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## Comparing the reporting and conduct quality of exercise and pharmacological randomized controlled trials: A systematic review

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Running Head: Exercise RCT reporting and conduct quality

# Comparing the reporting and conduct quality of exercise and pharmacological randomized controlled trials: A systematic review

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# ABSTRACT

**Objective.** Evaluate the quality of exercise randomized controlled trial (RCT) reporting and conduct in clinical populations (*i.e.*, adults with or at-risk of chronic conditions) and compare with matched pharmacological RCTs.

Design. Systematic review.

Data Sources. Embase (Elsevier), PubMed (NLM), and CINAHL (EBSCO)

Study Selection. RCTs of exercise in clinical populations with matching pharmacological RCTs published in leading clinical, medical and specialist journals with impact factors  $\geq$ 15. Review Methods. Overall RCT quality was evaluated by two independent reviewers using three research reporting guidelines (*i.e.*, Consolidated Standards of Reporting Trials (CONSORT; pharmacological RCTs) / CONSORT-Non-pharmacological trial (CONSORT-NPT; exercise RCTs), CONSORT-Harms, Template for Intervention Description and Replication (TIDieR)) and two risk of bias assessment (research conduct) tools (*i.e.*, Cochrane Risk of Bias, Jadad Scale). We compared research reporting and conduct quality within exercise RCTs with matched pharmacological RCTs, and examined factors associated with quality in exercise and pharmacological RCTs, separately. Findings. Forty-eight exercise RCTs (11,658 patients; median sample n=138) and 48 matched pharmacological RCTs were evaluated (18,501 patients; median sample n=160). RCTs were conducted primarily in cardiovascular medicine (43%) or oncology (31%). Overall quality score (composite of all research reporting and conduct quality scores; primary endpoint) for exercise RCTs was 58% (median score 46/80; interguartile range: 39-51) compared with 77% (53/68; interguartile range: 47-58) in the matched pharmacological RCTs ( $p \le 0.001$ ). Individual guality scores for trial reporting and conduct were lower in exercise RCTs compared with matched pharmacological RCTs (p ≤0.02). Factors associated with higher overall guality scores for exercise RCTs were journal impact factor ( $\geq$ 25), sample size ( $\geq$ 152) and publication year ( $\geq$ 2013).

**Conclusions and Relevance.** Research reporting and conduct quality within exercise RCTs is inferior to matched pharmacological RCTs. Suboptimal RCT reporting and conduct impact the fidelity,

interpretation, and reproducibility of exercise trials and, ultimately, implementation of exercise in clinical populations.

Registration. CRD42018095033

# STRENGTHS AND LIMITATIONS OF THIS STUDY

- A total of n=30,159 participants from ninety-six randomized controlled trials (RCTs) of exercise and pharmacological therapies published in high-impact journals were included.
- We used a combination of five established and one investigator developed inventories to comprehensively evaluate and compare the quality of research reporting and conduct of exercise and pharmacological RCTs.
- Main limitations of the study include the restriction to journals with impact factors ≥15 and the lack of broadly applicable or unified guidelines to compare across exercise and pharmacological therapy RCTs.

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## INTRODUCTION

Reports from epidemiological studies and randomized controlled trials (RCTs) indicate that exercise therapy is safe and well-tolerated, and associated with broad health benefits in adults.<sup>1</sup> Accordingly, exercise is considered standard of care therapy for many clinical populations (*i.e.*, adults with or at risk of chronic conditions), with established guidelines from numerous international agencies.<sup>2-4</sup>

Clinical recommendation of exercise for a particular clinical indication is predicated on evidence from RCTs.<sup>5</sup> Optimal reporting of RCTs evaluating pharmacological and non-pharmacological therapies is facilitated by multiple standardized guidelines [*e.g.*, Consolidated Standards of Reporting Trials (CONSORT),<sup>6,7</sup> Template for Intervention Description and Replication (TIDieR)<sup>8</sup>]. Reports of RCTs are required to conform to at least one of these guidelines when submitting to scientific journals across all areas of medicine. Relatedly, risk of bias (ROB) tools (*e.g.*, Cochrane ROB,<sup>9</sup> Jadad Scale<sup>10</sup>) evaluate RCT research conduct. However, the quality of exercise RCT reporting and conduct have received minimal attention.

Our primary objective was to evaluate the overall quality of exercise therapy RCT reporting and conduct in clinical populations. The primary outcome was overall quality score (*i.e.*, the combined quality scores from three research reporting and two research conduct inventories). We also compared the overall quality score from exercise RCTs to matched RCTs of pharmacological therapies (a well-established field of biomedical research with a long history of adopting RCT methods<sup>11</sup>) to provide context for our findings. Secondary objectives were to compare quality scores for research reporting and conduct inventories and to examine factors associated with overall quality score.

# METHODS

# Search Strategy

This review was conducted in accordance with the PRISMA<sup>12</sup> and AMSTAR 2<sup>13</sup> guidelines (PROSPERO identifier CRD42018095033; supplementary Methods 1 and 2). Full study search, selection, and data extraction methods are provided in supplementary Methods 3. Briefly, a Research Informationist (KM) conducted two sequential literature searches for exercise (first search) and pharmacological (second search) RCTs within the Embase (Elsevier), PubMed (NLM), and CINAHL (EBSCO) databases (fig 1). The search for exercise RCTs (supplementary Methods 4) was conducted on March 8<sup>th</sup>, 2018 using a combination of relevant keywords and controlled vocabulary: (1) exercise training intervention and (2) RCTs. Meta-data (*i.e.*, journal, cohort / population, sample size, and number of study sites) was extracted for eligible exercise RCTs and used to define the matching criteria for pharmacological RCTs. The pharmacological RCT search (supplementary Methods 5) was conducted on November 20<sup>th</sup>, 2018. The search was restricted by date (January 1<sup>st</sup>, 2008 to November 20<sup>th</sup>, 2018) and used a combination of relevant search terms and matching criteria for: (1) pharmaceutical intervention, (2) RCTs, (3) journal, (4) cohort / population, and (5) number of study sites (single or multi-center). We also purposefully restricted our search to medical journals with impact factors ≥15 since journals with higher impact factors are more likely to endorse and enforce reporting quality guidelines.14-16

# **Study Eligibility Criteria**

Exercise RCTs involving adults ( $\geq$ 18 years of age) with chronic conditions, written in English, and published in journals with impact factors  $\geq$ 15 according to the 2016 Journal Citation Reports (Clarivate Analytics) between January 1<sup>st</sup>, 2008 and the search date (March 8<sup>th</sup>, 2018) were eligible. Exercise therapy interventions were defined as those involving chronic (>3 weeks), repeated sessions of supervised (in person, with or without a distance-based component) aerobic training (i.e., endurance activity,  $\geq$ 15 minutes/session), resistance training (i.e., multiple large muscle group exercises involving repeated voluntary muscle contractions against a resistance greater than those normally encountered

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## Study Selection, Data Extraction and Additional Sources

Trained study reviewers (JM and KS; see supplementary Methods 3 for training description) independently screened and evaluated identified article titles and abstracts in the DistillerSR web platform (Evidence Partners, Ottawa, Canada; fig 1). Next, full manuscripts of potentially eligible articles were independently reviewed using DistillerSR. Excluded exercise records are listed in supplementary Table 1.<sup>19</sup> Matching criteria for exercise and pharmacological therapy RCTs included: (1) journal (±5 impact factor points according to the 2016 Journal Citation Reports (Clarivate Analytics)), (2) cohort / population (sharing similar disease characteristics), (3) sample size (±30% difference in study samples), and (4) number of study sites (single vs multiple sites). Exercise and pharmacological therapy RCTs had to be matched on a minimum of two of the four matching criteria to be eligible. The pharmacological therapy RCT with values closest to the target exercise RCT was used if more than one potential match was identified. Full data was extracted for all eligible RCTs from the primary article and all other publicly available supplemental data sources using DistillerSR and Reference Guides. Disagreements concerning eligibility, data extractions, and ROB assessments were resolved by consensus (JM and KS) and adjudicated by a third party (SCA) when consensus could not be obtained. The corresponding author for each article was contacted by investigators (SCA, JMS, LWJ) to request information on incomplete and missing items. After four weeks, non-responding authors were recontacted and provided an additional ~four weeks to respond. Reporting totals were revised after the close of data collection (*i.e.*, final author contact (September 1<sup>st</sup>, 2019)).

## **Evaluation measures**

Each trial was evaluated on two sets of criteria: (1) quality of research reporting and (2) quality of research conduct using four standardized inventories and one investigator developed inventory. Exercise RCTs were evaluated on a maximum of 78 potential items and pharmacological RCTs were

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evaluated on a maximum of 63 potential items. However, there were items within the CONSORT-based reporting quality guidelines that were not applicable (NA) based on the unique aspects of each RCT. Items rated as NA were excluded from the calculation of primary and secondary outcomes for each study (see *End Points* and *Data Analysis*). The quality of research reporting was assessed using either CONSORT [37 items]<sup>7</sup> (pharmacological only) or CONSORT-Nonpharmacologic Treatments (NPT) [52 items]<sup>6</sup> (exercise only), CONSORT-Harms [10 items],<sup>20</sup> and TIDieR [16 items].<sup>21</sup> The TIDieR guideline evaluates the reporting quality of exercise intervention prescription components.<sup>21</sup> Equivalent guidelines were not available for pharmacological intervention reporting thus we applied six relevant TIDieR-based criteria for comparison purposes [6 items; including intervention length, modality, location, frequency, dose, and adherence]. Exercise dose consisted of session intensity and duration (aerobic and resistance interventions) as well as the number of sets and repetitions (resistance interventions only). All research reporting quality items were rated (with equal weighting and maximum score of 1 point per item) as: 1 = 'properly reported'; or, 0 = 'unclear' (incompletely reported) or 'not reported' (missing); NA = 'not applicable.'

The quality of research conduct was assessed using the Cochrane ROB inventory [7 items]<sup>9</sup> and the Jadad scale [3 items].<sup>10</sup> Cochrane ROB was items were rated (with equal weighting) as: 2 ='low risk of bias'; 1 = 'unclear risk of bias'; or, 0 = 'high risk of bias'. The first two items in the Jadad scale were scored as 2 = 'low risk of bias' or 0 = 'high risk of bias' and the third item was scored as 1 = 'low risk of bias' or 0 = 'high risk of bias' and the third item was scored as 1 = 'low risk of bias.'

## End Points

The primary end point was overall quality score defined as the sum of numerical quality scores from all research reporting and conduct inventories relative to the total number of applicable items. Secondary end points were defined as the numerical quality scores for each research reporting guideline and conduct inventory relative to the total number of applicable items for the study.

## **Data Analysis**

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Characteristics of RCTs were summarized using descriptive statistics. Quality scores were calculated and reported in numerical and percentage score formats. Percentage quality scores were calculated for the primary end point (overall quality score) and secondary endpoints (individual scores for the quality of reporting guidelines and guality of conduct inventories) as the achieved score relative to the total number of applicable items per RCT. All items from the two research conduct inventories were applicable for every study and scored with values of 0.1 or 2 resulting in total quality score for research conduct-related items of 19 per study. The variation in the total number of applicable items per study was caused by different numbers of reporting quality guideline items being rated as 'Not Applicable', resulting in median numbers of eligible items (*i.e.*, denominators for percentage score calculations) of 80 for exercise RCTs and 68 for pharmacological RCTs. Generalized linear models (GLMs) were specified with a binomial family and logit link to compare the scores of exercise and pharmacological RCTs. The model accounted for differences in the number of eligible items and the matching between the exercise and pharmacological RCTs. GLMs were also used to evaluate factors associated with overall quality scores for exercise and pharmacological therapy RCTs separately. Potential factors included journal impact factor (<25 vs. ≥25), RCT sample size (<152 vs. ≥152 participants), number of study sites (single vs. multiple sites), and year of publication (<2013 vs. ≥2013). Cut offs for impact factor, sample size, and year of publication were based on the medians. For comparisons of the individual components of the composite scores, p-values were adjusted for multiple comparisons within research reporting and conduct inventories using a Bonferroni correction. Data are presented as median (Interguartile Range (IQR)) and odds ratios (OR; 95% confidence intervals (CI)). Inter-rater reliability was evaluated using intraclass correlation coefficient (ICC) calculated via one-way ANOVA.<sup>22</sup> Analyses were performed using R version 4.0.2.<sup>23</sup>

RESULTS

A total of 2836 potential exercise records were identified with 866 duplicate records removed using Endnote citation management software (Clarivate Analytics). A total of 1970 records underwent title and abstract screening (fig 1). Of these, 264 records underwent full review with 48 exercise RCTs

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meeting eligibility criteria.<sup>24-71</sup> The 48 primary searches for pharmacological therapy trials produced 2815 records. The median number of records returned per search was 15 (range: 0-853). Review of the primary search results produced 19 matched pharmacological RCTs; the remaining 29 were pharmacological RCTs were identified via review of modified secondary searches.<sup>72-119</sup> On average, exercise and pharmacological therapy RCTs were matched on 3 of 4 criteria (supplementary Table 2). The results of agreement for the two raters' assessments for the exercise and pharmaceutical studies publication scores were: overall quality score: ICC = 0.85 (95% CI: 0.78 to 0.89); quality of research reporting guidelines: ICC = 0.83 (95% CI: 0.75 to 0.88); and quality of research conduct inventories: ICC = 0.73 (95% CI: 0.62 to 0.81).

## Missing Information (Author Contact)

Each RCT had missing information. The median number of eligible reporting quality items for exercise RCTs was 61 (IQR 59, 62) and pharmacological RCTs was 49 (IQR 48, 50). The median percentage (numerical; numerical range) of missing or indeterminate reporting quality items in exercise RCTs was 46% (28/61 items; 13-49) compared to 27% (13/49 items; 5-26) in pharmacological RCTs. Sixteen (33%) and 7 (15%) corresponding authors of the exercise and pharmacological RCTs responded with a median of 12.5 (IQR: 10.0, 16.2) and 5.0 (IQR: 4.0, 6.5) additional items (supplementary Table 3).

## **RCT Characteristics**

RCT characteristics are summarized in Table 1. Individual RCT and intervention characteristics are provided in supplementary Tables 4-7. Exercise therapy RCTs included a total of 11,658 participants (7,411 (64%) were allocated to experimental arms; including studies with 1-3 intervention arms) compared with 18,501 participants (11,909 (64%) allocated to experimental arms) in the pharmacological therapy RCTs. The median sample size of exercise RCTs was 138 (IQR: 100, 236) and 160 (IQR: 98, 314) for pharmacological RCTs.

## **Primary and Secondary End Points**

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The median overall quality score for RCTs of exercise therapy was 58% (46/80; IQR: 49, 65) compared to 77% (53/68; IQR: 71, 84; p≤0.001) for pharmacological therapy RCTs (Table 2). For secondary end points, median research reporting quality scores across all guidelines were significantly lower in exercise RCTs in comparison with pharmacological RCTs (Table 2). The lowest scoring research reporting quality quideline was CONSORT-Harms for both exercise and pharmaceutical studies. In exercise RCTs, median CONSORT-Harms score was 32% (3/9; IQR: 11, 51) compared with 67% (6/10; IQR: 40, 73) in pharmacological RCTs (p≤0.001; Table 2). Harms reporting was missing entirely from 19% (9/48) of exercise RCTs and 4% (2/48) of pharmacological RCTs. Exercise RCTs reported 57% (8/15; IQR: 7, 10) of TIDieR items (Table 2). All exercise RCTs (100%) reported the intervention names, rationale, and total intervention lengths (Table 3); while >75% of exercise RCTs were missing details related to intervention personnel, progression, and participant adherence (Table 3). Additional summaries of individual reporting quality items are provided for CONSORT-NPT (supplementary Table 8; exercise trials), CONSORT (supplementary Table 9; pharmacological trials), CONSORT-Harms (supplementary Table 10; exercise and pharmacological trials), and TIDieR-based intervention items (supplementary Table 11; exercise and pharmacological trials). In exercise RCTs, median Cochrane ROB score was 71% (10/14; IQR: 64, 79) compared with 93% (13/14; IQR: 86, 93) in pharmacological RCTs (p≤0.001; Table 2). A summary of Cochrane ROB assessments for individual exercise and pharmacological therapy RCTs is provided in Table 4.

## Factors Associated with Reporting Quality

Journal impact factor  $\geq$ 25 (OR: 1.36; 95% CI: 1.18 to 1.57), larger sample size  $\geq$ 152 (OR: 1.29; 95% CI: 1.11 to 1.51), and more recent publication year  $\geq$ 2013 (OR: 1.18; 95% CI: 1.03 to 1.34) were significantly associated with higher overall quality scores in exercise RCTs (Table 5). The only factor associated with greater overall quality scores in pharmacological RCTs was more recent publication year  $\geq$ 2013 (OR: 1.35; 95% CI: 1.14 to 1.60; *p*<0.001).

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## DISCUSSION

We evaluated the quality of research reporting and conduct within exercise therapy RCTs in clinical populations, then compared with the quality of reporting and conduct in matched pharmacological therapy RCTs. Our findings demonstrate that the quality of exercise therapy RCT reporting and conduct is suboptimal according to all the research reporting guidelines and conduct inventories used in this study and is inferior to RCTs of pharmacological therapy.

To our knowledge, five systematic reviews<sup>120-124</sup> have evaluated the overall guality of research reporting and conduct within exercise RCTs in clinical populations. Our findings corroborate the findings of these systematic reviews demonstrating the overall quality of exercise RCT reporting and conduct is suboptimal. For instance, in 27 exercise RCTs involving 1,467 patients with metabolic syndrome, Ostman et al.<sup>123</sup> reported a median overall quality of 60% (range: 33-87%) using the TESTEX (Tool for the assEssment of Study qualiTy and reporting in EXercise<sup>125</sup>) guideline. Similarly, Borror and colleagues<sup>120</sup> evaluated 12 exercise RCTs (representing 135 patients) with type 2 diabetes using a combination of 16 items from CONSORT, Jadad, PEDro (Physiotherapy Evidence Database) guidelines,<sup>126</sup> and the Delphi list.<sup>127</sup> The combined trial reporting and conduct guality score was 49% (range: 38%-58%). Nevertheless, prior reviews have several important limitations. First, these reviews<sup>120-124</sup> did not use the complete versions of comprehensive and widely accepted guidelines (e.g., CONSORT, Cochrane ROB) and, thus, did not rigorously evaluate the quality of all salient aspects of trial reporting and conduct. In addition, the number of exercise trials evaluated were small, comparisons of reporting with matched pharmacological trials were not performed, and no data extraction training or standardization were described within these studies. Thus, our review that was conducted by welltrained independent reviewers using specialized reference guides to facilitate standardized data extraction according to five distinct but complementary established guidelines / tools to assess and compare a large number of exercise trials and matched pharmacological trials provides the most rigorous evaluation of exercise research quality to date.

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Atthough overall quality scores were poor in RCTs of exercise therapy, these findings were generally driven by poor research reporting quality scores across select individual guidelines rather than suboptimal RCT conduct per se. Foremost among these, the finding that harms were the most poorly reported aspects of exercise RCTs is concerning. Previous reviews in patients with cancer,<sup>128</sup> chronic fatigue,<sup>129</sup> and multiple sclerosis<sup>130</sup> have specifically focused on evaluating the reporting of adverse event frequency and descriptions; this information was completely missing within 23-88% of included exercise trials.<sup>128,130</sup> Our study extends these findings by demonstrating that harms-related monitoring and reporting were missing or incompletely reported in ≥75% of exercise RCTs; and, relatedly, >50% of articles failed to provide a balanced discussion of risks to benefits for the tested interventions. Based on our findings, we cannot support or refute the prevailing dogma that exercise is a safe and tolerable intervention strategy in most areas of clinical medicine.<sup>1</sup> However, it is not possible to fully evaluate the harms to benefit ratio of exercise without accurate monitoring and reporting of adverse events within exercise RCTs - a critical consideration in the clinical recommendation of any medical intervention.

Reporting of intervention methods is the most commonly assessed quality metric in exercise RCTs to date. Our findings support previous reviews of exercise interventions in patients with peripheral arterial disease,<sup>131</sup> cancer,<sup>132</sup> hypertension,<sup>133</sup> and recovering from stroke<sup>134</sup> demonstrating essential elements, including details on the exercise prescription regimen itself, are incompletely reported. For example, Hacke et al. used TIDieR to assess intervention reporting quality in 24 exercise RCTs involving 1,195 patients with hypertension and reported that 91% of exercise intervention studies in were missing information about intervention supervisors and 52% were missing details of intervention adherence.<sup>133</sup> Relatedly, Tew et al. also used TIDieR and reported that 20-26% of reports failed to describe several of the most fundamental exercise intervention elements (*i.e.*, exercise mode, intensity, tailoring, and progression) in 58 exercise RCTs in patients with peripheral arterial disease.<sup>131</sup> In our study, information on patient compliance to the planned exercise regimen as well as the expertise of the individuals implementing the intervention was missing or incomplete in >90% of trials; fundamental

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details pertaining to dose of prescribed exercise were also missing in over a third of trials. Incomplete intervention description not only hinders study reproducibility and cross-study integration (for meta-analyses) but also precludes quantification of exercise therapy dose – a key metric for elucidation of dose/exposure-response relationships and translation into clinical practice.<sup>135</sup>

A major strength of this review is that, to our knowledge, it is the first to compare the quality of research reporting and conduct within exercise and pharmacological therapy RCTs. We used rigorous data extraction and evaluation processes to provide the first direct evidence that the quality of research reporting and conduct within exercise RCTs is inferior to similar pharmacological RCTs. For context, the reporting quality of pharmacological RCTs in our review is comparable with previous reviews. For example, using CONSORT, Peron and colleagues<sup>136</sup> found that reporting quality of pharmacological RCTs in oncology ranged from 72% to 74%; the mean CONSORT-Harms score was 63%.<sup>137</sup> A similar review conducted by Ritchie et al. reported a CONSORT score of 72% in 57 pharmacological RCTs (33% of studies involved patients with metabolic and cardiorespiratory diseases).<sup>138</sup> Our findings are consistent with these studies and suggest that comparable research reporting quality scores for exercise RCTs are, on average, 15%-20% lower.

Several factors may contribute to the lower quality scores for research reporting and conduct within exercise trials. For instance, CONSORT was developed primarily to support the reporting of pharmacological trials and may not adequately capture aspects unique to the conduct of non-pharmacological trials such as exercise.<sup>139</sup> This issue should have been addressed, in theory, with publication of the CONSORT-NPT extension in 2008.<sup>6,140</sup> Indeed, this extension was developed to facilitate complete reporting across the fundamental aspects of RCTs applicable to all non-pharmacologic trials, including exercise. Reporting quality of traditional biomedical therapy RCTs (*e.g.*, surgical, pharmaceutical) has improved since the publication of the CONSORT guidelines and superior in journals adopting these guidelines.<sup>141-143</sup> We similarly found that exercise RCTs published more recently (>2013) had higher overall quality scores. These findings are encouraging and suggest that the awareness and use of established guidelines and inventories to support research reporting and conduct

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may be increasing, although there remains marked room for improvement. Continued improvement in this context will require continued education of exercise investigators to conform with such guidelines and journals / reviewers hold authors accountable to use of such guidelines. Stricter adherence to CONSORT-NPT, for example, would improve the reporting quality of most fundamental trial aspects; however, this tool may still be too generic to support the comprehensive reporting of features unique to exercise trials, especially intervention description. To this end, adoption of TIDieR, or the more recent exercise-specific CERT (*i.e.*, Consensus on Exercise Reporting Template) guidelines,<sup>144</sup> is warranted to improve the reporting and reproducibility of exercise interventions within exercise RCTs.

Our study has several limitations. First, the restriction to journals with impact factors ≥15 may overestimate the quality of research reporting and conduct within the included exercise and pharmacological therapy RCTs. Nevertheless, we felt it was necessary to selectively draw from this subset of journals given they are most likely to endorse and enforce reporting quality guidelines<sup>14-16</sup> to impartially compare and contextualize our findings. Second, the lack of broadly applicable or unified guidelines to compare across exercise and pharmacological therapy RCTs also merits consideration. Guidelines used to evaluate the quality of RCT reporting were either different between study types (*i.e.*, CONSORT-NPT<sup>6</sup> vs. CONSORT<sup>7</sup>), developed specifically for harms reporting in pharmacological trials,<sup>20</sup> or investigator-derived given that there are formal standards for non-pharmacological (*i.e.*, TIDieR<sup>21</sup>), but not pharmacological, intervention reporting. Nevertheless, we controlled for differences in the numbers of evaluable and applicable items across the reporting quality guidelines.

In summary, the overall quality of research reporting and conduct within exercise RCTs is suboptimal and inferior to pharmacological RCTs. Stricter adherence to established guidelines and inventories is warranted to facilitate the generation of high-quality evidence needed to optimize the safety, efficacy, and implementation of exercise therapy in clinical populations.

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**Contributors:** LWJ conceived the study idea. SCA and JMS coordinated the systematic review. SCA, LWJ and JMS wrote the first draft of the manuscript. KM designed the search strategy. KS and JM screened abstracts and full texts. JM, KS and SCA acquired the data and judged risk of bias in the studies. JL and CM performed the data analyses. SCA, JM, KS, KM, NMI, ABW, JL, CSM, MMZC, DSM, JMS and LWJ interpreted the data analysis. SCA, JM, KS, KM, NMI, ABW, JL, CSM, MMZC, DSM, JMS and LWJ critically revised the manuscript. LWJ had full access to all study data and takes responsibility for the integrity of the data and the accuracy of the data analysis. The findings of this study have been presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. LWJ is the guarantor.

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40 41

42 43

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Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in

Mezzani A, Hamm LF, Jones AM, et al. Aerobic exercise intensity assessment and prescription

Rochester CL, Vogiatzis I, Holland AE, et al. An official American Thoracic Society/European

Sanft T, Denlinger CS, Armenian S, et al. NCCN Guidelines Insights: Survivorship, Version

Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of

# REFERENCES 1. 26 different chronic diseases. Scand J Med Sci Sports 2015;25 Suppl 3:1-72. 2. in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. Eur J Prev Cardiol 2013;20:442-67. 3. Respiratory Society policy statement: Enhancing implementation, use, and delivery of pulmonary rehabilitation. Am J Respir Crit Care Med 2015;192:1373-86. 4. 2.2019: Featured Updates to the NCCN Guidelines. J Natl Compr Canc Netw 2019;17:784-94. 5. evidence and strength of recommendations. Br Med J 2008;336:924-6.

6. Boutron I, Altman DG, Moher D, Schulz KF, Ravaud P, Consort NPT Group. CONSORT statement for randomized trials of nonpharmacologic treatments: A 2017 update and a CONSORT extension for nonpharmacologic trial abstracts. Ann Intern Med 2017;167:40-7.

7. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med 2010;152:726-32.

8. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. Br Med J 2014;348:g1687.

9. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Br Med J 2011;343:d5928.

10. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clin Trials 1996;17:1-12.

58 59 60

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright

#### **BMJ** Open

 Exercise RCT reporting and conduct quality 17

11. Bothwell L, Greene J, Podolsky S, Jones D. Assessing the Gold Standard--Lessons from the History of RCTs. The New England journal of medicine 2016;374:2175.

12. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Ann Intern Med 2009;151:264-9.

13. Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. Bmc Med Res Methodol 2007;7:10.

14. Kunath F, Grobe HR, Rücker G, et al. Do journals publishing in the field of urology endorse reporting guidelines? A survey of author instructions. Urologia Internationalis 2012;88:54-9.

15. Samaan Z, Mbuagbaw L, Kosa D, et al. A systematic scoping review of adherence to reporting guidelines in health care literature. J Multidiscip Healthc 2013;6:169-88.

16. Mills E, Wu P, Gagnier J, Heels-Ansdell D, Montori VM. An analysis of general medical and specialist journals that endorse CONSORT found that reporting was not enforced consistently. Journal of clinical epidemiology 2005;58:662-7.

17. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription:Wolters Kluwer; 2018.

18. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. Public Health Rep 1985;100:126-31.

19. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. Br Med J 2017:j4008.

20. Ioannidis JP, Evans SJ, Gotzsche PC, et al. Better reporting of harms in randomized trials: an extension of the CONSORT statement. Ann Intern Med 2004;141:781-8.

21. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014;348:g1687.

22. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. Journal of chiropractic medicine 2016;15:155-63.

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#### **BMJ** Open

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright.

23. R Core Team. R: A Language and Environment for Statistical Computing. 467. Vienna, Austria2020.

24. Adamsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. BMJ 2009;339:b3410.

25. Beckers PJ, Denollet J, Possemiers NM, Wuyts FL, Vrints CJ, Conraads VM. Combined endurance-resistance training vs. endurance training in patients with chronic heart failure: a prospective randomized study. Eur Heart J 2008;29:1858-66.

26. Beer M, Wagner D, Myers J, et al. Effects of exercise training on myocardial energy metabolism and ventricular function assessed by quantitative phosphorus-31 magnetic resonance spectroscopy and magnetic resonance imaging in dilated cardiomyopathy. J Am Coll Cardiol 2008;51:1883-91.

27. Belardinelli R, Georgiou D, Cianci G, Purcaro A. 10-year exercise training in chronic heart failure: a randomized controlled trial. J Am Coll Cardiol 2012;60:1521-8.

28. Campbell KL, Foster-Schubert KE, Alfano CM, et al. Reduced-calorie dietary weight loss, exercise, and sex hormones in postmenopausal women: randomized controlled trial. J Clin Oncol 2012;30:2314-26.

29. Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. JAMA 2010;304:2253-62.

30. Courneya KS, Sellar CM, Stevinson C, et al. Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. J Clin Oncol 2009;27:4605-12.

31. Daumit GL, Dickerson FB, Wang NY, et al. A behavioral weight-loss intervention in persons with serious mental illness. N Engl J Med 2013;368:1594-602.

32. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Effects of Aerobic and Resistance Exercise on Metabolic Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright.

Overweight or Obese Survivors of Breast Cancer: A Randomized Controlled Trial. J Clin Oncol 2018;36:875-83.

33. Duijts SF, van Beurden M, Oldenburg HS, et al. Efficacy of cognitive behavioral therapy and physical exercise in alleviating treatment-induced menopausal symptoms in patients with breast cancer: results of a randomized, controlled, multicenter trial. J Clin Oncol 2012;30:4124-33.

34. Edelmann F, Gelbrich G, Dungen HD, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot study. J Am Coll Cardiol 2011;58:1780-91.

35. Ehlken N, Lichtblau M, Klose H, et al. Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial. Eur Heart J 2016;37:35-44.

36. Fakhry F, Spronk S, van der Laan L, et al. Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial. JAMA 2015;314:1936-44.

37. Friedenreich CM, Neilson HK, O'Reilly R, et al. Effects of a High vs Moderate Volume of Aerobic Exercise on Adiposity Outcomes in Postmenopausal Women: A Randomized Clinical Trial. JAMA Oncol 2015;1:766-76.

38. Friedenreich CM, Woolcott CG, McTiernan A, et al. Alberta physical activity and breast cancer prevention trial: sex hormone changes in a year-long exercise intervention among postmenopausal women. Journal of Clinical Oncology 2010;28:1458.

39. Galvao DA, Spry N, Denham J, et al. A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 2014;65:856-64.

40. Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate

#### **BMJ** Open

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright.

cancer without bone metastases: a randomized controlled trial. Journal of clinical oncology 2010;28:340-7.

41. Hallsworth K, Fattakhova G, Hollingsworth KG, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic fatty liver disease independent of weight loss. Gut 2011;60:1278-83.

42. Hollekim-Strand SM, Bjorgaas MR, Albrektsen G, Tjonna AE, Wisloff U, Ingul CB. High-intensity interval exercise effectively improves cardiac function in patients with type 2 diabetes mellitus and diastolic dysfunction: a randomized controlled trial. J Am Coll Cardiol 2014;64:1758-60.

43. Irwin ML, Cartmel B, Gross CP, et al. Randomized exercise trial of aromatase inhibitor–induced arthralgia in breast cancer survivors. Journal of Clinical Oncology 2015;33:1104.

44. Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA 2017;318:637-46.

45. Jones LW, Hornsby WE, Freedland SJ, et al. Effects of nonlinear aerobic training on erectile dysfunction and cardiovascular function following radical prostatectomy for clinically localized prostate cancer. Eur Urol 2014;65:852-5.

46. Kitzman DW, Brubaker P, Morgan T, et al. Effect of Caloric Restriction or Aerobic Exercise Training on Peak Oxygen Consumption and Quality of Life in Obese Older Patients With Heart Failure With Preserved Ejection Fraction: A Randomized Clinical Trial. JAMA 2016;315:36-46.

47. Kitzman DW, Brubaker PH, Herrington DM, et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. J Am Coll Cardiol 2013;62:584-92.

48. Ligibel JA, Campbell N, Partridge A, et al. Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors. J Clin Oncol 2008;26:907-12.

49. Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med 2008;149:869-

78.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright.

#### **BMJ** Open

50. McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial. JAMA 2009;301:165-74.

 McDermott MM, Ferrucci L, Tian L, et al. Effect of Granulocyte-Macrophage Colony-Stimulating Factor With or Without Supervised Exercise on Walking Performance in Patients With Peripheral Artery Disease: The PROPEL Randomized Clinical Trial. JAMA 2017;318:2089-98.

52. McDermott MM, Spring B, Berger JS, et al. Effect of a Home-Based Exercise Intervention of Wearable Technology and Telephone Coaching on Walking Performance in Peripheral Artery Disease: The HONOR Randomized Clinical Trial. JAMA 2018;319:1665-76.

53. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA 2013;310:1263-73.

54. Monninkhof EM, Velthuis MJ, Peeters PH, Twisk JW, Schuit AJ. Effect of exercise on postmenopausal sex hormone levels and role of body fat: a randomized controlled trial. J Clin Oncol 2009;27:4492-9.

55. Murphy TP, Cutlip DE, Regensteiner JG, et al. Supervised exercise, stent revascularization, or medical therapy for claudication due to aortoiliac peripheral artery disease: the CLEVER study. Journal of the American College of Cardiology 2015;65:999-1009.

56. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. JAMA 2009;301:1439-50.

57. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA 2014;311:2387-96.

58. Patwala AY, Woods PR, Sharp L, Goldspink DF, Tan LB, Wright DJ. Maximizing patient benefit from cardiac resynchronization therapy with the addition of structured exercise training: a randomized controlled study. J Am Coll Cardiol 2009;53:2332-9.

#### **BMJ** Open

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59. Pitkälä KH, Pöysti MM, Laakkonen M, et al. Effects of the Finnish Alzheimer disease exercise trial (FINALEX): a randomized controlled trial. JAMA internal medicine 2013;173:894-901.

60. Ross R, Hudson R, Stotz PJ, Lam M. Effects of exercise amount and intensity on abdominal obesity and glucose tolerance in obese adults: a randomized trial. Ann Intern Med 2015;162:325-34.

61. Saberi S, Wheeler M, Bragg-Gresham J, et al. Effect of Moderate-Intensity Exercise Training on Peak Oxygen Consumption in Patients With Hypertrophic Cardiomyopathy: A Randomized Clinical Trial. JAMA 2017;317:1349-57.

62. Sandri M, Kozarez I, Adams V, et al. Age-related effects of exercise training on diastolic function in heart failure with reduced ejection fraction: the Leipzig Exercise Intervention in Chronic Heart Failure and Aging (LEICA) Diastolic Dysfunction Study. Eur Heart J 2012;33:1758-68.

63. Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med 2009;361:664-73.

64. Schmitz KH, Ahmed RL, Troxel AB, et al. Weight lifting for women at risk for breast cancerrelated lymphedema: a randomized trial. JAMA 2010;304:2699-705.

65. Segal RJ, Reid RD, Courneya KS, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 2009;27:344-51.

66. Taaffe DR, Newton RU, Spry N, et al. Effects of Different Exercise Modalities on Fatigue in
Prostate Cancer Patients Undergoing Androgen Deprivation Therapy: A Year-long Randomised
Controlled Trial. Eur Urol 2017;72:293-9.

67. van Waart H, Stuiver MM, van Harten WH, et al. Effect of Low-Intensity Physical Activity and
Moderate- to High-Intensity Physical Exercise During Adjuvant Chemotherapy on Physical Fitness,
Fatigue, and Chemotherapy Completion Rates: Results of the PACES Randomized Clinical Trial. J Clin
Oncol 2015;33:1918-27.

68. Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. N Engl J Med 2017;376:1943-55.

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright.

**BMJ** Open

69. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 2011;364:1218-29.

70. Winter MM, van der Bom T, de Vries LC, et al. Exercise training improves exercise capacity in adult patients with a systemic right ventricle: a randomized clinical trial. Eur Heart J 2012;33:1378-85.

71. Zhang HJ, He J, Pan LL, et al. Effects of Moderate and Vigorous Exercise on Nonalcoholic Fatty Liver Disease: A Randomized Clinical Trial. JAMA Intern Med 2016;176:1074-82.

72. Ahmed S, Rienstra M, Crijns HJ, et al. Continuous vs episodic prophylactic treatment with amiodarone for the prevention of atrial fibrillation: a randomized trial. JAMA 2008;300:1784-92.

73. Caminiti G, Volterrani M, Iellamo F, et al. Effect of long-acting testosterone treatment on functional exercise capacity, skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure a double-blind, placebo-controlled, randomized study. J Am Coll Cardiol 2009;54:919-27.

74. Cortelazzo S, Tarella C, Gianni AM, et al. Randomized Trial Comparing R-CHOP Versus High-Dose Sequential Chemotherapy in High-Risk Patients With Diffuse Large B-Cell Lymphomas. J Clin Oncol 2016;34:4015-22.

75. Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial. JAMA 2015;314:1242-54.

76. Cusi K, Orsak B, Bril F, et al. Long-Term Pioglitazone Treatment for Patients With Nonalcoholic Steatohepatitis and Prediabetes or Type 2 Diabetes Mellitus: A Randomized Trial. Ann Intern Med 2016;165:305-15.

77. Devereux G, Cotton S, Fielding S, et al. Effect of theophylline as adjunct to inhaled corticosteroids on exacerbations in patients with COPD: a randomized clinical trial. JAMA 2018;320:1548-59.

78. Ellis MJ, Suman VJ, Hoog J, et al. Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and exemestane for postmenopausal women with estrogen receptor-rich stage 2

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to 3 breast cancer: clinical and biomarker outcomes and predictive value of the baseline PAM50-based intrinsic subtype--ACOSOG Z1031. J Clin Oncol 2011;29:2342-9. 79. Ford I, Scott NW, Herd V, Mitchell LR, Williams DJ, Brittenden J. A randomized controlled trial of platelet activity before and after cessation of clopidogrel therapy in patients with stable cardiovascular disease. J Am Coll Cardiol 2014;63:233-9. 80. Frustaci A, Russo MA, Chimenti C. Randomized study on the efficacy of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy: the TIMIC study. Eur Heart J 2009;30:1995-2002. 81. Gheorghiade M, Blair JE, Filippatos GS, et al. Hemodynamic, echocardiographic, and neurohormonal effects of istaroxime, a novel intravenous inotropic and lusitropic agent: a randomized controlled trial in patients hospitalized with heart failure. J Am Coll Cardiol 2008;51:2276-85. 82. Gheorghiade M, Bohm M, Greene SJ, et al. Effect of aliskiren on postdischarge mortality and heart failure readmissions among patients hospitalized for heart failure: the ASTRONAUT randomized trial. JAMA 2013;309:1125-35. 83. Goebel A, Bisla J, Carganillo R, et al. Low-Dose Intravenous Immunoglobulin Treatment for Long-Standing Complex Regional Pain Syndrome. Annals of Internal Medicine 2017;167:476-83. 84. Greenspan SL, Brufsky A, Lembersky BC, et al. Risedronate prevents bone loss in breast

cancer survivors: a 2-year, randomized, double-blind, placebo-controlled clinical trial. J Clin Oncol 2008;26:2644-52.

85. Grudell AB, Sweetser S, Camilleri M, et al. A controlled pharmacogenetic trial of sibutramine on weight loss and body composition in obese or overweight adults. Gastroenterology 2008;135:1142-54.
86. Hamshere S, Arnous S, Choudhury T, et al. Randomized trial of combination cytokine and adult autologous bone marrow progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy: the REGENERATE-DCM clinical trial. Eur Heart J 2015;36:3061-9.

### **BMJ** Open

87. Han Y, Zhu G, Han L, et al. Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in patients with diabetes and chronic kidney disease. J Am Coll Cardiol 2014;63:62-70.

88. Harman SM, Black DM, Naftolin F, et al. Arterial imaging outcomes and cardiovascular risk factors in recently menopausal women: a randomized trial. Ann Intern Med 2014;161:249-60.

89. Hoendermis ES, Liu LC, Hummel YM, et al. Effects of sildenafil on invasive haemodynamics and exercise capacity in heart failure patients with preserved ejection fraction and pulmonary hypertension: a randomized controlled trial. Eur Heart J 2015;36:2565-73.

90. Hurvitz SA, Dirix L, Kocsis J, et al. Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer. J Clin Oncol 2013;31:1157-63.

91. Irani J, Celhay O, Hubert J, et al. Continuous versus six months a year maximal androgen blockade in the management of prostate cancer: a randomised study. Eur Urol 2008;54:382-91.

92. Johnston SRD, Hegg R, Im SA, et al. Phase III, Randomized Study of Dual Human Epidermal Growth Factor Receptor 2 (HER2) Blockade With Lapatinib Plus Trastuzumab in Combination With an Aromatase Inhibitor in Postmenopausal Women With HER2-Positive, Hormone Receptor-Positive Metastatic Breast Cancer: ALTERNATIVE. J Clin Oncol 2018;36:741-8.

93. Kim JM, Stewart R, Lee YS, et al. Effect of Escitalopram vs Placebo Treatment for Depression on Long-term Cardiac Outcomes in Patients With Acute Coronary Syndrome: A Randomized Clinical Trial. JAMA 2018;320:350-8.

94. Klotz LH, McNeill IY, Kebabdjian M, Zhang L, Chin JL, Canadian Urology Research C. A phase 3, double-blind, randomised, parallel-group, placebo-controlled study of oral weekly alendronate for the prevention of androgen deprivation bone loss in nonmetastatic prostate cancer: the Cancer and Osteoporosis Research with Alendronate and Leuprolide (CORAL) study. Eur Urol 2013;63:927-35.

#### **BMJ** Open

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright.

95. Kosmala W, Holland DJ, Rojek A, Wright L, Przewlocka-Kosmala M, Marwick TH. Effect of Ifchannel inhibition on hemodynamic status and exercise tolerance in heart failure with preserved ejection fraction: a randomized trial. J Am Coll Cardiol 2013;62:1330-8.

96. Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of Aldosterone Antagonism on Exercise Tolerance in Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol 2016;68:1823-34.

97. Krankenberg H, Tubler T, Ingwersen M, et al. Drug-Coated Balloon Versus Standard Balloon for Superficial Femoral Artery In-Stent Restenosis: The Randomized Femoral Artery In-Stent Restenosis (FAIR) Trial. Circulation 2015;132:2230-6.

98. Lapperre TS, Snoeck-Stroband JB, Gosman MM, et al. Effect of fluticasone with and without salmeterol on pulmonary outcomes in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med 2009;151:517-27.

99. Loprinzi CL, Qin R, Balcueva EP, et al. Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for alleviating hot flashes, N07C1. J Clin Oncol 2010;28:641-7.

100. McKay RR, Zurita AJ, Werner L, et al. A Randomized Phase II Trial of Short-Course Androgen Deprivation Therapy With or Without Bevacizumab for Patients With Recurrent Prostate Cancer After Definitive Local Therapy. J Clin Oncol 2016;34:1913-20.

101. Nissen SE, Nicholls SJ, Wolski K, et al. Comparison of pioglitazone vs glimepiride on progression of coronary atherosclerosis in patients with type 2 diabetes: the PERISCOPE randomized controlled trial. JAMA 2008;299:1561-73.

102. Poole J, Mavromatis K, Binongo JN, et al. Effect of progenitor cell mobilization with granulocytemacrophage colony-stimulating factor in patients with peripheral artery disease: a randomized clinical trial. JAMA 2013;310:2631-9.

103. Pradhan AD, Everett BM, Cook NR, Rifai N, Ridker PM. Effects of initiating insulin and metformin on glycemic control and inflammatory biomarkers among patients with type 2 diabetes: the LANCET randomized trial. JAMA 2009;302:1186-94.

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### BMJ Open

104. Ratziu V, Giral P, Jacqueminet S, et al. Rosiglitazone for nonalcoholic steatohepatitis: one-year results of the randomized placebo-controlled Fatty Liver Improvement with Rosiglitazone Therapy (FLIRT) Trial. Gastroenterology 2008;135:100-10.
105. Rimawi M, Ferrero JM, de la Haba-Rodriguez J, et al. First-Line Trastuzumab Plus an Aromatase Inhibitor, With or Without Pertuzumab, in Human Epidermal Growth Factor Receptor 2-

Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer (PERTAIN): A Randomized, Open-Label Phase II Trial. J Clin Oncol 2018;36:2826-35.

106. Rosenheck RA, Krystal JH, Lew R, et al. Long-acting risperidone and oral antipsychotics in unstable schizophrenia. N Engl J Med 2011;364:842-51.

107. Schmid P, Pinder SE, Wheatley D, et al. Phase II Randomized Preoperative Window-ofOpportunity Study of the PI3K Inhibitor Pictilisib Plus Anastrozole Compared With Anastrozole Alone in
Patients With Estrogen Receptor-Positive Breast Cancer. J Clin Oncol 2016;34:1987-94.

108. Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. N Engl J Med 2010;363:245-56.

109. Soiffer RJ, Kim HT, McGuirk J, et al. Prospective, Randomized, Double-Blind, Phase III Clinical
Trial of Anti-T-Lymphocyte Globulin to Assess Impact on Chronic Graft-Versus-Host Disease-Free
Survival in Patients Undergoing HLA-Matched Unrelated Myeloablative Hematopoietic Cell
Transplantation. J Clin Oncol 2017;35:4003-11.

110. Spitzer M, Basaria S, Travison TG, et al. Effect of testosterone replacement on response to sildenafil citrate in men with erectile dysfunction: a parallel, randomized trial. Ann Intern Med 2012;157:681-91.

111. Taplin ME, Montgomery B, Logothetis CJ, et al. Intense androgen-deprivation therapy with abiraterone acetate plus leuprolide acetate in patients with localized high-risk prostate cancer: results of a randomized phase II neoadjuvant study. J Clin Oncol 2014;32:3705-15.

#### **BMJ** Open

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Exercise RCT reporting and conduct quality 28 Tsujita K, Sugiyama S, Sumida H, et al. Impact of Dual Lipid-Lowering Strategy With Ezetimibe 112. and Atorvastatin on Coronary Plaque Regression in Patients With Percutaneous Coronary Intervention: The Multicenter Randomized Controlled PRECISE-IVUS Trial. J Am Coll Cardiol 2015;66:495-507. 113. Ulrich S, Keusch S, Hildenbrand FF, et al. Effect of nocturnal oxygen and acetazolamide on exercise performance in patients with pre-capillary pulmonary hypertension and sleep-disturbed breathing: randomized, double-blind, cross-over trial. Eur Heart J 2015;36:615-23. Urruticoechea A, Rizwanullah M, Im SA, et al. Randomized Phase III Trial of Trastuzumab Plus 114. Capecitabine With or Without Pertuzumab in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer Who Experienced Disease Progression During or After Trastuzumab-Based Therapy. J Clin Oncol 2017;35:3030-8. van der Bom T, Winter MM, Bouma BJ, et al. Effect of valsartan on systemic right ventricular 115. function: a double-blind, randomized, placebo-controlled pilot trial. Circulation 2013;127:322-30. 116. Wapnir IL, Price KN, Anderson SJ, et al. Efficacy of Chemotherapy for ER-Negative and ER-Positive Isolated Locoregional Recurrence of Breast Cancer: Final Analysis of the CALOR Trial. J Clin Oncol 2018;36:1073-9. 117. Wysham C, Bhargava A, Chaykin L, et al. Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients With Type 2 Diabetes: The SWITCH 2 Randomized Clinical Trial. JAMA 2017;318:45-56. Yardley DA, Ismail-Khan RR, Melichar B, et al. Randomized phase II, double-blind, placebo-118. controlled study of exemestane with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptor-positive breast cancer progressing on treatment with a nonsteroidal aromatase inhibitor. J Clin Oncol 2013;31:2128-35. Yoshimura K, Minami T, Nozawa M, et al. A Phase 2 Randomized Controlled Trial of 119. Personalized Peptide Vaccine Immunotherapy with Low-dose Dexamethasone Versus Dexamethasone

Alone in Chemotherapy-naive Castration-resistant Prostate Cancer. Eur Urol 2016;70:35-41.

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#### **BMJ** Open

120. Borror A, Zieff G, Battaglini C, Stoner L. The effects of postprandial exercise on glucose control in individuals with type 2 diabetes: A systematic review. Sports Med 2018;48:1479-91.
121. Chan E, Giallauria F, Vigorito C, Smart NA, Exercise training in heart failure patients with

121. Chan E, Giallauria F, Vigorito C, Smart NA. Exercise training in heart failure patients with preserved ejection fraction: a systematic review and meta-analysis. Monaldi Arch Chest Dis 2016;86:759.

122. Grace A, Chan E, Giallauria F, Graham PL, Smart NA. Clinical outcomes and glycaemic responses to different aerobic exercise training intensities in type II diabetes: a systematic review and meta-analysis. Cardiovasc Diabetol 2017;16.

123. Ostman C, Smart NA, Morcos D, Duller A, Ridley W, Jewiss D. The effect of exercise training on clinical outcomes in patients with the metabolic syndrome: a systematic review and meta-analysis. Cardiovasc Diabetol 2017;16.

124. Van Rosendal SP, Osborne MA, Fassett RG, Coombes JS. Guidelines for glycerol use in hyperhydration and rehydration associated with exercise. Sports Med 2010;40:113-29.

125. Smart NA, Waldron M, Ismail H, et al. Validation of a new tool for the assessment of study quality and reporting in exercise training studies. Int J Evid Based Healthc 2015;13:9-18.

126. Maher CG, Moseley AM, Sherrington C, Elkins MR, Herbert RD. A description of the trials,

reviews, and practice guidelines indexed in the PEDro Database. Phys Ther 2008;88:1068-77.

127. Verhagen AP, De Vet HCW, De Bie RA, et al. The Delphi List. Journal of clinical epidemiology 1998;51:1235-41.

128. McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. Can Med Assoc J 2006;175:34-41.

129. Larun L, Brurberg KG, Odgaard-Jensen J, Price JR. Exercise therapy for chronic fatigue syndrome. Cochrane Database Syst Rev 2019;10:CD003200.

130. Pilutti LA, Platta ME, Motl RW, Latimer-Cheung AE. The safety of exercise training in multiple sclerosis: a systematic review. J Neurol Sci 2014;343:3-7.

#### **BMJ** Open

131. Tew GA, Brabyn S, Cook L, Peckham E. The completeness of intervention descriptions in randomised trials of supervised exercise training in peripheral arterial disease. PLoS One 2016;11:e0150869.

132. Meneses-Echavez JF, Rodriguez-Prieto I, Elkins M, Martinez-Torres J, Nguyen L, Bidonde J.
Analysis of reporting completeness in exercise cancer trials: a systematic review. Bmc Med Res
Methodol 2019;19:220.

133. Hacke C, Nunan D, Weisser B. Do exercise trials for hypertension adequately report interventions? A reporting quality study. Int J Sports Med 2018;39:902-8.

134. McEwen D, O'Neil J, Miron-Celis M, Brosseau L. Content reporting in post-stroke therapeutic circuit-class exercise programs in randomized control trials. Top Stroke Rehabil 2019;26:281-7.

135. Scott JM, Zabor EC, Schwitzer E, et al. Efficacy of Exercise Therapy on Cardiorespiratory

Fitness in Patients With Cancer: A Systematic Review and Meta-Analysis. J Clin Oncol 2018;36:2297-

305.

136. Peron J, Pond GR, Gan HK, et al. Quality of reporting of modern randomized controlled trials in medical oncology: a systematic review. J Natl Cancer Inst 2012;104:982-9.

137. Peron J, Maillet D, Gan HK, Chen EX, You B. Adherence to CONSORT adverse event reporting guidelines in randomized clinical trials evaluating systemic cancer therapy: a systematic review. J Clin Oncol 2013;31:3957-63.

138. Ritchie A, Seubert L, Clifford R, Perry D, Bond C. Do randomised controlled trials relevant to pharmacy meet best practice standards for quality conduct and reporting? A systematic review. Int J Pharm Pract 2020;28:220-32.

139. Begg C, Cho M, Eastwood S, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. JAMA 1996;276:637-9.

140. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, Group C. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. Ann Intern Med 2008;148:295-309.

BMJ Open: first published as 10.1136/bmjopen-2020-048218 on 11 August 2021. Downloaded from http://bmjopen.bmj.com/ on April 16, 2024 by guest. Protected by copyright

141. Han C, Kwak KP, Marks DM, et al. The impact of the CONSORT statement on reporting of randomized clinical trials in psychiatry. Contemp Clin Trials 2009;30:116-22.

142. Moher D, Jones A, Lepage L, Group C. Use of the CONSORT statement and guality of reports of randomized trials: a comparative before-and-after evaluation. JAMA 2001;285:1992-5.

143. Plint AC, Moher D, Morrison A, et al. Does the CONSORT checklist improve the quality of

reports of randomised controlled trials? A systematic review. Med J Aust 2006;185:263.

.ε .erwood κ. .ation statement. b. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on exercise reporting template 144.

(CERT): Explanation and elaboration statement. Br J Sports Med 2016;50:1428-37.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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Table 1. Characteristics of exercise and pharr	macological therapy RCTs
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Characteristic	Exercise Therapy RCTs <sup>1</sup>	Pharmacological Therapy RCTs <sup>2</sup>	
	No. (%)	No. (%)	
Journal (Impact Factors <sup>3</sup> )			
Annals of Internal Medicine (19.315)	2 (4.2%)	4 (8.3%)	
British Medical Journal (27.604)	1 (2.1%)	0 (0%)	
Circulation (23.054)	0 (0%)	2 (4.2%)	
European Heart Journal (24.889)	4 (8.3%)	4 (8.3%)	
European Urology (17.298)	3 (6.2%)	3 (6.2%)	
Gastroenterology (19.809)	0 (0%)	2 (4.2%)	
Gut (17.943)	1 (2.1%)	0 (0%)	
Journal of the American College of Cardiology (18.639)	7 (15%)	7 (15%)	
Journal of the American Medical Association (JAMA; 51.273)	12 (25%)	9 (19%)	
JAMA Internal Medicine (20.768)	2 (4.2%)	1 (2.1%)	
JAMA Oncology (22.416)	1 (2.1%)	0 (0%)	
Journal of Clinical Oncology (28.349)	11 (23%)	13 (27%)	
Lancet (59.102)	0 (0%)	1 (2.1%)	
New England Journal of Medicine (70.670)	4 (8.3%)	2 (4.2%)	
Journal impact factor			
Overall (median [IQR])	28 (19, 51)	28 (19, 34)	
Number of sites			
Single	33 (69%)	15 (31%)	
Multi-center	15 (31%)	33 (69%)	
Sample size			
Overall (median [IQR])	138 (100, 236)	160 (98, 314)	
Year of publication			
<2013	24 (50%)	17 (35%)	
≥2013	24 (50%)	31 (65%)	
Author response	16 (33%)	7 (15%)	

**Notes:** %, percent; IQR, interquartile range; No., number; RCTs, randomized controlled trials <sup>1</sup> n=48 exercise therapy RCTs; <sup>2</sup> n=48 pharmacological therapy RCTs; <sup>3</sup> Clarivate (2018)

Table 2. Quality of exercise and pharmacological therapy RCT reporting and conduct
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0	Exercise RCTs <sup>1</sup>		Pharmaco	Pharmacological RCTs <sup>2</sup>	
Outcomes	Median	IQR	Median	IQR	p-values*
Primary Outcome					
Overall Quality Score	45.5	38.8, 51.2	52.5	46.8, 58.0	<0.001
Eligible score <sup>3a,b</sup>	80.0	78.0, 81.0	68.0	67.0, 69.0	
Percent	58.2	48.6, 64.5	77.1	70.5, 83.9	
Secondary Outcomes					
Research Reporting Guidelines					
CONSORT Score	25.0	23.0, 28.0	25.0	22.0, 28.0	<0.001
Eligible score <sup>4a,b</sup>	45.0	44.0, 47.0	33.0	32.0, 34.0	
Percent	56.8	50.0, 62.8	75.4	69.7, 84.7	
CONSORT-Harms Score	3.0	1.0, 5.0	6.0	4.0, 7.2	<0.001
Eligible score <sup>5</sup>	9.0	9.0, 10.0	10.0	10.0, 10.0	
Percent	31.7	11.1, 51.4	66.7	40.0, 72.5	
Intervention Score	4.0	3.0, 4.0	4.0	4.0, 4.2	0.02
Eligible score <sup>6</sup>	6.0	-	6.0	-	
Percent	66.7	50, 66.7	66.7	66.7, 70.8	
TIDieR Score	8.0	7.0, 10.0	-	-	-
Eligible score <sup>7</sup>	15.0	14.0, 15.0	-	-	
Percent	57.4	49.2, 67.9	-	-	
Research Conduct Inventories					
Cochrane ROB Score	10.0	9.0, 11.0	13.0	12.0, 13.0	<0.001
Eligible score <sup>8</sup>	14.0	-	14.0	-	
Percent	71.4	64.3, 78.6	92.9	85.7, 92.9	
Jadad Score	3.0	2.8, 5.0	5.0	4.0, 5.0	<0.001
Eligible score <sup>9</sup>	5.0	-	5.0	-	
Percent	60.0	55.0, 100.0	100.0	80.0, 100.0	

Notes: %, percent; IQR, interquartile range; RCTs, randomized controlled trials

<sup>1</sup> n=48 exercise therapy RCTs; <sup>2</sup> n=48 pharmacological therapy RCTs

\* p-values were adjusted for multiple comparisons within Research Reporting Guidelines and within Research Conduct Inventories using a Bonferroni correction.

Maximum possible quality scores:

<sup>3a,b</sup> Overall quality for exercise therapy RCTs = 87<sup>3a</sup> and pharmacological therapy RCTs = 72<sup>3b</sup>

<sup>4a,b</sup> CONSORT-NPT for exercise therapy RCTs = 52<sup>4a</sup>; CONSORT for pharmacological therapy RCTs = 37<sup>4b</sup> <sup>5</sup> CONSORT-Harms for all RCTs = 10

<sup>6</sup> Intervention for all RCTs = 6

<sup>7</sup> TIDieR for exercise RCTs = 16

<sup>8</sup> Cochrane ROB for all RCTs = 14

<sup>9</sup> Jadad scale for all RCTs = 5

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# Table 3. Individual TIDieR item reporting summary for exercise therapy RCTs

	e 3. Individual TIDieR item reporting summary for exercise therapy RCTs		20-0		
ltem No.	Expanded TIDieR Criteria	Evaluation Yes	Unclea	No No (%)	
1	Provide the name or a phrase that describes the intervention.	<b>No. (%)</b> 48 (100%)	<b>No. (%)</b> 0 (0%) ⊐	<b>No. (%)</b> 0 (0%)	<b>No. (%)</b> 0 (0%)
2	Describe any rationale, theory, or goal of the elements essential to the intervention.	48 (100%)	Augu 0 (0%) 0	0 (0%)	0 (0%)
3	Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of providers.	20 (42%)	5 (10%)22 	0 (0%)	23 (48%)
4	Describe each of the procedures, activities, & / or processes used in the intervention, including any enabling or support activities.	33 (69%)	5 (10%)	10 (21%)	0 (0%)
5	For each category of intervention provider, describe their expertise, background & any specific training given.	7 (15%)	4 (8%) oaded f	37 (77%)	0 (0%)
6	Describe the modes of delivery of the intervention & whether it was provided individually or in a group.	17 (35%)	3 (6%) In 100 100 100 100 100 100 100 100 100 10	28 (58%)	0 (0%)
7	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	36 (75%)	5 (10%)	7 (15%)	0 (0%)
8a	Describe the intensity of intervention sessions.	31 (65%)	0 (0%) <mark>6</mark>	17 (35%)	0 (0%)
8b	Describe the frequency of intervention sessions.	40 (83%)	0 (0%)	8 (17%)	0 (0%)
8c	Describe the duration of intervention sessions.	28 (58%)	0 (0%) <mark>00</mark>	20 (42%)	0 (0%)
8d	Describe the total length of the intervention period.	48 (100%)	0 (0%) <sup>0</sup> >	0 (0%)	0 (0%)
9i	If the intervention was planned to be personalised, then describe when & how.	19 (40%)	9 (19%) 	20 (42%)	0 (0%)
9ii	If the intervention was planned to be progressed, then describe when & how.	3 (6%)	6 (13%)م	39 (81%)	0 (0%)
10	If the intervention was modified during the course of the study, describe the changes (what, why, when, & how).	1 (2%)	0 (0%) <sup>24</sup> by <sub>9</sub>	0 (0%)	47 (98%)
11	If intervention adherence or fidelity was assessed, describe how and by whom, & if any strategies were used to maintain or improve fidelity, describe them.	16 (33%)	10 (21%) דיייייייייייייייייייייייייייייייייייי	22 (46%)	0 (0%)
12	If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	2 (4%)	3 (6%) rotected	43 (90%)	0 (0%)

# Table 4. Cochrane ROB ratings for individual exercise and pharmacological therapy RCTs

							BMJ	Open		136/bm					Pag
								Ex	ercise	RCT		ng and	condu	ct qua	lity 35
able 4. Cochrane ROB ratir	ngs fo	or indi	vidua	l exei	rcise	and p	harm			'n-2					
Exercise RCTs	Sequence Generation	Allocation Concealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other Sources	Pharmacological RCTs	Sequence Generation	→ Allocation Z tsfc00cealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other Sources
Beckers et al. (2008)	-	?	-	?	•	•	•	Ahmed et al. (2008)	?			•	•	•	•
Beer et al. (2008)	?	?	•	?	•	•	0	Gheorghiade et al. (2008)	?	021. <u>~</u>	•	•	•	•	•
Ligibel et al. (2008)	?	?	•	?	$\bullet$	•	•	Greenspan et al. (2008)	•	• Dov		•	?	$\bullet$	•
Maltais et al. (2008)	+	•	0	?	•	•	•	Grudell et al. (2008)	?			•	•	•	•
Adamsen et al. (2009)	•	•	0	?	•	?	•	Irani et al. (2008)	?	wnloade	0	?	•	•	•
Courneya et al. (2009)	•	•	•	?	•	•	•	Nissen et al. (2008)	?	d fro	•	•	?	•	•
McDermott et al. (2009)	+	?	-	•	?	?	•	Ratziu et al. (2008)	?	• M	•	•	•	•	•
Monninkhof et al. (2009)	+	?	-	?	•	?	€	Caminiti et al. (2009)	?	?	•	?	•	•	•
O'Connor et al. (2009)	•	•	•	•	•	•	0	Frustaci et al. (2009)	•	e Ma	•	$\bullet$	•	$\bullet$	•
Patwala et al. (2009)	•	•	•	?	?	•	$\bullet$	Lapperre et al. (2009)	•	? pe	•	•	0	•	•
Schmitz et al. (2009)	•	?	•	?	•	?	•	Pradhan et al. (2009)	•	n.bn		$\bullet$	•	$\bullet$	•
Segal et al. (2009)	+	•	•	0	•	•	?	Loprinzi et al. (2010)	•	۳ <u>ار</u> ۲		$\bullet$	?	$\bullet$	•
Church et al. (2010)	+	•	-	•	•	•	•	Smith et al. (2010)	•	• •	•	•	?	$\bullet$	•
Friedenreich et al. (2010)	+	•	-	•	•	?	•	Ellis et al. (2011)	•	on A	•	?	•	$\bullet$	•
Galvao et al. (2010)	+	•	•	0	•	•	•	Rosenheck et al. (2011)	$\bullet$	• •	?	?	•	•	0
Schmitz et al. (2010)	+	•	-	•	•	•	•	Spitzer et al. (2012)	•	<b>•</b> ,	•	•	•	$\bullet$	•
Edelmann et al. (2011)	•	•	•	•	•	•	•	Gheorghiade et al. (2013)	?	2024	•	$\bullet$	•	$\bullet$	•
Hallsworth et al. (2011)	?	?	?	?	•	?	•	Hurvitz et al. (2013)	•	- by	0	•	•	•	•
Villareal et al. (2011)	•	?	0	?	•	•	•	Klotz et al. (2013)	•	guest. P	•	?	?	•	•
Belardinelli et al. (2012)	?	?	•	•	?	•	•	Kosmala et al. (2013)	•	St. F	•	?	•	$\bullet$	•
Campbell et al. (2012)	•	?	•	•	•	•	•	Poole et al. (2013)	•	orote	•	•	•	•	•
Duijts et al. (2012)	•	•	•	?	?	•	•	van der Bom et al. (2013)	•	rotected	•	•	•	•	•
Sandri et al. (2012)		•	0	?	?	•	•	Yardley et al. (2013)		oy oy	•	•	•	•	•
Winter et al. (2012)		$\bullet$		?	?	•	•	Ford et al. (2014)		copyright.	•	$\bullet$	•	$\bullet$	

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Exercise RCTs	Sequence Generation	Allocation Concealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other Sources	Pharmacological RCTs	Sequence Generation	Allocation C905ealment Particinant	Blinding	Blinding	Attrition Bias	Selective Reporting	Other
Daumit et al. (2013)	•	•	•	•	•	•	•	Han et al. (2014)	•	• Au		•	•	•	•
Kitzman et al. (2013)	?	?	0	•	•	•	•	Harman et al. (2014)	•	August	•	•	•	•	•
Messier et al. (2013)	?	?		•	•	•	•	Taplin et al. (2014)	?	? 202	•	•	•	•	•
Pitkala et al. (2013)		•	•	?	•	•	•	Cummings et al. (2015)	?		•	•	•	•	•
Galvao et al. (2014)	•	•	O		•	•	•	Hamshere et al. (2015)	•	? mloa	•	•	•	•	•
Hollekim-Strand et al. (2014)	?	?	O	?	•	•	•	Hoendermis et al. (2015)	•	10a	•	•	•	•	·
Jones et al. (2014)	?	?	•	?	•	•	•	Krankenberg et al. (2015)	?		•	•	?	•	•
Pahor et al. (2014)	•	?	•	•	e	?	•	Tsujita et al. (2015)	•	? from	•	•	?	•	+
Fakhry et al. (2015)	•	•	-	•	÷	Ð	•	Ulrich et al. (2015)	•	<u>? ਜ</u>	•	•	•	•	•
Friedenreich et al. (2015)	•	•	0	•	•	•	•	Cortelazzo et al. (2016)	•		•	?	•	•	•
Irwin et al. (2015)	?	?	•	?	?	•	•	Cusi et al. (2016)	•		•	•	•	•	•
Murphy et al. (2015)	•	?	•	•	Đ	+	?	Kosmala et al. (2016)	?		•	•	•	•	•
Ross et al. (2015)	•	•	•	•	•	+	?	McKay et al. (2016)	?	E 🤊	•	?	•	•	•
van Waart et al. (2015)	•	?	•	?	D	-	•	Schmid et al. (2016)	•	2 2 9	•	•	•	•	•
Ehlken et al. (2016)	?	?	•	•	•	+	•	Yoshimura et al. (2016)	?	• • •	•	?	•	•	•
Kitzman et al. (2016)	•	?	•	?	•	+	•	Goebel et al. (2017)			•	•	•	•	•
Zhang et al. (2016)	•	•	•	•	•	•	•	Soiffer et al. (2017)	•	? 16	•	?	0	•	•
Johansen et al. (2017)	•	•	0	•	•	•	•	Urruticoechea et al. (2017)	$\bigcirc$		•	?	$\bullet$	•	•
McDermott et al. (2017)	•	?	0	•	•	•	•	Wysham et al. (2017)	?	• 2024 I	•	•	$\bullet$	•	•
Saberi et al. (2017)	•	?	0	•	•	+	•	Devereux et al. (2018)	•	• v ⊇v	•	?	•	•	•
Taaffe et al. (2017)	•	?	•	?	•	•	?	Johnson et al. (2018)	•	by guest ●	•	?	•	•	•
Villareal et al. (2017)	•	?	•	•	•	•	•	Kim et al. (2018)	•		•	•	•	•	•
Dieli-Conwright et al. (2018)	•	•	•	?	•	•	•	Rimawi et al. (2018)	•	<ul> <li>Protected by copyright</li> <li> <ul> <li></li></ul></li></ul>	•	?	$\bullet$	•	•
McDermott et al. (2018)	•	?	-	?	+	•	•	Wapnir et al. (2018)	•		•	?	•	•	•

Exercise RCT eporting and conduct quality 37

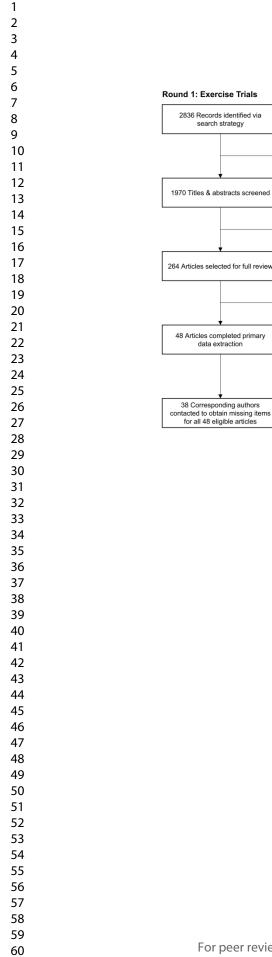
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# Table 5. Factors associated with overall quality score, stratified by study type

Outeeme	Study	Analysis	Exercis	e Therapy RCT	S <sup>1</sup>	Pharm	macological Therapy RCTs <sup>2</sup>			
Outcome	Characteristics	Dichotomy	OR	95% CI	<i>p</i> -value	OR S	95% CI	<i>p</i> -value		
Overall quality score	Impact factor	≥25 vs <25	1.36	1.18, 1.57	<0.001	1.02	0.84, 1.24	0.80		
	Sample size	≥152 vs <152	1.29	1.11, 1.51	0.001	1.02 1.20	0.97, 1.47	0.089		
	Number of sites	Multi- vs Single Centre	1.08	0.92, 1.27	0.30	1.21	0.98, 1.49	0.078		
	Publication year	≥2013 vs <2013	1.18	1.03, 1.34	0.015	1.35	1.14, 1.60	<0.001		
		ratio; RCTs, randomized co armacological therapy RCTs				prownloaded from http://prilippen.prilip.com/ on April 16, 2024 by guest. Protected				

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2 3	Figure Caption
4 5	Fig 1. PRISMA Flow Diagram
6 7	Notes: RCT, randomized controlled trial
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10 11	
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18 19	
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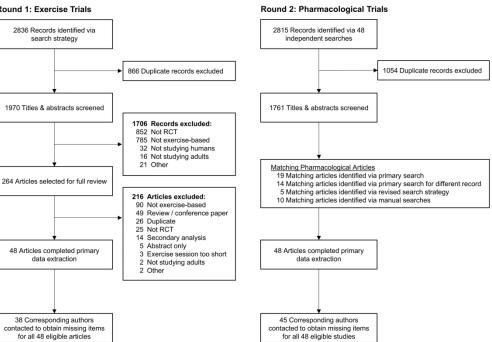


Fig 1. PRISMA Flow Diagram



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# Supplementary Methods 1: PRISMA Checklist

pplementary Methods pplementary Method			Page 42
Section/topic	#	Checklist item	Reported
TITLE			on page #
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS		n n n n n n n n n n n n n n n n n n n	
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6, eMethods
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	eMethod
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if appli able, included in the meta-analysis).	6,7, eMethod
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6,7, eMethod
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumption and simplifications made.	7,8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7,8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., l <sup>2</sup> ) for each meta-analysis.	8
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Section/topic	#	BMJ Open     3000000000000000000000000000000000000	Reported on page #
Risk of bias across	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within	7,8
studies		studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-	8,9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10, eMethods Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	eResults
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	eResults
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each antervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	eResults
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Table 2, eResul
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Iter 16]).	11, Table 3, eResul
DISCUSSION		<u> </u>	
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future regarch.	15
FUNDING		ح	
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1
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#### Supplementary Methods 2: AMSTAR 2 Checklist

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

For Yes:		Optiona	al (recommended)		
X	Population		Timeframe for follow-up	x	Yes
X	Intervention				No
X	Comparator group				
	Outcome				
2.			explicit statement that the review eview and did the report justify a		
For Part	ial Yes:	For Yes	5:		
The auth	nors state that they had a written	As for p	partial yes, plus the protocol		
protocol	or guide that included ALL the	should	be registered and should also		
followin	g:	have sp	ecified:		
				X	Yes
	review question(s)		a meta-analysis/synthesis plan,		Partial Yes
	a search strategy		if appropriate, and		No
	inclusion/exclusion criteria		a plan for investigating causes		
	a risk of bias assessment		of heterogeneity		
	a rist of ords assossment		justification for any deviations		
			from the protocol		
3.	Did the review authors explain	their sele	ction of the study designs for incl	lusion	in the review?
For Yes,	the review should satisfy ONE of	the follo	wing:		
$\boxtimes$	Explanation for including only R	CTs		X	Yes
	OR Explanation for including on	ly NRSI			No
	OR Explanation for including both	th RCTs a	and NRSI		
4.	Did the review authors use a co	mprehen	sive literature search strategy?		
For Part	ial Yes (all the following):	For Yes	s, should also have (all the		
	, <u> </u>	followin			
	searched at least 2 databases	X	searched the reference lists /	X	Yes
	(relevant to research question)		bibliographies of included		Partial Yes
	provided key word and/or		studies		No
	search strategy	X	searched trial/study registries		
	justified publication restrictions	X	included/consulted content		
	(e.g. language)		experts in the field		
		x	where relevant, searched for		
			grey literature		
		X	conducted search within 24		
			months of completion of the		
			review		
5.	Did the review authors perform	study se	election in duplicate?		
For Yes,	either ONE of the following:				
x	at least two reviewers independer			X	Yes
	and achieved consensus on which				No
	OR two reviewers selected a sam				
	agreement (at least 80 percent), w	vith the re	mainder selected by one		
	reviewer.				

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

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For Yes	s, either ONE of the following:				
x	at least two reviewers achieved co included studies	onsensus	on which data to extract from		Yes No
	OR two reviewers extracted data achieved good agreement (at leas extracted by one reviewer.				
7.	Did the review authors provide	a list of e	excluded studies and justify the ex	clusio	ns?
For Par	tial Yes:	For Yes	s, must also have:		
	provided a list of all potentially relevant studies that were read in full-text form but excluded from the review	X	Justified the exclusion from the review of each potentially relevant study		Yes Partial Yes No
8.	Did the review authors describe	the inclu	uded studies in adequate detail?		
For Par	tial Yes (ALL the following):	For Yes followin	-		
	described populations	X	described population in detail	X	Yes
	described interventions	X	described intervention in		Partial Yes
	described comparators		detail (including doses where relevant)		No
	described outcomes	X	described comparator in detail		
	described research designs	ы	(including doses where relevant)		
		x	described study's setting		
		X	timeframe for follow-up		
9. RCTs	Did the review authors use a sa individual studies that were inc		v technique for assessing the risk of the review?	of bias	(RoB) in
	tial Yes, must have assessed RoB	For Yes from:	s, must also have assessed RoB		
	unconcealed allocation, and	$\mathbf{x}$	allocation sequence that was	x	Yes
	lack of blinding of patients and		not truly random, and		Partial Yes
	assessors when assessing	x	selection of the reported result		No
	outcomes (unnecessary for		from among multiple measurements or analyses of a		Includes only NRSI
	objective outcomes such as all-		specified outcome		TOYINT
	cause mortality)				
NRSI	cause mortality)		The Transformed in a reference for the state of configuration		
	cause mortality) tial Yes, must have assessed	For Yes	s, must also have assessed RoB:		
		For Yes			Yes
For Par			s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i>		Partial Yes
For Par RoB:	tial Yes, must have assessed		s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i> selection of the reported result		Partial Yes No
For Par RoB:	tial Yes, must have assessed from confounding, and		s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i>		Partial Yes
For Par RoB:	tial Yes, must have assessed from confounding, <i>and</i> from selection bias		s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i> selection of the reported result from among multiple measurements or analyses of a		Partial Yes No Includes only RCTs
For Par RoB:	tial Yes, must have assessed from confounding, <i>and</i> from selection bias . <b>Did the review authors report o</b> es	n the sou	s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome	□ □ ⊠	Partial Yes No Includes only RCTs

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

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11. If meta-analysis was performed did the review authors use appropria combination of results?	te meth	ous for statistical
RCTs		
For Yes:	_	
□ The authors justified combining the data in a meta-analysis		Yes
AND they used an appropriate weighted technique to combine		No
study results and adjusted for heterogeneity if present.	x	No meta-analysis
AND investigated the causes of any heterogeneity		conducted
For NRSI		
For Yes:		Var
The authors justified combining the data in a meta-analysis		Yes No
AND they used an appropriate weighted technique to combine		No meta-analysis
study results, adjusting for heterogeneity if present		conducted
AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data,		conducted
or justified combining raw data when adjusted effect estimates		
were not available		
AND they reported separate summary estimates for RCTs and		
NRSI separately when both were included in the review		
12. If meta-analysis was performed, did the review authors assess the pote individual studies on the results of the meta-analysis or other evidence		
For Yes:		
included only low risk of bias RCTs		🗆 Yes
OR, if the pooled estimate was based on RCTs and/or NRSI at variable	1	🗆 No
RoB, the authors performed analyses to investigate possible impact of	Į.	No meta-analysis
RoB on summary estimates of effect.		conducted
13. Did the review authors account for RoB in individual studies when in results of the review?	terpret	ing/ discussing the
For Yes:		
included only low risk of bias RCTs	1	🕱 Yes
OR, if RCTs with moderate or high RoB, or NRSI were included the		🗆 No
review provided a discussion of the likely impact of RoB on the results		
14. Did the review authors provide a satisfactory explanation for, and dis heterogeneity observed in the results of the review?	cussion	of, any
For Yes:		
There was no significant heterogeneity in the results		X Yes
OR if heterogeneity was present the authors performed an investigation of		□ No
sources of any heterogeneity in the results and discussed the impact of this on the results of the review		
		- J
15. If they performed quantitative synthesis did the review authors carry investigation of publication bias (small study bias) and discuss its likel the review?		
For Yes:		
performed graphical or statistical tests for publication bias and discussed		□ Yes
the likelihood and magnitude of impact of publication bias		🗆 No
		No meta-analysis
		conducted

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

16.	Did the review authors report any potential sources of conflict of int they received for conducting the review?	terest, ind	cluding any funding
For Yes			
x	The authors reported no competing interests OR	X	Yes
	The authors described their funding sources and how they managed potential conflicts of interest		No

**To cite this tool:** Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

This review was conducted in accordance with the PRISMA<sup>1</sup> and AMSTAR 2<sup>2</sup> guidelines (PROSPERO identifier CRD42018095033) (eMethods 1 and 2).

#### **Data Sources and Searches**

A Research Informationist (KM) conducted two sequential literature searches for articles from RCTs of exercise (first search) and pharmacological (second search) therapies within the Cochrane Central Register of Controlled Trials (Wiley), Embase (Elsevier), PubMed (NLM), and CINAHL (EBSCO) databases (eFigure 1). The exercise literature search was conducted on March 8<sup>th</sup>, 2018 and consisted of two component concepts using a combination of relevant keywords and controlled vocabulary: (1) exercise training intervention and (2) RCTs (eMethods 4). The Round 1 search was limited to trials published between January 1<sup>st</sup> 2008 (the year the CONSORT extension for Non-Pharmacologic Treatments was first published<sup>3</sup>) and the search date (March 8<sup>th</sup>, 2018). The searches were also limited to publications within leading clinical, general medicine and specialist medical journals based on having impact factors  $\geq$ 15 according to the 2016 Journal Citation Reports (Clarivate Analytics, formerly ISI Web of Knowledge). We purposefully restricted our search to medical journals with higher impact factors are more likely to endorse and enforce reporting quality guidelines;<sup>14-16</sup> and, therein (2) we believed that more homogeneous publication standards would allow us to better contextualize our findings comparing the quality of research reporting and conduct between exercise and pharmacological therapy RCTs. This approach is also consistent with the methods from similar reviews of medical, psychosocial, and behavioural RCTs.<sup>4-10</sup>

Trial meta-data (i.e., publishing journal, cohort / population, sample size, and number of study sites) was extracted from eligible exercise studies and used as 'matching criteria' to define search parameters for the pharmacological trial searches. In Round 2, 48 independent searches were initially conducted to identify pharmacological trials to match each of the 48 eligible exercise RCTs identified in Round 1. The initial Round 2 searches were conducted on November 20<sup>th</sup>, 2018. Each search consisted of five component concepts using a combination of relevant search terms and 'matching criteria' for: 1) pharmacological intervention, 2) RCTs, 3) publishing journal, 4) population, and 5) number of study sites (single- vs. multi-site studies). The Round 2 searches were similarly limited to trials published between January 1<sup>st</sup> 2008 and the search date within leading clinical, general medicine and specialist medical journals based on having impact factors ≥15 according to the 2016 Journal Citation Reports (eMethods 4). Per Round, search strategy components were first searched individually

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Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

(combining synonyms describing that concept with the Boolean operator OR), followed by the individual component search sets combined together using the Boolean operator AND.

#### **Study Eligibility**

Published RCTs of exercise and pharmacological interventions involving human adults ( $\geq$ 18 years of age), written in English, published after January 1<sup>st</sup> 2008, and published in leading clinical, general medicine and specialist medical journals were eligible (eMethods 4 and 5). Exercise therapy interventions were defined as those involving chronic (>3 weeks), repeated sessions of supervised (in person, with or without a distance-based component) aerobic training (i.e., endurance activity,  $\geq$ 15 minutes/session), resistance training (i.e., multiple large muscle group exercises involving repeated voluntary muscle contractions against a resistance greater than those normally encountered in activities of daily living), or the combination, with the objective of improving health-related outcomes.<sup>11,12</sup> Pharmacological interventions were defined as studies involving the administration of established or experimental pharmacological agents with the objective of improving health.

#### Data Extractor Training

Study reviewers (JM and KS) were trained in eligibility screening and data extraction over the course of eight weeks (>25 hours of group training), consisting of: (1) independent screening and data extraction from 12 "training" articles of both exercise and pharmacological RCTs using custom study Data Extraction Reference Guides (eMethods 6 and 7), and (2) regular investigator-led (SCA) review sessions to evaluate extraction completeness.

#### Study Selection, Data Extraction and Additional Sources

Article screening and data extraction for all trials was conducted sequentially following each round of literature searches (fig 1). First, two trained reviewers (JM and KS) independently screened and evaluated exercise article titles and abstracts (n=1,970) against review eligibility criteria using DistillerSR (Evidence Partners, Ottawa, Canada). Second, full manuscripts (n=264) of potentially eligible exercise articles were independently reviewed (JM and KS) using DistillerSR. Third, meta-data from each eligible exercise RCT (n=48) was extracted and used to develop the targeted systematic search strategies for Round 2 (i.e., pharmacological trial search). Fourth, detailed data from all studies (e.g., study design and methods, patient characteristics and flow, intervention descriptions) were extracted for each eligible exercise RCT from the primary manuscript and all data sources that were publicly available at the time the primary manuscript was published, including online

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Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

supplements, clinical trial registries, and related publications as appropriate using DistillerSR and a custom Exercise Therapy RCT Data Extraction Reference Guide (**eMethods 6**). Fourth, "incomplete" and "missing" items were compiled, and corresponding authors were emailed (from SCA, JMS, LWJ) with a request to provide missing items within ~4 weeks. Non-responding authors were sent a reminder email within 3 weeks providing up to an additional ~4 weeks to respond.

The Round 2 pharmacological therapy RCT searches were conducted (KM, SCA) concurrently with the author contact step from round 1. Titles, abstracts, and full texts (n=1,761) were screened (SCA) to identify pharmacological therapy RCTs that were best matched to the n=48 eligible exercise therapy RCTs according to our matching criteria. The specific matching criteria used included: (1) journal (±5 impact factor points according to the 2016 Journal Citation Reports (Clarivate Analytics, formerly ISI Web of Knowledge)), (2) population (sharing similar disease characteristics), (3) sample size (±30% difference in study samples), and (4) number of study sites (single vs multiple sites). Nineteen of the initial 48 searches (40%) successfully identified 'matching' pharmacological trials, leaving 29 exercise trials unmatched. Matching pharmacological trials were found for the remaining 29 exercise trials within the search results for different records (n=14 (29%); SCA), by running revised searches (n=5 (10%); KM), and by manual searches of journal databases (n=10 (21%); SCA). Once all exercise trials had been matched, the team (JM and KS) independently extracted data from the primary manuscript and all data sources that were publicly available at the time the primary manuscript was published, including online supplements, clinical trial registries, and related publications as appropriate using DistillerSR and a custom Pharmacological Therapy RCT Data Extraction Reference Guide (eMethods 7). Finally, "incomplete" and "missing" items were compiled, and corresponding authors were emailed (from SCA, JMS, LWJ) with a request to provide missing items within ~4 weeks. Non-responding authors were sent a reminder email within 3-4 weeks providing up to an additional  $\sim$ 4 weeks to respond. Disagreements concerning eligibility, data extractions, and risk of bias assessments were resolved by consensus (JM and KS). Disagreements were adjudicated by a third party (SCA) when a consensus could not be reached.

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Supplementary Methods 4: Exercise RCT Search Strategies

Supplementary Methods 4: Exercise RCT Search Strategies

#### Exercise Search Strategies

Comprehensive searches were conducted (March 8th, 2018) in three electronic databases:

- 1) PubMed/Medline (NLM)
- 2) EMBASE (Elsevier)
- 3) CINAHL (EBSCO)

The literature search strategy was developed first in PubMed and then translated to the other databases. A combination of relevant keywords and controlled vocabulary (MeSH - Medical Subject Headings in PubMed and Emtree in EMBASE) were used in the PubMed and EMBASE searches. Comparable keyword search strategies were used in CINAHL. A "Last 10 years" (2008-2018) date range was applied. No language restrictions were applied.

Two component parts made up the search strategy:

- 1) Exercise training intervention
- 2) RCTs

Date range limit: Last 10 years Publications limit: 45 target journals

Search filters were used for finding RCTs in PubMed and EMBASE. Available database limiters were used in CINAHL (Publication Type: Clinical Trial, Randomized Controlled Trial).

For the RCT search set, we used Cochrane Handbook recommended search filters for finding RCTs: <u>http://work.cochrane.org/pubmed</u>

#### sensitivity- and precision-maximizing version (2008 revision); PubMed format<sup>1</sup>

(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans [mh])) http://work.cochrane.org/embase

#### Embase search strategy for finding RCTs in Embase<sup>1</sup>

('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (random\* OR factorial\* OR crossover\* OR cross NEXT/1 over\* OR placebo\* OR doubl\* NEAR/1 blind\* OR singl\* NEAR/1 blind\* OR assign\* OR allocat\* OR volunteer\*):de,ab,ti)

1. Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from **www.cochrane-handbook.org** 

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Each of the two components of the search strategy was first searched upon individually, combining synonyms describing that concept with the Boolean operator OR. The three individual component search sets were then combined together using the Boolean operator AND. Resulting citations were managed and duplicates removed using the Endnote citation management software program (Clarivate Analytics).

# PubMed/MEDLINE Search Strategy

("Exercise" [Mesh] OR "exercise" OR "exercises" OR "Exercise Therapy" [Mesh] OR "exercise therapy" OR "exercise therapies" OR "exercise prescription" OR "training program" OR "exercise program" OR "Physical Conditioning, Human" [Mesh] OR "physical conditioning" OR "physical activity" OR "physical activities" OR "Motor Activity"[Mesh] OR "motor activity" OR "motor activities" OR "Muscle Contraction"[Mesh] OR "muscle contraction" OR "Resistance Training"[Mesh] OR "resistance training" OR "Circuit-Based Exercise" [Mesh] OR "circuit-based exercise" OR "circuit training" OR "Muscle Stretching Exercises" [Mesh] OR "muscle stretching exercises" OR "aerobic exercise" OR "anaerobic exercise" OR "Locomotion" [Mesh] OR "locomotion" OR "Running" [Mesh] OR "running" OR "Jogging"[Mesh] OR "jogging" OR "Swimming"[Mesh] OR "swimming" OR "Walking"[Mesh] OR "walking" OR "Sports"[Mesh] OR "sports") AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("CA Cancer J Clin"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "JAMA"[Journal] OR "Nat Biotechnol" [Journal] OR "Nature" [Journal] OR "Science" [Journal] OR "Lancet Oncol" [Journal] OR "Cell" [Journal] OR "Nat Med" [Journal] OR "Nat Genet" [Journal] OR "Cancer Cell"[Journal] OR "World Psychiatry"[Journal] OR "Lancet Neurol"[Journal] OR "Nat Chem"[Journal] OR "J Clin Oncol"[Journal] OR "Cell Stem Cell"[Journal] OR "Immunity" [Journal] OR "Nat Immunol" [Journal] OR "BMJ" [Journal] OR "Eur Heart J" [Journal] OR "Nat Cell Biol" [Journal] OR "Cancer Discov" [Journal] OR "J Am Coll Cardiol"[Journal] OR "Lancet Infect Dis"[Journal] OR "Lancet Diabetes Endocrinol"[Journal] OR "Circulation"[Journal] OR "Lancet Respir Med"[Journal] OR "Gastroenterology"[Journal] OR "Cell Metab"[Journal] OR "Nat Neurosci"[Journal] OR "Lancet Glob Health"[Journal] OR "Ann Intern Med"[Journal] OR "Psychol Bull"[Journal] OR "Sci Transl Med"[Journal] OR "Gut"[Journal] OR "Trends Biochem Sci"[Journal] OR "JAMA Oncol"[Journal] OR "JAMA Intern Med"[Journal] OR "Psychol Ing"[Journal] OR "Eur Uro]"[Journal] OR "Cell Res"[Journal] OR "Trends Cogn Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal]) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT])

Abbreviations: Mesh = Medical Subject Heading, pt = Publication Type, tiab = Title/Abstract, ti = Title, mh = MeSH Terms

#### **EMBASE Search Strategy**

1	('exercise'/exp OR 'exercise' OR 'exercises' OR 'kinesiotherapy/exp OR 'exercise therapy' OR 'exercise therapies' OR 'exercise prescription' OR 'training program' OR 'exercise program' OR 'physical conditioning' OR 'physical activity' OR 'physical activities' OR 'motor activity/exp OR 'motor activity' or 'motor active' active apticon''''''''''''''''''''''''''''''''''''
2	(('15424863':is OR 'CA Cancer Journal for Clinicians'/jt) OR ('15334406':is OR 'New England Journal of Medicine'/jt) OR ('1474547X':is OR 'The Lancet'/jt) OR ('15383598':is OR 'JAMA - Journal of the American Medical Association'/jt) OR ('15461696':is OR 'Nature Biotechnology'/jt) OR ('14764687':is OR 'Nature'/jt) OR ('10959203':is OR 'Science'/jt) OR ('14745488':is OR 'The Lancet Oncology'/jt) OR ('10974172':is OR 'Cell'/jt) OR ('1546170X':is OR 'Nature Medicine'/jt) OR ('15461718':is OR 'Nature Genetics'/jt) OR ('18783686':is OR 'Cancer Cell'/jt) OR ('10974172':is OR 'World Psychiatry'/jt) OR ('14744465':is OR 'The Lancet Neurology'/jt) OR ('15277755':is OR 'Journal of Clinical Oncology'/jt) OR ('18759777':is OR 'Cell Stem Cell'/jt) OR ('10974180':is OR 'Immunity'/jt) OR ('17561833':is OR 'BMJ (Online'/jt) OR ('15229645':is OR 'European Heart Journal'/jt) OR ('14744457':is OR 'The Lancet Infectious Diseases'/jt) OR ('12218595':is OR 'The Lancet Diabetes and Endocrinology'/jt) OR ('15244539':is OR 'Circulation'/jt) OR ('14744457':is OR 'The Lancet Respiratory Medicine'/jt) OR ('15280012':is OR 'Gastroenterology'/jt) OR ('19327420':is OR 'Cell Metabolism'/jt) OR ('15461726':is OR 'Nature Neuroscience'/jt) OR ('14683288':is OR 'Gut'/jt) OR ('13624326':is OR 'Trends in Biochemical Sciences'/jt) OR ('21686106':is OR 'JAMA Internal Medicine'/jt) OR ('18737560':is OR 'European Urology'/jt) OR ('1879307X':is OR 'Trends in Cognitive Sciences'/jt) OR ('21686202':is OR 'JAMA Internal Medicine'/jt) OR ('1473456':is OR 'Nature Chemical Biology'/jt) OR ('1879307X':is OR 'Trends in Cognitive Sciences'/jt) OR ('2168622X':is OR 'JAMA Internal Medicine'/jt) OR ('14737560':is OR 'Lancet Chemical Biology'/jt) OR ('1879307X':is OR 'Trends in Cognitive Sciences'/jt) OR ('21686202X':is OR 'JAMA Internal Medicine'/jt) OR ('14737560':is OR 'Lancet Chemical Biology'/jt))
	-Nature Immunology -Psychological Bulletin -JAMA Oncology -Psychological Inquiry -Cell Research

# Supplementary Methods 4: Exercise RCT Search Strategies

	CINAHL Search Strategy
1	("exercise" OR "exercises" OR "exercise therapy" OR "exercise therapies" OR "exercise prescription" OR "training program" OR "exercise program" OR "physical conditioning" OR "physical activity" OR "motor activity" OR "motor activities" OR "muscle contraction" OR "resistance training" OR "circuit- based exercise" OR "circuit training" OR "muscle stretching exercises" OR "aerobic exercise" OR "anaerobic exercise" OR "locomotion" OR "running" OR "jogging" OR "swimming" OR "walking" OR "sports")
	AND
	Limiters - Publication Type: Clinical Trial, Randomized Controlled Trial
2	(((ZJ "new england journal of medicine")) or ((ZJ "lancet")) or ((ZJ "jama journal of the american medical association")) or ((ZJ "lancet oncology")) or ((ZJ "journal of clinical oncology")) or ((ZJ "bmj british medical journal international edition")) or ((ZJ "journal of the american college of cardiology jacc"))) or ((ZJ "clinical oncology")) or ((ZJ "annals of internal medicine")) or ((ZJ "jama internal medicine"))) or ((ZJ "annals of internal medicine")) or ((ZJ "jama internal medicine")))
	AND
	Limiters - Published Date: 20080101-20181231
	AND
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Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

# Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

#### Summary:

Database: PubMed (searched run on November 20th, 2018)

Total (including duplicates): 2815 records

**Duplicates:** 1054 records

Total (without duplicates): 1761 records to be reviewed

#### PubMed search strategies for each identified Population from the 48 included EXERCISE papers

#### 1) Exercise trial matching search: ID 33

("Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD OR "Chronic Obstructive Pulmonary Disease" OR COAD OR "Chronic Obstructive Airway Disease" OR "Chronic Airflow Obstructions" OR "Chronic Airflow Obstruction" OR ("chronic" AND "obstructive" AND "pulmonary" AND "disease")) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmaceutical Preparations" (Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmaceutical Preparations" (Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmaceutical Preparations" (Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmaceutical Preparations" (Mesh] OR "drug therapy" OR "therapeutic use" OR "therapeutic

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Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000073/public/

Pharma trial match: Found in original search - Lapperre et al. (2009)

#### 2) Exercise trial matching search: ID 51

(cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumors OR tumours OR malignan\* OR malignant OR "hematooncological" OR "hemato oncological" OR "hemato-oncological" OR hematologic neoplasms OR hematolos\*) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter"

Results: 14 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000123/public/

Pharma trial match: Found in original search from an alternate record (#36) – Rimawi et al. (2018)

#### 3) Exercise trial matching search: ID 96

(("peripheral arterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug "or "drugs" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug "OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal])

Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000170/public/

Pharma trial match: Found in original search from an alternate record (#31) - Ford et al. (2014)

4) Exercise trial matching search: ID 103

("Heart Failure"[Mesh] OR "heart failure" OR "Cardiac Failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapy" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR

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Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

"pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) Results: 29 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tIOrYmkO/collections/55000252/public/ Pharma trial match: Found in original search - Gheorghiade et al. (2013) 5) Exercise trial matching search: ID 107 10 (("Breast Cancer Lymphedema"[Mesh] OR (("lymphedema" OR "lymphedemas") AND ("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasms OR carcinoma OR carcinom\* OR tumor OR tumor OR 11 tumors OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multice 12 13 Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "therapeutic use" OR "pharmacotherapy" OR "therapeutic use" OR "therapeutic use" OR "pharmacotherapy" OR "therapeutic use" OR "therapeuti 14 "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR 15 controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans 16 [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR 17 "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) 18 Results: NONE - check how match found 19 Pharma trial match: Found in original search from an alternate record (#35) – Wapnir et al. (2018) 20 21 6) Exercise trial matching search: ID 133 22 23 (("Diabetes Mellitus, Type 2"[Mesh] OR "NIDDM" OR "type 2 diabetes mellitus" OR "diabetes mellitus type 2") NOT ("Multicenter Study" [Publication Type] OR 24 "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy" [Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR 25 "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR 26 "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR 27 "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern 28 Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) 29 Results: 18 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/55000319/public/ 30 31 Pharma trial match: Found in manual search - Nissen et al. (2008) 32 33 7) Exercise trial matching search: ID 180 34 ("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR 35 neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant)) NOT ("Multicenter Study" 36 [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR 37 "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR 38 "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 39 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical 40 trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) 41 42 Results: 6 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000333/public/ 43 Pharma trial match: Found in original search from an alternate record (#35) - Hurvitz et al. (2013) 44 45 8) Exercise trial matching search: ID 282 46 47 (("Obesity"[Mesh]OR "obesity" OR "obese") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical 48 Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "therapeutic use" OR 49 "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR 50 "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans 51 [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR 52 "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) 53 Results: 14 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000364/public/ 54 55 Pharma trial match: Found in manual search - Smith et al. (2010) 56 9) Exercise trial matching search: ID 394 57 58 15 59

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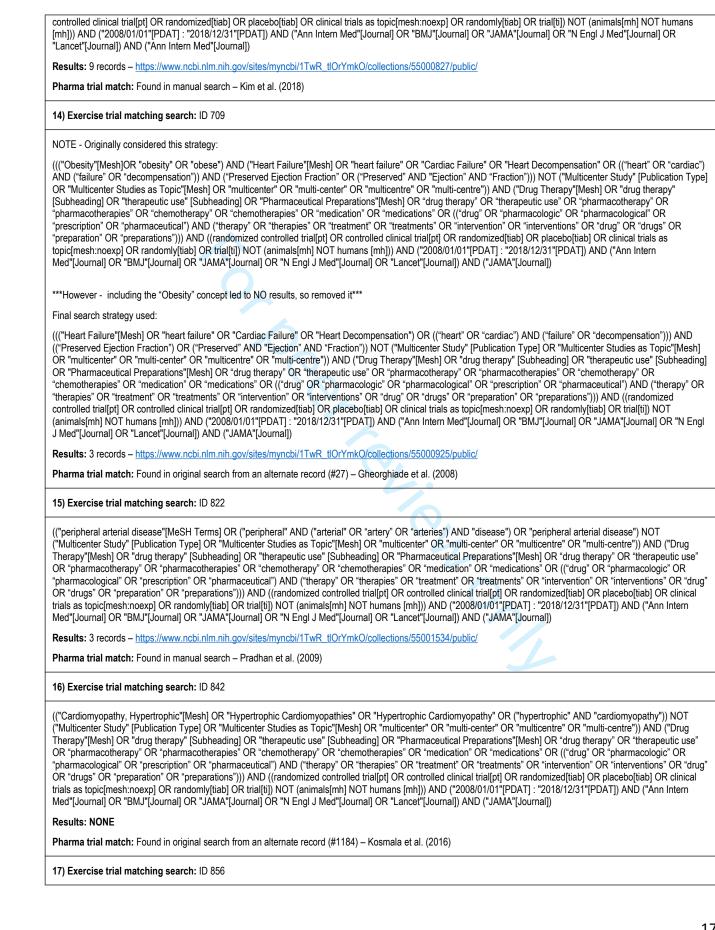
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("Mental Disorders" [Mesh] OR ((mental\* OR psycholog\* OR brain OR mind) AND ("disorder" OR "disorders" OR "illness" OR "illness" OR "diseases"))) AND "Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) Results: 79 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000661/public/ Pharma trial match: Found in original search – Rosenheck et al. (2011) 10) Exercise trial matching search: ID 431 ((((((("Obesity"[Mesh] OR "obesity" OR "obese" OR "Overweight"[Mesh] OR "overweight" OR "Weight Loss"[MeSH Terms] OR "Body Mass Index"[MeSH Terms]))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-centre")) AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations")))) AND (((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])))) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]))) AND ("CA Cancer J Clin"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "JAMA"[Journal] OR "Nat Biotechnol"[Journal] OR "Nature"[Journal] OR "Science"[Journal] OR "Lancet Oncol"[Journal] OR "Cell"[Journal] OR "Nat Med"[Journal] OR "Nat Genet"[Journal] OR "Cancer Cell"[Journal] OR "World Psychiatry"[Journal] OR "Lancet Neurol"[Journal] OR "Nat Chem"[Journal] OR "J Clin Oncol"[Journal] OR "Cell Stem Cell"[Journal] OR "Immunity"[Journal] OR "Nat Immunol"[Journal] OR "BMJ"[Journal] OR "Eur Heart J"[Journal] OR "Nat Cell Biol"[Journal] OR "Cancer Discov"[Journal] OR "J Am Coll Cardiol"[Journal] OR "Lancet Infect Dis"[Journal] OR "Lancet Diabetes Endocrinol"[Journal] OR "Circulation"[Journal] OR "Lancet Respir Med"[Journal] OR "Gastroenterology"[Journal] OR "Cell Metab"[Journal] OR "Nat Neurosci"[Journal] OR "Lancet Glob Health"[Journal] OR "Ann Intern Med"[Journal] OR "Psychol Bull"[Journal] OR "Sci Transi Med"[Journal] OR "Gut"[Journal] OR "Trends Biochem Sci"[Journal] OR "JAMA Oncol"[Journal] OR "JAMA Intern Med"[Journal] OR "Psychol Ing"[Journal] OR "Eur Urol"[Journal] OR "Cell Res"[Journal] OR "Trends Cogn Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal]) Results: 187 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57349993/public/ Pharma trial match: Found in original search - Spitzer et al. (2012) 11) Exercise trial matching search: ID 528 ("Aged" [Mesh] OR (("aged" OR "elderly" OR "older") AND ("adult" OR "adults"))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy" [Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) Results: 310 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000777/public/ Pharma trial match: Found in manual search – Devereux et al. (2018) 12) Exercise trial matching search: ID 585 ("peripheral arterial disease" [MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tIOrYmkO/collections/55000794/public/ Pharma trial match: Found in original search - Poole et al. (2013) 13) Exercise trial matching search: ID 631 (("Obesity"IMeshIQR "obesity" OR "obese") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"IMeshI OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR 16

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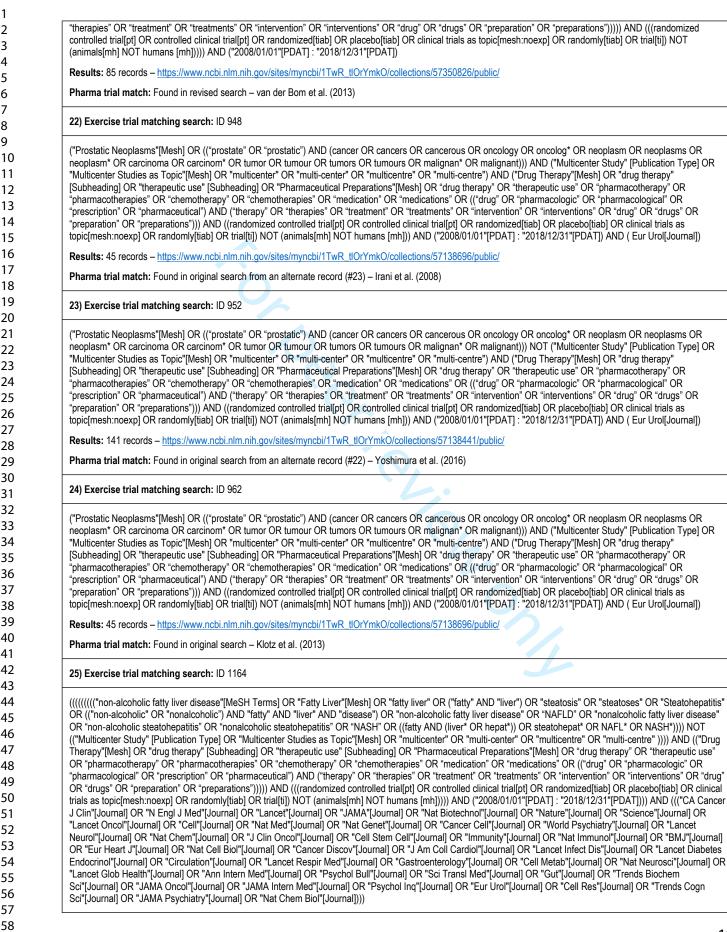
# Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

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<ul> <li>(a) Exercise trial matching search: ID 892</li> <li>("Heart Falue"[Mesh] OR "heat failure" OR "Cardiac Failure" OR "Heart Decompensation" OR (("heart 'OR "cardiac") AND ("failure" OR "decompensation")))) NOT Therapy ("Bubbication Type) OR "Nutlicenter Studies as Topic"[Mesh] OR "haraceutical Preparations"[Mesh] OR "rule-center" OR "multi-center" OR "mul</li></ul>	("Multicenter Therapy"[Me OR "pharmacolog OR "drugs" C trials as topic Clin"[Journal] "Lancet Onco Neurol"[Journ OR "Eur Hea Endocrinol"[J "Lancet Glob Sci"[Journal] Sci"[Journal] Results: 187	Study" [Publication Type] OR " sh] OR "drug therapy" [Subheal cotherapy" OR "pharmacotherap gical" OR "prescription" OR "pha- DR "preparation" OR "preparatic c[mesh:noexp] OR randomly[tial ] OR "N Engl J Med"[Journal] O ol"[Journal] OR "Cell"[Journal] O and J CR "Nat Chem"[Journal] O ant J"[Journal] OR "Nat Cell Biol" Journal] OR "Circulation"[Journal De Health"[Journal] OR "Ann Inter OR "JAMA Oncol"[Journal] OR "AMA Psychiatry"[Journal 7 records – https://www.ncbi.nlm	Multicenter Studies as Topic ding] OR "therapeutic use" [ pies" OR "chemotherapy" OI armaceutical") AND ("therap ons")))) AND (((randomized b) OR trial[ti]) NOT (animals DR "Lancet"[Journal] OR "JAI OR "Nat Med"[Journal] OR "JAI OR "Nat Med"[Journal] OR "[Journal] OR "Cancer Disco al] OR "Lancet Respir Med"[, rn Med"[Journal] OR "Psych R "JAMA Intern Med"[Journal I] OR "Nat Chem Biol"[Journal	"[Mesh] OR "multicenter" OR " Subheading] OR "Pharmaceuti R "chemotherapies" OR "medic y" OR "therapies" OR "treatmer controlled trial[pt] OR controlled [mh] NOT humans [mh])))) ANI MA"[Journal] OR "Nat Biotechn Vat Genet"[Journal] OR "Cance R "Cell Stem Cell"[Journal] OR "Cance Journal] OR "J Am Coll Carc Journal] OR "Gastroenterology" of Bull"[Journal] OR "Sci Transl ] OR "Psychol Inq"[Journal] OR al])	nulti-center" OR "multicentre" OR "multi- cal Preparations" [Mesh] OR "drug there ation" OR "medications" OR (("drug" Of tt" OR "treatments" OR "intervention" O I clinical trial[pt] OR randomized[tiab] C ("2008/01/01"[PDAT] : "2018/12/31"[P 0"[Journal] OR "Nature"[Journal] OR " r Cell"[Journal] OR "World Psychiatry"[ Immunity"[Journal] OR "Nat Immunol"[ iol"[Journal] OR "Lancet Infect Dis"[Jou [Journal] OR "Cell Metab"[Journal] OR Med"[Journal] OR "Cetl Metab"[Journal] OR " "Eur Urol"[Journal] OR "Cetl Res"[Jour	ti-centre"))) AND (("Drug py" OR "therapeutic use" R "pharmacologic" OR R "interventions" OR "dru R placebo[tiab] OR clinic DAT]))) AND ("CA Cance Science"[Journal] OR Journal] OR "Lancet Journal] OR "Lancet Journal" Journal] OR "Lancet Journal" Journal] OR "Lancet Journal" Journal] OR "Lancet Journal" Journal Journal Journal Journal" Journal Journal Journal Journal Journal (Alternal Journal Journal (Alternal Journal Journ
(Heart Failure"[Mesh] OR "heart failure" OR "Cardiac Failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND (failure" OR "decompensation")) NOT "Multicenter Study" [Publication Type) OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter Study" [Publication Type] OR Multicenter Study S as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "harmacoulical" OR pharmacoulical OR chance Study (Publication Type] OR Multicenter Study S as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "harmacoulical Preparations ("Mesh] OR "therapy" OR "harmacoulical Preparations ("Mesh] OR "therapy" OR "harmacoulical Preparations ("Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "harmacoulical Preparations ("Mesh] OR "therapy" OR "harmacoulical Preparations ("Mesh] OR "therapy" OR "harmacoulical Preparations ("Mesh] OR "therapy" OR "harmacoulical Preparations ("Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "harmacoulical Preparations ("Mesh] OR "therapy" OR "harmacoulical Preparations ("Mesh] OR "multicenter" ("Mesh] OR "multicenter" ("Mesh] OR "multicenter") OR "multicenter" ("Mesh] OR "multicenter") OR "multicenter" Stu	Pharma trial	match: Found in manual sear	ch – Grudell et al. (2008)			
"Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR	18) Exercise	etrial matching search: ID 892	2			
Pharma trial match: Found in original search – Hoendermis et al. (2015) 19) Exercise trial matching search: ID 901 ("hypertension, pulmonary"[MeSH Terms] OR ("hypertension" AND "pulmonary") OR "pulmonary hypertension") NOT ("Multicenter Study" [Publication Type] OR Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicenter" (DR "multicenter") AND ("therapy") Subheading] OR "therapy" (DR "hormacotherapy" OR pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "multicated Peparations"(Mesh) OR "fut gitterapy" OR pharmacotherapy" OR pharmacotherapy" OR pharmacotherapy" OR "chemotherapy" OR "therapy" OR "therapy" OR "therapy" OR "therapy" OR pharmacotherapy" OR "chemotherapy" OR "therapy" OR "t	("Multicenter Therapy"[Me OR "pharmac or "pharmacolog OR "drugs" C	Study" [Publication Type] OR " esh] OR "drug therapy" [Subhea cotherapy" OR "pharmacothera gical" OR "prescription" OR "pha DR "preparation" OR "preparatic	'Multicenter Studies as Topic ding] OR "therapeutic use" [ pies" OR "chemotherapy" OI armaceutical") AND ("therap ons"))) AND ((randomized co	"[Mesh] OR "multicenter" OR " Subheading] OR "Pharmaceuti R "chemotherapies" OR "medic y" OR "therapies" OR "treatmen ntrolled trial[pt] OR controlled c	nulti-center" OR "multicentre" OR "mul cal Preparations"[Mesh] OR "drug thera ation" OR "medications" OR (("drug" Of tt" OR "treatments" OR "intervention" O linical trial[pt] OR randomized[tiab] OR	ti-centre")) AND ("Drug py" OR "therapeutic use' R "pharmacologic" OR R "interventions" OR "dru placebo[tiab] OR clinical
19) Exercise trial matching search: ID 901 ("hypertension, pulmonary"[MeSH Terms] OR ("hypertension" AND "pulmonary") OR "pulmonary hypertension") NOT ("Multicenter Study" [Publication Type] OR Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "interventions" OR "interacenter of "pharmacologic" OR "preparation" OR "interventions" OR interventions" OR interventions" OR interventions" OR interventions" OR interventions "OR interventions" OR interventions" OR interventions "OR interventions" OR interventions" OR interventions" OR interventions" OR interventions" OR interventions" OR interventions "OR interventions" OR interventions "OR interventions" OR interventions" OR	Results: 87	records – https://www.ncbi.nlm.	.nih.gov/sites/myncbi/1TwR	tlOrYmkO/collections/5713795	<u>B/public/</u>	
("hypertension, pulmonary"[MeSH Terms] OR ("hypertension" AND "pulmonary") OR "pulmonary hypertension") NOT ("Multicenter Study" [Publication Type] OR Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter") AND ("Dug Therapy"[Mesh] OR "drug therapy" or "herapeutic use" (Subheading) OR "heraneoutical Preparations"[Mesh] OR "drug therapy" OR "herapeutic use" OR "pharmacological" OR preceription" OR "pharmacological" OR preceription "OR "pharmacological" OR preceription "OR "pharmacological" OR preceription "OR "pharmacological" OR preceription "OR "pharmacological" OR preparations")]) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR plantacological" OR preparations" OR "index prediction" OR "interventions" OR "index predictions" OR "index predictions" OR "index prediction" OR "interventions" OR "index predictions" OR "index prediction" OR "index prediction" OR "index predictions" OR "index prediction" OR "index predictio	Pharma trial	I match: Found in original searc	ch – Hoendermis et al. (201	5)		
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"heart failure"[MeSH Terms] OR "heart failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND (("ejection fractio DR "Ventricular Dysfunction"[Mesh] OR ("ejection" AND "fraction") OR ("ventricular" AND "dysfunction"))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-centre" OR "multicenter" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacological" OR "perscription" OR "pharmacoutherapy" OR "chemotherapy" OR "therapies" OR "therapeutic use" or "pharmacological" OR "preparation" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "preparation" OR "pharmacoutherapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "treatmace" or "pharmacoutherapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "pharmacoutherapy" (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ VOT (animals[mh] NOT humans [mh])) AND ("2008/01/10"[PDAT] : "2018/12/31"[PDAT]) AND (Eur Heart J[Journal]) Results: 33 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_ttOrYmkO/collections/57138774/public/ Pharma trial match: Found in original search – Frustaci et al. (2009) ((((("transposition of great arteries" OR "Ventricular Dysfunction, Right"[Mesh] OR "Right Ventricular Dysfunction") AND ("right ventricles" OR "right ventricles" O	"Multicenter s [Subheading] "pharmacothe "prescription" "preparation" topic[mesh:n <b>Results:</b> 6 re	Studies as Topic"[Mesh] OR "m ] OR "therapeutic use" [Subhea erapies" OR "chemotherapy" O " OR "pharmaceutical") AND ("ti ' OR "preparations"))) AND ((rar ioexp] OR randomly[tiab] OR tri- ecords – <u>https://www.ncbi.nlm.n</u>	nulticenter" OR "multi-center" ading] OR "Pharmaceutical P IR "chemotherapies" OR "me herapy" OR "therapies" OR " ndomized controlled trial[pt] ial[ti]) NOT (animals[mh] NO hih.gov/sites/myncbi/1TwR_tt	OR "multicentre" OR "multi-ce reparations" [Mesh] OR "drug th dication" OR "medications" OR treatment" OR "treatments" OF OR controlled clinical trial[pt] O T humans [mh])) AND ("2008/0	htre")) AND ("Drug Therapy"[Mesh] OR lerapy" OR "therapeutic use" OR "pharn (("drug" OR "pharmacologic" OR "phar "intervention" OR "interventions" OR "( R randomized[tiab] OR placebo[tiab] O 1/01"[PDAT] : "2018/12/31"[PDAT]) AN	"drug therapy" nacotherapy" OR macological" OR drug" OR "drugs" OR R clinical trials as
OR "Ventricular Dysfunction"[Mesh] OR ("ejection" AND "fraction") OR ("ventricular" AND "dysfunction"))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter" OR "multicenter" OR "multicenter") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "harmaceutical Preparations"[Mesh] OR "multicenter") AND ("drug therapy" (A "pharmaceutical Preparations"] [Mesh] OR "therapeutic use" (Subheading] OR "harmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacological" OR "pharmaceutical OR "medication" OR "medications" OR ("drug "OR "therapeutic use" OR "pharmacological" OR "preparation" OR "preparation" OR "medications" OR ("drug" OR "therapeutic use" OR "drugs" OR "preparation" OR "preparations"))) AND ("andomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[t] (OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[NOT (unimals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (Eur Heart J[Journal]) Results: 33 records – <a href="https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57138774/public/">https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57138774/public/</a> Pharma trial match: Found in original search – Frustaci et al. (2009) 21) Exercise trial matching search: ID 942 ((((("transposition of great arteries" OR "Ventricular Dysfunction, Right"[Mesh] OR ("systemic" or dysfunction") AND ("right ventricle" OR "right ventricles" OR "heart ventricles") AND ("Multicenter Study" [Publication Type] OR "heart ventricles" OR "heart ventricles"])) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "heart ventricles" OR "heart ventricles" OR "heart ventricles"])) AND ("Systemic" or dysfunction") OR "Right Ventricular Dysfunctions" OR ("Right" AN Ventricular AND ("systemic" OR "beart ventricles"]))) AND ("Multicenter Study" [	20) Exercise	trial matching search: ID 927	7		2/	
Pharma trial match: Found in original search – Frustaci et al. (2009) 21) Exercise trial matching search: ID 942 (((((("transposition of great arteries" OR "Ventricular Dysfunction, Right"[Mesh] OR "Right Ventricular Dysfunction" OR "Right Ventricular Dysfunctions" OR ("Right" AN Ventricular" AND ("systemic" OR "Dysfunction")) OR "systemic right ventricle" OR (("systemic" or dysfunction") AND ("right ventricle" OR "right ventricles" OR "heart ventricles"[MeSH Terms] OR "heart ventricles" OR "heart ventricle")))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR 'multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR	OR "Ventricu Studies as To "therapeutic of "chemotherap AND ("therap ((randomized	Jar Dysfunction"[Mesh] OR ("eji opic"[Mesh] OR "multicenter" O use" [Subheading] OR "Pharma py" OR "chemotherapies" OR "r oy" OR "therapies" OR "treatmen d controlled trial[pt] OR controlle	ection" AND "fraction") OR (" R "multi-center" OR "multice aceutical Preparations"[Mesh medication" OR "medications nt" OR "treatments" OR "inte ed clinical trial[pt] OR randon	ventricular" AND "dysfunction") entre" OR "multi-centre") AND ( 1] OR "drug therapy" OR "thera s" OR (("drug" OR "pharmacolo ervention" OR "interventions" OI nized[tiab] OR placebo[tiab] OF	)) NOT ("Multicenter Study" [Publication Drug Therapy"[Mesh] OR "drug therap beutic use" OR "pharmacotherapy" OR gic" OR "pharmacological" OR "prescrip R "drug" OR "drugs" OR "preparation" O clinical trials as topic[mesh:noexp] OR	n Type] OR "Multicenter y" [Subheading] OR "pharmacotherapies" OF otion" OR "pharmaceutic DR "preparations"))) AND
21) Exercise trial matching search: ID 942 ((((("transposition of great arteries" OR "Ventricular Dysfunction, Right"[Mesh] OR "Right Ventricular Dysfunction" OR "Right Ventricular Dysfunctions" OR ("Right" AN Ventricular" AND ("systemic" OR "Dysfunction")) OR "systemic right ventricle" OR (("systemic" or dysfunction*) AND ("right ventricle" OR "right ventricles" OR "heart ventricles"[MeSH Terms] OR "heart ventricles" OR "heart ventricle")))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR 'multicenter" OR "multi-center" OR "multi-center") AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR	Results: 33	records - https://www.ncbi.nlm.	.nih.gov/sites/myncbi/1TwR_	tlOrYmkO/collections/5713877	4/public/	
((((("transposition of great arteries" OR "Ventricular Dysfunction, Right"[Mesh] OR "Right Ventricular Dysfunction" OR "Right Ventricular Dysfunctions" OR ("Right" AN Ventricular" AND ("systemic" OR "Dysfunction")) OR "systemic right ventricle" OR (("systemic" or dysfunction*) AND ("right ventricle" OR "right ventricles" OR "heart rentricles"[MeSH Terms] OR "heart ventricles" OR "heart ventricle")))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR 'multicenter" OR "multi-center" OR "multicentre")) AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR	Pharma trial	i match: Found in original searc	ch – Frustaci et al. (2009)			
Ventricular" AND ("systemic" OR "Dysfunction")) OR "systemic right ventricle" OR (("systemic" or dysfunction*) AND ("right ventricle" OR "right ventricles" OR "heart ventricles"[MeSH Terms] OR "heart ventricles" OR "heart ventricle")))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR 'multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR	21) Exercise	e trial matching search: ID 942	2			
	"Ventricular" ventricles"[M "multicenter" OR "Pharma	AND ("systemic" OR "Dysfuncti leSH Terms] OR "heart ventricle OR "multi-center" OR "multicer ceutical Preparations"[Mesh] O	ion")) OR "systemic right ver es" OR "heart ventricle"))))) / ntre" OR "multi-centre")) ANI IR "drug therapy" OR "therap	tricle" OR (("systemic" or dysfu AND ("Multicenter Study" [Publi D (("Drug Therapy"[Mesh] OR " eutic use" OR "pharmacothera	nction*) AND ("right ventricle" OR "right cation Type] OR "Multicenter Studies a drug therapy" [Subheading] OR "therap by" OR "pharmacotherapies" OR "chem	t ventricles" OR "heart s Topic"[Mesh] OR eutic use" [Subheading otherapy" OR

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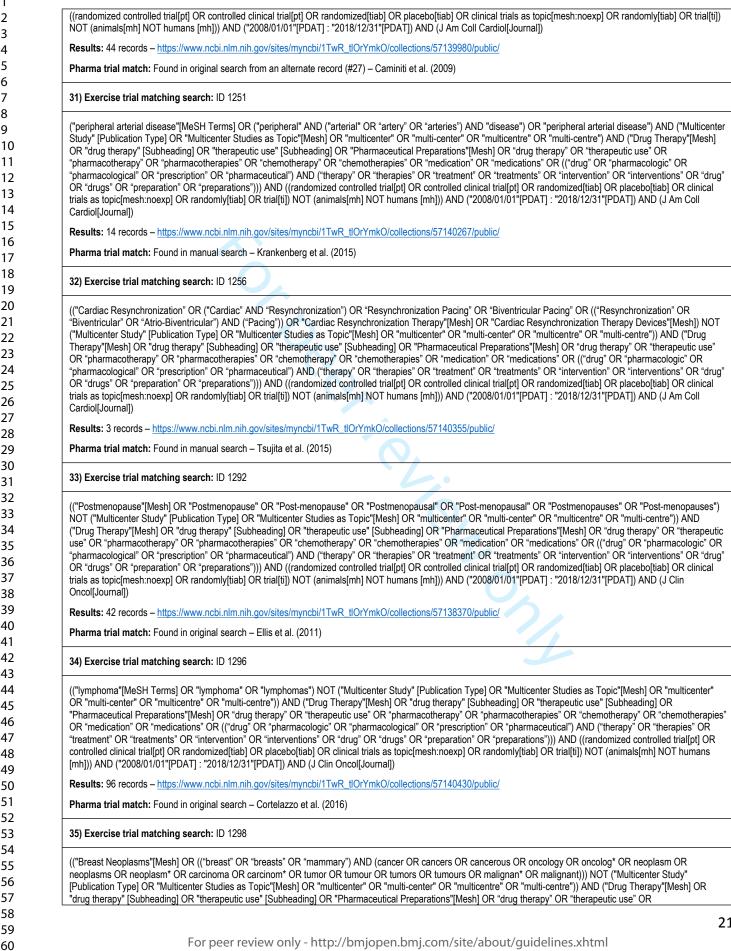
Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches



Pharma trial n	ecords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57351095/public/
	natch: Found in revised search – Ratziu et al. (2008)
26) Exercise t	rial matching search: ID 1183
cardiomyopath center" OR "m Preparations"[I "medication" O "treatment" OF controlled clinic	athy, dilated"[MeSH Terms] OR (("cardiomyopathy" OR "cardiomyopathies") AND ("dilated" OR "familial idiopathic" OR "Congestive")) OR "dilated y" OR "dilated cardiomyopathies") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "m ulticentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceut Wesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapies" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" or "therapies" OR treatments" OR (intervention" OR "interventions" OR "drug" OR "drugs" OR "prescription" OR "peparations"))) AND ((randomized controlled tria cal trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT hu 008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
Results: 2 rec	ords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140665/public/
Pharma trial r	natch: Found in original search from an alternate record (#18) – Hamshere et al. (2015)
27) Exercise t	rial matching search: ID 1184
ÖR (("heart" O OR "multi-cent "Pharmaceutic OR "medicatio "treatment" OF controlled clinic	[MeSH Terms] OR "heart failure" OR ("chronic" AND "heart" AND "failure") OR "chronic heart failure" OR "Cardiac Failure" OR "Heart Decomper R "cardiac") AND ("failure" OR "decompensation"))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "m er" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR al Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapy" OR "therapeutic use" or "multi-centre") AND ("Therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapy" OR "therapeutic use" or "pharmacological" OR "pharmacotherapies" OR "pharmaceutical") AND ("therapy" OR "therapeutic "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled tria cal trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT hu 008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
Results: 117 r	ecords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57138880/public/
Pharma trial r	natch: Found in manual search – Goebel et al. (2017)
28) Exercise t	rial matching search: ID 1198
OR "Ventricula Studies as Top "therapeutic us "chemotherapy AND ("therapy ((randomized of NOT (animals]	"[MeSH Terms] OR "heart failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND ("ejectior r Dysfunction"[Mesh] OR ("ejection" AND "fraction") OR ("ventricular" AND "dysfunction"))) NOT ("Multicenter Study" [Publication Type] OR "Multi bic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-center")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] be" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapy" "OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "preparation" OR "pharmacotherap" "OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug or "drugs" OR "preparation" OR "preparations"] controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] O mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal]) cords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57139980/public/
	natch: Found in original search – Kosmala et al. (2013)
29) Exercise t	rial matching search: ID 1218
Dysfunction"[M Topic"[Mesh] ( [Subheading] ( "chemotherapi "therapies" OR controlled trial[	"Diabetes Mellitus, Type 2"[Mesh] OR "NIDDM" OR "type 2 diabetes mellitus" OR "diabetes mellitus type 2" OR "diabetes") AND ("Ventricular lesh] OR "diastolic dysfunction" OR ("diastolic" AND "dysfunction") OR "diastolic")) NOT ("Multicenter Study" [Publication Type] OR "Multicenter S DR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therap DR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemoth es" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("the "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomize pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT IOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
(animals[mh] N	ord – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57139674/public/
	natch: Found in original search from an alternate record (#27) – Han et al. (2014)
Results: 1 rec	
Results: 1 rec Pharma trial r	rial matching search: ID 1232

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#### Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

"pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "drugs" OR "preparation" OR "pharmacological" OR "pharmacological" OR "therapy" OR "therapy" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal])

Results: 242 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57139370/public/

Pharma trial match: Found in revised search – Greenspan et al. (2008)

#### 36) Exercise trial matching search: ID 1299

("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "chemotherapy" OR "medication" OR "medications" OR ("drug therapy" OR "therapeutic use" OR "therapeutic or C "medication" OR "medications" OR ("drug "OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapes" OR "therapes"

Results: 179 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57140047/public/

Pharma trial match: Found in original search – Urruticoechea et al. (2017)

37) Exercise trial matching search: ID 1301

("Postmenopause" [Mesh] OR "Postmenopause" OR "Post-menopause" OR "Postmenopausal" OR "Post-menopausal" OR "Postmenopause" OR "Post-menopauses" OR "Post-menopauses" OR "Post-menopauses" AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "mul

Results: 49 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138311/public/

Pharma trial match: Found in original search from an alternate record (#35) - Johnston et al. (2018)

38) Exercise trial matching search: ID 1303

("Prostatic Neoplasms"[Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacological" OR "medications" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "preparation" OR "herapeuticause" OR "therapeuticause" OR "therapise" OR "therapise" OR "therapeuticause" OR "therapeuticause" OR "therapeuticause" OR "therapeuticause" OR "therapeuticause" OR "therapise" OR "therapise" OR "therapeuticause" OR "therapeuticause" OR "therapeuticause" OR "therapise" OR "ther

Results: 85 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138499/public/

Pharma trial match: Found in original search – Taplin et al. (2014)

#### 39) Exercise trial matching search: ID 1310

(("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasms OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicentre" OR "multicentre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapies" OR "chemotherapies" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacotherapies" OR "chemotherapy" OR "therapeis" OR "therapeutic use" (OR "pharmacological" OR "preparation" OR "pharmacotherapies" OR "therapy" OR "therapy" OR "therapeits" OR "therapeutic use" OR "pharmacotherapies" OR "pharmacotherapies" OR "therapeutic use" (Subheading) OR "therapy" OR "therapeis" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacotherapies" OR "therapeutic use" OR "therapeits" OR "therapy" OR "therapies" OR "therapeits" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "pharmacotherapies" OR "therapies" OR "therapies" OR "treatment" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"]))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:neoxp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]))

Results: 242 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57139370/public/

Pharma trial match: Found in original search – Yardley et al. (2013)

40) Exercise trial matching search: ID 1314

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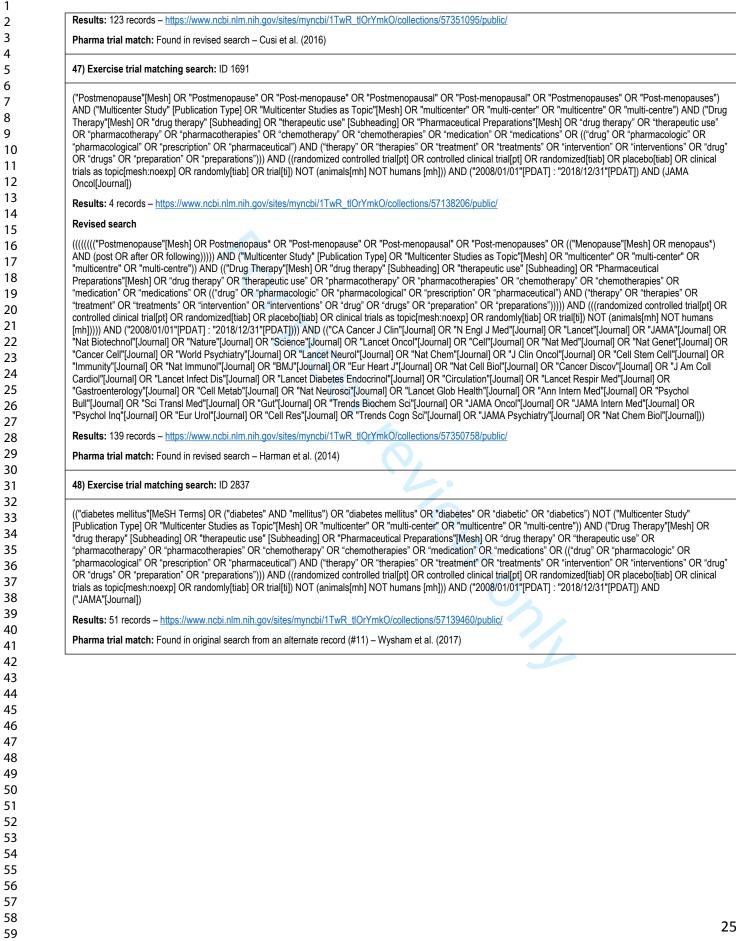
#### **BMJ** Open

Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

(("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) Results: 242 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57139370/public/ 10 11 Pharma trial match: Found in original search - Schmid et al. (2016) 12 41) Exercise trial matching search: ID 1320 13 14 (("Postmenopause"[Mesh] OR "Postmenopause" OR "Post-menopause" OR "Postmenopausal" OR "Post-menopausal" OR "Postmenopauses" OR "Post-menopauses") 15 NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND 16 ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR 17 "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 18 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical 19 trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tij] NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin 20 Oncol[Journal]) 21 Results: 42 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tIOrYmkO/collections/57138370/public/ 22 Pharma trial match: Found in original search - Loprinzi et al. (2010) 23 24 42) Exercise trial matching search: ID 1328 25 26 ("Prostatic Neoplasms"[Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR 27 "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy" [Mesh] OR "drug therapy" 28 [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR 29 "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR 30 "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as 31 topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) 32 Results: 85 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tIOrYmkO/collections/57138499/public/ 33 Pharma trial match: Found in original search from an alternate record (#38) - McKay et al. (2016) 34 35 43) Exercise trial matching search: ID 1332 36 37 (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR 38 tumors OR tumours OR malignan\* OR malignant OR "hematooncological" OR "hemato oncological" OR "hemato-oncological" OR hematologic neoplasms OR hematolo\*) 39 AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multicenter" OR "multicentre" OR "multicentre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" 40 OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR 41 "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 42 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical 43 trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) 44 45 Results: 853 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57140190/public/ 46 Pharma trial match: Found in original search - Soiffer et al. (2017) 47 48 44) Exercise trial matching search: ID 1385 49 (("peripheral arterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") NOT 50 ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug 51 Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" 52 OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 53 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placeboltiab] OR clinical 54 trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND 55 ("JAMA"[Journal]) 56 Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138957/public/ 57 58 59

Pharma trial mate	h: Found in manual search – Ahmed et al. (2008)
45) Exercise trial	natching search: ID 1599
,	•
Study" [Publication OR "drug therapy" "pharmacotherapy" "pharmacological" OR "drugs" OR "pr	e"[Mesh] OR "Alzheimer Disease" OR "Alzheimer's Disease" OR ("alzheimer's" AND "disease") OR ("alzheimer" AND "disease")) AND ("Mu Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-center") AND ("Drug Therap [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OI OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" exparation" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OF :noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAM/
Results: 0 records	
NOTE: Since this s	tring let to zero results, changed journal title limit to JAMA:
("Multicenter Study Therapy"[Mesh] O OR "pharmacother "pharmacological" OR "drugs" OR "pr	zheimer Disease"[Mesh] OR "Alzheimer Disease" OR "Alzheimer's Disease" OR ("alzheimer's" AND "disease") OR ("alzheimer" AND "disea " [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center" OR "therape apy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic DR "prescription" OR "pharmacoutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" aparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OF moexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAM/
Results: 10 record	s – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140943/public/
Pharma trial mate	h: Found in original search – Cummings et al. (2015)
46) Exercise trial	natching search: ID 1610
"pharmacological" OR "drugs" OR "pr	otherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmaco DR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" eparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OF incexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAM/
Result: 1 record -	https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140841/public/
NOTE: Also tried of	hanging the journal title to JAMAsee below:
(("non-alcoholic" C NOT ("Multicenter ("Drug Therapy"[M use" OR "pharmac "pharmacological" OR "drugs" OR "pr	ty liver disease"[MeSH Terms] OR "Fatty Liver"[Mesh] OR "fatty liver" OR ("fatty" AND "liver") OR "steatosis" OR "steatoses" OR "Steatohep, R "nonalcoholic") AND "fatty" AND "liver" AND "disease") OR "non-alcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver dis Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multicenter OR "multi-center") // esh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "medication" OR "medications" OR ("drug therapy" OR "pharmaceutical Preparations"] // otherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmaceutical") CR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" eparation" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OF cnoexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAM/
Result: 2 records	- https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140782/public/
Revised search:	
OR (("non-alcoholi OR "non-alcoholic (("Multicenter Stud Therapy"[Mesh] O/ OR "pharmacother "pharmacological" OR "drugs" OR "pr trials as topic[mesl J Clin"[Journal] OF "Lancet Oncol"[Jou Neurol"[Journal] O OR "Eur Heart J"[J Endocrinol"[Journa	ic fatty liver disease"[MeSH Terms] OR "Fatty Liver"[Mesh] OR "fatty liver" OR ("fatty" AND "liver") OR "steatosis" OR "steatoses" OR "Steatoses" OR "Steatoses" OR "non-alcoholic") AND "fatty" AND "liver" AND "disease") OR "non-alcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver steatohepatitis" OR "nonalcoholic steatohepatitis" OR "NASH" OR ((fatty AND (liver* OR hepat*)) OR steatohepat* OR NAFL* OR NASH*))) wight of the steatohepatitis or "NaSH" OR ((fatty AND (liver* OR hepat*)) OR steatohepat* OR NAFL* OR NASH*))) wight of the steatohepatitis or "non-alcoholic fatty liver" OR "multicenter" OR "featoward" OR "featoward" OR "featoward" OR "

#### Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches



Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

# Data Extraction Reference Guide – Exercise RCTs



Memorial Sloan Kettering Cancer Center

# BMJ Open

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

# EXTRACTION ABBREVIATIONS

- %: percent
- 1-RM: 1 repetition maximum (strength test)
- AET: Aerobic exercise training
- BL: baseline
- BMI: body mass index
- bpm: heart beats per minute
- d: days
- EX: exercise
- FU: follow-up
- HR: heart rate
- HRR: heart rate reserve
- hr/hrs: hour/hours
- Man: manuscript
- MAX: maximum
- MIN: minimum
- mins: minutes
- mo: months
- PA: physical activity
- Reg: registry
- RET: Resistance exercise training
- RPE: rate of perceived exertion (self-reported exercise intensity)
- sec: seconds
- UC: usual care/control
- VO<sub>2peak</sub>: peak aerobic exercise capacity
- wk/wks: week/weeks
- yrs: years

# **GENERAL NOMENCLATURE & EXTRACTION GUIDELINES**

# Nomenclature Guidelines

- Ranges:
  - $\circ$  Use 'to' and not '-' (e.g., 150 bpm to 175 bpm)
- Units:
  - o List all units of measure including percentages
- Significant figures:
  - o Raw values / averages T round to the nearest 0.1
  - Percentages T round to the nearest whole number
- Averages:
  - Mean value is preferred and assumed
  - o Only list median values if mean are not reported
    - If listing median values, please label appropriately
- Lists:
  - o Be succinct T only include pertinent details and use bullet form with semicolon separated values

- o List details in the same order as it is presented in the manuscript
- Examples:
  - Inclusion/exclusion criteria: e.g., 40 to 65 yrs; BMI<40; sedentary</li>
  - Primary/secondary outcomes: e.g., resting HR; body weight; PA mins/wk

# **Extraction Guidelines**

- Multiple intervention arms
  - Base group numbering on layout of flow diagram (e.g., AET 1 = left-most group; AET 2 = group immediately to the right, etc.)
  - In the case of discrepancies between data sources:
    - Prioritize the data provided in the primary manuscript.
    - Report both sets of numbers (e.g., Man: ##; Reg: ##)

# ARTICLE INCLUSION/EXCLUSION

- Should this article be included in our systematic review?
  - Yes T Does not meet any exclusion criteria.
  - No T Meets one or more exclusion criteria.

# DATA SOURCES

# • Data Sources:

- Please list all sources of information included in this extraction.
- Options:
  - Primary manuscript
  - Online supplement
  - Protocol paper
  - Clinical trial registry
  - Clinical trial protocol
  - Other
- If Other, please list.

# PUBLICATION INFORMATION

- Country of publication?
  - Please provide the <u>full name</u> of the country where the study was conducted/where the primary author is based

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

٠	CONSORT (1a) – Identification as a randomized trial in the title.
	• Options:
	<ul> <li>Yes T Either randomized controlled trial; randomized trial; randomized</li> <li>No T Not mentioned</li> </ul>
٠	CONSORT (1b) – Structured summary of trial design, methods, results, and conclusions. o Options:
	<ul> <li>Options:</li> <li>Yes T Introduction/Background + Methods + Results + Discussion/Conclusion</li> <li>No T Not properly structured</li> </ul>
•	CONSORT (2a) – Scientific background and explanation of rationale.
	<ul> <li>Yes T Reviews relevant literature AND identifies a knowledge gap/question</li> <li>No T Did not adequately review the literature and/or identify the knowledge gap/question study attempted to address</li> </ul>
•	CONSORT (2b) – Specific objectives or hypothesis. o Options:
	<ul> <li>Yes (objectives) T Must provide a specific purpose/objective for study in the context of the intervention AND the specific outcomes of interest OR</li> </ul>
	<ul> <li>Yes (hypothesis) T Must provide a specific hypothesis in the context of a group-related change a specific outcome of interest AND the expected direction of change</li> <li>Unclear T Provided the specific purpose/objective or hypothesis but only 1 of 2 additional required components</li> <li>No T Failed to provide either (1) the specific purpose/objective OR hypothesis, and/or (2) additional required components</li> <li>TIP:</li> </ul>
	<ul> <li>This information is typically reported within final paragraph of the introduction or early in the methods section.</li> </ul>
METH	ODS
•	CONSORT (3ai) – Description of trial design (such as parallel, factorial) including allocation ratio.
	<ul> <li>Options:</li> <li>Yes T Must provide both a description of overall study design (e.g., parallel arm, crossove allocation ratio</li> </ul>
	<ul> <li>Unclear T Description of study design is provided but NOT allocation ratio</li> <li>No T If missing the study design (even if allocation ratio is provided)</li> <li>• EXAMPLES:</li> </ul>
	<ul> <li>Parallel trials, cross-over trials, factorial trials AND 1:1, 1:2, 1:1:1</li> </ul>
•	CONSORT (4b) – Settings and locations where the data were collected. o Options:
	<ul> <li>Options.</li> <li>Yes T Provided details of where the data were collected for the trial</li> </ul>

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

- This includes single-location trials when the authors clearly state the entire trial took place
   onsite
- Unclear T Specifies that data was collected in a lab/testing room but does not provide the actual location of said room (e.g., at a hospital or university)
- **No** T Details not provided

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• TIP:
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This does NOT include where the recruitment or intervention took place.

#### • DETAILS – Population:

- List the population being studied
- **NR** T If not reported

#### DETAILS – Disease setting:

- Identify the disease phase [Prevention (P) vs. Management (M)] during which the exercise intervention took place.
- o NR T If not reported
- o NA T If the intervention was not conducted in the context of a disease

# • CONSORT (3aii) – When applicable, how care providers were allocated to each trial group.

• Options:

- NA T Only one interventionist involved with study no allocation strategy required.
- Yes T Must describe how the interventionists were assigned to supervise intervention arms
  - This applies to all components of the intervention (e.g., AET, RET, counseling)
  - Yes T Authors clearly state that no allocation strategy was used
- No T Fails to report any details
- o **TIP:** 
  - These details are seldom reported in exercise-based RCTs.
- CONSORT (3b) Important changes to methods after trial commencement (such as eligibility criteria), with reasons.
  - Options:
    - NA T The methods did not change
      - Yes T Methods changed and reasons were provided
        - Examples include (but are not limited to): study design, sample size % ± 10%), eligibility criteria, recruitment strategy, randomization, blinding, data analysis, etc.
    - Unclear T It appears that methods may have changed but there is not enough information to make assessment
    - No T Methods changed but no reasons were provided
  - TIPS:
    - This includes under/over recruitment according to the a priori-defined sample size without adequate justification.
    - Does NOT include changes to the intervention T that data is captured in the TIDieR inventory
    - Does *NOT* include changes in trial outcomes T that data is captured in a separate CONSORT item

# Eligibility Criteria

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Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

•	CONSORT (4ai) – Eligibility criteria for participants.
	<ul> <li>Options:</li> </ul>
	<ul> <li>Yes T Provided details/criteria for BOTH inclusion AND exclusion of participants</li> </ul>
	<ul> <li>Unclear T Only provides details of inclusion OR exclusion but NOT both</li> </ul>
	<ul> <li>No T Details not provided</li> </ul>
	CONCORT (Asii) When employed a cligibility exiteria for contern and for core providers
•	CONSORT (4aii) – When applicable, eligibility criteria for centers and for care providers. o Options:
	<ul> <li>Options:</li> <li>Yes (multicenter trials) T Provided criteria for eligible centers AND interventionists</li> </ul>
	<ul> <li>Unclear (<i>multicenter trials</i>) T Provided criteria for interventionists but <i>NOT</i> centers or vice versa</li> </ul>
	<ul> <li>Yes (single center trials) T Provided criteria for interventionists</li> </ul>
	<ul> <li>Yes T Authors clearly state there were no eligibility criteria for centers and/or care providers</li> </ul>
	<ul> <li>Unclear (multi and single center trials) T Stated professional background and/or study-specific</li> </ul>
	training for interventionists but did not describe them as requirements
	<ul> <li>No T Eligibility criteria not specifically stated</li> </ul>
	• TIPS:
	<ul> <li>Eligibility criteria for centers is applicable for all multi-center trials.</li> </ul>
	<ul> <li>Eligibility criteria for care providers is applicable for all trials.</li> </ul>
	<ul> <li>This is seldom reported.</li> </ul>
Data	Comparison: Eligibility Criteria
<u>Data</u>	Comparison: Eligibility Criteria
<u>Data</u>	Comparison: Eligibility Criteria Was there a difference in Eligibility Criteria between the Registry and the Manuscript?
<u>Data</u>	Was there a difference in Eligibility Criteria between the Registry and the Manuscript?
<u>Data</u>	<ul> <li>Was there a difference in Eligibility Criteria between the Registry and the Manuscript?</li> <li>Options:         <ul> <li>Yes T One or more differences between the two data sources.</li> </ul> </li> </ul>
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<u>Data</u> •	<ul> <li>Was there a difference in Eligibility Criteria between the Registry and the Manuscript?</li> <li>Options: <ul> <li>Yes T One or more differences between the two data sources.</li> <li>No T No difference between the two data sources.</li> <li>Unclear T Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable T No clinical trial registry data available.</li> </ul> </li> <li>Was the change noted in the Manuscript? <ul> <li>Options:</li> </ul> </li> </ul>
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<u>Data</u> • •	<ul> <li>Was there a difference in Eligibility Criteria between the Registry and the Manuscript? <ul> <li>Options:</li> <li>Yes T One or more differences between the two data sources.</li> <li>No T No difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable T No clinical trial registry data available.</li> </ul> </li> <li>Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes T The change in eligibility criteria was clearly stated and explained.</li> <li>Not Applicable T hore was no difference in the eligibility criteria between the Registry and the Manuscript.</li> <li>Not Applicable T No clinical trial registry data available.</li> </ul> </li> <li>Most the change in eligibility criteria was clearly stated and explained.</li> <li>Not Applicable T There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> <li>Not Applicable T No clinical trial registry data available.</li> </ul> <li>Mot Applicable T No clinical trial registry data available.</li> <li>Mot Applicable T No clinical trial registry data available.</li> <li>Mot Applicable T No clinical trial registry data available.</li> <li>Mot Applicable T No clinical trial registry data available.</li>
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- o Please record the total number of individual Inclusion Criteria listed in the Manuscript.
- DC DETAILS Please list the Inclusion Criteria reported in the Manuscript.
  - Please record each individual Inclusion Criteria listed in the Manuscript.
- How many Exclusion Criteria were listed in the Registry?
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- DC DETAILS Please list the Exclusion Criteria reported in the Registry.
  - Please record each individual Exclusion Criteria listed in the Registry.
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- DC DETAILS Please list the Exclusion Criteria reported in the Manuscript.
  - $\circ$   $\;$  Please record each individual Exclusion Criteria listed in the Manuscript.

### **Outcome Measures**

- CONSORT (6a) Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.
  - Options:
    - Yes T Clearly defined a single primary outcome (*co-primary outcomes at max*), all relevant secondary outcomes *AND* provide all requisite details of the timing *AND* procedures used to assess these outcomes
    - Unclear T Primary and secondary outcomes defined but the descriptions of the timing and procedures used to assess the outcomes were lacking details required to reproduce the measurements
    - No T If no primary or secondary outcomes are clearly defined OR if the assessment details (e.g., how & when) were missing altogether
  - o **TIPS**:
    - Some studies may identify multiple primary outcomes. Although this type of study design is inappropriate in the context of medical oncology research, we are evaluating the quality of reporting and not the quality of the study design. Therefore, a 'Yes' can be assigned provided the authors clearly identify which outcomes are considered primary and secondary.
- CONSORT (6b) Any changes to trial outcomes after the trial commenced, with reasons.
  - Options:
    - NA T No observable changes to trial outcomes were made
    - Yes T Describes changes in outcomes according to all pertinent features (e.g., what, why & when)
    - Unclear T Describes changes according to all but one pertinent feature
    - No T If the description is missing or unclear on two or more pertinent features

Data	Comparison: Primary Outcome
•	Was there a difference in the Primary Outcome(s) between the Registry and the Manuscript?
	• Options:
	<ul> <li>Yes T Z; difference between the two data sources.</li> </ul>
	<ul> <li>No T No difference between the two data sources.</li> </ul>
	<ul> <li>Unclear T Possible difference between the two data sources, but insufficient information to make</li> </ul>
	a determination.
	<ul> <li>NR T No clinical trial registry data available.</li> </ul>
٠	Was the change in Primary Outcome noted in the Manuscript?
	• Options:
	<ul> <li>Yes T The change in Primary Outcome was clearly stated and explained.</li> </ul>
	<ul> <li>No T The change in Primary Outcome was apparent but not explained.</li> </ul>
	<ul> <li>NR T No clinical trial registry data available.</li> <li>NA T No difference (i.e., Q1 = No)</li> </ul>
	- <b>NA</b> T NO difference (i.e., $QT = NO$ )
٠	Was a new Primary Outcome reported in the Manuscript which was not reported in the Registry?
	• Options:
	<ul> <li>Yes T Z; Primary Outcome reported in the Manuscript that was not listed in the Registry.</li> </ul>
	<ul> <li>No T No new Primary Outcome added to the Manuscript.</li> </ul>
	<ul> <li>Unclear T Possible difference between the two data sources, but insufficient information to make a determination.</li> </ul>
	<ul> <li>NR T No clinical trial registry data available.</li> </ul>
•	DC DETAILS – If Yes/Unclear, please provide the details?
	<ul> <li>Please list all pertinent details.</li> </ul>
•	Was the Primary Outcome reported in the Registry reported as a Secondary Outcome in the Manuscript?
	• Options:
	<ul> <li>Yes T Z; Primary Outcome reported in the Registry listed as a Secondary Outcome in the</li> </ul>
	Manuscript.
	<ul> <li>No T No Primary Outcome from the Registry listed as a Secondary Outcome in the Manuscript.</li> </ul>
	<ul> <li>Unclear T Possible difference between the two data sources, but insufficient information to make a determination.</li> </ul>
	<ul> <li>NR T No clinical trial registry data available.</li> </ul>
•	DC DETAILS – If Yes/Unclear, please provide the details?
	<ul> <li>Please list all pertinent details.</li> </ul>
•	Was the Primary Outcome reported in the Registry omitted from the Manuscript?
	• Options:
	<ul> <li>Yes T The Primary Outcomes reported in the Registry was omitted from the Manuscript.</li> </ul>
	<ul> <li>No T The Primary Outcome reported in the Registry was included in the Manuscript.</li> </ul>
	<ul> <li>Unclear T Possible difference between the two data sources, but insufficient information to make a determination.</li> </ul>
	33
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- NR T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.

### Data Comparison: Secondary Outcomes

- Were <u>different</u> (new) Secondary Outcomes reported in the Manuscript which were not reported in the Registry?
  - Options:
    - Yes T Z; Secondary Outcomes reported in the Manuscript were not reported in the Registry.
    - No T The Secondary Outcomes reported in the Manuscript were consistent with the Registry.
    - Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
    - NR T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- If different (new) Secondary Outcomes were added to the Manuscript, were the reasons noted in the Manuscript?
  - Options:
    - Yes T The change(s) in Secondary Outcomes were clearly stated and explained
    - No T The changes in Secondary Outcomes were apparent but not explained
    - NR T No clinical trial registry data available
    - NA T No difference in Secondary Outcomes (i.e., Q6 = No)
- Was one or more of the Secondary Outcomes reported in the Registry reported as Primary Outcomes in the Manuscript?
  - $\circ$  Options:
    - Yes T A Secondary Outcome reported in the Registry was reported as a Primary Outcome in the Manuscript.
    - No T None of the Secondary Outcomes reported in the Registry were reported as Primary Outcomes in the Manuscript.
    - Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
    - NR T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.

### **Randomization & Blinding**

- CONSORT (8a) Method used to generate the random allocation sequence.
  - Options:

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

1		
2 3		• Vee T. Clearly stated the apositie presses used to generate the rendemization (e.g., e.g.) fin
4		<ul> <li>Yes T Clearly stated the specific process used to generate the randomization (e.g., a coin flip, computer generated)</li> </ul>
5		<ul> <li>No T Not provided</li> </ul>
6 7		
7 8	٠	CONSORT (8b) – Type of randomization; details of any restriction (such as blocking and block size).
9		<ul> <li>Options:</li> </ul>
10		<ul> <li>Yes T Provided the details of how the randomization accounted for key confounding variables</li> </ul>
11		<ul><li>(e.g., blocking, minimization, stratification)</li><li>No T Not provided</li></ul>
12 13		
14	•	CONSORT (9) – Mechanism used to implement the random allocation sequence (such as sequentially
15		numbered containers), describing any steps taken to conceal the sequence until interventions were
16		assigned.
17 19		• Options:
18 19		<ul> <li>Yes T Provided details of how the physical randomization was performed or how the participants</li> </ul>
20		were notified of their allocation (e.g., phone call, sealed envelopes, centralized allocation)
21		<ul> <li>No T Not provided</li> </ul>
22	•	CONSORT (10) – Who generated the random allocation sequence, who enrolled participants, and who
23 24	·	assigned participants to interventions.
24		• Options:
26		<ul> <li>Yes T Must include a clear description of who performed ALL of these tasks</li> </ul>
27		<ul> <li>Unclear T If description of one of these tasks is inadequate or missing</li> </ul>
28		<ul> <li>No T If two or more of these tasks are poorly described or not described at all</li> </ul>
29 30		<ul> <li>TIP:</li> <li>An exception can be made for participant assignment criteria for studies using centralized</li> </ul>
31		allocation.
32		
33	•	CONSORT (11a) – If done, who was blinded after assignment to interventions (for example, participants, care
34 35		providers, those assessing outcomes) and how.
35 36		• Options:
37		<ul> <li>Yes T Details regarding testers AND data analyzers are provided</li> </ul>
38		<ul> <li>Unclear T If any of the aforementioned details are provided but poorly described</li> <li>No T If any of the aforementioned details are missing</li> </ul>
39		<ul> <li>No T If any of the aforementioned details are missing</li> <li>TIP:</li> </ul>
40 41		<ul> <li>Remember, we are assessing if the reporting is complete NOT how good the methods are.</li> </ul>
41		Therefore, if authors state that the testers and data analyzers were not blinded, we would consider
43		this good reporting and assign a 'Yes' for this category.
44		
45	٠	CONSORT (11c) – If blinding not possible, description of attempts to limit bias.
46 47		• Options:
47 48		<ul> <li>NA T If testers AND data analyzers were blinded</li> <li>Xee T Clearly stated that a specific strategy (a.g., physical or statistical) was employed to help</li> </ul>
49		<ul> <li>Yes T Clearly stated that a specific strategy (e.g., physical or statistical) was employed to help reduce the potential confounding influence of unblinded investigators</li> </ul>
50		• Example strategies: Identified strategy following standardized procedures' <b>AND</b> provided
51		requisite details
52 53		<ul> <li>Yes T Authors stated that no strategy was used limit bias related to lack of blinding</li> </ul>
53 54		<ul> <li>Unclear T If strategies were identified OR described for ALL unblinded personnel but not</li> </ul>
55		identified <b>AND</b> described
56		<ul> <li>No T If not clearly stated either in the methods, results or discussion</li> </ul>
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58 59		35
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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Simply listing lack of blinding in the limitations does not count TIP: 0 Remember, we are evaluating these studies according to the quality of their reporting and not their methods. We are looking for transparency in methods. As such, it does not matter, per se, if investigators were not blinded - rather, it matters how they report it and how well they report the strategies used to compensate for it. CONSORT (11b) – If relevant, description of the similarity of interventions. **Options:** 0 **NA** T If it is a 2-arm trial with a non-exercise control group comparison **OR** a 3+ -arm trial with obviously different intervention groups (e.g., AET v RET v UC) Yes T If details are adequately provided for two or more intervention arms with similar modalities of exercise No T If details are not adequately provided for two or more intervention arms with similar modalities of exercise TIP: 0 NA is not an option for superiority trials (i.e., exercise trials with only two similar intervention arms) Intervention Details TIDieR (1) – Provide the name or a phrase that describes the intervention. • Options: **Yes** T Provided a phrase to describe the intervention No T A clear summary phrase describing the intervention was not provided TIDieR (2) – Describe any rationale, theory, or goal of the elements essential to the intervention. • **Options:** Yes T Provides any rationale, theory **OR** goal of the elements essential to the intervention **No** T Did not provide at least one of the above **INTERVENTION TYPE – Exercise or Pharmaceutical** 0 **Options:** Exercise T Stated methods included delivery of a structured exercise program with a stated goal • of improving a health/fitness/psychosocial outcome. Pharmaceutical T Stated methods included delivery of a pharmaceutical intervention with a stated goal of improving health. TIDieR (4) – Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities. **Options:** 0 Yes T Provides complete details for each of the major intervention procedures, activities, and processes, including enabling or supporting activities Unclear (multi-component interventions) T If a single component of the intervention is identified but not adequately described (e.g., the aerobic exercise component is well described but the behavioral support component is not) No T If the primary component or more than one secondary component of the intervention is (are) not adequately described 36

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Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

3		
4		CONCORT (5ii) Descise details of both the ownering and the stream and some proton
5	•	CONSORT (5ii) – Precise details of both the experimental treatment and comparator.
6		• Options:
7		<ul> <li>Yes T Clear descriptions of the intervention arm(s) and control group</li> </ul>
8		<ul> <li>No T Control group conditions/requirements not defined</li> </ul>
9		
10	•	TIDieR (8d) – Describes length of the intervention period.
11		• Options:
12		<ul> <li>Yes T Must define the period over which the intervention was delivered according to a specific</li> </ul>
13		number of weeks/months or life period
14		<ul> <li>No T Not clearly defined (e.g., stated during chemotherapy without providing the average number</li> </ul>
15		
16		of weeks/months)
10 17		
	٠	DETAILS – What was the total length of the program/intervention (weeks)?
18		<ul> <li>Note the total duration of the intervention in weeks</li> </ul>
19		<ul> <li>NR T If not reported</li> </ul>
20		o TIP:
21		<ul> <li>Actual intervention length preferred (if provided); proposed intervention length if actual is not</li> </ul>
22		reported
23		
24		
25	•	DETAILS – How many phases did the intervention have?
26		<ul> <li>Note the total number of intervention phases</li> </ul>
27		• TIP:
28		<ul> <li>Lead-in period considered part of the intervention but not necessarily a separate phase</li> </ul>
29		
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34	PHAS	E I/II – DETAILS
35		
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50	•	
30 37	•	How many weeks was this phase?
	•	How many weeks was this phase? • Note number of weeks
37	•	How many weeks was this phase?
37 38 39	•	How many weeks was this phase? <ul> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul>
37 38 39 40	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary
37 38 39 40 41	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.
37 38 39 40 41 42	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> </ul>
37 38 39 40 41 42 43	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.
37 38 39 40 41 42 43 44	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> </ul>
37 38	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> </ul>
37 38 39 40 41 42 43 44 45	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> </ul>
37 38 39 40 41 42 43 44 45 46 47	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> </ul>
<ol> <li>37</li> <li>38</li> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>43</li> <li>44</li> <li>45</li> <li>46</li> <li>47</li> <li>48</li> </ol>	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul>
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37 38 39 40 41 42 43 44 45 46 47 48 49 50	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> <li>TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.</li> <li>Options: <ul> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by</li> </ul> </li> </ul>
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options: <ul> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> </ul> </li> </ul>
37 38 39 40 41 42 43 44 45 46	•	<ul> <li>How many weeks was this phase? <ul> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> </li> <li>TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists</li> </ul> </li> </ul>
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options: <ul> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> </ul> </li> </ul>
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> <li>TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.</li> <li>Options: <ul> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists (e.g., medical center or university).</li> </ul> </li> </ul>
<ol> <li>37</li> <li>38</li> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>43</li> <li>44</li> <li>45</li> <li>46</li> <li>47</li> <li>48</li> <li>49</li> <li>50</li> <li>51</li> <li>52</li> <li>53</li> <li>54</li> <li>55</li> </ol>	•	<ul> <li>How many weeks was this phase? <ul> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> </li> <li>TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists</li> </ul> </li> </ul>
<ol> <li>37</li> <li>38</li> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>43</li> <li>44</li> <li>45</li> <li>46</li> <li>47</li> <li>48</li> <li>49</li> <li>50</li> <li>51</li> <li>52</li> <li>53</li> <li>54</li> <li>55</li> <li>56</li> </ol>	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> <li>TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.</li> <li>Options: <ul> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists (e.g., medical center or university).</li> </ul> </li> </ul>
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> <li>TIP:</li> <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists (e.g., medical center or university).</li> </ul> Where did this phase of the intervention take place?</ul>
<ul> <li>37</li> <li>38</li> <li>39</li> <li>40</li> <li>41</li> <li>42</li> <li>43</li> <li>44</li> <li>45</li> <li>46</li> <li>47</li> <li>48</li> <li>49</li> <li>50</li> <li>51</li> <li>52</li> <li>53</li> <li>54</li> <li>55</li> <li>56</li> <li>57</li> <li>58</li> </ul>	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> <li>TIDieR (7) - Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.</li> <li>Options: <ul> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> </ul> </li> <li>TIP: <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists (e.g., medical center or university).</li> </ul> </li> </ul>
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	•	<ul> <li>How many weeks was this phase?</li> <li>Note number of weeks</li> <li>NR T If not reported</li> </ul> TIDieR (7) – Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features. <ul> <li>Options:</li> <li>Yes T If specifically described</li> <li>This includes single-location trials when the authors clearly state the entire trial took place onsite.</li> <li>Unclear T Inadequate description provided</li> <li>No T Details not provided</li> <li>TIP:</li> <ul> <li>Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.</li> <li>However, these trials should be further identified according to the location of the interventionists (e.g., medical center or university).</li> </ul> Where did this phase of the intervention take place?</ul>

- Check off which of these intervention settings apply
  - Medical Center
  - Rehabilitation Center
  - University
  - Public Gym
  - Home
  - Other

o TIP:

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- Check off more than one if needed (e.g., telephone-based or mixed facility- / home-based interventions).
- TIDieR (5) For each category of intervention provider (e.g. physiologist, psychologist, nursing assistant), describe their expertise/background AND any specific training given.
  - Options:
    - Yes T Must provide formal education, professional designation, OR certified designation with certifying organization AND any study-specific training they received
    - Unclear T If education/designation AND study-specific training are provided BUT are poorly described
    - No T If either education/designation OR study specific training are not provided
  - Background Examples:
    - Kinesiologist (KIN), Exercise Physiologist (EP), Physiotherapist (PhT), Cancer Exercise Specialist (CES), Personal Trainer + certifying organization (PT-org)
  - Training Examples:
    - Interventionists were required to complete 3 hours of training pertaining to intervention delivery and participant follow-up.
    - Interventionists completed 4 online training modules related to delivering the exercise and behavioral support components of the intervention.
- PHASE I (AET / RET / CET) Was aerobic (AET), resistance (RET), combined (CET) exercise training
  prescribed.
  - Options:
    - Yes T It/they were
    - No T lt/they were not
- DETAILS How many AET / RET / CET groups were there?
  - Indicate 1 or 2 groups as appropriate.

### • DETAILS – What modalities of AET / RET / CET were prescribed?

- Check off which of these intervention modalities apply
  - AET
    - Cycle ergometer
    - Treadmill
    - Elliptical ergometer
    - Walking (e.g., outdoors, indoor track)
    - Other
    - NR T If not reported
  - RET
    - Machine weights
    - Free weights
    - Resistance bands

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1		
2 3		
4		Body weight
5		• Other
6		NR T If not reported
7		o <b>TIP</b> :
8		<ul> <li>Check off more than one modality when applicable (e.g., RET trials which list the names of</li> </ul>
9		exercises but not the specific modalities should be assigned Machine weights and Free weights)
10		
11	•	TIDieR (6) – Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet
12		or telephone) of the intervention and whether it was provided individually or in a group.
13		• Options:
14		<ul> <li>Yes T If clearly described for ALL phases AND components of the intervention</li> </ul>
15		<ul> <li>Unclear T If clearly described for one phase/component BUT is poorly described for another</li> </ul>
16		<ul> <li>No T If not described OR is unclear for more than one intervention phase/component</li> </ul>
17		• TIP:
18		<ul> <li>Must be specifically stated and NOT just implied (e.g., home based programs)</li> </ul>
19		- Must be specifically stated and <b>NOT</b> just implied (e.g., nome based programs)
20		DETAILS Mode of AET / DET / CET auromyleion
21	•	DETAILS – Mode of AET / RET / CET supervision:
22		<ul> <li>Check off which of these supervision modes apply</li> </ul>
23		<ul> <li>Individual</li> </ul>
24		Group
25		<ul> <li>Mixed</li> </ul>
26		<ul> <li>Not applicable</li> </ul>
27		<ul> <li>Not reported</li> </ul>
28		
29	٠	DETAILS – Method of AET / RET / CET supervision:
30		<ul> <li>Check off which of these supervision modes apply</li> </ul>
31		<ul> <li>In person</li> </ul>
32		Phone
33		<ul> <li>Other</li> </ul>
34 35		<ul><li>Other</li></ul>
35 36	•	DETAILS – If Other, please list:
37		<ul> <li>Please list the method of exercise supervision</li> </ul>
38		
39	•	TIDieR (8b) – Describes the frequency of intervention sessions.
40	-	• Options:
41		<ul> <li>Yes T Must define a specific minimum OR range of sessions per week</li> </ul>
42		<ul> <li>No T Not provided</li> </ul>
43		
44	-	DETAILS How many appaions not weak was AET / DET / CET preseribed?
45	•	DETAILS – How many sessions per week was AET / RET / CET prescribed?
46		<ul> <li>Note the number or the range</li> </ul>
47		
48	•	TIDieR (8a) – Describes the intensity of intervention sessions.
49		• Options:
50		<ul> <li>Yes T Must define prescribed intensity according to a standardized and measurable unit (e.g.,</li> </ul>
51		%VO <sub>2peak</sub> , %HR <sub>max</sub> , %1-RM, RPE range)
52		No T Not provided
53		• TIP:
54		It is acceptable if authors state in the Methods that participants were asked to train between XX%
55		and XX% without specifically stating that the intensity was prescribed between these values.
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59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
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However, this information must be apriori defined (i.e., Methods) and not reported after the fact (i.e., Results).

### DETAILS – How was the intensity of AET / RET / CET prescribed?

Note the test/scale (e.g., VO<sub>2peak</sub>, HR<sub>max</sub>, 1-RM, RPE) upon which the relative intensity of exercise was prescribed.

### • DETAILS – Minimum prescribed AET / RET / CET intensity:

- o Note the lowest relative intensity of exercise prescribed
- NR T If not reported

### • DETAILS – Maximum prescribed AET / RET / CET intensity:

- o Note the highest relative intensity of exercise prescribed
- NR T If not reported

### • TIDieR (8c) – Describes the duration of AET / RET / CET sessions.

• **Options:** 

- Yes T Must define a specific minimum OR range for exercise session durations
- No T Not provided

### • DETAILS – Minimum prescribed AET / RET / CET session duration (minutes):

- Note the shortest duration of exercise prescribed in minutes
- **NR** T If not reported

### • DETAILS – Maximum prescribed AET / RET / CET session duration (minutes):

- Note the longest duration of exercise prescribed in minutes
- **NR** T If not reported
- DETAILS Number of prescribed sets (RET only):
  - Provide details
  - **NR** T If not reported
- DETAILS Number of prescribed repetitions (RET only):
  - Provide details
  - **NR** T If not reported
- CONSORT (5a) Description of the different components of the interventions and, when applicable, description of the procedure for tailoring the interventions to individual participants?

### • Options:

- Yes T Must describe the major (primary and secondary) intervention components and, when applicable, <u>when</u> AND <u>how</u> the intervention was individually tailored (personalized or progressed)
- Unclear T If any of the major intervention components are not well described and/or if either the timing or manner in which the intervention was tailored was not well described
- No T If any of the major intervention components and/or tailoring was not described
- No T If multiple intervention components and/or tailoring was not well described

## TIDieR (9i) – If the intervention was planned to be personalized / individualized, then describe when and how. Options:

Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

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2	
3	<ul> <li>Yes T Must at least describe when AND how the intervention was personalized</li> </ul>
4	
5	<ul> <li>Unclear T If either the timing or manner in which the intervention was personalized was not well</li> </ul>
6	described
7	<ul> <li>No T If either the timing or manner in which the intervention was personalized was missing</li> </ul>
8	
	<ul> <li>TIDieR (9ii) – If the intervention was planned to be progressed, then describe when and how.</li> </ul>
9	• Options:
10	<ul> <li>Yes T Must at least describe when AND how the intervention was progressed</li> </ul>
11	
12	<ul> <li>Unclear T If either the timing or manner in which the intervention was progressed was not well</li> </ul>
13	described
14	<ul> <li>No T If either the timing or manner in which the intervention was progressed was missing</li> </ul>
15	o TIP:
16	<ul> <li>Progressions must be defined according to the timing and increment of change throughout the</li> </ul>
17	intervention
18	<ul> <li>Lead-in periods are not considered progressions</li> </ul>
19	
20	TIDIAD (44) If intervention adherence on fidelity and according to the base of the base of the
21	• TIDieR (11) – If intervention adherence or fidelity was assessed, describe how and by whom, and if any
22	strategies were used to maintain or improve fidelity, describe them.
23	• Options:
24	<ul> <li>Yes T Must both identify the strategy AND provide requisite details describing how the strategy</li> </ul>
25	was implemented (including how & by whom)
	<ul> <li>Unclear T If the strategy was identified but not adequately described</li> </ul>
26	<ul> <li>No T If the strategy was identified but not described OR no strategy identified</li> </ul>
27	• TIP:
28	
29	<ul> <li>This only applies to strategies related to supporting the exercise or physical activity component of interpretations</li> </ul>
30	interventions.
31	
32	<ul> <li>CONSORT (5b) – Details of whether and how the AET / RET / CET interventions were standardized.</li> </ul>
33	• Options:
34	<ul> <li>Yes T Provided enough detail related to the consistency of how the exercise intervention was</li> </ul>
35	prescribed AND progressed AND/OR modified in a structured manner
36	This could also apply to how participants were coached or counseled.
37	<ul> <li>Unclear T Used the word 'standardized' but failed to provide the requisite details</li> </ul>
38	
39	<ul> <li>Unclear T Attempted to provide the requisite details but a key aspect is not well described</li> </ul>
40	<ul> <li>No T Failed to describe the intervention as standardized and/or failed to describe more than one</li> </ul>
41	key aspect of the exercise prescription, progression, and/or modification process
42	
43	• CONSORT (5c) – Details of whether and how adherence of care providers to the protocol was assessed or
44	enhanced.
45	• Options:
46	<ul> <li>Yes T Provided details as to how AND when the actions of the interventionists were evaluated</li> </ul>
40	
	by study investigators
48	<ul> <li>Yes T Authors stated that interventionist adherence was not tracked</li> </ul>
49	<ul> <li>Unclear T Provided details as to how OR when the actions of the interventionists were</li> </ul>
50	evaluated by study investigators
51	<ul> <li>No T Details not provided</li> </ul>
52	o TIPS:
53	<ul> <li>This specifically pertains to someone evaluating the interventionists' performance and NOT training</li> </ul>
54	or supporting the interventionists in any way.
55	
56	
57	
58	
59	41
60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# CONSORT (5d), TIDieR (12) – Details of whether and how intervention fidelity or adherence of participants to interventions was assessed or enhanced – describe the extent to which the intervention was delivered as planned.

• Options:

- Yes T Provided details <u>AND</u> data related to how much of the prescribed dose of exercise was actually delivered to each participant relative to <u>what was intended</u>
- Yes T Authors stated that participant adherence was not tracked
- Unclear T Provides details (i.e., intensity AND volume) AND data but one or both are unclear
- No T Failed to report the method **OR** the results of this assessment
- TIPS:
  - Although a participant must attend a session in order to adhere to the prescription, attendance does **NOT** count toward adherence.
  - Authors must describe the method of assessing participant adherence which captures both <u>target</u> <u>intensity</u> (e.g., % VO<sub>2peak</sub> or % HR<sub>max</sub>) *AND* <u>target volume</u> (e.g., total exercise time) *as well as* the results data comparing actual vs target exercise dose delivery.
  - Must describe findings in the context of the planned dose.
  - This ONLY applies to the exercise-specific components of the interventions.

### Other Phase I/II Information

- DETAILS Was there a co-intervention prescribed in this trial?
  - Options:
    - Yes T There was/were
      - Unclear T There was/were but not well described
      - No T There was/were not
  - o TIP:
    - Behavioral support strategies are counted as non-exercise intervention components and the data should be extracted here and for the formal CONSORT behavioral support item.
- DETAILS Please describe the co-intervention.
  - Note all pertinent details of the non-exercise intervention component(s)

TIDieR (3) – Describe any physical or informational materials used in the intervention, including those
provided to participants or used in intervention delivery or in training of intervention providers. Provide
information on where the materials can be accessed (e.g. online appendix, URL).

- Options:
  - NA T No physical or informational material was provided (stated or not)
  - **Yes** T Provides details on any physical or informational materials used in the intervention (including those provided to participants or used to train interventionists)
  - Unclear T Appears physical or informational material was provided but the details were not well described
  - No T Appears physical or informational material was provided but the details were not provided
- TIPS:
  - This pertains to physical or informational material which are only provided to the intervention group(s) and NOT the usual care/control group.
- TIDieR (10) If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).

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	○ Options:
	<ul> <li>NA T No observable modification to the intervention</li> </ul>
	<ul> <li>Yes T Describes modification according to all pertinent features (e.g., what, why, when &amp; how)</li> </ul>
	<ul> <li>Unclear T Notes intervention modification but fails to describe and justify it appropriately</li> </ul>
	<ul> <li>No T If the description or justification is missing</li> </ul>
	o TIPS:
	<ul> <li>Again, base this evaluation solely on the information provided in the primary paper (and online</li> </ul>
	supplement, when applicable) for <i>Round I - Data Extraction</i> .
ntervei	ntion Summary
•	CONSORT (5i) – Described the interventions for each group with sufficient details to allow replication,
	including how and when they were actually administered.
	<ul> <li>Options:</li> </ul>
	<ul> <li>Yes T Provided a complete description of the intervention, such that you could confidently</li> </ul>
	reproduce the intervention
	<ul> <li>No T If they failed to provide sufficient detail (even if they provided a reasonable amount)</li> </ul>
	• TIP:
	<ul> <li>Wait to answer this question until after you have gone through the TIDieR questions. If you assign</li> </ul>
	'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT-
	based item will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign a
	'No' to this CONSORT-based inventory item (this may often be the case).
Sample	Size & Statistics
•	CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes.
	• Options:
	<ul> <li>Yes T The methods used to compare the groups on the primary and secondary outcomes are</li> </ul>
	clearly described
	<ul> <li>Unclear T There is any ambiguity in the description</li> </ul>
	<ul> <li>No T Any aspect is not described</li> </ul>
•	CONSORT (7ai) – How sample size was determined.
-	
	$\circ$ Options:
	<ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable,</li> </ul>
	adjustment for drop-outs – how many participants were needed per group/overall)
	<ul> <li>Yes T Authors specifically stated that no power calculation was performed</li> </ul>
	<ul> <li>No T Any details not provided</li> </ul>
•	CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care providers
	or centers was addressed.
	○ Options:
	43
	43 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

· · ·	<ul> <li>NA T If study was conducted at a single center and under the supervision of the same group of interventionists</li> <li>Yes (<i>multicenter trials</i>) T If details of how the analyses were adjusted to account for potential differences across intervention sites and interventionists</li> <li>Yes (<i>single center/multi-intervention location</i>) T If details of how the analyses were adjusted to account for potential differences across interventionists</li> <li>Yes T Authors clearly stated that no clustering was performed</li> <li>No T Details not provided</li> </ul>
	<ul> <li>When applicable, explanation of any interim analysis or stopping guidelines.</li> </ul>
<ul> <li>Options</li> </ul>	
:	NA T No interim analysis or apriori defined stopping criteria Yes T Authors apriori defined the rationale, nature and methods for interim analyses or stopping criteria
•	<b>Unclear</b> T If any aspect of the rationale, nature and methods for the interim analysis or stopping criteria are poorly described
•	<b>No</b> T If any aspect of the rationale, nature and methods are missing or if results are reported without details provided in the methods section
○ TIPS:	
•	Interim analyses: Typically used to assess the safety, feasibility, or establish the preliminary efficacy of an intervention at a prespecified time-point in a trial with the express purpose of making decisions around whether the trial should continue as planned, if modifications are required, or if the trial should be stopped altogether. Do not mistake this type of analysis for a midpoint assessment wherein the primary and/or secondary outcome data are collected and reported as another testing time-point in the overall trial. Stopping criteria: Likely related to the outcome of the aforementioned interim analyses. Must be apriori defined and described and <i>NOT</i> just reported on after the fact.
CONSORT (12a)     or centers was	ii; <i>statistics</i> ) – When applicable, details of whether and how the clustering by care providers addressed.
<ul> <li>Options</li> </ul>	S:
•	<b>NA</b> T If study was conducted at a single center and under the supervision of the same group of interventionists
:	<b>NA T</b> If multicenter trial stratified by center and no further exploratory analyses were performed <b>Yes</b> ( <i>multicenter trials</i> ) T If details of how the analyses were adjusted to account for potential differences across intervention sites and interventionists
	Yes (single center/multi-intervention location) T If details of how the analyses were adjusted to account for potential differences across interventionists Yes T Authors stated that clustering was not performed
•	No T Details not provided
CONSORT (12b         Options	) – Methods for additional analyses, such as subgroup analyses and adjusted analyses. s:
•	NA T If no additional subgroup analyses were performed
:	<b>Yes</b> T If any analysis other than the primary/secondary intervention effects are described <b>No</b> T If any analysis other than the primary/secondary intervention effects are reported but not
	described

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Data Comparison: Sample Size

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	Sample Size Calculated	Sample Size Recruited
Sample size – calculated vs actual?	Number:	Number:
• <b>TIP:</b>		
<ul> <li>If the calculated sample values (e.g., Reg: ##; N</li> </ul>	e size listed in the Registry and Manuso /an: ##).	cript are different, please note both
<ul> <li>DETAILS – If different, were the change</li> <li>Options:</li> </ul>	es noted in the Manuscript?	
<ul> <li>Yes T The difference(s)</li> </ul>	) in Sample Size were clearly stated ar	
<ul> <li>Not Applicable T Then</li> </ul>	in Sample Size were apparent but not e was no difference in the Sample Size	
and the Manuscript. <ul> <li>Not Applicable T No c</li> </ul>	linical trial registry data available.	
	6	
RESULTS		
Participant Flow		
<ul> <li>CONSORT (13) – Participant flow diagr</li> <li>Options:</li> </ul>	ram (a diagram is strongly recomme	nded).
<ul> <li>Yes T A clear depiction</li> <li>No T Not provided</li> </ul>	of participant flow was provided	
• CONSORT (13b) – For each group, loss	ses and exclusions after randomizat	ion, together with reasons.
<ul> <li>Options:</li> <li>NA T If authors specific</li> </ul>	ally state there were no losses/exclusi	ons post randomization
•	lete account of all randomized particip ized participants are accounted for but	
unclear		The details of any participant are
<ul> <li>No T If any details of an</li> </ul>	ny participant are missing	

• CONSORT (13aii) – The number of care providers and/or centers performing the intervention in each group and the number of patients treated by each care provider or in each center.

	<ul> <li>Options:</li> <li>Yes T (Multi-site trials) List the number of intervention sites OR individually identify each site AND must clearly state the number of interventionists at each study site.</li> </ul>
	<ul> <li>Yes T (Single-site trials) Must clearly state the number of interventionists at the study site.</li> <li>No T (Multi-site trials) Data not provided for number of centers and/or number of interventionists.</li> <li>No T (Single-site trials) Data not provided for number of interventionists.</li> </ul>
•	CONSORT (15ii) – When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group.
	<ul> <li>Options:</li> <li>Yes T (Multi-site trials) Must at least provide the background education or training of the interventionists <i>AND</i> the volume of participants at each site.</li> </ul>
	<ul> <li>Yes T (Single-site trials) Must at least provide the background education or training of the interventionists.</li> </ul>
	<ul> <li>No T (Multi-site trials) Data not provided for interventionists and/or centers.</li> <li>No T (Single-site trials) Data not provided for interventionists.</li> </ul>
Partici	pants, Analyses & Outcomes
•	CONSORT (15i) – A table showing baseline demographic and clinical characteristics for each group.
•	<ul> <li>Options:</li> </ul>
	<ul> <li>Yes T A unique table displaying demographic data is provided</li> <li>No T Table not provided</li> </ul>
•	CONSORT (13ai) – For each group, the number of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome.
	<ul> <li>Options:</li> <li>Yes T All requisite details were provided</li> </ul>
	<ul> <li>No T Any of the requisite details are not provided</li> </ul>
	<ul> <li>TIP:</li> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> </ul>
•	CONSORT (16) – For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.
	<ul> <li>Options:</li> <li>Yes T Must provide details of how many participants from each group were included within each analysis</li> </ul>
	<ul> <li>Unclear T The authors suggest that analyses were performed according to intention-to-treat but failed to provide a description of how missing data from drop-outs or testing errors was accounted</li> </ul>
	<ul> <li>Unclear T The authors provided numbers for the analysis but did not indicate that analyses adhered to intention-to-treat principles</li> </ul>
	<ul> <li>No T Data not provided</li> <li>TIPS:</li> </ul>
	<ul> <li>This information is typically reported in the main results tables in the form of (n = #) but may also be found in the results section.</li> </ul>
	<ul> <li>Double check the flow diagram to check for potential dropouts/missing data.</li> </ul>
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	• If any participants withdraw or wore last to follow up, the authors should displace how
	<ul> <li>If any participants withdrew or were lost to follow-up, the authors should disclose how their missing data was treated.</li> </ul>
	<ul> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> </ul>
•	CONSORT (17a) – For each primary and secondary outcome, results for each group, and the estimated effect
•	size and its precision (such as 95% confidence interval).
	• Options:
	<ul> <li>Yes T Authors must provide the raw baseline data, raw or adjusted follow-up data, change scores</li> </ul>
	or effect sizes, AND 95% CI data
	<ul> <li>No T Missing any of the aforementioned data</li> </ul>
•	CONSORT (17b) – For binary outcomes, presentation of both absolute and relative effect sizes is
-	recommended.
	• Options:
	<ul> <li>NA T If no binary outcomes are tracked/reported</li> </ul>
	<ul> <li>Yes T Authors provide an indication of the actual number of observations relative to the expected</li> </ul>
	number of observations <b>AND</b> whether the ratio of observations differed between groups
	<ul> <li>No T Missing any of the aforementioned data</li> </ul>
•	CONSORT (18) – Results of any other analyses performed, including subgroup analyses and adjusted
-	analyses, distinguishing pre-specified from exploratory.
	• Options:
	<ul> <li>NA T If no subgroup or sensitivity analysis were performed</li> </ul>
	<ul> <li>Yes T If the results of any analysis other than the main intervention effects were performed and</li> </ul>
	reported
	<ul> <li>No T If the results of any analysis other than the main intervention effects were performed but not</li> </ul>
	reported
	2
•	DETAILS – What was the outcome of this trial?
2	• Options:
	<ul> <li>Positive T As hypothesized, there was a significant difference in the primary outcome</li> </ul>
	<ul> <li>Positive → As hypothesized, equivalency was demonstrated</li> </ul>
	<ul> <li>Negative T Contrary to the hypothesis, there was no significant difference in the primary outcome</li> </ul>
	<ul> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> </ul>
	<ul> <li>Unclear T If the primary findings are not well defined or not interpretable</li> </ul>
	<ul> <li>Mixed T Only an option for trials with more than one primary outcome (rare)</li> </ul>
rial C	characteristics
٠	CONSORT (13d) – Details of the experimental treatment and comparator as they were implemented.
	• Options:
	<ul> <li>Yes T Clearly reported findings for the intervention arms(s) and control group</li> </ul>
	<ul> <li>No T Results not clearly defined for each group</li> </ul>
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	47 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**NA** T If the trial appeared to finish as planned (i.e., achieved target sample size and concluded

**Unclear** T If the trial stopped early or was extended **AND** the authors made special note of that

**Unclear** T If the trial stopped early or was extended **AND** an inadequate discussion was provided No T If the trial stopped early or was extended **BUT** an adequate justification was not provided

Yes T Must provide both the dates of when the trial was open to recruitment AND at least indicate

Unclear T Authors provided recruitment dates but only eluded to how long the follow-up period

Yes T If the trial stopped early or was extended AND a full justification was provided

The majority of studies will finish as planned and will be assigned an NA

Supplet	memary Methods 6. Data Extraction Reference Guide – Exercise RC1s
•	CONSORT (14b) – Why the trial ended or was stopped.
	<ul> <li>Options:</li> </ul>
	<ul> <li>NA T If the trial appeared to finish as planned (i.e., achie</li> </ul>
	the intervention and follow-up tested as intended)
	<ul> <li>Yes T If the trial stopped early or was extended AND a function</li> </ul>
	<ul> <li>Unclear T If the trial stopped early or was extended ANI</li> </ul>
	fact without providing an adequate justification
	<ul> <li>Unclear T If the trial stopped early or was extended ANI</li> </ul>
	<ul> <li>No T If the trial stopped early or was extended BUT an a</li> </ul>
	<ul> <li>The majority of studies will finish as planned and will be</li> </ul>
٠	CONSORT (14a) – Dates defining the periods of recruitment and follo
	• Options:
	<ul> <li>Yes T Must provide both the dates of when the trial was</li> </ul>
	a specific date as to when participant follow-up finished
	<ul> <li>Unclear T Authors provided recruitment dates but only e</li> </ul>
	lasted (e.g., 12 months)
	<ul> <li>No T Only provided dates of recruitment but not follow-u</li> </ul>
	No i only provided dates of redultment but not follow-u
DETAI	
•	Recruitment (enrollment) start date:
	<ul> <li>Note details</li> </ul>
	<ul> <li>Nomenclature: Date format T MM/YY</li> </ul>
	<ul> <li>NR T If not reported</li> </ul>
•	Recruitment (enrollment) end date:
	<ul> <li>Note details</li> </ul>
	<ul> <li>Nomenclature: Date format T MM/YY</li> </ul>
	<ul> <li>NR T If not reported</li> </ul>
	<ul> <li>Note details</li> <li>Nomenclature: Date format T MM/YY</li> <li>NR T If not reported</li> </ul> Recruitment (enrollment) end date: <ul> <li>Note details</li> <li>Nomenclature: Date format T MM/YY</li> <li>NR T If not reported</li> </ul>
-	Trial start date:
•	
	• Note details
	<ul> <li>Nomenclature: Date format T MM/YY</li> </ul>
	<ul> <li>NR T If not reported</li> </ul>
٠	Trial end date:
	<ul> <li>Note details</li> </ul>
	<ul> <li>Nomenclature: Date format T MM/YY</li> </ul>
	<ul> <li>NR T If not reported</li> </ul>
Timing	g of Assessments

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- CONSORT (13c) For each group, the delay between randomization and the initiation of the intervention. • **Options:**
- ts

- lasted (e.g., 12 months) No T Only provided dates of recruitment but not follow-up OR not at all
- nrollment) start date:
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  - clature: Date format T MM/YY
  - not reported
- nrollment) end date:
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  - clature: Date format T MM/YY
  - not reported

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	<ul> <li>Yes T Explicitly states an average or maximum time (days/weeks) between randomization intervention start</li> <li>No T Data not provided</li> </ul>
Rando	mization & Testing
•	<ul> <li>Number of subjects randomized to Exercise:</li> <li>AET (2) / RET (2) / COMB (2) T Note details for each group as relevant</li> <li>NR T If not reported</li> </ul>
•	Number of subjects randomized to Usual Care/Control: <ul> <li>Note details</li> <li>NR T If not reported</li> </ul>
•	Number of Exercise participants with baseline data: • AET (2) / RET (2) / COMB (2) T Note details for each group as relevant • NR T If not reported
•	Number of Usual Care/Control participants with baseline data: <ul> <li>Note details</li> <li>NR T If not reported</li> </ul>
•	<ul> <li>Number of Exercise participants with follow-up data:</li> <li>AET (2) / RET (2) / COMB (2) T Note details for each group as relevant</li> <li>NR T If not reported</li> </ul>
•	Number of Usual Care/Control participants with follow-up data: <ul> <li>Note details</li> </ul>
	• NR T If not reported
Demo	graphics
•	Note details       NR T If not reported
•	Number of male participants: <ul> <li>Note details</li> <li>NR T If not reported</li> </ul>
•	Number of female participants: <ul> <li>Note details</li> </ul>

- o NR T If not reported
- Average age of all participants:
  - Note details

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- o NR T If not reported
- Average age of Exercise participants:
  - Note details
  - o NR T If not reported
- Average age of Usual Care/Control participants:
  - Note details
  - o NR T If not reported
- Medical Characteristics
  - Average disease duration (months):
    - Not Applicable
    - <6 months</li>
    - <12 months</li>
    - <24 months</li>
    - o <60 months
    - o <120 months
    - **ﷺ**nonths
    - NR T If not reported

### Comorbidities

### Hypertension (n):

- Note details
- NR T If not reported
- NA T If listed in exclusion criteria

### Hypercholesterolemia (n):

- Note details
- NR T If not reported
- NA T If listed in exclusion criteria

### Diabetes (n):

- Note details
- NR T If not reported
- NA T If listed in exclusion criteria

Hypercholesterolemia (%): Note details

Hypertension (%): Note details

Diabetes (%): Note details

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sessions mber: Note details NR T If not reported OR sessions mber: Note details NR T If not reported OR sessions	<ul> <li>if trial reports attendance as X% attende</li> <li>Percent: Note details</li> <li>if trial reports attendance as X% attende</li> <li>Percent: Note details</li> <li>if trial reports attendance as X% attende</li> <li>if trial reports attendance as X% attende</li> <li>ise-based components of the intervention a punseling sessions).</li> </ul>
sessions mber: Note details NR T If not reported OR sessions mber: Note details NR T If not reported OR sessions attendance with the exerce	Percent: Note details if trial reports attendance as X% attende Percent: Note details if trial reports attendance as X% attende
Note details NR T If not reported OR sessions mber: Note details NR T If not reported OR sessions attendance with the exerce	<ul> <li>if trial reports attendance as X% attende</li> <li><b>Percent:</b> Note details</li> <li>if trial reports attendance as X% attende</li> <li>iise-based components of the intervention a</li> </ul>
NR T If not reported OR sessions mber: Note details NR T If not reported OR sessions attendance with the exerce	<b>Percent:</b> <i>Note details</i> if trial reports attendance as X% attende ise-based components of the intervention a
Note details NR T If not reported OR sessions attendance with the exerc	if trial reports attendance as X% attende
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mber:	Percent: Note details
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mber:	Percent: Note details
Note details	
NR T If not reported	
nber:	Percent: Note details
Note details	
NR T If not reported	
	nber: Note details NR T If not reported nber: Note details NR T If not reported nber: Note details

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

### 

# HARMS (19a) – If the study collected data on harms and benefits, the title or abstract should so state. Options:

- Yes T If authors mention safety or AEs anywhere in the title or abstract
- No T If safety or AEs are not mentioned in these sections

o TIPS:

**CONSORT – HARMS** 

- IMPORTANT All Phase I-III, by definition, should report safety outcomes. Thus, the safety
  of the intervention should be assessed and reported on.
- HARMS (19b) If the trial addresses both harms and benefits, the introduction should so state.
  - Options:
    - Yes T Authors should state the safety of the intervention is in question **OR** they should state that one of the trial objectives (typically last paragraph of the intro) is to assess the safety of the intervention.
    - No T Not mentioned
- HARMS (19c) List addressed adverse events with definitions for each (when relevant, attention to grading, expected vs. unexpected AEs, reference to standardized and validated definition, and description of new definitions).
  - Options:
    - Yes T Authors listed AND defined the potential/anticipated AEs being studied
    - Unclear T Authors listed the AEs but failed to define them
    - No T Details not provided
  - TIPS:
    - For trials reporting AEs as the primary and secondary outcomes, the definitions for the outcomes count towards defining the AEs.
- HARMS (19d) Clarify how harms-related data was collected (mode of collection, timing, attribution methods, intensity of ascertainment, and harms-related monitoring and stopping rules).
  - Options:
    - Yes T Authors should clearly state how, when AND by whom AE data was collected
    - Unclear T Authors fail to properly describe a single aspect (how, when, by whom) of how the AE
      data was collected but adequately describe all other aspects
    - No T Details not provided
  - o TIPS:
    - For trials reporting AEs as the primary and secondary outcomes, the collection methods for the outcomes count towards collecting the AEs.
- HARMS (19e) Describe plans for presenting and analyzing information on harms (including coding, handling of recurrent event, specification of timing issues, handling of continuous measures, and statistical analyses).
   Options:
  - Yes T Authors should clearly state how AE data was analyzed
  - Unclear T Authors fail to properly describe a single aspect of how the AE data was analyzed but adequately describe all other aspects
  - No T Details not provided

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### GENERAL TIPS FOR HARMS:

- If authors fail to explicitly state if AEs were attributable to the intervention, check to see if there were analyses comparing AE frequency or relative risk per arm.
  - If analyses were performed:
    - For AEs which occur significantly more frequently within the intervention group(s) T list details for those specific AEs under 'intervention-related'
    - For AEs which do not occur significantly more frequently within the intervention group(s) T list details for those specific AEs under 'non-intervention-related'
  - $\circ$   $\;$  If analyses were not performed:
    - Rate 'intervention-related' AEs as NR
    - List all reported AEs for both groups as 'non-intervention-related'
- For trials reporting AEs as the primary and secondary outcomes, the analysis methods for the outcomes count towards analyzing the AEs.

### Testing-related AEs

- DETAILS Did any testing-related AE occur?
  - o NA T Specifically stated that no testing-related AEs occurred
  - Yes T Specifically stated the type and number of testing-related AEs
  - o Unclear T The numbers are provided but the details were unclear
  - **No** T Details not provided

### • DETAILS – If so, how many?

- Note pertinent details
- **NR** T If not reported
- TIPS:
  - Report both values if there are discrepancies between the Registry and Manuscript
- DETAILS How were testing-related AE defined?
  - Note pertinent details
  - **NR** T If not reported
- DETAILS How were testing-related AE monitored/tracked?
  - Note pertinent details
  - NR T If not reported

### Intervention-related AEs

- DETAILS Did any intervention-related AE occur?
  - NA T Specifically stated that no intervention-related AEs occurred
  - Yes T Specifically stated the type and number of intervention-related AEs
  - Unclear T The numbers are provided but the details are unclear
  - **No** T Details not provided
- DETAILS If so, how many?
  - Note pertinent details
  - **NR** T If not reported

- o TIPS:
  - Report both values if there are discrepancies between the Registry and Manuscript

### • DETAILS – How were intervention-related AE defined?

- Note pertinent details
- **NR** T If not reported

### DETAILS – How were intervention-related AE monitored/tracked?

- o Note pertinent details
- **NR** T If not reported

### Non-Intervention-related AEs

- DETAILS Did any non-intervention-related AE occur?
  - NA T Specifically stated that no intervention-related AEs occurred
  - Yes T Specifically stated the type and number of intervention-related AEs
  - Unclear T The numbers are provided but the details are unclear
  - No T Details not provided

### • DETAILS – If so, how many?

- Note pertinent details
- **NR** T If not reported
- TIPS:
  - Report both values if there are discrepancies between the Registry and Manuscript

### DETAILS – How were non-intervention-related AE defined?

- Note pertinent details
- **NR** T If not reported

### DETAILS – How were non-intervention-related AE monitored/tracked?

- Note pertinent details
- **NR** T If not reported

### **AEs Per Group**

- DETAILS How many AEs were reported for the PHARMA (4) & UC groups?
  - Note pertinent details
  - NR T If not reported

### HARMS Continued...

- HARMS (19f) Describe for each arm the participant withdrawals that are due to harms and their experiences with the allocated treatment.
  - $\circ$  Options:
    - **NA** T If the authors specifically stated there were no AEs **OR** that no participant withdrew/was lost to follow-up due to AEs

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1 2 3 4 5 6	<ul> <li>Yes T If the authors clearly identify the number of participants who withdrew or were lost to follow-up due to AEs</li> <li>No T If the reasons why participants withdrew or were lost-to-follow-up are not provided for every applicable case</li> </ul>
7 8 9 10 11 12 13 14	<ul> <li>HARMS (19g) – Provide denominators for analyses on harms.</li> <li>Options:         <ul> <li>NA T If the authors specifically stated there were no AEs</li> <li>Yes T Reference numbers provided for AE risk calculations</li> <li>No T Details not provided</li> </ul> </li> </ul>
15 16 17 18 19 20 21 22	<ul> <li>HARMS (19h) – Presents absolute risk per arm and per AE type, grade, and seriousness, and present appropriate metrics for recurrent events, continuous variables, and scale variables.</li> <li>Options:         <ul> <li>NA T If the authors specifically stated there were no AEs</li> <li>Yes T If the authors present the absolute risk per arm <i>AND</i> per adverse event type/grade <i>AND</i> describe the frequency of AEs</li> <li>No T Details not provided</li> </ul> </li> </ul>
23 24 25 26 27 28 29 30 31 32	<ul> <li>HARMS (19i) – Describes any subgroup analyses and exploratory analyses for harms.</li> <li>Options:         <ul> <li>NA T If the authors specifically stated there were no AEs</li> <li>NA T There were no subgroup / exploratory analyses proposed or reported</li> <li>NA T If the number of AEs were so small that it was not reasonable to perform subgroup or exploratory analyses</li> <li>Yes T If the authors present the results of subgroup analyses or exploratory analyses</li> <li>No T Details not provided</li> </ul> </li> </ul>
33 34 35 36 37 38 39 40 41 42 43	<ul> <li>HARMS (19j) – Provide a balanced discussion of benefits and harms with emphasis on study limitation, generalizability, and other sources of information on harms.</li> <li>Options:         <ul> <li>NA T If the authors specifically stated there were no AEs</li> <li>Yes T Should formally address any AEs in the Discussion in the context of trial limitations and whether the risk intervention-related AEs should be considered when implementing or conducting further tests of the intervention in question.</li> <li>No T Not discussed</li> </ul> </li> </ul>
43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20i) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.         <ul> <li>Options:</li> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> </ul> </li> </ul>
58 59 60	55 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

 No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations

# • CONSORT (20ii) – Trial limitations: taking into account the choice of comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group.

 $\circ$  Options:

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- Yes T If authors listed sources of potential bias related to the control group(s), incomplete or lack
  of blinding, and/or between care providers/intervention sites AND provided basic details as to how
  these factors may have influenced results
- Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors
- No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations
- o TIPS:
  - Trials with only PROs: *analysis* must be blinded to be rated *Low*.
  - Trials with only physiologic outcomes: *testing* must be blinded to be rated *Low*.
  - Trials with both physiologic and PROs: *testing* and *analysis* must be blinded to be rated *Low*. In these mixed outcome trials, an Unclear can be assigned if the *analysis* details are missing.

# • CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.

- Options:
  - Yes T Authors must discuss their findings in the context of similar interventions, comparators, patient groups, and care provider/centers.
  - No T None of these aspects were not adequately discussed within the context of other research (past and future)
- CONSORT (22) Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.
  - $\circ$  Options:
    - Yes T Authors should not overstate non-significant or modestly altered endpoints; nor should they dismiss/ignore/fail to adequately describe non-significant findings for any of the primary outcomes in favor of discussing secondary outcomes
    - No T Authors do not present an unbiased interpretation of their findings
  - o **TIP:** 
    - Look closely at the results for the primary outcomes (data tables). The first paragraph of the Discussion should summarize these results without inflating/downplaying the findings. Similarly, the Conclusion should also provide an unbiased summary of the main trial findings.

### • CONSORT (23) – Registration number and name of trial registry.

- Options:
  - Yes T If the number was provided
  - Yes T If authors clearly stated the trial was not registered
  - No T If the number was not provided
  - o TIP:
    - Check the abstract, methods, and footnotes/margins of the paper to locate this number.
- DETAILS If so, please list.
  - o Note pertinent details

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3	<ul> <li>CONSORT (24) – Where the <u>full trial protocol</u> can be accessed, if available.</li> </ul>
4	$\circ$ Options:
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6	<ul> <li>Yes T If the full protocol or a link to the full protocol is provided in the primary manuscript or as an</li> </ul>
8 7	online supplement
	No T Data not provided
8	
9	DETAILS – If so, please provide the URL:
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11	<ul> <li>Note pertinent details</li> </ul>
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13	<ul> <li>CONSORT (25) – Sources of funding and other support, role of funders.</li> </ul>
14	• Options:
15	<ul> <li>Yes T If funder and funder's role are both described</li> </ul>
16	
17	<ul> <li>Unclear T If either funder OR funder's role are described</li> </ul>
18	<ul> <li>No T Neither funder nor funder's role are described</li> </ul>
	o TIP:
19	<ul> <li>Similar to the registration number, check the footnotes, margins, and any supplemental information</li> </ul>
20	listed between the Conclusion and the Reference list.
21	
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23	<ul> <li>DETAILS – If so, please provide the details:</li> </ul>
24	<ul> <li>Note pertinent details</li> </ul>
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### **COCHRANE – Risk of Bias**

### • Selection Bias: Random sequence generation

- **High** T Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence
- o Low T Random sequence generation method should produce comparable groups
- o Unclear T Not described in sufficient detail to permit judgement

### • Selection Bias: Allocation concealment

- High T Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
- o Low T Intervention allocations likely could not have been foreseen in before or during enrollment
- o Unclear T Not described in sufficient detail to permit judgement

### • Performance Bias: Blinding (participants & personnel)

- **High** T Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
- Low T Blinding was likely effective
- Unclear T Not described in sufficient detail to permit judgement

### Detection Bias: Blinding (outcome assessment)

- o High T Detection bias due to knowledge of the allocated interventions by outcome assessors
- o Low T Blinding was likely effective
- o Unclear T Not described in sufficient detail to permit judgement
- $\circ$  TIPS:
  - Trials with only PROs: *analysis* must be blinded to be rated *Low*.
  - Trials with only physiologic outcomes: testing must be blinded to be rated Low.
  - Trials with both physiologic and PROs: *testing* and *analysis* must be blinded to be rated *Low*. In these mixed outcome trials, an Unclear can be assigned if the *analysis* details are missing.

### • Attrition Bias: Incomplete outcome data

- High T Attrition bias due to amount, nature or handling of incomplete outcome data
- o Low T Handling of incomplete outcome data was complete and unlikely to have produced bias
- **Unclear** T Insufficient reporting of attrition/exclusions to permit judgment (e.g., number randomized not stated, no reasons for missing data provided)

### • Reporting Bias: Selective reporting

- High T Reporting bias due to selective outcome reporting
- Low T Selective reporting bias not detected
- Unclear T Insufficient information to permit judgment

### • Other sources of bias

- o High T Bias due to problems not covered elsewhere in the criteria
- Low T No other bias detected
- **Unclear** T There may be a risk of bias, but there is insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem will introduce bias

### Quality Comments: Justify 'high-risk' & 'unclear' decisions

o Please note pertinent details

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### JADAD Score

- Randomization Score:
  - 1 point if randomization is mentioned
  - o 1 additional point if the method of randomization is appropriate
  - Deduct 1 point if the method of randomization is inappropriate (minimum 0)

### • Blinding Score:

- 1 point if blinding is mentioned
- 1 additional point if the method of blinding is appropriate
- Deduct 1 point if the method of blinding is inappropriate (minimum 0)
- o TIPS:
  - For trials reporting exclusively PROs the analysis must be blinded.
  - For trials reporting any physiologic outcomes the testing must be blinded.
  - For trials with both physiologic and PROs the testing and analysis must be blinded.

### • Account of All Patient Score:

• 1 point if the fate of all patients in the trial is known. If there are no data the reason is stated.

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# Data Extraction Reference Guide – Pharmacological RCTs



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### EXTRACTION ABBREVIATIONS

- %: percent
- BL: baseline
- d: days
- FU: follow-up
- hr/hrs: hour/hours
- IN: injection
- INH: inhalent
- IO: intraosseous
- mins: minutes
- mo: months
- PHARMA: pharmaceutical intervention
- PO: oral
- PR: per rectum
- SL: sublingual
- TD: transdermal
- Top: topical
- UC: usual care/control
- wk/wks: week/weeks
- yrs: years

### **GENERAL NOMENCLATURE & EXTRACTION GUIDELINES**

### **Nomenclature Guidelines**

- Ranges:
  - Use 'to' and not '-' (e.g., 150 bpm to 175 bpm)
- Units:
  - List all units of measure including percentages
- Significant figures:
  - Raw values / averages T round to the nearest 0.1
  - Percentages T round to the nearest whole number
- Averages:

0

- $\circ$   $\,$  Mean value is preferred and assumed  $\,$ 
  - Only list median values if mean are not reported
    - If listing median values, please label appropriately
- Lists:
  - $\circ$   $\;$  Be succinct T only include pertinent details and use bullet form with semicolon separated values
  - $\circ$   $\;$  List details in the same order as it is presented in the manuscript
  - Examples:
    - Inclusion/exclusion criteria: e.g., 40 to 65 yrs; BMI<40; sedentary</li>
    - Primary/secondary outcomes: e.g., resting HR; body weight; PA mins/wk

### **Extraction Guidelines**

- Multiple intervention arms
  - Base group numbering on layout of flow diagram (e.g., PHARMA 1 = left-most group; PHARMA 2 = group immediately to the right, etc.)
- Placebo group
  - Extract data into Control group fields
- In the case of discrepancies between conflicting sources of data, prioritize the data provided in the primary manuscript.

### ARTICLE INCLUSION/EXCLUSION

- Should this article be included in our systematic review?
  - Yes T Does not meet any exclusion criteria.
  - No T Meets one or more exclusion criteria.

### **PUBLICATION INFORMATION**

- Country of publication?
  - Please provide the <u>full name</u> of the country where the study was conducted/where the primary author is based

### TITLE, ABSTRACT & INTRODUCTION

- CONSORT (1a) Identification as a randomized trial in the title.
  - Options:
    - Yes T Either randomized controlled trial; randomized trial; randomized
    - No T Not mentioned
- CONSORT (1b) Structured summary of trial design, methods, results, and conclusions.
  - Options:
    - Yes T Introduction/Background + Methods + Results + Discussion/Conclusion
    - No T Not properly structured
- CONSORT (2a) Scientific background and explanation of rationale.
  - Options:
    - Yes T Reviews relevant literature AND identifies a knowledge gap/question
    - No T Did not adequately review the literature and/or identify the knowledge gap/question the study attempted to address
- CONSORT (2b) Specific objectives or hypothesis.
  - Options:

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3		<ul> <li>Yes (objectives) T Must provide a specific purpose/objective for study in the context of the</li> </ul>	
4		intervention AND the specific outcomes of interest	
5		OR	
6		<ul> <li>Yes (hypothesis) T Must provide a specific hypothesis in the context of a group-related change</li> </ul>	in ؛
7		a specific outcome of interest <b>AND</b> the expected direction of change	<u></u> .
8		<ul> <li>Unclear T Provided the specific purpose/objective or hypothesis but only 1 of 2 additional</li> </ul>	
9			
10		required components	
11		<ul> <li>No T Failed to provide either (1) the specific purpose/objective OR hypothesis, and/or (2) both</li> </ul>	
12		additional required components	
13	0		
14		<ul> <li>This information is typically reported within final paragraph of the introduction or early in the</li> </ul>	
15		methods section.	
16			
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23	<ul> <li>CONSO</li> </ul>	ORT (3a) – Description of trial design (such as parallel, factorial) including allocation ratio.	
24	0	Options:	
25		<ul> <li>Yes T Must provide both a description of overall study design (e.g., parallel arm, crossover) AN</li> </ul>	٧D
26		allocation ratio	
27		<ul> <li>Unclear T Description of study design is provided but NOT allocation ratio</li> </ul>	
28		<ul> <li>No T If missing the study design (even if allocation ratio is provided)</li> </ul>	
29	0	EXAMPLES:	
30	Ũ	<ul> <li>Parallel trials, cross-over trials, factorial trials AND 1:1, 1:2, 1:1:1</li> </ul>	
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32	0010		
33		ORT (4b) – Settings and locations where the data were collected.	
34	0		
35		<ul> <li>Yes T Provided details of where the data were collected for the trial</li> </ul>	
36		<ul> <li>This includes single-location trials when the authors clearly state the entire trial took plant</li> </ul>	lace
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38		<ul> <li>Unclear T Specifies that data was collected in a lab/office but does not provide the actual locat</li> </ul>	tion
39		of said room (e.g., at which hospital)	
40		<ul> <li>No T Details not provided</li> </ul>	
41	0	TIP:	
42	-	<ul> <li>This does NOT include where the recruitment or intervention took place.</li> </ul>	
43		<ul> <li>Listing the institutional / ethics review board does not count.</li> </ul>	
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45		I.S. Clinical nonulation	
46		LS – Clinical population:	
47	0	List the clinical population being studied	
48	0	NR T If not reported	
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50	<ul> <li>DETAI</li> </ul>	LS – Disease setting:	
51	0	Identify the disease phase [Prevention (P) vs. Management (M)] during and after) during which the	
52		PHARMA intervention took place.	
53			
54	CONS	ORT (3b) – Important changes to methods after trial commencement (such as eligibility criteria), wi	ith
55	reason		
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# Options: NA T The methods did not change Yes T Methods changed and reasons were provided

- Examples include (but are not limited to): study design, sample size (± 10%), eligibility criteria, recruitment strategy, randomization, blinding, data analysis, etc.
- **Unclear** T Described change in methods but no reasons were provided
- No → It appears that methods may have changed but there is not enough information to make assessment

### o TIPS:

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- This includes under/over recruitment according to the a priori-defined sample size without adequate justification.
- Does NOT include changes in trial outcomes T that data is captured in a separate CONSORT item

### Eligibility Criteria

CONSORT (4a) – Eligibility criteria for participants.

### • Options:

- Yes T Provided details/criteria for BOTH inclusion AND exclusion of participants
- Unclear T Only provides details of inclusion OR exclusion but NOT both
- No T Details not provided

### Data Comparison: Eligibility Criteria

• Was there a difference in Eligibility Criteria between the Registry and the Manuscript?

### • Options:

- Yes T One or more differences between the two data sources.
- **No** T No difference between the two data sources.
- Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
- Not Applicable T No clinical trial registry data available.

### • Was the change noted in the Manuscript?

### • Options:

- Yes T The change in eligibility criteria was clearly stated and explained.
- No T The change in eligibility criteria was apparent but not explained.
- Not Applicable T There was no difference in the eligibility criteria between the Registry and the Manuscript.
- Not Applicable T No clinical trial registry data available.
- How many Inclusion Criteria were listed in the Registry?
  - Please record the total number of individual Inclusion Criteria listed in the Registry.

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3 4 5	•	<ul> <li>DC DETAILS - Please list the Inclusion Criteria reported in the Registry.</li> <li>Please record each individual Inclusion Criteria listed in the Registry.</li> </ul>
6 7 8	•	<ul> <li>How many Inclusion Criteria were listed in the Manuscript?</li> <li>Please record the total number of individual Inclusion Criteria listed in the Manuscript.</li> </ul>
9 10 11 12	•	DC DETAILS - Please list the Inclusion Criteria reported in the Manuscript. O Please record each individual Inclusion Criteria listed in the Manuscript.
12 13 14 15	•	<ul> <li>How many Exclusion Criteria were listed in the Registry?</li> <li>Please record the total number of individual Exclusion Criteria listed in the Registry.</li> </ul>
16 17 18	•	<ul> <li>DC DETAILS - Please list the Exclusion Criteria reported in the Registry.</li> <li>Please record each individual Exclusion Criteria listed in the Registry.</li> </ul>
19 20 21 22	•	<ul> <li>How many Exclusion Criteria were listed in the Manuscript?</li> <li>Please record the total number of individual Exclusion Criteria listed in the Manuscript.</li> </ul>
23 24 25	•	<ul> <li>DC DETAILS - Please list the Exclusion Criteria reported in the Manuscript.</li> <li>Please record each individual Exclusion Criteria listed in the Manuscript.</li> </ul>
26 27 28		
31 32 33 34	Outco •	me Measures CONSORT (6a) – Completely defined pre-specified primary and secondary outcome measures, including how
35		and when they were assessed. • Options:
36 37 38 39		<ul> <li>Options:</li> <li>Yes T Clearly defined a single primary outcome (<i>co-primary outcomes at max</i>), all relevant secondary outcomes <i>AND</i> provide all requisite details of the timing <i>AND</i> procedures used to assess these outcomes</li> </ul>
40 41 42		<ul> <li>Unclear T Primary and secondary outcomes defined but the descriptions of the timing and procedures used to assess the outcomes were lacking details required to reproduce the measurements</li> </ul>
43 44 45		<ul> <li>No T If no primary or secondary outcomes are clearly defined OR if the assessment details (e.g., how &amp; when) were missing altogether</li> <li>TIPS:</li> </ul>
46 47 48 49 50		<ul> <li>Some studies may identify multiple primary outcomes. Although this type of study design is inappropriate in the context of medical oncology research, we are evaluating the quality of reporting and not the quality of the study design. Therefore, a 'Yes' can be assigned provided the authors clearly identify which outcomes are considered primary and secondary.</li> </ul>
51 52 53 54	•	<ul> <li>DETAILS – Please list the primary endpoint(s):</li> <li>When entering data, list the primary endpoint(s) using a semicolon to separate individual criteria</li> <li>NR T If not reported.</li> </ul>
55 56	•	DETAILS – Please list the secondary endpoint(s):
57	-	
58 59		65

- o When entering data, list the secondary endpoints using a semicolon to separate individual criteria
- **NR** T If not reported.
- CONSORT (6b) Any changes to trial outcomes after the trial commenced, with reasons.
  - Options:

- NA T No observable changes to trial outcomes were made
- Yes T Describes changes in outcomes according to all pertinent features (e.g., what, why & when)
- Unclear T Describes changes according to all but one pertinent feature
- No T If the description is missing or unclear on two or more pertinent features

### Data Comparison: Primary Outcome

- Was there a difference in the Primary Outcome(s) between the Registry and the Manuscript?
   Options:
  - Options:
    - Yes T Z; difference between the two data sources.
      - No T No difference between the two data sources.
      - Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
      - NR T No clinical trial registry data available.
- Was the change in Primary Outcome noted in the Manuscript?
  - Options:
    - Yes T The change in Primary Outcome was clearly stated and explained.
    - No T The change in Primary Outcome was apparent but not explained.
    - NR T No clinical trial registry data available.
    - NA T No difference (i.e., Q1 = No)
- Was a new Primary Outcome reported in the Manuscript which was not reported in the Registry?
   Options:
  - Yes T Z; Primary Outcome reported in the Manuscript that was not listed in the Registry.
  - No T No new Primary Outcome added to the Manuscript.
  - Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
  - **NR** T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- Was the Primary Outcome reported in the Registry reported as a Secondary Outcome in the Manuscript?
   Options:
  - Yes T Z; Primary Outcome reported in the Registry listed as a Secondary Outcome in the Manuscript.
  - **No** T No Primary Outcome from the Registry listed as a Secondary Outcome in the Manuscript.

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- Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
- **NR** T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- Was the Primary Outcome reported in the Registry omitted from the Manuscript?
  - Yes T The Primary Outcomes reported in the Registry was omitted from the Manuscript.
  - No T The Primary Outcome reported in the Registry was included in the Manuscript.
  - **Unclear** T Possible difference between the two data sources, but insufficient information to make a determination.
  - **NR** T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.

## Data Comparison: Secondary Outcomes

- Were different (new) Secondary Outcomes reported in the Manuscript which were not reported in the
  - **Yes** T Z: Secondary Outcomes reported in the Manuscript were not reported in the Registry.
  - **No** T The Secondary Outcomes reported in the Manuscript were consistent with the Registry.
  - Unclear T Possible difference between the two data sources, but insufficient information to make a determination.
  - **NR** T No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- If different (new) Secondary Outcomes were added to the Manuscript, were the reasons noted in the
  - Yes T The change(s) in Secondary Outcomes were clearly stated and explained
  - No T The changes in Secondary Outcomes were apparent but not explained
  - **NR** T No clinical trial registry data available
  - **NA** T No difference in Secondary Outcomes (i.e., Q6 = No)
- Was one or more of the Secondary Outcomes reported in the Registry reported as Primary Outcomes in the
  - Yes T A Secondary Outcome reported in the Registry was reported as a Primary Outcome in the Manuscript.
  - **No** T None of the Secondary Outcomes reported in the Registry were reported as Primary Outcomes in the Manuscript.
  - Unclear T Possible difference between the two data sources, but insufficient information to make a determination.

• NR T No clinical trial registry data available.

#### • DC DETAILS - If Yes/Unclear, please provide the details?

• Please list all pertinent details.

## Randomization & Blinding

- CONSORT (8a) Method used to generate the random allocation sequence.
  - Options:
    - Yes T Clearly stated the specific process used to generate the randomization (e.g., a coin flip, computer generated)
    - No T Not provided
- CONSORT (8b) Type of randomization; details of any restriction (such as blocking and block size).
   Options:
  - Yes T Provided the details of how the randomization accounted for key confounding variables (e.g., blocking, minimization, stratification)
  - No T Not provided
- CONSORT (9) Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.
  - Options:
    - **Yes** T Provided details of how the physical randomization was performed or how the participants were notified of their allocation (e.g., phone call, sealed envelopes, centralized allocation)
    - No T Not provided
- CONSORT (10) Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.
  - Options:
    - Yes T Must include a clear description of who performed ALL of these tasks
    - Unclear T If description of one of these tasks is inadequate or missing
    - No T If two or more of these tasks are poorly described or not described at all
  - TIP:
    - An exception can be made for participant assignment criteria for studies using centralized allocation.
- CONSORT (11a) If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.
  - Options:
    - Yes T Details regarding testers AND data analyzers are provided
    - Unclear T If any of the aforementioned details are provided but poorly described
    - No T If any of the aforementioned details are missing
  - TIP:

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2 3 4 5 6 7 8	<ul> <li>Remember, we are assessing if the <u>reporting is complete</u> <i>NOT</i> how good the methods are. Therefore, if authors state that the outcome assessors were not blinded, we would consider this good reporting and assign a 'Yes' for this category.</li> <li>Trials listing "double-blind" or "open label" qualify as complete reporting</li> <li>CONSORT (11b) – If relevant, description of the similarity of interventions.</li> </ul>
9 10	<ul> <li>Options:</li> </ul>
10	<ul> <li>NA T If it is a 2-arm trial with a non-pharma control group comparison OR a 3+ -arm trial with</li> </ul>
12 13	<ul> <li>obviously different intervention groups</li> <li>Yes T If details are adequately provided for two or more in<u>tervention arms with similar pharma</u></li> </ul>
14 15	<ul> <li>interventions</li> <li>No T If details are not adequately provided for two or more intervention arms with similar pharma</li> </ul>
16 17	interventions
17 18	• TIP:
19	<ul> <li>NA is not an option for superiority trials (i.e., pharma trials with only two similar intervention arms)</li> </ul>
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24 25	Intervention Details
25 26	
20	INTERVENTION TYPE – Exercise or Pharmaceutical
28	• Options:
29	<ul> <li>Exercise T Stated methods included delivery of a structured exercise program with a stated goal</li> </ul>
30	of improving a health/fitness/psychosocial outcome.
31	<ul> <li>Pharmaceutical T Stated methods included delivery of a pharmaceutical intervention with a</li> </ul>
32	stated goal of improving health.
33	
34	<ul> <li>DETAILS – Was there a run-in / lead-in period?</li> </ul>
35	• Options:
36	<ul> <li>Yes T Authors clearly stated there was a run-in period</li> </ul>
37	<ul> <li>Unclear T Appears to be a run-in period, but it was not well described</li> </ul>
38	<ul> <li>No T No evidence of a run-in period</li> </ul>
39	
40	DETAILS – How many weeks was the run-in period?
41	<ul> <li>Note the total duration of the run-in period in weeks</li> </ul>
42	• NR T If not reported
43	
44	• DETAILS – Please provide the details of the run-in period, including the modality of drug administration,
45 46	dose and frequency.
46 47	<ul> <li>Note all pertinent details</li> </ul>
47 48	
40 49	<ul> <li>DETAILS – What was the total length of the program/intervention (weeks)?</li> </ul>
50	<ul> <li>Note the total duration of the intervention in weeks</li> </ul>
51	
52	
53	<ul> <li>Options:</li> <li>Yes T Must define the period over which the intervention was delivered according to a specific</li> </ul>
54	<ul> <li>res i must define the period over which the intervention was derivered according to a specific number of weeks/months or life period</li> </ul>
55	
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60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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- No T Not clearly defined (e.g., stated during chemotherapy without providing the average number of weeks/months)
- DETAILS How many phases did the intervention have?
  - Note the total number of intervention phases
- DETAILS How many pharmaceutical intervention groups were there?
  - Indicate 1, 2, 3 or 4 groups, as appropriate.

# PHASE I/II – DETAILS

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- DETAILS How many weeks was this phase?
  - Note number of weeks
  - NR T If not reported

# DETAILS – Where did this phase of the intervention take place?

- Check off which of these intervention settings apply
  - Hospital
  - Research laboratory
  - Outpatient medical clinic
  - Home
  - Other
- o TIP:
  - Check off more than one if needed
  - Check off Home if regular (e.g., daily) doses are prescribed and no other locations are described

# • DETAILS – If Other, please list.

- Note location of intervention
- **NR** T If not reported

# • DETAILS – What was the modality of drug administration?

- Check off which of these intervention modalities apply
  - Oral (PO)
  - Injection (IN)
  - Topical (Top)
  - Intraosseous (IO)
  - Transdermal (TD)
  - Inhalent (INH)
  - Per rectum (PR)
  - Sublingual (SL)
  - Other
  - Not Reported
- o TIP:
  - Check off more than one modality when applicable

# • DETAILS – If Other, please list.

- Note modality of drug administration
- **NR** T If not reported

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Pharma Dose and Frequency Extraction Example:	
Definite tables the 500 mer as an electric days (table 1000 mer) tables a days	
<ul> <li>Patients taking two 500 mg capsules of a drug (total 1000 mg) twice a day</li> </ul>	
• <b>Dose:</b> 1000 mg / 2	
<ul> <li>Frequency: 2x / day</li> </ul>	
DETAILS – What dose of drug was administered?	
<ul> <li>Note the dose of drug administered</li> </ul>	
<ul> <li>NR T If not reported</li> <li>TIP:</li> </ul>	
<ul> <li>List total dose and fractionation (e.g., two 500 mg capsules T 1000 mg / 2)</li> </ul>	
• DETAILS – What was the frequency of drug administration (# per day or week)?	
<ul> <li>Note the frequency (number or range) of drug administration</li> </ul>	
• NR T If not reported	
o TIP:	
<ul> <li>List frequency per day or week (e.g., twice daily T 2x / day)</li> </ul>	
DETAILS – Was there a co-intervention prescribed for this group?	
<ul> <li>Options:</li> <li>Yes T If the details of a non-pharmacologic co-intervention was described</li> </ul>	
<ul> <li>If yes, write 'Yes' and provide details</li> </ul>	
<ul> <li>No T If there was no non-pharmacologic co-intervention described</li> </ul>	
<ul> <li>If no, write 'No' only</li> </ul>	
• TIP:	
<ul> <li>Co-interventions do not include concomitant use of medications or therapies</li> </ul>	unless they have
been specifically administered/prescribed in the context of the intervention	
Intervention Summary	
	n <i>(</i> 1
CONSORT (5) – Described the interventions for each group with sufficient details to allo	w replication,
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allo including how and when they were actually administered.</li> </ul>	w replication,
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allo including how and when they were actually administered.</li> <li>Options:</li> </ul>	•
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allo including how and when they were actually administered.</li> </ul>	•
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allouincluding how and when they were actually administered.         <ul> <li>Options:</li> <li>Yes T Provided a complete description of the intervention, such that you conreproduce the intervention</li> <li>No T If they failed to provide sufficient detail (even if they provided a reason</li> </ul> </li> </ul>	uld confidently
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allow including how and when they were actually administered.         <ul> <li>Options:</li> <li>Yes T Provided a complete description of the intervention, such that you converge reproduce the intervention</li> <li>No T If they failed to provide sufficient detail (even if they provided a reason</li> <li>TIP:</li> </ul> </li> </ul>	uld confidently able amount)
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<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allow including how and when they were actually administered.         <ul> <li>Options:</li> <li>Yes T Provided a complete description of the intervention, such that you converge reproduce the intervention</li> <li>No T If they failed to provide sufficient detail (even if they provided a reason</li> <li>TIP:</li> <li>Must describe the type, modality, dose, frequency and any co-interventions</li> </ul> </li> </ul>	uld confidently able amount)
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allow including how and when they were actually administered.         <ul> <li>Options:</li> <li>Yes T Provided a complete description of the intervention, such that you converge reproduce the intervention</li> <li>No T If they failed to provide sufficient detail (even if they provided a reason</li> <li>TIP:</li> <li>Must describe the type, modality, dose, frequency and any co-interventions</li> </ul> </li> </ul>	uld confidently able amount)
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<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allow including how and when they were actually administered.         <ul> <li>Options:</li> <li>Yes T Provided a complete description of the intervention, such that you courreproduce the intervention</li> <li>No T If they failed to provide sufficient detail (even if they provided a reason</li> <li>TIP:                 <ul> <li>Must describe the type, modality, dose, frequency and any co-interventions (intervention location not necessarily required).</li> </ul> </li> </ul> </li> <li>Sample Size &amp; Statistics         <ul> <li>CONSORT (12a) – Statistical methods used to compare groups for primary and secondary</li> </ul> </li> </ul>	uld confidently able amount) to warrant a Yes
<ul> <li>CONSORT (5) – Described the interventions for each group with sufficient details to allow including how and when they were actually administered.         <ul> <li>Options:</li> <li>Yes T Provided a complete description of the intervention, such that you conception of the intervention</li> <li>No T If they failed to provide sufficient detail (even if they provided a reason</li> <li>TIP:</li> <li>Must describe the type, modality, dose, frequency and any co-interventions (intervention location not necessarily required).</li> </ul> </li> <li>Sample Size &amp; Statistics</li> <li>CONSORT (12a) – Statistical methods used to compare groups for primary and seconda o Options:</li> </ul>	uld confidently able amount) to warrant a Yes
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<ul> <li>CONSORT (7a) – How sample size was determined.         <ul> <li>Options:                 <ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes T Authors specifically stated that no power calculation was performed</li> <li>No T Any details not provided</li> </ul> </li> </ul> </li> <li>CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.                     <ul> <li>Options:</li></ul></li></ul>	<ul> <li>CONSORT (7a) – How sample size was determined.</li> <li>Options:         <ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes T Authors specifically stated that no power calculation was performed</li> <li>No T Any details not provided</li> </ul> </li> <li>CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.         <ul> <li>Options:</li> <li>NA T No interim analysis or apriori defined stopping criteria</li> <li>Yes T Authors apriori defined the rationale, nature and methods for interim analysis or stop criteria</li> <li>Unclear T If any aspect of the rationale, nature and methods for the interim analysis or stop criteria are poorly described</li> <li>No T If any aspect of the rationale, nature and methods are missing or if results are reporte without details provided in the methods section</li> <li>TIPS:                 <ul> <li>Interim analyses: Typically used to assess the safety, feasibility, or establish the prelimina efficacy of an intervention at a prespecified time-point in a trial with the express purpose of</li> <li>A method an intervention at a prespecified time-point in a trial with the express purpose of</li></ul></li></ul></li></ul>	<ul> <li>CONSORT (7a) – How sample size was determined.</li> <li>Options:         <ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes T Authors specifically stated that no power calculation was performed</li> <li>No T Any details not provided</li> </ul> </li> <li>CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.</li> <li>Options:         <ul> <li>NA T No interim analysis or apriori defined stopping criteria</li> <li>Yes T Authors apriori defined the rationale, nature and methods for interim analyses or stop criteria</li> <li>Unclear T If any aspect of the rationale, nature and methods for the interim analysis or stop criteria are poorly described</li> <li>No T If any aspect of the rationale, nature and methods are missing or if results are reporte without details provided in the methods section</li> <li>TIPS:                 <ul> <li>Interim analyses: Typically used to assess the safety, feasibility, or establish the preliminal efficacy of an intervention at a prespecified time-point in a trial with the express purpose of the section</li> <li>TIPS:</li> <li>Intervention at a prespecified time-point in a trial with the express purpose of the section</li> <li>TIPS</li> <li>Intervention at a prespecified time-point in a trial with the express purpose of the section</li> <li>Tipose the section</li></ul></li></ul></li></ul>	<ul> <li>Options:         <ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes T Authors specifically stated that no power calculation was performed</li> <li>No T Any details not provided</li> </ul> </li> <li>CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.         <ul> <li>Options:</li> <li>NA T No interim analysis or apriori defined stopping criteria</li> <li>Yes T Authors apriori defined the rationale, nature and methods for interim analysis or stop criteria</li> <li>Unclear T If any aspect of the rationale, nature and methods for the interim analysis or stop criteria are poorly described</li> <li>No T If any aspect of the rationale, nature and methods are missing or if results are reporter without details provided in the methods section</li> <li>TIPS:</li> <li>Interim analyses: Typically used to assess the safety, feasibility, or establish the preliminate efficacy of an intervention at a prespecified time-point in a trial with the express purpose of the section</li> </ul> </li> </ul>		the trial should be stopped altogether. <u>Do n</u>	not mistake this type of analysis for a midpo
<ul> <li>CONSORT (7a) – How sample size was determined.         <ul> <li>Options:                 <ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes T Authors specifically stated that no power calculation was performed</li> <li>No T Any details not provided</li> </ul> </li> </ul> </li> <li>CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.                     <ul> <li>Options:</li> <li>NA T No interim analysis or apriori defined stopping criteria</li> <li>Yes T Authors apriori defined the rationale, nature and methods for interim analyses or stocriteria</li> <li>Unclear T If any aspect of the rationale, nature and methods for the interim analysis or stopriteria are poorly described</li> <li>No T If any aspect of the rationale, nature and methods are missing or if results are reporte without details provided in the methods section</li> <li>TIPS:</li></ul></li></ul>	<ul> <li>CONSORT (7a) – How sample size was determined.</li> <li>Options:         <ul> <li>Yes T Provides the details of the power calculation (i.e., based on \] and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes T Authors specifically stated that no power calculation was performed</li> <li>No T Any details not provided</li> </ul> </li> <li>CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.         <ul> <li>Options:</li> <li>NA T No interim analysis or apriori defined stopping criteria</li> <li>Yes T Authors apriori defined the rationale, nature and methods for interim analyses or stop criteria</li> <li>Unclear T If any aspect of the rationale, nature and methods for the interim analysis or stop criteria are poorly described</li> <li>No T If any aspect of the rationale, nature and methods are missing or if results are reporte without details provided in the methods section</li> <li>TIPS:</li> <li>Interim analyses: Typically used to assess the safety, feasibility, or establish the prelimina efficacy of an intervention at a prespecified time-point in a trial with the express purpose of decisions around whether the trial should continue as planned, if modifications are required the trial should be stopped altogether. 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					No T Any aspect is not described	

If the calculated sample size listed in the Registry and Manuscript are different, please note both values (e.g., Reg: ##; Man: ##).

Supplementary Methods 7: Data Extraction Reference Guide - Pharmacological RCTs

	DETAILS – If different, were the changes noted in the Manuscript? <ul> <li>Options:</li> </ul>
	<ul> <li>Yes T The difference(s) in Sample Size were clearly stated and explained.</li> <li>No T The difference(s) in Sample Size were apparent but not explained.</li> <li>Not Applicable T There was no difference in the Sample Size calculations between the Re and the Manuscript.</li> <li>Not Applicable T No clinical trial registry data available.</li> </ul>
RESU	LTS
Partic	ipant Flow
•	CONSORT (13) – Participant flow diagram (a diagram is strongly recommended). o Options:
	<ul> <li>Options:</li> <li>Yes T A clear depiction of participant flow was provided</li> <li>No T Not provided</li> </ul>
•	<ul> <li>CONSORT (13b) – For each group, losses and exclusions after randomization, together with reasons.</li> <li>Options:         <ul> <li>NA T If authors specifically state there were no losses/exclusions post randomization</li> <li>Yes T Provided a complete account of all randomized participants</li> <li>Unclear T If all randomized participants are accounted for but the details of any participant unclear</li> <li>No T If any details of any participant are missing</li> </ul> </li> </ul>
Partic	ipants, Analyses & Outcomes
•	<ul> <li>CONSORT (15) – A table showing baseline demographic and clinical characteristics for each group.</li> <li>Options:         <ul> <li>Yes T A unique table displaying demographic data is provided</li> <li>No T Table not provided</li> </ul> </li> </ul>
•	CONSORT (13a) – For each group, the number of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome. <ul> <li>Options:</li> </ul>
	<ul> <li>Yes T All requisite details were provided</li> <li>No T Any of the requisite details are not provided</li> </ul>
	∘ TIP:
	<ul> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> </ul>
•	<ul> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> <li>CONSORT (16) – For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.</li> <li>Options:</li> </ul>

•	<b>Yes</b> T Must provide details of how many participants from each group were included within each analysis
•	<b>Unclear</b> T The authors suggest that analyses were performed according to intention-to-treat but failed to provide a description of how missing data from drop-outs or testing errors was accounted for
•	<b>Unclear</b> T The authors provided numbers for the analysis but did not indicate that analyses adhered to intention-to-treat principles <b>No</b> T Data not provided
• TIPS:	
•	This information is typically reported in the main results tables in the form of $(n = #)$ but may also be found in the results section.
•	Double check the flow diagram to check for potential dropouts/missing data.
	<ul> <li>If any participants withdrew or were lost to follow-up, the authors should disclose how their missing data was treated.</li> </ul>
•	Must include sample sizes in the body of the Results or directly within the Results tables.
size and its pred	) – For each primary and secondary outcome, results for each group, and the estimated effect cision (such as 95% confidence interval).
<ul> <li>Options</li> </ul>	Yes T Authors must provide the raw baseline data, raw or adjusted follow-up data, change scores or effect sizes, <i>AND</i> 95% CI data
•	No T Missing any of the aforementioned data
recommended.	) – For binary outcomes, presentation of both absolute and relative effect sizes is
<ul> <li>Options</li> </ul>	
	<b>NA</b> T If no binary outcomes are tracked/reported <b>Yes</b> T Authors provide an indication of the actual number of observations relative to the expected number of observations <b>AND</b> whether the ratio of observations differed between groups
	No T Missing any of the aforementioned data
	<ul> <li>Results of any other analyses performed, including subgroup analyses and adjusted guishing pre-specified from exploratory.</li> </ul>
	<b>NA</b> T If no subgroup or sensitivity analysis were performed <b>Yes</b> T If the results of any analysis other than the main intervention effects were performed and
•	reported No T If the results of any analysis other than the main intervention effects were performed but not reported
DETAILS – What Options	t was the outcome of this trial?
•	Positive T As hypothesized, there was a significant difference in the primary outcome
÷	<b>Negative</b> T Contrary to the hypothesis, there was no significant difference in the primary outcome <b>Unclear</b> T If the primary findings are not well defined or not interpretable <b>Mixed T</b> Only an option for trials with more than one primary outcome (rare)
•	<b>Mixed T</b> Only an option for trials with more than one primary outcome (rare)
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#### BMJ Open

	CONSORT (14b) Why the trial and d or was standed
•	CONSORT (14b) – Why the trial ended or was stopped. o Options:
	<ul> <li>Options:</li> <li>NA T If the trial appeared to finish as planned (i.e., achieved target sample size and conditional structure)</li> </ul>
	the intervention and follow-up tested as intended)
	<ul> <li>Yes T If the trial stopped early or was extended AND a full justification was provided</li> </ul>
	<ul> <li>Unclear T if the trial stopped early of was extended AND a full justification was provided</li> <li>Unclear T if the trial stopped early or was extended AND the authors made special note</li> </ul>
	fact without providing an adequate justification
	<ul> <li>Unclear T If the trial stopped early or was extended AND an inadequate discussion was</li> </ul>
	<ul> <li>No T If the trial stopped early or was extended BUT an adequate justification was not pro</li> </ul>
	• TIP:
	<ul> <li>The majority of studies will finish as planned and will be assigned an NA</li> </ul>
•	CONSORT (14a) – Dates defining the periods of recruitment and follow-up. o Options:
	<ul> <li>Yes T Must provide both the dates of when the trial was open to recruitment AND at leas</li> </ul>
	a specific date as to when participant follow-up finished
	<ul> <li>Unclear T Authors provided recruitment dates but only eluded to how long the follow-up  </li> </ul>
	lasted (e.g., 12 months)
	<ul> <li>No T Only provided dates of recruitment but not follow-up OR not at all</li> </ul>
DETA	ILS
•	Recruitment (enrollment) start date:
	<ul> <li>Note details</li> </ul>
	Nomenclature: Date format T MM/YY
	<ul> <li>NR T If not reported</li> </ul>
•	Recruitment (enrollment) end date: ○ Note details
	New years left was Detailed and TANADOA
•	Trial start date:
	<ul> <li>Note details</li> </ul>
	<ul> <li>Nomenclature: Date format T MM/YY</li> </ul>
	<ul> <li>NR T If not reported</li> </ul>
•	Trial end date:
	<ul> <li>Note details</li> </ul>
	• Nomenclature: Date format T MM/YY
	<ul> <li>NR T If not reported</li> </ul>

#### 

# **Randomization & Testing**

- Number of subjects randomized to PHARMA intervention:
  - PHARMA (4) T Note details for each group as relevant
  - o NR T If not reported
- Number of subjects randomized to Usual Care/Control:
  - Note details
  - NR T If not reported
- Number of PHARMA participants tested at baseline:
  - PHARMA (4) T Note details for each group as relevant
  - NR T If not reported
- Number of Usual Care/Control participants tested at baseline:
  - Note details
  - NR T If not reported
- Number of PHARMA participants tested at follow-up:
  - PHARMA (4) T Note details for each group as relevant
  - **NR** T If not reported

## Number of Usual Care/Control participants tested at follow-up:

- Note details
- o NR T If not reported

## Demographics

- Total number of subjects:
  - Note details
  - NR T If not reported

## • Number of male participants:

- Note details
- NR T If not reported
- Number of female participants:
  - Note details
  - NR T If not reported
- Average age of all participants:
  - Note details
  - o NR T If not reported
- Average age of PHARMA participants:

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- Note details
- NR T If not reported
- Average age of Usual Care/Control participants:
  - Note details
  - o NR T If not reported

#### **Medical Characteristics**

- Average disease duration (*months*):
  - Not Applicable
  - <6 months</li>
  - <12 months</li>
  - <24 months</li>
  - o <60 months
  - <120 months
  - **ﷺ**nonths
  - **NR** T If not reported

## Comorbidities

#### Hypertension (n):

- Note details
- NR T If not reported
- NA T If listed in exclusion criteria

#### Hypercholesterolemia (n):

- Note details
- NR T If not reported
- NA T If listed in exclusion criteria

#### Diabetes (n):

- Note details
- NR T If not reported
- NA T If listed in exclusion criteria

## **Pharmaceutical Outcomes**

#### PHARMA (4) & UC Compliance: Number:

- Note details
- NR T If not reported OR if trial reports compliance as X% attended X% of sessions

**Percent:** Note details

Hypertension (%): Note details

Diabetes (%): Note details

Hypercholesterolemia (%): Note details

PHARMA (4) & UC RDI:		
	Number:	Percent: Note details
	Note details	
	<ul> <li>NR T If not reported</li> <li>Cannot be NA</li> </ul>	
PHARMA (4) & UC Dose		
	Number:	Percent: Note details
	Note details	
	NR T If not reported     If no dose modifications	occurred list as '0' not NA
PHARMA (4) & UC Treat		Demonstration 1.4.1
	<ul><li>Number:</li><li>Note details</li></ul>	Percent: Note details
	NR T If not reported	
		occurred list as '0' not NA
l		
Exclusion		
PHARMA (4) Exclusion -		
	Number:	Percent: Note details
	Note details	
	<ul> <li>NR T If not reported</li> <li>If no participants were ex</li> </ul>	cluded list as '0' not NA
UC Exclusion –	Number:	Percent: Note details
	Note details	
	<ul> <li>NR T If not reported</li> <li>If no participants were ex</li> </ul>	cluded list as '0' not NA
• TIP ( <i>if patient attritic</i>		moutation) and authors confirm that the rea
	without the imputed data.	mputation) and authors confirm that the res
<ul> <li>For trials rep</li> </ul>	orting intention to treat analyses, 'zero	exclusion' cannot be assigned unless confir
analysis san	ple sizes defined in either the body of t	he results or the results tables.

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3	CONSORT – HARMS
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5	HARMS (19a) – If the study collected data on harms and benefits, the title or abstract should so state.
6	
7	<ul> <li>Options:</li> <li>NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented</li> </ul>
8	
9	risks and is no longer the question
10	<ul> <li>Yes T If authors mention safety or AEs anywhere in the title or abstract</li> </ul>
11	<ul> <li>No T If safety or AEs are not mentioned in these sections</li> </ul>
12	• TIPS:
13	<ul> <li>IMPORTANT – All Phase I-II, by definition, should report safety outcomes. Thus, the safety</li> </ul>
14	of the intervention should be assessed and reported on.
15	
16	<ul> <li>HARMS (19b) – If the trial addresses both harms and benefits, the introduction should so state.</li> </ul>
17	• Options:
18	• <b>NA</b> T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented
19	risks and is no longer the question
20	Yes T Authors should state the safety of the intervention is in question OR they should state that
21	one of the trial objectives (typically last paragraph of the intro) is to assess the safety of the
22	intervention.
23	<ul> <li>No T Not mentioned</li> </ul>
24	
25	LADNO (40a) List addressed advance such a with definitions for each (when relevant attention to provide
26	<ul> <li>HARMS (19c) – List addressed adverse events with definitions for each (when relevant, attention to grading,</li> </ul>
27	expected vs. unexpected AEs, reference to standardized and validated definition, and description of new definitions).
28	• Options:
29	<ul> <li>NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented</li> </ul>
30	risks and is no longer the question
31	<ul> <li>Yes T Authors listed AND defined the potential/anticipated AEs being studied</li> </ul>
32	<ul> <li>Unclear T Authors listed the AEs but failed to define them</li> </ul>
33	<ul> <li>No T Details not provided</li> </ul>
34 25	• TIPS:
35	<ul> <li>For trials reporting AEs as the primary and secondary outcomes, the definitions for the outcomes</li> </ul>
36 37	count towards defining the AEs.
38	• HARMS (19d) – Clarify how harms-related data was collected (mode of collection, timing, attribution methods,
39 40	intensity of ascertainment, and harms-related monitoring and stopping rules).
40	• Options:
41 42	<ul> <li>NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented</li> </ul>
42 43	risks and is no longer the question
43 44	<ul> <li>Yes T Authors should clearly state how, when AND by whom AE data was collected</li> </ul>
44 45	• •
45	<ul> <li>Unclear T Authors fail to properly describe a single aspect (how, when, by whom) of how the AE</li> </ul>
40	data was collected but adequately describe all other aspects
47	No T Details not provided
48 49	o TIPS:
	<ul> <li>For trials reporting AEs as the primary and secondary outcomes, the collection methods for the</li> </ul>
50 51	outcomes count towards collecting the AEs.
52	
52 53	• HARMS (19e) – Describe plans for presenting and analyzing information on harms (including coding, handling
55 54	of recurrent event, specification of timing issues, handling of continuous measures, and statistical analyses).
54 55	• Options:
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- NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
- Yes T Authors should clearly state how AE data was analyzed
- Unclear T Authors fail to properly describe a single aspect of how the AE data was analyzed but adequately describe all other aspects
- No T Details not provided

## **GENERAL TIPS FOR HARMS:**

- If authors fail to explicitly state if AEs were attributable to the intervention, check to see if there were analyses comparing AE frequency or relative risk per arm.
  - o If analyses were performed:
    - For AEs which occur significantly more frequently within the intervention group(s) T list details for those specific AEs under 'intervention-related'
    - For AEs which do not occur significantly more frequently within the intervention group(s) T list details for those specific AEs under 'non-intervention-related'
  - If analyses were not performed:
    - Rate 'intervention-related' AEs as NR
    - List all reported AEs for both groups as 'non-intervention-related'
- For trials reporting AEs as the primary and secondary outcomes, the analysis methods for the outcomes count towards analyzing the AEs.

## Intervention-related AEs

- DETAILS Did any intervention-related AE occur?
  - NA T Specifically stated that no intervention-related AEs occurred
  - Yes T Specifically stated the type and number of intervention-related AEs
  - o Unclear T The numbers are provided but the details are unclear
  - **No** T Details not provided

## • DETAILS – If so, how many?

- o Note pertinent details
- **NR** T If not reported

## • DETAILS – How were intervention-related AE defined?

- Note pertinent details
- **NR** T If not reported

## DETAILS – How were intervention-related AE monitored/tracked?

- o Note pertinent details
- **NR** T If not reported

## Non-Intervention-related AEs

• DETAILS – Did any non-intervention-related AE occur?

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- **NA** T Specifically stated that no intervention-related AEs occurred 0
- Yes T Specifically stated the type and number of intervention-related AEs
- **Unclear** T The numbers are provided but the details are unclear
- **No** T Details not provided

## DETAILS – If so, how many?

- Note pertinent details
- **NR** T If not reported

## DETAILS – How were non-intervention-related AE defined?

- Note pertinent details
- NR T If not reported

## DETAILS - How were non-intervention-related AE monitored/tracked?

- Note pertinent details
- NR T If not reported

# **AEs Per Group**

- DETAILS How many AEs were reported for the PHARMA (4) & UC groups?
  - Note pertinent details
  - **NR** T If not reported

# HARMS Continued...

HARMS (19f) – Describe for each arm the participant withdrawals that are due to harms and their experiences with the allocated treatment.

#### Options: 0

- NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
- NA T If the authors specifically stated there were no AEs OR that no participant withdrew/was lost . to follow-up due to AEs
- Yes T If the authors clearly identify the number of participants who withdrew or were lost to . follow-up due to AEs
- No T If the reasons why participants withdrew or were lost-to-follow-up are not provided for every • applicable case
- HARMS (19g) Provide denominators for analyses on harms.
  - **Options:** 
    - NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
    - **NA** T If the authors specifically stated there were no AEs
    - Yes T Reference numbers provided for AE risk calculations •
    - **No** T Details not provided •
- HARMS (19h) Presents absolute risk per arm and per AE type, grade, and seriousness, and present appropriate metrics for recurrent events, continuous variables, and scale variables.

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	○ Options:
	<ul> <li>NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented</li> </ul>
	risks and is no longer the question
	<ul> <li>NA T If the authors specifically stated there were no AEs</li> </ul>
	<ul> <li>Yes T If the authors present the absolute risk per arm AND per adverse event type/grade AND</li> </ul>
	describe the frequency of AEs
	<ul> <li>No T Details not provided</li> </ul>
•	HARMS (19i) – Describes any subgroup analyses and exploratory analyses for harms.
•	<ul> <li>Options:</li> </ul>
	<ul> <li>NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented</li> </ul>
	risks and is no longer the question
	<ul> <li>NA T If the authors specifically stated there were no AEs</li> </ul>
	<ul> <li>Yes T If the authors present the results of subgroup analyses or exploratory analyses</li> </ul>
	<ul> <li>No T Details not provided</li> </ul>
	- NOT Details not provided
•	HARMS (19j) – Provide a balanced discussion of benefits and harms with emphasis on study limitation,
	generalizability, and other sources of information on harms.
	○ Options:
	<ul> <li>NA T Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented</li> </ul>
	risks and is no longer the question
	<ul> <li>NA T If the authors specifically stated there were no AEs</li> </ul>
	<ul> <li>Yes T Should formally address any AEs in the Discussion in the context of trial limitations and</li> </ul>
	whether the risk intervention-related AEs should be considered when implementing or conductin
	further tests of the intervention in question.
	<ul> <li>No T Not discussed</li> </ul>
DISCUS	SION & OTHER
•	CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant,
•	CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.
•	CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses. o Options:
•	CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses. • Options: • Yes T If authors listed major sources of potential bias or measurement error AND provided basic
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and</li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.         <ul> <li>Options:</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basid details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.         <ul> <li>Options:</li> <li>Yes T Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options:</li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.         <ul> <li>Options:</li> <li>Yes T Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.         <ul> <li>Options:</li> <li>Yes T Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
•	<ul> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes T If authors listed major sources of potential bias or measurement error AND provided basid details as to how these factors may have influenced results</li> <li>Unclear T Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No T Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.         <ul> <li>Options:</li> <li>Yes T Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>

- No T None of these aspects were not adequately discussed within the context of other research (past and future)
- CONSORT (22) Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.
  - Options:

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- Yes T Authors should not overstate non-significant or modestly altered endpoints; nor should they
  dismiss/ignore/fail to adequately describe non-significant findings for any of the primary outcomes
  in favor of discussing secondary outcomes
- No T Authors do not present an unbiased interpretation of their findings
- o TIP:
  - Look closely at the results for the primary outcomes (data tables). The first paragraph of the Discussion should summarize these results without inflating/downplaying the findings. Similarly, the Conclusion should also provide an unbiased summary of the main trial findings.
- CONSORT (23) Registration number and name of trial registry.
  - Options:
    - Yes T If the number was provided
    - Yes T If authors clearly stated the trial was not registered
    - No T If the number was not provided
  - o TIP:
    - Check the abstract, methods, and footnotes/margins of the paper to locate this number.
- DETAILS If so, please list.
  - Note pertinent details
- CONSORT (24) Where the full trial protocol can be accessed, if available.
  - Options:
    - Yes T If the full protocol or a link to the full protocol is provided in the primary manuscript or as an online supplement
    - No T Data not provided
  - o TIP:
    - Check the abstract, methods, and footnotes/margins of the paper to locate this number.
- DETAILS If so, please provide the URL:
  - Note pertinent details
- CONSORT (25) Sources of funding and other support, role of funders.
  - Options:
    - Yes T If described
    - Unclear T If described either the funder or the role but not both
    - No T Not described
  - o **TIP:** 
    - Similar to the registration number, check the footnotes, margins, and any supplemental information listed between the Conclusion and the Reference list.
- DETAILS If so, please provide the details:
  - o Note pertinent details

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# COCHRANE – Risk of Bias

# • Selection Bias: Random sequence generation

- **High** T Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence
- $\circ$  Low T Random sequence generation method should produce comparable groups
- o Unclear T Not described in sufficient detail to permit judgement

# • Selection Bias: Allocation concealment

- **High** T Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
- o Low T Intervention allocations likely could not have been foreseen in before or during enrollment
- o Unclear T Not described in sufficient detail to permit judgement

# Performance Bias: Blinding (participants & personnel)

- **High** T Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
- Low T Blinding was likely effective
- o Unclear T Not described in sufficient detail to permit judgement

# • Detection Bias: Blinding (outcome assessment)

- High T Detection bias due to knowledge of the allocated interventions by outcome assessors
- o Low T Blinding was likely effective
- o Unclear T Not described in sufficient detail to permit judgement

# Attrition Bias: Incomplete outcome data

- o High T Attrition bias due to amount, nature or handling of incomplete outcome data
- Low T Handling of incomplete outcome data was complete and unlikely to have produced bias
- Unclear T Insufficient reporting of attrition/exclusions to permit judgment (e.g., number randomized not stated, no reasons for missing data provided)

# Reporting Bias: Selective reporting

- High T Reporting bias due to selective outcome reporting
- Low T Selective reporting bias not detected
- $\circ \quad \textbf{Unclear} \ \mathsf{T} \ \mathsf{Insufficient} \ \mathsf{information} \ \mathsf{to} \ \mathsf{permit} \ \mathsf{judgment}$

# • Other sources of bias

- $\circ$   $\,$  High T Bias due to problems not covered elsewhere in the criteria
- Low T No other bias detected
- **Unclear** T There may be a risk of bias, but there is insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem will introduce bias

# Quality Comments: Justify 'high-risk' & 'unclear' decisions

• Please note pertinent details

# JADAD Score

- Randomization Score:
  - 1 point if randomization is mentioned
  - o 1 additional point if the method of randomization is appropriate
  - Deduct 1 point if the method of randomization is inappropriate (minimum 0)

#### • Blinding Score:

- o 1 point if blinding is mentioned
- o 1 additional point if the method of blinding is appropriate
- Deduct 1 point if the method of blinding is inappropriate (minimum 0)

## • Account of All Patient Score:

o 1 point if the fate of all patients in the trial is known. If there are no data the reason is stated.

## Supplementary Table 1: List of Excluded Exercise Records

Supplementary Table 1: List of Excluded Exercise R
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Author	Year	Title	Primary Exclusi Criteria
Cumming et al.	2008	Cluster randomised trial of a targeted multifactorial intervention to prevent falls among older people in hospital	Not exercise-base
Dixon et al.	2008	Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial	Not exercise-base
Hollinghurst et al.	2008	Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain: economic evaluation	Not exercise-base
Kerse et al.	2008	Does a functional activity programme improve function, quality of life, and falls for residents in long term care? Cluster randomised controlled trial	Exercise session duration too short
Kinmonth et al.	2008	Efficacy of a theory-based behavioural intervention to increase physical activity in an at-risk group in primary care (ProActive UK): a randomised trial	Not exercise-base
Lautenschlager et al.	2008	Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial	Not exercise-base
Li et al.	2008	The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study	Secondary analys
Little et al.	2008	Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain	Not exercise-base
Lloyd & Barnett	2008	Physical activity and risk of diabetes	Not a RCT
Lloyd et al.	2008	Physical activity and risk of diabetes	R/C paper
Mitka, M.	2008	Therapies aim to boost "good" cholesterol	R/C paper
NA	2008	Summaries for patients. A combination treatment for pulmonary hypertension	Not a RCT
Pasanen et al.	2008	Neuromuscular training and the risk of leg injuries in female floorball players: cluster randomised controlled study	Exercise session duration too short
Barton et al.	2009	Lifestyle interventions for knee pain in overweight and obese adults aged $\geq$ 45: Economic evaluation of randomised controlled trial	Secondary analys
Boysen et al.	2009	ExStroke Pilot Trial of the effect of repeated instructions to improve physical activity after ischaemic stroke: A multinational randomised controlled clinical trial	Not exercise-base
Engebretsen et al.	2009	Radial extracorporeal shockwave treatment compared with supervised exercises in patients with subacromial pain syndrome: Single blind randomised study	Not exercise-base
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-action randomized controlled trial	Secondary analys
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial	Duplicate
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial	Secondary analys
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-action randomized controlled trial.	Secondary analys
Hupperets et al.	2009	Effect of unsupervised home based proprioceptive training on recurrences of ankle sprain: Randomised controlled trial	Not exercise-base
Jafar et al.	2009	Community-based interventions to promote blood pressure control in a developing country: A cluster randomized trial	Not exercise-base
Jarvik et al.	2009	Surgery versus non-surgical therapy for carpal tunnel syndrome: a randomised parallel-group trial	Not exercise-base
Jenkinson et al.	2009	Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: Randomised controlled trial	Not exercise-base
Karthikeyan et al.	2009	Treatment of intermittent claudication	R/C paper
Khattri, S.	2009	Treadmill exercise or resistance training in patients with peripheral arterial disease	R/C paper
Khattri, S.	2009	Treadmill exercise or resistance training in patients with peripheral arterial disease	Not a RCT
Kuijper et al.	2009	Cervical collar or physiotherapy versus wait and see policy for recent onset cervical radiculopathy: Randomised trial	Not exercise-base
Lautenschlager et al.	2009	Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: A randomized trial	Duplicate
Lautenschlager et al.	2009	Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: A randomized trial.	Not exercise-base

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclus Criteria
Lawton et al.	2009	Exercise on prescription for women aged 40-74 recruited through primary care: Two year randomised controlled trial	Not exercise-bas
Marshall et al.	2009	Losing weight in moderate to severe obstructive sleep apnoea	R/C paper
McDermott et al.	2009	Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial	Duplicate
Mead, G.	2009	Exercise after stroke Is beneficial but how best to increase physical activity is unknown	R/C paper
Misra, A.	2009	Prevention of type 2 diabetes: the long and winding road	R/C paper
Morey et al.	2009	Effects of home-based diet and exercise on functional outcomes among older, overweight long- term cancer survivors: RENEW: a randomized controlled trial	Not exercise-bas
O'Connor et al.	2009	Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial	Duplicate
Patwala et al.	2009	Maximizing Patient Benefit From Cardiac Resynchronization Therapy With the Addition of Structured Exercise Training. A Randomized Controlled Study	Duplicate
Ravaud et al.	2009	ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: Pragmatic randomised controlled trial	Not exercise-ba
Sackley et al.	2009	Effects of a physiotherapy and occupational therapy intervention on mobility and activity in care home residents: A cluster randomised controlled trial	Not exercise-ba
Schmitz et al.	2009	Weight lifting in women with breast-cancer-related lymphedema	Duplicate
Schweickert et al	2009	Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial	Not exercise-ba
Soligard et al.	2009	Comprehensive warm-up programme to prevent injuries in young female footballers: Cluster randomised controlled trial	Not studying ad
Subak et al.	2009	Weight loss to treat urinary incontinence in overweight and obese women	Not exercise-ba
Van Linschoten et al.	2009	Supervised exercise therapy versus usual care for patellofemoral pain syndrome: An open label randomised controlled trial	Not exercise-ba
Bennell et al.	2010	Efficacy of standardised manual therapy and home exercise programme for chronic rotator cuff disease: Randomised placebo controlled trial	Not exercise-ba
Bleakley et al.	2010	Effect of accelerated rehabilitation on function after ankle sprain: Randomised controlled trial	Not exercise-ba
Crawshaw et al.	2010	Exercise therapy after corticosteroid injection for moderate to severe shoulder pain: Large pragmatic randomised trial	Not exercise-ba
Frobell et al.	2010	A randomized trial of treatment for acute anterior cruciate ligament tears	Not exercise-ba
Goodpaster et al.	2010	Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial	Not exercise-ba
Lacomba et al.	2010	Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: Randomised, single blinded, clinical trial	Not exercise-ba
Lo et al.	2010	Robot-assisted therapy for long-term upper-limb impairment after stroke	Not exercise-ba
Logan et al.	2010	Community falls prevention for people who call an emergency ambulance after a fall: randomised controlled trial	Not exercise-ba
Lombard et al.	2010	A low intensity, community based lifestyle programme to prevent weight gain in women with young children: Cluster randomised controlled trial	Not exercise-ba
Rock et al.	2010	Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial	Not exercise-ba
Schmitz et al.	2010	Weight lifting for women at risk for breast cancer-related lymphedema: a randomized trial	Duplicate
Sixt et al.	2010	Long- but not short-term multifactorial intervention with focus on exercise training improves coronary endothelial dysfunction in diabetes mellitus type 2 and coronary artery disease	Not exercise-ba
van Eijk-Hustings et al.	2010	A randomized trial of tai chi for fibromyalgia	R/C paper
Van Gelder et al.	2010	Lenient versus strict rate control in patients with atrial fibrillation	Not exercise-ba
Wang et al.	2010	A randomized trial of tai chi for fibromyalgia	Not exercise-ba
Wearden et al.	2010	Nurse led, home based self help treatment for patients in primary care with chronic fatigue syndrome: randomised controlled trial	Not exercise-ba
Zhan & Wu	2010	A randomized trial of tai chi for fibromyalgia	Duplicate
Zhou et al.	2010	A randomized trial of tai chi for fibromyalgia	Duplicate

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclusion Criteria
Andrews et al.	2011	Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial	Not exercise-base
Bleijenberg & Knoop	2011	Chronic fatigue syndrome: Where to PACE from here?	Not a RCT
Church et al.	2011	Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: A randomized controlled trial	Duplicate
Church et al.	2011	Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: A randomized controlled trial	Duplicate
Devoogdt et al.	2011	Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: Randomised controlled trial	Not exercise-base
Dubowitz et al.	2011	Exercise interventions and glycemic control in patients with diabetes	R/C paper
Dubowitz et al.	2011	Exercise interventions and glycemic control in patients with diabetes	Not a RCT
Duncan et al.	2011	Body-weight-supported treadmill rehabilitation after stroke	R/C paper
Duncan et al.	2011	Body-weight-supported treadmill rehabilitation after stroke	Not a RCT
Edelmann et al.	2011	Exercise Training Improves Exercise Capacity and Diastolic Function in Patients With Heart Failure With Preserved Ejection Fraction Results of the Ex-DHF (Exercise training in Diastolic Heart Failure) Pilot Study	Duplicate
Engel, C	2011	Tailored cognitive-behavioral therapy plus exercise training improved clinical and functional outcomes in fibromyalgia	R/C paper
Giakoumakis, J.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
Glazener et al.	2011	Urinary incontinence in men after formal one-to-one pelvic-floor muscle training following radical prostatectomy or transurethral resection of the prostate (MAPS): two parallel randomised controlled trials	Not exercise-base
Gondoni & Liuzzi	2011	Diet and physical activity interventions in severely obese adults	R/C paper
Gondoni & Liuzzi	2011	Diet and physical activity interventions in severely obese adults	Not a RCT
Hemmingsson et al.	2011	Diet and physical activity interventions in severely obese adults	Duplicate
Hemmingsson et al.	2011	Diet and physical activity interventions in severely obese adults	Not a RCT
Hu, F.	2011	Diet and exercise for new-onset type 2 diabetes?	R/C paper
Jebb et al.	2011	Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial	Not exercise-base
Jolly et al.	2011	Comparison of range of commercial or primary care led weight reduction programmes with minimal intervention control for weight loss in obesity: Lighten Up randomised controlled trial	Not exercise-base
Kewley, A.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
Khan et al.	2011	Prescribing exercise in primary care	R/C paper
Kindlon, T.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
Langhorne et al.	2011	Stroke rehabilitation	R/C paper
McArthur et al.	2011	Post-acute care and secondary prevention after ischaemic stroke	R/C paper
Mitchell, J.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
Pearse et al.	2011	Managing perioperative risk in patients undergoing elective non-cardiac surgery	R/C paper
Rice, K.	2011	A COPD disease management program reduced a composite of hospitalizations or emergency department visits	wrong journal
Rolla & Bucca	2011	Placebo and other interventions in asthma	Not a RCT
Shinohara, M.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
Spink et al.	2011	Effectiveness of a multifaceted podiatry intervention to prevent falls in community dwelling older people with disabling foot pain: randomised controlled trial	Not exercise-base
Stouten et al.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
Tilbrook et al.	2011	Yoga for chronic low back pain: A randomized trial	Not exercise-base
Villareal et al.	2011	Weight loss, exercise, or both and physical function in obese older adults	Duplicate
Vlaeyen et al.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT
White et al.	2011	Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial	Duplicate

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclu Criteria			
Bennell et al.	2012	Management of osteoarthritis of the knee	R/C paper			
Blumenthal et al.	2012	Effects of exercise training on depressive symptoms in patients with chronic heart failure: The HF-ACTION randomized trial.	Duplicate			
Blumenthal et al.	2012	Effects of exercise training on depressive symptoms in patients with chronic heart failure: the HF- ACTION randomized trial	Secondary analy			
Blumenthal et al.	2012	Exercise and pharmacological treatment of depressive symptoms in patients with coronary heart disease: results from the UPBEAT (Understanding the Prognostic Benefits of Exercise and Antidepressant Therapy) study	Secondary anal			
Bronfort et al.	2012	Spinal manipulation, medication, or home exercise with advice for acute and subacute neck pain: a randomized trial	Not exercise-ba			
Chalder et al.	2012	Facilitated physical activity as a treatment for depressed adults: Randomised controlled trial	Not exercise-ba			
Clemson et al.	2012	Integration of balance and strength training into daily life activity to reduce rate of falls in older people (the LiFE study): Randomised parallel trial	Not exercise-ba			
Ernst, E.	2012	Acute and subacute neck pain	R/C paper			
Franklin, B.	2012	Multifactorial cardiac rehabilitation did not reduce mortality or morbidity after acute myocardial infarction	R/C paper			
Holmgren et al.	2012	Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: Randomised controlled study	Not exercise-ba			
Jakicic et al.	2012	Effect of a stepped-care intervention approach on weight loss in adults: a randomized clinical trial	Not exercise-ba			
Layden et al.	2012	Diagnosis and management of lower limb peripheral arterial disease: Summary of NICE guidance	R/C paper			
Lazzeri et al.	2012	Pelvic floor muscle training after prostate surgery	R/C paper			
Li et al.	2012	Tai chi and postural stability in patients with Parkinson's disease	Not exercise-ba			
Li et al.	2012	Tai chi and postural stability in patients with Parkinson's disease	Not exercise-ba			
McDermott et al.	2012	Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: A randomized trial.				
McDermott et al.	2012	Treadmill exercise and resistance training in patients with peripheral arterial disease with and I without intermittent claudication: A randomized trial.				
Morris, M.	2012	Preventing falls in older people	R/C paper			
O'Connor & Ahmad	2012	Can We Prevent Heart Failure with Exercise?	Not a RCT			
Rejeski et al.	2012	Lifestyle change and mobility in obese adults with type 2 diabetes	Not exercise-ba			
Sossai & Sponga	2012	Physical activity to combat depression in chronic heart failure	R/C paper			
Van De Port et al.	2012	Effects of circuit training as alternative to usual physiotherapy after stroke: Randomised controlled trial	Not exercise-ba			
Waldén et al.	2012	Prevention of acute knee injuries in adolescent female football players: Cluster randomised controlled trial	Not studying ac			
Belardinelli et al.	2013	A 10-year exercise program improved oxygen consumption and quality of life in stable chronic heart failure	R/C paper			
Katz, J.	2013	Surgery and physical therapy did not differ for function in meniscal tears with knee osteoarthritis	Not exercise-ba			
Labrie et al.	2013	Surgery versus physiotherapy for stress urinary incontinence	Not exercise-ba			
Lamb et al.	2013	Emergency department treatments and physiotherapy for acute whiplash: a pragmatic, two-step, randomised controlled trial	Not exercise-ba			
Mascitelli & Goldstein	2013	Statin and exercise prescription	R/C paper			
Mascitelli & Goldstein	2013	Statin and exercise prescription	Not a RCT			
McDermott et al.	2013	Home-based walking exercise intervention in peripheral artery disease: a randomized clinical trial	Not exercise-ba			
Messier et al.	2013	Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes	Not exercise-ba			
Solomon et al.	2013	among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial The influence of hyperglycemia on the therapeutic effect of exercise on glycemic control in	Not a RCT			
		patients with type 2 diabetes mellitus				
Underwood et al.	2013	Exercise for depression in elderly residents of care homes: a cluster-randomised controlled trial	Duplicate			
Van Nimwegen, et al.	2013	Promotion of physical activity and fitness in sedentary patients with Parkinson's disease: Randomised controlled trial	Not exercise-ba			
Wing et al.	2013	Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes	Secondary analy			

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclus Criteria
Wing, R.	2013	A lifestyle intervention did not reduce cardiovascular outcomes in overweight or obese patients with type 2 diabetes	R/C paper
Bennell et al.	2014	Effect of physical therapy on pain and function in patients with hip osteoarthritis: a randomized clinical trial	Not exercise-bas
Bronfort et al.	2014	Spinal manipulation and home exercise with advice for subacute and chronic back-related leg pain: a trial with adaptive allocation	Not exercise-bas
Cooney et al.	2014	Exercise for depression	R/C paper
Goonewardene et al.	2014	Letter to the Editor: Re: Bourke et al., Lifestyle changes for improving disease-specific quality of life in sedentary men on long-term androgen-deprivation therapy for advanced prostate cancer: a randomised controlled trial. Eur Urol 2014;65:865-72; Re: Galvão et al., A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 2014;65:856-64; Re: Keating et al., Androgen-deprivation therapy and diabetes control among diabetic men with prostate cancer. Eur Urol 2014;65:816-24; Re: Jespersen et al., Androgen-deprivation therapy in treatment of prostate cancer and risk of myocardial infarction and stroke: a nationwide Danish population-based cohort study. Eur Urol 2014;65:704-9	Not a RCT
Hunt et al.	2014	A gender-sensitised weight loss and healthy living programme for overweight and obese men delivered by Scottish Premier League football clubs (FFIT): a pragmatic randomised controlled trial	Not exercise-bas
Latham et al.	2014	Effect of a home-based exercise program on functional recovery following rehabilitation after hip fracture: a randomized clinical trial	Not exercise-ba
Li et al.	2014	Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study	Secondary analy
Michaleff et al.	2014	Comprehensive physiotherapy exercise programme or advice for chronic whiplash (PROMISE): a pragmatic randomised controlled trial	Not exercise-ba
Michaleff et al.	2014	Comprehensive physiotherapy exercise programme or advice for chronic whiplash (PROMISE): a pragmatic randomised controlled trial	Not exercise-ba
Pahor et al.	2014	Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial	Not exercise-ba
Pugliese & Balducci	2014	NAVIGATOR: Physical activity for cardiovascular health?	R/C paper
Rhon et al.	2014	One-year outcome of subacromial corticosteroid injection compared with manual physical therapy for the management of the unilateral shoulder impingement syndrome: A pragmatic randomized trial	Not exercise-ba
Sanders & Wyse	2014	In overweight or obese patients with atrial fibrillation, a weight reduction program reduced symptoms	R/C paper
Westman, E.	2014	In overweight or obese patients with diabetes, a lifestyle intervention increased weight loss at 8 years	R/C paper
El-Khoury et al.	2015	Effectiveness of two year balance training programme on prevention of fall induced injuries in at risk women aged 75-85 living in community: Ossébo randomised controlled trial	Not exercise-ba
Fakhry et al.	2015	Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial	Duplicate
Fritz et al.	2015	Early Physical Therapy vs Usual Care in Patients With Recent-Onset Low Back Pain: A Randomized Clinical Trial	Not exercise-ba
Lamb et al.	2015	Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial	Not exercise-ba
Lamb et al.	2015	Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial	Not exercise-ba
Lipscombe, L.	2015	In high-risk pregnant women, an individualized lifestyle intervention reduced gestational diabetes mellitus	R/C paper
March, L.	2015	An exercise program for hands and arms improved hand function in RA controlled with medication	R/C paper
McDermott, M.	2015	Erasing disability in peripheral artery disease: The role of endovascular procedures and supervised exercise	R/C paper
McDermott, M.	2015	Erasing disability in peripheral artery disease: The role of endovascular procedures and supervised exercise	Not a RCT
Moseley et al.	2015	Rehabilitation After Immobilization for Ankle Fracture: The EXACT Randomized Clinical Trial	Not exercise-ba

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclus Criteria
Moseley et al.	2015	Rehabilitation After Immobilization for Ankle Fracture: The EXACT Randomized Clinical Trial	Not exercise-bas
Opava & Bjök	2015	Towards evidence-based hand exercises in rheumatoid arthritis	R/C paper
Sink et al.	2015	Effect of a 24-Month Physical Activity Intervention vs Health Education on Cognitive Outcomes in Sedentary Older Adults: The LIFE Randomized Trial	Secondary analy
Sink et al.	2015	Effect of a 24-Month Physical Activity Intervention vs Health Education on Cognitive Outcomes in Sedentary Older Adults: The LIFE Randomized Trial	Not exercise-bas
Skou et al.	2015	A Randomized, Controlled Trial of Total Knee Replacement	Not exercise-bas
Sussman et al.	2015	Improving diabetes prevention with benefit based tailored treatment: Risk based reanalysis of diabetes prevention program	Not exercise-bas
Anokye et al.	2016	The short-term and long-term cost-effectiveness of a pedometer-based intervention in primary care: A within trial analysis and beyond-trial modelling	R/C paper
Charante et al.	2016	Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial	Not exercise-bas
Gill et al.	2016	Effect of Structured Physical Activity on Overall Burden and Transitions Between States of Major Mobility Disability in Older Persons: Secondary Analysis of a Randomized Trial	Secondary analy
Gill et al.	2016	Effect of structured physical activity on prevention of serious fall injuries in adults aged 70-89: Randomized clinical trial (LIFE study)	Secondary analy
Guralnik et al.	2016	Effect of a Structured Exercise Program on the Overall Burden of Major Mobility Disability Among Older Adults	R/C paper
Iwashyna et al.	2016	Early mobilisation in ICU is far more than just exercise	R/C paper
Jakicic et al.	2016	Effect of Wearable Technology Combined With a Lifestyle Intervention on Long-term Weight Loss: The IDEA Randomized Clinical Trial	Not exercise-bas
Kise et al.	2016	Exercise therapy versus arthroscopic partial meniscectomy for degenerative meniscal tear in middle aged patients: Randomised controlled trial with two year follow-up	Not exercise-bas
Kitzman et al.	2016	Effect of Caloric Restriction or Aerobic Exercise Training on Peak Oxygen Consumption and Quality of Life in Obese Older Patients With Heart Failure With Preserved Ejection Fraction: A Randomized Clinical Trial	Duplicate
Mirelman et al.	2016	Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial	Not exercise-bas
Mirelman et al.	2016	Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial	Not exercise-bas
Morris et al.	2016	Standardized Rehabilitation and Hospital Length of Stay Among Patients With Acute Respiratory Failure: A Randomized Clinical Trial	Not exercise-bas
Mutsaerts et al.	2016	Randomized Trial of a Lifestyle Program in Obese Infertile Women	Not exercise-bas
Patel et al.	2016	Framing Financial Incentives to Increase Physical Activity Among Overweight and Obese Adults: A Randomized, Controlled Trial	Not exercise-bas
Prenner & Rinella	2016	Moderate exercise for nonalcoholic fatty liver disease	Not a RCT
Saposnik et al.	2016	Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVREST): a randomised, multicentre, single-blind, controlled trial	Not exercise-bas
Sit et al.	2016	A smartphone-based exercise adherence intervention for people with metabolic syndrome: A feasibility pilot study	Abstract only
Skou et al.	2016	A Randomized, Controlled Trial of Total Knee Replacement	Duplicate
Teuscher et al.	2016	A Randomized, Controlled Trial of Total Knee Replacement	Duplicate
Wang et al.	2016	Effectiveness of a health promotion programme on self-efficacy and practice of exercise in Chinese metabolic syndrome population: A single-centre, open-label, randomised controlled trial	Abstract only
Winstein et al.	2016	Effect of a Task-Oriented Rehabilitation Program on Upper Extremity Recovery Following Motor Stroke: The ICARE Randomized Clinical Trial	Not exercise-bas
Wise, J.	2016	Moderate physical activity in older adults is not associated with reduced cardiovascular events	R/C paper
Wise, J.	2016	Activity trackers, even with cash incentives, do not improve health	R/C paper
Allen et al.	2017	Patient, Provider, and Combined Interventions for Managing Osteoarthritis in Primary Care: A Cluster Randomized Trial	Not exercise-bas
Bayer et al.	2017	Early versus delayed rehabilitation after acute muscle injury	R/C paper
Bennell et al.	2017	Effectiveness of an Internet-Delivered Exercise and Pain-Coping Skills Training Intervention for Persons With Chronic Knee Pain: A Randomized Trial	Not exercise-bas

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclusi Criteria
Bennell et al.	2017	Internet-delivered exercise and pain-coping skills training for chronic knee pain	R/C paper
Brach et al.	2017	Effectiveness of a Timing and Coordination Group Exercise Program to Improve Mobility in Community-Dwelling Older Adults: A Randomized Clinical Trial	Not exercise-base
Brindal, E.	2017	Weight management programmes of extended duration	R/C paper
Buhagiar et al.	2017	Effect of Inpatient Rehabilitation vs a Monitored Home-Based Program on Mobility in Patients With Total Knee Arthroplasty: the HIHO Randomized Clinical Trial	Not exercise-base
Clark et al.	2017	Guided graded exercise self-help plus specialist medical care versus specialist medical care alone for chronic fatigue syndrome (GETSET): a pragmatic randomised controlled trial	Not exercise-base
Clauw, D.	2017	Guided graded exercise self-help as a treatment of fatigue in chronic fatigue syndrome	R/C paper
Dawes et al.	2017	Impact of volunteer-led running groups for women affected by homelessness: A qualitative study of the charity, A Mile in Her Shoes	Not a RCT
Fong et al.	2017	Novel aquatic physiotherapy programme for elderly Chinese adults with osteoarthritis of the knee: A randomised controlled trial	Abstract only
Juch et al.	2017	Effect of Radiofrequency Denervation on Pain Intensity Among Patients With Chronic Low Back Pain: The Mint Randomized Clinical Trials	Not exercise-base
Kwakkel & van Wegen	2017	Family-delivered rehabilitation services at home: is the glass empty?	Not a RCT
Liu et al.	2017	Effect of health literacy and exercise interventions on glycated haemoglobin levels in Chinese patients with type 2 diabetes: A cluster-randomised controlled trial	Abstract only
Mayor, S.	2017	Self help approach to graded exercise may help chronic fatigue syndrome	R/C paper
McDermott & Kibbe	2017	Improving lower extremity functioning in peripheral artery disease: Exercise, endovascular revascularization, or both?	R/C paper
Owens & Cappola	2017	Recreational exercise in hypertrophic cardiomyopathy	R/C paper
Saberi et al.	2017	Effect of Moderate-Intensity Exercise Training on Peak Oxygen Consumption in Patients With Hypertrophic Cardiomyopathy: A Randomized Clinical Trial	Duplicate
Saper et al.	2017	Yoga, physical therapy, or education for chronic low back pain: A randomized noninferiority trial	Not exercise-base
Villareal et al.	2017	Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults	Duplicate
Wahlich et al.	2017	Primary care pedometer-based walking intervention: Mixed-methods results from 3 year follow- up of PACE-UP cluster-randomised controlled trial	Abstract only
Wanigatunga et al.	2017	Association Between Structured Physical Activity and Sedentary Time in Older Adults	R/C paper
Wanigatunga et al.	2017	Association Between Structured Physical Activity and Sedentary Time in Older Adults	Not a RCT
Crawford, J.	2018	Graded exercise self-help for chronic fatigue syndrome in GETSET	R/C paper
Trombetti et al.	2018	Effect of Physical Activity on Frailty: Secondary Analysis of a Randomized Controlled Trial	Secondary analys

Notes: R/C, review or conference paper; RCT, randomized controlled trial

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# Supplementary Table 2: Exercise & Pharmacological RCT Matching

## Supplementary Table 2: Exercise & Pharmacological RCT Matching

Exercise Studies	Journal	Population	Size	Sites	Pharmacological Studies	Journal	Population	Size	Sites	% Matcl
Beckers et al., (2008) <sup>13</sup>	Eur Heart J	Heart Failure	58	Single	Hoendermis et al., (2015) <sup>77</sup>	Eur Heart J	HFpEF	52	Single	100%
Beer et al., (2008) <sup>14</sup>	JACC	Dilated Cardiomyopathy	24	Single	Hamshere et al., (2015) <sup>74</sup>	Eur Heart J	Dilated Cardiomyopathy	60	Single	75%
Ligibel et al., (2008) <sup>36</sup>	JCO	Breast CA	82	Single	Schmid et al., (2016) <sup>95</sup>	JCO	Breast CA	75	Multiple	75%
Maltais et al. (2008) <sup>37</sup>	AIM	COPD	252	Multiple	Lapperre et al., (2009) <sup>86</sup>	AIM	COPD	114	Multiple	75%
Adamsen et al., (2009) <sup>12</sup>	BMJ	Mixed CA	269	Multiple	Rimawi et al., (2018) <sup>93</sup>	JCO	Breast CA	258	Multiple	100%
Courneya et al., (2009) <sup>18</sup>	JCO	Lymphoma	122	Single	Cortelazzo et al., (2016) <sup>62</sup>	JCO	Lymphoma	246	Multiple	50%
McDermott et al., $(2009)^{38}$	JAMA	PAD	156	Single	Ford et al., (2014) <sup>67</sup>	JACC	PAD	171	Multiple	50%
Monninkhof et al., (2009) <sup>42</sup>	JCO	Postmenopausal women	189	Single	Loprinzi et al., (2010) <sup>87</sup>	JCO	Women with hot flashes	207	Multiple	75%
O'Connor et al., (2009) <sup>44</sup>	JAMA	Heart Failure	2331	Multiple	Gheorghiade et al., (2013) <sup>70</sup>	JAMA	Heart Failure	1639	Multiple	75%
Patwala et al., (2009) <sup>46</sup>	JACC	Cardiac Resynch	50	Single	Tsujita et al., (2015) <sup>100</sup>	JACC	Percutaneous Coronary Inter	246	Multiple	50%
Schmitz et al., (2009) <sup>51</sup>	NEJM	Breast CA	141	Single	Wapnir et al., (2018) <sup>104</sup>	Lancet	Breast CA	162	Multiple	50%
Segal et al., (2009) <sup>53</sup>	JCO	Prostate CA	121	Single	McKay et al., (2016) <sup>88</sup>	ЈСО	Prostate CA	102	Multiple	75%
Church et al., (2010) <sup>17</sup>	JAMA	T2DM	262	Single	Nissen et al., (2008) <sup>89</sup>	JAMA	T2DM & CAD	547	Multiple	50%
Friedenreich et al., $(2010)^{26}$	JCO	Postmenopausal women	320	Multiple	Johnston et al., (2018) <sup>80</sup>	JCO	Postmenopausal Breast CA	355	Multiple	100%
Galvao et al., (2010) <sup>28</sup>	JCO	Prostate CA	57	Single	Taplin et al., (2014) <sup>99</sup>	JCO	Prostate CA	58	Single	100%
Schmitz et al., (2010) <sup>52</sup>	NEJM	Breast CA	154	Single	Hurvitz et al., (2013) <sup>78</sup>	JCO	Breast CA	137	Multiple	50%
Edelmann et al., $(2011)^{22}$	JACC	HFpEF	64	Single	Kosmala et al., (2013) <sup>83</sup>	JACC	HFpEF	61	Single	100%

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Supplementary Table 2: Exercise & Pharmacological RCT Matching

Exercise Studies	Journal	Population	Size	Sites	Pharmacological Studies	Journal	Population	Size	Sites	% Matcl
Hallsworth et al., (2011) <sup>29</sup>	Gut	NAFLD	19	Single	Ratziu et al., (2008) <sup>92</sup>	Gastroenterol	NASH	64	Single	75%
Villareal et al., (2011) <sup>57</sup>	NEJM	Obese	107	Single	Smith et al., (2010) <sup>96</sup>	NEJM	Obese	3182	Multiple	50%
Belardinelli et al., (2012) <sup>15</sup>	JACC	CHF	123	Single	Goebel et al., (2017) <sup>71</sup>	AIM	Complex Pain Syndrome	111	Multiple	50%
Campbell et al., (2012) <sup>16</sup>	JCO	Postmenopausal women	439	Single	Ellis et al., (2011) <sup>66</sup>	JCO	Postmenopausal Breast CA	377	Multiple	75%
Duijts et al., (2012) <sup>21</sup>	JCO	Breast CA	422	Multiple	Urruticoechea et al., $(2017)^{102}$	JCO	Breast CA	452	Multiple	100%
Sandri et al., (2012) <sup>50</sup>	Eur Heart J	HFrEF	60	Single	Frustaci et al., (2009) <sup>68</sup>	Eur Heart J	CHF w Cardio- myopathy	85	Single	75%
Winter et al., (2012) <sup>58</sup>	Eur Heart J	Systemic Right Ventricle	54	Multiple	van der Bom et al., (2013) <sup>103</sup>	Circulation	Systemic Right Ventricle	88	Multiple	75%
Daumit et al., (2013) <sup>19</sup>	NEJM	Mental Illness	291	Multiple	Rosenheck et al., (2011) <sup>94</sup>	NEJM	Mental Illness	382	Multiple	75%
Kitzman et al., (2013) <sup>35</sup>	JACC	HFpEF	63	Single	Caminiti et al., (2009) <sup>61</sup>	JACC	CHF	70	Single	100%
Messier et al., (2013) <sup>41</sup>	JAMA	Overweight & Obese	454	Single	Spitzer et al., (2012) <sup>98</sup>	AIM	Obese w ED	140	Single	50%
Pitkala et al., (2013) <sup>47</sup>	JAMA Int Med	Alzheimer's Disease	210	Multiple	Cummings et al., (2015) <sup>63</sup>	JAMA	Alzheimer's Disease	220	Multiple	75%
Galvao et al., (2014) <sup>27</sup>	Eur Urol	Prostate CA	100	Multiple	Irani et al., (2008) <sup>79</sup>	Eur Urol	Prostate CA	138	Single	50%
Hollekim-Strand et al., (2014) <sup>30</sup>	JACC	T2DM & DD	47	Single	Han et al., (2014) <sup>75</sup>	JACC	T2DM & CKD	3082	Multiple	50%
Jones et al., (2014) <sup>33</sup>	Eur Urol	Prostate CA	50	Single	Yoshimura et al., (2016) <sup>107</sup>	Eur Urol	Prostate CA	73	Multiple	50%
Pahor et al., (2014) <sup>45</sup>	JAMA	Elderly	1635	Multiple	Devereux et al., (2018) <sup>65</sup>	JAMA	Elderly w COPD	1578	Multiple	100%
Fakhry et al., (2015) <sup>24</sup>	JAMA	PAD	212	Multiple	Poole et al., (2013) <sup>90</sup>	JAMA	PAD	159	Multiple	100%
Friedenreich et al., (2015) <sup>25</sup>	JAMA Oncol	Postmenopausal women	400	Multiple	Harman et al., (2014) <sup>76</sup>	JAMA Int Med	Postmenopausal women	727	Multiple	75%
Irwin et al., (2015) <sup>31</sup>	JCO	Breast CA	121	Single	Yardley et al., (2013) <sup>106</sup>	JCO	Breast CA	130	Multiple	75%

Supplementary Table 2: Exercise & Pharmacological RCT Matching

Exercise Studies	Journal	Population	Size	Sites	Pharmacological Studies	Journal	Population	Size	Sites	% Mate
Murphy et al., (2015) <sup>43</sup>	JACC	PAD	111	Multiple	Krankenberg et al., (2015) <sup>85</sup>	Circulation	PAD	119	Multiple	100%
Ross et al., (2015) <sup>48</sup>	AIM	Obese	300	Single	Kim et al., (2018) <sup>81</sup>	JAMA	Acute Coronary Syndrome	300	Single	50%
van Waart et al., (2015) <sup>55</sup>	JCO	Mixed CA	230	Multiple	Soiffer et al., (2017) <sup>97</sup>	JCO	HSCT	260	Multiple	100%
Ehlken et al., (2016) <sup>23</sup>	Eur Heart J	Pulmonary HTN	87	Single	Ulrich et al., (2015) <sup>101</sup>	Eur Heart J	Pulmonary HTN	23	Single	75%
Kitzman et al., (2016) <sup>34</sup>	JAMA	HFpEF & Obese	100	Single	Gheorghiade et al., (2008) <sup>69</sup>	JACC	Heart Failure	120	Multiple	50%
Zhang et al., (2016) <sup>59</sup>	JAMA Int Med	NAFLD	220	Single	Cusi et al., (2016) <sup>64</sup>	AIM	NASH	101	Single	75%
Johansen et al., $(2017)^{32}$	JAMA	T2DM	98	Single	Wysham et al., (2017) <sup>105</sup>	JAMA	T2DM	721	Multiple	50%
McDermott et al., (2017) <sup>39</sup>	JAMA	PAD	210	Single	Pradhan et al., (2009) <sup>91</sup>	JAMA	PAD	500	Multiple	50%
Saberi et al., (2017) <sup>49</sup>	JAMA	Hypertrophic Cardiomyopathy	136	Single	Kosmala et al., (2016) <sup>84</sup>	JACC	HFpEF	150	Single	75%
Taaffe et al., (2017) <sup>54</sup>	Eur Urol	Prostate CA	163	Multiple	Klotz et al., (2013) <sup>82</sup>	Eur Urol	Prostate CA	186	Multiple	100%
Villareal et al., (2017) <sup>56</sup>	NEJM	Obese	160	Single	Grudell et al., (2008) <sup>73</sup>	Gastroenterol	Overweight & Obese	181	Single	75%
Dieli-Conwright et al., (2018) <sup>20</sup>	JCO	Breast CA	100	Single	Greenspan et al., (2008) <sup>72</sup>	JCO	Breast CA	87	Single	100%
McDermott et al., (2018) <sup>40</sup>	JAMA	PAD	200	Single	Ahmed et al., (2008) <sup>60</sup>	JAMA	A-Fib w Cardiac Resynch	214	Multiple	50%

Notes: A-Fib. atrial fibrillation; AIM, Annals of Internal Medicine; BMJ, British Medical Journal; CA, cancer; CAD, coronary artery disease; CHF, chronic heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disorder; CVD, cardiovascular disease; DD, diastolic dysfunction; ED, erectile dysfunction; Eur Heart J, European Heart Journal; Eur Urol, European Urology; HCL, hypercholesterolemia; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HSCT, hematopoietic stem cell transplantation; HTN, hypertension; Inter, intervention; JACC, Journal of the American College of Cardiology; JAMA, Journal of the American Medical Association; JAMA Int Med, JAMA Internal Medicine; JAMA Oncol, JAMA Oncology; JCO, Journal of Clinical Oncology; MDS, myelodisplastic syndrome; NEJM, New England Journal of Medicine: NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; PAD, peripheral arterial disease; Resynch, resynchronization; T2DM, type 2 diabetes mellitus 

#### Supplementary Table 4: Exercise RCT Characteristics

#### Supplementary Table 3: Pre vs. Post Author Contact

Ostassa		Exercise Studie	es (n=16)		Pharmacological Studies (n=7)			
Outcomes		Pre	Post	Δ	Pre	Post	Δ	
Study Reporting Score	Median	30.5	43.0	12.5	33.0	39.0	5.0	
	IQR	27.8, 35.0	41.5, 45.8	10.0, 16.2	30.0, 37.0	35.5, 41.5	4.0, 6.5	
CONSORT	Median	24.5	36.5	10.5	24.0	27.0	4.0	
	IQR	24.0, 26.5	31.8, 38.2	8.8, 13.2	23.0, 27.5	27.0, 29.5	2.0, 4.0	
CONSORT-Harms	Median	1.0	2.0	1.0	6.0	6.0	0.0	
	IQR	0.0, 3.0	1.8, 5.0	0.0, 2.0	4.0, 6.5	4.0, 6.5	0.0, 0.0	
TIDieR	Median	9.5	12.5	3.0	NA	NA	NA	
	IQR	7.0, 10.2	10.0, 13.0	2.0, 4.0	NA	NA	NA	

Notes: Δ, change; CONSORT, Consolidated Standards for Reporting Trials; CONSORT-Harms, CONSORT Extension for Harms Reporting; IQR, interquartile range; Pre, original score (prior to author contact); Post, updated score (following author contact); TIDieR, Template for Intervention Description and Replication

#### Supplementary Table 4: Exercise RCT Characteristics

## Supplementary Table 4: Exercise RCT Characteristics

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Beckers et al., (2008) <sup>14</sup>	Heart Failure	58	AET1: 30; CET1: 30	NR	16 (28)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Beer et al., $(2008)^{15}$	Dilated Cardiomyopathy	24	AET1: 12; UC: 12	56	NR	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Ligibel et al., (2008) <sup>37</sup>	Breast CA	101	CET1: 51; UC: 50	NR	101 (100)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Maltais et al. (2008) <sup>38</sup>	COPD	252	CET1: 126; CET2: 126	66	112 (44)	HTN: 112 (44); HCL: NR (NR); T2DM: 30 (12)
Adamsen et al., $(2009)^{13}$	Mixed CA	269	CET1: 135; UC: 134	47.2	196 (73)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Courneya et al., (2009) <sup>19</sup>	Lymphoma	122	AET1: 60; UC: 62	53	50 (41)	HTN: 35 (29); HCL: 36 (30); T2DM: NR (NR)
McDermott et al., (2009) <sup>39</sup>	PAD	156	AET1: 51; RET1: 52; UC: 53	73.7	81 (52)	HTN: NR (NR); HCL: NR (NR) T2DM: 69 (44)
Monninkhof et al., (2009) <sup>43</sup>	Postmenopausal Women	189	CET1: 96; UC: 93	NR	189 (100)	HTN: NR (NR); HCL: NR (NR) T2DM: NA (NA)
O'Connor et al., (2009) <sup>45</sup>	Heart Failure	2331	AET1: 1159; UC: 1172	59.2 <sup>MED</sup>	661 (28)	HTN: 1388 (60); HCL: NR (NR T2DM: 748 (32)
Patwala et al., (2009) <sup>47</sup>	Congestive Heart Failure	50	AET1: 25; UC: 25	64	4 (8)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Schmitz et al., (2009) <sup>52</sup>	Breast CA	141	RET1: 71; UC: 70	NR	NR	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Segal et al., (2009) <sup>54</sup>	Prostate CA	121	AET1: 40; CET1: 40; UC: 41	66	NA	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Church et al., (2010) <sup>18</sup>	T2DM	262	AET1: 72; RET1: 73; CET1: 76; UC: 41	56	165 (63)	HTN: 208 (79); HCL: 168 (64); T2DM: 262 (100)
Friedenreich et al., (2010) <sup>27</sup>	Postmenopausal Women	320	AET1: 160; UC: 160	61	320 (100)	HTN: NR (NR); HCL: NA (NA T2DM: NR (NR)
Galvao et al., (2010) <sup>29</sup>	Prostate CA	57	CET1: 29; UC: 28	NR	NA	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Schmitz et al., (2010) <sup>53</sup>	Breast CA	154	RET1: 71; UC: 77	NR	154 (100)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Edelmann et al., $(2011)^{23}$	Heart Failure	64	CET1: 46; UC: 21	65	36 (56)	HTN: 55 (86); HCL: 30 (47); T2DM: 9 (14)
Hallsworth et al., $(2011)^{30}$	NAFLD	19	RET1: 11; UC: 10	NR	NR	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)

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Supplementary Table 4: Exercise RCT Characteristics

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Villareal et al., (2011) <sup>58</sup>	Obese Elderly	107	AET1: 26; CET1: 26; CET2: 28; UC: 27	70	67 (63)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Belardinelli et al., (2012) <sup>16</sup>	Heart Failure	123	AET1: 63; UC: 60	59	27 (22)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Campbell et al., (2012) <sup>17</sup>	Postmenopausal Women	439	AET1: 117; AET2: 117; RET1: 118; UC: 87	58	439 (100)	HTN: NR (NR); HCL: NR (NR T2DM: NA (NA)
Duijts et al., $(2012)^{22}$	Breast CA	422	AET1: 104; AET2: 106; RET1: 109; UC: 103	48	422 (100)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Sandri et al., (2012) <sup>51</sup>	HFrEF	120	AET1: 60; UC: 60	NR	23 (19)	HTN: 90 (75); HCL: 72 (60); T2DM: 35 (29)
Winter et al., (2012) <sup>59</sup>	Systemic Right Ventricle	46	AET1: 28; UC: 26	32	23 (50)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Daumit et al., (2013) <sup>20</sup>	Serious Mental Illness	291	AET1: 144; UC: 147	45	146 (50)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Kitzman et al., (2013) <sup>36</sup>	HFpEF	63	AET1: 32; UC: 31	70	48 (76)	HTN: 56 (89); HCL: NA (NA) T2DM: 15 (24)
Messier et al., $(2013)^{42}$	Overweight & Obese w Osteoarthritis	454	AET1: 152; CET1: 150; CET2: 152	66	325 (72)	HTN: 273 (60); HCL: NR (NR T2DM: 59 (13)
Pitkala et al., (2013) <sup>48</sup>	Alzheimer's Diesase	210	AET1: 70; CET1: 70; UC: 70	78	81 (39	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Galvao et al., (2014) <sup>28</sup>	Prostate CA	100	CET1: 50; UC: 50	NR	NA	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Hollekim-Strand et al., (2014) <sup>31</sup>	T2DM w Diastolic Dysfunction	37	AET1: 23; AET2: 24	56	17 (46)	HTN: NR (NR); HCL: NR (NR T2DM: NA (NA)
Jones et al., $(2014)^{34}$	Prostate CA	50	AET1: 25; UC: 25	59	NA	HTN: 27 (54); HCL: 30 (60); T2DM: 8 (16)
Pahor et al., (2014) <sup>46</sup>	Elderly	1635	CET1: 818; UC: 817	79	1098 (67)	HTN: 1151 (70); HCL: NR (NI T2DM: 412 (25)
Fakhry et al., (2015) <sup>25</sup>	PAD	212	AET1: 106; AET2: 106	65	80 (38)	HTN: 128 (60); HCL: 91 (43); T2DM: 44 (21)
Friedenreich et al., (2015) <sup>26</sup>	Postmenopausal Women	400	AET1: 200; AET2: 200	59	400 (100)	HTN: NR (NR); HCL: NA (NA T2DM: NA (NA)
Irwin et al., $(2015)^{32}$	Breast CA	121	CET1: 61; UC: 60	61	121 (100)	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Murphy et al., (2015) <sup>44</sup>	PAD	111	AET1: 43; Stent: 46; UC: 22	64	42 (38)	HTN: 94 (85); HCL: 89 (80); T2DM: 26 (24)
Ross et al., (2015) <sup>49</sup>	Obese	300	AET1: 73; AET2: 76; CET1: 76; UC: 75	51	196 (65)	HTN: NR (NR); HCL: NR (NF T2DM: NA (NA)

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
van Waart et al., (2015) <sup>56</sup>	Breast CA	230	AET1: 77; CET1: 76; UC: 77	51	228 (99)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Ehlken et al., (2016) <sup>24</sup>	Pulmonary Artery HTN	87	CET1: 46; UC: 41	56	47 (54)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Kitzman et al., (2016) <sup>35</sup>	HFpEF	100	AET1: 26; AET2: 25; RET1: 24; UC: 25	67	81 (81)	HTN: 95 (95); HCL: NR (NR); T2DM: 32 (32)
Zhang et al., (2016) <sup>60</sup>	NAFLD	220	AET1: 73; AET2: 73; UC: 74	54	149 (68)	HTN: NA (NA); HCL: NR (NR); T2DM: NA (NA)
Johansen et al., $(2017)^{33}$	T2DM	98	CET1: 64; UC: 34	55	47 (48)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
McDermott et al., (2017) <sup>40</sup>	PAD	210	AET1: 53; AET2: 53; RET1: 53; UC: 51	67	82 (39)	HTN: 175 (83); HCL: NR (NR); T2DM: 80 (38)
Saberi et al., (2017) <sup>50</sup>	Hypertrophic Cardiomyopathy	136	AET1: 67; UC: 69	50	57 (42)	HTN: 30 (22); HCL: NR (NR); T2DM: 9 (7)
Taaffe et al., (2017) <sup>55</sup>	Prostate CA	163	AET1: 51; RET1: 58; CET1: 54	NR	NA	HTN: 58 (36); HCL: 35 (21); T2DM: 20 (12)
Villareal et al., (2017) <sup>57</sup>	Obese Elderly	160	AET1: 40; RET1: 40; CET1: 40; UC: 40	70	103 (64)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Dieli-Conwright et al., (2018) <sup>21</sup>	Overweight & Obese Breast CA	100	CET1: 50; UC: 50	54	100 (100)	HTN: NA (NA); HCL: NR (NR); T2DM: NA (NA)
McDermott et al., (2018) <sup>41</sup>	PAD	200	AET1: 99; UC: 101	70	105 (53)	HTN: NR (NR); HCL: NR (NR); T2DM: 67 (34)

**Notes**: AET1, aerobic exercise training (group 1); AET2, aerobic exercise training (group 2); CA, cancer; CET1, combined aerobic and resistance exercise training (group 1); CET2, combined aerobic and resistance exercise training (group 2); COPD, chronic obstructive pulmonary disorder; CVD, cardiovascular disease; HCL, hypercholesterolemia; HFpEF, heart failure with preserved ejection fraction; HTN, hypertension; LTF, loss-to-follow up; PAD, peripheral arterial disease; n, number; NA, not applicable; NAFLD, non-alcoholic fatty liver disease; NR, not reported; RET1, resistance exercise training (group 1); RET2, resistance exercise training (group 2); T2DM, type 2 diabetes mellitus; UC, usual care

## Supplementary Table 5: Pharmacological RCT Characteristics

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Ahmed et al. (2008) <sup>61</sup>	Atrial Fibrillation	214	Grp1: 106; Grp2: 108	NR	73 (34.11)	HTN: 84 (39); HCL: NR (NR); T2DM: 21 (10)
Gheorghiade et al. (2008) <sup>70</sup>	Heart Failure	120	Grp1: 29; Grp2: 30; Grp3: 30; UC: 31	55	15 (12.5)	HTN: NA (NA); HCL: NR (NR) T2DM: 21 (18)
Greenspan et al. $(2008)^{73}$	Breast CA	87	Grp1: 43; UC: 44	NR	87 (100)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Grudell et al. (2008) <sup>74</sup>	Obese & Overweight	181	Grp1: 58; Grp2: 61; UC: 62	NR	161 (88.95)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Irani et al. (2008) <sup>80</sup>	Prostate CA	129	Grp1: 62; Grp2: 67	73	NA	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Nissen et al. (2008) <sup>90</sup>	T2DM	547	Grp1: 273; Grp2: 274	60	181 (33.09)	HTN: 475 (87); HCL: NR (NR); T2DM: NA (NA)
Ratziu et al. (2008) <sup>93</sup>	NASH	64	Grp1: 32; UC: 32	54	26 (40.63)	HTN: 22 (35); HCL: NR (NR); T2DM: 20 (32)
Caminiti et al. (2009) <sup>62</sup>	Heart Failure	70	Grp1: 35; UC: 35	$70^{\text{MED}}$	NA	HTN: 25 (36); HCL: 39 (56); T2DM: 20 (29)
Frustaci et al. (2009) <sup>69</sup>	Cardiomyopathy	85	Grp1: 43; UC: 42	NR	34 (40)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Lapperre et al. (2009) <sup>87</sup>	COPD	114	Grp1: 26; Grp2: 31; Grp3: 28; UC: 29	NR	27 (23.68)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Pradhan et al. (2009) <sup>92</sup>	T2DM	500	Grp1: 126; Grp2: 126; Grp3: 124; UC: 124	54	281 (56.2)	HTN: 341 (68); HCL: 299 (60); T2DM: 500 (100)
Loprinzi et al. (2010) <sup>88</sup>	Women with Hot Flashes	207	Grp1: 69; Grp2: 69; UC: 69	NR	207 (100)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Smith et al. (2010) <sup>97</sup>	Overweight & Obese	3182	Grp1: 1595; UC: 1587	44	2652 (83.34)	HTN: NA (NA); HCL: NR (NR) T2DM: NA (NA)
Ellis et al. (2011) <sup>67</sup>	Breast CA	377	Grp1: 124; Grp2: 128; Grp3: 125	NR	377 (100)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Rosenheck et al. (2011) <sup>95</sup>	Schizophrenia	382	Grp1: 190; UC: 192	51	32 (8.38)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Spitzer et al. (2012) <sup>99</sup>	Erectile Dysfunction	140	Grp1: 70; Grp2: 70	55	NA	HTN: 56 (40); HCL: NR (NR); T2DM: 27 (19)
Gheorghiade et al. (2013) <sup>71</sup>	Heart Failure	1639	Grp1: 821; UC: 818	65	368 (22.45)	HTN: 1225 (76); HCL: NR (NR T2DM: 662 (41)

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Hurvitz et al. (2013) <sup>79</sup>	Breast CA	137	Grp1: 67; Grp2: 70	NR	NR	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Klotz et al. $(2013)^{83}$	Prostate CA	186	Grp1: 84; Grp2: 102	NR	NA	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Kosmala et al. (2013) <sup>84</sup>	HFpEF	61	Grp1: 30; UC: 31	67	50 (81.97)	HTN: 51 (84); HCL: NR (NR); T2DM: 22 (36)
Poole et al. $(2013)^{91}$	PAD	159	Grp1: 80; UC: 79	64	20 (12.58)	HTN: 153 (96); HCL: 134 (87); T2DM: 58 (37)
van der Bom et al. $(2013)^{104}$	Systemic Right Ventricle	88	Grp1: 44; UC: 44	33	31 (35.23)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Yardley et al. (2013) <sup>107</sup>	Breast CA	130	Grp1: 64; Grp2: 66	NR	130 (100)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Ford et al. $(2014)^{68}$	Cardiovascular Disease	171	Grp1: 86; UC: 85	65	26 (15.2)	HTN: 52 (30); HCL: NR (NR); T2DM: 14 (9)
Han et al. (2014) <sup>76</sup>	T2DM & Chronic Kidney Disease	3082	Grp1: 1543; UC: 1539	61	1044 (33.87)	HTN: 2156 (70); HCL: 256 (8); T2DM: 3082 (100)
Harman et al. (2014) <sup>77</sup>	Menopausal	727	Grp1: 230; Grp2: 222; UC: 275	53	727 (100)	HTN: NA (NA); HCL: NA (NA T2DM: NA (NA)
Taplin et al. (2014) <sup>100</sup>	Prostate CA	58	Grp1: 28; Grp2: 30	58 MED	NA	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Cummings et al. (2015) <sup>64</sup>	Alzheimer's	220	Grp1: 93; UC: 127	78	126 (57.27)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Hamshere et al. $(2015)^{75}$	Dilated Cardiomyopathy	60	Grp1: 15; Grp2: 15; Grp3: 15; UC: 15	55	17 (28.33)	HTN: 6 (10); HCL: 6 (10); T2DM: 6 (10)
Hoendermis et al. (2015) <sup>78</sup>	HFpEF	52	Grp1: 26; UC: 26	74	37 (71.15)	HTN: 47 (90); HCL: 27 (52); T2DM: 18 (35)
Krankenberg et al. (2015) <sup>86</sup>	PAD	119	Grp1: 62; Grp2: 57	NR	37 (31.09)	HTN: 105 (88); HCL: 93 (78); T2DM: 45 (38)
Tsujita et al. (2015) <sup>101</sup>	Coronary Artery Disease	246	Grp1: 122; Grp2: 124	NR	44 (17.89)	HTN: 142 (58); HCL: 142 (58); T2DM: 60 (24)
Ulrich et al. (2015) <sup>102</sup>	Pulmonary Artery HTN	23	Grp1: 23; Grp2: 23; UC: 23	66	15 (65.22)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Cortelazzo et al. $(2016)^{63}$	Lymphoma	246	Grp1: 126; Grp2: 120	51 MED	99 (40.24)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Cusi et al. (2016) <sup>65</sup>	NASH & Prediabetes or T2DM	101	Grp1: 50; UC: 51	NR	30 (29.7)	HTN: NR (NR); HCL: NR (NR T2DM: 52 (52)
Kosmala et al. (2016) <sup>85</sup>	HFpEF	150	Grp1: 75; UC: 75	67	110 (73.33)	HTN: 120 (80); HCL: NR (NR) T2DM: 52 (35)

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Supplementary Table 5: Pharmacological RCT Characteristics

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Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
McKay et al. (2016) <sup>89</sup>	Prostate CA	102	Grp1: 66; Grp2: 36; UC: NA	65 MED	NA	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Schmid et al. (2016) <sup>96</sup>	Breast CA	75	Grp1: 26; Grp2: 49	NR	75 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
Yoshimura et al. (2016) <sup>108</sup>	Prostate CA	73	Grp1: 36; Grp2: 37	NR	NA	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Goebel et al. $(2017)^{72}$	Complex Regional Pain Syndrome	111	Grp1: 55; UC: 56	NR	75 (67.57)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Soiffer et al. (2017) <sup>98</sup>	Acute Leukemia or MDS w HSCT	260	Grp1: 128; UC: 132	NR	115 (44.23)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Urruticoechea et al. (2017) <sup>103</sup>	Breast CA	452	Grp1: 224; Grp2: 228	NR	452 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
Wysham et al. (2017) <sup>106</sup>	T2DM	721	Grp1: 361; Grp2: 360	61	338 (46.88)	HTN: NR (NR); HCL: NR (NR); T2DM: 721 (100)
Devereux et al. $(2018)^{66}$	COPD	1578	Grp1: 791; UC: 787	68	724 (45.88)	HTN: 594 (38); HCL: NR (NR); T2DM: 176 (11)
Johnson et al. $(2018)^{81}$	Breast CA	355	Grp1: 120; Grp2: 117; Grp3: 118	NR	355 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Kim et al. (2018) <sup>82</sup>	Depression & Acute Coronary Syndrome	300	Grp1: 149; UC: 151	60	119 (39.67)	HTN: 184 (61); HCL: 144 (48); T2DM: 85 (28)
Rimawi et al. (2018) <sup>94</sup>	Breast CA	258	Grp1: 129; Grp2: 129	60	258 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Wapnir et al. (2018) <sup>105</sup>	Breast CA	162	Grp1: 85; UC: 77	56 MED	162 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)

**Notes**: CA, cancer; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; Grp, group; HCL, hypercholesterolemia; HFpEF, heart failure with preserved ejection fraction; HSCT, hematopoietic stem cell transplantation; HTN, hypertension; kg, kilogram; LTF, loss to follow up; MDS, myelodisplastic syndrome; MED, median; PAD, peripheral arterial disease; n, number; NA, not applicable; NASH, non-alcoholic steatohepatitis; NR, not reported; T2DM, type 2 diabetes mellitus; UC, usual care

## **Supplementary Table 6: Exercise Intervention Characteristics**

		Length		Exercise Dose				
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]	
Beckers et al., (2008) <sup>13</sup>	MC	Total (single-phase): 26 wks	AET1: CE, TM CAET1: NR CRET1: MW	AET1: 3 CAET1: 3 CRET1: 3	AET1: 40-45 CAET1: 10-45 CRET1: 10-40	AET1: 90% HR at AT CAET1: 90% HR at AT CRET1: 50-60% 1RM; 10-15 reps, 1-2 sets	NA	
Beer et al., (2008) <sup>14</sup>	NR	Total (single-phase): 36 wks	AET1: CE, NR	AET1: 5	AET1: 45	AET1: 60-80% VO <sub>2</sub> <sup>max</sup> ; 13-15 RPE	NA	
Ligibel et al., (2008) <sup>36</sup>	PG, HM	Total (single-phase): 16 wks	CAET1: NR CRET1: MW, BW	CAET1: NR CRET1: 2	CAET1: NR CRET1: 35	CAET1: 55-80% HR <sup>max</sup> CRET1: 80% 1RM; 10 reps, 4 sets	NA	
Maltais et al. (2008) <sup>37</sup>	MC, HM, Other	Total: 52 wks Lead-in: 4 wks	Lead-in: NA	Lead-in: NA	Lead-in: NA	Lead-in: NA	Lead-in: 4 wk education progra	
		Phase 1: 8 wks	Phase 1 CAET1: CE CRET1: RB, BW, NR CAET2: CE CRET2: RB, BW, NR	<u>Phase 1</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	Phase 1 CAET1: 25-30 CRET1: 30 CAET2: 40 CRET2: 30	<u>Phase 1</u> CAET1: 80% peak work CRET1: NR; 10 reps, 1-3 sets CAET2: 60% maximum work capacity CRET2: NR; 10 reps, 1-3 sets		
		Phase 2: 40 wks	<u>Phase 2</u> CRET1: NR CAET1: NR CAET2: NR CRET2: NR	<u>Phase 2</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	Phase 2 CAET1: NR CRET1: NR CAET2: NR CRET2: NR	<u>Phase 2</u> CAET1: NR (NR) CRET1: NR (NR) CAET2: NR (NR) CRET2: NR (NR)		
Adamsen et al., (2009) <sup>12</sup>	MC	Total (single-phase): 6 wks	CAET1: CE CRET1: MW	CAET1: 3 CRET1: 3	CAET1: 15 CRET1: 45	CAET1: 85-95% HR <sup>max</sup> CRET1: 70-100% 1RM; 5-8 reps, 3 sets	Body awareness restoration; rela ation; massage	
Courneya et al., (2009) <sup>18</sup>	NR	Total (single-phase): 12 wks	AET1: CE	AET1: 3	AET1: 15-45	AET1: 60-75% PPO at VO <sub>2</sub> <sup>peak</sup>	NA	
McDermott et al., (2009) <sup>38</sup>	UNI, Other	Total (single-phase): 24 wks	AET1: TM RET1: MW, BW	AET1: 3 RET1: 3	AET1: 15-40 RET1: NR	AET1: 12-14 RPE RET1: 50-80% 1RM, 12-14 RPE; 8 reps, 3 sets	NA	
Monninkhof et al., (2009) <sup>42</sup>	PG, HM	Total (single-phase): 52 wks	CAET1: CE, WK, NR CRET1: NR	CAET1: 3 CRET1: 2	CAET1: 20-30 CRET1: 25	CAET1: 60-85% HR <sup>max</sup> CRET1: NR; NR; NR	NA	

Supplementary Table 6: Exercise Intervention Characteristics

Length		Length		<b>Exercise Dose</b>			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	<sup>–</sup> Co-interventio [Group: Details]
O'Connor et al., (2009) <sup>44</sup>	Other	Total: 130 wks <sup>MED</sup> Phase 1: 12 wks	Phase 1 AET1: CE, TM, WK	Phase 1 AET1: 3	<u>Phase 1</u> AET1: 15-35	<u>Phase 1</u> AET1: 60-70% HRR	NA
		Phase 2: 118 wks <sup>MED</sup>	Phase 2 AET1: CE, TM, WK	Phase 2 AET1: 5	<u>Phase 2</u> AET1: 40	<u>Phase 2</u> AET1: 60-70% HRR	
Patwala et al., (2009) <sup>46</sup>	UNI	Total (single-phase): 12 wks	AET1: CE, TM	AET1: 3	AET1: 30	AET1: 80-90% HR <sup>peak</sup>	NA
Schmitz et al., (2009) <sup>51</sup>	PG	Total: 52 wks Phase 1: 13 wks	Phase 1 RET1: MW, FW	<u>Phase 1</u> RET1: 2	<u>Phase 1</u> RET1: 90	Phase 1 RET: NR; 10 reps, 2-3 sets	NA
		Phase 2: 39 wks	Phase 2 RET1: NR	Phase 2 RET1: 2	<u>Phase 2</u> RET1: NR	<u>Phase 2</u> RET1: NR; NR, NR	
Segal et al., (2009) <sup>53</sup>	RC	Total (single-phase): 24 wks	AET1: CE, TM, EE RET1: MW, FW	AET1: 3 RET1: 3	AET1: 15-45 RET1: NR	AET1: 50-75% VO <sub>2</sub> <sup>peak</sup> RET1: 60-70% 1RM; 8-12 reps, 2 sets	NA
Church et al., (2010) <sup>17</sup>	МС	Total (single-phase): 40 wks	AET1: NR RET1: MW, BW CAET1: NR CRET1: MW, BW	AET1: NR RET1: 3 CAET1: NR CRET1: 2	AET1: NR RET1: NR CAET1: NR CRET1: NR	AET1: 50-80% VO <sub>2</sub> <sup>peak</sup> RET1: NR; 10-12 reps, 2-3 sets CAET1: 50-80% VO <sub>2</sub> <sup>peak</sup> CRET1: NR, 10-12 reps, 1 set	NA
Friedenreich et al., (2010) <sup>26</sup>	UNI, PG, HM	Total (single-phase): 52 wks	AET1: NR	AET1: 3-5	AET1: 15-45	AET1: 50- 80% HRR	NA
Galvao et al., (2010) <sup>28</sup>	RC, HM	Total (single-phase): 12 wks	CAET1: CE, WK, JG CRET1: MW, FW	CAET1: 2 CRET1: 2	CAET1: 15-20 CRET1: NR	CAET1: 65-80% HR <sup>max</sup> ; 11-13 RPE CRET1: 6-12 RM; NR, 2-4 sets	NA
Schmitz et al., (2010) <sup>52</sup>	PG	Total: 52 wks Phase 1: 13 wks	<u>Phase 1</u> RET1: MW, FW	<u>Phase 1</u> RET1: 2	<u>Phase 1</u> RET1: 60-90	Phase 1 RET1: NR; 10 reps, 3 sets	NA
		Phase 2: 39 wks	Phase 2 RET1: MW, FW	Phase 2 RET1: 2	<u>Phase 2</u> RET1: NR	<u>Phase 2</u> RET1: NR; NR, NR	
Edelmann et al., $(2011)^{22}$	Other (Facility Based)	Total: 12 wks Phase 1: 4 wks	<u>Phase 1</u> CAET1: CE CRET1: NR	<u>Phase 1</u> CAET1: 2 CRET1: NR	<u>Phase 1</u> CAET1: 20-40 CRET1: NR	$\frac{\text{Phase 1}}{\text{CAET1: 50-60\% VO}_2^{\text{peak}}}$ CRET1: NR	NA

Supplementary Table 6: Exercise Intervention Characteristics

		Length		Exercise Dose	<u>)</u>		—a · , , ,
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	<sup>–</sup> Co-intervention [Group: Details]
Edelmann cont'd		Phase 2: 8 wks	<u>Phase 2</u> CAET1: CE CRET1: MW	<u>Phase 2</u> CAET1: 3 CRET1: 2	<u>Phase 2</u> CAET1: NR CRET1: NR	Phase 2 CAET1: 70% VO <sub>2</sub> <sup>peak</sup> CRET1: 60-65% 1RM; 15 reps, NR	
Hallsworth et al., (2011) <sup>29</sup>	NR	Total (single-phase): 8 wks	RET1: MW	RET1: 3	RET1: 25-40	RET1: 50% 1RM; 8-12 reps, 2-4 sets	NA
Villareal et al., (2011) <sup>57</sup>	UNI	Total (single-phase): 52 wks	CAET1: CE, TM, SC CRET1: MW, FW CAET2: CE, TM CRET2: MW, FW	CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	CAET1: 30 CRET1: 30 CAET2: 30 CRET2: 30	CAET1: 65-85% VO <sub>2</sub> <sup>peak</sup> CRET1: 65-85% 1RM; 6-12 reps, 1-3 sets CAET2: 65-85% VO <sub>2</sub> <sup>peak</sup> CRET2: 65-85% 1RM; 6-12 reps, 1-3 sets	CET1: Diet CET2: NA
Belardinelli et al., (2012) <sup>15</sup>	MC	Total: 120 mo Phase 1: 8 wks	Phase 1 AET1: CE, TM	Phase 1 AET1: 3	<u>Phase 1</u> AET1: 40	Phase 1 AET1: 60% VO <sub>2</sub> <sup>peak</sup>	Phase 1 & Phase Counselling (smoking, stre
		Phase 2: 118 mo	Phase 2 AET1: CE, TM	Phase 2 AET1: 3	<u>Phase 2</u> AET1: 40	Phase 2 AET1: 70% VO2 peak	& diet)
Campbell et al., $(2012)^{16}$	MC, HM	Total (single-phase): 52 wks	AET1: WK AET2: WK	AET1: 5 AET2: 5	AET1: 45 AET2: 45	AET1: 70-85% HR <sup>max</sup> AET2: 70-85% HR <sup>max</sup>	AET1 & AET2 Diet
Duijts et al., (2012) <sup>21</sup>	НМ	Total (single-phase): 12 wks	AET1: NR AET2: NR	AET1: NR AET2: NR	AET1: NR AET2: NR	AET1: 60-80% HR - Karvonen AET2: 60-80% HR - Karvonen	AET1 & AET 2 CBT
Sandri et al., (2012) <sup>50</sup>	NR	Total (single-phase): 4 days	AET1: NR CAET1: CE, WK CRET1: BW	AET1: NR CAET1: 5 CRET1: 1	AET1: NR CAET1: CE: 20 4x/day; WK: NR CRET1: NR	AET1: NR CAET1: 70% VO <sub>2</sub> <sup>max</sup> CRET1: NR; NR, NR	NA
Winter et al., (2012) <sup>58</sup>	НМ	Total (single-phase): 10 wks	AET11: NR	AET1: 3	AET1: 32	AET1: 60-90% HR <sup>max</sup>	NA
Daumit et al., (2013) <sup>19</sup>	НМ	Total: 78 wks Phase 1: 26 wks	Phase 1 AET1: WK	Phase 1 AET1: 3	Phase 1 AET1: 10-30	Phase 1 AET1: 50-69% HR <sup>max</sup>	Phase 1 & Phase AET1: Ind & g weight manag
		Phase 2: 52 wks	Phase 2 AET1: WK	<u>Phase 2</u> AET1: 3	Phase 2 AET1: NR	<u>Phase 2</u> AET1: NR	ment

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Supplementary Table 6: Exercise Intervention Characteristics

	Length			<b>Exercise Dose</b>			~ • •
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	<sup>–</sup> Co-intervention [Group: Details]
Kitzman et al., (2013) <sup>35</sup>	NR	Total (single-phase): 16 wks	AET1: CE, WK	AET1: 3	AET1: 10-40	AET1: 40-70% HRR	NA
Messier et al., (2013) <sup>41</sup>	MC, UNI	Total: 78 wks Phase 1: 26 wks	<u>Phase 1</u> CAET1: CE, WK CRET1: MW CAET2: CE, WK CRET2: MW	<u>Phase 1</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	Phase 1 CAET1: 30 CRET1: 20 CAET2: 30 CRET2: 20	<u>Phase 1</u> CAET1: 50-75% HRR CRET1: NR; 10-12 reps, 1-2 sets CAET2: 50-75% HRR CRET2: NR; 10-12 reps, 1-2 sets	Phase 1 & Phase CET1: Diet CET2: NA
		Phase 2: 52 wks	Phase 2 CAET1: CE, WK CRET1: MW, RB CAET2: CE, WK, NR CRET2: MW, RB	<u>Phase 2</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	Phase 2 CAET1: 30 CRET1: 20 CAET2: 30 CRET2: 20	<u>Phase 2</u> CAET1: 50-75% HRR CRET1: NR; 10-12 reps, 1-2 sets CAET2: 50-75% HRR CRET2: NR; 10-12 reps, 1-2 sets	
Pitkala et al., (2013) <sup>47</sup>	RC, HM	Total (single-phase): 52 wks	AET1: NR CAET1: CE CRET1: MW	AET1: 2 CAET1: 2 CRET1: 2	AET1: 60 CAET1: NR CRET1: NR	AET1: NR CAET1: NR CRET1: NR; NR, NR	NA
Galvao et al., (2014) <sup>27</sup>	NR	Total: 52 wks Phase 1: 26 wks	Phase 1 CAET1: CE, WK/JG CRET1: MW, FW, BW	Phase 1 CAET1: 4 CRET1: 2	<u>Phase 1</u> CAET1: 20-30 CRET1: NR	<u>Phase 1</u> CAET1: 70-85% HR <sup>max</sup> , 11-13 RPE CRET1: 6-12RM; NR, 2-4 sets	NA
		Phase 2: 26 wks	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR; NR, NR	
Hollekim-Strand et al., (2014) <sup>30</sup>	HM, Other	Total: 52 wks Phase 1: 12 wks Phase 2: 40 wks	Phase 1 AET1: CE, WK, SW AET2: TM Phase 2 AET1: CE, WK, SW AET2: TM, CE, SW	Phase 1 AET1: NR AET2: 3 Phase 2 AET1: NR AET2: NR	Phase 1 AET1: 10-NR AET2: 40 Phase 2 AET1: NR AET2: NR	Phase 1 AET1: 70% HR <sup>max</sup> AET2: 90-95% HR <sup>max</sup> Phase 2 AET1: NR AET2: NR	NA
Jones et al., (2014) <sup>33</sup>	HM, Other	Total (single-phase): 26 wks	AET1: TM	AET1: 5	AET1: 30-45	AET1: 55-100% VO <sub>2</sub> <sup>peak</sup>	NA
Pahor et al., (2014) <sup>45</sup>	МС	Total: 135 wks Phase 1: 52 wks	<u>Phase 1</u> CAET1: WK CRET1: FW	<u>Phase 1</u> CAET1: 3-6 CRET1: 3	<u>Phase 1</u> CAET1: NR CRET1: 10	<u>Phase 1</u> CAET1: 13 RPE (Borg) CRET1: 15-16 RPE (Borg); 10 reps, 2 sets	NA
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Supplementary Table 6: Exercise Intervention Characteristics

		Length		Exercise Dose				
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]	
		Phase 2: 83 wks	<u>Phase 2</u> CAET1: WK CRET1: FW	Phase 2 CAET1: 5-6 CRET1: 3	<u>Phase 2</u> CAET1: NR CRET1: 10	<u>Phase 2</u> CAET1: 13 RPE (Borg) CRET1: 15-16 RPE (Borg); 10 reps, 2 sets		
Fakhry et al., (2015) <sup>24</sup>	RC	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> AET1: TM AET2: TM	<u>Phase 1</u> AET1: 2-3 AET2: 2-3	Phase 1 AET1: 30-45 AET2: 30-45	<u>Phase 1</u> AET1: NR AET2: NR	Phase 1 & Phase 2 AET1: NA AET2: Endovasc revascularizatio	
		Phase 2: 26 wks	<u>Phase 2</u> AET1: TM AET2: TM	<u>Phase 2</u> AET1: 1 AET2: 1	Phase 2 AET1: 30-45 AET2: 30-45	<u>Phase 2</u> AET1: NR AET2: NR	Tevascularizatio	
Friedenreich et al., (2015) <sup>25</sup>	PG, HM	Total: 52 wks Phase 1: 12 wks	Phase 1 AET1: NR AET2: NR	<u>Phase 1</u> AET1: 3-5 AET2: 3-5	Phase 1 AET1: 15-60 AET2: 10-30	<u>Phase 1</u> AET1: 50-75% HRR AET2: 50-75% HRR	NA	
		Phase 2: 40 wks	Phase 2 AET1: WK, EG, CE, RG, NR AET2: NR	<u>Phase 2</u> AET1: 5 AET2: 5	<u>Phase 2</u> AET1: 60 AET2: 30	<u>Phase 2</u> AET1: 65-75% HRR AET2: 65-75% HRR		
Irwin et al., (2015) <sup>31</sup>	PG, HM	Total (single-phase): 52 wks	CAET1: CE, TM, WK, NR CRET1: MW	CAET1: NR CRET1: 2	CAET1: NR CRET1: NR	CAET1: 50-80% HR <sup>max</sup> CRET1: NR; NR, NR	NA	
Murphy et al., (2015) <sup>43</sup>	RC	Total: 78 wks Phase 1: 26 wks	Phase 1 AET1: TM	Phase 1 AET1: 5	Phase 1 AET1: 15-50	Phase 1 AET1: 2-4 claudication pain scale	Phase 1 Cilostazol, EX counselling	
		Phase 2: 52 wks	<u>Phase 2</u> AET1: NR	<u>Phase 2</u> AET1: NR	<u>Phase 2</u> AET1: NR	<u>Phase 2</u> AET1: NR	Phase 2 EX counselling	
Ross et al., (2015) <sup>48</sup>	NR	Total (single-phase): 24 wks	AET1: TM AET2: TM CAET1: TM	AET1: 5 AET2: 5 CAET1: 5	AET1: 31.2 AET2: 58.4 CAET1: 40	AET1: 50% $VO_2^{peak}$ AET2: 50% $VO_2^{peak}$ CAET1: 75% $VO_2^{peak}$	NA	
van Waart et al., (2015) <sup>55</sup>	RC, HM	Total (single-phase): NR	AET1: NR CAET1: NR CRET1: MW, FW, BW	AET1: 5 CAET1: 2 CRET1: 2	AET1: 30-NR CAET1: 30 CRET1: 20	AET1: 12-14 RPE CAET1: 50-80% workload max CRET1: 70-80% 1RM; 8-12 reps, NR	NA	

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Supplementary Table 6: Exercise Intervention Characteristics

		Length		Exercise Dose			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]
Ehlken et al., (2016) <sup>23</sup>	MC	Total: 15 wks Phase 1: 3 wks	<u>Phase 1</u> CAET1: CE, WK CRET1: FW	<u>Phase 1</u> CAET1: 7 CRET1: 5	<u>Phase 1</u> CAET1: 70-85 CRET1: 30	$\frac{\text{Phase 1}}{\text{CAET1: 60-80\% HR at VO}_2^{\text{max}}}$ CRET: NR; NR, 1-3 sets	<u>Phase 1</u> Respiratory & "mental" training
		Phase 2: 12 wks	<u>Phase 2</u> CAET1: CE CRET1: FW	<u>Phase 2</u> CAET1: 5 CRET1: 3-4	<u>Phase 2</u> CAET1: 15-30 CRET1: 15-30	<u>Phase 2</u> CAET1: NR CRET1: NR; NR, 1-2 sets	<u>Phase 2</u> Respiratory training
Kitzman et al., (2016) <sup>34</sup>	MC	Total (single-phase): 20 wks	AET1: WK AET2: WK	AET1: 3 AET2: 3	AET1: 18-48 AET2: 19-50	AET1: HRR (NR) AET2: HRR (NR)	AET1 & AET2: Diet
Zhang et al., (2016) <sup>59</sup>	PG, HM	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> AET1: TM AET2: WK	Phase 1 AET1: 5 AET2: 5	<u>Phase 1</u> AET1: 15-30 AET2: 30	Phase 1 AET1: 45-50%; 65-80% HR <sup>max</sup> AET2: 45-55% HR <sup>max</sup>	Phase 1 & Phase 2 AET1 & AET2: Health education
		Phase 2: 26 wks	<u>Phase 2</u> AET1: WK AET2: WK	Phase 2 AET1: 5 AET2: 5	<u>Phase 2</u> AET1: 30 AET2: 30	Phase 2 AET1: 45-55% HR <sup>max</sup> AET2: 45-55% HR <sup>max</sup>	w EX behavioral support
Johansen et al., $(2017)^{32}$	REC, Other	Total: 52 wks Phase 1: 16 wks	<u>Phase 1</u> CAET1: NR CRET1: NR	<u>Phase 1</u> CAET1: 6 CRET1: 2	<u>Phase 1</u> CAET1: 30-60 CRET1: 30	<u>Phase 1</u> CAET1: 62-80% HRR CRET1: NR; NR, NR	<u>Phase 1 &amp; Phase 2</u> Diet & sleep
		Phase 2: 36 wks	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR	Phase 2 CAET1: 45-60 CRET1: 30	<u>Phase 2</u> CAET1: 68-88% HRR CRET1: NR; NR, NR	
McDermott et al., (2017) <sup>39</sup>	MC	Total (single-phase): 26 wks	AET1: TM AET2: TM	AET1: 3 AET2: 3	AET1: 15-50 AET2: 15-50	AET1: 12-14 RPE AET2: 12-14 RPE	AET1: GM-CSF injections AET2: NA
Saberi et al., (2017) <sup>49</sup>	НМ	Total (single-phase): 16 wks	AET1: EE, WK	AET1: 3-7	AET1: 20-60	AET1: 60-70% HRR, 11-14 RPE	NA
Taaffe et al., (2017) <sup>54</sup>	UNI	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> RET1: MW CAET1: CE, TM, RE; MW CRET1: MW	Phase 1 RET1: 2 CAET1: 2 CRET1: 2	<u>Phase 1</u> RET1: NR CAET1: 20-30 CRET1: NR	Phase 1 RET1: 6-12 RM CAET1: 60-75% HR <sup>max</sup> CRET1: 6-12 RM; NR, 2-4 sets	Phase 1 RET1: Impact- loading activities CET1: NA
							10

Supplementary Table 6: Exercise Intervention Characteristics

		Length		<b>Exercise Dose</b>			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]
Taaffe cont'd		Phase 2: 26 wks	Phase 2 AET1: CE	Phase 2 AET1: 2	<u>Phase 2</u> AET1: NR	Phase 2 AET1: 70% HR <sup>max</sup>	<u>Phase 2</u> AET1: NA
Villareal et al., (2017) <sup>56</sup>	MC	Total (single-phase): 26 wks	AET1: CE, TM RET1: MW, FW CAET1: CE, TM, SC CRET1: MW, FW	AET1: 3 RET1: 3 CAET1: 3 CRET1: 3	AET1: 40 RET1: 40 CAET1: 30-40 CRET1: 30-40	AET1: 65-85% VO <sub>2</sub> <sup>max</sup> RET1: 65-85% 1RM; 8-12 reps, 1-3 sets CAET1: 65-85% VO <sub>2</sub> <sup>max</sup> CRET1: 65-85% 1RM	AET1, RET1 & CET1: Diet & dieticia support theraj
Dieli-Conwright et al., (2018) <sup>20</sup>	UNI	Total (single-phase): 16 wks	CAET1: CE, TM, WK, RE CRET1: MW	CAET1: 3 CRET1: 2	CAET1: 30-50 CRET1: NR	CAET1: 65-80% HR <sup>max</sup> CRET1: 60% 1RM (upper); 10-15 reps, 3 sets; 80% 1RM (lower); 10-15 reps, 3 sets	NA
McDermott et al., $(2018)^{40}$	НМ	Total: 40 wks Phase 1: 4 wks	Phase 1 AET1: WK	Phase 1 AET1: 1	<u>Phase 1</u> AET1: NR	Phase 1 AET1: NR	NA
		Phase 2: 36 wks	<u>Phase 2</u> AET1: WK	Phase 2 AET1: 5	<u>Phase 2</u> AET1: 10-50	<u>Phase 2</u> AET1: 12-14 RPE	
combined aerobic CET1: combined combined aerobic CE: elliptical ergo nedical center; m owing ergometer	e and resistand aerobic and r e and resistand ometer; EX: e hin: minutes; r; REC: recrea rate of percei	ce exercise training (gro resistance exercise training ce exercise training (gro exercise; FW: free weigh MW: machine weights; ational center; reps: repo ved exertion; SC: stair of	up 1); CAET2: aerobic cc ng (group 1); CET2: com up 1); CRET2: resistance nts; HM: home; HR: heart NA: not applicable; n: nu etitions; RET1: resistance	imponent of com bined aerobic and component of co rate; HR <sup>max</sup> : max mber; NR: not re exercise training	bined aerobic and res d resistance exercise ombined aerobic and ximal heart rate; HR <sup>p</sup> ported; PG: public gy (group 1); RET2: res	d; BW: body weight; CAET1: aerobic cc sistance exercise training (group 2); CE: training (group 2); CRET1: resistance cc resistance exercise training (group 2); d/ eak: peak heart rate; HRR: heart rate rese ym; RB: resistance bands; RC: rehabilita sistance exercise training (group 2); RM iversity; VO2max: maximal oxygen upta	cycle ergometer; omponent of wk: days per week rve; JG: jogging; N tion center; RE: : repetition

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# Supplementary Table 7: Pharmacological Intervention Characteristics

# Supplementary Table 7: Pharmacological Intervention Characteristics

I		Length		Pharmaceutical Dose		
Study	Location		Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	<sup>—</sup> Co-intervention [Group: Details]
Ahmed et al. (2008) <sup>60</sup>	NR	Total (single-phase): 109.2 wks	Grp1: NR Grp2: NR	Grp1: 1x/day Grp2: 1x/day	Grp1: Amiodarone 200mg, 600mg Grp2: Amiodarone 200mg	NA
Gheorghiade et al. (2008) <sup>69</sup>	HSP	Total (single-phase): 1 day	Grp1: IV Grp2: IN Grp3: IN	Grp1: 1x dose Grp2: 1x dose Grp3: 1x dose	Grp1: Istaroxime 0.5ug/kg/min Grp2: Istaroxime 1.0ug/kg/min Grp3: Istaroxime 1.5ug/kg/min	NA
Greenspan et al. (2008) <sup>72</sup>	NR	Total (single-phase): 104 wks	Grp1: PO	Grp1: 1x/wk	Grp1: Risendronate 35 mg	Calcium & Vitamin I needed
Grudell et al. (2008) <sup>73</sup>	OMC	Total (single-phase): 12 wks	Grp1: NR Grp2: NR	Grp1: 1x/day Grp2: 1x/day	Grp1: Sibutramine 10mg Grp2: Sibutramine 15mg	Grp1 & Grp2: Writte psychologist-based weight managemen behavioral therapy
Irani et al. (2008) <sup>79</sup>	NR	Total (single-phase): 193.5 wks	Grp1: PO, IN Grp2: PO, IN	Grp1: 1x/3mo (Goserelin) Grp1: 3x/day (Flutamide) Grp2: 1x/3mo (Goserelin) Grp2: 3x/day (Flutamide) 6 mths, no drugs 6mths, repeat	Grp1: Goserelin 10.8mg Grp1: Flutamide 250mg Grp2: Goserelin 10.8mg Grp2: Flutamide 250mg	NA
Nissen et al. (2008) <sup>89</sup>	NR	Total (single-phase): 52 wks	Grp1: PO Grp2: PO	Grp1: 1x/day Grp2: 1x/day	Grp1: Glimepiride 2.9 mg (1-4mg) Grp2: Pioglitazone 37.4 mg (15-45mg)	Grp1 & Grp2: Insulin Metformin, or both needed
Ratziu et al. (2008) <sup>92</sup>	NR	Total: 51.3 wks Phase 1: 4 wks	<u>Phase 1</u> Grp1: NR	<u>Phase 1</u> Grp1: 1x/day	Phase 1 Grp1: Rosiglitazone 4mg	NA
		Phase 2: 47.3 wks	Phase 2 Grp1: NR	Phase 2 Grp1: 1x/day	<u>Phase 2</u> Grp1: Rosiglitazone 8mg	
Caminiti et al. $(2009)^{61}$	NR	Total (single-phase): 12 wks	Grp1: IN	Grp1: 1x/6wks	Grp1: Testosterone undecanoate 1000mg	NA
Frustaci et al. (2009) <sup>68</sup>	NR	Total (single-phase): 26 wks	Grp1: PO	Grp1: 2x/day	Grp1: Prednisone 0.33mg/kg/day, 1mg/kg/day Grp1: Azathioprine 2mg/kg/day	NA

Supplementary Table 7: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose	-Co intervention	
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	<sup>–</sup> Co-intervention [Group: Details]
Lapperre et al. (2009) <sup>86</sup>	NR	Total: 130 wks Phase 1: 26 wks	<u>Phase 1</u> Grp1: INH Grp2: INH Grp3: INH	Phase 1 Grp1: 2x/day Grp2: 2x/day Grp3: 2x/day	<u>Phase 1</u> Grp1: Fluticasone propionate 500ug Grp2: Fluticasone propionate 500ug Grp3: Fluticasone propionate 500ug Grp3: Salmeterol 50ug	NA
		Phase 2: 104 wks	Phase 2 Grp1: INH Grp2: INH Grp3: INH	Phase 2 Grp1: 2x/day Grp2: 2x/day Grp3: 2x/day	Phase 2 Grp1: Fluticasone propionate 500ug Grp2: Placebo 0mg Grp3: Fluticasone propionate 500ug Grp3: Salmeterol 50ug	
Pradhan et al. (2009) <sup>91</sup>	HSP	Total (single-phase): 14 wks	Grp1: IN Grp2: PO Grp3: PO, IN	Grp1: 1x/day Grp2: 2x/day Grp3: 1x/day (Insulin) Grp3: 1-2x/day (Metformin)	Grp1: Insulin glargine 5U starting Grp2: Metformin 500mg, 1000mg Grp3: Insulin glargine 5U starting Grp3: Metformin 500mg, 1000mg	NA
Loprinzi et al. (2010) <sup>87</sup>	NR	Total (single-phase): 6 wks	Grp1: PO Grp2: PO	Grp1: 1x/day; 2x/day Grp2: 1x/day; 2x/day	Grp1: Pregabalin 50mg, 75mg Grp2: Pregabalin 50mg, 75mg, 150mg	NA
Smith et al. (2010) <sup>96</sup>	NR	Total (single-phase): 52 wks	Grp1: PO	Grp1: 2x/day	Grp1: Lorcaserin 10mg	NA
Ellis et al. (2011) <sup>66</sup>	NR	Total (single-phase): 3-4 wks	Grp1: PO Grp2: PO Grp3: PO	Grp1: 1x/day Grp2: 1x/day GrGrp3: 1x/day	Grp1: Exemestane 25mg Grp2: Letrozole 2.5mg Grp3: Anastrozole 1mg	NA
Rosenheck et al. (2011) <sup>94</sup>	HSP	Total (single-phase): 104 wks	Grp1: IN	Grp1: 1x/2wk	Grp1: Risperidone 25mg, 37.5mg, 50mg	NA
Spitzer et al. (2012) <sup>98</sup>	NR	Total (single-phase): 14 wks	Grp1: PO, TD Grp2: PO	Grp1: 2.7 x/wk (Sildenafil) Grp1: 3 x/day (Testosterone) Grp2: 2.7 x/wk (Sildenafil)	Grp1: Sildenafil 25mg, 50mg, 100mg Grp1: Testosterone 5g, 10g, 15g Grp2: Sildenafil 25mg, 50mg, 100mg	NA
Gheorghiade et al. (2013) <sup>70</sup>	NR	Total (single-phase): 48.6 wks <sup>MED</sup>	Grp1: PO	Grp1: 1x/day	Grp1: Aliskiren 150mg or 300mg	NA
Hurvitz et al. (2013) <sup>78</sup>	NR	Total (single-phase): 43.9 wks <sup>MED</sup>	Grp1: IV Grp2: Other, IV	Grp1: 1x/3wks Grp2: 1x/3wks	Grp1: Trastuzumab emtansine 3.6 mg/kg Grp2: Trastuzumab 8mg/kg load, 6mg/kg Grp2: Docetaxel 75mg/m <sup>2</sup> or 100mg/m <sup>2</sup>	NA

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# Supplementary Table 7: Pharmacological Intervention Characteristics

•	Location NR	2 (when applicable)]	Modalities	Frequency	N7 11 41	<sup>—</sup> Co-intervention
	NR			[x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	[Group: Details]
		Total (single-phase): 52 wks	Grp1: PO, IN Grp2: PO, IN	Grp1: 1x/4mo (Leuoprolide) Grp1: 1x/wk (Alendonrate) Grp1: 1x/day (Calcium) Grp1: 1x/day (Vitamin D) Grp2: 1x/4mo (Leuoprolide) Grp2: 1x/day (Calcium) Grp2: 1x/day (Vitamin D)	Grp1: Leuoprolide 30mg Grp1: Alendonrate 70mg Grp1: Calcium 500mg Grp1: Vitamin D 500Iu Grp2: Leuoprolide 30mg Grp2: Calcium 500mg Grp2: Vitamin D 500Iu	NA
Kosmala et al. (2013) <sup>83</sup>	HSP	Total (single-phase): 1 wk	Grp1: PO	Grp1: 2x/day	Grp1: Ivabradine 5mg	NA
Poole et al. (2013) <sup>90</sup>	HSP	Total (single-phase): 4 wks	Grp1: IN	Grp1: 3x/wk	Grp1: Granulocyte-macrophage-colony stimulating factor 500ug	NA
van der Bom et al. $(2013)^{103}$	NR	Total (single-phase): 166.4 wks	Grp1: PO	Grp1: 2x/day	Grp1: Valsartan 160mg	NA
Yardley et al. (2013) <sup>106</sup>	HSP	Total (single-phase): Grp1: 18.5 wks <sup>MED</sup> Grp2: 9.89 wks <sup>MED</sup>	Grp1: PO Grp2: PO	Grp1: 1x/day (Exemestane) Grp1: 1x/wk (Entinostat) Grp2: 1x/day	Grp1: Exemestane 25mg; Grp1: Entinostat 5mg Grp2: Exemestane 25mg	NA
Ford et al. (2014) <sup>67</sup>	NR	Total (single-phase): 30 days	Grp1: PO	Grp1: 1x/day	Grp1: Clopidogrel 75mg	NA
Han et al. (2014) <sup>75</sup>	NR	Total (single-phase): 5 days	Grp1: PO	Grp1: 1x/day	Grp1: Rosuvastatin 10mg	Isotonic saline (0.9 Na at 1ml/kg/h) as needed
Harman et al. (2014) <sup>76</sup>	NR	Total (single-phase): 208 wks	Grp1: PO Grp2: TD	Grp1: 1x/day Grp2: 1x/wk	Grp1: Equine estrogen 0.45mg Grp2: Transdermal 17B-estradiol 50ug/d	Grp1& Grp2: Progest- erone (200 mg/d; firs 12 days / mth)
Taplin et al. (2014) <sup>99</sup>	NR	Total: 24 wks Phase 1: 12 wks	<u>Phase 1</u> Grp1: IN Grp2: IN, NR	Phase 1 Grp1: 1x/4wk Grp2: 1x/4wk (LHRH agonist) Grp2: 1x/day (Abiraterone acetate) Grp2: 1x/day (Prednisone)	Phase 1 Grp1: Leuprolide acetate 7.5mg Grp2: LHRH agonist 7.5 mg Grp2: Abiraterone acetate 1000 mg Grp2: Prednisone 5 mg	Phase 1 & Phase 2: Radical prostatectom at end of Phase 2

Supplementary Table 7: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		— a ·
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Taplin cont'd		Phase 2: 12 wks	<u>Phase 2</u> Grp1: IN, NR Grp2: IN, NR	Phase 2 Grp1: 1x/day (Abiraterone acetate) Grp1: 1x/4wk (Leuprolide acetate) Grp1: 1x/day (Prednisone) Grp2: 1x/day (Abiraterone acetate) Grp2: 1x/4wk (Leuprolide acetate) Grp2: 1x/day (Prednisone)	Grp1: Leuprolide acetate 7.5mg Grp1: Prednisone 5mg Grp2: Abiraterone acetate 1000mg	
Cummings et al. (2015) <sup>63</sup>	HSP, OMC	Total (single-phase): 5 wks	Grp1: PO	Grp1: 1x/day (active drug) & 1x/day placebo (wk 1) Grp1: 2x/day active drug (wks 2-5)	Grp1: Dextromethorphan 20mg, 30mg Grp1: Quinidine 10mg	NA
Hamshere et al. (2015) <sup>74</sup>	HSP	Total (single-phase): 5 days	Grp1: IN Grp2: IN Grp3: IN	Grp1: 1x/day Grp2: 1x/day Grp3: 1x/day	Grp1: GCSF 10 ug/kg/day Grp2: GCSF 10 ug/kg/day Grp3: GCSF 10 ug/kg/day	Grp1: NA Grp2: BM harvest & intracoronary injection of bone marrow-derived co Grp3: BM harvest & intracoronary seru injection
Hoendermis et al. (2015) <sup>77</sup>	NR	Total (single-phase): 10 wks	Grp1: PO	Grp1: 3x/day	Grp1: Sildenafil 60 mg	NA
Krankenberg et al. (2015) <sup>85</sup>	OMC	Total (single-phase): 1 day	Grp1: Intra-lesion via coated balloon Grp2: NR	Grp1: 1x dose (Paclitaxel); Grp1: 1x/day (Aspirin); Grp1: 1x/day (Clopidogrel) Grp2: 1x/day (Aspirin); Grp2: 1x/day (Clopidogrel)	Grp1: Paclitaxel 3.5ug/mm <sup>2</sup> of balloon; Grp1: Aspirin 100mg; Grp1: Clopidogrel 75mg Grp2: Aspirin 100mg; Grp2: Clopidogrel 75mg	Grp1 & Grp2: Hepar (5,000 - 10,000U based on body weight during Sx
Tsujita et al. (2015) <sup>100</sup>	NR	Total (single-phase): Grp1: 43.4 wks Grp2: 41.7 wks	Grp1: NR Grp2: NR	Grp1: 1x/day Grp2: NR	Grp1: Atorvastatin NR Grp1: Ezemtimibe 10mg Grp2: Atorvastatin NR	NA
Ulrich et al. (2015) <sup>101</sup>	HSP	Total (single-phase): 1 wk	Grp1: PO Grp2: PO	Grp1: 2x/day Grp2: 2x/day	Grp1: Acetazolamide 250mg Grp2: Placebo 0mg	Grp1: Sham nocturna oxygen therapy Grp2: Real nocturnal oxygen therapy

Supplementary Table 7: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		- 0 • 1 • •
Study	Location       [Total; Phase 1 & Phase       Modalities         2 (when applicable)]       Frequency       Medication         [x/time]       [Grp#: Med 1 dose; med 2 dose, etc.]			Co-intervention [Group: Details]		
Cortelazzo et al. (2016) <sup>62</sup>	NR	Total: Grp1: 4 wks Grp2: 4.6 wks Phase 1: Grp1: 2 wks Grp2: 3 wks	Phase 1 Grp1: PO, IN, IV Grp2: PO, IN, IV	<u>Phase 1</u> Grp1: 1x/2wk <b>RCHOP</b> (w 1x/d P;	Phase 1           Grp1: R (375mg/m²); C (750 mg/m²); H (50mg/m²); O (1.4 mg/m²); P (100mg); Filgrastim (5ug/kg)           Grp2: R (375mg/m²); C (7g/m²); H (50mg/m²; 75mg/m²); O (1.4 mg/m²); P (40mg/m²); Filgrastim (5ug/kg and 10ug/kg); Cytarabine (2g/m²)	Phase 1 & Phase 2 Grp1: CNS prophylaxis (high risk patients) Grp1: PCP prophylaxis Grp1: HSV prophylaxi Grp2: Peripheral blood progenitor cell reinfusion (day 77) Grp2: CNS prophylaxis (high risk patients) Grp2: PCP prophylaxis Grp2: HSV prophylaxi
		Phase 2: Grp1: 2 wks Grp2: 1.6 wks	<u>Phase 2</u> Grp1: PO, IN, IV Grp2: IV	Phase 2 Grp1: 1x/2wk RCHOP (w 1x/d P; days 1-5 per cycle) Grp1: 1x/d Filgrastim; days 7-11 per cycle) Grp2: 1x/d Etoposide; day 112 Grp2: 1x/d Cisplatin; day 113 Grp2: 1x/d Filgrastim; day 114	Phase 2 Grp1: <b>R</b> (375mg/m <sup>2</sup> ); <b>C</b> (750 mg/m <sup>2</sup> ); <b>H</b> (50mg/m <sup>2</sup> ); <b>O</b> (1.4 mg/m <sup>2</sup> ); <b>P</b> (100 mg/m <sup>2</sup> ); Filgrastim (5ug/kg) Grp2: Etoposide 2.4 g/ m <sup>2</sup> Grp2: Cisplatin 100mg/ m <sup>2</sup> Grp2: Filgrastim 5ug/kg	
				Conditional Grp2: 1x/d Mitoxantrone; day 133 Grp2: 1x/day Melphalan; day 135 or 137 OR Grp2: 1x/d Carmustine; day 133 Grp2: 1x/d Etoposide; day 134- 137 Grp2: 12hr Cytarabine; day 134- 137 Grp2: 1x/d Melphalan; day 138	Conditional Grp2: Mitoxantrone 60mg/ m <sup>2</sup> Grp2: Melphalan 180mg/ m <sup>2</sup> OR Grp2: Carmustine 300mg/m <sup>2</sup> Grp2: Etoposide 200mg/m <sup>2</sup> Grp2: Cytarabine 200mg/m <sup>2</sup> Grp2: Melphalen 140mg/m <sup>2</sup>	
Cusi et al. (2016) <sup>64</sup>	NR	Total: 77 wks Phase 1: 8 wks Phase 2: 69 wks	Phase 1 Grp1: PO	Phase 1 Grp1: 1x/day	Phase 1 Grp1: Pioglitazone 30mg	Phase 1 & Phase 2 Hypocaloric diet
			Phase 2 Grp1: PO	Phase 2 Grp1: 1x/day	Phase 2 Grp1: Pioglitazone 45mg	
						1

Supplementary Table 7: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		— Ca :=+
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Kosmala et al. (2016) <sup>84</sup>	NR	Total (single-phase): 26 wks	Grp1: PO	Grp1: 1x/day	Grp1: Spironolactone 25mg	NA
McKay et al. (2016) <sup>88</sup>	NR	Total (single-phase): 26 wks	Grp1: PO, IN, IV Grp2: PO, IN	Grp1: 1x/3mo (Leuprolide OR Goserelin); Grp1: 1x/day (Bicalutamide) Grp1: 1x/3wk (Bevacizumab) Grp2: 1x/3mo (Leuprolide OR Goserelin) Grp2: 1x/day (Bicalutamide)	Grp1: Leuprolide acetate 22.5mg or Goserelin acetate 10.8mg Grp1: Bicalutamide 10mg Grp1: Bevacizumab 15mg/kg Grp2: Leuprolide acetate 22.5mg or Goserelin acetate 10.8mg Grp2: Bicalutamide 50mg	NA
Schmid et al. (2016) <sup>95</sup>	NR	Total (single-phase): 2 wks	Grp1: PO Grp2: PO	Grp1: 1x/day Grp2: 1x/day	Grp1: Anastrazole 1mg Grp2: Anaztrazole 1mg Grp2: Pictilisib 260mg, 340mg	NA
Yoshimura et al. (2016) <sup>107</sup>	NR	Total (single-phase): Grp1: 30 wks <sup>MED</sup> Grp2: 94.6 wks <sup>MED</sup>	Grp1: NR Grp2: IN, NR	Grp1: 1x/day Grp2: 1x/day (Dexamethasone) Grp2: 1x/2wk (Peptide vaccine)	Grp1: Dexamethasone 1mg Grp2: Dexamethasone 1mg Grp2: Peptide vaccine 3mg	NA
Goebel et al. (2017) <sup>71</sup>	NR	Total (single-phase): 6 wks	Grp1: IV	Grp1: 2x/6wks	Grp1: Intratectivig 0.5g/kg	NA
Soiffer et al. (2017) <sup>97</sup>	NR	Total (single-phase): 3 days	Grp1: IV	Grp1: 1x/day Anti–T- lymphocyte globulin (3 days) Grp1: Antihistamine (NR) Grp1: 1x/day Methylprednisolone (3 days) Grp1: 1x/day Methotrexate (4 days)	Grp1: Anti–T- lymphocyte globulin Grp1: Antihistamine 20mg/kg Grp1: Methylprednisolone 2mg/kg, 1mg/kg Grp1: Methotrexate 10-15 mg/m <sup>2</sup>	NA
Urruticoechea et al. (2017) <sup>102</sup>		Total (single-phase): Grp1: 36 wks (Trastuzumab) 30 wks (Capecitabine) Grp2: 45 wks (Trastuzumab) 36 wks (Capecitabine) 45 wks (Pertuzumab)	Grp1: PO, IV Grp2: PO, IV	Grp1: 1x/3wk Trastuzumab Grp1: 2x/day Capecitabine (2 wks on / 1wk off) Grp2: 1x/3wk Pertuzumab Grp2: 1x/3wk Trastuzumab Grp2: 2x/day Capecitabine (2 wks on / 1wk off)	Grp1: Trastuzumab (8mg/kg loading; 6mg/kg maintenance) Grp1: Capecitabine 1250 mg/m <sup>2</sup> Grp2: Pertuzumab (840mg loading; 420mg maintenance) Grp2: Trastuzumab (8mg/kg loading; 6mg/kg maintenance) Grp2: Capecitabine 1000 mg/m <sup>2</sup>	NA
Wysham et al. (2017) <sup>105</sup>	NR	Total: 64 wks Phase 1: 32 wks	<u>Phase 1</u> Grp1: IN Grp2: IN	Phase 1 Grp1: 1x/day Grp2: 1x/day	Phase 1 Grp1: Insulin degludec 70U Grp2: Insulin glargine 74U	NA

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Supplementary Table 7: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		<u> </u>
Study	Location [Total; Phase 1 & Phase Modalities 2 (when applicable)] [x/time]			Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]	
		Phase 2: 32 wks	<u>Phase 2</u> Grp1: IN Grp2: IN	Phase 2 Grp1: 1x/day Grp2: 1x/day	<u>Phase 2</u> Grp1: Insulin glargine 83U Grp2: Insulin degludec 83U	
Devereux et al. (2018) <sup>65</sup>	NR	Total (single-phase): 52 wks	Grp1: PO	Grp1: 1-2x/day	Grp1: Theophylline 200mg	NA
Johnson et al. (2018) <sup>80</sup>	NR	Total (single-phase): 53.6 wks	Grp1: PO, IV Grp2: IV Grp3: PO	Grp1: 1x/day (Lapatinib) Grp1: 1x/3wk (Trastuzumab) Grp2: 1x/3wk Trastuzumab GrGrp3: 1x/day Lapatinib	Grp1: Lapatinib 1000mg; Grp1: Trastuzumab (8mg/kg loading, 6mg/kg maintenance) Grp2: Trastuzumab (8mg/kg loading, 6mg/kg maintenance) Grp3: Lapatinib 1500 mg	Grp1, Grp2 & GrGrp3 Aromatase inhibitor (as needed): Letrozo 2.5mg/day, Anas- trozole 1mg/day, or Exemestane 25mg/d
Kim et al. (2018) <sup>81</sup>	NR	Total (single-phase): 24 wks	Grp1: PO	Grp1: 1x/day	Grp1: Escitalopram 7.6mg (5mg, 10mg, 15mg or 20mg)	NA
Rimawi et al. (2018) <sup>93</sup>	OMC	Total (single-phase): 52 wks	Grp1: PO, IV Grp2: PO, IN	Grp1: 1x/3wk (Pertuzumab or Trastuzumab); Grp1: 1x/day (Letrozole) Grp2: 1x/3wk (Trastuzumab); Grp2: 1x/day (Anastrozole or Letrozole)	<ul> <li>Grp1: Pertuzumab (840mg loading, 420mg maintenance)</li> <li>Grp1: Trastuzumab (8mg/kg loading, 6mg/kg maintenance)</li> <li>Grp1: Anastrozole 1mg or Letrozole 2.5mg</li> <li>Grp2: Trastuzumab (8mg/kg loading, 6mg/kg maintenance)</li> <li>Grp2: Anastrozole 1mg or Letrozole 2.5mg</li> </ul>	Grp1 & Grp2: Inducti IV Docetaxel q3wk Paclitaxel q1wk for 18-24wk as needed (decided prior to random assignment)
Wapnir et al. (2018) <sup>104</sup>	NR 4	Total (single-phase): 12-26 wks	Grp1: NR	Grp1: NR	Grp1: NR	Grp1: Radiotherapy & endocrine therapy required by surgica margins & tumor hormone markers.

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# Supplementary Table 8: Exercise RCT CONSORT-NPT Data Extraction Summary

Item		Evaluation Outcomes				
No.	Criterion	Yes	Unclear	No	NA	
1a	Identification as a randomized trial in the title.	<b>No. (%)</b> 36 (75.0%)	<b>No. (%)</b> 0 (0.0%)	<b>No. (%)</b> 12 (25.0%)	<b>No. (%)</b> 0 (0.0%)	
		· · · · · ·		× /		
b	Structured summary of trial design, methods, results, and conclusions.	× ,	0 (0.0%)	2 (4.2%)	0 (0.0%)	
2a	Scientific background and explanation of rationale.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
2b	Specific objectives or hypothesis.	44 (91.7%)	4 (8.3%)	0 (0.0%)	0 (0.0%)	
Bai	Description of trial design (such as parallel, factorial) including allocation ratio.	13 (27.1%)	20 (41.7%)	15 (31.3%)	0 (0.0%)	
Baii	When applicable, how care providers were allocated to each trial group.	0 (0.0%)	0 (0.0%)	46 (95.8%)	2 (4.2%)	
3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons.	9 (18.8%)	0 (0.0%)	6 (12.5%)	33 (68.8%	
4ai	Eligibility criteria for participants.	38 (79.2%)	10 (20.8%)	0 (0.0%)	0 (0.0%)	
4aii	When applicable, eligibility criteria for centers and for care providers.	3 (6.3%)	16 (33.3%)	29 (60.4%)	0 (0.0%)	
4b	Settings and locations where the data were collected.	18 (37.5%)	3 (6.3%)	27 (56.3%)	0 (0.0%)	
5i	The interventions for each group with sufficient details to allow replication, including how and when they	0 (0.0%)	0 (0.0%)	48 (100.0%)	0 (0.0%)	
	were actually administered.			× ,		
511	Precise details of both the experimental treatment and comparator.	47 (97.9%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	
5a	Description of the different components of the interventions and, when applicable, description of the procedure for tailoring the interventions to individual participants.	8 (16.7%)	16 (33.3%)	24 (50.0%)	0 (0.0%)	
5b	Details of whether and how the interventions were standardized.	5 (10.4%)	2 (4.2%)	41 (85.4%)	0 (0.0%)	
5c	Details of whether and how adherence of care providers to the protocol was assessed or enhanced.	2 (4.2%)	3 (6.3%)	43 (89.6%)	0 (0.0%)	
5d	Details of whether and how adherence of participants to interventions was assessed or enhanced.	2 (4.2%)	3 (6.3%)	43 (89.6%)	0 (0.0%)	
6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they	40 (83.3%)	2 (4.2%)	6 (12.5%)	0 (0.0%)	
	were assessed.					
6b	Any changes to trial outcomes after the trial commenced, with reasons.	2 (4.2%)	0 (0.0%)	1 (2.1%)	45 (93.8%	
7ai	How sample size was determined.	42 (87.5%)	0 (0.0%)	6 (12.5%)	0 (0.0%)	
	When applicable, details of whether and how the clustering by care providers or centers was addressed.	0 (0.0%)	0 (0.0%)	30 (62.5%)	18 (37.5%	

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# Supplementary Table 8: Exercise RCT CONSORT-NPT Data Extraction Summary

[tem		Evaluation (			
No.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)
7b	When applicable, explanation of any interim analyses and stopping guidelines.	5 (10.4%)	0 (0.0%)	0 (0.0%)	43 (89.6%
Ba	Method used to generate random allocation sequence.	33 (68.8%)	0 (0.0%)	15 (31.3%)	0 (0.0%)
ßb	Type of randomization; details of any restriction (such as blocking and block size).	39 (81.3%)	0 (0.0%)	9 (18.8%)	0 (0.0%)
	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.	15 (31.3%)	0 (0.0%)	33 (68.8%)	0 (0.0%)
	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.	3 (6.3%)	7 (14.6%)	38 (79.2%)	0 (0.0%)
	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	18 (37.5%)	0 (0.0%)	30 (62.5%)	0 (0.0%)
l 1b	If relevant, description of the similarity of interventions.	12 (25.0%)	0 (0.0%)	0 (0.0%)	36 (75.0%
11c	If blinding was not possible, description of any attempts to limit bias.	12 (25.0%)	1 (2.1%)	22 (45.8%)	13 (27.1%
12ai	Statistical methods used to compare groups for primary and secondary outcomes.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
12aii	When applicable, details of whether and how the clustering by care providers or centers was addressed.	5 (10.4%)	0 (0.0%)	21 (43.8%)	22 (45.8%
12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses.	27 (56.3%)	0 (0.0%)	0 (0.0%)	21 (43.8%
13a	Participant flow diagram.	42 (87.5%)	0 (0.0%)	6 (12.5%)	0 (0.0%)
	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome.	41 (85.4%)	0 (0.0%)	7 (14.6%)	0 (0.0%)
	The number of care providers or centers performing the intervention in each group and the number of patients treated by each care provider or in each center.	7 (14.6%)	0 (0.0%)	41 (85.4%)	0 (0.0%)
13b	For each group, the delay between randomization and the initiation of the intervention.	43 (89.6%)	2 (4.2%)	3 (6.3%)	0 (0.0%)
13c	For each group, the delay between randomization and the initiation of the intervention.	1 (2.1%)	0 (0.0%)	47 (97.9%)	0 (0.0%)
13d	Details of the experimental treatment and comparator as they were implemented.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
14a	Dates defining the periods of recruitment and follow-up.	18 (37.5%)	22 (45.8%)	8 (16.7%)	0 (0.0%)
14b	Why the trial ended or was stopped.	7 (14.6%)	0 (0.0%)	3 (6.3%)	38 (79.2%
l 5i	A table showing baseline demographic and clinical characteristics for each group.	45 (93.8%)	0 (0.0%)	3 (6.3%)	0 (0.0%)

Supplementary Table 8: Exercise RCT CONSORT-NPT Data Extraction Summary

14		Evaluation Outcomes				
Item No.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)	
15ii	When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group.	13 (27.1%)	0 (0.0%)	35 (72.9%)	0 (0.0%)	
16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.	37 (77.1%)	9 (18.8%)	2 (4.2%)	0 (0.0%)	
17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval).	36 (75.0%)	0 (0.0%)	12 (25.0%)	0 (0.0%)	
17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended.	13 (27.1%)	0 (0.0%)	3 (6.3%)	32 (66.7%)	
18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory.	29 (60.4%)	0 (0.0%)	1 (2.1%)	18 (37.5%)	
19	See CONSORT-Harms					
20i	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.	33 (68.8%)	8 (16.7%)	7 (14.6%)	0 (0.0%)	
20ii	In addition, take into account the choice of the comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group.	9 (18.8%)	7 (14.6%)	32 (66.7%)	0 (0.0%)	
21	Generalizability (external validity) of the trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
23	Registration number and name of trial registry.	39 (81.3%)	0 (0.0%)	9 (18.8%)	0 (0.0%)	
24	Where the full trial protocol can be accessed, if available.	10 (20.8%)	0 (0.0%)	38 (79.2%)	0 (0.0%)	
25	Sources of funding and other support (such as supply of drugs), role of funders.	24 (50.0%)	20 (41.7%)	4 (8.3%)	0 (0.0%)	

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Supplementary Table 9: Pharmacological RCT CONSORT Data Extraction Summary

## Supplementary Table 9: Pharmacological RCT CONSORT Data Extraction Summary

Item		Evaluation Outcomes				
No.	Criterion	Yes	Unclear	No	NA	
		No. (%)	No. (%)	No. (%)	No. (%)	
1a	Identification as a randomized trial in the title.	43 (89.6%)	0 (0.0%)	5 (10.4%)	0 (0.0%)	
1b	Structured summary of trial design, methods, results, and conclusions.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
2a	Scientific background and explanation of rationale.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
2b	Specific objectives or hypothesis.	37 (77.1%)	11 (22.9%)	0 (0.0%)	0 (0.0%)	
3a	Description of trial design (such as parallel, factorial) including allocation ratio.	30 (62.5%)	9 (18.8%)	9 (18.8%)	0 (0.0%)	
3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons.	10 (20.8%)	0 (0.0%)	5 (10.4%)	33 (68.8%	
4a	Eligibility criteria for participants.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
4b	Settings and locations where the data were collected.	10 (20.8%)	7 (14.6%)	31 (64.6%)	0 (0.0%)	
5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered.	32 (66.7%)	0 (0.0%)	16 (33.3%)	0 (0.0%)	
6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.	42 (87.5%)	5 (10.4%)	1 (2.1%)	0 (0.0%)	
6b	Any changes to trial outcomes after the trial commenced, with reasons.	1 (2.1%)	0 (0.0%)	0 (0.0%)	47 (97.9%	
7a	How sample size was determined.	46 (95.8%)	0 (0.0%)	2 (4.2%)	0 (0.0%)	
7b	When applicable, explanation of any interim analyses and stopping guidelines.	10 (20.8%)	0 (0.0%)	1 (2.1%)	37 (77.1%	
8a	Method used to generate random allocation sequence.	26 (54.2%)	0 (0.0%)	22 (45.8%)	0 (0.0%)	
8b	Type of randomization; details of any restriction (such as blocking and block size).	38 (79.2%)	0 (0.0%)	10 (20.8%)	0 (0.0%)	
9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.	21 (43.8%)	0 (0.0%)	27 (56.3%)	0 (0.0%)	
10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.	4 (8.3%)	10 (20.8%)	34 (70.8%)	0 (0.0%)	
11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	47 (97.9%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	
11b	If relevant, description of the similarity of interventions.	22 (45.8%)	0 (0.0%)	0 (0.0%)	26 (54.2%	

# Supplementary Table 9: Pharmacological RCT CONSORT Data Extraction Summary

Itom		<b>Evaluation</b>	Outcomes		
Item No.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)
12a	Statistical methods used to compare groups for primary and secondary outcomes.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses.	30 (62.5%)	0 (0.0%)	11 (22.9%)	7 (14.6%
13	Participant flow diagram.	43 (89.6%)	0 (0.0%)	5 (10.4%)	0 (0.0%)
13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome.	46 (95.8%)	0 (0.0%)	2 (4.2%)	0 (0.0%)
13b	For each group, the delay between randomization and the initiation of the intervention.	39 (81.3%)	6 (12.5%)	1 (2.1%)	2 (4.2%)
14a	Dates defining the periods of recruitment and follow-up.	32 (66.7%)	14 (29.2%)	2 (4.2%)	0 (0.0%)
14b	Why the trial ended or was stopped.	7 (14.6%)	0 (0.0%)	6 (12.5%)	35 (72.99
15	A table showing baseline demographic and clinical characteristics for each group.	47 (97.9%)	0 (0.0%)	1 (2.1%)	0 (0.0%)
16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.	36 (75.0%)	11 (22.9%)	1 (2.1%)	0 (0.0%)
17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval).	39 (81.3%)	0 (0.0%)	9 (18.8%)	0 (0.0%)
17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended.	34 (70.8%)	0 (0.0%)	3 (6.3%)	11 (22.9
18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory.	41 (85.4%)	0 (0.0%)	1 (2.1%)	6 (12.5%
19	See CONSORT-Harms				
20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.	29 (60.4%)	9 (18.8%)	10 (20.8%)	0 (0.0%)
21	Generalizability (external validity) of the trial findings.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
23	Registration number and name of trial registry.	40 (83.3%)	0 (0.0%)	8 (16.7%)	0 (0.0%)
24	Where the full trial protocol can be accessed, if available.	12 (25.0%)	0 (0.0%)	36 (75.0%)	0 (0.0%)
25	Sources of funding and other support (such as supply of drugs), role of funders.	23 (47.9%)	23 (47.9%)	2 (4.2%)	0 (0.0%)
Notes	NA, not applicable; No., number				
	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.x	html			1

# Supplementary Table 10: Exercise & Pharmacological RCT CONSORT-Harms Data Extraction Summary

Item No.	Criterion	Evaluation Outcomes	Exercise No. (%)	Pharma No. (%)
1	If the study collected data on harms and benefits, the title or	Yes	17 (35.4%)	34 (70.8%)
	abstract should so state.	Unclear	0 (0.0%)	0 (0.0%)
		No	31 (64.6%)	14 (29.2%)
		NA	0 (0.0%)	0 (0.0%)
2	If the trial addresses both harms and benefits, the introduction	Yes	10 (20.8%)	16 (33.3%)
	should so state.	Unclear	0 (0.0%)	0 (0.0%)
		No	38 (79.2%)	32 (66.7%)
		NA	0 (0.0%)	0 (0.0%)
3	List addressed adverse events with definitions for each (with	Yes	31 (64.6%)	41 (85.4%)
	attention, when relevant, to grading, expected vs. unexpected	Unclear	1 (2.1%)	3 (6.3%)
	events, reference to standardized and validated definitions, and	No	16 (33.3%)	4 (8.3%)
	description of new definitions).	NA	0 (0.0%)	0 (0.0%)
4	Clarify how harms-related information was collected (mode of	Yes	12 (25.0%)	17 (35.4%)
	data collection, timing, attribution methods, intensity of	Unclear	5 (10.4%)	12 (25.0%)
	ascertainment, and harms-related monitoring and stopping rules,	No	31 (64.6%)	19 (39.6%)
	if pertinent).	NA	0 (0.0%)	0 (0.0%)
5	Describe plans for presenting and analyzing information on	Yes	8 (16.7%)	27 (56.3%)
	harms (including coding, handling of recurrent events,	Unclear	0 (0.0%)	1 (2.1%)
	specification of timing issues, handling of continuous measures,	No	39 (81.3%)	20 (41.7%)
	and any statistical analyses).	NA	1 (2.1%)	0 (0.0%)
6	Describe for each arm the participant withdrawals that are due to	Yes	26 (54.2%)	31 (64.6%)
	harms and their experiences with the allocated treatment.	Unclear	0 (0.0%)	0 (0.0%)
		No	16 (33.3%)	12 (25.0%)
		NA	6 (12.5%)	5 (10.4%)
7	Provide the denominators for analyses on harms.	Yes	22 (45.8%)	39 (81.3%)
	·	Unclear	0 (0.0%)	0 (0.0%)
		No	18 (37.5%)	8 (16.7%)
		NA	8 (16.7%)	1 (2.1%)
8	Present the absolute risk per arm and per adverse event type,	Yes	13 (27.1%)	33 (68.8%)
	grade, and seriousness, and present appropriate metrics for	Unclear	0 (0.0%)	0 (0.0%)
	recurrent events, continuous variables, and scale variables,	No	29 (60.4%)	14 (29.2%)
	whenever pertinent.	NA	6 (12.5%)	1 (2.1%)
9	Describe any subgroup analyses and exploratory analyses for	Yes	3 (6.3%)	3 (6.3%)
	harms.	Unclear	0 (0.0%)	0 (0.0%)
		No	24 (50.0%)	44 (91.7%)
		NA	21 (43.8%)	1 (2.1%)
10	Provide a balanced discussion of benefits and harms with	Yes	15 (31.3%)	31 (64.6%)
	emphasis on study limitations, generalizability, and other	Unclear	0 (0.0%)	0 (0.0%)
	sources of information on harms.	No	25 (52.1%)	16 (33.3%)
		NA	8 (16.7%)	1 (2.1%)

# Supplementary Table 10: Exercise & Pharmacological RCT CONSORT-Harms Data Extraction Summary

Notes: NA, not applicable; No., number

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Item No.	Criterion	Evaluation Outcomes	Exercise No. (%)	Pharma No. (%)
1	Intervention Modality	Yes	22 (45.8%)	40 (83.3%)
		Unclear	17 (35.4%)	0 (0.0%)
		No	9 (18.8%)	8 (16.7%)
		NA	0 (0.0%)	0 (0.0%)
2	Intervention Setting	Yes	36 (75.0%)	10 (20.8%)
	C	Unclear	5 (10.4%)	2 (4.2%)
		No	7 (14.6%)	36 (75.0%)
		NA	0 (0.0%)	0 (0.0%)
3	Intervention Frequency	Yes	40 (83.3%)	46 (95.8%)
	1 5	Unclear	0 (0.0%)	0 (0.0%)
		No	8 (16.7%)	2 (4.2%)
		NA	0 (0.0%)	0 (0.0%)
4	Total Intervention Time	Yes	48 (100.0%)	47 (97.9%)
		Unclear	0 (0.0%)	0 (0.0%)
		No	0 (0.0%)	1 (2.1%)
		NA	0 (0.0%)	0 (0.0%)
5	Intervention Dose*	Yes	22 (45.8%)	46 (95.8%)
		Unclear	0 (0.0%)	0 (0.0%)
		No	26 (54.2%)	2 (4.2%)
		NA	0 (0.0%)	0 (0.0%)
6	Intervention Compliance & Adherence	Yes	2 (4.2%)	8 (16.7%)
		Unclear	3 (6.3%)	0 (0.0%)
		No	43 (89.6%)	40 (83.3%)
		NA	0 (0.0%)	0 (0.0%)

\*Complete reporting of exercise therapy dose required complete reporting of:

- Exercise session intensity (aerobic and resistance training interventions)
- Exercise session duration (aerobic and resistance training interventions) •
- Number of sets (resistance training interventions only) •
- • Number of repetitions (resistance training interventions only)

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1 2 4 5 6 7 8	Online Supplement References		
	1.	Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols	
		(PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.	
	2.	Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological	
9 10		quality of systematic reviews. Bmc Med Res Methodol. 2007;7:10.	
11 12 13 14	3.	Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, Group C. Extending the CONSORT statement to randomized trials	
		of nonpharmacologic treatment: explanation and elaboration. Ann Intern Med. 2008;148(4):295-309.	
15 16	4.	Hoffmann TC, Erueti C, Glasziou PP. Poor description of non-pharmacological interventions: analysis of consecutive sample	
17		of randomised trials. BMJ. 2013;347:f3755.	
18 19 20	5.	Mills E, Loke YK, Wu P, et al. Determining the reporting quality of RCTs in clinical pharmacology. Br J Clin Pharmacol.	
20 21 22		2004;58(1):61-65.	
23	6.	Mills EJ, Wu P, Gagnier J, Devereaux PJ. The quality of randomized trial reporting in leading medical journals since the	
24 25		revised CONSORT statement. Contemp Clin Trials. 2005;26(4):480-487.	
26 27	7.	Khan MS, Lateef N, Siddiqi TJ, et al. Level and Prevalence of Spin in Published Cardiovascular Randomized Clinical Trial	
28 29		Reports With Statistically Nonsignificant Primary Outcomes: A Systematic Review. JAMA Netw Open. 2019;2(5):e192622.	
30 31	8.	Pandis N, Polychronopoulou A, Eliades T. An assessment of quality characteristics of randomised control trials published in	
32 33		dental journals. J Dent. 2010;38(9):713-721.	
34 35	9.	Grant SP, Mayo-Wilson E, Melendez-Torres GJ, Montgomery P. Reporting quality of social and psychological intervention	
36 37		trials: a systematic review of reporting guidelines and trial publications. PLoS One. 2013;8(5):e65442.	
38 39	10.	Ghimire S, Kyung E, Kang W, Kim E. Assessment of adherence to the CONSORT statement for quality of reports on	
40 41		randomized controlled trial abstracts from four high-impact general medical journals. Trials. 2012;13(1):77.	
42	11.	Caspersen CJ, Powell KE, Christenson GM. Physical Activity, Exercise, and Physical Fitness: Definitions and Distinctions	
43 44 45		for Health-Related Research. Public Health Reports (1974-). 1985;100(2):126-131.	
46	12.	Adamsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients	
47 48		undergoing chemotherapy: randomised controlled trial. BMJ. 2009;339(7726):b3410.	
49 50	13.	Beckers PJ, Denollet J, Possemiers NM, Wuyts FL, Vrints CJ, Conraads VM. Combined endurance-resistance training vs.	
51 52		endurance training in patients with chronic heart failure: a prospective randomized study. Eur Heart J. 2008;29(15):1858-	
53 54		1866.	
55 56			
57 58			

**Online Supplement References** 

1 14. Beer M, Wagner D, Myers J, et al. Effects of exercise training on myocardial energy metabolism and ventricular function 2 3 assessed by quantitative phosphorus-31 magnetic resonance spectroscopy and magnetic resonance imaging in dilated 4 5 cardiomyopathy. J Am Coll Cardiol. 2008;51(19):1883-1891. 6 7 15. Belardinelli R, Georgiou D, Cianci G, Purcaro A. 10-year exercise training in chronic heart failure: a randomized controlled 8 9 trial. J Am Coll Cardiol. 2012;60(16):1521-1528. 10 11 16. Campbell KL, Foster-Schubert KE, Alfano CM, et al. Reduced-calorie dietary weight loss, exercise, and sex hormones in 12 13 postmenopausal women: randomized controlled trial. J Clin Oncol. 2012;30(19):2314-2326. 14 Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with 15 17. 16 type 2 diabetes: a randomized controlled trial. JAMA. 2010;304(20):2253-2262. 17 18 18. Courneya KS, Sellar CM, Stevinson C, et al. Randomized controlled trial of the effects of aerobic exercise on physical 19 20 functioning and quality of life in lymphoma patients. J Clin Oncol. 2009;27(27):4605-4612. 21 22 19. Daumit GL, Dickerson FB, Wang NY, et al. A behavioral weight-loss intervention in persons with serious mental illness. N 23 24 Engl J Med. 2013;368(17):1594-1602. 25 26 20. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Effects of Aerobic and Resistance Exercise on Metabolic 27 28 Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in Overweight or Obese Survivors of Breast Cancer: A 29 30 Randomized Controlled Trial. J Clin Oncol. 2018;36(9):875-883. 31 32 21. Duijts SF, van Beurden M, Oldenburg HS, et al. Efficacy of cognitive behavioral therapy and physical exercise in alleviating 33 34 treatment-induced menopausal symptoms in patients with breast cancer: results of a randomized, controlled, multicenter trial. 35 36 J Clin Oncol. 2012;30(33):4124-4133. 37 Edelmann F, Gelbrich G, Dungen HD, et al. Exercise training improves exercise capacity and diastolic function in patients 22. 38 39 with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot 40 41 study. J Am Coll Cardiol. 2011;58(17):1780-1791. 42 43 23. Ehlken N, Lichtblau M, Klose H, et al. Exercise training improves peak oxygen consumption and haemodynamics in patients 44 45 with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, 46 47 randomized, controlled trial. Eur Heart J. 2016;37(1):35-44. 48 49 24. Fakhry F, Spronk S, van der Laan L, et al. Endovascular Revascularization and Supervised Exercise for Peripheral Artery 50 51 Disease and Intermittent Claudication: A Randomized Clinical Trial. JAMA. 2015;314(18):1936-1944. 52 53 25. Friedenreich CM, Neilson HK, O'Reilly R, et al. Effects of a High vs Moderate Volume of Aerobic Exercise on Adiposity 54 55 Outcomes in Postmenopausal Women: A Randomized Clinical Trial. JAMA Oncol. 2015;1(6):766-776. 56 57 58 126 59 60

Page 167 of 176

# BMJ Open

Online Supplement References
------------------------------

26.	Friedenreich CM, Woolcott CG, McTiernan A, et al. Alberta physical activity and breast cancer prevention trial: sex hormone
	changes in a year-long exercise intervention among postmenopausal women. Journal of Clinical Oncology. 2010;28(9):1458.
27.	Galvao DA, Spry N, Denham J, et al. A multicentre year-long randomised controlled trial of exercise training targeting
	physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG
	03.04 RADAR. Eur Urol. 2014;65(5):856-864.
28.	Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle
	loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled
	trial. Journal of clinical oncology. 2010;28(2):340-347.
29.	Hallsworth K, Fattakhova G, Hollingsworth KG, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic
	fatty liver disease independent of weight loss. Gut. 2011;60(9):1278-1283.
30.	Hollekim-Strand SM, Bjorgaas MR, Albrektsen G, Tjonna AE, Wisloff U, Ingul CB. High-intensity interval exercise
	effectively improves cardiac function in patients with type 2 diabetes mellitus and diastolic dysfunction: a randomized
	controlled trial. J Am Coll Cardiol. 2014;64(16):1758-1760.
31.	Irwin ML, Cartmel B, Gross CP, et al. Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer
	survivors. Journal of Clinical Oncology. 2015;33(10):1104.
32.	Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in
	Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA. 2017;318(7):637-646.
33.	Jones LW, Hornsby WE, Freedland SJ, et al. Effects of nonlinear aerobic training on erectile dysfunction and cardiovascular
	function following radical prostatectomy for clinically localized prostate cancer. Eur Urol. 2014;65(5):852-855.
34.	Kitzman DW, Brubaker P, Morgan T, et al. Effect of Caloric Restriction or Aerobic Exercise Training on Peak Oxygen
	Consumption and Quality of Life in Obese Older Patients With Heart Failure With Preserved Ejection Fraction: A
	Randomized Clinical Trial. JAMA. 2016;315(1):36-46.
35.	Kitzman DW, Brubaker PH, Herrington DM, et al. Effect of endurance exercise training on endothelial function and arterial
	stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. J Am
	Coll Cardiol. 2013;62(7):584-592.
36.	Ligibel JA, Campbell N, Partridge A, et al. Impact of a mixed strength and endurance exercise intervention on insulin levels
	in breast cancer survivors. J Clin Oncol. 2008;26(6):907-912.
37.	Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive
	pulmonary disease: a randomized trial. Ann Intern Med. 2008;149(12):869-878.
	127 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
	<ol> <li>27.</li> <li>28.</li> <li>29.</li> <li>30.</li> <li>31.</li> <li>32.</li> <li>33.</li> <li>34.</li> <li>35.</li> <li>36.</li> </ol>

Online Supplement References

1 2	38.	McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial
3 4		disease with and without intermittent claudication: a randomized controlled trial. JAMA. 2009;301(2):165-174.
5 6	39.	McDermott MM, Ferrucci L, Tian L, et al. Effect of Granulocyte-Macrophage Colony-Stimulating Factor With or Without
7 8		Supervised Exercise on Walking Performance in Patients With Peripheral Artery Disease: The PROPEL Randomized
9 10		Clinical Trial. JAMA. 2017;318(21):2089-2098.
11	40.	McDermott MM, Spring B, Berger JS, et al. Effect of a Home-Based Exercise Intervention of Wearable Technology and
12 13		Telephone Coaching on Walking Performance in Peripheral Artery Disease: The HONOR Randomized Clinical Trial. JAMA.
14 15		2018;319(16):1665-1676.
16 17	41.	Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and
18 19		clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA.
20 21		2013;310(12):1263-1273.
22 23	42.	Monninkhof EM, Velthuis MJ, Peeters PH, Twisk JW, Schuit AJ. Effect of exercise on postmenopausal sex hormone levels
24 25		and role of body fat: a randomized controlled trial. J Clin Oncol. 2009;27(27):4492-4499.
26 27	43.	Murphy TP, Cutlip DE, Regensteiner JG, et al. Supervised exercise, stent revascularization, or medical therapy for
28 29		claudication due to aortoiliac peripheral artery disease: the CLEVER study. Journal of the American College of Cardiology.
30 31		2015;65(10):999-1009.
32	44.	O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-
33 34		ACTION randomized controlled trial. JAMA. 2009;301(14):1439-1450.
35 36	45.	Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability
37 38		in older adults: the LIFE study randomized clinical trial. JAMA. 2014;311(23):2387-2396.
39 40	46.	Patwala AY, Woods PR, Sharp L, Goldspink DF, Tan LB, Wright DJ. Maximizing patient benefit from cardiac
41 42		resynchronization therapy with the addition of structured exercise training: a randomized controlled study. J Am Coll
43 44		Cardiol. 2009;53(25):2332-2339.
45 46	47.	Pitkälä KH, Pöysti MM, Laakkonen M, et al. Effects of the Finnish Alzheimer disease exercise trial (FINALEX): a
47 48		randomized controlled trial. JAMA internal medicine. 2013;173(10):894-901.
49 50	48.	Ross R, Hudson R, Stotz PJ, Lam M. Effects of exercise amount and intensity on abdominal obesity and glucose tolerance in
51 52		obese adults: a randomized trial. Ann Intern Med. 2015;162(5):325-334.
52 53 54	49.	Saberi S, Wheeler M, Bragg-Gresham J, et al. Effect of Moderate-Intensity Exercise Training on Peak Oxygen Consumption
55		in Patients With Hypertrophic Cardiomyopathy: A Randomized Clinical Trial. JAMA. 2017;317(13):1349-1357.
56 57		
58 59		128
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Page 169 of 176

Online Supplement References

# BMJ Open

1 2	50.	Sandri M, Kozarez I, Adams V, et al. Age-related effects of exercise training on diastolic function in heart failure with
- 3 4		reduced ejection fraction: the Leipzig Exercise Intervention in Chronic Heart Failure and Aging (LEICA) Diastolic
5 6		Dysfunction Study. Eur Heart J. 2012;33(14):1758-1768.
7	51.	Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med.
8 9		2009;361(7):664-673.
10 11	52.	Schmitz KH, Ahmed RL, Troxel AB, et al. Weight lifting for women at risk for breast cancer-related lymphedema: a
12 13		randomized trial. JAMA. 2010;304(24):2699-2705.
14 15	53.	Segal RJ, Reid RD, Courneya KS, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving
16 17		radiation therapy for prostate cancer. J Clin Oncol. 2009;27(3):344-351.
18 19	54.	Taaffe DR, Newton RU, Spry N, et al. Effects of Different Exercise Modalities on Fatigue in Prostate Cancer Patients
20 21		Undergoing Androgen Deprivation Therapy: A Year-long Randomised Controlled Trial. Eur Urol. 2017;72(2):293-299.
22 23	55.	van Waart H, Stuiver MM, van Harten WH, et al. Effect of Low-Intensity Physical Activity and Moderate- to High-Intensity
23 24 25		Physical Exercise During Adjuvant Chemotherapy on Physical Fitness, Fatigue, and Chemotherapy Completion Rates:
26		Results of the PACES Randomized Clinical Trial. J Clin Oncol. 2015;33(17):1918-1927.
27 28	56.	Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. <i>N Engl J</i>
29 30		Med. 2017;376(20):1943-1955.
31 32	57.	Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. <i>N Engl J</i>
33 34		Med. 2011;364(13):1218-1229.
35 36	58.	Winter MM, van der Bom T, de Vries LC, et al. Exercise training improves exercise capacity in adult patients with a
37 38		systemic right ventricle: a randomized clinical trial. Eur Heart J. 2012;33(11):1378-1385.
39 40	59.	Zhang HJ, He J, Pan LL, et al. Effects of Moderate and Vigorous Exercise on Nonalcoholic Fatty Liver Disease: A
41 42		Randomized Clinical Trial. JAMA Intern Med. 2016;176(8):1074-1082.
43 44	60.	Ahmed S, Rienstra M, Crijns HJ, et al. Continuous vs episodic prophylactic treatment with amiodarone for the prevention of
45 46		atrial fibrillation: a randomized trial. JAMA. 2008;300(15):1784-1792.
47	61.	Caminiti G, Volterrani M, Iellamo F, et al. Effect of long-acting testosterone treatment on functional exercise capacity,
48 49		skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure a
50 51		double-blind, placebo-controlled, randomized study. J Am Coll Cardiol. 2009;54(10):919-927.
52 53	62.	Cortelazzo S, Tarella C, Gianni AM, et al. Randomized Trial Comparing R-CHOP Versus High-Dose Sequential
54 55		Chemotherapy in High-Risk Patients With Diffuse Large B-Cell Lymphomas. J Clin Oncol. 2016;34(33):4015-4022.
56 57		
58 59		129
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Online Supplement References** 

59

60

1 63. Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of Dextromethorphan-Quinidine on Agitation in Patients With 2 3 Alzheimer Disease Dementia: A Randomized Clinical Trial. JAMA. 2015;314(12):1242-1254. 4 5 64. Cusi K, Orsak B, Bril F, et al. Long-Term Pioglitazone Treatment for Patients With Nonalcoholic Steatohepatitis and 6 7 Prediabetes or Type 2 Diabetes Mellitus: A Randomized Trial. Ann Intern Med. 2016;165(5):305-315. 8 9 65. Devereux G, Cotton S, Fielding S, et al. Effect of theophylline as adjunct to inhaled corticosteroids on exacerbations in 10 11 patients with COPD: a randomized clinical trial. JAMA. 2018;320(15):1548-1559. 12 13 66. Ellis MJ, Suman VJ, Hoog J, et al. Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and 14 exemestane for postmenopausal women with estrogen receptor-rich stage 2 to 3 breast cancer: clinical and biomarker 15 16 outcomes and predictive value of the baseline PAM50-based intrinsic subtype--ACOSOG Z1031. J Clin Oncol. 17 18 2011;29(17):2342-2349. 19 20 67. Ford I, Scott NW, Herd V, Mitchell LR, Williams DJ, Brittenden J. A randomized controlled trial of platelet activity before 21 22 and after cessation of clopidogrel therapy in patients with stable cardiovascular disease. J Am Coll Cardiol. 2014;63(3):233-23 24 239. 25 26 68. Frustaci A, Russo MA, Chimenti C. Randomized study on the efficacy of immunosuppressive therapy in patients with virus-27 28 negative inflammatory cardiomyopathy: the TIMIC study. Eur Heart J. 2009;30(16):1995-2002. 29 30 69. Gheorghiade M, Blair JE, Filippatos GS, et al. Hemodynamic, echocardiographic, and neurohormonal effects of istaroxime, a 31 32 novel intravenous inotropic and lusitropic agent: a randomized controlled trial in patients hospitalized with heart failure. J Am 33 34 Coll Cardiol. 2008;51(23):2276-2285. 35 36 70. Gheorghiade M, Bohm M, Greene SJ, et al. Effect of aliskiren on postdischarge mortality and heart failure readmissions 37 among patients hospitalized for heart failure: the ASTRONAUT randomized trial. JAMA. 2013;309(11):1125-1135. 38 39 71. Goebel A, Bisla J, Carganillo R, et al. Low-Dose Intravenous Immunoglobulin Treatment for Long-Standing Complex 40 41 Regional Pain Syndrome. Annals of Internal Medicine. 2017;167(7):476-483. 42 43 72. Greenspan SL, Brufsky A, Lembersky BC, et al. Risedronate prevents bone loss in breast cancer survivors: a 2-year, 44 45 randomized, double-blind, placebo-controlled clinical trial. J Clin Oncol. 2008;26(16):2644-2652. 46 47 Grudell AB, Sweetser S, Camilleri M, et al. A controlled pharmacogenetic trial of sibutramine on weight loss and body 73. 48 49 composition in obese or overweight adults. Gastroenterology. 2008;135(4):1142-1154. 50 51 74. Hamshere S, Arnous S, Choudhury T, et al. Randomized trial of combination cytokine and adult autologous bone marrow 52 53 progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy: the REGENERATE-DCM clinical 54 55 trial. Eur Heart J. 2015;36(44):3061-3069. 56 57 58

Page 171 of 176

Online Supplement References

# BMJ Open

1 2	75.	Han Y, Zhu G, Han L, et al. Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in
3 4		patients with diabetes and chronic kidney disease. J Am Coll Cardiol. 2014;63(1):62-70.
5 6	76.	Harman SM, Black DM, Naftolin F, et al. Arterial imaging outcomes and cardiovascular risk factors in recently menopausal
7 8		women: a randomized trial. Ann Intern Med. 2014;161(4):249-260.
9	77.	Hoendermis ES, Liu LC, Hummel YM, et al. Effects of sildenafil on invasive haemodynamics and exercise capacity in heart
10 11		failure patients with preserved ejection fraction and pulmonary hypertension: a randomized controlled trial. Eur Heart J.
12 13		2015;36(38):2565-2573.
14 15	78.	Hurvitz SA, Dirix L, Kocsis J, et al. Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel
16 17		in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer. J Clin Oncol. 2013;31(9):1157-
18 19		1163.
20 21	79.	Irani J, Celhay O, Hubert J, et al. Continuous versus six months a year maximal androgen blockade in the management of
22 23		prostate cancer: a randomised study. Eur Urol. 2008;54(2):382-391.
24 25	80.	Johnston SRD, Hegg R, Im SA, et al. Phase III, Randomized Study of Dual Human Epidermal Growth Factor Receptor 2
26 27		(HER2) Blockade With Lapatinib Plus Trastuzumab in Combination With an Aromatase Inhibitor in Postmenopausal
28 29		Women With HER2-Positive, Hormone Receptor-Positive Metastatic Breast Cancer: ALTERNATIVE. J Clin Oncol.
30 31		2018;36(8):741-748.
32 33	81.	Kim JM, Stewart R, Lee YS, et al. Effect of Escitalopram vs Placebo Treatment for Depression on Long-term Cardiac
34 35		Outcomes in Patients With Acute Coronary Syndrome: A Randomized Clinical Trial. JAMA. 2018;320(4):350-358.
36	82.	Klotz LH, McNeill IY, Kebabdjian M, Zhang L, Chin JL, Canadian Urology Research C. A phase 3, double-blind,
37 38		randomised, parallel-group, placebo-controlled study of oral weekly alendronate for the prevention of androgen deprivation
39 40		bone loss in nonmetastatic prostate cancer: the Cancer and Osteoporosis Research with Alendronate and Leuprolide
41 42		(CORAL) study. Eur Urol. 2013;63(5):927-935.
43 44	83.	Kosmala W, Holland DJ, Rojek A, Wright L, Przewlocka-Kosmala M, Marwick TH. Effect of If-channel inhibition on
45 46		hemodynamic status and exercise tolerance in heart failure with preserved ejection fraction: a randomized trial. J Am Coll
47 48		Cardiol. 2013;62(15):1330-1338.
49 50	84.	Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of Aldosterone Antagonism on
51 52		Exercise Tolerance in Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol. 2016;68(17):1823-1834.
53 54	85.	Krankenberg H, Tubler T, Ingwersen M, et al. Drug-Coated Balloon Versus Standard Balloon for Superficial Femoral Artery
55 56		In-Stent Restenosis: The Randomized Femoral Artery In-Stent Restenosis (FAIR) Trial. Circulation. 2015;132(23):2230-
57 58		2236.
59 60		131 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Online Supplement References** 

60

1 86. Lapperre TS, Snoeck-Stroband JB, Gosman MM, et al. Effect of fluticasone with and without salmeterol on pulmonary 2 3 outcomes in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med. 2009;151(8):517-527. 4 5 87. Loprinzi CL, Qin R, Balcueva EP, et al. Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for 6 7 alleviating hot flashes, N07C1. J Clin Oncol. 2010;28(4):641-647. 8 9 88. McKay RR, Zurita AJ, Werner L, et al. A Randomized Phase II Trial of Short-Course Androgen Deprivation Therapy With 10 11 or Without Bevacizumab for Patients With Recurrent Prostate Cancer After Definitive Local Therapy. J Clin Oncol. 12 13 2016;34(16):1913-1920. 14 Nissen SE, Nicholls SJ, Wolski K, et al. Comparison of pioglitazone vs glimepiride on progression of coronary 15 89. 16 atherosclerosis in patients with type 2 diabetes: the PERISCOPE randomized controlled trial. JAMA. 2008;299(13):1561-17 18 1573. 19 20 90. Poole J, Mavromatis K, Binongo JN, et al. Effect of progenitor cell mobilization with granulocyte-macrophage colony-21 22 stimulating factor in patients with peripheral artery disease: a randomized clinical trial. JAMA. 2013;310(24):2631-2639. 23 24 91. Pradhan AD, Everett BM, Cook NR, Rifai N, Ridker PM. Effects of initiating insulin and metformin on glycemic control and 25 26 inflammatory biomarkers among patients with type 2 diabetes: the LANCET randomized trial. JAMA. 2009;302(11):1186-27 28 1194. 29 30 92. Ratziu V, Giral P, Jacqueminet S, et al. Rosiglitazone for nonalcoholic steatohepatitis: one-year results of the randomized 31 32 placebo-controlled Fatty Liver Improvement with Rosiglitazone Therapy (FLIRT) Trial. Gastroenterology. 2008;135(1):100-33 34 110. 35 Rimawi M, Ferrero JM, de la Haba-Rodriguez J, et al. First-Line Trastuzumab Plus an Aromatase Inhibitor, With or Without 36 93. 37 Pertuzumab, in Human Epidermal Growth Factor Receptor 2-Positive and Hormone Receptor-Positive Metastatic or Locally 38 39 Advanced Breast Cancer (PERTAIN): A Randomized, Open-Label Phase II Trial. J Clin Oncol. 2018;36(28):2826-2835. 40 41 Rosenheck RA, Krystal JH, Lew R, et al. Long-acting risperidone and oral antipsychotics in unstable schizophrenia. N Engl J 94. 42 43 Med. 2011;364(9):842-851. 44 45 95. Schmid P, Pinder SE, Wheatley D, et al. Phase II Randomized Preoperative Window-of-Opportunity Study of the PI3K 46 47 Inhibitor Pictilisib Plus Anastrozole Compared With Anastrozole Alone in Patients With Estrogen Receptor-Positive Breast 48 49 Cancer. J Clin Oncol. 2016;34(17):1987-1994. 50 51 Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. N 96. 52 53 Engl J Med. 2010;363(3):245-256. 54 55 56 57 58 132 59

Page 173 of 176

60

## **BMI Open**

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	Online	Supplement References
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17	97.	Soiffer RJ, Kim HT, McGuirk J, et al. Prospective, Randomized, Double-Blind, Phase III Clinical Trial of Anti-T-
		Lymphocyte Globulin to Assess Impact on Chronic Graft-Versus-Host Disease-Free Survival in Patients Undergoing HLA-
		Matched Unrelated Myeloablative Hematopoietic Cell Transplantation. J Clin Oncol. 2017;35(36):4003-4011.
	98.	Spitzer M, Basaria S, Travison TG, et al. Effect of testosterone replacement on response to sildenafil citrate in men with
		erectile dysfunction: a parallel, randomized trial. Ann Intern Med. 2012;157(10):681-691.
	99.	Taplin ME, Montgomery B, Logothetis CJ, et al. Intense androgen-deprivation therapy with abiraterone acetate plus
		leuprolide acetate in patients with localized high-risk prostate cancer: results of a randomized phase II neoadjuvant study. J
		<i>Clin Oncol.</i> 2014;32(33):3705-3715.
	100.	Tsujita K, Sugiyama S, Sumida H, et al. Impact of Dual Lipid-Lowering Strategy With Ezetimibe and Atorvastatin on
18 19		Coronary Plaque Regression in Patients With Percutaneous Coronary Intervention: The Multicenter Randomized Controlled
20 21 22 23		PRECISE-IVUS Trial. J Am Coll Cardiol. 2015;66(5):495-507.
	101.	Ulrich S, Keusch S, Hildenbrand FF, et al. Effect of nocturnal oxygen and acetazolamide on exercise performance in patients
24 25		with pre-capillary pulmonary hypertension and sleep-disturbed breathing: randomized, double-blind, cross-over trial. Eur
25 26 27 28 29		Heart J. 2015;36(10):615-623.
28	102.	Urruticoechea A, Rizwanullah M, Im SA, et al. Randomized Phase III Trial of Trastuzumab Plus Capecitabine With or
30 31		Without Pertuzumab in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer Who
32 33		Experienced Disease Progression During or After Trastuzumab-Based Therapy. J Clin Oncol. 2017;35(26):3030-3038.
34	103.	van der Bom T, Winter MM, Bouma BJ, et al. Effect of valsartan on systemic right ventricular function: a double-blind,
35 36		randomized, placebo-controlled pilot trial. Circulation. 2013;127(3):322-330.
37 38	104.	Wapnir IL, Price KN, Anderson SJ, et al. Efficacy of Chemotherapy for ER-Negative and ER-Positive Isolated Locoregional
39 40		Recurrence of Breast Cancer: Final Analysis of the CALOR Trial. J Clin Oncol. 2018;36(11):1073-1079.
41 42	105.	Wysham C, Bhargava A, Chaykin L, et al. Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients
43 44		With Type 2 Diabetes: The SWITCH 2 Randomized Clinical Trial. JAMA. 2017;318(1):45-56.
45 46	106.	Yardley DA, Ismail-Khan RR, Melichar B, et al. Randomized phase II, double-blind, placebo-controlled study of exemestane
47 48		with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptor-positive breast
49 50		cancer progressing on treatment with a nonsteroidal aromatase inhibitor. J Clin Oncol. 2013;31(17):2128-2135.
51 52	107.	Yoshimura K, Minami T, Nozawa M, et al. A Phase 2 Randomized Controlled Trial of Personalized Peptide Vaccine
52 53 54		Immunotherapy with Low-dose Dexamethasone Versus Dexamethasone Alone in Chemotherapy-naive Castration-resistant
55		Prostate Cancer. Eur Urol. 2016;70(1):35-41.
56 57		
58 59		133

**Online Supplement References** 

60

1 108. Pitkälä KH, Pöysti MM, Laakkonen M-L, et al. Effects of the Finnish Alzheimer disease exercise trial (FINALEX): a 2 3 randomized controlled trial. JAMA internal medicine. 2013;173(10):894-901. 4 5 109. Gheorghiade M, Blair JEA, Filippatos GS, et al. Hemodynamic, Echocardiographic, and Neurohormonal Effects of 6 7 Istaroxime, a Novel Intravenous Inotropic and Lusitropic Agent. A Randomized Controlled Trial in Patients Hospitalized 8 9 With Heart Failure. 2008;51(23):2276-2285. 10 11 110. Greenspan SL, Brufsky A, Lembersky BC, et al. Risedronate prevents bone loss in breast cancer survivors: a 2-year, 12 13 randomized, double-blind, placebo-controlled clinical trial. J Clin Oncol. 2008;26(16):2644-2652. 14 Grudell AB, Sweetser S, Camilleri M, et al. A controlled pharmacogenetic trial of sibutramine on weight loss and body 15 111. 16 composition in obese or overweight adults. Gastroenterology. 2008;135(4):1142-1154. 17 18 112. Irani J, Celhay O, Hubert J, et al. Continuous versus six months a year maximal androgen blockade in the management of 19 20 prostate cancer: a randomised study. European urology. 2008;54(2):382-391. 21 22 113. Ratziu V, Giral P, Jacqueminet S, et al. Rosiglitazone for Nonalcoholic Steatohepatitis: One-Year Results of the Randomized 23 24 Placebo-Controlled Fatty Liver Improvement With Rosiglitazone Therapy (FLIRT) Trial. Gastroenterology. 25 26 2008;135(1):100-110. 27 28 114. Caminiti G, Volterrani M, Iellamo F, et al. Effect of long-acting testosterone treatment on functional exercise capacity, 29 30 skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure: a 31 32 double-blind, placebo-controlled, randomized study. Journal of the American College of Cardiology, 2009;54(10):919-927. 33 115. 34 Frustaci A, Russo MA, Chimenti C. Randomized study on the efficacy of immunosuppressive therapy in patients with virus-35 36 negative inflammatory cardiomyopathy: the TIMIC study. European Heart Journal. 2009;30(16):1995-2002. 37 Loprinzi CL, Qin R, Balcueva EP, et al. Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for 116. 38 39 alleviating hot flashes, N07C1. J Clin Oncol. 2010;28(4):641-647. 40 41 117. Ellis MJ, Suman VJ, Hoog J, et al. Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and 42 43 exemestane for postmenopausal women with estrogen receptor-rich stage 2 to 3 breast cancer: clinical and biomarker 44 45 outcomes and predictive value of the baseline PAM50-based intrinsic subtype--ACOSOG Z1031. J Clin Oncol. 46 47 2011;29(17):2342-2349. 48 49 Klotz LH, McNeill IY, Kebabdjian M, Zhang L, Chin JL. A Phase 3, Double-blind, Randomised, Parallel-group, Placebo-118. 50 51 controlled Study of Oral Weekly Alendronate for the Prevention of Androgen Deprivation Bone Loss in Nonmetastatic 52 53 Prostate Cancer: The Cancer and Osteoporosis Research with Alendronate and Leuprolide (CORAL) Study. European 54 55 Urology. 2013;63(5):927-935. 56 57 58 59

2 3

4 5

6

### **BMJ** Open

Online Supplement References

- 119. Kosmala W, Holland DJ, Rojek A, Wright L, Przewlocka-Kosmala M, Marwick TH. Effect of If-channel inhibition on hemodynamic status and exercise tolerance in heart failure with preserved ejection fraction: a randomized trial. *Journal of the American College of Cardiology*. 2013;62(15):1330-1338.
- van der Bom T, Winter MM, Bouma BJ, et al. Effect of valsartan on systemic right ventricular function: a double-blind,
   randomized, placebo-controlled pilot trial. *Circulation*. 2013;127(3):322-330.
- Yardley DA, Ismail-Khan RR, Melichar B, et al. Randomized phase II, double-blind, placebo-controlled study of exemestane
   with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptor-positive breast
   cancer progressing on treatment with a nonsteroidal aromatase inhibitor. *J Clin Oncol.* 2013;31(17):2128-2135.
- Ford I, Scott NW, Herd V, Mitchell LR, Williams DJP, Brittenden J. A Randomized Controlled Trial of Platelet Activity
   Before and After Cessation of Clopidogrel Therapy in Patients With Stable Cardiovascular Disease. *Journal of the American College of Cardiology*. 2014;63(3):233-239.
- Han Y, Zhu G, Han L, et al. Short-Term Rosuvastatin Therapy for Prevention of Contrast-Induced Acute Kidney Injury in
   Patients With Diabetes and Chronic Kidney Disease. *Journal of the American College of Cardiology*. 2014;63(1):62-70.
- Harman SM, Black DM, Naftolin F, et al. Arterial imaging outcomes and cardiovascular risk factors in recently menopausal
   women: a randomized trial. *Annals of internal medicine*. 2014;161(4):249-260.
- Taplin M-E, Montgomery B, Logothetis CJ, et al. Intense androgen-deprivation therapy with abiraterone acetate plus
   leuprolide acetate in patients with localized high-risk prostate cancer: results of a randomized phase II neoadjuvant study. J
   *Clin Oncol.* 2014;32(33):3705-3715.
- Hamshere S, Arnous S, Choudhury T, et al. Randomized trial of combination cytokine and adult autologous bone marrow
   progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy: the REGENERATE-DCM clinical
   trial. *European Heart Journal*. 2015;36(44):3061-3069.
- Hoendermis ES, Liu LC, Hummel YM, et al. Effects of sildenafil on invasive haemodynamics and exercise capacity in heart
  failure patients with preserved ejection fraction and pulmonary hypertension: a randomized controlled trial. *European heart journal.* 2015;36(38):2565-2573.
- 47
  48
  48
  49
  50
  49
  49. Krankenberg H, Tübler T, Ingwersen M, et al. Drug-Coated Balloon Versus Standard Balloon for Superficial Femoral Artery
  49. In-Stent Restenosis. *Circulation*. 2015;132(23):2230-2236.
- Tsujita K, Sugiyama S, Sumida H, et al. Impact of Dual Lipid-Lowering Strategy With Ezetimibe and Atorvastatin on
   Coronary Plaque Regression in Patients With Percutaneous Coronary Intervention. *The Multicenter Randomized Controlled PRECISE-IVUS Trial.* 2015;66(5):495-507.

57 58

Online Supplement References

1 130. Ulrich S, Keusch S, Hildenbrand FF, et al. Effect of nocturnal oxygen and acetazolamide on exercise performance in patients 2 3 with pre-capillary pulmonary hypertension and sleep-disturbed breathing: randomized, double-blind, cross-over trial. 4 5 European heart journal. 2015;36(10):615-623. 6 7 131. Cortelazzo S, Tarella C, Gianni AM, et al. Randomized Trial Comparing R-CHOP Versus High-Dose Sequential 8 9 Chemotherapy in High-Risk Patients With Diffuse Large B-Cell Lymphomas. Journal of Clinical Oncology. 10 11 2016;34(33):4015-4022. 12 13 132. Long-Term Pioglitazone Treatment for Patients With Nonalcoholic Steatohepatitis and Prediabetes or Type 2 Diabetes 14 Mellitus. Annals of internal medicine. 2016;165(5):305-315. 15 16 133. Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of aldosterone antagonism on 17 18 exercise tolerance in heart failure with preserved ejection fraction. Journal of the American College of Cardiology. 19 20 2016;68(17):1823-1834. 21 22 McKay RR, Zurita AJ, Werner L, et al. A Randomized Phase II Trial of Short-Course Androgen Deprivation Therapy With 134. 23 24 or Without Bevacizumab for Patients With Recurrent Prostate Cancer After Definitive Local Therapy. J Clin Oncol. 25 26 2016;34(16):1913-1920. 27 28 135. Schmid P, Pinder SE, Wheatley D, et al. Phase II Randomized Preoperative Window-of-Opportunity Study of the PI3K 29 30 Inhibitor Pictilisib Plus Anastrozole Compared With Anastrozole Alone in Patients With Estrogen Receptor-Positive Breast 31 32 Cancer. J Clin Oncol. 2016;34(17):1987-1994. 33 34 136. Yoshimura K, Minami T, Nozawa M, et al. A Phase 2 Randomized Controlled Trial of Personalized Peptide Vaccine 35 36 Immunotherapy with Low-dose Dexamethasone Versus Dexamethasone Alone in Chemotherapy-naive Castration-resistant 37 Prostate Cancer. European Urology. 2016;70(1):35-41. 38 39 Low-Dose Intravenous Immunoglobulin Treatment for Long-Standing Complex Regional Pain Syndrome. Annals of internal 137. 40 41 medicine. 2017;167(7):476-483. 42 43 138. Urruticoechea A, Rizwanullah M, Im S-A, et al. Randomized Phase III Trial of Trastuzumab Plus Capecitabine With or 44 45 Without Pertuzumab in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer Who 46 47 Experienced Disease Progression During or After Trastuzumab-Based Therapy. Journal of Clinical Oncology. 48 49 2017;35(26):3030-3038. 50 51 139. Johnston SRD, Hegg R, Im S-A, et al. Phase III, Randomized Study of Dual Human Epidermal Growth Factor Receptor 2 52 53 (HER2) Blockade With Lapatinib Plus Trastuzumab in Combination With an Aromatase Inhibitor in Postmenopausal 54 55 Women With HER2-Positive, Hormone Receptor-Positive Metastatic Breast Cancer: ALTERNATIVE. Journal of Clinical 56 57 Oncology. 2018;36(8):741-748. 58 136 59 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml 60

#### **BMJ** Open

**Online Supplement References** 

- 140. Kim J-M, Stewart R, Lee Y-S, et al. Effect of escitalopram vs placebo treatment for depression on long-term cardiac outcomes in patients with acute coronary syndrome: a randomized clinical trial. Jama. 2018;320(4):350-357.
- 141. Rimawi M, Ferrero J-M, Haba-Rodriguez Jdl, et al. First-Line Trastuzumab Plus an Aromatase Inhibitor, With or Without Pertuzumab, in Human Epidermal Growth Factor Receptor 2-Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer (PERTAIN): A Randomized, Open-Label Phase II Trial. Journal of Clinical Oncology.
- 2018;36(28):2826-2835.
- <text> 142. Wapnir IL, Price KN, Anderson SJ, et al. Efficacy of Chemotherapy for ER-Negative and ER-Positive Isolated Locoregional Recurrence of Breast Cancer: Final Analysis of the CALOR Trial. J Clin Oncol. 2018;36(11):1073-1079.

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## Comparing the reporting and conduct quality of exercise and pharmacological randomized controlled trials: A systematic review

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Running Head: Exercise RCT reporting and conduct quality

# Comparing the reporting and conduct quality of exercise and pharmacological randomized controlled trials: A systematic review

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## ABSTRACT

**Objective.** Evaluate the quality of exercise randomized controlled trial (RCT) reporting and conduct in clinical populations (*i.e.*, adults with or at-risk of chronic conditions) and compare with matched pharmacological RCTs.

Design. Systematic review.

Data Sources. Embase (Elsevier), PubMed (NLM), and CINAHL (EBSCO)

Study Selection. RCTs of exercise in clinical populations with matching pharmacological RCTs published in leading clinical, medical and specialist journals with impact factors  $\geq 15$ . Review Methods. Overall RCT quality was evaluated by two independent reviewers using three research reporting guidelines (*i.e.*, Consolidated Standards of Reporting Trials (CONSORT; pharmacological RCTs) / CONSORT-Non-pharmacological trial (CONSORT-NPT; exercise RCTs), CONSORT-Harms, Template for Intervention Description and Replication (TIDieR)) and two risk of bias assessment (research conduct) tools (*i.e.*, Cochrane Risk of Bias, Jadad Scale). We compared research reporting and conduct quality within exercise RCTs with matched pharmacological RCTs, and examined factors associated with quality in exercise and pharmacological RCTs, separately. Findings. Forty-eight exercise RCTs (11,658 patients; median sample n=138) and 48 matched pharmacological RCTs were evaluated (18,501 patients; median sample n=160). RCTs were conducted primarily in cardiovascular medicine (43%) or oncology (31%). Overall quality score (composite of all research reporting and conduct quality scores; primary endpoint) for exercise RCTs was 58% (median score 46/80; interguartile range: 39-51) compared with 77% (53/68; interguartile range: 47-58) in the matched pharmacological RCTs ( $p \le 0.001$ ). Individual guality scores for trial reporting and conduct were lower in exercise RCTs compared with matched pharmacological RCTs (p ≤0.03). Factors associated with higher overall guality scores for exercise RCTs were journal impact factor ( $\geq$ 25), sample size ( $\geq$ 152) and publication year ( $\geq$ 2013).

**Conclusions and Relevance.** Research reporting and conduct quality within exercise RCTs is inferior to matched pharmacological RCTs. Suboptimal RCT reporting and conduct impact the fidelity,

interpretation, and reproducibility of exercise trials and, ultimately, implementation of exercise in clinical

populations.

Registration. CRD42018095033

# STRENGTHS AND LIMITATIONS OF THIS STUDY

- A total of n=30,159 participants from ninety-six randomized controlled trials (RCTs) of exercise and pharmacological therapies published in high-impact journals were included.
- We used a combination of five established and one investigator developed inventories to comprehensively evaluate and compare the quality of research reporting and conduct of exercise and pharmacological RCTs.
- Main limitations of the study include the restriction to journals with impact factors ≥15 and the lack of broadly applicable or unified guidelines to compare across exercise and pharmacological therapy RCTs.

## INTRODUCTION

Reports from epidemiological studies and randomized controlled trials (RCTs) indicate that exercise therapy is safe and well-tolerated, and associated with broad health benefits in adults.<sup>1</sup> Accordingly, exercise is considered standard of care therapy for many clinical populations (ie, adults with or at risk of chronic conditions), with established guidelines from numerous international agencies.<sup>2-4</sup>

Clinical recommendation of exercise for a particular clinical indication is predicated on evidence from RCTs.<sup>5</sup> Optimal reporting of RCTs evaluating pharmacological and non-pharmacological therapies is facilitated by multiple standardized guidelines [eg, Consolidated Standards of Reporting Trials (CONSORT),<sup>6,7</sup> Template for Intervention Description and Replication (TIDieR)<sup>8</sup>]. Reports of RCTs are required to conform to at least one of these guidelines when submitting to scientific journals across all areas of medicine. Relatedly, risk of bias (ROB) tools (eg, Cochrane ROB,<sup>9</sup> Jadad Scale<sup>10</sup>) evaluate RCT research conduct. Numerous reviews have evaluated reporting quality and conduct of medical (eg, surgical,<sup>11</sup> medical device<sup>12</sup> and pharmacological<sup>13</sup> interventions) RCTs. Only a few previous systematic reviews have assessed the quality of exercise RCT reporting and conduct.<sup>14-18</sup> However, these reviews were limited in scope (eg, did not use comprehensive guidelines like CONSORT and Cochrane ROB; included a small number of trials) and incompletely reported key aspects of study methods (eg, item rating criteria, reviewer training). To our knowledge, no exercise reviews have contextualized their findings via direct comparison with trials in other research disciplines.

Therefore, our primary objective was to comprehensively evaluate the overall quality of exercise RCT reporting and conduct in clinical populations. The primary outcome was overall quality score (ie, the combined quality scores from three research reporting and two research conduct inventories). We also compared the quality of research reporting and conduct from exercise RCTs to matched RCTs of pharmacological therapies (a well-established field of biomedical research with a long history of adopting RCT methods<sup>19</sup>) using (1) the complete guidelines and (2) only key items from the guidelines (ie, those generally applicable to both intervention types) to provide context for our findings. Secondary

objectives were to compare individual items within the research reporting and conduct inventories as well as to examine factors associated with overall quality score.

# METHODS Search Strategy

This review was conducted in accordance with the PRISMA<sup>20</sup> and AMSTAR 2<sup>21</sup> guidelines (PROSPERO identifier CRD42018095033; supplementary Methods 1 and 2). Full study methods are provided within Supplementary Methods 3-7 and Supplementary Table 1. Briefly, a Research Informationist (KM) conducted two sequential literature searches for exercise (first search) and pharmacological (second search) RCTs within the Embase (Elsevier), PubMed (NLM), and CINAHL (EBSCO) databases (fig 1). The search for exercise RCTs was conducted using a combination of relevant keywords and controlled vocabulary: (1) exercise training intervention and (2) RCTs. The search was restricted to trials published between January 1<sup>st</sup> 2008 (the year the CONSORT extension for Non-Pharmacologic Treatments (CONSORT-NPT) was first published<sup>22</sup>) and the search date (March 8<sup>th</sup>, 2018). Meta-data (ie, journal, cohort / population, sample size, and number of study sites) was extracted for eligible exercise RCTs and used to define the matching criteria for pharmacological RCTs. The pharmacological RCT search was conducted on November 20th, 2018. The search was similarly restricted by date (January 1<sup>st</sup>, 2008 to November 20<sup>th</sup>, 2018) and used a combination of relevant search terms and matching criteria for: (1) pharmaceutical intervention, (2) RCTs, (3) journal, (4) cohort / population, and (5) number of study sites (single or multi-center). We purposefully restricted our search to medical journals with impact factors ≥15 because journals with higher impact factors are more likely to endorse and enforce reporting guality guidelines<sup>23-25</sup> and publish both exercise and pharmacological RCTs – leading to a more balanced foundation for comparison between study types. Study Eligibility Criteria

Exercise RCTs involving adults (≥18 years of age) with chronic conditions, written in English, and published in journals with impact factors ≥15 according to the 2016 Journal Citation Reports (Clarivate

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Analytics) between January 1<sup>st</sup>, 2008 and the search date (March 8<sup>th</sup>, 2018) were eligible. Exercise therapy interventions were defined as those involving chronic (>3 weeks), repeated sessions of supervised (in person, with or without a distance-based component) aerobic training (ie, endurance activity, ≥15 minutes/session), resistance training (ie, multiple large muscle group exercises involving repeated voluntary muscle contractions against a resistance greater than those normally encountered in activities of daily living), or the combination, with the objective of improving health-related outcomes.<sup>26,27</sup> Pharmacological interventions were defined as studies involving the administration of established or experimental pharmacological agents with the objective of improving health.

## Study Selection, Matching, Data Extraction and Additional Sources

Trained study reviewers (JM and KS; see supplementary Methods 3 for training description) independently screened and evaluated identified article titles and abstracts in the DistillerSR web platform (Evidence Partners, Ottawa, Canada; fig 1). Next, full manuscripts of potentially eligible articles were independently reviewed using DistillerSR. Excluded exercise records are listed in supplementary Table 1.<sup>28</sup> Matching criteria for exercise and pharmacological therapy RCTs included: (1) publishing journal (±5 impact factor points according to the 2016 Journal Citation Reports [Clarivate Analytics, formerly ISI Web of Knowledge]), (2) study population (sharing similar disease characteristics), (3) study sample size (±30% difference in study sample size), and (4) number of study sites (single vs. multi-site). These specific matching criteria were selected to establish impartial comparison between exercise and pharmacological RCTs. The 'publishing journal' criteria was selected because studies published within the same journal should, in theory, be held to similar reporting standards. If no direct match could be identified within the same journal, we used an investigator-defined cut-off of ±5 impact factor points to find alternate matches because impact factor has been shown to be associated with RCT reporting and methodological quality.<sup>29,30</sup> The 'study population' criteria was chosen to account for differences in the research methods and standards across specific clinical populations and specialties. If no direct population match could be identified, we considered closely related populations. For example, for trials among patients with cardiac diseases, cardiomyopathy or heart failure were

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considered surrogates. We selected the 'study sample size' and 'number of study sites' as criterion to control for differences in the methods (eg, human and physical resources, infrastructure) used to conduct smaller versus larger trials. To this end, an investigator-defined cut-point of a 30% difference in sample size was used to match RCTs of similar scale and logistical complexity. Exercise and pharmacological therapy RCTs had to be matched on a minimum of two of the four matching criteria to be eligible. The pharmacological therapy RCT with values closest to the target exercise RCT was used if more than one potential match was identified. Full data was extracted for all eligible RCTs from the primary article and all other publicly available supplemental data sources using DistillerSR and Reference Guides. Disagreements concerning eligibility, data extractions, and ROB assessments were resolved by consensus (JM and KS) and adjudicated by a third party (SCA) when consensus could not be obtained. The corresponding author for each article was contacted by investigators (SCA, JMS, LWJ) to request information on incomplete and missing items. After four weeks, non-responding authors were re-contacted and provided an additional ~four weeks to respond. Reporting totals were revised after the close of data collection (ie, final author contact (September 1<sup>st</sup>, 2019)).

## Evaluation measures

Each trial was evaluated on two sets of criteria: (1) quality of research reporting and (2) quality of research conduct using complete standardized inventories and/or key items from these inventories, as needed. Exercise RCTs were evaluated on a maximum of 78 potential items and pharmacological RCTs were evaluated on a maximum of 63 potential items. The quality of exercise research reporting was first assessed using CONSORT-Nonpharmacologic Treatments (NPT) [52 items],<sup>6</sup> CONSORT-Harms [10 items],<sup>31</sup> and TIDieR [16 items].<sup>32</sup> The quality of pharmacological research reporting was assessed using CONSORT [37 items]<sup>7</sup> and CONSORT-Harms [10 items]. However, there are no TIDieR-equivalent guidelines available to assess pharmacological intervention reporting. Therefore, intervention reporting for pharmacological interventions was assessed using six key items from TIDieR (including intervention length, modality, location, frequency, dose, and adherence). Exercise dose consisted of session intensity and duration (aerobic and resistance interventions) as well as the number

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of sets and repetitions (resistance interventions only). Exercise RCT reporting was also re-evaluated using just the 37 items from the CONSORT guidelines that are common to both intervention types.<sup>7</sup> Notably, there were items within the CONSORT-based reporting quality guidelines (and TIDieR guidelines for exercise RCTs) that were not applicable (NA) based on the unique aspects of individual exercise and pharmacological RCTs. Items rated as NA were excluded from the calculation of primary and secondary outcomes for each study (see *End Points* and *Data Analysis*). All research reporting quality items were rated (with equal weighting and maximum score of 1 point per item) as: 1 = 'properly reported'; or, 0 = 'unclear' (incompletely reported) or 'not reported' (missing); NA = 'not applicable.'

The quality of research conduct was assessed using the Cochrane ROB inventory [7 items]<sup>9</sup> and the Jadad scale [3 items].<sup>10</sup> Cochrane ROB was items were rated (with equal weighting) as: 2 = 'low risk of bias'; 1 = 'unclear risk of bias'; or, 0 = 'high risk of bias'. The first two items in the Jadad scale were scored as 2 = 'low risk of bias' or 0 = 'high risk of bias' and the third item was scored as 1 = 'low risk of bias' or 0 = 'high risk of bias' and the third item was scored as 1 = 'low risk of bias' or 0 = 'high risk of bias' and the third item was scored as 1 = 'low risk of bias' or 0 = 'high risk of bias.'

## **End Points**

The primary end point was overall quality score defined as the sum of numerical quality scores from all research reporting and conduct inventories relative to the total number of applicable items. Secondary end points were defined as the numerical quality scores for each research reporting guideline and conduct inventory relative to the total number of applicable items for the study.

## Data Analysis

Characteristics of RCTs were summarized using descriptive statistics. Quality scores were calculated and reported in numerical and percentage score formats. Percentage quality scores were calculated for the primary end point (overall quality score) and secondary endpoints (individual scores for the quality of reporting guidelines and quality of conduct inventories) as the achieved score relative to the total number of applicable items per RCT. All items from the two research conduct inventories were applicable for every study and scored with values of 0,1 or 2 resulting in total quality score for research conduct-related items of 19 per study. The variation in the total number of applicable items per

study was caused by different numbers of reporting guality guideline items being rated as 'Not Applicable', resulting in median numbers of eligible items (ie, denominators for percentage score calculations) of 80 for exercise RCTs and 68 for pharmacological RCTs. Generalized linear models (GLMs) were specified with a binomial family and logit link to compare the scores of exercise and pharmacological RCTs. For the quality of research conduct scales (Cochrane ROB, Jadad), item ratings were analyzed as low or unknown risk of bias versus high risk of bias. The model accounts for differences in the number of eligible items and the matching between the exercise and pharmacological RCTs. GLMs were also used to evaluate factors associated with overall quality scores for exercise and pharmacological therapy RCTs separately. Potential factors included journal impact factor (<25 vs.  $\geq$ 25), RCT sample size (<152 vs.  $\geq$ 152 participants), number of study sites (single vs. multiple sites), and year of publication (<2013 vs. ≥2013). Cut offs for impact factor, sample size, and year of publication were based on the medians. Exploratory one-way ANOVAs were used to assess whether reporting guality varied across studies matched on 50%, 75%, and 100% of matching criteria. For comparisons of the individual components of the composite scores, p-values were adjusted for multiple comparisons within research reporting and conduct inventories using a Bonferroni correction. Data are presented as median (Interguartile Range (IQR)) and odds ratios (OR; 95% confidence intervals (CI)). Inter-rater reliability was evaluated using intraclass correlation coefficient (ICC) calculated via one-way ANOVA.<sup>33</sup> Analyses were performed using R version 4.0.2.<sup>34</sup>

## Patient and Public Involvement

Patients were not included in the design and conduct of this review. However, optimizing patient safety and benefit is the fundamental purpose of this review. Specifically, the proximal objective of the review is to identify opportunities to improve the rigour and reproducibility of exercise research that, in turn, will facilitate the delivery of robust evidence-based exercise interventions across diverse clinical populations and settings.

## RESULTS

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See Supplementary Tables 2-12 for full study characteristics and results. A total of 2836 potential exercise records were identified with 866 duplicate records removed using Endnote citation management software (Clarivate Analytics). A total of 1970 records underwent title and abstract screening (fig 1). Of these, 264 records underwent full review with 48 exercise RCTs meeting eligibility criteria.<sup>35-82</sup> The 48 primary searches for pharmacological therapy trials produced 2815 records. The median number of records returned per search was 15 (range: 0-853). Review of the primary search results produced 19 matched pharmacological RCTs; the remaining 29 were pharmacological RCTs were identified via review of modified secondary searches.<sup>83-130</sup> Overall, 13 pairs of exercise and pharmacological RCTs were matched on 100% of our four matching criteria, 18 pairs of RCTs were matched on 75%, and 17 pairs of RCTs were matched on 50%. On average, exercise and pharmacological therapy RCTs were matched on 3 of 4 criteria. The results of agreement for the two raters' assessments for the exercise and pharmaceutical studies publication scores were: overall quality score: ICC = 0.85 (95% CI: 0.78 to 0.89); quality of research reporting guidelines: ICC = 0.83 (95% CI: 0.75 to 0.88); and quality of research conduct inventories: ICC = 0.73 (95% CI: 0.62 to 0.81).

## **Missing Information (Author Contact)**

Each RCT had missing information. The median number of eligible reporting quality items for exercise RCTs was 61 (IQR 59, 62) and pharmacological RCTs was 49 (IQR 48, 50). The median percentage (numerical; numerical range) of missing or indeterminate reporting quality items in exercise RCTs was 46% (28/61 items; 13-49) compared to 27% (13/49 items; 5-26) in pharmacological RCTs. Sixteen (33%) and 7 (15%) corresponding authors of the exercise and pharmacological RCTs responded with a median of 12.5 (IQR: 10.0, 16.2) and 5.0 (IQR: 4.0, 6.5) additional items.

## **RCT Characteristics**

RCT characteristics are summarized in Table 1. Exercise therapy RCTs included a total of 11,658 participants (7,411 (64%) were allocated to experimental arms; including studies with 1-3 intervention arms) compared with 18,501 participants (11,909 (64%) allocated to experimental arms) in the pharmacological therapy RCTs. The median sample size of exercise RCTs was 138 (IQR: 100, 236)

and 160 (IQR: 98, 314) for pharmacological RCTs. Overall, 34 of 48 exercise RCTs (71%) and 31 of 48 pharmacological RCTs (65%) reported positive primary outcomes.

# **Primary and Secondary End Points**

The median overall quality score for RCTs of exercise therapy was 58% (46/80; IQR: 49, 65) compared to 77% (53/68; IQR: 71, 84;  $p \le 0.001$ ) for pharmacological therapy RCTs (Table 2). For secondary end points, median research reporting quality scores across all complete guidelines were significantly lower in exercise RCTs in comparison with pharmacological RCTs (Table 2). The lowest scoring research reporting quality guideline was CONSORT-Harms for both exercise and pharmaceutical studies. In exercise RCTs, median CONSORT-Harms score was 32% (3/9; IQR: 11, 51) compared with 67% (6/10; IQR: 40, 73) in pharmacological RCTs ( $p \le 0.001$ ; Table 2). Harms reporting was missing entirely from 19% (9/48) of exercise RCTs and 4% (2/48) of pharmacological RCTs. Exercise RCTs reported 57% (8/15; IQR: 7, 10) of TIDieR items (Table 2). Over 75% of exercise RCTs were missing details related to intervention personnel, progression, and participant adherence (Table 3).

In exercise RCTs, median Cochrane ROB score was 71% (10/14; IQR: 64, 79) compared with 93% (13/14; IQR: 86, 93) in pharmacological RCTs ( $p \le 0.001$ ; Table 2). A summary of Cochrane ROB assessments for individual exercise and pharmacological therapy RCTs is provided in Table 4. Exploratory one-way ANOVAs did not indicate a difference in reporting quality outcomes between exercise and pharmacological RCTs matched on 50%, 75%, or 100% of the matching criteria.

## Comparison of Key Items

Thirty-seven of 52 CONSORT items, all ten CONSORT-Harms items, and six of 16 TIDieR items were considered key items. Median reporting scores for the key items from CONSORT and TIDieR were not significantly different between exercise and pharmacological RCTs; whereas, reporting scores for CONSORT-Harms was significantly lower for exercise RCTs (Table 2). Compared to pharmacological RCTs, exercise RCTs had lower reporting of key study methods (e.g. blinding after group assignment [60% vs. 98%], balanced discussion of harms vs. benefits [39% vs. 66%],

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intervention modality [39% vs. 66%], intervention dose [50% vs. 98%], and complete intervention descriptions [0% vs. 67%]).

## Factors Associated with Reporting Quality

Journal impact factor  $\ge 25$  (OR: 1.36; 95% CI: 1.18 to 1.57), larger sample size  $\ge 152$  (OR: 1.29; 95% CI: 1.11 to 1.51), and more recent publication year  $\ge 2013$  (OR: 1.18; 95% CI: 1.03 to 1.34) were associated with higher overall quality scores in exercise RCTs (Table 5). The only factor associated with greater overall quality scores in pharmacological RCTs was more recent publication year  $\ge 2013$  (OR: 1.35; 95% CI: 1.14 to 1.60; *p*<0.001).

## DISCUSSION

We evaluated the quality of research reporting and conduct within exercise therapy RCTs in clinical populations, then compared with the quality of reporting and conduct in matched pharmacological therapy RCTs. Our findings demonstrate that the quality of exercise therapy RCT reporting and conduct is suboptimal according to all complete guidelines and inventories used in this study and is inferior to RCTs of pharmacological therapy. However, the mean overall reporting quality for RCT methods and interventions, but not harms, was similar between intervention types when considering key items within the respective guidelines.

To our knowledge, five systematic reviews<sup>14-18</sup> have evaluated the overall quality of research reporting and conduct within exercise RCTs in clinical populations. Our findings corroborate the findings of these systematic reviews demonstrating the overall quality of exercise RCT reporting and conduct is suboptimal. For instance, in 27 exercise RCTs involving 1,467 patients with metabolic syndrome, Ostman et al.<sup>17</sup> reported a median overall quality of 60% (range: 33-87%) using the TESTEX (Tool for the assEssment of Study qualiTy and reporting in EXercise<sup>131</sup>) guideline. Similarly, Borror and colleagues<sup>14</sup> evaluated 12 exercise RCTs (representing 135 patients) with type 2 diabetes using a combination of 16 items from CONSORT, Jadad, PEDro (Physiotherapy Evidence Database) guidelines,<sup>132</sup> and the Delphi list.<sup>133</sup> The combined trial reporting and conduct quality score was 49% (range: 38%-58%). Nevertheless, prior reviews have several important limitations. For instance, these

reviews<sup>14-18</sup> did not use the complete versions of comprehensive and widely accepted guidelines (*e.g.*, CONSORT, Cochrane ROB) and, thus, did not rigorously evaluate the quality of all salient aspects of trial reporting and conduct. In addition, the number of exercise trials evaluated were small, comparisons of reporting with matched pharmacological trials were not performed, and no data extraction training or standardization were described within these studies. Thus, our review that was conducted by well-trained independent reviewers using specialized reference guides to facilitate standardized data extraction according to five distinct but complementary established guidelines / tools to assess and compare a large number of exercise trials and matched pharmacological trials provides the most rigorous evaluation of exercise research quality to date.

Although overall quality scores were poor in RCTs of exercise therapy, these findings were generally driven by poor research reporting quality scores across select individual guidelines rather than suboptimal RCT conduct per se. Foremost among these, the finding that harms were the most poorly reported aspects of exercise RCTs is concerning. Previous reviews in patients with cancer.<sup>134</sup> chronic fatigue,<sup>135</sup> and multiple sclerosis<sup>136</sup> have specifically focused on evaluating the reporting of adverse event frequency and descriptions; this information was completely missing within 23-88% of included exercise trials.<sup>134-136</sup> Our study extends these findings by demonstrating that harms-related monitoring and reporting were missing or incompletely reported in ≥75% of exercise RCTs; and, relatedly, >50% of articles failed to provide a balanced discussion of risks to benefits for the tested interventions. In contrast, a related assessment of 325 chemotherapy trials reported a mean CONSORT-Harms score of 63%,<sup>137</sup> compared to mean harms scores of 36% (exercise RCTs) and 57% (pharmacological RCTs) in our study. Based on our findings, we cannot support or refute the prevailing dogma that exercise is a safe and tolerable intervention strategy in most areas of clinical medicine.<sup>1</sup> However, it is not possible to fully evaluate the harms to benefit ratio of exercise without accurate monitoring and reporting of adverse events within exercise RCTs - a critical consideration in the clinical recommendation of any medical intervention.

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Reporting of intervention methods is the most commonly assessed quality metric in exercise RCTs to date. Our findings support previous reviews of exercise interventions in patients with peripheral arterial disease,<sup>138</sup> cancer,<sup>139</sup> hypertension,<sup>140</sup> and recovering from stroke<sup>141</sup> demonstrating essential elements, including details on the exercise prescription regimen itself, are incompletely reported. For example, Hacke et al. used TIDieR to assess intervention reporting quality in 24 exercise RCTs involving 1,195 patients with hypertension and reported that 91% of exercise intervention studies in were missing information about intervention supervisors and 52% were missing details of intervention adherence.<sup>140</sup> Relatedly, Tew et al. also used TIDieR and reported that 20-26% of reports failed to describe several of the most fundamental exercise intervention elements (*i.e.*, exercise mode, intensity, tailoring, and progression) in 58 exercise RCTs in patients with peripheral arterial disease.<sup>138</sup> In our study, information on patient compliance to the planned exercise regimen as well as the expertise of the individuals implementing the intervention was missing or incomplete in >90% of trials; fundamental details pertaining to dose of prescribed exercise were also missing in 50% trials. By contrast, pharmacological intervention compliance was similarly missing in ~80% of trials; however, prescribed pharmacotherapy dose was only missing in 2% of studies. Incomplete intervention description not only hinders study reproducibility and cross-study integration (for meta-analyses) but also precludes quantification of exercise and pharmacotherapy therapy dose – a key metric for elucidation of dose/exposure-response relationships and translation into clinical practice.<sup>142</sup>

A major strength of this review is that, to our knowledge, it is the first to compare the quality of research reporting and conduct within exercise and pharmacological therapy RCTs. We used rigorous data extraction and evaluation processes to provide the first direct evidence that the quality of research reporting and conduct within exercise RCTs is inferior to similar pharmacological RCTs using the complete reporting guidelines (CONSORT and CONSORT-NPT). For context, the reporting quality of pharmacological RCTs in our review is comparable with previous reviews. For example, using CONSORT, Peron and colleagues<sup>143</sup> found that reporting quality of pharmacological RCTs in oncology ranged from 72% to 74%. A similar review conducted by Ritchie et al. reported a CONSORT score of

72% in 57 pharmacological RCTs (33% of studies involved patients with metabolic and cardiorespiratory diseases).<sup>13</sup> Our findings are consistent with these studies and suggest that comparable research reporting quality scores for exercise RCTs are, on average, 15%-20% lower. There were no differences observed in mean overall reporting quality when comparing exercise and pharmacological RCTs according to key items from the CONSORT guidelines; however, the reporting of several critical individual items was suboptimal within exercise RCTs (e.g. complete intervention descriptions, intervention dose, blinding status). Our findings provide important direction to improve the completeness and rigor of exercise trial reporting.

Several factors may contribute to the lower quality scores for research reporting and conduct within exercise trials. For instance, CONSORT was developed primarily to support the reporting of pharmacological trials and may not adequately capture aspects unique to the conduct of nonpharmacological trials such as exercise.<sup>144</sup> This issue should have been addressed, in theory, with publication of the CONSORT-NPT extension in 2008.<sup>6,22</sup> Indeed, this extension was developed to facilitate complete reporting across the fundamental aspects of RCTs applicable to all nonpharmacologic trials, including exercise. Reporting quality of traditional biomedical therapy RCTs (e.g., surgical, pharmaceutical) has improved since the publication of the CONSORT guidelines and superior in journals adopting these guidelines.<sup>145-147</sup> We similarly found that exercise RCTs published more recently (>2013) had higher overall guality scores. These findings are encouraging and suggest that the awareness and use of established guidelines and inventories to support research reporting and conduct may be increasing, although there remains marked room for improvement. Continued improvement in this context will require continued education of exercise investigators to conform with such guidelines and journals / reviewers hold authors accountable to use of such guidelines. Stricter adherence to CONSORT-NPT, for example, would improve the reporting quality of most fundamental trial aspects; however, this tool may still be too generic to support the comprehensive reporting of features unique to exercise trials, especially intervention description. To this end, adoption of TIDieR, or the more recent

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exercise-specific CERT (*i.e.*, Consensus on Exercise Reporting Template) guidelines,<sup>148</sup> is warranted to improve the reporting and reproducibility of exercise interventions within exercise RCTs.

Our study has several limitations. First, the restriction to journals with impact factors  $\geq$ 15 may overestimate the quality of research reporting and conduct within the included exercise and pharmacological therapy RCTs. Relatedly, the exclusion of exercise RCTs published within sports science journals may underestimate the quality of exercise studies. Nevertheless, we felt it was necessary to selectively draw from this subset of journals given they are most likely to publish RCTs of both intervention types and endorse and enforce reporting guality guidelines<sup>23-25</sup> to impartially compare and contextualize our findings. Second, the lack of broadly applicable or unified guidelines to compare across exercise and pharmacological therapy RCTs also merits consideration. Guidelines used to evaluate the quality of RCT reporting were either different between study types (*i.e.*, CONSORT-NPT<sup>6</sup> vs. CONSORT<sup>7</sup>), developed specifically for harms reporting in pharmacological trials,<sup>31</sup> or investigatorderived given that there are formal standards for non-pharmacological (*i.e.*, TIDieR<sup>32</sup>), but not pharmacological, intervention reporting. We controlled for differences in the numbers of evaluable and applicable items across the reporting quality guidelines and used four matching criteria to control the influence of differences in (1) journal editorial standards and policies, (2) population-specific research methods and standards, and (3) the methods, resources, and infrastructure required to conduct smaller vs. larger trials. Future research could be strengthened by the establishment of standardized matching criteria to facilitate comparisons between branches of biomedical research. Third, we did not update the search following the extraction of the 96 included studies published from 2008-2018, which may have introduced bias related to search recency. However, the association between year of publication and reporting quality was evaluated and discussed as herein. Finally, we acknowledge that using nonspecific assessment tools (e.g., using CONSORT-NPT to evaluate exercise trials or TIDieR to evaluate pharmacological interventions) potentially introduces measurement bias. We limited our evaluations and comparisons to include only reporting and conduct quality items that were applicable to the type of intervention to address this concern and selected six of TIDieR's 16 items to facilitate comparisons of

intervention reporting quality between exercise and pharmacological RCTs. Development of disciplinespecific measurement tools such as CONSORT extensions for acupuncture interventions<sup>149</sup> and patient-reported outcomes<sup>150</sup> may be needed to improve reporting of exercise trials.

In summary, the overall quality of research reporting and conduct within exercise RCTs is suboptimal and inferior to pharmacological RCTs. Stricter adherence to established guidelines and inventories is warranted to facilitate the generation of high-quality evidence needed to optimize the safety, efficacy, and implementation of exercise therapy in clinical populations.

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Data sharing: All relevant data was provided. All data available upon request.

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**Transparency:** The senior author (the manuscript's guarantor) confirms that the manuscript is an honest, accurate, and transparent account of the conducted review; that no important aspects of the study or data have been omitted; and that any discrepancies from the study as planned (i.e., reported in the trial registry) have been explained.

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# REFERENCES

Pedersen BK, Saltin B. Exercise as medicine - evidence for prescribing exercise as therapy in
 26 different chronic diseases. Scand J Med Sci Sports 2015;25 Suppl 3:1-72.

 Mezzani A, Hamm LF, Jones AM, et al. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. Eur J Prev Cardiol 2013;20:442-67.

3. Rochester CL, Vogiatzis I, Holland AE, et al. An official American Thoracic Society/European Respiratory Society policy statement: Enhancing implementation, use, and delivery of pulmonary rehabilitation. Am J Respir Crit Care Med 2015;192:1373-86.

Sanft T, Denlinger CS, Armenian S, et al. NCCN Guidelines Insights: Survivorship, Version
 2.2019: Featured Updates to the NCCN Guidelines. J Natl Compr Canc Netw 2019;17:784-94.

5. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Br Med J 2008;336:924-6.

6. Boutron I, Altman DG, Moher D, Schulz KF, Ravaud P, Consort NPT Group. CONSORT statement for randomized trials of nonpharmacologic treatments: A 2017 update and a CONSORT extension for nonpharmacologic trial abstracts. Ann Intern Med 2017;167:40-7.

7. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med 2010;152:726-32.

8. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. Br Med J 2014;348:g1687.

9. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Br Med J 2011;343:d5928.

10. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clin Trials 1996;17:1-12.

11. Jacquier I, Boutron I, Moher D, Roy C, Ravaud P. The reporting of randomized clinical trials using a surgical intervention is in need of immediate improvement: a systematic review. Annals of surgery 2006;244:677.

12. Chen W, Yu J, Zhang L, et al. Quality of reporting in randomized controlled trials of therapeutic cardiovascular medical devices. Surgery 2019;165:965-9.

13. Ritchie A, Seubert L, Clifford R, Perry D, Bond C. Do randomised controlled trials relevant to pharmacy meet best practice standards for quality conduct and reporting? A systematic review. Int J Pharm Pract 2020;28:220-32.

14. Borror A, Zieff G, Battaglini C, Stoner L. The effects of postprandial exercise on glucose control in individuals with type 2 diabetes: A systematic review. Sports Med 2018;48:1479-91.

15. Chan E, Giallauria F, Vigorito C, Smart NA. Exercise training in heart failure patients with preserved ejection fraction: a systematic review and meta-analysis. Monaldi Arch Chest Dis 2016;86:759.

16. Grace A, Chan E, Giallauria F, Graham PL, Smart NA. Clinical outcomes and glycaemic responses to different aerobic exercise training intensities in type II diabetes: a systematic review and meta-analysis. Cardiovasc Diabetol 2017;16.

17. Ostman C, Smart NA, Morcos D, Duller A, Ridley W, Jewiss D. The effect of exercise training on clinical outcomes in patients with the metabolic syndrome: a systematic review and meta-analysis.
Cardiovasc Diabetol 2017;16.

18. Van Rosendal SP, Osborne MA, Fassett RG, Coombes JS. Guidelines for glycerol use in hyperhydration and rehydration associated with exercise. Sports Med 2010;40:113-29.

19. Bothwell L, Greene J, Podolsky S, Jones D. Assessing the Gold Standard--Lessons from the History of RCTs. The New England journal of medicine 2016;374:2175.

20. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. Ann Intern Med 2009;151:264-9.

21. Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. Bmc Med Res Methodol 2007;7:10.

22. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, Group C. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. Ann Intern Med 2008;148:295-309.

23. Kunath F, Grobe HR, Rücker G, et al. Do journals publishing in the field of urology endorse reporting guidelines? A survey of author instructions. Urologia Internationalis 2012;88:54-9.

24. Samaan Z, Mbuagbaw L, Kosa D, et al. A systematic scoping review of adherence to reporting guidelines in health care literature. J Multidiscip Healthc 2013;6:169-88.

25. Mills E, Wu P, Gagnier J, Heels-Ansdell D, Montori VM. An analysis of general medical and specialist journals that endorse CONSORT found that reporting was not enforced consistently. Journal of clinical epidemiology 2005;58:662-7.

26. American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription:Wolters Kluwer; 2018.

27. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. Public Health Rep 1985;100:126-31.

28. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. Br Med J 2017:j4008.

29. Fleming PS, Koletsi D, Seehra J, Pandis N. Systematic reviews published in higher impact clinical journals were of higher quality. Journal of clinical epidemiology 2014;67:754-9.

30. Gluud LL, Sørensen TIA, Gøtzsche PC, Gluud C. The Journal Impact Factor as a Predictor of Trial Quality and Outcomes: Cohort Study of Hepatobiliary Randomized Clinical Trials. American Journal of Gastroenterology 2005;100:2431-5.

31. Ioannidis JP, Evans SJ, Gotzsche PC, et al. Better reporting of harms in randomized trials: an extension of the CONSORT statement. Ann Intern Med 2004;141:781-8.

#### BMJ Open

32. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014;348:g1687.

33. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. Journal of chiropractic medicine 2016;15:155-63.

34. R Core Team. R: A Language and Environment for Statistical Computing. 467. Vienna, Austria2020.

35. Adamsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: randomised controlled trial. BMJ 2009;339:b3410.

36. Beckers PJ, Denollet J, Possemiers NM, Wuyts FL, Vrints CJ, Conraads VM. Combined endurance-resistance training vs. endurance training in patients with chronic heart failure: a prospective randomized study. Eur Heart J 2008;29:1858-66.

37. Beer M, Wagner D, Myers J, et al. Effects of exercise training on myocardial energy metabolism and ventricular function assessed by quantitative phosphorus-31 magnetic resonance spectroscopy and magnetic resonance imaging in dilated cardiomyopathy. J Am Coll Cardiol 2008;51:1883-91.

38. Belardinelli R, Georgiou D, Cianci G, Purcaro A. 10-year exercise training in chronic heart failure: a randomized controlled trial. J Am Coll Cardiol 2012;60:1521-8.

39. Campbell KL, Foster-Schubert KE, Alfano CM, et al. Reduced-calorie dietary weight loss, exercise, and sex hormones in postmenopausal women: randomized controlled trial. J Clin Oncol 2012;30:2314-26.

40. Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. JAMA 2010;304:2253-62.

41. Courneya KS, Sellar CM, Stevinson C, et al. Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients. J Clin Oncol 2009;27:4605-12.

42. Daumit GL, Dickerson FB, Wang NY, et al. A behavioral weight-loss intervention in persons with serious mental illness. N Engl J Med 2013;368:1594-602.

43. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Effects of Aerobic and Resistance Exercise on Metabolic Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in Overweight or Obese Survivors of Breast Cancer: A Randomized Controlled Trial. J Clin Oncol 2018;36:875-83.

44. Duijts SF, van Beurden M, Oldenburg HS, et al. Efficacy of cognitive behavioral therapy and physical exercise in alleviating treatment-induced menopausal symptoms in patients with breast cancer: results of a randomized, controlled, multicenter trial. J Clin Oncol 2012;30:4124-33.

45. Edelmann F, Gelbrich G, Dungen HD, et al. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot study. J Am Coll Cardiol 2011;58:1780-91.

46. Ehlken N, Lichtblau M, Klose H, et al. Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial. Eur Heart J 2016;37:35-44.

47. Fakhry F, Spronk S, van der Laan L, et al. Endovascular Revascularization and Supervised
Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial.
JAMA 2015;314:1936-44.

48. Friedenreich CM, Neilson HK, O'Reilly R, et al. Effects of a High vs Moderate Volume of Aerobic
Exercise on Adiposity Outcomes in Postmenopausal Women: A Randomized Clinical Trial. JAMA
Oncol 2015;1:766-76.

49. Friedenreich CM, Woolcott CG, McTiernan A, et al. Alberta physical activity and breast cancer prevention trial: sex hormone changes in a year-long exercise intervention among postmenopausal women. Journal of Clinical Oncology 2010;28:1458.

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**BMJ** Open

50. Galvao DA, Spry N, Denham J, et al. A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 2014;65:856-64.

51. Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled trial. Journal of clinical oncology 2010;28:340-7.

52. Hallsworth K, Fattakhova G, Hollingsworth KG, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic fatty liver disease independent of weight loss. Gut 2011;60:1278-83.

53. Hollekim-Strand SM, Bjorgaas MR, Albrektsen G, Tjonna AE, Wisloff U, Ingul CB. High-intensity interval exercise effectively improves cardiac function in patients with type 2 diabetes mellitus and diastolic dysfunction: a randomized controlled trial. J Am Coll Cardiol 2014;64:1758-60.

54. Irwin ML, Cartmel B, Gross CP, et al. Randomized exercise trial of aromatase inhibitor–induced arthralgia in breast cancer survivors. Journal of Clinical Oncology 2015;33:1104.

55. Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA 2017;318:637-46.

56. Jones LW, Hornsby WE, Freedland SJ, et al. Effects of nonlinear aerobic training on erectile dysfunction and cardiovascular function following radical prostatectomy for clinically localized prostate cancer. Eur Urol 2014;65:852-5.

57. Kitzman DW, Brubaker P, Morgan T, et al. Effect of Caloric Restriction or Aerobic Exercise Training on Peak Oxygen Consumption and Quality of Life in Obese Older Patients With Heart Failure With Preserved Ejection Fraction: A Randomized Clinical Trial. JAMA 2016;315:36-46.

58. Kitzman DW, Brubaker PH, Herrington DM, et al. Effect of endurance exercise training on endothelial function and arterial stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. J Am Coll Cardiol 2013;62:584-92.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

59. Ligibel JA, Campbell N, Partridge A, et al. Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors. J Clin Oncol 2008;26:907-12.

60. Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med 2008;149:869-

78.

61. McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial. JAMA 2009;301:165-74.

62. McDermott MM, Ferrucci L, Tian L, et al. Effect of Granulocyte-Macrophage Colony-Stimulating Factor With or Without Supervised Exercise on Walking Performance in Patients With Peripheral Artery Disease: The PROPEL Randomized Clinical Trial. JAMA 2017;318:2089-98.

63. McDermott MM, Spring B, Berger JS, et al. Effect of a Home-Based Exercise Intervention of Wearable Technology and Telephone Coaching on Walking Performance in Peripheral Artery Disease: The HONOR Randomized Clinical Trial. JAMA 2018;319:1665-76.

64. Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA 2013;310:1263-73.

65. Monninkhof EM, Velthuis MJ, Peeters PH, Twisk JW, Schuit AJ. Effect of exercise on postmenopausal sex hormone levels and role of body fat: a randomized controlled trial. J Clin Oncol 2009;27:4492-9.

66. Murphy TP, Cutlip DE, Regensteiner JG, et al. Supervised exercise, stent revascularization, or medical therapy for claudication due to aortoiliac peripheral artery disease: the CLEVER study. Journal of the American College of Cardiology 2015;65:999-1009.

67. O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. JAMA 2009;301:1439-50.

68. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA 2014;311:2387-96.

69. Patwala AY, Woods PR, Sharp L, Goldspink DF, Tan LB, Wright DJ. Maximizing patient benefit from cardiac resynchronization therapy with the addition of structured exercise training: a randomized controlled study. J Am Coll Cardiol 2009;53:2332-9.

70. Pitkälä KH, Pöysti MM, Laakkonen M, et al. Effects of the Finnish Alzheimer disease exercise trial (FINALEX): a randomized controlled trial. JAMA internal medicine 2013;173:894-901.

71. Ross R, Hudson R, Stotz PJ, Lam M. Effects of exercise amount and intensity on abdominal obesity and glucose tolerance in obese adults: a randomized trial. Ann Intern Med 2015;162:325-34.

72. Saberi S, Wheeler M, Bragg-Gresham J, et al. Effect of Moderate-Intensity Exercise Training on Peak Oxygen Consumption in Patients With Hypertrophic Cardiomyopathy: A Randomized Clinical Trial. JAMA 2017;317:1349-57.

73. Sandri M, Kozarez I, Adams V, et al. Age-related effects of exercise training on diastolic function in heart failure with reduced ejection fraction: the Leipzig Exercise Intervention in Chronic Heart Failure and Aging (LEICA) Diastolic Dysfunction Study. Eur Heart J 2012;33:1758-68.

74. Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med 2009;361:664-73.

75. Schmitz KH, Ahmed RL, Troxel AB, et al. Weight lifting for women at risk for breast cancerrelated lymphedema: a randomized trial. JAMA 2010;304:2699-705.

76. Segal RJ, Reid RD, Courneya KS, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. J Clin Oncol 2009;27:344-51.

Taaffe DR, Newton RU, Spry N, et al. Effects of Different Exercise Modalities on Fatigue in
Prostate Cancer Patients Undergoing Androgen Deprivation Therapy: A Year-long Randomised
Controlled Trial. Eur Urol 2017;72:293-9.

78. van Waart H, Stuiver MM, van Harten WH, et al. Effect of Low-Intensity Physical Activity and Moderate- to High-Intensity Physical Exercise During Adjuvant Chemotherapy on Physical Fitness, Fatigue, and Chemotherapy Completion Rates: Results of the PACES Randomized Clinical Trial. J Clin Oncol 2015;33:1918-27.

79. Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. N Engl J Med 2017;376:1943-55.

80. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 2011;364:1218-29.

81. Winter MM, van der Bom T, de Vries LC, et al. Exercise training improves exercise capacity in adult patients with a systemic right ventricle: a randomized clinical trial. Eur Heart J 2012;33:1378-85.

82. Zhang HJ, He J, Pan LL, et al. Effects of Moderate and Vigorous Exercise on Nonalcoholic Fatty Liver Disease: A Randomized Clinical Trial. JAMA Intern Med 2016;176:1074-82.

83. Ahmed S, Rienstra M, Crijns HJ, et al. Continuous vs episodic prophylactic treatment with amiodarone for the prevention of atrial fibrillation: a randomized trial. JAMA 2008;300:1784-92.

84. Caminiti G, Volterrani M, Iellamo F, et al. Effect of long-acting testosterone treatment on functional exercise capacity, skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure a double-blind, placebo-controlled, randomized study. J Am Coll Cardiol 2009;54:919-27.

85. Cortelazzo S, Tarella C, Gianni AM, et al. Randomized Trial Comparing R-CHOP Versus High-Dose Sequential Chemotherapy in High-Risk Patients With Diffuse Large B-Cell Lymphomas. J Clin Oncol 2016;34:4015-22.

86. Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of Dextromethorphan-Quinidine on Agitation in Patients With Alzheimer Disease Dementia: A Randomized Clinical Trial. JAMA 2015;314:1242-54.

87. Cusi K, Orsak B, Bril F, et al. Long-Term Pioglitazone Treatment for Patients With Nonalcoholic Steatohepatitis and Prediabetes or Type 2 Diabetes Mellitus: A Randomized Trial. Ann Intern Med 2016;165:305-15.

88. Devereux G, Cotton S, Fielding S, et al. Effect of theophylline as adjunct to inhaled corticosteroids on exacerbations in patients with COPD: a randomized clinical trial. JAMA 2018;320:1548-59.

89. Ellis MJ, Suman VJ, Hoog J, et al. Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and exemestane for postmenopausal women with estrogen receptor-rich stage 2 to 3 breast cancer: clinical and biomarker outcomes and predictive value of the baseline PAM50-based intrinsic subtype--ACOSOG Z1031. J Clin Oncol 2011;29:2342-9.

90. Ford I, Scott NW, Herd V, Mitchell LR, Williams DJ, Brittenden J. A randomized controlled trial of platelet activity before and after cessation of clopidogrel therapy in patients with stable cardiovascular disease. J Am Coll Cardiol 2014;63:233-9.

91. Frustaci A, Russo MA, Chimenti C. Randomized study on the efficacy of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy: the TIMIC study. Eur Heart J 2009;30:1995-2002.

92. Gheorghiade M, Blair JE, Filippatos GS, et al. Hemodynamic, echocardiographic, and neurohormonal effects of istaroxime, a novel intravenous inotropic and lusitropic agent: a randomized controlled trial in patients hospitalized with heart failure. J Am Coll Cardiol 2008;51:2276-85.

93. Gheorghiade M, Bohm M, Greene SJ, et al. Effect of aliskiren on postdischarge mortality and heart failure readmissions among patients hospitalized for heart failure: the ASTRONAUT randomized trial. JAMA 2013;309:1125-35.

94. Goebel A, Bisla J, Carganillo R, et al. Low-Dose Intravenous Immunoglobulin Treatment for Long-Standing Complex Regional Pain Syndrome. Annals of Internal Medicine 2017;167:476-83.

95. Greenspan SL, Brufsky A, Lembersky BC, et al. Risedronate prevents bone loss in breast cancer survivors: a 2-year, randomized, double-blind, placebo-controlled clinical trial. J Clin Oncol 2008;26:2644-52.

96. Grudell AB, Sweetser S, Camilleri M, et al. A controlled pharmacogenetic trial of sibutramine on weight loss and body composition in obese or overweight adults. Gastroenterology 2008;135:1142-54.
97. Hamshere S, Arnous S, Choudhury T, et al. Randomized trial of combination cytokine and adult autologous bone marrow progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy: the REGENERATE-DCM clinical trial. Eur Heart J 2015;36:3061-9.

98. Han Y, Zhu G, Han L, et al. Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in patients with diabetes and chronic kidney disease. J Am Coll Cardiol 2014;63:62-

70.

99. Harman SM, Black DM, Naftolin F, et al. Arterial imaging outcomes and cardiovascular risk factors in recently menopausal women: a randomized trial. Ann Intern Med 2014;161:249-60.

100. Hoendermis ES, Liu LC, Hummel YM, et al. Effects of sildenafil on invasive haemodynamics and exercise capacity in heart failure patients with preserved ejection fraction and pulmonary hypertension: a randomized controlled trial. Eur Heart J 2015;36:2565-73.

101. Hurvitz SA, Dirix L, Kocsis J, et al. Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer. J Clin Oncol 2013;31:1157-63.

102. Irani J, Celhay O, Hubert J, et al. Continuous versus six months a year maximal androgen blockade in the management of prostate cancer: a randomised study. Eur Urol 2008;54:382-91.

103. Johnston SRD, Hegg R, Im SA, et al. Phase III, Randomized Study of Dual Human Epidermal Growth Factor Receptor 2 (HER2) Blockade With Lapatinib Plus Trastuzumab in Combination With an Aromatase Inhibitor in Postmenopausal Women With HER2-Positive, Hormone Receptor-Positive Metastatic Breast Cancer: ALTERNATIVE. J Clin Oncol 2018;36:741-8.

**BMJ** Open

104. Kim JM, Stewart R, Lee YS, et al. Effect of Escitalopram vs Placebo Treatment for Depression on Long-term Cardiac Outcomes in Patients With Acute Coronary Syndrome: A Randomized Clinical Trial. JAMA 2018;320:350-8.

Klotz LH, McNeill IY, Kebabdjian M, Zhang L, Chin JL, Canadian Urology Research C. A phase
 double-blind, randomised, parallel-group, placebo-controlled study of oral weekly alendronate for the prevention of androgen deprivation bone loss in nonmetastatic prostate cancer: the Cancer and Osteoporosis Research with Alendronate and Leuprolide (CORAL) study. Eur Urol 2013;63:927-35.
 Kosmala W, Holland DJ, Rojek A, Wright L, Przewlocka-Kosmala M, Marwick TH. Effect of If-channel inhibition on hemodynamic status and exercise tolerance in heart failure with preserved ejection fraction: a randomized trial. J Am Coll Cardiol 2013;62:1330-8.

107. Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of Aldosterone Antagonism on Exercise Tolerance in Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol 2016;68:1823-34.

108. Krankenberg H, Tubler T, Ingwersen M, et al. Drug-Coated Balloon Versus Standard Balloon for Superficial Femoral Artery In-Stent Restenosis: The Randomized Femoral Artery In-Stent Restenosis (FAIR) Trial. Circulation 2015;132:2230-6.

109. Lapperre TS, Snoeck-Stroband JB, Gosman MM, et al. Effect of fluticasone with and without salmeterol on pulmonary outcomes in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med 2009;151:517-27.

110. Loprinzi CL, Qin R, Balcueva EP, et al. Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for alleviating hot flashes, N07C1. J Clin Oncol 2010;28:641-7.

111. McKay RR, Zurita AJ, Werner L, et al. A Randomized Phase II Trial of Short-Course Androgen Deprivation Therapy With or Without Bevacizumab for Patients With Recurrent Prostate Cancer After Definitive Local Therapy. J Clin Oncol 2016;34:1913-20.

112. Nissen SE, Nicholls SJ, Wolski K, et al. Comparison of pioglitazone vs glimepiride on progression of coronary atherosclerosis in patients with type 2 diabetes: the PERISCOPE randomized controlled trial. JAMA 2008;299:1561-73.

113. Poole J, Mavromatis K, Binongo JN, et al. Effect of progenitor cell mobilization with granulocytemacrophage colony-stimulating factor in patients with peripheral artery disease: a randomized clinical trial. JAMA 2013;310:2631-9.

114. Pradhan AD, Everett BM, Cook NR, Rifai N, Ridker PM. Effects of initiating insulin and metformin on glycemic control and inflammatory biomarkers among patients with type 2 diabetes: the LANCET randomized trial. JAMA 2009;302:1186-94.

115. Ratziu V, Giral P, Jacqueminet S, et al. Rosiglitazone for nonalcoholic steatohepatitis: one-year results of the randomized placebo-controlled Fatty Liver Improvement with Rosiglitazone Therapy (FLIRT) Trial. Gastroenterology 2008;135:100-10.

116. Rimawi M, Ferrero JM, de la Haba-Rodriguez J, et al. First-Line Trastuzumab Plus an
Aromatase Inhibitor, With or Without Pertuzumab, in Human Epidermal Growth Factor Receptor 2Positive and Hormone Receptor-Positive Metastatic or Locally Advanced Breast Cancer (PERTAIN): A
Randomized, Open-Label Phase II Trial. J Clin Oncol 2018;36:2826-35.

117. Rosenheck RA, Krystal JH, Lew R, et al. Long-acting risperidone and oral antipsychotics in unstable schizophrenia. N Engl J Med 2011;364:842-51.

118. Schmid P, Pinder SE, Wheatley D, et al. Phase II Randomized Preoperative Window-of-Opportunity Study of the PI3K Inhibitor Pictilisib Plus Anastrozole Compared With Anastrozole Alone in

Patients With Estrogen Receptor-Positive Breast Cancer. J Clin Oncol 2016:34:1987-94.

119. Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. N Engl J Med 2010;363:245-56.

120. Soiffer RJ, Kim HT, McGuirk J, et al. Prospective, Randomized, Double-Blind, Phase III Clinical Trial of Anti-T-Lymphocyte Globulin to Assess Impact on Chronic Graft-Versus-Host Disease-Free

BMJ Open

Survival in Patients Undergoing HLA-Matched Unrelated Myeloablative Hematopoietic Cell Transplantation. J Clin Oncol 2017;35:4003-11.

121. Spitzer M, Basaria S, Travison TG, et al. Effect of testosterone replacement on response to sildenafil citrate in men with erectile dysfunction: a parallel, randomized trial. Ann Intern Med 2012;157:681-91.

122. Taplin ME, Montgomery B, Logothetis CJ, et al. Intense androgen-deprivation therapy with abiraterone acetate plus leuprolide acetate in patients with localized high-risk prostate cancer: results of a randomized phase II neoadjuvant study. J Clin Oncol 2014;32:3705-15.

123. Tsujita K, Sugiyama S, Sumida H, et al. Impact of Dual Lipid-Lowering Strategy With Ezetimibe and Atorvastatin on Coronary Plaque Regression in Patients With Percutaneous Coronary Intervention: The Multicenter Randomized Controlled PRECISE-IVUS Trial. J Am Coll Cardiol 2015;66:495-507.

124. Ulrich S, Keusch S, Hildenbrand FF, et al. Effect of nocturnal oxygen and acetazolamide on exercise performance in patients with pre-capillary pulmonary hypertension and sleep-disturbed breathing: randomized, double-blind, cross-over trial. Eur Heart J 2015;36:615-23.

125. Urruticoechea A, Rizwanullah M, Im SA, et al. Randomized Phase III Trial of Trastuzumab Plus
Capecitabine With or Without Pertuzumab in Patients With Human Epidermal Growth Factor Receptor
2-Positive Metastatic Breast Cancer Who Experienced Disease Progression During or After
Trastuzumab-Based Therapy. J Clin Oncol 2017;35:3030-8.

126. van der Bom T, Winter MM, Bouma BJ, et al. Effect of valsartan on systemic right ventricular function: a double-blind, randomized, placebo-controlled pilot trial. Circulation 2013;127:322-30.

127. Wapnir IL, Price KN, Anderson SJ, et al. Efficacy of Chemotherapy for ER-Negative and ER-Positive Isolated Locoregional Recurrence of Breast Cancer: Final Analysis of the CALOR Trial. J Clin Oncol 2018;36:1073-9.

128. Wysham C, Bhargava A, Chaykin L, et al. Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients With Type 2 Diabetes: The SWITCH 2 Randomized Clinical Trial. JAMA 2017;318:45-56.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

129. Yardley DA, Ismail-Khan RR, Melichar B, et al. Randomized phase II, double-blind, placebocontrolled study of exemestane with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptor-positive breast cancer progressing on treatment with a nonsteroidal aromatase inhibitor. J Clin Oncol 2013;31:2128-35.

130. Yoshimura K, Minami T, Nozawa M, et al. A Phase 2 Randomized Controlled Trial of
Personalized Peptide Vaccine Immunotherapy with Low-dose Dexamethasone Versus Dexamethasone
Alone in Chemotherapy-naive Castration-resistant Prostate Cancer. Eur Urol 2016;70:35-41.

131. Smart NA, Waldron M, Ismail H, et al. Validation of a new tool for the assessment of study quality and reporting in exercise training studies. Int J Evid Based Healthc 2015;13:9-18.

132. Maher CG, Moseley AM, Sherrington C, Elkins MR, Herbert RD. A description of the trials, reviews, and practice guidelines indexed in the PEDro Database. Phys Ther 2008;88:1068-77.

133. Verhagen AP, De Vet HCW, De Bie RA, et al. The Delphi List. Journal of clinical epidemiology 1998;51:1235-41.

134. McNeely ML, Campbell KL, Rowe BH, Klassen TP, Mackey JR, Courneya KS. Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. Can Med Assoc J 2006;175:34-41.

135. Larun L, Brurberg KG, Odgaard-Jensen J, Price JR. Exercise therapy for chronic fatigue syndrome. Cochrane Database Syst Rev 2019;10:CD003200.

136. Pilutti LA, Platta ME, Motl RW, Latimer-Cheung AE. The safety of exercise training in multiple sclerosis: a systematic review. J Neurol Sci 2014;343:3-7.

137. Peron J, Maillet D, Gan HK, Chen EX, You B. Adherence to CONSORT adverse event reporting guidelines in randomized clinical trials evaluating systemic cancer therapy: a systematic review. J Clin Oncol 2013;31:3957-63.

 Tew GA, Brabyn S, Cook L, Peckham E. The completeness of intervention descriptions in randomised trials of supervised exercise training in peripheral arterial disease. PLoS One 2016;11:e0150869.

139. Meneses-Echavez JF, Rodriguez-Prieto I, Elkins M, Martinez-Torres J, Nguyen L, Bidonde J. Analysis of reporting completeness in exercise cancer trials: a systematic review. Bmc Med Res Methodol 2019;19:220.

140. Hacke C, Nunan D, Weisser B. Do exercise trials for hypertension adequately report interventions? A reporting quality study. Int J Sports Med 2018;39:902-8.

141. McEwen D, O'Neil J, Miron-Celis M, Brosseau L. Content reporting in post-stroke therapeutic circuit-class exercise programs in randomized control trials. Top Stroke Rehabil 2019;26:281-7.

142. Scott JM, Zabor EC, Schwitzer E, et al. Efficacy of Exercise Therapy on Cardiorespiratory

Fitness in Patients With Cancer: A Systematic Review and Meta-Analysis. J Clin Oncol 2018;36:2297-305.

143. Peron J, Pond GR, Gan HK, et al. Quality of reporting of modern randomized controlled trials in medical oncology: a systematic review. J Natl Cancer Inst 2012;104:982-9.

144. Begg C, Cho M, Eastwood S, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. JAMA 1996;276:637-9.

145. Han C, Kwak KP, Marks DM, et al. The impact of the CONSORT statement on reporting of randomized clinical trials in psychiatry. Contemp Clin Trials 2009;30:116-22.

146. Moher D, Jones A, Lepage L, Group C. Use of the CONSORT statement and quality of reports of randomized trials: a comparative before-and-after evaluation. JAMA 2001;285:1992-5.

147. Plint AC, Moher D, Morrison A, et al. Does the CONSORT checklist improve the quality of reports of randomised controlled trials? A systematic review. Med J Aust 2006;185:263.

148. Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on exercise reporting template (CERT): Explanation and elaboration statement. Br J Sports Med 2016;50:1428-37.

149. MacPherson H, Altman DG, Hammerschlag R, et al. Revised standards for reporting interventions in clinical trials of acupuncture (STRICTA): extending the CONSORT statement. The Journal of Alternative and Complementary Medicine 2010;16:ST-1-ST-14.

150. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized

trials: the CONSORT PRO extension. Jama 2013;309:814-22.

# Table 1. Characteristics of exercise and pharmacological therapy RCTs

No. (%)           2 (4.2%)           1 (2.1%)           0 (0%)           4 (8.3%)           3 (6.2%)           0 (0%)           1 (2.1%)           7 (15%)           12 (25%)           2 (4.2%)           1 (2.1%)           1 (2.1%)           1 (2.1%)           1 (2.1%)	No. (%) 4 (8.3%) 0 (0%) 2 (4.2%) 4 (8.3%) 3 (6.2%) 2 (4.2%) 0 (0%) 7 (15%) 9 (19%) 1 (2.1%) 0 (0%)
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1 (2.1%) 7 (15%) 12 (25%) 2 (4.2%) 1 (2.1%)	0 (0%) 7 (15%) 9 (19%) 1 (2.1%) 0 (0%)
7 (15%) 12 (25%) 2 (4.2%) 1 (2.1%)	7 (15%) 9 (19%) 1 (2.1%) 0 (0%)
12 (25%) 2 (4.2%) 1 (2.1%)	9 (19%) 1 (2.1%) 0 (0%)
2 (4.2%) 1 (2.1%)	1 (2.1%) 0 (0%)
1 (2.1%)	0 (0%)
1 (2.1%)	0 (0%)
, ,	
	13 (27%)
0 (0%)	1 (2.1%)
4 (8.3%)	2 (4.2%)
28 (19, 51)	28 (19, 34)
. ,	. ,
33 (69%)	15 (31%)
15 (31%)	33 (69%)
, ,	
38 (100, 236)	160 (98, 314)
24 (50%)	17 (35%)
24 (50%)	31 (65%)
16 (33%)	7 (15%)
	38 (100, 236) 24 (50%)

#### Table 2. Quality of exercise and pharmacological therapy RCT reporting and conduct **Exercise RCTs<sup>1</sup>** Pharmacological RCTs<sup>2</sup> Outcomes p-values\* Median IQR Median IQR **Primary Outcome Overall Quality Score** 45.5 38.8, 51.2 52.5 46.8, 58.0 < 0.001 Eligible score 3a,b 80.0 78.0, 81.0 68.0 67.0, 69.0 Percent 58.2 48.6, 64.5 77.1 70.5, 83.9 **Secondary Outcomes** Research Reporting: Complete Guidelines **CONSORT Score** 25.0 23.0, 28.0 25.0 22.0, 28.0 < 0.001 45.0 Eligible score <sup>4a,b</sup> 44.0, 47.0 33.0 32.0, 34.0 75.4 Percent 56.8 50.0, 62.8 69.7, 84.7 3.0 < 0.001 CONSORT-Harms Score 1.0, 5.0 6.0 4.0.7.2 Eligible score 5 9.0 9.0, 10.0 10.0 10.0, 10.0 Percent 31.7 11.1, 51.4 66.7 40.0, 72.5 **TIDieR Score** 8.0 7.0, 10.0 Eligible score 7 15.0 14.0, 15.0 \_ \_ Percent 57.4 49.2, 67.9 **Research Reporting:** 0.68 Key Items 24.0 CONSORT Score 21.0, 27.0 26.5 22.8, 28.0 30.0. 32.0 Eligible score 31.0 33.0 32.0. 34.0 Percent 75.4 68.0, 84.8 79.4 70.7.85.7 Intervention Score 4.0 3.0, 4.0 4.0 4.0, 4.2 0.03 Eligible score 6 6.0 6.0 \_ \_ 66.7 66.7 Percent 50, 66.7 66.7, 70.8 Research Conduct Inventories Cochrane ROB Score 10.0 9.0, 11.0 13.0 12.0, 13.0 < 0.001 Eligible score 8 14.0 14.0 Percent 71.4 64.3, 78.6 92.9 85.7, 92.9 Jadad Score 3.0 2.8, 5.0 5.0 4.0, 5.0 < 0.001 Eligible score 9 5.0 5.0

60.0 Notes: %, percent; IQR, interquartile range; RCTs, randomized controlled trials

<sup>1</sup> n=48 exercise therapy RCTs; <sup>2</sup> n=48 pharmacological therapy RCTs

\* p-values were adjusted for multiple comparisons within Research Reporting and within Research Conduct Inventories using a Bonferroni correction.

Maximum possible quality scores:

 $^{3a,b}$  Overall quality for exercise therapy RCTs = 87<sup>3a</sup> and pharmacological therapy RCTs = 72<sup>3b</sup>

<sup>4a,b</sup> CONSORT-NPT for exercise therapy RCTs = 52<sup>4a</sup>; CONSORT for pharmacological therapy RCTs = 37<sup>4b</sup>

55.0, 100.0

100.0

80.0, 100.0

<sup>5</sup> CONSORT-Harms for all RCTs = 10

<sup>6</sup> Intervention for all RCTs = 6

Percent

<sup>7</sup> TIDieR for exercise RCTs = 16

<sup>8</sup> Cochrane ROB for all RCTs = 14

<sup>9</sup> Jadad scale for all RCTs = 5

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# Table 3: Individual TIDieR item reporting summary for exercise therapy RCTs

Itom		Evaluation			
Item No.	Expanded TIDieR Criteria	Yes	Unclear	Νο	NA
		No. (%)	No. (%)	No. (%)	No. (%)
1	Provide the name or a phrase that describes the intervention.	48 (100%)	0 (0%)	0 (0%)	0 (0%)
2	Describe any rationale, theory, or goal of the elements essential to the intervention.	48 (100%)	0 (0%)	0 (0%)	0 (0%)
3	Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of providers.	20 (42%)	5 (10%)	0 (0%)	23 (48%
4	Describe each of the procedures, activities, & / or processes used in the intervention, including any enabling or support activities.	33 (69%)	5 (10%)	10 (21%)	0 (0%)
5	For each category of intervention provider, describe their expertise, background & any specific training given.	7 (15%)	4 (8%)	37 (77%)	0 (0%)
6	Describe the modes of delivery of the intervention & whether it was provided individually or in a group.	17 (35%)	3 (6%)	28 (58%)	0 (0%)
7	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	36 (75%)	5 (10%)	7 (15%)	0 (0%)
8a	Describe the intensity of intervention sessions.	31 (65%)	0 (0%)	17 (35%)	0 (0%)
8b	Describe the frequency of intervention sessions.	40 (83%)	0 (0%)	8 (17%)	0 (0%)
8c	Describe the duration of intervention sessions.	28 (58%)	0 (0%)	20 (42%)	0 (0%)
8d	Describe the total length of the intervention period.	48 (100%)	0 (0%)	0 (0%)	0 (0%)
9i	If the intervention was planned to be personalized, then describe when & how.	19 (40%)	9 (19%)	20 (42%)	0 (0%)
9ii	If the intervention was planned to be progressed, then describe when & how.	3 (6%)	6 (13%)	39 (81%)	0 (0%)
10	If the intervention was modified during the course of the study, describe the changes (what, why, when, & how).	1 (2%)	0 (0%)	0 (0%)	47 (98%
11	If intervention adherence or fidelity was assessed, describe how and by whom, & if any strategies were used to maintain or improve fidelity, describe them.	16 (33%)	10 (21%)	22 (46%)	0 (0%)
12	If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	2 (4%)	3 (6%)	43 (90%)	0 (0%)

# Table 4. Cochrane ROB ratings for individual exercise and pharmacological therapy RCTs

Exercise RCTs	Sequence Generation	Allocation Concealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other Sources	Pharmacological RCTs	Sequence Generation	Allocation Concealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other
Beckers et al. (2008)	0	?	•	?	•	•	•	Ahmed et al. (200	3) ?	?	•	•	•	•	•
Beer et al. (2008)	?	?	•	?	+	•	0	Gheorghiade et al. (200	3) ?	?	•	•	•	•	•
Ligibel et al. (2008)	?	?	Đ	?	+	•	•	Greenspan et al. (200	3) 💿	•	•	•	?	•	•
Maltais et al. (2008)	+	•	P	?	+	•	•	Grudell et al. (200	3) ?	?	•	•	•	•	•
Adamsen et al. (2009)	•	•	-	?	•	?	•	Irani et al. (200	3) ?	?	•	?	•	•	•
Courneya et al. (2009)	•	•	•	?	•	•	•	Nissen et al. (200	3) ?	•	•	•	?	•	÷
McDermott et al. (2009)	+	?	-	•	?	?	•	Ratziu et al. (200	3) ?	•	•	+	•	•	•
Monninkhof et al. (2009)	+	?	-	?	•	?	•	Caminiti et al. (200	) ?	?	•	?	•	•	•
O'Connor et al. (2009)	•	•	-	•	•	•	•	Frustaci et al. (200	9) 💿	•	•	•	•	•	•
Patwala et al. (2009)	•	•	0	?	?	•	•	Lapperre et al. (200	9) 💿	?	•	•	0	•	•
Schmitz et al. (2009)	•	?	0	?	•	?	•	Pradhan et al. (200	9) 💿	•	$\bullet$	•	•	•	•
Segal et al. (2009)	+	•	0	0	•	•	?	Loprinzi et al. (201	) 💿	?	•	•	?	•	•
Church et al. (2010)	+	•	0	•	•	•	•	Smith et al. (201	)) 💽	•	•	•	?	•	•
Friedenreich et al. (2010)	+	•	-	•	•	?	•	Ellis et al. (201	1) 💿	?	•	?	•	•	•
Galvao et al. (2010)	+	•	0	0	•	•	•	Rosenheck et al. (201	1) 💿	•	?	?	•	•	e
Schmitz et al. (2010)	•	•	•	•	•	•	•	Spitzer et al. (201)	2) 💿	$\bullet$	$\bullet$	•	•	•	•
Edelmann et al. (2011)	•	•	•	•	•	•	•	Gheorghiade et al. (201	3) ?	?	$\bullet$	•	•	•	•
Hallsworth et al. (2011)	?	?	?	?	•	?	•	Hurvitz et al. (201	3) 💿	?	•	0	•	•	•
Villareal et al. (2011)	•	?	•	?	•	•	•	Klotz et al. (201	3) 💿	?	•	?	?	•	•
Belardinelli et al. (2012)	?	?	•	•	?	•	•	Kosmala et al. (201	3) 💿	•	•	?	•	•	•
Campbell et al. (2012)	•	?	•	•	•	•	•	Poole et al. (201	3) 💿	?	•	•	•	•	•
Duijts et al. (2012)	•	•	•	?	?	•	•	van der Bom et al. (201	3) 💿	$\bullet$	•	•	•	•	•
Sandri et al. (2012)	•	•	•	?	?	•	•	Yardley et al. (201	3) 💿	?	•	•	•	•	•
Winter et al. (2012)	•	•	-	?	?	•	•	Ford et al. (201	1) 💿	?	$\bullet$	•	•	•	•

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Exercise RCTs	Sequence Generation	Allocation Concealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other Sources	Pharmacological RCTs	Sequence Generation	Allocation Concealment	Participant Blinding	Assessment Blinding	Attrition Bias	Selective Reporting	Other
Daumit et al. (2013)	•	•	•	$\overline{\bullet}$	$\overline{\bullet}$	•	•	Han et al. (2014)		•	•	$\bullet$	•	•	•
Kitzman et al. (2013)	?	?	0	•	$\bullet$	•	•	Harman et al. (2014)	•	•	•	•	•	•	•
Messier et al. (2013)	?	?		•	$\bullet$	•	•	Taplin et al. (2014)	?	?	•	•	•	•	•
Pitkala et al. (2013)	•	•	0	?	$\bullet$	•	•	Cummings et al. (2015)	?	•	•	•	•	•	•
Galvao et al. (2014)	•	•	0	. 🖯	•	•	•	Hamshere et al. (2015)	•	?	•	•	•	•	•
Hollekim-Strand et al. (2014)	?	?	0	?	?	•	•	Hoendermis et al. (2015)	•	?	•	•	•	•	•
Jones et al. (2014)	?	?	•	?	•	•	•	Krankenberg et al. (2015)	?	•	•	•	?	•	·
Pahor et al. (2014)	+	?	-	•	$\mathbf{O}$	?	•	Tsujita et al. (2015)	•	?	•	•	?	•	•
Fakhry et al. (2015)	•	•	•	$\bullet$	•	$\mathbf{O}$	•	Ulrich et al. (2015)	•	?	$\bullet$	•	•	•	•
Friedenreich et al. (2015)	•	•	0	$\bullet$	$\bullet$	$\mathbf{\bullet}$	$\bullet$	Cortelazzo et al. (2016)	•	•	$\bullet$	?	•	•	•
Irwin et al. (2015)	?	?	•	?	?	•	•	Cusi et al. (2016)	•	•	•	•	•	•	•
Murphy et al. (2015)	•	?	-	•	•	•	?	Kosmala et al. (2016)	?	•	•	•	•	•	•
Ross et al. (2015)	•	•	•	•	•	•	?	McKay et al. (2016)	?	?	•	?	•	•	•
van Waart et al. (2015)	+	?	-	?	0	-	•	Schmid et al. (2016)	•	?	•	•	•	•	•
Ehlken et al. (2016)	?	?	-	•	•	•	•	Yoshimura et al. (2016)	?	•	•	?	•	•	•
Kitzman et al. (2016)	•	?	•	?	•	•	•	Goebel et al. (2017)		•	•	•	•	•	•
Zhang et al. (2016)	•	•	0	$\bullet$	$\bullet$	•	•	Soiffer et al. (2017)	•	?	•	?	0	•	•
Johansen et al. (2017)	•	•	0	$\bullet$	$\bullet$	•	•	Urruticoechea et al. (2017)	$\odot$	•	•	?	•	•	•
McDermott et al. (2017)	•	?	0	•	•	•	•	Wysham et al. (2017)	?	•	•	•	•	•	•
Saberi et al. (2017)	•	?	0	•	•	•	•	Devereux et al. (2018)	•	•	•	?	•	•	•
Taaffe et al. (2017)	+	?	•	?	•	•	?	Johnson et al. (2018)	•	•	•	?	•	•	÷
Villareal et al. (2017)	+	?	•	•	•	•	•	Kim et al. (2018)	•	?	•	•	•	•	÷
Dieli-Conwright et al. (2018)	+	•	•	?	•	•	•	Rimawi et al. (2018)	•	•	•	?	•	•	•
McDermott et al. (2018)	•	?	-	?	$\bullet$	•	$\bullet$	Wapnir et al. (2018)	•	•	•	?	$\bullet$	•	•

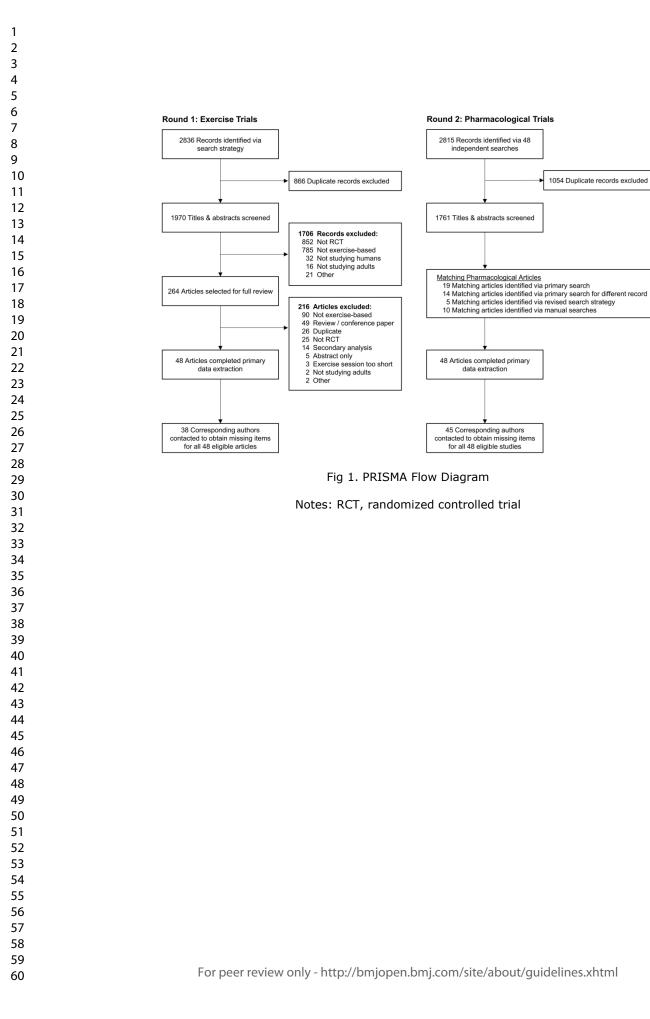
# Table 5. Factors associated with overall quality score, stratified by study type

Outeene	Study	Analysis	Exercis	e Therapy RCT	'S¹	Pharmacological Therapy RCTs <sup>2</sup>			
Outcome	Characteristics	Dichotomy	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value	
Overall quality score	Impact factor	≥25 vs <25	1.36	1.18, 1.57	<0.001	1.02	0.84, 1.24	0.80	
	Sample size	≥152 vs <152	1.29	1.11, 1.51	0.001	1.20	0.97, 1.47	0.089	
	Number of sites	Multi- vs Single Centre	1.08	0.92, 1.27	0.30	1.21	0.98, 1.49	0.078	
	Publication year	≥2013 vs <2013	1.18	1.03, 1.34	0.015	1.35	1.14, 1.60	<0.001	

Notes: CI, confidence interval; OR, odds ratio; RCTs, randomized controlled trials

1 n=48 exercise therapy RCTs; 2 n=48 pharmacological therapy RCTs

1 2	Figure Caption
3 4	Fig 1. PRISMA Flow Diagram
5 6	Notes: RCT, randomized controlled trial
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59 60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



# **Online Supplement**

# Comparing the quality of reporting and conduct of exercise therapy and pharmacological randomized controlled trials: A systematic review

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# Supplementary Methods 1: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration			6
Eligibility criteria 6 Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years publication status) used as criteria for eligibility, giving rationale.		Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources 7 Describe all information sources (e.g., o the search and date last searched.		Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6, eMethods
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	eMethods
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6,7, eMethods
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6,7, eMethods
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7,8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7,8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.	8

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Supplementary Methods 1: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7,8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre- specified.	8,9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10, eMethods Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	eResults
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	eResults
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	eResults
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Table 2, eResul
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11, Table 3, eResul
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

# Supplementary Methods 2: AMSTAR 2 Checklist

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

For Yes	:	Optiona	ll (recommended)				
X	Population		Timeframe for follow-up	X	Yes		
X	Intervention		house and the second seco		No		
X	Comparator group				110		
x	Outcome						
2.			explicit statement that the review eview and did the report justify a				
	ial Yes:	For Yes					
	hors state that they had a written l or guide that included ALL the ng:		vartial yes, plus the protocol be registered and should also ecified:				
				X	Yes		
	review question(s)		a meta-analysis/synthesis plan,		Partial Yes		
	a search strategy		if appropriate, and		No		
	inclusion/exclusion criteria		a plan for investigating causes				
	a risk of bias assessment		of heterogeneity				
			justification for any deviations from the protocol				
3.			ction of the study designs for incl	lusion	in the review?		
For Yes	, the review should satisfy ONE o		wing:				
$\boxtimes$	Explanation for including only R			X	Yes		
	OR Explanation for including on				No		
	OR Explanation for including bo	th RCTs a	ind NRSI				
4.	Did the review authors use a co	mprehen	sive literature search strategy?				
For Part	ial Yes (all the following):	For Yes followin					
	searched at least 2 databases	X	searched the reference lists /		Yes		
_	(relevant to research question)		bibliographies of included		Partial Yes		
	provided key word and/or	_	studies		No		
_	search strategy	X	searched trial/study registries				
	justified publication restrictions	x	included/consulted content experts in the field				
	(e.g. language)	x	where relevant, searched for				
		LAI	grey literature				
		X	conducted search within 24				
		<u>кл</u>	months of completion of the				
			review				
5.	Did the review authors perform	n study se	lection in duplicate?				
	, either ONE of the following:						
x	at least two reviewers independent	ntly agree	d on selection of eligible studies	X	Yes		
	and achieved consensus on which				No		
	OR two reviewers selected a sam				TAC		
IJ	agreement (at least 80 percent), v reviewer.						

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

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	s, either ONE of the following:				
x	at least two reviewers achieved control included studies	onsensus	on which data to extract from		Yes No
	OR two reviewers extracted data achieved good agreement (at leas extracted by one reviewer.				
7.		a list of	excluded studies and justify the ex	clusio	ns?
For Par	tial Yes:	For Yes	s, must also have:		
	provided a list of all potentially	x	Justified the exclusion from	X	Yes
	relevant studies that were read		the review of each potentially		Partial Yes
	in full-text form but excluded from the review		relevant study		No
8.	Did the review authors describe	e the incl	uded studies in adequate detail?		
For Par	tial Yes (ALL the following):	For Yes followi	s, should also have ALL the ng:		
	described populations	X	described population in detail	X	Yes
	described interventions	X	described intervention in		Partial Yes
	described comparators		detail (including doses where		No
	described outcomes	_	relevant)		
	described research designs	X	described comparator in detail (including doses where		
		_	relevant)		
		x	described study's setting		
		x	timeframe for follow-up		
9.			timeframe for follow-up technique for assessing the risk of	of bias	(RoB) in
	Did the review authors use a sa individual studies that were inc	tisfactor	v technique for assessing the risk of	of bias	(RoB) in
<b>RCTs</b> For Par		tisfactory luded in	v technique for assessing the risk of	of bias	(RoB) in
RCTs	individual studies that were inc	tisfactor: luded in For Yes	y technique for assessing the risk of the review?	of bias	(RoB) in Yes
<b>RCTs</b> For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, and	tisfactory luded in For Yes from:	y <b>technique for assessing the risk of</b> <b>the review?</b> s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i>		
RCTs For Par from	individual studies that were inc	tisfactory luded in For Yes from:	y <b>technique for assessing the risk of</b> <b>the review?</b> s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result	x	Yes
RCTs For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for	tisfactory luded in For Yes from: ⊠	y <b>technique for assessing the risk of</b> <b>the review?</b> s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple		Yes Partial Yes No Includes only
RCTs For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing	tisfactory luded in For Yes from: ⊠	y <b>technique for assessing the risk of</b> <b>the review?</b> s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result		Yes Partial Yes No
RCTs For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality)	tisfactory luded in For Yes from: ⊠	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome		Yes Partial Yes No Includes only
RCTs For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-	fisfactory luded in For Yes from: For Yes	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB:		Yes Partial Yes No Includes only NRSI
RCTs For Par rom D NRSI For Par RoB:	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality) tial Yes, must have assessed	tisfactory luded in For Yes from: ⊠	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB: methods used to ascertain		Yes Partial Yes No Includes only NRSI Yes
RCTs For Par Trom	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality) tial Yes, must have assessed from confounding, <i>and</i>	fisfactory luded in For Yes from: For Yes	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i>		Yes Partial Yes No Includes only NRSI Yes Partial Yes
RCTs For Par rom D NRSI For Par RoB:	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality) tial Yes, must have assessed	fisfactory luded in For Yes from: For Yes	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i> selection of the reported result		Yes Partial Yes No Includes only NRSI Yes Partial Yes No
RCTs For Par Trom	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality) tial Yes, must have assessed from confounding, <i>and</i>	fisfactory luded in For Yes from: For Yes	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i>		Yes Partial Yes No Includes only NRSI Yes Partial Yes
RCTs For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, <i>and</i> lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality) tial Yes, must have assessed from confounding, <i>and</i> from selection bias	for Yes from: For Yes from: S For Yes C	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i> selection of the reported result from among multiple measurements or analyses of a		Yes Partial Yes No Includes only NRSI Yes Partial Yes No Includes only RCTs
RCTs For Par from	individual studies that were inc tial Yes, must have assessed RoB unconcealed allocation, and lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all- cause mortality) tial Yes, must have assessed from confounding, and from selection bias	for Yes from: For Yes from: S For Yes C	y technique for assessing the risk of the review? s, must also have assessed RoB allocation sequence that was not truly random, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome s, must also have assessed RoB: methods used to ascertain exposures and outcomes, <i>and</i> selection of the reported result from among multiple measurements or analyses of a specified outcome		Yes Partial Yes No Includes only NRSI Yes Partial Yes No Includes only RCTs

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

RCTs	combination of results?		
For Yes:			
	The authors justified combining the data in a meta-analysis		Yes
			No
	study results and adjusted for heterogeneity if present.	x	No meta-analysis
	AND investigated the causes of any heterogeneity		conducted
For NR	SI		
For Yes:			
	The authors justified combining the data in a meta-analysis		Yes
			No No moto analonia
_	study results, adjusting for heterogeneity if present	x	No meta-analysis conducted
	AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data,		conducted
	or justified combining raw data when adjusted effect estimates		
	were not available		
	AND they reported separate summary estimates for RCTs and		
	NRSI separately when both were included in the review		
12.	If meta-analysis was performed, did the review authors assess the poten individual studies on the results of the meta-analysis or other evidence s		
For Yes:			
	included only low risk of bias RCTs	Ţ	□ Yes
	OR, if the pooled estimate was based on RCTs and/or NRSI at variable		🗆 No
	RoB, the authors performed analyses to investigate possible impact of		x No meta-analys
	RoB on summary estimates of effect.		conducted
13.	Did the review authors account for RoB in individual studies when interesults of the review?	rpret	ing/ discussing the
For Yes:			
	included only low risk of bias RCTs		x Yes
X	OR, if RCTs with moderate or high RoB, or NRSI were included the		] No
	review provided a discussion of the likely impact of RoB on the results		
14.	Did the review authors provide a satisfactory explanation for, and disc heterogeneity observed in the results of the review?	ussion	of, any
For Yes:			
	There was no significant heterogeneity in the results		🛛 Yes
X	OR if heterogeneity was present the authors performed an investigation of		$\square$ No
	sources of any heterogeneity in the results and discussed the impact of this on the results of the review		and the second s
15		ut an	adaguata
15.	If they performed quantitative synthesis did the review authors carry or investigation of publication bias (small study bias) and discuss its likely the review?		
For Yes:			
	performed graphical or statistical tests for publication bias and discussed		□ Yes
	the likelihood and magnitude of impact of publication bias	1	🗆 No
		1	🗴 No meta-analysi
			conducted

Supplementary Methods 2: AMSTAR 2 Checklist

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or nonrandomised studies of healthcare interventions, or both

16.	Did the review authors report any potential sources of conflict of inter they received for conducting the review?	rest, ind	cluding any funding
For Yes			
X	The authors reported no competing interests OR	X	Yes
	The authors described their funding sources and how they managed		No
	potential conflicts of interest		

**To cite this tool:** Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

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Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

#### Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

This review was conducted in accordance with the PRISMA<sup>1</sup> and AMSTAR 2<sup>2</sup> guidelines (PROSPERO identifier CRD42018095033) (eMethods 1 and 2).

#### **Data Sources and Searches**

A Research Informationist (KM) conducted two sequential literature searches for articles from RCTs of exercise (first search) and pharmacological (second search) therapies within the Cochrane Central Register of Controlled Trials (Wiley), Embase (Elsevier), PubMed (NLM), and CINAHL (EBSCO) databases (eFigure 1). The exercise literature search was conducted on March 8<sup>th</sup>, 2018 and consisted of two component concepts using a combination of relevant keywords and controlled vocabulary: (1) exercise training intervention and (2) RCTs (eMethods 4). The Round 1 search was limited to trials published between January 1<sup>st</sup> 2008 (the year the CONSORT extension for Non-Pharmacologic Treatments was first published<sup>3</sup>) and the search date (March 8<sup>th</sup>, 2018). The searches were also limited to publications within leading clinical, general medicine and specialist medical journals based on having impact factors  $\geq$ 15 according to the 2016 Journal Citation Reports (Clarivate Analytics, formerly ISI Web of Knowledge). We purposefully restricted our search to medical journals with higher impact factors are more likely to endorse and enforce reporting quality guidelines<sup>4-6</sup> and publish both exercise and pharmacological RCTs – leading to a more balanced foundation for comparison between study types. This impact factor-based restriction is also consistent with the methods from similar reviews of medical, psychosocial, and behavioural RCTs.<sup>7-13</sup>

Trial meta-data (i.e., publishing journal, cohort / population, sample size, and number of study sites) was extracted from eligible exercise studies and used as 'matching criteria' to define search parameters for the pharmacological trial searches. See RCT matching criteria below. In Round 2, 48 independent searches were initially conducted to identify pharmacological trials to match each of the 48 eligible exercise RCTs identified in Round 1. The initial Round 2 searches were conducted on November  $20^{th}$ , 2018. Each search consisted of five component concepts using a combination of relevant search terms and 'matching criteria' for: 1) pharmacological intervention, 2) RCTs, 3) publishing journal, 4) population, and 5) number of study sites (single- vs. multi-site studies). The Round 2 searches were similarly limited to trials published between January 1<sup>st</sup> 2008 and the search date within leading clinical, general medicine and specialist medical journals based on having impact factors  $\geq 15$  according to the 2016 Journal Citation Reports (eMethods 4). Per Round, search strategy components were first searched

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Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

individually (combining synonyms describing that concept with the Boolean operator OR), followed by the individual component search sets combined together using the Boolean operator AND.

#### **Study Eligibility**

Published RCTs of exercise and pharmacological interventions involving human adults ( $\geq$ 18 years of age), written in English, published after January 1<sup>st</sup> 2008, and published in leading clinical, general medicine and specialist medical journals were eligible (eMethods 4 and 5). Exercise therapy interventions were defined as those involving chronic (>3 weeks), repeated sessions of supervised (in person, with or without a distance-based component) aerobic training (i.e., endurance activity,  $\geq$ 15 minutes/session), resistance training (i.e., multiple large muscle group exercises involving repeated voluntary muscle contractions against a resistance greater than those normally encountered in activities of daily living), or the combination, with the objective of improving health-related outcomes.<sup>14,15</sup> Pharmacological interventions were defined as studies involving the administration of established or experimental pharmacological agents with the objective of improving health.

#### **Data Extractor Training**

Study reviewers (JM and KS) were trained in eligibility screening and data extraction over the course of eight weeks (>25 hours of group training), consisting of: (1) independent screening and data extraction from 12 "training" articles of both exercise and pharmacological RCTs using custom study Data Extraction Reference Guides (eMethods 6 and 7), and (2) regular investigator-led (SCA) review sessions to evaluate extraction completeness.

#### **RCT Matching**

The <u>specific matching criteria</u> used included: (1) **publishing journal** ( $\pm$ 5 impact factor points according to the 2016 Journal Citation Reports (Clarivate Analytics, formerly ISI Web of Knowledge)), (2) **study population** (sharing similar disease characteristics), (3) **study sample size** ( $\pm$ 30% difference in study samples), and (4) **number of study sites** (single vs multisite). These specific matching criteria were selected to establish impartial comparison between exercise and pharmacological RCTs. The 'publishing journal' criteria was selected because studies published within the same journal should, in theory, be held to similar reporting standards. If no direct match could be identified within the same journal, we used an investigatordefined cut-off of  $\pm$ 5 impact factor points to find alternate matches because impact factor has been shown to be associated with RCT reporting and methodological quality.<sup>16,17</sup> The 'study population' criteria was chosen to account for differences in the

Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

research methods and standards across specific clinical populations and specialties. If no direct population match could be identified, we considered closely related populations. For example, for trials among patients with cardiac diseases, cardiomyopathy or heart failure were considered surrogates. We selected the 'study sample size' and 'number of study sites' as criterion to control for differences in the methods (eg, human and physical resources, infrastructure) used to conduct smaller versus larger trials. To this end, an investigator-defined cut-point of a 30% difference in sample size was used to match RCTs of similar scale and logistical complexity. Exercise and pharmacological therapy RCTs had to be matched on a minimum of two of the four matching criteria to be eligible. The pharmacological therapy RCT with values closest to the target exercise RCT was used if more than one potential match was identified.

#### Study Selection, Data Extraction and Additional Sources

Article screening and data extraction for all trials was conducted sequentially following each round of literature searches (fig 1). First, two trained reviewers (JM and KS) independently screened and evaluated exercise article titles and abstracts (n=1,970) against review eligibility criteria using DistillerSR (Evidence Partners, Ottawa, Canada). Second, full manuscripts (n=264) of potentially eligible exercise articles were independently reviewed (JM and KS) using DistillerSR. Third, meta-data from each eligible exercise RCT (n=48) was extracted and used to develop the targeted systematic search strategies for Round 2 (i.e., pharmacological trial search). Fourth, detailed data from all studies (e.g., study design and methods, patient characteristics and flow, intervention descriptions) were extracted for each eligible exercise RCT from the primary manuscript and all data sources that were publicly available at the time the primary manuscript was published, including online supplements, clinical trial registries, and related publications as appropriate using DistillerSR and a custom Exercise Therapy RCT Data Extraction Reference Guide (eMethods 6). Fourth, "incomplete" and "missing" items were compiled, and corresponding authors were emailed (from SCA, JMS, LWJ) with a request to provide missing items within ~4 weeks. Non-responding authors were sent a reminder email within 3 weeks providing up to an additional ~4 weeks to respond.

The Round 2 pharmacological therapy RCT searches were conducted (KM, SCA) concurrently with the author contact step from round 1. Titles, abstracts, and full texts (n=1,761) were screened (SCA) to identify pharmacological therapy RCTs that were best matched to the n=48 eligible exercise therapy RCTs according to our matching criteria. Nineteen of the initial 48 searches (40%) successfully identified 'matching' pharmacological trials, leaving 29 exercise trials unmatched. Matching pharmacological trials were found for the remaining 29 exercise trials within the search results for different records (n=14 (29%); SCA), by running revised searches (n=5 (10%); KM), and by manual searches of journal databases (n=10 (21%); SCA).

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Supplementary Methods 3: Study Search, Selection & Data Extraction Methods

Once all exercise trials had been matched, the team (JM and KS) independently extracted data from the primary manuscript and all data sources that were publicly available at the time the primary manuscript was published, including online ran supplements, clinical trial registries, and related publications as appropriate using DistillerSR and a custom Pharmacological Therapy RCT Data Extraction Reference Guide (eMethods 7). Finally, "incomplete" and "missing" items were compiled, and corresponding authors were emailed (from SCA, JMS, LWJ) with a request to provide missing items within ~4 weeks. Nonresponding authors were sent a reminder email within 3-4 weeks providing up to an additional ~4 weeks to respond. Disagreements concerning eligibility, data extractions, and risk of bias assessments were resolved by consensus (JM and KS). Disagreements were adjudicated by a third party (SCA) when a consensus could not be reached.

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## Supplementary Methods 4: Exercise RCT Search Strategies

### **Exercise Search Strategies**

Comprehensive searches were conducted (March 8th, 2018) in three electronic databases:

- 1) PubMed/Medline (NLM)
- 2) EMBASE (Elsevier)
- 3) CINAHL (EBSCO)

The literature search strategy was developed first in PubMed and then translated to the other databases. A combination of relevant keywords and controlled vocabulary (MeSH - Medical Subject Headings in PubMed and Emtree in EMBASE) were used in the PubMed and EMBASE searches. Comparable keyword search strategies were used in CINAHL. A "Last 10 years" (2008-2018) date range was applied. No language restrictions were applied.

Two component parts made up the search strategy:

- 1) Exercise training intervention
- 2) RCTs

Date range limit: Last 10 years Publications limit: 45 target journals

Search filters were used for finding RCTs in PubMed and EMBASE. Available database limiters were used in CINAHL (Publication Type: Clinical Trial, Randomized Controlled Trial).

For the RCT search set, we used Cochrane Handbook recommended search filters for finding RCTs: <u>http://work.cochrane.org/pubmed</u>

#### sensitivity- and precision-maximizing version (2008 revision); PubMed format<sup>1</sup>

(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti] NOT (animals[mh] NOT humans [mh])) http://work.cochrane.org/embase

#### Embase search strategy for finding RCTs in Embase<sup>1</sup>

('crossover procedure':de OR 'double-blind procedure':de OR 'randomized controlled trial':de OR 'single-blind procedure':de OR (random\* OR factorial\* OR crossover\* OR cross NEXT/1 over\* OR placebo\* OR doubl\* NEAR/1 blind\* OR singl\* NEAR/1 blind\* OR assign\* OR allocat\* OR volunteer\*):de,ab,ti)

1. Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from **www.cochrane-handbook.org** 

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Each of the two components of the search strategy was first searched upon individually, combining synonyms describing that concept with the Boolean operator OR. The three individual component search sets were then combined together using the Boolean operator AND. Resulting citations were managed and duplicates removed using the Endnote citation management software program (Clarivate Analytics).

Supplementary Methods 4: Exercise RCT Search Strategies

# PubMed/MEDLINE Search Strategy

("Exercise"[Mesh] OR "exercise" OR "exercises" OR "Exercise Therapy"[Mesh] OR "exercise therapy" OR "exercise therapies" OR "exercise program" OR "Physical Conditioning, Human"[Mesh] OR "physical conditioning" OR "physical activity" OR "physical activities" OR "Motor Activity"[Mesh] OR "motor activity" OR "motor activities" OR "Muscle Contraction"[Mesh] OR "muscle contraction" OR "Resistance Training"[Mesh] OR "resistance training" OR "Circuit-Based Exercise"[Mesh] OR "circuit-based exercise" OR "circuit training" OR "Muscle Stretching Exercises"[Mesh] OR "muscle stretching exercises" OR "aerobic exercise" OR "anaerobic exercise" OR "Locomotion"[Mesh] OR "locomotion" OR "Running"[Mesh] OR "running" OR "Jogging"[Mesh] OR "jogging" OR "Swimming"[Mesh] OR "swimming" OR "Valking"[Mesh] OR "sole trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) **AND** ("CA Cancer J Clin"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "JAMA"[Journal] OR "Nat Beiotechnol"[Journal] OR "Nature"[Journal] OR "Science"[Journal] OR "N Engl J Med"[Journal] OR "Cell"[Journal] OR "Nat Med"[Journal] OR "Nat Beiotechnol"[Journal] OR "Nat Med"[Journal] OR "Nat metro bis/[Journal] OR "Lancet Neurol"[Journal] OR "Nat Cell Biol"[Journal] OR "Cancer Disco"[Journal] OR "Nat Chem "Journal] OR "Nat Med"[Journal] OR "Cancer Cell"[Journal] OR "Lancet Infect Dis"[Journal] OR "Nat Med"[Journal] OR "Cancer Cell"[Journal] OR "Cancer Cells [Journal] OR "Cancer Cells [Journal] OR "Cell Mesh"[Journal] OR "Nat Neurosci"[Journal] OR "Circulation"[Journal] OR "Cancer Disco"[Journal] OR "Lancet Circo

Abbreviations: Mesh = Medical Subject Heading, pt = Publication Type, tiab = Title/Abstract, ti = Title, mh = MeSH Terms

### **EMBASE Search Strategy**

1	(exercise/exp OR 'exercise' OR 'exercises' OR 'kinesiotherapy/exp OR 'exercise therapy' OR 'exercise therapies' OR 'exercise prescription' OR 'training program' OR 'exercise program' OR 'physical conditioning' OR 'physical activity' OR 'physical activities' OR 'motor activity' exp OR 'motor activity' OR 'motor activities' OR 'motor activity' OR 'motor activity' OR 'motor activities' OR 'muscle contraction'/exp OR 'muscle contraction' OR 'resistance training'/exp OR 'exercise' OR 'anaerobic exercise' OR 'accounties' or 'accounties' or OR 'accounti
2	(('15424863':is OR 'CA Cancer Journal for Clinicians'/jt) OR ('15334406':is OR 'New England Journal of Medicine'/jt) OR ('1474547X':is OR 'The Lancet'/jt) OR ('15383598':is OR 'JAMA - Journal of the American Medical Association'/jt) OR ('15461696':is OR 'Nature Biotechnology'/jt) OR ('14764687':is OR 'Nature'/jt) OR ('10959203':is OR 'Science'/jt) OR ('14745488':is OR 'The Lancet Oncology/jt) OR ('10974172':is OR 'Cell'/jt) OR ('1546170X':is OR 'Nature Medicine'/jt) OR ('15461718':is OR 'Nature Genetics'/jt) OR ('1776183369':is OR 'Cancer Cell'/jt) OR ('120515545':is OR 'Northe Psychiatry'/jt) OR ('14744465':is OR 'The Lancet Neurology'/jt) OR ('15277755':is OR 'Journal of Clinical Oncology/jt) OR ('147597777':is OR 'Cell Stem Cell'/jt) OR ('10974180':is OR 'Immunity/jt) OR ('17561833':is OR 'BMJ (Online)'/jt) OR ('15229645':is OR 'European Heart Journal'/jt) OR ('14744457':is OR 'Nature Cell Biology'/jt) OR ('12598290':is OR 'Cancer Discovery'/jt) OR ('15583597':is OR 'Journal of the American College of Cardiology'/jt) OR ('14744457':is OR 'The Lancet Infectious Diseases'/jt) OR ('122138595':is OR 'The Lancet Diabetes and Endocrinology'/jt) OR ('15244539':is OR 'Circulation'/jt) OR ('12432619':is OR 'The Lancet Respiratory Medicine'/jt) OR ('15280012':is OR 'Gastroenterology'/jt) OR ('19327420':is OR 'Cell Metabolism'/jt) OR ('15461726':is OR 'Nature Neuroscience'/jt) OR ('2214109X':is OR 'The Lancet Global Health'/jt) OR ('15393704':is OR 'Annals of Internal Medicine'/jt) OR ('19466242':is OR 'Science Translational Medicine'/jt) OR ('1463288':is OR 'Gut'/jt) OR ('13624326':is OR 'Trends in Biochemical Sciences'/jt) OR ('21686106':is OR 'JAMA Internal Medicine'/jt) OR ('18737560':is OR 'European Urology'/jt) OR ('187307X':is OR 'Trends in Cognitive Sciences'/jt) OR ('2168622X':is OR 'JAMA Psychiatry'/jt) OR ('15524469':is OR 'Nature Chemical Biology'/jt))
	**Note: EMBASE does not index the following 6 titles so they were not included in the search string: -Nature Chemistry -Nature Immunology -Psychological Bulletin -JAMA Oncology -Psychological Inquiry -Cell Research

# Supplementary Methods 4: Exercise RCT Search Strategies

# **CINAHL Search Strategy**

1 ("exercise" OR "exercises" OR "exercise therapy" OR "exercise therapies" OR "exercise prescription" OR "training program" OR "exercise program" OR "physical conditioning" OR "physical activity" OR "motor activity" OR "motor activities" OR "muscle contraction" OR "resistance training" OR "circuit-based exercise" OR "circuit training" OR "muscle stretching exercises" OR "aerobic exercise" OR "anaerobic exercise" OR "locomotion" OR "running" OR "jogging" OR "swimming" OR "walking" OR "sports")

AND

Limiters - Publication Type: Clinical Trial, Randomized Controlled Trial

2 (((ZJ "new england journal of medicine")) or ((ZJ "lancet")) or ((ZJ "jama journal of the american medical association")) or ((ZJ "lancet oncology")) or ((ZJ "journal of clinical oncology")) or ((ZJ "bmj british medical journal international edition")) or ((ZJ "journal of the american college of cardiology jacc"))) or ((ZJ "circulation"))) or ((ZJ "annals of internal medicine")) or ((ZJ "jama internal medicine")))

AND

Limiters - Published Date: 20080101-20181231

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Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

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Supplementary	viernous 5:	Pharmacological	KU I Search	Strategies &	мателея
~ approntent j				~	

## Summary:

**Database:** PubMed (searched run on November 20<sup>th</sup>, 2018)

Total (including duplicates): 2815 records

Duplicates: 1054 records

Total (without duplicates): 1761 records to be reviewed

## PubMed search strategies for each identified Population from the 48 included EXERCISE papers

#### 1) Exercise trial matching search: ID 33

("Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD OR "Chronic Obstructive Pulmonary Disease" OR COAD OR "Chronic Obstructive Airway Disease" OR Chronic Obstructive Lung Disease" OR "Chronic Airflow Obstructions" OR "Chronic Airflow Obstruction" OR ("chronic" AND "obstructive" AND "pulmonary" AND "disease")) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("Ann Intern Med"[Journal]) Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000073/public/ Pharma trial match: Found in original search - Lapperre et al. (2009) 2) Exercise trial matching search: ID 51 (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumors OR tumours OR malignan\* OR malignant OR "hematooncological" OR "hemato oncological" OR "hemato-oncological" OR hematologic neoplasms OR hematolo\*) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multicenter" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("BMJ"[Journal]) Results: 14 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/55000123/public/ Pharma trial match: Found in original search from an alternate record (#36) - Rimawi et al. (2018) 3) Exercise trial matching search: ID 96 (("peripheral arterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal])

Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/55000170/public/

Pharma trial match: Found in original search from an alternate record (#31) – Ford et al. (2014)

4) Exercise trial matching search: ID 103

("Heart Failure"[Mesh] OR "heart failure" OR "Cardiac Failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR

#### Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

"pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) Results: 29 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/55000252/public/ Pharma trial match: Found in original search - Gheorghiade et al. (2013) 5) Exercise trial matching search: ID 107 (("Breast Cancer Lymphedema" [Mesh] OR (("lymphedema" OR "lymphedemas") AND ("Breast Neoplasms" [Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumors OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) Results: NONE - check how match found Pharma trial match: Found in original search from an alternate record (#35) - Wapnir et al. (2018) 6) Exercise trial matching search: ID 133 (("Diabetes Mellitus, Type 2"[Mesh] OR "NIDDM" OR "type 2 diabetes mellitus" OR "diabetes mellitus type 2") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy" [Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) Results: 18 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/55000319/public/ Pharma trial match: Found in manual search - Nissen et al. (2008) 7) Exercise trial matching search: ID 180 ("Breast Neoplasms" [Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant)) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) Results: 6 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tIOrYmkO/collections/55000333/public/ Pharma trial match: Found in original search from an alternate record (#35) - Hurvitz et al. (2013) 8) Exercise trial matching search: ID 282 (("Obesity"[Mesh]OR "obesity" OR "obese") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "therapeutic use" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("N Engl J Med"[Journal]) Results: 14 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/55000364/public/ Pharma trial match: Found in manual search - Smith et al. (2010) 9) Exercise trial matching search: ID 394 16

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## **BMJ** Open

## Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

(' T C "F C tr	Mental Disorders" [Mesh] OR ((mental* OR psycholog* OR brain OR mind) AND ("disorder" OR "disorders" OR "illness" OR "ill" OR "disease" OR "diseases"))) AND Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center") AND ("Drug herapy" [Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" or "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR oharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug oharmacological" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" oharmacological" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" or "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical ials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01" [PDAT] : "2018/12/31" [PDAT]) AND ("Ann Intern fed" [Journal] OR "BMJ" [Journal] OR "JAMA" [Journal] OR "N Engl J Med" [Journal] OR "Lancet" [Journal]) AND ("N Engl J Med" [Journal])
R	Results: 79 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_ttOrYmkO/collections/55000661/public/
	Pharma trial match: Found in original search – Rosenheck et al. (2011)
-	
1	0) Exercise trial matching search: ID 431
	((((((("Obesity"[Mesh] OR "obesity" OR "obese" OR "Overweight"[Mesh] OR "overweight" OR "Weight Loss"[MeSH Terms] OR "Body Mass Index"[MeSH Terms]))) NOT (Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter"))) AND (("Drug iherapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR oharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" PR "drugs" OR "preparation" OR "pharmaceutical") AND (("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" PR "drugs" OR "preparation" OR "pharmaceutical") AND (("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" PR "drugs" OR "preparation" OR "pharmaceutical") AND (("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" PR "drugs" OR "preparation" OR "pharmaceutical") AND (("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" PR "drugs" OR "preparation" OR "pharmaceutical") ON (("animals[mh] NOT humans [mh])))) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]))) AND ("CA Cancer J Clin"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "JAMA"[Journal] OR "Nat Biotechnol"[Journal] OR "Nature"[Journal] OR "Lancet [Journal] OR "Nature"[Journal] OR "Nature"[Journal] OR "Lancet [Journal] OR "Nat Med"[Journal] OR "Lancet [Journal] OR "Cancer Cell"[Journal] OR "Nat Immunol"[Journal] OR "BAJ"[Journal] PR "Lancet Oncol"[Journal] OR "Nat Chem [Journal] OR "Cancer Discov"[Journal] OR "Lancet Inabetes Endocrinol
R	Results: 187 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57349993/public/
	Pharma trial match: Found in original search – Spitzer et al. (2012)
1	1) Exercise trial matching search: ID 528
"i "I C "t c [r	'Aged"[Mesh] OR (("aged" OR "elderly" OR "older") AND ("adult" OR "adults"))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" (OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapy" OR "therapeutic use" [Subheading] OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmacotherapies") AND ("therapy" OR "therapey" OR "therapey" OR "therapey" OR "therapeited trial[pt] OR "reatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND (randomized (trial[pt] OR ontrolled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "hand"[Journal]) AND ("JAMA"[Journal])
R	Results: 310 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tIOrYmkO/collections/55000777/public/
P	Pharma trial match: Found in manual search – Devereux et al. (2018)
1	2) Exercise trial matching search: ID 585
S C "H C tr	'peripheral arterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") AND ("Multicenter tudy" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR oharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug therapy" OR "pharmacologic" OR oharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "interventions" OR "interventions" OR "drug "drugs" OR "preparations" OR "preparations"])) AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug "a drugs" OR "preparation" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical tials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal])
R	Results: 3 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/55000794/public/
	Pharma trial match: Found in original search – Poole et al. (2013)
1	3) Exercise trial matching search: ID 631
י" P "ו	"Obesity"[Mesh]OR "obesity" OR "obese") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR multicenter" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapeies" OR medication" OR "medications" OR (interventions" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR reatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparations" OR "preparations")) AND ((randomized controlled trial[pt] OR
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#### Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

<ul> <li>((*)Desky[WeblyOR *: obesky]* OR *: obesky]* OR *: obesky]* AND [*Heart Failure*] Meshy] OR *: heart failure* OR *: Cardiac Failure* OR *: Cardiac Failure* OR *: Cardiac *: Desky]* OR *: obesky]* OR *: o</li></ul>	[mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "JAMA"[Journal] OR "I Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("Ann Intern Med"[Journal]) Results: 9 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/55000827/public/	ans
Pharma trial match: Found in manual search – Kim et al. (2018)  14) Exercise trial matching search: 10 709  NOTE - Originally considered this strategy: (('Description of the strategy): ('Description of the str		
<ul> <li>14) Exercise trial matching search: 10 709</li> <li>NOTE - Originally considered this strategy:</li> <li>(("Desiry (Net)(Sear)) (AR) (Sear) (AR) (Preserved Ejection Fraction OR (Preserved ARD Ejection' AND Fractorn')) NOT ("Multicents Study" Publication Type (Network) (Search Study (Publication Type)) (Search Study (Publica</li></ul>	Pharma trial match: Found in manual search – Kim et al. (2018)	
NOTE - Originally considered this strategy: (('Deskyf) Mesh)OR 'obeshy' OR 'obesh' AND ('Heart Failure')Mesh) OR 'heart failure' OR 'Cardiac Failure' OR 'Heart Decompensation' OR (('heart' OR 'cardiac') AND (Failure' OR decompensation') AND ('Heart Failure')Mesh) OR 'heart failure' OR 'Cardiac Failure' OR 'theoremethy of the thome of the multicenter' (IAU OT) Tractory (IAU) (Pailotation Type G'Autocardia San Cord Charter (IAU) (Pailotation') OR 'Heart failure') OR 'theoremethy of the multicenter') IAU OT ('theoremethy of theoremethy OR pharmacohanges OR theoremethy OR 'theoremethy OR 'theoremethy OR 'theoremethy' OR 'theore		
<ul> <li>(If Obeshy DR 'obeshy' DR 'obeshy' AND ('Heart Failure' Mesh) DR 'heart failure' OR 'Cardiac Failure' DR 'decompensation' OR ('heart OR 'cardiac') AND (Fleasened Type) (The served AND 'Ejection' AND 'Fractori')) NOT ('Multicente' Study' Publication Type) (The 'Nuticente' OR 'multicente' O</li></ul>	14) Exercise trial matching search: ID 709	
<ul> <li>Alb C faluer OR 'decomposition'') AND (Preserved Ejection Factor'' OR (Preserved 'AND 'Ejection'' AND 'Factor'') ("Autilicanter Study' Publication Type)</li> <li>OR 'vulcionet's OK 'shorthered OR ''nulcionet' OR ''nulcionet'') ("Antilocanter' OR ''nulcionet'') (AND (Charpertocuse') (Shorthered) (OR ''nulcionet'') (Shorthered) (OR ''nulcionet') (Shorthered) (OR ''nulcionet') (Shorthered) (Shorthere</li></ul>	NOTE - Originally considered this strategy:	
Final search strategy used: ((("Heart Failure")Mesh) OR "heart failure" OR "Cardiac Failure" OR "Heart Decompensation") OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND ((Preserved Ejection Fraction") OR ("Preserved" AND "Ejection") AND ("Dug Theraciton") Study Entry") (Subteading) OR "therapeeter of R" multic-anter" of R" multic-anter") or R" multic-anter" of R" multic-anter" of R" multic-anter" of R" multic-anter") AND ("therapey") (Mesh) (OR "therapeeter of R" multic-anter") AND ("therapeeter of R" fundamentary") (Pathamacologic")	AND ("failure" OR "decompensation")) AND ("Preserved Ejection Fraction" OR ("Preserved" AND "Ejection" AND "Fraction"))) NOT ("Multicenter Study" [Publication OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapies" OR "medications" OR ("drug therapy" OR "therapeutic use" OR "pharmacotherapies" OR "chemotherapies" OR "medication" OR "medications" OR ("drug therapy" OR "therapeutic use" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug or "drugs" OR "preparation" OR "preparations"))) AND ((trandomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern	n Type
(("Heart Failure"(Mesh) QR "heart failure" OR "Cardiac Failure" OR "Heart Decompensation") OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) NOT ("Multicenter Studies as Topic"(Mesh) QR "multicenter QR ("multicenter QR "multicenter QR "	***However - including the "Obesity" concept led to NO results, so removed it***	
((Preserved Ejection Fraction') OR (Preserved' AND Ejection' AND Fraction') NOT ("Multicenter Study" (Publication Type) OR "Multicenter OR multicenter' OR "metanocherapy" OR "hereapy" (Stubheading) OR "hereapic use 'I (Stubheading) OR "hereapic use' OR "pharmacologic' OR "preservations" (Preparations") OR Tradument' OR "hereapic use' OR "hereapy" (Stubheading) OR "hereapic use' Stubheading OR "hereapics" OR "chemotherapy" OR "hereapics" OR "chemotherapy" OR "hereapics" OR "retenters") OR "intervention" OR "interventions" OR "trauge OR "preparation" OR "preparation" (OR "preparation") ND (Catodomicaed controlled trialing) OR readomized (Path) OR placeboltab) OR clinical trialing or a non-explicit preparation" (OR multicenter') OR "interventions" OR "trauge OR "preparation" OR "reduced or "JAMA" (Journal) OR "Net (Journal) OR "Lancet (Journal) O	Final search strategy used:	
Pharma trial match: Found in original search from an alternate record (#27) – Gheorghiade et al. (2008)         15) Exercise trial matching search: ID 822         (("peripheral arterial disease"]MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "arteries") AND "disease") OR "multicenter" OR "intervention" OR "interve	(("Preserved Ejection Fraction") OR ("Preserved" AND "Ejection" AND "Fraction")) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[N OR "multicenter" OR "multi-center" OR "multi-centre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subhe OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapies" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacotherapy" OR "pharmaceutical") AND ("therapeutic use" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapeutic use" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapeutic use" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "drugs" OR "preparation")) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT	Mesh] eading] by" OR
15) Exercise trial matching search: ID 822          ("peripheral aterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease"] NOT ("Multicenter Study: [Publication Type] OR "Multicenter Study: Subheading] OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter OR "multicenter" OR "multicenter or OR "peripheral arterial disease"] NOT ("Multicenter Study: [Subheading] OR "therapeutic use" OR "hearnacotherapy" OR "pharmacotherapy" OR "therapeutic use" (Subheading] OR "therapeited Preparations" (Mesh] OR "drug therapy" OR "therapeutic use" OR "themcotherapy" OR "prescription" OR "pharmacotical" NAD ("therapies" OR "therapeutic use" OR "medication" OR "medication" OR "medication" OR "interventions" OR ("drug" OR "preparations" OR "preparations")) AND (Or animals(mh) NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intervention") OR "interventions" OR "therapeutic use" OR "hearnacotherapy" (Subheading) OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intervention" OR "intervention" OR "interventind"	Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/55000925/public/	
("peripheral atterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral atterial disease") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "medication" OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "perparation" OR "preparation" OR "therapeuti	Pharma trial match: Found in original search from an alternate record (#27) – Gheorghiade et al. (2008)	
(*Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "mult	15) Exercise trial matching search: ID 822	
Pharma trial match: Found in manual search – Pradhan et al. (2009)         16) Exercise trial matching search: ID 842         (("Cardiomyopathy, Hypertrophic"[Mesh] OR "Hypertrophic Cardiomyopathies" OR "Hypertrophic Cardiomyopathy" OR ("hypertrophic" AND "cardiomyopathy")) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "hypertrophic OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "herapeutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "therapeuse" OR "medications" OR (("drug" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "medication" OR "medications" OR (("drug" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "theratment" OR "treatments" OR "intervention" OR "interventions" OR "drug OR "pharmacelogical" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "theratment" OR "treatments" OR "intervention" OR "interventions" OR "drug OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "interventions" OR "pharmaceutical") AND ("therapy" OR "herapies" OR "therative of "used intial[pt] OR candomized (table) OR placebo[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR "andomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Interm Med"[Journal] OR "BAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]))	("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multicenter") AND ("Dr Therapy"[Mesh] OR "drug therapy" (Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" ([drug" OR "drug therapy" OR "therapeutic OR "pharmacological" OR "pharmacotherapies" OR "chemotherapies" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinit trials as topic[mesh:noexp] OR randomized[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Interventions")) AND ("Ann Interventions") OR "BAJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal])	use" R R "drug' nical
16) Exercise trial matching search: ID 842 (("Cardiomyopathy, Hypertrophic"[Mesh] OR "Hypertrophic Cardiomyopathies" OR "Hypertrophic Cardiomyopathy" OR ("hypertrophic" AND "cardiomyopathy")) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multicenter" OR "multi-center")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapies" OR "therapeutication" OR "medications" OR (("drug" OR "pharmacodogical" OR "pharmacotological" OR "preparations" OR "pharmaceutical") AND ("therapy" OR "therapeus"		
(("Cardiomyopathy, Hypertrophic"[Mesh] OR "Hypertrophic Cardiomyopathies" OR "Hypertrophic Cardiomyopathy" OR ("hypertrophic" AND "cardiomyopathy")) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentere" OR "multi-center")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapeis" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "interventions" OR "drug OR "drugs" OR "preparation" OR "pharmaceutical") AND ((tandomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("Ann Intern Med"[Journal] OR "BMJ"[Journal] OR "JAMA"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal]) AND ("JAMA"[Journal]) <b>Results: NONE</b> <b>Pharma trial match:</b> Found in original search from an alternate record (#1184) – Kosmala et al. (2016)		
("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multice		
Pharma trial match: Found in original search from an alternate record (#1184) – Kosmala et al. (2016)	("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter") AND ("Dn Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic") "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clin	ug use" R R "drug nical
	Results: NONE	
	Pharma trial match: Found in original search from an alternate record (#1184) - Kosmala et al. (2016)	

## Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

	(((((("Obesity"[Mesh] OR "obesity" OR "obese" OR "Overweight"[Mesh] OR "overweight" OR "Weight Loss"[MeSH Terms] OR "Body Mass Index"[MeSH Terms]))) NOT
	"Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre"))) AND (("Drug
	[herapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use"
	DR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR
	pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug"
	DR "drugs" OR "preparation" OR "preparations"))))) AND (((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical
	rials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])))) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]))) AND ("CA Cancer J
C	Clin"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "JAMA"[Journal] OR "Nat Biotechnol"[Journal] OR "Nature"[Journal] OR "Science"[Journal] OR
	Lancet Oncol"[Journal] OR "Cell"[Journal] OR "Nat Med"[Journal] OR "Nat Genet"[Journal] OR "Cancer Cell"[Journal] OR "World Psychiatry"[Journal] OR "Lancet
	Neurol"[Journal] OR "Nat Chem"[Journal] OR "J Cin Oncol"[Journal] OR "Cell Stem Cell"[Journal] OR "Immunity"[Journal] OR "Nat Immunol"[Journal] OR "BMJ"[Journal]
	DR "Eur Heart J"[Journal] OR "Nat Cell Biol"[Journal] OR "Cancer Discov"[Journal] OR "J Am Coll Cardiol"[Journal] OR "Lancet Infect Dis"[Journal] OR "Lancet Diabetes
	Endocrinol"[Journal] OR "Circulation"[Journal] OR "Lancet Respir Med"[Journal] OR "Gastroenterology"[Journal] OR "Cell Metab"[Journal] OR "Nat Neurosci"[Journal] OR
	Lancet Glob Health"[Journal] OR "Ann Intern Med"[Journal] OR "Psychol Bull"[Journal] OR "Sci Transl Med"[Journal] OR "Gut"[Journal] OR "Trends Biochem
	Sci"[Journal] OR "JAMA Oncol"[Journal] OR "JAMA Intern Med"[Journal] OR "Psychol Ing"[Journal] OR "Eur Urol"[Journal] OR "Cell Res"[Journal] OR "Trends Cogn
S	Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal])
E	Results: 187 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tIOrYmkO/collections/57349993/public/
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F	Pharma trial match: Found in manual search – Grudell et al. (2008)
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	D Formation stately a second by D 000
1	8) Exercise trial matching search: ID 892
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	("Heart Failure"[Mesh] OR "heart failure" OR "Cardiac Failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) NOT
	"Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug
Ť	[herapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use"
C	DR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR
"	pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug"
Ċ	DR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical
	rials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (Eur Heart
F	Results: 87 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_ttOrYmkO/collections/57137958/public/
	Dearma trial matchy Found in ariginal aparts Upandomia et al. (2015)
۲	Pharma trial match: Found in original search – Hoendermis et al. (2015)
1	I9) Exercise trial matching search: ID 901
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1	("hypertension, nulmonany"[MaSH Terms] OP ("hypertension" AND "hypertension") OP "hypertension") NOT ("Multiscater Study" [Dublisation Type] OP
- (*	("hypertension, pulmonary"[MeSH Terms] OR ("hypertension" AND "pulmonary") OR "pulmonary hypertension") NOT ("Multicenter Study" [Publication Type] OR
"	Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multicenter" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" Subbactive OB "therapy" (Subbactive OB "Dharmaceutical Properties" (Nach) OB "therapy" (OB "therapy") OB "therapy"
"  [{	Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR
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" [9] "	Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR pharmacotherapies" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "drugs" OR "drugs" OR "drugs" OR "drugs" OR "treatments" OR "treatments" OR "treatments" OR "interventions" OR "drugs"
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"  "  "  to	Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR pharmacotherapy" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug "OR "pharmacologic" OR "pharmacological" OR prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug "OR "drugs" OR "drugs" OR "drugs" OR "drugs" OR "drugs" OR "therapeutic use" OR "therapeutic use" OR "pharmacological" OR prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as opic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (Eur Heart J[Journal]))
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#### Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

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"therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations")))) AND (((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])))) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT])

Results: 85 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57350826/public/

Pharma trial match: Found in revised search - van der Bom et al. (2013)

### 22) Exercise trial matching search: ID 948

("Prostatic Neoplasms"[Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR malignan\* OR malignan\*) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatments" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "pharmacological" OR "preparations"])) AND (("andomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ( Eur Urol[Journal])

Results: 45 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138696/public/

Pharma trial match: Found in original search from an alternate record (#23) – Irani et al. (2008)

23) Exercise trial matching search: ID 952

("Prostatic Neoplasms"[Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR malignan\* OR malignan\*) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatments" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparations"]) AND ("therapy" OR "therapies" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatments" OR "intervention" OR "interventions" OR "drugs" OR "preparation" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (Eur Urol[Journal])

Results: 141 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138441/public/

Pharma trial match: Found in original search from an alternate record (#22) – Yoshimura et al. (2016)

24) Exercise trial matching search: ID 962

("Prostatic Neoplasms"[Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasm OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmaceological" OR "medication" OR "medications" OR ("drug therapy" OR "therapeutic use" OR "pharmaceological" OR "pharmaceological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapeutical") AND ("therapy" OR "therapeutical") AND ("therapy" OR "therapeutical") OR "therapeutical") AND ("therapy" OR "therapies" OR "therapeutical") OR "therapeutical" OR "multicenter" OR "multicenter" OR "multicenter" OR "multicenter") OR "therapeutic use" OR "pharmaceological" OR "pharmaceological" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "therapies" OR "therapeutical") AND ("therapy" OR "therapies" OR "treatment" OR "theratements" OR "interventions" OR "interventions" OR "drug "OR "therapeutical") AND ("therapy" OR "therapies" OR "treatment" OR "theratements" OR "interventions" OR "interventions" OR "drug "OR "therapeutical") AND ("therapy" OR "therapies" OR "therapies" OR "treatments" OR "interventions" OR "interventions" OR "drug "OR "therapeutical" or "treatments" OR "preparations")) AND ("therapy" OR "therapies" OR "treatment" OR "therapies") OR "treatments" OR "interventions" OR "interventions" OR "drug or "drugs" OR "preparation")) AND (trandomized controlled trial[pt] OR controlled clinical trial[pt] OR candomized[tiab] OR placebo[tiab] OR clinical trial sas topic[tesh:noexp] OR trial[tib] OR trial[tib] ONT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (teur Urol[Journal]))

Results: 45 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138696/public/

Pharma trial match: Found in original search – Klotz et al. (2013)

#### 25) Exercise trial matching search: ID 1164

((((((("non-alcoholic fatty liver disease"[MeSH Terms] OR "Fatty Liver"[Mesh] OR "fatty liver" OR ("fatty" AND "liver") OR "steatosis" OR "steatoses" OR "Steatohepatitis" OR (("non-alcoholic" OR "nonalcoholic") AND "fatty" AND "liver" AND "disease") OR "non-alcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver disease" OR "non-alcoholic steatohepatitis" OR "nonalcoholic steatohepatitis" OR "NASH" OR ((fatty AND (liver\* OR hepat\*)) OR steatohepat\* OR NAFL\* OR NASH\*)))) NOT (("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre" )))) AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations")))) AND (((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])))) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]))) AND ((("CA Cancer J Clin" [Journal] OR "N Engl J Med" [Journal] OR "Lancet" [Journal] OR "JAMA" [Journal] OR "Nat Biotechnol" [Journal] OR "Nature" [Journal] OR "Science" [Journal] OR "Lancet Oncol"[Journal] OR "Cell"[Journal] OR "Nat Med"[Journal] OR "Nat Genet"[Journal] OR "Cancer Cell"[Journal] OR "World Psychiatry"[Journal] OR "Lancet Neurol"[Journal] OR "Nat Chem"[Journal] OR "J Clin Oncol"[Journal] OR "Cell Stem Cell"[Journal] OR "Immunity"[Journal] OR "Nat Immunol"[Journal] OR "BMJ"[Journal] OR "Eur Heart J"[Journal] OR "Nat Cell Biol"[Journal] OR "Cancer Discov"[Journal] OR "J Am Coll Cardiol"[Journal] OR "Lancet Infect Dis"[Journal] OR "Lancet Diabetes" Endocrinol"[Journal] OR "Circulation"[Journal] OR "Lancet Respir Med"[Journal] OR "Gastroenterology"[Journal] OR "Cell Metab"[Journal] OR "Nat Neurosci"[Journal] OR "Lancet Glob Health"[Journal] OR "Ann Intern Med"[Journal] OR "Psychol Bull"[Journal] OR "Sci Transl Med"[Journal] OR "Gut"[Journal] OR "Trends Biochem Sci"[Journal] OR "JAMA Oncol" [Journal] OR "JAMA Intern Med" [Journal] OR "Psychol Ing" [Journal] OR "Eur Urol" [Journal] OR "Cell Res" [Journal] OR "Trends Cogn Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal])))

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# Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

26) Exercise	trial matching search: ID 1183
cardiomyopa center" OR "h Preparations "medication" "treatment" C controlled clii [mh])) AND (	bathy, dilated"[MeSH Terms] OR (("cardiomyopathy" OR "cardiomyopathies") AND ("dilated" OR "familial idiopathic" OR "Congestive")) OR "di hy" OR "dilated cardiomyopathies") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" O nulticentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmac [Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapy" OR "therapeutical") AND ("therapy" OR "therapeutical trial[pt] OR randomized[tiab] OR linical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] No 2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
Results: 2 re	cords - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140665/public/
Pharma tria	match: Found in original search from an alternate record (#18) – Hamshere et al. (2015)
27) Exercise	trial matching search: ID 1184
OR (("heart" OR "multi-ce "Pharmaceut OR "medicat "treatment" C controlled clin	"[MeSH Terms] OR "heart failure" OR ("chronic" AND "heart" AND "failure") OR "chronic heart failure" OR "Cardiac Failure" OR "Heart Decord DR "cardiac") AND ("failure" OR "decompensation"))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OL ter" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] O cal Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "c on" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "the R "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"])) AND ((randomized controlle icical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NO 2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
Results: 117	records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57138880/public/
Pharma trial	match: Found in manual search – Goebel et al. (2017)
28) Exercise	trial matching search: ID 1198
OR "Ventricu Studies as To "therapeutic "chemothera AND ("therap ((randomized	re"[MeSH Terms] OR "heart failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND ("eje ar Dysfunction"[Mesh] OR ("ejection" AND "fraction") OR ("ventricular" AND "dysfunction"))) NOT ("Multicenter Study" [Publication Type] OR " pic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subhead ise" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pt y" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "drugs" OR "drugs" OR "prescription" OR "preparation controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tias [mh] NOT humans [mh]]) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
Results: 44	ecords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57139980/public/
	match: Found in original search – Kosmala et al. (2013)
29) Exercise	trial matching search: ID 1218
Dysfunction" Topic"[Mesh] [Subheading] "chemothera "therapies" C controlled tria	R "Diabetes Mellitus, Type 2"[Mesh] OR "NIDDM" OR "type 2 diabetes mellitus" OR "diabetes mellitus type 2" OR "diabetes") AND ("Ventricula Mesh] OR "diastolic dysfunction" OR ("diastolic" AND "dysfunction") OR "diastolic")) NOT ("Multicenter Study" [Publication Type] OR "Multicer OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "th OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "che pies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND R "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"])) AND ((rando [[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Coll Cardiol[Journal])
Results: 1 re	cord – <u>https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57139674/public/</u>
Pharma trial	match: Found in original search from an alternate record (#27) – Han et al. (2014)
30) Exercise	trial matching search: ID 1232
OR "Ventricu Studies as To "therapeutic	re"[MeSH Terms] OR "heart failure" OR "Heart Decompensation" OR (("heart" OR "cardiac") AND ("failure" OR "decompensation"))) AND ("eje ar Dysfunction"[Mesh] OR ("ejection" AND "fraction") OR ("ventricular" AND "dysfunction"))) NOT ("Multicenter Study" [Publication Type] OR " pic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheac ise" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacoth by" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "ph

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Results	: 44 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57139980/public/
	trial match: Found in original search from an alternate record (#27) – Caminiti et al. (2009)
31) Exe	rcise trial matching search: ID 1251
Study" [I OR "drug "pharma "pharma OR "drug trials as	eral arterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") AND ("Mult Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multicentre") AND ("Drug Therapy"[M g therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR cotherapy" OR "pharmacotherapies" OR "chemotherapies" OR "medications" OR ("medications" OR (("drug" OR "pharmacologic" OR cological" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" gs" OR "preparation" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clir topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Col Journal])
Results	: 14 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140267/public/
Pharma	trial match: Found in manual search – Krankenberg et al. (2015)
32) Exe	rcise trial matching search: ID 1256
"Biventri ("Multice Therapy OR "pha "pharma OR "drug trials as	ac Resynchronization" OR ("Cardiac" AND "Resynchronization") OR "Resynchronization Pacing" OR "Biventricular Pacing" OR (("Resynchronization" OR cular" OR "Atrio-Biventricular") AND ("Pacing")) OR "Cardiac Resynchronization Therapy"[Mesh] OR "Cardiac Resynchronization Therapy Devices"[Mesh]] enter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center")) AND ("Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "therapeutic on "Redication" OR "medications" OR ("drug therapy" OR "therapeutic use" [Subheading] OR "therapeutic on "OR "medications" OR ("drug therapy" OR "therapeutic use" [Subheading] OR "therapeutic on "Redication" OR "medications" OR ("drug therapy" OR "therapeutic use" [Subheading] OR "therapeutic on "OR "medication" OR "medications" OR ("drug 'OR "pharmacologic" OI coological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR gs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clir topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Am Col Journal])
Results	: 3 records – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140355/public/
Pharma	trial match: Found in manual search – Tsujita et al. (2015)
33) Exe	rcise trial matching search: ID 1292
NOT ("M ("Drug T use" OR "pharma OR "drug	nenopause"[Mesh] OR "Postmenopause" OR "Post-menopause" OR "Postmenopausal" OR "Post-menopausal" OR "Postmenopauses" OR "Post-menopause" fulticenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center") AND herapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapy" OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapy" OR "therapy" (Mesh] OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacolog icological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "interventions" OR gs" OR "preparation" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clin topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh]])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin purnal])
Results	: 42 records – <u>https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57138370/public/</u>
Pharma	trial match: Found in original search – Ellis et al. (2011)
34) Exe	rcise trial matching search: ID 1296
OR "mul "Pharma OR "med "treatme controlle	oma"[MeSH Terms] OR "lymphoma" OR "lymphomas") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicent tit-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR acceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapy" OR "medications" OR ("furg" OR "medications" OR ("furg" OR "medications" OR ("furg" OR "pharmacologic" OR "pharmacological" OR "pharmacotherapy" OR "pharmaceutical") AND ("therapy" OR "therapeutic use" OR "pharmacological" OR "pharmaceutical") AND ("therapy" OR "therapies" int" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "pharmaceutical") AND ((randomized controlled trial[pt ed clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT human ND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal])
Results	: 96 records – <u>https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140430/public/</u>
	trial match: Found in original search – Cortelazzo et al. (2016)
Pharma	raina trial matahing aparah. ID 1208
	rcise trial matching search: ID 1298

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1 "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR 2 "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 3 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical 4 trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tij] NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin 5 Oncol[Journal]) 6 Results: 242 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57139370/public/ 7 Pharma trial match: Found in revised search – Greenspan et al. (2008) 8 9 36) Exercise trial matching search: ID 1299 10 11 ("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) AND ("Multicenter Study" 12 [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug 13 therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR 14 "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR 15 "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as 16 topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) 17 Results: 179 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57140047/public/ 18 Pharma trial match: Found in original search - Urruticoechea et al. (2017) 19 20 37) Exercise trial matching search: ID 1301 21 22 ("Postmenopause" [Mesh] OR "Postmenopause" OR "Post-menopause" OR "Postmenopausal" OR "Post-menopausal" OR "Post-menopauses" OR "Post-menopauses") 23 AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug 24 Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug" OR "pharmacologic" OR 25 "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 26 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical 27 trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) 28 29 Results: 49 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138311/public/ 30 Pharma trial match: Found in original search from an alternate record (#35) – Johnston et al. (2018) 31 32 38) Exercise trial matching search: ID 1303 33 34 ("Prostatic Neoplasms" [Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR 35 "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR 36 37 "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR 38 "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as 39 topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) 40 Results: 85 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138499/public/ 41 42 Pharma trial match: Found in original search - Taplin et al. (2014) 43 39) Exercise trial matching search: ID 1310 44 45 (("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR 46 neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" 47 [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy" [Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "therapeutic use" on the second se 48 49 "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" 50 OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tij] NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin 51 Oncol[Journal]) 52 Results: 242 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57139370/public/ 53 54 Pharma trial match: Found in original search - Yardley et al. (2013) 55 56 40) Exercise trial matching search: ID 1314 57 58 59 60

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(("Breast Neoplasms"[Mesh] OR (("breast" OR "breasts" OR "mammary") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tii]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) Results: 242 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57139370/public/ Pharma trial match: Found in original search - Schmid et al. (2016) 41) Exercise trial matching search: ID 1320 (("Postmenopause"[Mesh] OR "Postmenopause" OR "Post-menopause" OR "Postmenopausal" OR "Post-menopausal" OR "Postmenopauses" OR "Post-menopauses") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tij] NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) Results: 42 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR\_tlOrYmkO/collections/57138370/public/ Pharma trial match: Found in original search - Loprinzi et al. (2010) 42) Exercise trial matching search: ID 1328 ("Prostatic Neoplasms"[Mesh] OR (("prostate" OR "prostatic") AND (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumours OR tumours OR malignan\* OR malignant))) NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) Results: 85 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57138499/public/ Pharma trial match: Found in original search from an alternate record (#38) - McKay et al. (2016) 43) Exercise trial matching search: ID 1332 (cancer OR cancers OR cancerous OR oncology OR oncolog\* OR neoplasm OR neoplasms OR neoplasm\* OR carcinoma OR carcinom\* OR tumor OR tumour OR tumors OR tumours OR malignan\* OR malignant OR "hematooncological" OR "hemato oncological" OR "hemato-oncological" OR hematologic neoplasms OR hematolo\*) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multicenter" OR "multicentre" OR "multicentre") AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tij] NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (J Clin Oncol[Journal]) Results: 853 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57140190/public/ Pharma trial match: Found in original search - Soiffer et al. (2017) 44) Exercise trial matching search: ID 1385 (("peripheral arterial disease"[MeSH Terms] OR ("peripheral" AND ("arterial" OR "artery" OR "arteries") AND "disease") OR "peripheral arterial disease") NOT ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR "pharmacological" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drugs" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[tij] NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND ("JAMA"[Journal]) Results: 3 records - https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR tlOrYmkO/collections/57138957/public/

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#### **BMJ** Open

#### Supplementary Methods 5: Pharmacological RCT Search Strategies & Matches

45) Exercise trial n	natching search: ID 1599
("Alzheimer Disease Study" [Publication OR "drug therapy" [ "pharmacotherapy" "pharmacological" C OR "drugs" OR "pre	a"[Mesh] OR "Alzheimer Disease" OR "Alzheimer's Disease" OR ("alzheimer's" AND "disease") OR ("alzheimer" AND "disease")) AND ("Multice Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre") AND ("Drug Therapy"[N Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR ("drug therapy" OR "pharmacologic" OR PR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OF paration" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clin noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAMA Intervention)
Results: 0 records	
NOTE: Since this st	ring let to zero results, changed journal title limit to JAMA:
("Multicenter Study" Therapy"[Mesh] OR OR "pharmacothera "pharmacological" C OR "drugs" OR "pre	heimer Disease" [Mesh] OR "Alzheimer Disease" OR "Alzheimer's Disease" OR ("alzheimer's" AND "disease") OR ("alzheimer" AND "disease" [Publication Type] OR "Multicenter Studies as Topic" [Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center") AND ("Dru "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic py" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" O PR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OF paration" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clin noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01" [PDAT] : "2018/12/31" [PDAT]) AND (JAMA [Jo
Results: 10 records	= https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140943/public/
Pharma trial match	a: Found in original search – Cummings et al. (2015)
46) Exercise trial n	natching search: ID 1610
use" OR "pharmaco "pharmacological" O OR "drugs" OR "pre	sh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapy" OR "therapy" OR "pharmacotherapies" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacolog Prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "intervention" OR "interventions" OF paration" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clin noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAMA Interventions) of the statement of the stateme
Result: 1 record -	https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140841/public/
NOTE: Also tried ch	anging the journal title to JAMAsee below:
(("non-alcoholic" OF NOT ("Multicenter S ("Drug Therapy"[Me use" OR "pharmaco "pharmacological" C OR "drugs" OR "pre	v liver disease"[MeSH Terms] OR "Fatty Liver"[Mesh] OR "fatty liver" OR ("fatty" AND "liver") OR "steatosis" OR "steatoses" OR "Steatohepatiti t "nonalcoholic") AND "fatty" AND "liver" AND "disease") OR "non-alcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver disease tudy" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicenter" OR "multi-center")) AND sh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacolog PR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OF paration" OR "preparations"])) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR cli noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAMA[Jo
Result: 2 records -	https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57140782/public/
Revised search:	
OR (("non-alcoholic OR "non-alcoholic s (("Multicenter Study Therapy"[Mesh] OR OR "pharmacothera "pharmacological" C OR "drugs" OR "pre trials as topic[mesh: J Clin"[Journal] OR "Lancet Oncol"[Journal] OR "Eur Heart J"[Jo Endocrinol"[Journal] "Lancet Glob Health"	c fatty liver disease"[MeSH Terms] OR "Fatty Liver"[Mesh] OR "fatty liver" OR ("fatty" AND "liver") OR "steatosis" OR "steatoses" OR "Steatoher "OR "nonalcoholic") AND "fatty" AND "liver" AND "disease") OR "non-alcoholic fatty liver disease" OR "NAFLD" OR "nonalcoholic fatty liver dis teatohepatitis" OR "nonalcoholic steatohepatitis" OR "NASH" OR ((fatty AND (liver* OR hepat*)) OR steatohepat* OR NAFL* OR NASH*)))) NO " [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre" )))) AND (i "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic py" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" O R "prescription" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OF paration" OR "preparations"))))) AND (((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])))) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]))) AND (("CA "N Engl J Med"[Journal] OR "Lancet [Journal] OR "JAMA"[Journal] OR "Nat Biotechnol"[Journal] OR "Nature"[Journal] OR "Science"[Journal] OR "Nat Cell"[Journal] OR "Lancet [Journal] OR "JAMA"[Journal] OR "Cancer Cell"[Journal] OR "Nature"[Journal] OR "Lancet [Journal] OR "Nat Genet"[Journal] OR "Cell "[Journal] OR "Nat Med"[Journal] OR "Lancet Discov"[Journal] OR "JAM Cell Biol"[Journal] OR "Lancet Respir Med"[Journal] OR "JAm Coll Cardiol"[Journal] OR "Cell Metab*[Journal] OR "Lancet Respir Med"[Journal] OR "Sci Transl Med"[Journal] OR "Cell Metab*[Journal] OR "Trends Biochem "[Journal] OR "JAMA Intern Med"[Journal] OR "Psychol Ing"[Journal] OR "Cell Wetab*[Journal] OR "Trends Sci "[Journal] OR "JAMA Intern Med"[Journal] OR "Psychol Ing"[Journal] OR "Cell Wetab*[Journal] OR "Trends Sci

Pharma trial m	natch: Found in revised search – Cusi et al. (2016)
47) Exercise ti	rial matching search: ID 1691
AND ("Multicer Therapy"[Mesh OR "pharmaco "pharmacologic OR "drugs" OR	use"[Mesh] OR "Postmenopause" OR "Post-menopause" OR "Postmenopausal" OR "Post-menopausal" OR "Postmenopauses" OR "Post-menopause" OR "Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multi-center" OR "multi-center" OR "multi-center") AND ] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations" [Mesh] OR "drug therapy" OR "therapeutic therapy" OR "pharmacotherapies" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" Of cal" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapeus" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "pharmaceutical") AND ((therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "preparation"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR climenses] OR "needication"] OR "andomized[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND (JAMA
Results: 4 reco	ords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57138206/public/
Revised searc	h
AND (post OR "multicentre" O Preparations"[N "medication" O "treatment" OR controlled clinic [mh])))) AND (" "Nat Biotechno "Cancer Cell"[J "Immunity"[Jou Cardiol"[Journal Gastroenterold Bull"[Journal] C "Psychol Inq"[J Results: 139 ref	nopause"[Mesh] OR Postmenopaus* OR "Post-menopause" OR "Post-menopausal" OR "Post-menopauses" OR (("Menopause"[Mesh] OR menopau after OR following))))) AND ("Multicenter Study" [Publication Type] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR R "multi-centre")) AND (("Drug Therapy"[Mesh] OR "drug therapy" [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Mesh] OR "drug therapy" OR "therapeutic use" OR "pharmacotherapy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR R "medications" OR (("drug" OR "pharmacologic" OR "pharmacotherapy" OR "prescription" OR "pharmaceutical") AND ("therapy" OR "therapeus" OR "treatments" OR "intervention" OR "interventions" OR "drug" OR "drug" OR "druge" OR "preparation" OR "preparations"))))) AND (((randomized controlled trial[ trial[ti]] OR randomized[tiab] OR placebo[tiab] OR clinical trials as topic[mesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT huma 2008/01/01"[PDAT] : "2018/12/31"[PDAT]))) AND (("CA Cancer J Clin"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "Att Genet"[Journal] OR "Nature"[Journal] OR "Science"[Journal] OR "Lancet Oncol"[Journal] OR "N Engl J Med"[Journal] OR "Lancet"[Journal] OR "Lancet Neurol"[Journal] OR "Nat Chem [Journal] OR "J Ath Med"[Journal] OR "Lancet [Journal] OR "Nat Immunol"[Journal] OR "Lancet Neurol"[Journal] OR "Nat Chem [Journal] OR "Lancet Respir Med"[Journal] OR "Lancet Infect Dis"[Journal] OR "Nat Neurosci"[Journal] OR "Lancet Glob Health"[Journal] OR "Lancet Respir Med"[Journal] OR "Nat Chem Biol"[Journal] OR "Sci Transl Med"[Journal] OR "Gut"[Journal] OR "Trends Biochem Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal] OR "Sci Transl Med"[Journal] OR "Cell Res"[Journal] OR "Trends Biochem Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal] OR "Sci Transl Med"[Journal] OR "Cell Res"[Journal] OR "Trends Biochem Sci"[Journal] OR "JAMA Psychiatry"[Journal] OR "Nat Chem Biol"[Journal]) "Sci Transl Med"[Journal] OR "Cell Res"
48) Exercise ti	rial matching search: ID 2837
[Publication Ty] "drug therapy" "pharmacothera "pharmacologic OR "drugs" OR	litus"[MeSH Terms] OR ("diabetes" AND "mellitus") OR "diabetes mellitus" OR "diabetes" OR "diabetic" OR "diabetics") NOT ("Multicenter Study" pe] OR "Multicenter Studies as Topic"[Mesh] OR "multicenter" OR "multi-center" OR "multicentre" OR "multi-centre")) AND ("Drug Therapy"[Mesh] O [Subheading] OR "therapeutic use" [Subheading] OR "Pharmaceutical Preparations"[Mesh] OR "drug therapy" OR "therapeutic use" OR apy" OR "pharmacotherapies" OR "chemotherapy" OR "chemotherapies" OR "medication" OR "medications" OR (("drug" OR "pharmacologic" OR ap" OR "pharmacotherapies" OR "chemotherapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR al" OR "preparation" OR "pharmaceutical") AND ("therapy" OR "therapies" OR "treatment" OR "treatments" OR "intervention" OR "interventions" OR "preparation" OR "preparations"))) AND ((randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR clim hesh:noexp] OR randomly[tiab] OR trial[ti]) NOT (animals[mh] NOT humans [mh])) AND ("2008/01/01"[PDAT] : "2018/12/31"[PDAT]) AND al])
Results: 51 ree	cords – https://www.ncbi.nlm.nih.gov/sites/myncbi/1TwR_tlOrYmkO/collections/57139460/public/
Pharma trial m	natch: Found in original search from an alternate record (#11) – Wysham et al. (2017)

## **BMJ** Open

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

Data Extraction Reference Guide – Exercise RCTs

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Memorial Sloan Kettering Cancer Center

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## EXTRACTION ABBREVIATIONS

- %: percent
- 1-RM: 1 repetition maximum (strength test)
- AET: Aerobic exercise training
- BL: baseline
- BMI: body mass index
- bpm: heart beats per minute
- d: days
- EX: exercise
- FU: follow-up
- HR: heart rate
- HRR: heart rate reserve
- hr/hrs: hour/hours
- Man: manuscript
- MAX: maximum
- MIN: minimum
- mins: minutes
- mo: months
- PA: physical activity
- Reg: registry
- RET: Resistance exercise training
- RPE: rate of perceived exertion (self-reported exercise intensity)
- sec: seconds
- UC: usual care/control
- VO<sub>2peak</sub>: peak aerobic exercise capacity
- wk/wks: week/weeks
- yrs: years

# **GENERAL NOMENCLATURE & EXTRACTION GUIDELINES**

# Nomenclature Guidelines

- Ranges:
  - Use 'to' and not '-' (e.g., 150 bpm to 175 bpm)
- Units:
  - o List all units of measure including percentages
- Significant figures:
  - $\circ$  Raw values / averages  $\rightarrow$  round to the nearest 0.1
  - $\circ$  Percentages  $\rightarrow$  round to the nearest whole number
- Averages:
  - Mean value is preferred and assumed
  - o Only list median values if mean are not reported
    - If listing median values, please label appropriately
- Lists:
  - $\circ$  Be succinct  $\rightarrow$  only include pertinent details and use bullet form with semicolon separated values



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Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

- $\circ$   $\;$  List details in the same order as it is presented in the manuscript
- Examples:
  - Inclusion/exclusion criteria: e.g., 40 to 65 yrs; BMI<40; sedentary</li>
  - Primary/secondary outcomes: e.g., resting HR; body weight; PA mins/wk

# **Extraction Guidelines**

- Multiple intervention arms
  - Base group numbering on layout of flow diagram (e.g., AET 1 = left-most group; AET 2 = group immediately to the right, etc.)
  - In the case of discrepancies between data sources:
    - Prioritize the data provided in the primary manuscript.
    - Report both sets of numbers (e.g., Man: ##; Reg: ##)

# ARTICLE INCLUSION/EXCLUSION

• Should this article be included in our systematic review?

- $\circ$  Yes  $\rightarrow$  Does not meet any exclusion criteria.
- $\circ$  No  $\rightarrow$  Meets one or more exclusion criteria.

# DATA SOURCES

- Data Sources:
  - Please list all sources of information included in this extraction.
  - Options:
    - Primary manuscript
    - Online supplement
    - Protocol paper
    - Clinical trial registry
    - Clinical trial protocol
    - Other
- If Other, please list.

# PUBLICATION INFORMATION

- Country of publication?
  - Please provide the <u>full name</u> of the country where the study was conducted/where the primary author is based

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

1

TITI F	ABSTRACT & INTRODUCTION
٠	CONSORT (1a) – Identification as a randomized trial in the title.
	<ul> <li>Options:</li> <li>Yes → Either randomized controlled trial; randomized trial; randomized</li> </ul>
	• No $\rightarrow$ Not mentioned
٠	CONSORT (1b) – Structured summary of trial design, methods, results, and conclusions.
	• Options:
	<ul> <li>Yes → Introduction/Background + Methods + Results + Discussion/Conclusion</li> <li>No → Not properly structured</li> </ul>
•	CONSORT (2a) – Scientific background and explanation of rationale.
	• Options:
	<ul> <li>Yes → Reviews relevant literature AND identifies a knowledge gap/question</li> </ul>
	<ul> <li>No → Did not adequately review the literature and/or identify the knowledge gap/question the study attempted to address</li> </ul>
	Siddy allempted to address
•	CONSORT (2b) – Specific objectives or hypothesis.
	• Options:
	<ul> <li>Yes (objectives) → Must provide a specific <u>purpose/objective</u> for study in the context of the</li> </ul>
	intervention AND the specific outcomes of interest
	<ul> <li>OR</li> <li>Yes (hypothesis) → Must provide a specific hypothesis in the context of a group-related change in</li> </ul>
	a specific outcome of interest AND the expected direction of change
	<ul> <li>Unclear → Provided the specific purpose/objective or hypothesis but only 1 of 2 additional</li> </ul>
	required components
	<ul> <li>No → Failed to provide either (1) the specific purpose/objective OR hypothesis, and/or (2) both additional required components</li> </ul>
	• TIP:
	<ul> <li>This information is typically reported within final paragraph of the introduction or early in the</li> </ul>
	methods section.
METH	ODS
•	CONSORT (3ai) – Description of trial design (such as parallel, factorial) including allocation ratio.
	• Options:
	<ul> <li>Yes → Must provide both a description of overall study design (e.g., parallel arm, crossover) AND allocation ratio</li> </ul>
	• <b>Unclear</b> $\rightarrow$ Description of study design is provided but <b>NOT</b> allocation ratio
	<ul> <li>No → If missing the study design (even if allocation ratio is provided)</li> </ul>
	• EXAMPLES:
	<ul> <li>Parallel trials, cross-over trials, factorial trials AND 1:1, 1:2, 1:1:1</li> </ul>
•	CONSORT (4b) – Settings and locations where the data were collected.
•	$\circ$ Options:
	• Yes $\rightarrow$ Provided details of where the <u>data were collected</u> for the trial
	30
	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### BMJ Open

Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

	<ul> <li>This includes single-location trials when the authors clearly so onsite</li> </ul>	tate the entire trial took place
	<ul> <li>Unclear → Specifies that data was collected in a lab/testing room but location of said room (e.g., at a hospital or university)</li> </ul>	does not provide the actual
	<ul> <li>No → Details not provided</li> <li>TIP:</li> </ul>	
	<ul> <li>This does <i>NOT</i> include where the recruitment or intervention took place</li> </ul>	æ.
•	DETAILS – Population:	
	<ul> <li>List the population being studied</li> </ul>	
	$\circ$ <b>NR</b> $\rightarrow$ If not reported	
•	DETAILS – Disease setting:	
	<ul> <li>Identify the disease phase [Prevention (P) vs. Management (M)] during which the place.</li> </ul>	ne exercise intervention took
	• <b>NR</b> $\rightarrow$ If not reported	
	$\circ$ NA $\rightarrow$ If the intervention was not conducted in the context of a disease	
•	CONSORT (3aii) – When applicable, how care providers were allocated to each tria	al group.
	<ul> <li>Options:</li> <li>NA → Only one interventionist involved with study – no allocation stra</li> </ul>	toov required
	• Yes $\rightarrow$ Must describe how the interventionists were assigned to super	<b>0</b> , 1
	<ul> <li>This applies to all components of the intervention (e.g., AET,</li> </ul>	
	• Yes $\rightarrow$ Authors clearly state that no allocation strategy was used	
	• No $\rightarrow$ Fails to report any details $\circ$ TIP:	
	<ul> <li>These details are seldom reported in exercise-based RCTs.</li> </ul>	
•	CONSORT (3b) – Important changes to methods after trial commencement (such a	is eligibility criteria), with
	o Options:	
	<ul> <li>Options:</li> <li>NA → The methods did not change</li> </ul>	
	• Yes $\rightarrow$ Methods changed and reasons were provided	
	<ul> <li>Examples include (but are not limited to): study design, samp</li> </ul>	
	criteria, recruitment strategy, randomization, blinding, data ar	-
	<ul> <li>Unclear → It appears that methods may have changed but there is no make assessment</li> </ul>	or enough mormation to
	<ul> <li>No → Methods changed but no reasons were provided</li> </ul>	
	• TIPS:	
	<ul> <li>This includes under/over recruitment according to the a priori-defined adequate justification.</li> </ul>	sample size without
	Does <b>NOT</b> include changes to the intervention $\rightarrow$ that data is captured	d in the TIDieR inventorv
	■ Does <b>NOT</b> include changes in trial outcomes → that data is captured	
	item	
aihi	bility Criteria	
gibli		

•	
	<ul> <li>CONSORT (4ai) – Eligibility criteria for participants.</li> <li>Options:         <ul> <li>Yes → Provided details/criteria for BOTH inclusion AND exclusion of participants</li> <li>Unclear → Only provides details of inclusion OR exclusion but NOT both</li> <li>No → Details not provided</li> </ul> </li> </ul>
•	CONSORT (4aii) – When applicable, eligibility criteria for centers and for care providers.
	<ul> <li>Options:         <ul> <li>Yes (multicenter trials) → Provided criteria for eligible centers AND interventionists</li> <li>Unclear (multicenter trials) → Provided criteria for interventionists but NOT centers or vice versa</li> <li>Yes (single center trials) → Provided criteria for interventionists</li> <li>Yes → Authors clearly state there were no eligibility criteria for centers and/or care providers</li> <li>Unclear (multi and single center trials) → Stated professional background and/or study-specific training for interventionists but did not describe them as requirements</li> <li>No → Eligibility criteria not specifically stated</li> </ul> </li> </ul>
	<ul> <li>Eligibility criteria for centers is applicable for all multi-center trials.</li> <li>Eligibility criteria for care providers is applicable for all trials.</li> <li>This is seldom reported.</li> </ul>
Data	Comparison: Eligibility Criteria
•	Was there a difference in Eligibility Criteria between the Registry and the Manuscript? <ul> <li>Options:</li> </ul>
	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> How many Inclusion Criteria were listed in the Registry? <ul> <li>Please record the total number of individual Inclusion Criteria listed in the Registry.</li> </ul>
•	<ul> <li>Yes → One or more differences between the two data sources.</li> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> <li>Was the change noted in the Manuscript? <ul> <li>Options:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript.</li> <li>Not Applicable → No clinical trial registry data available.</li> </ul> </li> <li>How many Inclusion Criteria were listed in the Registry? <ul> <li>Please record the total number of individual Inclusion Criteria listed in the Registry.</li> <li>Please record each individual Inclusion Criteria listed in the Registry.</li> </ul> </li> </ul>

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• Please record the total number of individual Inclus	sion Criteria listed in the Manuscript.
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# • DC DETAILS - Please list the Inclusion Criteria reported in the Manuscript.

o Please record each individual Inclusion Criteria listed in the Manuscript.

# How many Exclusion Criteria were listed in the Registry?

• Please record the total number of individual Exclusion Criteria listed in the Registry.

## • DC DETAILS - Please list the Exclusion Criteria reported in the Registry.

• Please record each individual Exclusion Criteria listed in the Registry.

## How many Exclusion Criteria were listed in the Manuscript?

o Please record the total number of individual Exclusion Criteria listed in the Manuscript.

# DC DETAILS - Please list the Exclusion Criteria reported in the Manuscript.

• Please record each individual Exclusion Criteria listed in the Manuscript.

# **Outcome Measures**

- CONSORT (6a) Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.
  - Options:
    - Yes → Clearly defined a single primary outcome (co-primary outcomes at max), all relevant secondary outcomes AND provide all requisite details of the timing AND procedures used to assess these outcomes
    - Unclear → Primary and secondary outcomes defined but the descriptions of the timing and procedures used to assess the outcomes were lacking details required to reproduce the measurements
    - No → If no primary or secondary outcomes are clearly defined OR if the assessment details (e.g., how & when) were missing altogether
  - o **TIPS**:
    - Some studies may identify multiple primary outcomes. Although this type of study design is
      inappropriate in the context of medical oncology research, we are evaluating the quality of
      reporting and not the quality of the study design. Therefore, a 'Yes' can be assigned provided the
      authors clearly identify which outcomes are considered primary and secondary.

# • CONSORT (6b) – Any changes to trial outcomes after the trial commenced, with reasons.

- Options:
  - $\bullet \quad \mathbf{NA} \rightarrow \mathbf{No} \text{ observable changes to trial outcomes were made}$
  - Yes → Describes changes in outcomes according to all pertinent features (e.g., what, why & when)
  - Unclear  $\rightarrow$  Describes changes according to all but one pertinent feature
  - No  $\rightarrow$  If the description is missing or unclear on two or more pertinent features

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# **Data Comparison: Primary Outcome**

•	Was there a difference in the Primary Outcome(s) between the Registry and the Manuscript? o Options:
	• Yes $\rightarrow \geq 1$ difference between the two data sources.
	• No $\rightarrow$ No difference between the two data sources.
	■ Unclear → Possible difference between the two data sources, but insufficient information to make
	a determination.
	• NR $\rightarrow$ No clinical trial registry data available.
•	Was the change in Primary Outcome noted in the Manuscript?
	• Options:
	• Yes $\rightarrow$ The change in Primary Outcome was clearly stated and explained.
	• No $\rightarrow$ The change in Primary Outcome was apparent but not explained.
	• $NR \rightarrow No$ clinical trial registry data available.
	• NA $\rightarrow$ No difference (i.e., Q1 = No)
•	Was a new Primary Outcome reported in the Manuscript which was not reported in the Registry? o Options:
	• Yes $\rightarrow \geq 1$ Primary Outcome reported in the Manuscript that was not listed in the Registry.
	• No $\rightarrow$ No new Primary Outcome added to the Manuscript.
	<ul> <li>Unclear → Possible difference between the two data sources, but insufficient information to make</li> </ul>
	a determination.
	• $NR \rightarrow No$ clinical trial registry data available.
•	<ul> <li>DC DETAILS – If Yes/Unclear, please provide the details?</li> <li>Please list all pertinent details.</li> </ul>
•	Was the Primary Outcome reported in the Registry reported as a Secondary Outcome in the Manuscript?
	• Options:
	• Yes $\rightarrow \geq 1$ Primary Outcome reported in the Registry listed as a Secondary Outcome in the
	Manuscript.
	• No $\rightarrow$ No Primary Outcome from the Registry listed as a Secondary Outcome in the Manuscript.
	<ul> <li>Unclear → Possible difference between the two data sources, but insufficient information to make</li> </ul>
	a determination.
	• $\mathbf{NR} \rightarrow \mathbf{No}$ clinical trial registry data available.
•	DC DETAILS – If Yes/Unclear, please provide the details? <ul> <li>Please list all pertinent details.</li> </ul>
•	Was the Primary Outcome reported in the Registry omitted from the Manuscript? <ul> <li>Options:</li> </ul>
	• Yes $\rightarrow$ The Primary Outcomes reported in the Registry was omitted from the Manuscript.
	<ul> <li>No → The Primary Outcome reported in the Registry was included in the Manuscript.</li> </ul>
	<ul> <li>Unclear → Possible difference between the two data sources, but insufficient information to make a determination.</li> </ul>
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•  $NR \rightarrow No$  clinical trial registry data available.

# • DC DETAILS – If Yes/Unclear, please provide the details?

• Please list all pertinent details.

## Data Comparison: Secondary Outcomes

# • Were <u>different</u> (new) Secondary Outcomes reported in the Manuscript which were not reported in the Registry?

- Options:
  - Yes  $\rightarrow \geq 1$  Secondary Outcomes reported in the Manuscript were not reported in the Registry.
  - No  $\rightarrow$  The Secondary Outcomes reported in the Manuscript were consistent with the Registry.
  - Unclear → Possible difference between the two data sources, but insufficient information to make a determination.
  - NR → No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- If different (new) Secondary Outcomes were added to the Manuscript, were the reasons noted in the Manuscript?
  - Options:
    - Yes  $\rightarrow$  The change(s) in Secondary Outcomes were clearly stated and explained
    - No  $\rightarrow$  The changes in Secondary Outcomes were apparent but not explained
    - NR → No clinical trial registry data available
    - NA  $\rightarrow$  No difference in Secondary Outcomes (i.e., Q6 = No)
- Was one or more of the Secondary Outcomes reported in the Registry reported as Primary Outcomes in the Manuscript?
  - Options:
    - Yes → A Secondary Outcome reported in the Registry was reported as a Primary Outcome in the Manuscript.
    - No → None of the Secondary Outcomes reported in the Registry were reported as Primary Outcomes in the Manuscript.
    - Unclear → Possible difference between the two data sources, but insufficient information to make a determination.
    - **NR** → No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.

## **Randomization & Blinding**

- CONSORT (8a) Method used to generate the random allocation sequence.
  - Options:

- Yes → Clearly stated the specific process used to generate the randomization (e.g., a coin flip, computer generated)
- No  $\rightarrow$  Not provided

# CONSORT (8b) – Type of randomization; details of any restriction (such as blocking and block size). Options:

- Yes → Provided the details of how the randomization accounted for key confounding variables (e.g., blocking, minimization, stratification)
- No  $\rightarrow$  Not provided
- CONSORT (9) Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.
  - Options:

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- Yes → Provided details of how the physical randomization was performed or how the participants were notified of their allocation (e.g., phone call, sealed envelopes, centralized allocation)
- No  $\rightarrow$  Not provided
- CONSORT (10) Who generated the random allocation sequence, who enrolled participants, and who
  assigned participants to interventions.
  - Options:
    - Yes  $\rightarrow$  Must include a clear description of who performed ALL of these tasks
    - **Unclear**  $\rightarrow$  If description of one of these tasks is inadequate or missing
    - No  $\rightarrow$  If two or more of these tasks are poorly described or not described at all
  - o TIP:
    - An exception can be made for participant assignment criteria for studies using centralized allocation.
- CONSORT (11a) If done, who was blinded after assignment to interventions (for example, participants, care
  providers, those assessing outcomes) and how.
  - Options:
    - Yes  $\rightarrow$  Details regarding testers **AND** data analyzers are provided
    - Unclear  $\rightarrow$  If any of the aforementioned details are provided but poorly described
    - No  $\rightarrow$  If any of the aforementioned details are missing
  - o **TIP:** 
    - Remember, we are assessing if the <u>reporting is complete</u> **NOT** how good the methods are. Therefore, if authors state that the testers and data analyzers were not blinded, we would consider this good reporting and assign a 'Yes' for this category.
- CONSORT (11c) If blinding not possible, description of attempts to limit bias.
  - Options:
    - $NA \rightarrow If$  testers *AND* data analyzers were blinded
    - Yes → Clearly stated that a specific strategy (e.g., physical or statistical) was employed to help
      reduce the potential confounding influence of unblinded investigators
      - Example strategies: Identified strategy 'following standardized procedures' **AND** provided requisite details
    - Yes  $\rightarrow$  Authors stated that no strategy was used limit bias related to lack of blinding
    - Unclear → If strategies were identified OR described for ALL unblinded personnel but not identified AND described
    - $No \rightarrow$  If not clearly stated either in the methods, results or discussion

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4	<ul> <li>Simply listing lack of blinding in the limitations does not count</li> <li>TIP:</li> </ul>
5 6 7 8 9	<ul> <li>IP:</li> <li>Remember, we are evaluating these studies according to the quality of their reporting and not their methods. We are looking for transparency in methods. As such, it does not matter, per se, if investigators were not blinded – rather, it matters how they report it and how well they report the strategies used to compensate for it.</li> </ul>
10 11 •	CONSORT (11b) – If relevant, description of the similarity of interventions.
12 13 14 15 16 17	<ul> <li>Options:         <ul> <li>NA → If it is a 2-arm trial with a non-exercise control group comparison <i>OR</i> a 3+ -arm trial with obviously different intervention groups (e.g., AET v RET v UC)</li> <li>Yes → If details are adequately provided for two or more <u>intervention</u> arms with similar modalities of exercise</li> <li>No → If details are not adequately provided for two or more <u>intervention</u> arms with similar</li> </ul> </li> </ul>
18	modalities of exercise
19 20 21	<ul> <li>TIP:</li> <li>NA is not an option for superiority trials (i.e., exercise trials with only two similar intervention arms)</li> </ul>
22	
24	ention Details
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27 28	TIDieR (1) – Provide the name or a phrase that describes the intervention.
29 30	• Yes $\rightarrow$ Provided a phrase to describe the intervention
31	• No $\rightarrow$ A clear summary phrase describing the intervention was not provided
32 33 34	TIDieR (2) – Describe any rationale, theory, or goal of the elements essential to the intervention. o Options:
35 36	<ul> <li>Yes → Provides any rationale, theory OR goal of the elements essential to the intervention</li> <li>No → Did not provide at least one of the above</li> </ul>
37 38 39	INTERVENTION TYPE – Exercise or Pharmaceutical
40 41	<ul> <li>Exercise → Stated methods included delivery of a structured exercise program with a stated goal of improving a health/fitness/psychosocial outcome.</li> </ul>
42 43 44	<ul> <li>Pharmaceutical → Stated methods included delivery of a pharmaceutical intervention with a stated goal of improving health.</li> </ul>
45 46 ● 47	TIDieR (4) – Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.
48	• Options:
49	<ul> <li>Yes → Provides complete details for each of the major intervention procedures, activities, and processes, including enabling or supporting activities</li> </ul>
50 51 52	<ul> <li>Unclear (multi-component interventions) → If a single component of the intervention is identified but not adequately described (e.g., the aerobic exercise component is well described but</li> </ul>
53	the behavioral support component is not)
54 55	<ul> <li>No → If the primary component or more than one secondary component of the intervention is (are) not adequately described</li> </ul>
56	not adequately described
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# CONSORT (5ii) – Precise details of both the experimental treatment and comparator.

- Options:
  - Yes  $\rightarrow$  Clear descriptions of the intervention arm(s) and control group
  - $\bullet \quad \textbf{No} \rightarrow \textbf{Control group conditions/requirements not defined}$
- TIDieR (8d) Describes length of the intervention period.
  - Options:
    - Yes → Must define the period over which the intervention was delivered according to a specific number of weeks/months or life period
    - No → Not clearly defined (e.g., stated during chemotherapy without providing the average number of weeks/months)

#### DETAILS – What was the total length of the program/intervention (weeks)?

- Note the total duration of the intervention in weeks
- **NR**  $\rightarrow$  If not reported
- TIP:
  - Actual intervention length preferred (if provided); proposed intervention length if actual is not reported

#### DETAILS – How many phases did the intervention have?

- o Note the total number of intervention phases
- TIP:
  - Lead-in period considered part of the intervention but not necessarily a separate phase

# PHASE I/II – DETAILS

- How many weeks was this phase?
  - Note number of weeks
  - $\mathbf{NR} \rightarrow \mathbf{If} \text{ not reported}$
- TIDieR (7) Describe the type(s) of location(s) where the intervention occurred, including any necessary
  infrastructure or relevant features.
  - Options:
    - Yes  $\rightarrow$  If specifically described
      - This includes single-location trials when the authors clearly state the entire trial took place onsite.
    - **Unclear**  $\rightarrow$  Inadequate description provided
    - **No**  $\rightarrow$  Details not provided
  - o **TIP:** 
    - Interventions described as being telephone- / mail-based can be considered home-based by default – even if the authors do not specifically state the intervention took place at home.
    - However, these trials should be further identified according to the location of the interventionists (e.g., medical center or university).
- Where did this phase of the intervention take place?

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3		<ul> <li>Check off which of these intervention settings apply</li> </ul>
4		<ul> <li>Medical Center</li> </ul>
5		<ul> <li>Rehabilitation Center</li> </ul>
6		
7		University
8		Public Gym
9		<ul> <li>Home</li> </ul>
10		<ul> <li>Other</li> </ul>
10		o <b>TIP:</b>
12		<ul> <li>Check off more than one if needed (e.g., telephone-based or mixed facility- / home-based</li> </ul>
12		interventions).
14 15		TIDiaD (6) For each actory of intervention availar (a.g. abusial sist as what a logist a surging assistant)
15	•	TIDieR (5) – For each category of intervention provider (e.g. physiologist, psychologist, nursing assistant),
16		describe their expertise/background AND any specific training given.
17		• Options:
18		Yes → Must provide formal education, professional designation, OR certified designation with
19		certifying organization AND any study-specific training they received
20		<ul> <li>Unclear</li></ul>
21		described
22		• No $\rightarrow$ If either education/designation <b>OR</b> study specific training are not provided
23		<ul> <li>Background Examples:</li> </ul>
24		<ul> <li>Kinesiologist (KIN), Exercise Physiologist (EP), Physiotherapist (PhT), Cancer Exercise Specialist</li> </ul>
25		
26		(CES), Personal Trainer + certifying organization (PT-org)
27		• Training Examples:
28		<ul> <li>Interventionists were required to complete 3 hours of training pertaining to intervention delivery and</li> </ul>
29		participant follow-up.
30		Interventionists completed 4 online training modules related to delivering the exercise and
31		behavioral support components of the intervention.
32		
33	•	PHASE I (AET / RET / CET) – Was aerobic (AET), resistance (RET), combined (CET) exercise training
34	•	prescribed.
35		
36		• Options:
30		• Yes $\rightarrow$ It/they were
		• No $\rightarrow$ It/they were not
38		
39	•	DETAILS – How many AET / RET / CET groups were there? o Indicate 1 or 2 groups as appropriate.
40		<ul> <li>Indicate 1 or 2 groups as appropriate.</li> </ul>
41		
42		DETAILS What modelifies of AET / DET / CET ware preseribed?
43	•	DETAILS – What modalities of AET / RET / CET were prescribed?
44		<ul> <li>Check off which of these intervention modalities apply</li> </ul>
45		<ul> <li>AET</li> </ul>
46		Cycle ergometer
47		Treadmill
48		Elliptical ergometer
49		<ul> <li>Walking (e.g., outdoors, indoor track)</li> </ul>
50		<ul> <li>Other</li> </ul>
51		
52		• $\mathbf{NR} \rightarrow \mathbf{If}$ not reported
53		• RET
54		Machine weights
55		Free weights
56		Resistance bands
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- Body weight
- Other
- $NR \rightarrow If not reported$
- o TIP:
  - Check off more than one modality when applicable (e.g., RET trials which list the names of exercises but not the specific modalities should be assigned Machine weights and Free weights)
- TIDieR (6) Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.
  - Options:
    - Yes  $\rightarrow$  If clearly described for *ALL* phases *AND* components of the intervention
    - Unclear  $\rightarrow$  If clearly described for one phase/component **BUT** is poorly described for another
    - No → If not described OR is unclear for more than one intervention phase/component
  - o **TIP:** 
    - Must be specifically stated and NOT just implied (e.g., home based programs)
- DETAILS Mode of AET / RET / CET supervision:
  - Check off which of these supervision modes apply
    - Individual
    - Group
    - Mixed
    - Not applicable
    - Not reported

# DETAILS – Method of AET / RET / CET supervision:

- Check off which of these supervision modes apply
  - In person
  - Phone
  - Other

# • DETAILS – If Other, please list:

- o Please list the method of exercise supervision
- TIDieR (8b) Describes the frequency of intervention sessions.
  - Options:
    - Yes → Must define a specific minimum **OR** range of sessions per week
    - No  $\rightarrow$  Not provided

# • DETAILS – How many sessions per week was AET / RET / CET prescribed?

- Note the number or the range
- TIDieR (8a) Describes the intensity of intervention sessions.
  - Options:
    - Yes  $\rightarrow$  Must define prescribed intensity according to a standardized and measurable unit (e.g.,  $\% VO_{2peak}$ ,  $\% HR_{max}$ , % 1-RM, RPE range)
    - No → Not provided
  - o TIP:
    - It is acceptable if authors state in the Methods that participants were asked to train between XX% and XX% without specifically stating that the intensity was prescribed between these values.

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However, this information must be apriori defined (i.e., Methods) and not reported after the fact (i.e., Results).

## • DETAILS – How was the intensity of AET / RET / CET prescribed?

 Note the test/scale (e.g., VO<sub>2peak</sub>, HR<sub>max</sub>, 1-RM, RPE) upon which the relative intensity of exercise was prescribed.

# • DETAILS – Minimum prescribed AET / RET / CET intensity:

- o Note the lowest relative intensity of exercise prescribed
- $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

# • DETAILS – Maximum prescribed AET / RET / CET intensity:

- o Note the highest relative intensity of exercise prescribed
- $\circ \quad \mathbf{NR} \to \mathsf{lf not reported}$

# • TIDieR (8c) – Describes the duration of AET / RET / CET sessions.

- $\circ$  Options:
  - Yes  $\rightarrow$  Must define a specific minimum **OR** range for exercise session durations
  - No  $\rightarrow$  Not provided

# • DETAILS – Minimum prescribed AET / RET / CET session duration (minutes):

- Note the shortest duration of exercise prescribed in minutes
- $\circ \quad \mathbf{NR} \to \mathsf{If not reported}$

## • DETAILS – Maximum prescribed AET / RET / CET session duration (minutes):

- Note the longest duration of exercise prescribed in minutes
- $\circ \quad \mathbf{NR} \to \text{If not reported}$
- DETAILS Number of prescribed sets (RET only):
  - Provide details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- DETAILS Number of prescribed repetitions (RET only):
  - Provide details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- CONSORT (5a) Description of the different components of the interventions and, when applicable, description of the procedure for tailoring the interventions to individual participants?

## • **Options:**

- Yes → Must describe the major (primary and secondary) intervention components and, when applicable, <u>when</u> AND <u>how</u> the intervention was individually tailored (personalized or progressed)
- Unclear → If any of the major intervention components are not well described and/or if either the <u>timing</u> or <u>manner</u> in which the intervention was tailored was not well described
- No  $\rightarrow$  If any of the major intervention components and/or tailoring was not described
- $\bullet \quad \text{No} \rightarrow \text{If multiple intervention components and/or tailoring was not well described}$

# TIDieR (9i) – If the intervention was planned to be personalized / individualized, then describe when and how. Options:

Supplementary Methods 6: Data Extraction Reference Guide - Exercise RCTs

- Yes  $\rightarrow$  Must at least describe when AND how the intervention was personalized
- Unclear → If either the timing or manner in which the intervention was personalized was not well described
- No → If either the <u>timing</u> or <u>manner</u> in which the intervention was personalized was missing

#### • TIDieR (9ii) – If the intervention was planned to be progressed, then describe when and how.

#### • Options:

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- Yes → Must at least describe when AND how the intervention was progressed
- Unclear → If either the timing or manner in which the intervention was progressed was not well described
- No  $\rightarrow$  If either the <u>timing</u> or <u>manner</u> in which the intervention was progressed was missing
- TIP:
  - Progressions must be defined according to the timing and increment of change throughout the intervention
  - Lead-in periods are not considered progressions
- TIDieR (11) If intervention adherence or fidelity was assessed, describe how and by whom, and if any
  strategies were used to maintain or improve fidelity, describe them.
  - Options:
    - Yes → Must both identify the strategy AND provide requisite details describing how the strategy was implemented (including how & by whom)
    - Unclear → If the strategy was identified but not adequately described
    - No → If the strategy was identified but not described OR no strategy identified
  - o TIP:
    - This only applies to strategies related to supporting the exercise or physical activity component of interventions.
- CONSORT (5b) Details of whether and how the AET / RET / CET interventions were standardized.
  - Options:

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- Yes → Provided enough detail related to the consistency of how the exercise intervention was prescribed AND progressed AND/OR modified in a structured manner
  - This could also apply to how participants were coached or counseled.
  - **Unclear**  $\rightarrow$  Used the word 'standardized' but failed to provide the requisite details
- **Unclear** → Attempted to provide the requisite details but a key aspect is not well described
- No → Failed to describe the intervention as standardized and/or failed to describe more than one key aspect of the exercise prescription, progression, and/or modification process

 CONSORT (5c) – Details of whether and how adherence of care providers to the protocol was assessed or enhanced.

- **Options:** 
  - Yes → Provided details as to how AND when the actions of the interventionists were evaluated by study investigators
  - Yes  $\rightarrow$  Authors stated that interventionist adherence was not tracked
  - Unclear → Provided details as to how OR when the actions of the interventionists were evaluated by study investigators
  - No  $\rightarrow$  Details not provided
- $\circ$  TIPS:
  - This specifically pertains to someone evaluating the interventionists' performance and NOT training
    or supporting the interventionists in any way.

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3	• CONSORT (5d), TIDieR (12) – Details of whether and how intervention fidelity or adherence of participants to
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5	interventions was assessed or enhanced – describe the extent to which the intervention was delivered as
6	planned.
7	<ul> <li>Options:</li> </ul>
	Yes → Provided <u>details</u> AND <u>data</u> related to how much of the prescribed dose of exercise was
8	actually delivered to each participant relative to what was intended
9	• Yes $\rightarrow$ Authors stated that participant adherence was not tracked
10	• <b>Unclear</b> $\rightarrow$ Provides details (i.e., intensity <b>AND</b> volume) <b>AND</b> data but one or both are unclear
11	
12	• No $\rightarrow$ Failed to report the method <b>OR</b> the results of this assessment
13	• TIPS:
14	<ul> <li>Although a participant must attend a session in order to adhere to the prescription, attendance</li> </ul>
15	does <b>NOT</b> count toward adherence.
16	<ul> <li>Authors must describe the method of assessing participant adherence which captures both target</li> </ul>
17	intensity (e.g., % VO <sub>2peak</sub> or % HR <sub>max</sub> ) AND target volume (e.g., total exercise time) as well as
18	the results data comparing actual vs target exercise dose delivery.
19	<ul> <li>Must describe findings in the context of the planned dose.</li> </ul>
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20	<ul> <li>This ONLY applies to the exercise-specific components of the interventions.</li> </ul>
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25	Other Phase I/II Information
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27	<ul> <li>DETAILS – Was there a co-intervention prescribed in this trial?</li> </ul>
28	• Options:
29	• Yes $\rightarrow$ There was/were
30	
31	<ul> <li>Unclear → There was/were but not well described</li> </ul>
32	• No $\rightarrow$ There was/were not
33	o TIP:
	<ul> <li>Behavioral support strategies are counted as non-exercise intervention components and the data</li> </ul>
34	should be extracted here and for the formal CONSORT behavioral support item.
35	
36	DETAILO Disses describe the second second second
37	DETAILS – Please describe the co-intervention.
38	<ul> <li>Note all pertinent details of the non-exercise intervention component(s)</li> </ul>
39	
40	• TIDieR (3) – Describe any physical or informational materials used in the intervention, including those
41	provided to participants or used in intervention delivery or in training of intervention providers. Provide
42	
43	information on where the materials can be accessed (e.g. online appendix, URL).
44	<ul> <li>Options:</li> </ul>
44 45	<ul> <li>NA → No physical or informational material was provided (stated or not)</li> </ul>
	Yes → Provides details on any physical or informational materials used in the intervention
46	(including those provided to participants or used to train interventionists)
47	• <b>Unclear</b> $\rightarrow$ Appears physical or informational material was provided but the details were not well
48	described
49	• No $\rightarrow$ Appears physical or informational material was provided but the details were not provided
50	
51	$\circ$ TIPS:
52	<ul> <li>This pertains to physical or informational material which are only provided to the intervention</li> </ul>
53	group(s) and <b>NOT</b> the usual care/control group.
54	
55	• TIDieR (10) – If the intervention was modified during the course of the study, describe the changes (what,
56	why, when, and how).
57	wity, when, and nowj.
58	43
59	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
60	f or peer review only - http://binjopen.binj.com/site/about/guidelines.xhtml

'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT-	0	<ul> <li>Options:</li> <li>NA → No observable modification to the intervention</li> <li>Yes → Describes modification according to all pertinent features (e.g., what, why, when &amp; how)</li> <li>Unclear → Notes intervention modification but fails to describe and justify it appropriately</li> <li>No → If the description or justification is missing</li> <li>TIPS:</li> <li>Again, base this evaluation solely on the information provided in the primary paper (and online supplement, when applicable) for <i>Round I - Data Extraction</i>.</li> </ul>
including how and when they were actually administered. ○ Options: • Yes → Provided a complete description of the intervention, such that you could confidently reproduce the intervention • No → If they failed to provide sufficient detail (even if they provided a reasonable amount) • TIP: • Wait to answer this question until after you have gone through the TIDieR questions. If you assi 'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT- based item will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign 'No' to this CONSORT-based inventory item ( <i>this may often be the case</i> ). Sample Size & Statistics • CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes. • Options: • Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described • Unclear → There is any ambiguity in the description • No → Any aspect is not described • CONSORT (7ai) – How sample size was determined. • Options: • Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall) • Yes → Authors specifically stated that no power calculation was performed • No → Any details not provided • CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.	Intervention S	Summary
<ul> <li>Yes → Provided a complete description of the intervention, such that you could confidently reproduce the intervention</li> <li>No → If they failed to provide sufficient detail (even if they provided a reasonable amount)</li> <li>TIP:</li> <li>Wait to answer this question until after you have gone through the TIDieR questions. If you assi 'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8, 5.80, 5.80, 5.80, short 5.9, beam of the will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign 'No' to this CONSORT-based inventory item (<i>this may often be the case</i>).</li> </ul> Sample Size & Statistics <ul> <li>CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes.</li> <li>Options:         <ul> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> </ul> </li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> </ul>		
<ul> <li>No → If they failed to provide sufficient detail (even if they provided a reasonable amount)</li> <li>TIP:</li> <li>Wait to answer this question until after you have gone through the TIDieR questions. If you assi 'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT-based item will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign 'No' to this CONSORT-based inventory item (<i>this may often be the case</i>).</li> </ul> Sample Size & Statistics <ul> <li>CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes.</li> <li>Options:         <ul> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> </ul> </li> <li>CONSORT (7ai) – How sample size was determined.</li> <li>Options:         <ul> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> </ul>	0	
<ul> <li>TIP:         <ul> <li>Wait to answer this question until after you have gone through the TIDieR questions. If you assi 'Yes's to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT-based item will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign 'No' to this CONSORT-based inventory item (<i>this may often be the case</i>).</li> </ul> </li> <li>Sample Size &amp; Statistics         <ul> <li>CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes.</li> <li>Options:                 <ul> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li></ul></li></ul></li></ul>		
<ul> <li>Wait to answer this question until after you have gone through the TIDieR questions. If you assi 'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT-based item will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign 'No' to this CONSORT-based inventory item (<i>this may often be the case</i>).</li> <li>Sample Size &amp; Statistics</li> <li>CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes.         <ul> <li>Options:</li> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> </ul> </li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on c, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> </ul>		• No $\rightarrow$ If they failed to provide sufficient detail (even if they provided a reasonable amount)
<ul> <li>CONSORT (12ai) – Statistical methods used to compare groups for primary and secondary outcomes.         <ul> <li>Options:</li> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> </ul> </li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provide or centers was addressed.</li> </ul>	0	<ul> <li>Wait to answer this question until after you have gone through the TIDieR questions. If you assig 'Yes's' to TIDieR items 5.3, 5.4, 5.6, 5.7, 5.8a, 5.8b, 5.8c, 5.8d, and 5.9, then this CONSORT- based item will also be 'Yes'. If any of these TIDieR items are not labelled 'Yes', you will assign a</li> </ul>
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<ul> <li>Options:         <ul> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> </ul> </li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.</li> </ul>	Sample Size 8	& Statistics
<ul> <li>Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described</li> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.</li> </ul>		
<ul> <li>Unclear → There is any ambiguity in the description</li> <li>No → Any aspect is not described</li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.</li> </ul>		• Yes $\rightarrow$ The methods used to compare the groups on the primary and secondary outcomes are
<ul> <li>No → Any aspect is not described</li> <li>CONSORT (7ai) – How sample size was determined.         <ul> <li>Options:</li> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provided or centers was addressed.</li> </ul>		
<ul> <li>Options:         <ul> <li>Yes → Provides the details of the power calculation (i.e., based on α, β and, when applicable, adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> </ul> </li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.</li> </ul>		
<ul> <li>adjustment for drop-outs – how many participants were needed per group/overall)</li> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provided or centers was addressed.</li> </ul>		
<ul> <li>Yes → Authors specifically stated that no power calculation was performed</li> <li>No → Any details not provided</li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.</li> </ul>		• Yes $\rightarrow$ Provides the details of the power calculation (i.e., based on $\alpha$ , $\beta$ and, when applicable,
<ul> <li>No → Any details not provided</li> <li>CONSORT (7aii; sample size) – When applicable, details of whether and how the clustering by care provid or centers was addressed.</li> </ul>		
or centers was addressed.		
<ul> <li>○ Options:</li> </ul>		ters was addressed.
	0	Options:

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	• $NA \rightarrow If$ study was conducted at a single center and under the supervision of the same group of
	interventionists
	<ul> <li>Yes (multicenter trials) → If details of how the analyses were adjusted to account for potential</li> </ul>
	differences across intervention sites and interventionists
	<ul> <li>Yes (single center/multi-intervention location) → If details of how the analyses were adjusted to</li> </ul>
	account for potential differences across interventionists
	<ul> <li>Yes → Authors clearly stated that no clustering was performed</li> </ul>
	<ul> <li>No → Details not provided</li> </ul>
•	CONSORT (7b) – When applicable, explanation of any interim analysis or stopping guidelines.
	<ul> <li>Options:</li> </ul>
	<ul> <li>NA → No interim analysis or apriori defined stopping criteria</li> </ul>
	Yes → Authors apriori defined the rationale, nature and methods for interim analyses or stopping
	criteria
	<ul> <li>Unclear → If any aspect of the rationale, nature and methods for the interim analysis or stopping</li> </ul>
	criteria are poorly described
	• No $\rightarrow$ If any aspect of the rationale, nature and methods are missing or if results are reported
	without details provided in the methods section
	• TIPS:
	<ul> <li>Interim analyses: Typically used to assess the safety, feasibility, or establish the preliminary</li> </ul>
	efficacy of an intervention at a prespecified time-point in a trial with the express purpose of makir
	decisions around whether the trial should continue as planned, if modifications are required, or if
	the trial should be stopped altogether. <u>Do not mistake this type of analysis</u> for a midpoint
	assessment wherein the primary and/or secondary outcome data are collected and reported as
	another testing time-point in the overall trial.
	<ul> <li>Stopping criteria: Likely related to the outcome of the aforementioned interim analyses. Must be project defined and departies and NOT just reported on after the fact.</li> </ul>
	apriori defined and described and <b>NOT</b> just reported on after the fact.
	CONCORT ((0) " + (-('-(')) - Wither and ''(-) - () -
•	CONSORT (12aii; statistics) – When applicable, details of whether and how the clustering by care providers
	or centers was addressed.
	<ul> <li>Options:</li> <li>NA → If study was conducted at a single center and under the supervision of the same group of</li> </ul>
	interventionists
	<ul> <li>NA → If multicenter trial stratified by center and no further exploratory analyses were performed</li> </ul>
	• Yes (multicenter trials) $\rightarrow$ If details of how the analyses were adjusted to account for potential
	differences across intervention sites and interventionists
	• Yes (single center/multi-intervention location) $\rightarrow$ If details of how the analyses were adjusted to
	account for potential differences across interventionists
	• Yes $\rightarrow$ Authors stated that clustering was not performed
	• No $\rightarrow$ Details not provided
•	CONSORT (12b) – Methods for additional analyses, such as subgroup analyses and adjusted analyses.
•	$\circ$ Options:
	• NA $\rightarrow$ If no additional subgroup analyses were performed
	• Yes $\rightarrow$ If any analysis other than the primary/secondary intervention effects are described
	• No $\rightarrow$ If any analysis other than the primary/secondary intervention effects are reported but not
	described
	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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# Data Comparison: Sample Size

	Sample Size Calculated	Sample Size Recruited
Sample size – calculated vs actual?	Number:	Number:
<ul> <li>TIP:</li> <li>If the calculated sample values (e.g., Reg: ##; N</li> </ul>	e size listed in the Registry and Manus /lan: ##).	script are different, please note both
<ul> <li>No → The difference(s</li> <li>Not Applicable → The and the Manuscript.</li> </ul>	es noted in the Manuscript? (s) in Sample Size were clearly stated b) in Sample Size were apparent but n ere was no difference in the Sample S clinical trial registry data available.	ot explained.
RESULTS		
• CONSORT (13) – Participant flow diag	ram (a diagram is strongly recomm	anded)
• Options:	on of participant flow was provided	Shucuj.
<ul> <li>Yes → Provided a con</li> <li>Unclear → If all rando unclear</li> </ul>	ses and exclusions after randomization fically state there were no losses/exclu- nplete account of all randomized partic mized participants are accounted for b any participant are missing	usions post randomization cipants
Centers & Care Providers <ul> <li>CONSORT (13aii) – The number of care</li> </ul>	e providers and/or centers performi	ng the intervention in each grou

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3	<ul> <li>Options:</li> </ul>
4	• Yes $\rightarrow$ (Multi-site trials) List the number of intervention sites <b>OR</b> individually identify each site <b>AND</b>
5	must clearly state the number of interventionists at each study site.
6	• Yes $\rightarrow$ (Single-site trials) Must clearly state the number of interventionists at the study site.
7	• No $\rightarrow$ (Multi-site trials) Data not provided for number of centers and/or number of interventionists.
8	
9	• No $\rightarrow$ (Single-site trials) Data not provided for number of interventionists.
10	
11	<ul> <li>CONSORT (15ii) – When applicable, a description of care providers (case volume, qualification, expertise,</li> </ul>
12	etc.) and centers (volume) in each group.
13	• Options:
14	• Yes $\rightarrow$ (Multi-site trials) Must at least provide the background education or training of the
15	interventionists <b>AND</b> the volume of participants at each site.
16	• Yes $\rightarrow$ (Single-site trials) Must at least provide the background education or training of the
17	interventionists.
18	<ul> <li>No → (Multi-site trials) Data not provided for interventionists and/or centers.</li> </ul>
19	<ul> <li>No → (Single-site trials) Data not provided for interventionists.</li> </ul>
20	
21	
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23	
24	Participants, Analyses & Outcomes
25	
26	• CONSORT (15i) – A table showing baseline demographic and clinical characteristics for each group.
27	<ul> <li>Options:</li> </ul>
28	
29	• Yes $\rightarrow$ A unique table displaying demographic data is provided
30	• No $\rightarrow$ Table not provided
31	
32	<ul> <li>CONSORT (13ai) – For each group, the number of participants who were randomly assigned, received</li> </ul>
33	intended treatment, and were analyzed for the primary outcome.
	• Options:
34 25	• Yes $\rightarrow$ All requisite details were provided
35	
36	• No $\rightarrow$ Any of the requisite details are not provided
37	• TIP:
38	<ul> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> </ul>
39	
40	CONSORT (16) – For each group, number of participants (denominator) included in each analysis and
41	whether the analysis was by original assigned groups.
42	<ul> <li>Options:</li> </ul>
43	
44	<ul> <li>Yes → Must provide details of how many participants from each group were included within each</li> </ul>
45	analysis
46	<ul> <li>Unclear → The authors suggest that analyses were performed according to intention-to-treat but</li> </ul>
47	failed to provide a description of how missing data from drop-outs or testing errors was accounted
48	for
	■ Unclear → The authors provided numbers for the analysis but did not indicate that analyses
49 50	adhered to intention-to-treat principles
50	• No $\rightarrow$ Data not provided
51	
52	
53	<ul> <li>This information is typically reported in the main results tables in the form of (n = #) but may also</li> </ul>
54	be found in the results section.
55	<ul> <li>Double check the flow diagram to check for potential dropouts/missing data.</li> </ul>
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50	
58 59	47 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

	<ul> <li>If any participants withdrew or were lost to follow-up, the authors should disclose how</li> </ul>
	their missing data was treated.
	<ul> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> </ul>
•	CONSORT (17a) – For each primary and secondary outcome, results for each group, and the estimated e size and its precision (such as 95% confidence interval). o Options:
	<ul> <li>Yes → Authors must provide the raw baseline data, raw or adjusted follow-up data, change so or effect sizes, <i>AND</i> 95% CI data</li> <li>No → Missing any of the aforementioned data</li> </ul>
•	CONSORT (17b) – For binary outcomes, presentation of both absolute and relative effect sizes is recommended. • Options:
	<ul> <li>NA → If no binary outcomes are tracked/reported</li> </ul>
	<ul> <li>Yes → Authors provide an indication of the actual number of observations relative to the expension of observations <i>AND</i> whether the ratio of observations differed between groups</li> <li>No → Missing any of the aforementioned data</li> </ul>
•	CONSORT (18) – Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory. • Options:
	• $NA \rightarrow If$ no subgroup or sensitivity analysis were performed
	<ul> <li>Yes → If the results of any analysis other than the main intervention effects were performed a reported</li> </ul>
	• No $\rightarrow$ If the results of any analysis other than the main intervention effects were performed by reported
	4
•	DETAILS – What was the outcome of this trial?
•	• Options:
•	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> </ul>
•	<ul> <li>Options:         <ul> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary outcome</li> </ul> </li> </ul>
•	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary out</li> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> </ul>
•	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary out</li> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> <li>Unclear → If the primary findings are not well defined or not interpretable</li> </ul>
•	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary out</li> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> <li>Unclear → If the primary findings are not well defined or not interpretable</li> </ul>
•	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary out</li> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> <li>Unclear → If the primary findings are not well defined or not interpretable</li> </ul>
• Frial C	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary out</li> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> <li>Unclear → If the primary findings are not well defined or not interpretable</li> </ul>
• Frial C	<ul> <li>Options:</li> <li>Positive → As hypothesized, there was a significant difference in the primary outcome</li> <li>Positive → As hypothesized, equivalency was demonstrated</li> <li>Negative → Contrary to the hypothesis, there was no significant difference in the primary outcome</li> <li>Negative → Contrary to the hypothesis, equivalency was not demonstrated</li> <li>Unclear → If the primary findings are not well defined or not interpretable</li> <li>Mixed → Only an option for trials with more than one primary outcome (rare)</li> </ul>

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4	•	CONSORT (14b) – Why the trial ended or was stopped.
5	•	
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8		the intervention and follow-up tested as intended)
9		<ul> <li>Yes → If the trial stopped early or was extended AND a full justification was provided</li> </ul>
10		<ul> <li>Unclear → If the trial stopped early or was extended AND the authors made special note of that</li> </ul>
11		fact without providing an adequate justification
12		<ul> <li>Unclear → If the trial stopped early or was extended AND an inadequate discussion was provided</li> </ul>
13		<ul> <li>No → If the trial stopped early or was extended BUT an adequate justification was not provided</li> </ul>
14		o TIP:
15		<ul> <li>The majority of studies will finish as planned and will be assigned an NA</li> </ul>
16		
17	•	CONSORT (14a) – Dates defining the periods of recruitment and follow-up.
18	•	• Options:
19		
20		
21		a specific date as to when participant follow-up finished
22		<ul> <li>Unclear → Authors provided recruitment dates but only eluded to how long the follow-up period</li> </ul>
23		lasted (e.g., 12 months)
24		<ul> <li>No → Only provided dates of recruitment but not follow-up OR not at all</li> </ul>
25		
26	DETA	LS
27	•	Recruitment (enrollment) start date:
28		• Note details
29		• Nomenclature: Date format $\rightarrow$ MM/YY
30		$\circ$ NR $\rightarrow$ If not reported
31		
32		
33	•	Recruitment (enrollment) end date:
34		Note details
35		• Nomenclature: Date format $\rightarrow$ MM/YY
36		$\circ$ NR $\rightarrow$ If not reported
37		
38	•	Trial start date:
39		<ul> <li>Note details</li> </ul>
40		• Nomenclature: Date format $\rightarrow$ MM/YY
41		$\circ$ NR $\rightarrow$ If not reported
42		
43		Trial and data.
44	•	Trial end date:
45		<ul> <li>Note details</li> </ul>
46		• Nomenclature: Date format $\rightarrow$ MM/YY
47		$\circ$ <b>NR</b> $\rightarrow$ If not reported
48		
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52	T:	n of Annonements
53	rimin	g of Assessments
55		
55	•	CONSORT (13c) – For each group, the delay between randomization and the initiation of the intervention.
56		• Options:
50 57		
58		49
59		

- Yes → Explicitly states an average or maximum time (days/weeks) between randomization and intervention start
- No → Data not provided

#### **Randomization & Testing**

- Number of subjects randomized to Exercise:
  - AET (2) / RET (2) / COMB (2)  $\rightarrow$  Note details for each group as relevant
  - $\circ$  **NR**  $\rightarrow$  If not reported
- Number of subjects randomized to Usual Care/Control:
  - Note details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- Number of Exercise participants with baseline data:
  - $\circ$  AET (2) / RET (2) / COMB (2)  $\rightarrow$  Note details for each group as relevant
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- Number of Usual Care/Control participants with baseline data:
  - Note details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- Number of Exercise participants with follow-up data:
  - AET (2) / RET (2) / COMB (2)  $\rightarrow$  Note details for each group as relevant
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- Number of Usual Care/Control participants with follow-up data:
  - Note details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$

# Demographics

- Total number of subjects:
  - Note details
  - $\circ$  **NR**  $\rightarrow$  If not reported
- Number of male participants:
  - Note details
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- Number of female participants:
  - Note details

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- $NR \rightarrow If not reported$
- Average age of all participants:
  - Note details
  - $NR \rightarrow If not reported$
- Average age of Exercise participants:
  - Note details
  - $NR \rightarrow If not reported$
- Average age of Usual Care/Control participants:
  - Note details
  - $NR \rightarrow If not reported$
- **Medical Characteristics** 
  - r erez Average disease duration (months): •
    - Not Applicable
    - <6 months
    - <12 months
    - <24 months
    - <60 months
    - <120 months
    - ≥120 months
    - $NR \rightarrow If not reported$

# **Comorbidities**

# Hypertension (n):

- Note details
- $NR \rightarrow If not reported$ •
- $NA \rightarrow If$  listed in exclusion criteria •

# Hypercholesterolemia (n):

- Note details •
- $NR \rightarrow If not reported$ •
- $NA \rightarrow If$  listed in exclusion criteria •

# Diabetes (n):

- Note details
- $NR \rightarrow$  If not reported
- $NA \rightarrow If$  listed in exclusion criteria

Hypercholesterolemia (%): Note details

Hypertension (%): Note details

Diabetes (%): Note details

2 3	Attendance
3 4 5	Attendance
5 6	AET (2) At
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AET (2) Attendance –	<ul> <li>Number:</li> <li>Note details</li> <li>NR → If not reported OR if trial report sessions</li> </ul>	<b>Percent:</b> <i>Note details</i> s attendance as X% attended X% of
RET (2) Attendance –	Number: <ul> <li>Note details</li> <li>NP</li> <li>If not reported OP if trial report</li> </ul>	Percent: Note details
	<ul> <li>NR → If not reported OR if trial report sessions</li> </ul>	
CET (2) Attendance –	Number: • Note details	Percent: Note details
	<ul> <li>NR → If not reported OR if trial report sessions</li> </ul>	s attendance as X% attended X% of
• TIPS:		
	port attendance with the exercise-based con components (e.g., telephone counseling sess	•
Exclusion		
AET (2) Exclusion –	<ul> <li>Number:</li> <li>Note details</li> <li>NR → If not reported</li> </ul>	Percent: Note details
RET (2) Exclusion –	Number:	Percent: Note details
	<ul> <li>Note details</li> <li>NR → If not reported</li> </ul>	
CET (2) Exclusion –	Number:	Percent: Note details
	<ul> <li>Note details</li> <li>NR → If not reported</li> </ul>	
UC Exclusion –	<ul> <li>Number:</li> <li>Note details</li> <li>NR → If not reported</li> </ul>	Percent: Note details
differ with or without o For trials reporting in	g data strategies are used (e.g., imputation) a	nnot be assigned unless confirmed by

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3 4	CONSC	DRT – HARMS
5	•	HARMS (19a) – If the study collected data on harms and benefits, the title or abstract should so state.
6		• Options:
7		• Yes $\rightarrow$ If authors mention safety or AEs anywhere in the title or abstract
8		• No $\rightarrow$ If safety or AEs are not mentioned in these sections
9		• TIPS:
10		<ul> <li>IMPORTANT – All Phase I-III, by definition, should report safety outcomes. Thus, the safety</li> </ul>
11 12		of the intervention should be assessed and reported on.
13		
14	-	HADME (10h) If the twist addresses both harms and herefits the introduction should be state
15	•	HARMS (19b) – If the trial addresses both harms and benefits, the introduction should so state.
16		• Options:
17		• Yes $\rightarrow$ Authors should state the safety of the intervention is in question <b>OR</b> they should state that
18		one of the trial objectives (typically last paragraph of the intro) is to assess the safety of the
19		intervention.
20		• No $\rightarrow$ Not mentioned
21		
22	•	HARMS (19c) – List addressed adverse events with definitions for each (when relevant, attention to grading,
23		expected vs. unexpected AEs, reference to standardized and validated definition, and description of new definitions).
24		○ Options:
25		<ul> <li>Yes → Authors listed AND defined the potential/anticipated AEs being studied</li> </ul>
26		<ul> <li>Unclear → Authors listed the AEs but failed to define them</li> </ul>
27		• No $\rightarrow$ Details not provided
28		• TIPS:
29		For trials reporting AEs as the primary and secondary outcomes, the definitions for the outcomes
30		count towards defining the AEs.
31		
32	•	HARMS (19d) – Clarify how harms-related data was collected (mode of collection, timing, attribution methods,
33	•	intensity of ascertainment, and harms-related monitoring and stopping rules).
34		• Options:
35		• Yes $\rightarrow$ Authors should clearly state how, when <b>AND</b> by whom AE data was collected
36		• Unclear $\rightarrow$ Authors fail to properly describe a single aspect (how, when, by whom) of how the AE
37		
38		data was collected but adequately describe all other aspects
39		• No $\rightarrow$ Details not provided
40		$\circ$ TIPS:
41		<ul> <li>For trials reporting AEs as the primary and secondary outcomes, the collection methods for the</li> </ul>
42		outcomes count towards collecting the AEs.
43		
44	•	HARMS (19e) – Describe plans for presenting and analyzing information on harms (including coding, handling
45		of recurrent event, specification of timing issues, handling of continuous measures, and statistical analyses).
46		<ul> <li>Options:</li> </ul>
47		<ul> <li>Yes → Authors should clearly state how AE data was analyzed</li> </ul>
48		■ Unclear → Authors fail to properly describe a single aspect of how the AE data was analyzed but
49		adequately describe all other aspects
50		• No $\rightarrow$ Details not provided
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# GENERAL TIPS FOR HARMS:

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- If authors fail to explicitly state if AEs were attributable to the intervention, check to see if there were analyses comparing AE frequency or relative risk per arm.
  - o If analyses were performed:
    - For AEs which occur significantly more frequently within the intervention group(s) → list details for those specific AEs under 'intervention-related'
    - For AEs which do not occur significantly more frequently within the intervention group(s) → list details for those specific AEs under 'non-intervention-related'
  - o If analyses were not performed:
    - Rate 'intervention-related' AEs as NR
    - List all reported AEs for both groups as 'non-intervention-related'
- For trials reporting AEs as the primary and secondary outcomes, the analysis methods for the outcomes count towards analyzing the AEs.

## Testing-related AEs

- DETAILS Did any testing-related AE occur?
  - $\circ$  NA  $\rightarrow$  Specifically stated that no testing-related AEs occurred
  - Yes  $\rightarrow$  Specifically stated the type and number of testing-related AEs
  - $\circ$  Unclear  $\rightarrow$  The numbers are provided but the details were unclear
  - $\circ \quad \mathbf{No} \to \mathbf{Details} \text{ not provided}$

## • DETAILS – If so, how many?

- Note pertinent details
- $\circ \quad \mathbf{NR} \to \text{If not reported}$
- TIPS:
  - Report both values if there are discrepancies between the Registry and Manuscript
- DETAILS How were testing-related AE defined?
  - $\circ \quad \text{Note pertinent details} \\$
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- DETAILS How were testing-related AE monitored/tracked?
  - Note pertinent details
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$

# Intervention-related AEs

- DETAILS Did any intervention-related AE occur?
  - $\circ$  NA  $\rightarrow$  Specifically stated that no intervention-related AEs occurred
  - $\circ\quad \textbf{Yes} \rightarrow \textbf{Specifically stated the type and number of intervention-related AEs}$
  - $\circ$  **Unclear**  $\rightarrow$  The numbers are provided but the details are unclear
  - $\circ \quad \textbf{No} \rightarrow \textbf{Details not provided}$
- DETAILS If so, how many?
  - Note pertinent details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$

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- TIPS:
  - Report both values if there are discrepancies between the Registry and Manuscript

- Note pertinent details
- $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

#### • DETAILS – How were intervention-related AE monitored/tracked?

- o Note pertinent details
- $\circ \quad \mathbf{NR} \rightarrow \mathsf{lf} \mathsf{ not reported}$
- Non-Intervention-related AEs
  - DETAILS Did any non-intervention-related AE occur?
    - $\circ$  NA  $\rightarrow$  Specifically stated that no intervention-related AEs occurred
    - $\circ$  Yes  $\rightarrow$  Specifically stated the type and number of intervention-related AEs
    - $\circ$  Unclear  $\rightarrow$  The numbers are provided but the details are unclear
    - $\circ$  **No**  $\rightarrow$  Details not provided

#### • DETAILS – If so, how many?

- Note pertinent details
- $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- o TIPS:
  - Report both values if there are discrepancies between the Registry and Manuscript
- DETAILS How were non-intervention-related AE defined?
  - Note pertinent details
  - $\circ \quad \mathbf{NR} \rightarrow \text{If not reported}$
- DETAILS How were non-intervention-related AE monitored/tracked?
  - Note pertinent details
  - $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

## **AEs Per Group**

- DETAILS How many AEs were reported for the PHARMA (4) & UC groups?
  - Note pertinent details
  - $\circ \quad \mathbf{NR} \xrightarrow{} \mathsf{lf not reported}$

## HARMS Continued...

- HARMS (19f) Describe for each arm the participant withdrawals that are due to harms and their experiences with the allocated treatment.
  - Options:
    - NA → If the authors specifically stated there were no AEs OR that no participant withdrew/was lost to follow-up due to AEs

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**Yes**  $\rightarrow$  If the authors clearly identify the number of participants who withdrew or were lost to follow-up due to AEs  $No \rightarrow If$  the reasons why participants withdrew or were lost-to-follow-up are not provided for every applicable case HARMS (19g) – Provide denominators for analyses on harms. Options: 0  $NA \rightarrow If$  the authors specifically stated there were no AEs **Yes**  $\rightarrow$  Reference numbers provided for AE risk calculations  $No \rightarrow Details not provided$ HARMS (19h) – Presents absolute risk per arm and per AE type, grade, and seriousness, and present appropriate metrics for recurrent events, continuous variables, and scale variables. **Options:** 0  $NA \rightarrow If$  the authors specifically stated there were no AEs Yes  $\rightarrow$  If the authors present the absolute risk per arm AND per adverse event type/grade AND describe the frequency of AEs  $No \rightarrow$  Details not provided . HARMS (19i) – Describes any subgroup analyses and exploratory analyses for harms. Options: 0  $NA \rightarrow$  If the authors specifically stated there were no AEs NA → There were no subgroup / exploratory analyses proposed or reported .  $NA \rightarrow If$  the number of AEs were so small that it was not reasonable to perform subgroup or exploratory analyses **Yes**  $\rightarrow$  If the authors present the results of subgroup analyses or exploratory analyses  $No \rightarrow$  Details not provided HARMS (19j) - Provide a balanced discussion of benefits and harms with emphasis on study limitation, generalizability, and other sources of information on harms. **Options:** 0  $NA \rightarrow If$  the authors specifically stated there were no AEs **Yes**  $\rightarrow$  Should formally address any AEs in the Discussion in the context of trial limitations and whether the risk intervention-related AEs should be considered when implementing or conducting further tests of the intervention in question.  $No \rightarrow Not discussed$ **DISCUSSION & OTHER** CONSORT (20i) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses. • Options: **Yes**  $\rightarrow$  If authors listed major sources of potential bias or measurement error **AND** provided basic details as to how these factors may have influenced results **Unclear** → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors

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3	■ No → Failed to list and adequately discuss potential sources of bias within the description of trial
4	limitations
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6	CONCORT (2011) Trial limitations, taking into account the choice of comparator lock of an partial blinding
7 •	CONSORT (20ii) – Trial limitations: taking into account the choice of comparator, lack of or partial blinding,
8	and unequal expertise of care providers or centers in each group.
9	<ul> <li>Options:</li> </ul>
10	• Yes $\rightarrow$ If authors listed sources of potential bias related to the control group(s), incomplete or lack
11	of blinding, and/or between care providers/intervention sites AND provided basic details as to how
12	these factors may have influenced results
13	<ul> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential</li> </ul>
14	impact/implications of these factors
15	■ No → Failed to list and adequately discuss potential sources of bias within the description of trial
16	limitations
17	• TIPS:
18	<ul> <li>Trials with only PROs: analysis must be blinded to be rated Low.</li> </ul>
19	<ul> <li>Trials with only physiologic outcomes: testing must be blinded to be rated Low.</li> </ul>
20	<ul> <li>Trials with both physiologic and PROs: testing and analysis must be blinded to be rated Low. In</li> </ul>
21	these mixed outcome trials, an Unclear can be assigned if the analysis details are missing.
22	
23	
24	CONSORT (21) – Generalizability of trial findings according to the intervention, comparators, patients, and
25	care providers and centers involved in the trial.
26	• Options:
27	<ul> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul>
28	patient groups, and care provider/centers.
29	■ No → None of these aspects were not adequately discussed within the context of other research
	(past and future)
30	(past and ratare)
31	CONCORT (22) Intermediation consistent with results belowing boughts and borrise and considering other
32 •	CONSORT (22) – Interpretation consistent with results, balancing benefits and harms, and considering other
33	relevant evidence.
34	• Options:
35	• Yes $\rightarrow$ Authors should not overstate non-significant or modestly altered endpoints; nor should they
36	dismiss/ignore/fail to adequately describe non-significant findings for any of the primary outcomes
37	in favor of discussing secondary outcomes
38	• No $\rightarrow$ Authors do not present an unbiased interpretation of their findings
39	
40	
41	<ul> <li>Look closely at the results for the primary outcomes (data tables). The first paragraph of the</li> </ul>
42	Discussion should summarize these results without inflating/downplaying the findings. Similarly, the
43	Conclusion should also provide an unbiased summary of the main trial findings.
44	
45 •	CONSORT (23) – Registration number and name of trial registry.
	• Options:
46	• Yes $\rightarrow$ If the number was provided
47	
48	• Yes $\rightarrow$ If authors clearly stated the trial was not registered
49	• No $\rightarrow$ If the number was not provided
50	• TIP:
51	<ul> <li>Check the abstract, methods, and footnotes/margins of the paper to locate this number.</li> </ul>
52	
53	DETAILS – If so, please list.
54	
55	• Note pertinent details
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- CONSORT (24) Where the <u>full trial protocol</u> can be accessed, if available.
  - Options:

- Yes → If the full protocol or a link to the full protocol is provided in the primary manuscript or as an online supplement
- No  $\rightarrow$  Data not provided
- DETAILS If so, please provide the URL:
  - Note pertinent details
- CONSORT (25) Sources of funding and other support, role of funders.
  - Options:
    - Yes  $\rightarrow$  If funder and funder's role are both described
    - Unclear → If either funder OR funder's role are described
    - No → Neither funder nor funder's role are described
  - o TIP:
    - Similar to the registration number, check the footnotes, margins, and any supplemental information listed between the Conclusion and the Reference list.

- DETAILS If so, please provide the details:
  - Note pertinent details

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Supplementary Methods 6: Data Extraction Reference Guide – Exercise RCTs

# COCHRANE – Risk of Bias

- Selection Bias: Random sequence generation
  - $\circ$  High  $\rightarrow$  Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence
  - $\circ$  Low  $\rightarrow$  Random sequence generation method should produce comparable groups
  - $\circ \quad \textbf{Unclear} \rightarrow \text{Not described in sufficient detail to permit judgement}$

# Selection Bias: Allocation concealment

- $\circ$  **High**  $\rightarrow$  Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
- $\circ$  Low  $\rightarrow$  Intervention allocations likely could not have been foreseen in before or during enrollment
- $\circ$  **Unclear**  $\rightarrow$  Not described in sufficient detail to permit judgement

# Performance Bias: Blinding (participants & personnel)

- **High**  $\rightarrow$  Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
- $\circ \quad \text{Low} \rightarrow \text{Blinding was likely effective}$
- $\circ$  Unclear  $\rightarrow$  Not described in sufficient detail to permit judgement

# Detection Bias: Blinding (outcome assessment)

- $\circ$  High  $\rightarrow$  Detection bias due to knowledge of the allocated interventions by outcome assessors
- $\circ \quad \text{Low} \rightarrow \text{Blinding was likely effective}$
- $\circ \quad \textbf{Unclear} \rightarrow \text{Not described in sufficient detail to permit judgement}$
- $\circ$  TIPS:
  - Trials with only PROs: *analysis* must be blinded to be rated *Low*.
  - Trials with only physiologic outcomes: *testing* must be blinded to be rated *Low*.
  - Trials with both physiologic and PROs: *testing* and *analysis* must be blinded to be rated *Low*. In these mixed outcome trials, an Unclear can be assigned if the *analysis* details are missing.

# • Attrition Bias: Incomplete outcome data

- $\circ$  High  $\rightarrow$  Attrition bias due to amount, nature or handling of incomplete outcome data
- $\circ$  Low  $\rightarrow$  Handling of incomplete outcome data was complete and unlikely to have produced bias
- Unclear → Insufficient reporting of attrition/exclusions to permit judgment (e.g., number randomized not stated, no reasons for missing data provided)

# Reporting Bias: Selective reporting

- $\circ$  High  $\rightarrow$  Reporting bias due to selective outcome reporting
- $\circ$  Low  $\rightarrow$  Selective reporting bias not detected
- $\circ$  **Unclear**  $\rightarrow$  Insufficient information to permit judgment

# • Other sources of bias

- $\circ\quad \text{High} \rightarrow \text{Bias}$  due to problems not covered elsewhere in the criteria
- Low  $\rightarrow$  No other bias detected
- $\circ$  **Unclear**  $\rightarrow$  There may be a risk of bias, but there is insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem will introduce bias

# Quality Comments: Justify 'high-risk' & 'unclear' decisions

• Please note pertinent details

#### 

## JADAD Score

- Randomization Score:
  - 1 point if randomization is mentioned
  - $\circ$  1 additional point if the method of randomization is appropriate
  - Deduct 1 point if the method of randomization is inappropriate (minimum 0)

#### • Blinding Score:

- o 1 point if blinding is mentioned
- 1 additional point if the method of blinding is appropriate
- Deduct 1 point if the method of blinding is inappropriate (minimum 0)
- $\circ$  TIPS:
  - For trials reporting exclusively PROs the analysis must be blinded.
  - For trials reporting any physiologic outcomes the testing must be blinded.
  - For trials with both physiologic and PROs the testing and analysis must be blinded.

## Account of All Patient Score:

o 1 point if the fate of all patients in the trial is known. If there are no data the reason is stated.

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Supplementary Methods 7: Data Extraction Reference Guide - Pharmacological RCTs

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Data Extraction Reference Guide – Pharmacological RCTs



Memorial Sloan Kettering Cancer Center

## **EXTRACTION ABBREVIATIONS**

- %: percent
- BL: baseline
- d: days

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- FU: follow-up
- hr/hrs: hour/hours
- IN: injection
- INH: inhalent
- IO: intraosseous
- mins: minutes
- mo: months
- PHARMA: pharmaceutical intervention
- PO: oral
- PR: per rectum
- SL: sublingual
- TD: transdermal
- Top: topical
- UC: usual care/control
- wk/wks: week/weeks
- yrs: years

## **GENERAL NOMENCLATURE & EXTRACTION GUIDELINES**

#### **Nomenclature Guidelines**

- Ranges:
  - Use 'to' and not '-' (e.g., 150 bpm to 175 bpm)
- Units:
  - List all units of measure including percentages
- Significant figures:
  - $\circ$  Raw values / averages  $\rightarrow$  round to the nearest 0.1
  - $\circ$  Percentages  $\rightarrow$  round to the nearest whole number
- Averages:

0

- Mean value is preferred and assumed
  - Only list median values if mean are not reported
    - If listing median values, please label appropriately
- Lists:
  - $\circ$  ~ Be succinct  $\rightarrow$  only include pertinent details and use bullet form with semicolon separated values
  - $\circ$   $\;$  List details in the same order as it is presented in the manuscript
  - Examples:
    - Inclusion/exclusion criteria: e.g., 40 to 65 yrs; BMI<40; sedentary</li>
    - Primary/secondary outcomes: e.g., resting HR; body weight; PA mins/wk

# **Extraction Guidelines**

Supplementary Methods 7: Data Extraction Reference Guide – Pharmacological RCTs

- Multiple intervention arms
  - Base group numbering on layout of flow diagram (e.g., PHARMA 1 = left-most group; PHARMA 2 = group immediately to the right, etc.)
- Placebo group
  - Extract data into Control group fields
- In the case of discrepancies between conflicting sources of data, prioritize the data provided in the primary manuscript.

# ARTICLE INCLUSION/EXCLUSION

- Should this article be included in our systematic review?
  - Yes  $\rightarrow$  Does not meet any exclusion criteria.
  - $\circ$  No  $\rightarrow$  Meets one or more exclusion criteria.

## **PUBLICATION INFORMATION**

- Country of publication?
  - Please provide the <u>full name</u> of the country where the study was conducted/where the primary author is based

# **TITLE, ABSTRACT & INTRODUCTION**

- CONSORT (1a) Identification as a randomized trial in the title.
  - Options:
    - Yes  $\rightarrow$  Either randomized controlled trial; randomized trial; randomized
    - No  $\rightarrow$  Not mentioned
- CONSORT (1b) Structured summary of trial design, methods, results, and conclusions.
  - Options:
    - Yes  $\rightarrow$  Introduction/Background + Methods + Results + Discussion/Conclusion
    - No  $\rightarrow$  Not properly structured
- CONSORT (2a) Scientific background and explanation of rationale.
  - Options:
    - Yes  $\rightarrow$  Reviews relevant literature **AND** identifies a knowledge gap/question
    - No → Did not adequately review the literature and/or identify the knowledge gap/question the study attempted to address
- CONSORT (2b) Specific objectives or hypothesis.
  - **Options:**

 Yes (objectives) → Must provide a specific <u>purpose/objective</u> for study in the context of the intervention AND the <u>specific outcomes of interest</u>

#### OR

- Yes (hypothesis) → Must provide a specific hypothesis in the context of a group-related change in a specific outcome of interest AND the expected direction of change
- **Unclear** → Provided the specific purpose/objective or hypothesis but only 1 of 2 additional required components
- No → Failed to provide either (1) the specific purpose/objective OR hypothesis, and/or (2) both additional required components

#### o TIP:

 This information is typically reported within final paragraph of the introduction or early in the methods section.

## METHODS

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- CONSORT (3a) Description of trial design (such as parallel, factorial) including allocation ratio.
  - Options:
    - Yes → Must provide both a description of overall study design (e.g., parallel arm, crossover) AND allocation ratio
    - Unclear → Description of study design is provided but *NOT* allocation ratio
    - No → If missing the study design (even if allocation ratio is provided)

#### • EXAMPLES:

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- Parallel trials, cross-over trials, factorial trials AND 1:1, 1:2, 1:1:1
- CONSORT (4b) Settings and locations where the data were collected.

#### • Options:

- **Yes**  $\rightarrow$  Provided details of where the <u>data were collected</u> for the trial
  - This includes single-location trials when the authors clearly state the entire trial took place
     onsite
- Unclear → Specifies that data was collected in a lab/office but does not provide the actual location of said room (e.g., at which hospital)
- No → Details not provided
- TIP:
  - This does NOT include where the recruitment or intervention took place.
  - Listing the institutional / ethics review board does not count.

#### • DETAILS – Clinical population:

- List the clinical population being studied
- $\circ$  **NR**  $\rightarrow$  If not reported
- DETAILS Disease setting:
  - Identify the disease phase [Prevention (P) vs. Management (M)] during and after) during which the PHARMA intervention took place.
- CONSORT (3b) Important changes to methods after trial commencement (such as eligibility criteria), with reasons.

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	• Options	
		$NA \rightarrow$ The methods did not change
		<b>Yes</b> $\rightarrow$ Methods changed and reasons were provided
		<ul> <li>Examples include (but are not limited to): study design, sample size (± 10%), eligibilit</li> </ul>
		criteria, recruitment strategy, randomization, blinding, data analysis, etc.
	•	<b>Unclear</b> $\rightarrow$ Described change in methods but no reasons were provided
	•	$No \rightarrow$ It appears that methods may have changed but there is not enough information to mak
		assessment
	o TIPS:	
	•	This includes under/over recruitment according to the a priori-defined sample size without
	_	adequate justification.
	•	Does <b>NOT</b> include changes in trial outcomes $\rightarrow$ that data is captured in a <u>separate CONSOR</u>
		item
Eligibi	lity Criteria	
•		– Eligibility criteria for participants.
	<ul> <li>Options</li> </ul>	
		<b>Yes</b> $\rightarrow$ Provided details/criteria for <b>BOTH</b> inclusion <b>AND</b> exclusion of participants <b>Unclear</b> $\rightarrow$ Only provides details of <u>inclusion</u> <b>OR</b> exclusion but <b>NOT</b> both
		$No \rightarrow Details not provided$
	_	
•	omparison: Eli <u>c</u> Was there a diff ○ Options	erence in Eligibility Criteria between the Registry and the Manuscript?
	:	Yes → One or more differences between the two data sources. No → No difference between the two data sources. Unclear → Possible difference between the two data sources, but insufficient information to r a determination. Not Applicable → No clinical trial registry data available.
•		$No \rightarrow No$ difference between the two data sources. Unclear → Possible difference between the two data sources, but insufficient information to r a determination. Not Applicable → No clinical trial registry data available.
•		$No \rightarrow No$ difference between the two data sources. Unclear $\rightarrow$ Possible difference between the two data sources, but insufficient information to a determination. Not Applicable $\rightarrow$ No clinical trial registry data available.
•	Was the change	$No \rightarrow No$ difference between the two data sources. Unclear $\rightarrow$ Possible difference between the two data sources, but insufficient information to a determination. Not Applicable $\rightarrow$ No clinical trial registry data available.
•	Was the change	<ul> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to r a determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> <li>noted in the Manuscript?</li> <li>S:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> </ul>
•	Was the change	<ul> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to ra determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> <li>noted in the Manuscript?</li> <li>S:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and</li> </ul>
•	Was the change	No → No difference between the two data sources. Unclear → Possible difference between the two data sources, but insufficient information to a determination. Not Applicable → No clinical trial registry data available. noted in the Manuscript? S: Yes → The change in eligibility criteria was clearly stated and explained. No → The change in eligibility criteria was apparent but not explained. Not Applicable → There was no difference in the eligibility criteria between the Registry and Manuscript.
•	Was the change	<ul> <li>No → No difference between the two data sources.</li> <li>Unclear → Possible difference between the two data sources, but insufficient information to ra determination.</li> <li>Not Applicable → No clinical trial registry data available.</li> <li>noted in the Manuscript?</li> <li>S:</li> <li>Yes → The change in eligibility criteria was clearly stated and explained.</li> <li>No → The change in eligibility criteria was apparent but not explained.</li> <li>Not Applicable → There was no difference in the eligibility criteria between the Registry and</li> </ul>
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•	Was the change Options	No → No difference between the two data sources. Unclear → Possible difference between the two data sources, but insufficient information to r a determination. Not Applicable → No clinical trial registry data available. e noted in the Manuscript? S: Yes → The change in eligibility criteria was clearly stated and explained. No → The change in eligibility criteria was apparent but not explained. Not Applicable → There was no difference in the eligibility criteria between the Registry and Manuscript. Not Applicable → No clinical trial registry data available. sion Criteria were listed in the Registry?
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•	Was the change o Options • • • • • • • • • • • • •	No → No difference between the two data sources. Unclear → Possible difference between the two data sources, but insufficient information to ma determination. Not Applicable → No clinical trial registry data available. enoted in the Manuscript? S: Yes → The change in eligibility criteria was clearly stated and explained. No → The change in eligibility criteria was apparent but not explained. Not Applicable → There was no difference in the eligibility criteria between the Registry and the Manuscript. Not Applicable → No clinical trial registry data available. Sign Criteria were listed in the Registry?

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# • DC DETAILS - Please list the Inclusion Criteria reported in the Registry.

Please record each individual Inclusion Criteria listed in the Registry.

# • How many Inclusion Criteria were listed in the Manuscript?

o Please record the total number of individual Inclusion Criteria listed in the Manuscript.

#### • DC DETAILS - Please list the Inclusion Criteria reported in the Manuscript.

o Please record each individual Inclusion Criteria listed in the Manuscript.

#### • How many Exclusion Criteria were listed in the Registry?

o Please record the total number of individual Exclusion Criteria listed in the Registry.

# • DC DETAILS - Please list the Exclusion Criteria reported in the Registry.

o Please record each individual Exclusion Criteria listed in the Registry.

#### How many Exclusion Criteria were listed in the Manuscript?

o Please record the total number of individual Exclusion Criteria listed in the Manuscript.

#### • DC DETAILS - Please list the Exclusion Criteria reported in the Manuscript.

• Please record each individual Exclusion Criteria listed in the Manuscript.

# **Outcome Measures**

• CONSORT (6a) – Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.

# • Options:

- Yes → Clearly defined a single primary outcome (*co-primary outcomes at max*), all relevant secondary outcomes *AND* provide all requisite details of the timing *AND* procedures used to assess these outcomes
- Unclear → Primary and secondary outcomes defined but the descriptions of the timing and procedures used to assess the outcomes were lacking details required to reproduce the measurements
- No → If no primary or secondary outcomes are clearly defined OR if the assessment details (e.g., how & when) were missing altogether

#### o TIPS:

Some studies may identify multiple primary outcomes. Although this type of study design is
inappropriate in the context of medical oncology research, we are evaluating the quality of
reporting and not the quality of the study design. Therefore, a 'Yes' can be assigned provided the
authors clearly identify which outcomes are considered primary and secondary.

# • DETAILS – Please list the primary endpoint(s):

- When entering data, list the primary endpoint(s) using a semicolon to separate individual criteria
- **NR**  $\rightarrow$  If not reported.

# • DETAILS – Please list the secondary endpoint(s):

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3	<ul> <li>When entering data, list the secondary endpoints <u>using a semicolon to separate individual criteria</u></li> </ul>
4	$\circ$ <b>NR</b> $\rightarrow$ If not reported.
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6	<ul> <li>CONSORT (6b) – Any changes to trial outcomes after the trial commenced, with reasons.</li> </ul>
7	• Options:
8	• NA $\rightarrow$ No observable changes to trial outcomes were made
9	• Yes $\rightarrow$ Describes changes in outcomes according to all pertinent features (e.g., what, why &
10	
11	when)
12	<ul> <li>Unclear → Describes changes according to all but one pertinent feature</li> </ul>
13	• No $\rightarrow$ If the description is missing or unclear on two or more pertinent features
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20	Data Comparison: Primary Outcome
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22	<ul> <li>Was there a difference in the Primary Outcome(s) between the Registry and the Manuscript?</li> </ul>
23	• Options:
24	• Yes $\rightarrow \geq 1$ difference between the two data sources.
25	• No $\rightarrow$ No difference between the two data sources.
26	• <b>Unclear</b> $\rightarrow$ Possible difference between the two data sources, but insufficient information to make
27	a determination.
28	• NR $\rightarrow$ No clinical trial registry data available.
29	• <b>NR</b> $\rightarrow$ NO cirrical that registry data available.
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31	<ul> <li>Was the change in Primary Outcome noted in the Manuscript?</li> </ul>
32	<ul> <li>Options:</li> </ul>
33	Yes → The change in Primary Outcome was clearly stated and explained.
34	• No $\rightarrow$ The change in Primary Outcome was apparent but not explained.
35	• NR $\rightarrow$ No clinical trial registry data available.
36	• NA $\rightarrow$ No difference (i.e., Q1 = No)
37	
38	Was a new Primary Outcome reported in the Manuscript which was not reported in the Registry?
39	• was a new Primary Outcome reported in the manuscript which was not reported in the Registry?
40	• Options:
41	• Yes $\rightarrow \geq 1$ Primary Outcome reported in the Manuscript that was not listed in the Registry.
42	• No $\rightarrow$ No new Primary Outcome added to the Manuscript.
43	<ul> <li>Unclear → Possible difference between the two data sources, but insufficient information to make</li> </ul>
44	a determination.
45	<ul> <li>NR → No clinical trial registry data available.</li> </ul>
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40 47	<ul> <li>DC DETAILS – If Yes/Unclear, please provide the details?</li> </ul>
	<ul> <li>Please list all pertinent details.</li> </ul>
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49 50	Wes the Drimony Outcome reported in the Deviatory reported as a Case of Jam Outcome in the Manuscriptic
50 51	Was the Primary Outcome reported in the Registry reported as a Secondary Outcome in the Manuscript?
52	• Options:
	• Yes $\rightarrow \geq 1$ Primary Outcome reported in the Registry listed as a Secondary Outcome in the
53	Manuscript.
54	<ul> <li>No → No Primary Outcome from the Registry listed as a Secondary Outcome in the Manuscript.</li> </ul>
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60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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- Unclear → Possible difference between the two data sources, but insufficient information to make a determination.
- $NR \rightarrow No$  clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- Was the Primary Outcome reported in the Registry omitted from the Manuscript?
  - Options:
    - Yes  $\rightarrow$  The Primary Outcomes reported in the Registry was omitted from the Manuscript.
    - No  $\rightarrow$  The Primary Outcome reported in the Registry was included in the Manuscript.
    - Unclear → Possible difference between the two data sources, but insufficient information to make a determination.
    - $NR \rightarrow No$  clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.

# Data Comparison: Secondary Outcomes

- Were <u>different</u> (new) Secondary Outcomes reported in the Manuscript which were not reported in the Registry?
  - Options:
    - Yes  $\rightarrow \geq 1$  Secondary Outcomes reported in the Manuscript were not reported in the Registry.
    - No  $\rightarrow$  The Secondary Outcomes reported in the Manuscript were consistent with the Registry.
    - Unclear → Possible difference between the two data sources, but insufficient information to make a determination.
    - NR → No clinical trial registry data available.
- DC DETAILS If Yes/Unclear, please provide the details?
  - Please list all pertinent details.
- If different (new) Secondary Outcomes were added to the Manuscript, were the reasons noted in the Manuscript?
  - Options:
    - Yes  $\rightarrow$  The change(s) in Secondary Outcomes were clearly stated and explained
    - No  $\rightarrow$  The changes in Secondary Outcomes were apparent but not explained
    - $NR \rightarrow No$  clinical trial registry data available
    - NA → No difference in Secondary Outcomes (i.e., Q6 = No)
- Was one or more of the Secondary Outcomes reported in the Registry reported as Primary Outcomes in the Manuscript?
  - Options:
    - Yes → A Secondary Outcome reported in the Registry was reported as a Primary Outcome in the Manuscript.
    - No → None of the Secondary Outcomes reported in the Registry were reported as Primary Outcomes in the Manuscript.
    - **Unclear** → Possible difference between the two data sources, but insufficient information to make a determination.

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•	<ul> <li>NR → No clinical trial registry data available.</li> <li>DC DETAILS – If Yes/Unclear, please provide the details?         <ul> <li>Please list all pertinent details.</li> </ul> </li> </ul>
Rando	omization & Blinding
•	CONSORT (8a) – Method used to generate the random allocation sequence.
	<ul> <li>Options:</li> <li>Yes → Clearly stated the specific process used to generate the randomization (e.g., a coin flip, computer generated)</li> </ul>
	• No $\rightarrow$ Not provided
•	CONSORT (8b) – Type of randomization; details of any restriction (such as blocking and block size).
	<ul> <li>Options:         <ul> <li>Yes → Provided the details of how the randomization accounted for key confounding variables (e.g., blocking, minimization, stratification)</li> <li>No → Not provided</li> </ul> </li> </ul>
•	CONSORT (9) – Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.
	<ul> <li>Options:         <ul> <li>Yes → Provided details of how the physical randomization was performed or how the participants were notified of their allocation (e.g., phone call, sealed envelopes, centralized allocation)</li> <li>No → Not provided</li> </ul> </li> </ul>
•	CONSORT (10) – Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.
	<ul> <li>Options:</li> <li>Yes → Must include a clear description of who performed ALL of these tasks</li> <li>Unclear → If description of one of these tasks is inadequate or missing</li> </ul>
	• No $\rightarrow$ If two or more of these tasks are poorly described or not described at all
	<ul> <li>IIP:</li> <li>An exception can be made for participant assignment criteria for studies using centralized allocation.</li> </ul>
•	CONSORT (11a) – If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.
	<ul> <li>Options:</li> <li>Yes → Details regarding testers AND data analyzers are provided</li> <li>Unclear → If any of the aforementioned details are provided but poorly described</li> <li>No → If any of the aforementioned details are missing</li> </ul>
	• No $\rightarrow$ If any of the aforementioned details are missing $\circ$ TIP:
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	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

- Remember, we are assessing if the <u>reporting is complete</u> NOT how good the methods are. Therefore, if authors state that the outcome assessors were not blinded, we would consider this good reporting and assign a 'Yes' for this category.
- Trials listing "double-blind" or "open label" qualify as complete reporting

# • CONSORT (11b) – If relevant, description of the similarity of interventions.

# • Options:

- NA → If it is a 2-arm trial with a non-pharma control group comparison OR a 3+ -arm trial with obviously different intervention groups
- Yes → If details are adequately provided for two or more <u>intervention</u> arms with similar pharma interventions
- No → If details are not adequately provided for two or more <u>intervention</u> arms with similar pharma interventions

o TIP:

• NA is not an option for superiority trials (i.e., pharma trials with only two similar intervention arms)

# Intervention Details

- INTERVENTION TYPE Exercise or Pharmaceutical
  - Options:
    - Exercise → Stated methods included delivery of a structured exercise program with a stated goal of improving a health/fitness/psychosocial outcome.
    - **Pharmaceutical** → Stated methods included delivery of a pharmaceutical intervention with a stated goal of improving health.

# • DETAILS – Was there a run-in / lead-in period?

# • **Options:**

- Yes  $\rightarrow$  Authors clearly stated there was a run-in period
- **Unclear**  $\rightarrow$  Appears to be a run-in period, but it was not well described
- No  $\rightarrow$  No evidence of a run-in period

# • DETAILS – How many weeks was the run-in period?

- Note the total duration of the run-in period in weeks
- $\circ \quad \mathbf{NR} \to \text{If not reported}$
- DETAILS Please provide the details of the run-in period, including the modality of drug administration, dose and frequency.
  - Note all pertinent details
- DETAILS What was the total length of the program/intervention (weeks)?
  - $\circ$   $\;$  Note the total duration of the intervention in weeks
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
  - **Options:** 
    - Yes → Must define the period over which the intervention was delivered according to a specific number of weeks/months or life period

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 No → Not clearly defined (e.g., stated during chemotherapy without providing the average number of weeks/months)

- DETAILS How many phases did the intervention have?
  - Note the total number of intervention phases
- DETAILS How many pharmaceutical intervention groups were there?
  - Indicate 1, 2, 3 or 4 groups, as appropriate.

#### PHASE I/II – DETAILS

- DETAILS How many weeks was this phase?
  - Note number of weeks
  - $\circ$  **NR**  $\rightarrow$  If not reported

#### • DETAILS – Where did this phase of the intervention take place?

- Check off which of these intervention settings apply
  - Hospital
  - Research laboratory
  - Outpatient medical clinic
  - Home
  - Other
- o TIP:
  - Check off more than one if needed
  - Check off Home if regular (e.g., daily) doses are prescribed and no other locations are described

#### • DETAILS – If Other, please list.

- Note location of intervention
- $\circ$  **NR**  $\rightarrow$  If not reported

#### • DETAILS – What was the modality of drug administration?

- Check off which of these intervention modalities apply
  - Oral (PO)
  - Injection (IN)
  - Topical (Top)
  - Intraosseous (IO)
  - Transdermal (TD)
  - Inhalent (INH)
  - Per rectum (PR)
  - Sublingual (SL)
  - Other
  - Not Reported
- o TIP:
  - Check off more than one modality when applicable
- DETAILS If Other, please list.
  - Note modality of drug administration
  - $\circ$  **NR**  $\rightarrow$  If not reported

# Pharma Dose and Frequency Extraction Example:

- Patients taking two 500 mg capsules of a drug (total 1000 mg) twice a day
  - **Dose:** 1000 mg / 2
  - Frequency: 2x / day

# • DETAILS – What dose of drug was administered?

- Note the dose of drug administered
- $\circ \quad \mathbf{NR} \rightarrow \text{If not reported}$
- o TIP:
  - List total dose and fractionation (e.g., two 500 mg capsules  $\rightarrow$  1000 mg / 2)

# • DETAILS – What was the frequency of drug administration (# per day or week)?

- Note the frequency (number or range) of drug administration
- $\mathbf{NR} \rightarrow \mathbf{If} \text{ not reported}$
- o TIP:
  - List frequency per day or week (e.g., twice daily  $\rightarrow 2x / day$ )

#### • DETAILS – Was there a co-intervention prescribed for this group?

- Options:
  - Yes  $\rightarrow$  If the details of a non-pharmacologic co-intervention was described
    - If yes, write 'Yes' and provide details
  - No  $\rightarrow$  If there was no non-pharmacologic co-intervention described
    - If no, write 'No' only

#### o **TIP:**

 Co-interventions do not include concomitant use of medications or therapies unless they have been specifically administered/prescribed in the context of the intervention

# Intervention Summary

- CONSORT (5) Described the interventions for each group with sufficient details to allow replication, including how and when they were actually administered.
  - Options:
    - Yes → Provided a complete description of the intervention, such that you could confidently reproduce the intervention
    - No  $\rightarrow$  If they failed to provide sufficient detail (even if they provided a reasonable amount)
  - o TIP:
    - Must describe the type, modality, dose, frequency and any co-interventions to warrant a Yes (intervention location not necessarily required).

# Sample Size & Statistics

- CONSORT (12a) Statistical methods used to compare groups for primary and secondary outcomes.
  - Options:
    - Yes → The methods used to compare the groups on the primary and secondary outcomes are clearly described

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	C	
	e is any ambiguity in the description ct is not described	
CONSORT (7a) – How sample size	e was determined.	
• Options:		
	the details of the power calculation (i.e., ba	
	op-outs – how many participants were need specifically stated that no power calculation	
<ul> <li>Yes → Authors s</li> <li>No → Any details</li> </ul>		i was penoimed
	a not provided	
• CONSORT (7b) – When applicable	e, explanation of any interim analysis or	r stopping guidelines.
<ul> <li>Options:</li> </ul>		
	n analysis or apriori defined stopping criteria	
	apriori defined the rationale, nature and me	thods for interim analyses or stoppi
criteria ■ Unclear → If any	y aspect of the rationale, nature and metho	de for the interim analysis or storni
- Officiear → frans criteria are poorly		us for the internit analysis of stoppi
	ect of the rationale, nature and methods an	e missing or if results are reported
without details pro	ovided in the methods section	<b>v</b>
o <b>TIPS</b> :		
	s: Typically used to assess the safety, feasi	
	ervention at a prespecified time-point in a tr	
	whether the trial should continue as planne e stopped altogether. <u>Do not mistake this ty</u>	
	rein the primary and/or secondary outcome	
	me-point in the overall trial.	
•	a: Likely related to the outcome of the afore	ementioned interim analyses. Must
apriori defined an	nd described and <b>NOT</b> just reported on afte	r the fact.
CONSORT (12b) – Methods for a	dditional analyses, such as subgroup ar	aavlees and adjusted analyses
$\circ$ Options:	duttonal analyses, such as subgroup al	aryses and adjusted analyses.
•	tional subgroup analyses were performed	
• Yes $\rightarrow$ If any ana	alysis other than the primary/secondary inte	
	Its of any analysis other than the primary/s	econdary intervention effects are
reported but no m	nethods are described	
Data Comparison: Sample Size		
	Sample Size	Sample Size
	Calculated	Recruited
Sample size – calculated vs actual?	Number:	Number:
• <b>TIP:</b>		
	sample size listed in the Registry and Manu	iscript are different, please note bot
values (e.g., Reg	: ##; Man: ##).	

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RESULTS	
Participant Flow	
<ul> <li>CONSORT (13)</li> <li>Option:</li> </ul>	– Participant flow diagram (a diagram is strongly recommended). s:
:	$\textbf{Yes} \rightarrow \textbf{A}$ clear depiction of participant flow was provided $\textbf{No} \rightarrow \textbf{Not}$ provided
<ul> <li>CONSORT (13b</li> <li>Option:</li> </ul>	$NA \rightarrow$ If authors specifically state there were no losses/exclusions post randomization $Yes \rightarrow$ Provided a complete account of all randomized participants $Unclear \rightarrow$ If all randomized participants are accounted for but the details of any participant are
•	unclear $No \rightarrow If$ any details of any participant are missing
Participants, Analyses	s & Outcomes
<ul> <li>CONSORT (15)</li> <li>Option:</li> </ul>	A table showing baseline demographic and clinical characteristics for each group.
	$\textbf{Yes} \rightarrow \textbf{A}$ unique table displaying demographic data is provided $\textbf{No} \rightarrow \textbf{Table}$ not provided
•	) – For each group, the number of participants who were randomly assigned, received ent, and were analyzed for the primary outcome.
	Yes $\rightarrow$ All requisite details were provided No $\rightarrow$ Any of the requisite details are not provided
○ <b>TIP:</b> ■	Must include sample sizes in the body of the Results or directly within the Results tables.
. ,	– For each group, number of participants (denominator) included in each analysis and Ilysis was by original assigned groups. s:

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3	Yes → Must provide details of how many participants from each group were included within each
4	analysis
5	<ul> <li>Unclear → The authors suggest that analyses were performed according to intention-to-treat but</li> </ul>
6	failed to provide a description of how missing data from drop-outs or testing errors was accounted
7	for
8	• <b>Unclear</b> $\rightarrow$ The authors provided numbers for the analysis but did not indicate that analyses
9	adhered to intention-to-treat principles
10 11	• No $\rightarrow$ Data not provided
12	○ TIPS:
13	<ul> <li>This information is typically reported in the main results tables in the form of (n = #) but may also</li> </ul>
14	be found in the results section.
15	<ul> <li>Double check the flow diagram to check for potential dropouts/missing data.</li> </ul>
16	• If any participants withdrew or were lost to follow-up, the authors should disclose how
17	their missing data was treated.
18	<ul> <li>Must include sample sizes in the body of the Results or directly within the Results tables.</li> </ul>
19	
20	CONCORT (17a) For each primary and eccordary outcome results for each group and the estimated effect
21	• CONSORT (17a) – For each primary and secondary outcome, results for each group, and the estimated effect
22	size and its precision (such as 95% confidence interval).
23	• Options:
24	• Yes $\rightarrow$ Authors must provide the raw baseline data, raw or adjusted follow-up data, change scores
25	or effect sizes, AND 95% CI data
26	<ul> <li>No → Missing any of the aforementioned data</li> </ul>
27	
28	<ul> <li>CONSORT (17b) – For binary outcomes, presentation of both absolute and relative effect sizes is</li> </ul>
29	recommended.
30	• Options:
31	• $NA \rightarrow If$ no binary outcomes are tracked/reported
32	• Yes $\rightarrow$ Authors provide an indication of the actual number of observations relative to the expected
33	number of observations <b>AND</b> whether the ratio of observations differed between groups
34	• No $\rightarrow$ Missing any of the aforementioned data
35	
36	<ul> <li>CONSORT (18) – Results of any other analyses performed, including subgroup analyses and adjusted</li> </ul>
37	analyses, distinguishing pre-specified from exploratory.
38	• Options:
39	• NA $\rightarrow$ If no subgroup or sensitivity analysis were performed
40	<ul> <li>Yes → If the results of any analysis other than the main intervention effects were performed and</li> </ul>
41	reported
42	• No $\rightarrow$ If the results of any analysis other than the main intervention effects were performed but not
43	
44	reported
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49	DETAILS – What was the outcome of this trial?
50 <b>•</b>	• Options:
51 52	<ul> <li>■ Positive → As hypothesized, there was a significant difference in the primary outcome</li> </ul>
53	• <b>Negative</b> $\rightarrow$ Contrary to the hypothesis, there was no significant difference in the primary outcome
54	• <b>Unclear</b> $\rightarrow$ If the primary findings are not well defined or not interpretable
55	• <b>Mixed</b> $\rightarrow$ Only an option for trials with more than one primary outcome (rare)
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59	75
60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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# **Trial Characteristics**

•	CONSORT (14b) – Why the trial ended or was stopped.
	<ul> <li>Ontions:</li> </ul>

- Options:
  - NA → If the trial appeared to finish as planned (i.e., achieved target sample size and concluded the intervention and follow-up tested as intended)
  - Yes  $\rightarrow$  If the trial stopped early or was extended **AND** a full justification was provided
  - Unclear → If the trial stopped early or was extended AND the authors made special note of that fact without providing an adequate justification
  - Unclear → If the trial stopped early or was extended AND an inadequate discussion was provided
  - No 
     — If the trial stopped early or was extended BUT an adequate justification was not provided
- TIP:
  - The majority of studies will finish as planned and will be assigned an NA

# • CONSORT (14a) – Dates defining the periods of recruitment and follow-up.

- Options:
  - Yes → Must provide both the dates of when the trial was open to recruitment AND at least indicate a specific date as to when participant follow-up finished

- Unclear → Authors provided recruitment dates but only eluded to how long the follow-up period lasted (e.g., 12 months)
- No → Only provided dates of recruitment but not follow-up *OR* not at all

# DETAILS

- Recruitment (enrollment) start date:
  - Note details
  - $\circ \quad \text{Nomenclature: Date format} \rightarrow \text{MM/YY}$
  - $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$
- Recruitment (enrollment) end date:
  - Note details
  - **Nomenclature:** Date format  $\rightarrow$  MM/YY
  - $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

# • Trial start date:

- Note details
- $\circ \quad \text{Nomenclature: Date format} \rightarrow \text{MM/YY}$
- $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$

# • Trial end date:

- Note details
- **Nomenclature:** Date format  $\rightarrow$  MM/YY
- $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

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# Randomization & Testing

- Number of subjects randomized to PHARMA intervention:
  - $\circ$  **PHARMA (4)**  $\rightarrow$  *Note details* for each group as relevant
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- Number of subjects randomized to Usual Care/Control:
  - Note details
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- Number of PHARMA participants tested at baseline:
  - PHARMA (4)  $\rightarrow$  Note details for each group as relevant
  - $\circ$  **NR**  $\rightarrow$  If not reported
- Number of Usual Care/Control participants tested at baseline:
  - Note details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- Number of PHARMA participants tested at follow-up:
  - **PHARMA (4)**  $\rightarrow$  *Note details* for each group as relevant
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$
- Number of Usual Care/Control participants tested at follow-up:
  - Note details
  - $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$

#### Demographics

- Total number of subjects:
  - Note details
  - $\circ$  NR  $\rightarrow$  If not reported

#### • Number of male participants:

- Note details
- $\circ \quad \mathbf{NR} \to \text{If not reported}$
- Number of female participants:
  - Note details
  - $\circ$  NR  $\rightarrow$  If not reported
- Average age of all participants:
  - Note details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$
- Average age of PHARMA participants:

To 22

- o Note details
- $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

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# • Average age of Usual Care/Control participants:

- Note details
- $\circ \quad \mathbf{NR} \to \mathsf{lf} \text{ not reported}$

#### **Medical Characteristics**

• Average disease duration (months):

- Not Applicable
- <6 months</li>
- <12 months</li>
- o <24 months
- o <60 months
- o <120 months
- $\circ$  ≥120 months
- $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$

# Comorbidities

# Hypertension (n):

#### • Note details

- $NR \rightarrow If not reported$
- $NA \rightarrow$  If listed in exclusion criteria

# Hypercholesterolemia (n):

- Note details
- $NR \rightarrow If not reported$
- $NA \rightarrow If$  listed in exclusion criteria

# Diabetes (n):

- Note details
- $NR \rightarrow If not reported$
- $NA \rightarrow$  If listed in exclusion criteria

# **Pharmaceutical Outcomes**

#### PHARMA (4) & UC Compliance: Number:

• Note details

# $NR \rightarrow If$ not reported *OR* if trial reports compliance as X% attended X% of sessions

Percent: Note details

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# Hypertension (%): Note details

Hypercholesterolemia (%): Note details

Diabetes (%): Note details

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	Cannot be NA	
PHARMA (4) & UC RDI:		
	Number:	Percent: Note details
	Note details	
	• NR $\rightarrow$ If not reported	
	Cannot be <b>NA</b>	
PHARMA (4) & UC Dose Me	odification:	
	Number:	Percent: Note details
	Note details	
	• NR $\rightarrow$ If not reported	
	<ul> <li>If no dose modifications occ</li> </ul>	urred list as '0' not <b>NA</b>
PHARMA (4) & UC Treatme	ent Discontinuation:	
. ,	Number:	Percent: Note details
	Note details	
	• $\mathbf{NR} \rightarrow \mathbf{If} \text{ not reported}$	
	<ul> <li>If no dose modifications occ</li> </ul>	urred list as '0' not NA
Exclusion		
PHARMA (4) Exclusion –		
	Number:	Percent: Note details
	Note details	
	• <b>NR</b> $\rightarrow$ If not reported	
	<ul> <li>If no participants were exclu</li> </ul>	ided list as '0' not NA
UC Exclusion –	Number:	Percent: Note details
	Note details	
	• <b>NR</b> $\rightarrow$ If not reported	
	<ul> <li>If no participants were exclu</li> </ul>	ided list as 'U' not NA
	<i>k</i>	
• TIP ( <i>if patient attrition</i>		nutation) and authors confirm that the results do
$\circ$ <b>NA</b> $\rightarrow$ When n	nissing data strategies are used (e.g., im	putation) and authors confirm that the results do
$\circ$ <b>NA</b> $\rightarrow$ When n differ with or with	nissing data strategies are used (e.g., im ithout the imputed data.	
<ul> <li>NA → When n differ with or wi</li> <li>For trials repor</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data.	lusion' cannot be assigned unless confirmed by
<ul> <li>NA → When n differ with or wi</li> <li>For trials repor</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data. ting intention to treat analyses, 'zero excl	lusion' cannot be assigned unless confirmed by
<ul> <li>NA → When n differ with or wi</li> <li>For trials reportion</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data. ting intention to treat analyses, 'zero excl	lusion' cannot be assigned unless confirmed by
<ul> <li>NA → When n differ with or wi</li> <li>For trials repor</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data. ting intention to treat analyses, 'zero excl	lusion' cannot be assigned unless confirmed by
<ul> <li>NA → When n differ with or wi</li> <li>For trials reportion</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data. ting intention to treat analyses, 'zero excl	lusion' cannot be assigned unless confirmed by
<ul> <li>NA → When n differ with or wi</li> <li>For trials reportion</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data. ting intention to treat analyses, 'zero excl	lusion' cannot be assigned unless confirmed by
<ul> <li>NA → When n differ with or wi</li> <li>For trials repor</li> </ul>	nissing data strategies are used (e.g., im ithout the imputed data. ting intention to treat analyses, 'zero excl	

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#### **CONSORT – HARMS**

- HARMS (19a) If the study collected data on harms and benefits, the title or abstract should so state.
   Options:
  - NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
  - Yes  $\rightarrow$  If authors mention safety or AEs anywhere in the title or abstract
  - $No \rightarrow$  If safety or AEs are not mentioned in these sections
  - TIPS:
    - IMPORTANT All Phase I-II, by definition, should report safety outcomes. Thus, the safety
      of the intervention should be assessed and reported on.
- HARMS (19b) If the trial addresses both harms and benefits, the introduction should so state.
  - Options:
    - NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
    - Yes → Authors should state the safety of the intervention is in question OR they should state that one of the trial objectives (typically last paragraph of the intro) is to assess the safety of the intervention.
    - No  $\rightarrow$  Not mentioned
- HARMS (19c) List addressed adverse events with definitions for each (when relevant, attention to grading,
  - expected vs. unexpected AEs, reference to standardized and validated definition, and description of new definitions). • Options:
    - NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
    - Yes  $\rightarrow$  Authors listed AND defined the potential/anticipated AEs being studied
    - Unclear  $\rightarrow$  Authors listed the AEs but failed to define them
    - No → Details not provided
    - $\circ$  TIPS:
      - For trials reporting AEs as the primary and secondary outcomes, the definitions for the outcomes count towards defining the AEs.
- HARMS (19d) Clarify how harms-related data was collected (mode of collection, timing, attribution methods, intensity of ascertainment, and harms-related monitoring and stopping rules).
  - Options:
    - NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
    - Yes  $\rightarrow$  Authors should clearly state how, when **AND** by whom AE data was collected
    - **Unclear** → Authors fail to properly describe a single aspect (how, when, by whom) of how the AE data was collected but adequately describe all other aspects
    - No → Details not provided
  - $\circ$  TIPS:
    - For trials reporting AEs as the primary and secondary outcomes, the collection methods for the outcomes count towards collecting the AEs.
- HARMS (19e) Describe plans for presenting and analyzing information on harms (including coding, handling of recurrent event, specification of timing issues, handling of continuous measures, and statistical analyses).
  - **Options:**

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- NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
- Yes  $\rightarrow$  Authors should clearly state how AE data was analyzed
- Unclear → Authors fail to properly describe a single aspect of how the AE data was analyzed but adequately describe all other aspects
- No  $\rightarrow$  Details not provided

# **GENERAL TIPS FOR HARMS:**

- If authors fail to explicitly state if AEs were attributable to the intervention, check to see if there were analyses comparing AE frequency or relative risk per arm.
  - If analyses were performed:
    - For AEs which occur significantly more frequently within the intervention group(s) → list details for those specific AEs under 'intervention-related'
    - For AEs which do not occur significantly more frequently within the intervention group(s) → list details for those specific AEs under 'non-intervention-related'
  - o If analyses were not performed:
    - Rate 'intervention-related' AEs as NR
    - List all reported AEs for both groups as 'non-intervention-related'
- For trials reporting AEs as the primary and secondary outcomes, the analysis methods for the outcomes count towards analyzing the AEs.

# Intervention-related AEs

- DETAILS Did any intervention-related AE occur?
  - $\circ$  NA  $\rightarrow$  Specifically stated that no intervention-related AEs occurred
  - $\circ$  Yes  $\rightarrow$  Specifically stated the type and number of intervention-related AEs
  - $\circ$  Unclear  $\rightarrow$  The numbers are provided but the details are unclear
  - $\circ \quad \textbf{No} \rightarrow \textbf{Details not provided}$

# • DETAILS – If so, how many?

- Note pertinent details
- $\circ \quad \mathbf{NR} \to \text{If not reported}$
- DETAILS How were intervention-related AE defined?
  - Note pertinent details
  - $\circ \quad \mathbf{NR} \to \text{If not reported}$

# DETAILS – How were intervention-related AE monitored/tracked?

- o Note pertinent details
- $\circ \quad \textbf{NR} \rightarrow \textbf{If not reported}$

# Non-Intervention-related AEs

• DETAILS – Did any non-intervention-related AE occur?

- $\circ \quad \textbf{NA} \rightarrow \textbf{Specifically stated that no intervention-related AEs occurred}$
- $\circ$  Yes  $\rightarrow$  Specifically stated the type and number of intervention-related AEs
- $\circ\quad$  Unclear  $\rightarrow$  The numbers are provided but the details are unclear
- $\circ \quad \textbf{No} \rightarrow \textbf{Details not provided}$

# • DETAILS – If so, how many?

- Note pertinent details
- $\circ \quad \mathbf{NR} \rightarrow \text{If not reported}$

# • DETAILS – How were non-intervention-related AE defined?

- Note pertinent details
- $\circ \quad \mathbf{NR} \to \text{If not reported}$

# DETAILS – How were non-intervention-related AE monitored/tracked?

- Note pertinent details
- **NR**  $\rightarrow$  If not reported

# **AEs Per Group**

- DETAILS How many AEs were reported for the PHARMA (4) & UC groups?
  - Note pertinent details
  - $\circ$  **NR**  $\rightarrow$  If not reported

# HARMS Continued...

• HARMS (19f) – Describe for each arm the participant withdrawals that are due to harms and their experiences with the allocated treatment.

# • **Options:**

- NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
- NA → If the authors specifically stated there were no AEs OR that no participant withdrew/was lost to follow-up due to AEs
- Yes → If the authors clearly identify the number of participants who withdrew or were lost to follow-up due to AEs
- No → If the reasons why participants withdrew or were lost-to-follow-up are not provided for every applicable case
- HARMS (19g) Provide denominators for analyses on harms.

# • Options:

- NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented risks and is no longer the question
- $NA \rightarrow If$  the authors specifically stated there were no AEs
- Yes  $\rightarrow$  Reference numbers provided for AE risk calculations
- No  $\rightarrow$  Details not provided
- HARMS (19h) Presents absolute risk per arm and per AE type, grade, and seriousness, and present appropriate metrics for recurrent events, continuous variables, and scale variables.

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2	
3	<ul> <li>Options:</li> </ul>
4	■ NA → Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented
5	risks and is no longer the question
6	• $NA \rightarrow If$ the authors specifically stated there were no AEs
7	• Yes $\rightarrow$ If the authors present the absolute risk per arm <b>AND</b> per adverse event type/grade <b>AND</b>
8	
9	describe the frequency of AEs
10	<ul> <li>No → Details not provided</li> </ul>
11	
12	<ul> <li>HARMS (19i) – Describes any subgroup analyses and exploratory analyses for harms.</li> </ul>
13	• Options:
14	• NA $\rightarrow$ Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented
15	risks and is no longer the question
16	• $NA \rightarrow If$ the authors specifically stated there were no AEs
10	
	• Yes $\rightarrow$ If the authors present the results of subgroup analyses or exploratory analyses
18 10	<ul> <li>No → Details not provided</li> </ul>
19	
20	<ul> <li>HARMS (19j) – Provide a balanced discussion of benefits and harms with emphasis on study limitation,</li> </ul>
21	generalizability, and other sources of information on harms.
22	• Options:
23	• NA $\rightarrow$ Testing an intervention (e.g., calcium, insulin) which has either no risks or well documented
24	risks and is no longer the question
25	
26	• $NA \rightarrow If$ the authors specifically stated there were no AEs
27	• Yes $\rightarrow$ Should formally address any AEs in the Discussion in the context of trial limitations and
28	whether the risk intervention-related AEs should be considered when implementing or conducting
29	further tests of the intervention in question.
30	• No $\rightarrow$ Not discussed
30 31	• No $\rightarrow$ Not discussed
	• No $\rightarrow$ Not discussed
31	No → Not discussed
31 32	No → Not discussed
31 32 33	
31 32 33 34	<ul> <li>No → Not discussed</li> <li>DISCUSSION &amp; OTHER</li> </ul>
31 32 33 34 35	
31 32 33 34 35 36	DISCUSSION & OTHER
31 32 33 34 35 36 37	DISCUSSION & OTHER  • CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant,
31 32 33 34 35 36 37 38	DISCUSSION & OTHER • CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.
31 32 33 34 35 36 37 38 39	DISCUSSION & OTHER • CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses. • Options:
31 32 33 34 35 36 37 38 39 40	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) – Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options:         <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results.</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors.</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations.</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and</li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options:</li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options: <ul> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options:</li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options: <ul> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options: <ul> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	<ul> <li>DISCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, multiplicity of analyses.</li> <li>Options: <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>Options: <ul> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators,</li> </ul> </li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 40 41 42 43 44 45 46 47 48 49 50 51 51 52 53 54 55 56 57 58	<ul> <li>DSCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, nultiplicity of analyses.</li> <li>Options <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>9 Options</li> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators, patient groups, and care provider/centers.</li> </ul>
31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59	<section-header><section-header><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item><list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></list-item></section-header></section-header>
31 32 33 34 35 36 37 38 39 40 41 42 43 40 41 42 43 44 45 46 47 48 49 50 51 51 52 53 54 55 56 57 58	<ul> <li>DSCUSSION &amp; OTHER</li> <li>CONSORT (20) - Trial limitations: addressing sources of potential bias, imprecision, and if relevant, nultiplicity of analyses.</li> <li>Options <ul> <li>Yes → If authors listed major sources of potential bias or measurement error AND provided basic details as to how these factors may have influenced results</li> <li>Unclear → Authors listed sources of bias but failed to adequately discuss the potential impact/implications of these factors</li> <li>No → Failed to list and adequately discuss potential sources of bias within the description of trial limitations</li> </ul> </li> <li>CONSORT (21) - Generalizability of trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.</li> <li>9 Options</li> <li>Yes → Authors must discuss their findings in the context of similar interventions, comparators, patient groups, and care provider/centers.</li> </ul>

- No → None of these aspects were not adequately discussed within the context of other research (past and future)
- CONSORT (22) Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.
  - Options:

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- Yes → Authors should not overstate non-significant or modestly altered endpoints; nor should they
  dismiss/ignore/fail to adequately describe non-significant findings for any of the primary outcomes
  in favor of discussing secondary outcomes
- No → Authors do not present an unbiased interpretation of their findings
- o TIP:
  - Look closely at the results for the primary outcomes (data tables). The first paragraph of the Discussion should summarize these results without inflating/downplaying the findings. Similarly, the Conclusion should also provide an unbiased summary of the main trial findings.
- CONSORT (23) Registration number and name of trial registry.
  - Options:
    - Yes  $\rightarrow$  If the number was provided
    - Yes → If authors clearly stated the trial was not registered
    - No  $\rightarrow$  If the number was not provided
  - o TIP:
    - Check the abstract, methods, and footnotes/margins of the paper to locate this number.
- DETAILS If so, please list.
  - Note pertinent details
- CONSORT (24) Where the full trial protocol can be accessed, if available.
  - Options:
    - Yes → If the full protocol or a link to the full protocol is provided in the primary manuscript or as an online supplement
    - No  $\rightarrow$  Data not provided
  - o TIP:
    - Check the abstract, methods, and footnotes/margins of the paper to locate this number.
- DETAILS If so, please provide the URL:
  - Note pertinent details
- CONSORT (25) Sources of funding and other support, role of funders.
  - Options:
    - Yes  $\rightarrow$  If described
    - Unclear  $\rightarrow$  If described either the funder or the role but not both
    - No  $\rightarrow$  Not described
  - o **TIP:** 
    - Similar to the registration number, check the footnotes, margins, and any supplemental information listed between the Conclusion and the Reference list.
- DETAILS If so, please provide the details:
  - o Note pertinent details

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# COCHRANE – Risk of Bias

# • Selection Bias: Random sequence generation

- High → Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence
- $\circ \quad \text{Low} \rightarrow \text{Random sequence generation method should produce comparable groups}$
- $\circ \quad \textbf{Unclear} \rightarrow \text{Not described in sufficient detail to permit judgement}$

# • Selection Bias: Allocation concealment

- High → Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment
- $\circ$  Low  $\rightarrow$  Intervention allocations likely could not have been foreseen in before or during enrollment
- $\circ \quad \textbf{Unclear} \rightarrow \textbf{Not} \text{ described in sufficient detail to permit judgement}$

# Performance Bias: Blinding (participants & personnel)

- High → Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
- $\circ \quad \text{Low} \rightarrow \text{Blinding was likely effective}$
- $\circ$  Unclear  $\rightarrow$  Not described in sufficient detail to permit judgement

# • Detection Bias: Blinding (outcome assessment)

- $\circ$  High  $\rightarrow$  Detection bias due to knowledge of the allocated interventions by outcome assessors
- $\circ \quad \text{Low} \rightarrow \text{Blinding was likely effective}$
- $\circ \quad \textbf{Unclear} \rightarrow \textbf{Not} \text{ described in sufficient detail to permit judgement}$

# Attrition Bias: Incomplete outcome data

- $\circ$  High  $\rightarrow$  Attrition bias due to amount, nature or handling of incomplete outcome data
- $\circ$  Low  $\rightarrow$  Handling of incomplete outcome data was complete and unlikely to have produced bias
- Unclear → Insufficient reporting of attrition/exclusions to permit judgment (e.g., number randomized not stated, no reasons for missing data provided)

# • Reporting Bias: Selective reporting

- $\circ$  High  $\rightarrow$  Reporting bias due to selective outcome reporting
- $\circ \quad \text{Low} \rightarrow \text{Selective reporting bias not detected}$
- $\circ \quad \textbf{Unclear} \rightarrow \text{Insufficient information to permit judgment}$
- Other sources of bias
  - $\circ\quad \mbox{High} \rightarrow \mbox{Bias}$  due to problems not covered elsewhere in the criteria
  - $\circ \quad \mathbf{Low} \to \mathsf{No} \text{ other bias detected}$
  - $\circ$  **Unclear**  $\rightarrow$  There may be a risk of bias, but there is insufficient information to assess whether an important risk of bias exists or insufficient rationale or evidence that an identified problem will introduce bias

# Quality Comments: Justify 'high-risk' & 'unclear' decisions

• Please note pertinent details

# JADAD Score

- Randomization Score:
  - 1 point if randomization is mentioned
  - o 1 additional point if the method of randomization is appropriate
  - Deduct 1 point if the method of randomization is inappropriate (minimum 0)

#### • Blinding Score:

- o 1 point if blinding is mentioned
- 1 additional point if the method of blinding is appropriate
- Deduct 1 point if the method of blinding is inappropriate (minimum 0)

# • Account of All Patient Score:

o 1 point if the fate of all patients in the trial is known. If there are no data the reason is stated.

# Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclus Criteria		
Cumming et al.	2008	Cluster randomised trial of a targeted multifactorial intervention to prevent falls among older people in hospital	Not exercise-bas		
Dixon et al.	2008	Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial	Not exercise-bas		
Hollinghurst et al.	2008	Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain: economic evaluation	Not exercise-base		
Kerse et al.	2008	Does a functional activity programme improve function, quality of life, and falls for residents in long term care? Cluster randomised controlled trial	Exercise session duration too short		
Kinmonth et al.	2008	Efficacy of a theory-based behavioural intervention to increase physical activity in an at-risk group in primary care (ProActive UK): a randomised trial	Not exercise-base		
Lautenschlager et al.	2008	Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: a randomized trial	Not exercise-base		
Li et al.	2008	The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study	Secondary analys		
Little et al.	2008	Randomised controlled trial of Alexander technique lessons, exercise, and massage (ATEAM) for chronic and recurrent back pain	Not exercise-base		
Lloyd & Barnett	2008	Physical activity and risk of diabetes	Not a RCT		
Lloyd et al.	2008	Physical activity and risk of diabetes	R/C paper		
Mitka, M.	2008	Therapies aim to boost "good" cholesterol	R/C paper		
NA	2008	Summaries for patients. A combination treatment for pulmonary hypertension	Not a RCT		
Pasanen et al.	2008	Neuromuscular training and the risk of leg injuries in female floorball players: cluster randomised controlled study			
Barton et al.	2009	Lifestyle interventions for knee pain in overweight and obese adults aged ≥45: Economic evaluation of randomised controlled trial	Secondary analys		
Boysen et al.	2009	ExStroke Pilot Trial of the effect of repeated instructions to improve physical activity after ischaemic stroke: A multinational randomised controlled clinical trial	Not exercise-base		
Engebretsen et al.	2009	Radial extracorporeal shockwave treatment compared with supervised exercises in patients with subacromial pain syndrome: Single blind randomised study	Not exercise-base		
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-action randomized controlled trial	Secondary analys		
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION D randomized controlled trial			
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial	Secondary analys		
Flynn et al.	2009	Effects of exercise training on health status in patients with chronic heart failure: HF-action randomized controlled trial.	Secondary analys		
Hupperets et al.	2009	Effect of unsupervised home based proprioceptive training on recurrences of ankle sprain: Randomised controlled trial	Not exercise-base		
Jafar et al.	2009	Community-based interventions to promote blood pressure control in a developing country: A cluster randomized trial	Not exercise-base		
Jarvik et al.	2009	Surgery versus non-surgical therapy for carpal tunnel syndrome: a randomised parallel-group trial	Not exercise-base		
Jenkinson et al.	2009	Effects of dietary intervention and quadriceps strengthening exercises on pain and function in overweight people with knee pain: Randomised controlled trial	Not exercise-base		
Karthikeyan et al.	2009	Treatment of intermittent claudication	R/C paper		
Khattri, S.	2009	Treadmill exercise or resistance training in patients with peripheral arterial disease	R/C paper		
Khattri, S.	2009	Treadmill exercise or resistance training in patients with peripheral arterial disease	Not a RCT		
Kuijper et al.	2009	Cervical collar or physiotherapy versus wait and see policy for recent onset cervical radiculopathy: Randomised trial	Not exercise-base		
Lautenschlager et al.	2009	Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: A randomized trial	Duplicate		
Lautenschlager et al.	2009	Effect of physical activity on cognitive function in older adults at risk for Alzheimer disease: A randomized trial.	Not exercise-base		

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclus Criteria			
Lawton et al.	2009	Exercise on prescription for women aged 40-74 recruited through primary care: Two year randomised controlled trial	Not exercise-bas			
Marshall et al.	2009	Losing weight in moderate to severe obstructive sleep apnoea	R/C paper			
McDermott et al.	2009	Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial	Duplicate			
Mead, G.	2009	Exercise after stroke Is beneficial but how best to increase physical activity is unknown	R/C paper			
Misra, A.	2009	Prevention of type 2 diabetes: the long and winding road	R/C paper			
Morey et al.	2009	Effects of home-based diet and exercise on functional outcomes among older, overweight long- term cancer survivors: RENEW: a randomized controlled trial	Not exercise-bas			
O'Connor et al.	2009	Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial	Duplicate			
Patwala et al.	2009	Maximizing Patient Benefit From Cardiac Resynchronization Therapy With the Addition of Structured Exercise Training. A Randomized Controlled Study	Duplicate			
Ravaud et al.	2009	ARTIST (osteoarthritis intervention standardized) study of standardised consultation versus usual care for patients with osteoarthritis of the knee in primary care in France: Pragmatic randomised controlled trial				
Sackley et al.	2009	Effects of a physiotherapy and occupational therapy intervention on mobility and activity in care home residents: A cluster randomised controlled trial	Not exercise-bas			
Schmitz et al.	2009	Weight lifting in women with breast-cancer-related lymphedema	Duplicate			
Schweickert et al	randomised controlled trial					
Soligard et al.	2009	Comprehensive warm-up programme to prevent injuries in young female footballers: Cluster N randomised controlled trial				
Subak et al.	2009	Weight loss to treat urinary incontinence in overweight and obese women	Not exercise-bas			
Van Linschoten et al.	2009	Supervised exercise therapy versus usual care for patellofemoral pain syndrome: An open label randomised controlled trial	Not exercise-bas			
Bennell et al.	2010	Efficacy of standardised manual therapy and home exercise programme for chronic rotator cuff disease: Randomised placebo controlled trial				
Bleakley et al.	2010	Effect of accelerated rehabilitation on function after ankle sprain: Randomised controlled trial	Not exercise-bas			
Crawshaw et al.	2010	Exercise therapy after corticosteroid injection for moderate to severe shoulder pain: Large pragmatic randomised trial	Not exercise-bas			
Frobell et al.	2010	A randomized trial of treatment for acute anterior cruciate ligament tears	Not exercise-ba			
Goodpaster et al.	2010	Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial	Not exercise-ba			
Lacomba et al.	2010	Effectiveness of early physiotherapy to prevent lymphoedema after surgery for breast cancer: Randomised, single blinded, clinical trial	Not exercise-ba			
Lo et al.	2010	Robot-assisted therapy for long-term upper-limb impairment after stroke	Not exercise-ba			
Logan et al.	2010	Community falls prevention for people who call an emergency ambulance after a fall: randomised controlled trial	Not exercise-ba			
Lombard et al.	2010	A low intensity, community based lifestyle programme to prevent weight gain in women with young children: Cluster randomised controlled trial	Not exercise-ba			
Rock et al.	2010	Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial	Not exercise-ba			
Schmitz et al.	2010	Weight lifting for women at risk for breast cancer-related lymphedema: a randomized trial	Duplicate			
Sixt et al.	2010	Long- but not short-term multifactorial intervention with focus on exercise training improves coronary endothelial dysfunction in diabetes mellitus type 2 and coronary artery disease	Not exercise-bas			
van Eijk-Hustings et al.	2010	A randomized trial of tai chi for fibromyalgia	R/C paper			
Van Gelder et al.	2010	Lenient versus strict rate control in patients with atrial fibrillation	Not exercise-ba			
Wang et al.	2010	A randomized trial of tai chi for fibromyalgia	Not exercise-ba			
Wearden et al.	2010	Nurse led, home based self help treatment for patients in primary care with chronic fatigue syndrome: randomised controlled trial	Not exercise-ba			
Zhan & Wu	2010	A randomized trial of tai chi for fibromyalgia	Duplicate			
Zhou et al.	2010	A randomized trial of tai chi for fibromyalgia	Duplicate			

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclus Criteria			
Andrews et al.	2011	Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial	Not exercise-base			
Bleijenberg & Knoop	2011	Chronic fatigue syndrome: Where to PACE from here?	Not a RCT			
Church et al.	2011	Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: A randomized controlled trial	Duplicate			
Church et al.	2011	Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: A randomized controlled trial	Duplicate			
Devoogdt et al.	2011	Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: Randomised controlled trial	Not exercise-bas			
Dubowitz et al.	2011	Exercise interventions and glycemic control in patients with diabetes	R/C paper			
Dubowitz et al.	2011	Exercise interventions and glycemic control in patients with diabetes	Not a RCT			
Duncan et al.	2011	Body-weight-supported treadmill rehabilitation after stroke	R/C paper			
Duncan et al.	2011	Body-weight-supported treadmill rehabilitation after stroke	Not a RCT			
Edelmann et al.	2011	Exercise Training Improves Exercise Capacity and Diastolic Function in Patients With Heart Failure With Preserved Ejection Fraction Results of the Ex-DHF (Exercise training in Diastolic Heart Failure) Pilot Study				
Engel, C	2011	Tailored cognitive-behavioral therapy plus exercise training improved clinical and functional outcomes in fibromyalgia	R/C paper			
Giakoumakis, J.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
Glazener et al.	2011	Urinary incontinence in men after formal one-to-one pelvic-floor muscle training following radical prostatectomy or transurethral resection of the prostate (MAPS): two parallel randomised controlled trials	Not exercise-bas			
Gondoni & Liuzzi	2011	Diet and physical activity interventions in severely obese adults	R/C paper			
Gondoni & Liuzzi	2011	Diet and physical activity interventions in severely obese adults	Not a RCT			
Hemmingsson et al.	2011	Diet and physical activity interventions in severely obese adults	Duplicate			
Hemmingsson et al.	2011	Diet and physical activity interventions in severely obese adults	Not a RCT			
Hu, F.	2011	Diet and exercise for new-onset type 2 diabetes?	R/C paper			
Jebb et al.	2011	Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial	Not exercise-bas			
Jolly et al.	2011	Comparison of range of commercial or primary care led weight reduction programmes with minimal intervention control for weight loss in obesity: Lighten Up randomised controlled trial	Not exercise-bas			
Kewley, A.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
Khan et al.	2011	Prescribing exercise in primary care	R/C paper			
Kindlon, T.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
Langhorne et al.	2011	Stroke rehabilitation	R/C paper			
McArthur et al.	2011	Post-acute care and secondary prevention after ischaemic stroke	R/C paper			
Mitchell, J.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
Pearse et al.	2011	Managing perioperative risk in patients undergoing elective non-cardiac surgery	R/C paper			
Rice, K.	2011	A COPD disease management program reduced a composite of hospitalizations or emergency department visits	wrong journal			
Rolla & Bucca	2011	Placebo and other interventions in asthma	Not a RCT			
Shinohara, M.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
Spink et al.	2011	Effectiveness of a multifaceted podiatry intervention to prevent falls in community dwelling older people with disabling foot pain: randomised controlled trial	Not exercise-bas			
Stouten et al.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
Tilbrook et al.	2011	Yoga for chronic low back pain: A randomized trial	Not exercise-bas			
Villareal et al.	2011	Weight loss, exercise, or both and physical function in obese older adults	Duplicate			
Vlaeyen et al.	2011	The PACE trial in chronic fatigue syndrome	Not a RCT			
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#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclu Criteria		
Bennell et al.	2012	Management of osteoarthritis of the knee	R/C paper		
Blumenthal et al.	2012	Effects of exercise training on depressive symptoms in patients with chronic heart failure: The HF-ACTION randomized trial.	Duplicate		
Blumenthal et al.	2012	Effects of exercise training on depressive symptoms in patients with chronic heart failure: the HF- ACTION randomized trial	Secondary analy		
Blumenthal et al.	2012	Exercise and pharmacological treatment of depressive symptoms in patients with coronary heart disease: results from the UPBEAT (Understanding the Prognostic Benefits of Exercise and Antidepressant Therapy) study	Secondary analys		
Bronfort et al.	2012	Spinal manipulation, medication, or home exercise with advice for acute and subacute neck pain: a randomized trial	Not exercise-bas		
Chalder et al.	2012	Facilitated physical activity as a treatment for depressed adults: Randomised controlled trial	Not exercise-ba		
Clemson et al.	2012	Integration of balance and strength training into daily life activity to reduce rate of falls in older people (the LiFE study): Randomised parallel trial	Not exercise-ba		
Ernst, E.	2012	Acute and subacute neck pain	R/C paper		
Franklin, B.	2012	Multifactorial cardiac rehabilitation did not reduce mortality or morbidity after acute myocardial infarction	R/C paper		
Holmgren et al.	2012	Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: Randomised controlled study	Not exercise-ba		
Jakicic et al.	2012	Effect of a stepped-care intervention approach on weight loss in adults: a randomized clinical trial	Not exercise-ba		
Layden et al.	2012	Diagnosis and management of lower limb peripheral arterial disease: Summary of NICE guidance	R/C paper		
Lazzeri et al.	2012	Pelvic floor muscle training after prostate surgery	R/C paper		
Li et al.	2012	Tai chi and postural stability in patients with Parkinson's disease	Not exercise-ba		
Li et al.	2012	Tai chi and postural stability in patients with Parkinson's disease	Not exercise-ba		
McDermott et al.	2012	Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: A randomized trial.	Duplicate		
McDermott et al.	2012	Treadmill exercise and resistance training in patients with peripheral arterial disease with and like without intermittent claudication: A randomized trial.			
Morris, M.	2012	Preventing falls in older people	R/C paper		
O'Connor & Ahmad	2012	Can We Prevent Heart Failure with Exercise?	Not a RCT		
Rejeski et al.	2012	Lifestyle change and mobility in obese adults with type 2 diabetes	Not exercise-ba		
Sossai & Sponga	2012	Physical activity to combat depression in chronic heart failure	R/C paper		
Van De Port et al.	2012	Effects of circuit training as alternative to usual physiotherapy after stroke: Randomised controlled trial	Not exercise-ba		
Waldén et al.	2012	Prevention of acute knee injuries in adolescent female football players: Cluster randomised controlled trial	Not studying ad		
Belardinelli et al.	2013	A 10-year exercise program improved oxygen consumption and quality of life in stable chronic heart failure	R/C paper		
Katz, J.	2013	Surgery and physical therapy did not differ for function in meniscal tears with knee osteoarthritis	Not exercise-ba		
Labrie et al.	2013	Surgery versus physiotherapy for stress urinary incontinence	Not exercise-ba		
Lamb et al.	2013	Emergency department treatments and physiotherapy for acute whiplash: a pragmatic, two-step, randomised controlled trial	Not exercise-ba		
Mascitelli & Goldstein	2013	Statin and exercise prescription	R/C paper		
Mascitelli & Goldstein	2013	Statin and exercise prescription	Not a RCT		
McDermott et al.	2013	Home-based walking exercise intervention in peripheral artery disease: a randomized clinical trial	Not exercise-ba		
Messier et al.	2013	Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial	Not exercise-ba		
Solomon et al.	2013	The influence of hyperglycemia on the therapeutic effect of exercise on glycemic control in patients with type 2 diabetes mellitus	Not a RCT		
Underwood et al.	2013	Exercise for depression in elderly residents of care homes: a cluster-randomised controlled trial	Duplicate		
Van Nimwegen, et al.	2013	Promotion of physical activity and fitness in sedentary patients with Parkinson's disease: Randomised controlled trial	Not exercise-ba		
Wing et al.	2013	Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes	Secondary analy		

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclu Criteria				
Wing, R.	2013	A lifestyle intervention did not reduce cardiovascular outcomes in overweight or obese patients with type 2 diabetes	R/C paper				
Bennell et al.	2014	Effect of physical therapy on pain and function in patients with hip osteoarthritis: a randomized clinical trial	Not exercise-ba				
Bronfort et al.	2014	Spinal manipulation and home exercise with advice for subacute and chronic back-related leg pain: a trial with adaptive allocation	Not exercise-ba				
Cooney et al.	2014	Exercise for depression	R/C paper				
Goonewardene et al.	2014	Letter to the Editor: Re: Bourke et al., Lifestyle changes for improving disease-specific quality of life in sedentary men on long-term androgen-deprivation therapy for advanced prostate cancer: a randomised controlled trial. Eur Urol 2014;65:865-72; Re: Galvão et al., A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. Eur Urol 2014;65:856-64; Re: Keating et al., Androgen-deprivation therapy and diabetes control among diabetic men with prostate cancer. Eur Urol 2014;65:816-24; Re: Jespersen et al., Androgen-deprivation therapy in treatment of prostate cancer and risk of myocardial infarction and stroke: a nationwide Danish population-based cohort study. Eur Urol 2014;65:704-9					
Hunt et al.	2014 A gender-sensitised weight loss and healthy living programme for overweight and obese men delivered by Scottish Premier League football clubs (FFIT): a pragmatic randomised controlled trial						
Latham et al.	2014	Effect of a home-based exercise program on functional recovery following rehabilitation after hip N fracture: a randomized clinical trial					
Li et al.	2014	Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study	Secondary anal				
Michaleff et al.	2014	Comprehensive physiotherapy exercise programme or advice for chronic whiplash (PROMISE): a N pragmatic randomised controlled trial					
Michaleff et al.	2014	Comprehensive physiotherapy exercise programme or advice for chronic whiplash (PROMISE): a pragmatic randomised controlled trial	Not exercise-ba				
Pahor et al.	2014	Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial	Not exercise-ba				
Pugliese & Balducci	2014	NAVIGATOR: Physical activity for cardiovascular health?	R/C paper				
Rhon et al.	2014	One-year outcome of subacromial corticosteroid injection compared with manual physical therapy for the management of the unilateral shoulder impingement syndrome: A pragmatic randomized trial	Not exercise-ba				
Sanders & Wyse	2014	In overweight or obese patients with atrial fibrillation, a weight reduction program reduced symptoms	R/C paper				
Westman, E.	2014	In overweight or obese patients with diabetes, a lifestyle intervention increased weight loss at 8 years	R/C paper				
El-Khoury et al.	2015	Effectiveness of two year balance training programme on prevention of fall induced injuries in at risk women aged 75-85 living in community: Ossébo randomised controlled trial	Not exercise-ba				
Fakhry et al.	2015	Endovascular Revascularization and Supervised Exercise for Peripheral Artery Disease and Intermittent Claudication: A Randomized Clinical Trial	Duplicate				
Fritz et al.	2015	Early Physical Therapy vs Usual Care in Patients With Recent-Onset Low Back Pain: A Randomized Clinical Trial	Not exercise-ba				
Lamb et al.	2015	Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial	Not exercise-ba				
Lamb et al.	2015	Exercises to improve function of the rheumatoid hand (SARAH): a randomised controlled trial	Not exercise-ba				
Lipscombe, L.	2015	In high-risk pregnant women, an individualized lifestyle intervention reduced gestational diabetes mellitus	R/C paper				
March, L.	2015	An exercise program for hands and arms improved hand function in RA controlled with medication	R/C paper				
McDermott, M.	2015	Erasing disability in peripheral artery disease: The role of endovascular procedures and supervised exercise	R/C paper				
McDermott, M.	2015	Erasing disability in peripheral artery disease: The role of endovascular procedures and supervised exercise	Not a RCT				
Moseley et al.	2015	Rehabilitation After Immobilization for Ankle Fracture: The EXACT Randomized Clinical Trial	Not exercise-ba				

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclu Criteria					
Moseley et al.	2015	Rehabilitation After Immobilization for Ankle Fracture: The EXACT Randomized Clinical Trial	Not exercise-bas					
Opava & Bjök	2015	Towards evidence-based hand exercises in rheumatoid arthritis	R/C paper					
Sink et al.	2015	Effect of a 24-Month Physical Activity Intervention vs Health Education on Cognitive Outcomes in Sedentary Older Adults: The LIFE Randomized Trial	Secondary analy					
Sink et al.	2015	Effect of a 24-Month Physical Activity Intervention vs Health Education on Cognitive Outcomes in Sedentary Older Adults: The LIFE Randomized Trial	es Not exercise-bas					
Skou et al.	2015	A Randomized, Controlled Trial of Total Knee Replacement	Not exercise-bas					
Sussman et al.	2015	Improving diabetes prevention with benefit based tailored treatment: Risk based reanalysis of diabetes prevention program	Not exercise-bas					
Anokye et al.	2016	The short-term and long-term cost-effectiveness of a pedometer-based intervention in primary care: A within trial analysis and beyond-trial modelling	R/C paper					
Charante et al.	2016	Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial	Not exercise-bas					
Gill et al.	2016	Effect of Structured Physical Activity on Overall Burden and Transitions Between States of Major Mobility Disability in Older Persons: Secondary Analysis of a Randomized Trial	Secondary analy					
Gill et al.	2016	Effect of structured physical activity on prevention of serious fall injuries in adults aged 70-89: Randomized clinical trial (LIFE study)	Secondary analy					
Guralnik et al.	2016	Effect of a Structured Exercise Program on the Overall Burden of Major Mobility Disability Among Older Adults	R/C paper					
Iwashyna et al.	2016	Early mobilisation in ICU is far more than just exercise	R/C paper					
Jakicic et al.	2016							
Kise et al.	2016	Exercise therapy versus arthroscopic partial meniscectomy for degenerative meniscal tear in middle aged patients: Randomised controlled trial with two year follow-up						
Kitzman et al.	2016	Effect of Caloric Restriction or Aerobic Exercise Training on Peak Oxygen Consumption and Quality of Life in Obese Older Patients With Heart Failure With Preserved Ejection Fraction: A Randomized Clinical Trial						
Mirelman et al.	2016	Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial	Not exercise-bas					
Mirelman et al.	2016	Addition of a non-immersive virtual reality component to treadmill training to reduce fall risk in older adults (V-TIME): a randomised controlled trial	Not exercise-bas					
Morris et al.	2016	Standardized Rehabilitation and Hospital Length of Stay Among Patients With Acute Respiratory Failure: A Randomized Clinical Trial	Not exercise-bas					
Mutsaerts et al.	2016	Randomized Trial of a Lifestyle Program in Obese Infertile Women	Not exercise-bas					
Patel et al.	2016	Framing Financial Incentives to Increase Physical Activity Among Overweight and Obese Adults: A Randomized, Controlled Trial	Not exercise-bas					
Prenner & Rinella	2016	Moderate exercise for nonalcoholic fatty liver disease	Not a RCT					
Saposnik et al.	2016	Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVREST): a randomised, multicentre, single-blind, controlled trial	Not exercise-bas					
Sit et al.	2016	A smartphone-based exercise adherence intervention for people with metabolic syndrome: A feasibility pilot study	Abstract only					
Skou et al.	2016	A Randomized, Controlled Trial of Total Knee Replacement	Duplicate					
Teuscher et al.	2016	A Randomized, Controlled Trial of Total Knee Replacement	Duplicate					
Wang et al.	2016	Effectiveness of a health promotion programme on self-efficacy and practice of exercise in Chinese metabolic syndrome population: A single-centre, open-label, randomised controlled trial	Abstract only					
Winstein et al.	2016	Effect of a Task-Oriented Rehabilitation Program on Upper Extremity Recovery Following Motor Stroke: The ICARE Randomized Clinical Trial	Not exercise-bas					
Wise, J.	2016	Moderate physical activity in older adults is not associated with reduced cardiovascular events	R/C paper					
Wise, J.	2016	Activity trackers, even with cash incentives, do not improve health	R/C paper					
Allen et al.	2017	Patient, Provider, and Combined Interventions for Managing Osteoarthritis in Primary Care: A Cluster Randomized Trial	Not exercise-bas					
Bayer et al.	2017	Early versus delayed rehabilitation after acute muscle injury	R/C paper					
Bennell et al.	2017	Effectiveness of an Internet-Delivered Exercise and Pain-Coping Skills Training Intervention for Persons With Chronic Knee Pain: A Randomized Trial	Not exercise-bas					

#### Supplementary Table 1: List of Excluded Exercise Records

Author	Year	Title	Primary Exclusi Criteria			
Bennell et al.	2017	Internet-delivered exercise and pain-coping skills training for chronic knee pain	R/C paper			
Brach et al.	2017	Effectiveness of a Timing and Coordination Group Exercise Program to Improve Mobility in Community-Dwelling Older Adults: A Randomized Clinical Trial	Not exercise-bas			
Brindal, E.	2017	Weight management programmes of extended duration	R/C paper			
Buhagiar et al.	2017	Effect of Inpatient Rehabilitation vs a Monitored Home-Based Program on Mobility in Patients With Total Knee Arthroplasty: the HIHO Randomized Clinical Trial	Not exercise-bas			
Clark et al.	2017	Guided graded exercise self-help plus specialist medical care versus specialist medical care alone for chronic fatigue syndrome (GETSET): a pragmatic randomised controlled trial	Not exercise-bas			
Clauw, D.	2017	Guided graded exercise self-help as a treatment of fatigue in chronic fatigue syndrome	R/C paper			
Dawes et al.	2017	Impact of volunteer-led running groups for women affected by homelessness: A qualitative study of the charity, A Mile in Her Shoes	Not a RCT			
Fong et al.	2017	Novel aquatic physiotherapy programme for elderly Chinese adults with osteoarthritis of the knee: A randomised controlled trial	Abstract only			
Juch et al.	2017	Effect of Radiofrequency Denervation on Pain Intensity Among Patients With Chronic Low Back Pain: The Mint Randomized Clinical Trials	Not exercise-bas			
Kwakkel & van Wegen	2017	Family-delivered rehabilitation services at home: is the glass empty?	Not a RCT			
Liu et al.	2017	Effect of health literacy and exercise interventions on glycated haemoglobin levels in Chinese patients with type 2 diabetes: A cluster-randomised controlled trial	Abstract only			
Mayor, S.	2017	Self help approach to graded exercise may help chronic fatigue syndrome				
McDermott & Kibbe	2017	Improving lower extremity functioning in peripheral artery disease: Exercise, endovascular revascularization, or both?	R/C paper			
Owens & Cappola	2017	Recreational exercise in hypertrophic cardiomyopathy	R/C paper			
Saberi et al.	2017	Effect of Moderate-Intensity Exercise Training on Peak Oxygen Consumption in Patients With Hypertrophic Cardiomyopathy: A Randomized Clinical Trial	Duplicate			
Saper et al.	2017	Yoga, physical therapy, or education for chronic low back pain: A randomized noninferiority trial	Not exercise-bas			
Villareal et al.	2017	Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults	Duplicate			
Wahlich et al.	2017	Primary care pedometer-based walking intervention: Mixed-methods results from 3 year follow- up of PACE-UP cluster-randomised controlled trial	Abstract only			
Wanigatunga et al.	2017	Association Between Structured Physical Activity and Sedentary Time in Older Adults	R/C paper			
Wanigatunga et al.	2017	Association Between Structured Physical Activity and Sedentary Time in Older Adults	Not a RCT			
Crawford, J.	2018	Graded exercise self-help for chronic fatigue syndrome in GETSET	R/C paper			
	2018	Effect of Physical Activity on Frailty: Secondary Analysis of a Randomized Controlled Trial	Secondary analy			

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# Supplementary Table 2: Exercise & Pharmacological RCT Matching

# Supplementary Table 2: Exercise & Pharmacological RCT Matching

Exercise Studies	Journal	Population	Size	Sites	Pharmacological Studies	Journal	Population	Size	Sites	% Matcl
Beckers et al., (2008) <sup>18</sup>	Eur Heart J	Heart Failure	58	Single	Hoendermis et al., (2015) <sup>19</sup>	Eur Heart J	HFpEF	52	Single	100%
Beer et al., (2008) <sup>20</sup>	JACC	Dilated Cardiomyopathy	24	Single	Hamshere et al., $(2015)^{21}$	Eur Heart J	Dilated Cardiomyopathy	60	Single	75%
Ligibel et al., (2008) <sup>22</sup>	JCO	Breast CA	101	Single	Schmid et al., (2016) <sup>23</sup>	JCO	Breast CA	75	Multiple	75%
Maltais et al. (2008) <sup>24</sup>	AIM	COPD	252	Multiple	Lapperre et al., (2009) <sup>25</sup>	AIM	COPD	114	Multiple	75%
Adamsen et al., (2009) <sup>26</sup>	BMJ	Mixed CA	269	Multiple	Rimawi et al., (2018) <sup>27</sup>	JCO	Breast CA	258	Multiple	100%
Courneya et al., (2009) <sup>28</sup>	JCO	Lymphoma	122	Single	Cortelazzo et al., (2016) <sup>29</sup>	JCO	Lymphoma	246	Multiple	50%
McDermott et al., (2009) <sup>30</sup>	JAMA	PAD	156	Single	Ford et al., (2014) <sup>31</sup>	JACC	PAD	171	Multiple	50%
Monninkhof et al., $(2009)^{32}$	JCO	Postmenopausal women	189	Single	Loprinzi et al., (2010) <sup>33</sup>	JCO	Women with hot flashes	207	Multiple	75%
O'Connor et al., (2009) <sup>34</sup>	JAMA	Heart Failure	2331	Multiple	Gheorghiade et al., (2013) <sup>35</sup>	JAMA	Heart Failure	1639	Multiple	75%
Patwala et al., (2009) <sup>36</sup>	JACC	Cardiac Resynch	50	Single	Tsujita et al., (2015) <sup>37</sup>	JACC	Percutaneous Coronary Inter	246	Multiple	50%
Schmitz et al., (2009) <sup>38</sup>	NEJM	Breast CA	141	Single	Wapnir et al., (2018) <sup>39</sup>	Lancet	Breast CA	162	Multiple	50%
Segal et al., (2009) <sup>40</sup>	JCO	Prostate CA	121	Single	McKay et al., (2016) <sup>41</sup>	JCO	Prostate CA	102	Multiple	75%
Church et al., (2010) <sup>42</sup>	JAMA	T2DM	262	Single	Nissen et al., (2008) <sup>43</sup>	JAMA	T2DM & CAD	547	Multiple	50%
Friedenreich et al., (2010) <sup>44</sup>	JCO	Postmenopausal women	320	Multiple	Johnston et al., (2018) <sup>45</sup>	JCO	Postmenopausal Breast CA	355	Multiple	100%
Galvao et al., (2010) <sup>46</sup>	JCO	Prostate CA	57	Single	Taplin et al., (2014) <sup>47</sup>	JCO	Prostate CA	58	Single	100%
Schmitz et al., (2010) <sup>48</sup>	JAMA	Breast CA	154	Single	Hurvitz et al., (2013) <sup>49</sup>	JCO	Breast CA	137	Multiple	50%
Edelmann et al., (2011) <sup>50</sup>	JACC	HFpEF	64	Single	Kosmala et al., (2013) <sup>51</sup>	JACC	HFpEF	61	Single	100%

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Supplementary Table 2: Exercise & Pharmacological RCT Matching

Exercise Studies	Journal	Population	Size	Sites	Pharmacological Studies	Journal	Population	Size	Sites	% Matcl
Hallsworth et al., (2011) <sup>52</sup>	Gut	NAFLD	19	Single	Ratziu et al., (2008) <sup>53</sup>	Gastroenterol	NASH	64	Single	75%
Villareal et al., (2011) <sup>54</sup>	NEJM	Obese	107	Single	Smith et al., (2010) <sup>55</sup>	NEJM	Obese	3182	Multiple	50%
Belardinelli et al., (2012) <sup>56</sup>	JACC	CHF	123	Single	Goebel et al., (2017) <sup>57</sup>	AIM	Complex Pain Syndrome	111	Multiple	50%
Campbell et al., (2012) <sup>58</sup>	JCO	Postmenopausal women	439	Single	Ellis et al., (2011) <sup>59</sup>	JCO	Postmenopausal Breast CA	377	Multiple	75%
Duijts et al., (2012) <sup>60</sup>	JCO	Breast CA	422	Multiple	Urruticoechea et al., (2017) <sup>61</sup>	JCO	Breast CA	452	Multiple	100%
Sandri et al., (2012) <sup>62</sup>	Eur Heart J	HFrEF	120	Single	Frustaci et al., (2009) <sup>63</sup>	Eur Heart J	CHF w Cardio- myopathy	85	Single	75%
Winter et al., (2012) <sup>64</sup>	Eur Heart J	Systemic Right Ventricle	54	Multiple	van der Bom et al., (2013) <sup>65</sup>	Circulation	Systemic Right Ventricle	88	Multiple	75%
Daumit et al., (2013) <sup>66</sup>	NEJM	Mental Illness	291	Multiple	Rosenheck et al., (2011) <sup>67</sup>	NEJM	Mental Illness	382	Multiple	75%
Kitzman et al., (2013) <sup>68</sup>	JACC	HFpEF	63	Single	Caminiti et al., (2009) <sup>69</sup>	JACC	CHF	70	Single	100%
Messier et al., (2013) <sup>70</sup>	JAMA	Overweight & Obese	454	Single	Spitzer et al., (2012) <sup>71</sup>	AIM	Obese w ED	140	Single	50%
Pitkala et al., (2013) <sup>72</sup>	JAMA Int Med	Alzheimer's Disease	210	Multiple	Cummings et al., (2015) <sup>73</sup>	JAMA	Alzheimer's Disease	220	Multiple	75%
Galvao et al., (2014) <sup>74</sup>	Eur Urol	Prostate CA	100	Multiple	Irani et al., (2008) <sup>75</sup>	Eur Urol	Prostate CA	138	Single	50%
Hollekim-Strand et al., (2014) <sup>76</sup>	JACC	T2DM & DD	47	Single	Han et al., (2014) <sup>77</sup>	JACC	T2DM & CKD	3082	Multiple	50%
Jones et al., (2014) <sup>78</sup>	Eur Urol	Prostate CA	50	Single	Yoshimura et al., (2016) <sup>79</sup>	Eur Urol	Prostate CA	73	Multiple	50%
Pahor et al., (2014) <sup>80</sup>	JAMA	Elderly	1635	Multiple	Devereux et al., (2018) <sup>81</sup>	JAMA	Elderly w COPD	1578	Multiple	100%
Fakhry et al., (2015) <sup>82</sup>	JAMA	PAD	212	Multiple	Poole et al., (2013) <sup>83</sup>	JAMA	PAD	159	Multiple	100%
Friedenreich et al., (2015) <sup>84</sup>	JAMA Oncol	Postmenopausal women	400	Multiple	Harman et al., (2014) <sup>85</sup>	JAMA Int Med	Postmenopausal women	727	Multiple	75%
Irwin et al., (2015) <sup>86</sup>	JCO	Breast CA	121	Single	Yardley et al., (2013) <sup>87</sup>	JCO	Breast CA	130	Multiple	75%

Supplementary Table 2: Exercise & Pharmacological RCT Matching

Exercise Studies	Journal	Population	Size	Sites	Pharmacological Studies	Journal	Population	Size	Sites	% Matc
Murphy et al., (2015) <sup>88</sup>	JACC	PAD	111	Multiple	Krankenberg et al., (2015) <sup>89</sup>	Circulation	PAD	119	Multiple	100%
Ross et al., (2015) <sup>90</sup>	AIM	Obese	300	Single	Kim et al., (2018) <sup>91</sup>	JAMA	Acute Coronary Syndrome	300	Single	50%
van Waart et al., (2015) <sup>92</sup>	JCO	Mixed CA	230	Multiple	Soiffer et al., (2017) <sup>93</sup>	JCO	HSCT	260	Multiple	100%
Ehlken et al., (2016) <sup>94</sup>	Eur Heart J	Pulmonary HTN	87	Single	Ulrich et al., (2015) <sup>95</sup>	Eur Heart J	Pulmonary HTN	23	Single	75%
Kitzman et al., (2016) <sup>96</sup>	JAMA	HFpEF & Obese	100	Single	Gheorghiade et al., (2008) <sup>97</sup>	JACC	Heart Failure	120	Multiple	50%
Zhang et al., (2016) <sup>98</sup>	JAMA Int Med	NAFLD	220	Single	Cusi et al., (2016) <sup>99</sup>	AIM	NASH	101	Single	75%
Johansen et al., (2017) <sup>100</sup>	JAMA	T2DM	98	Single	Wysham et al., (2017) <sup>101</sup>	JAMA	T2DM	721	Multiple	50%
McDermott et al., (2017) <sup>102</sup>	JAMA	PAD	210	Single	Pradhan et al., (2009) <sup>103</sup>	JAMA	PAD	500	Multiple	50%
Saberi et al., (2017) <sup>104</sup>	JAMA	Hypertrophic Cardiomyopathy	136	Single	Kosmala et al., (2016) <sup>105</sup>	JACC	HFpEF	150	Single	75%
Taaffe et al., (2017) <sup>106</sup>	Eur Urol	Prostate CA	163	Multiple	Klotz et al., (2013) <sup>107</sup>	Eur Urol	Prostate CA	186	Multiple	100%
Villareal et al., (2017) <sup>108</sup>	NEJM	Obese	160	Single	Grudell et al., (2008) <sup>109</sup>	Gastroenterol	Overweight & Obese	181	Single	75%
Dieli-Conwright et al., (2018) <sup>110</sup>	JCO	Breast CA	100	Single	Greenspan et al., (2008) <sup>111</sup>	JCO	Breast CA	87	Single	100%
McDermott et al., (2018) <sup>112</sup>	JAMA	PAD	200	Single	Ahmed et al., (2008) <sup>113</sup>	JAMA	A-Fib w Cardiac Resynch	214	Multiple	50%

Notes: A-Fib, atrial fibrillation; AIM, Annals of Internal Medicine; BMJ, British Medical Journal; CA, cancer; CAD, coronary artery disease; CHF, chronic heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disorder; CVD, cardiovascular disease; DD, diastolic dysfunction; ED, erectile dysfunction; Eur Heart J, European Heart Journal; Eur Urol, European Urology; HCL, hypercholesterolemia; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HSCT, hematopoietic stem cell transplantation; HTN, hypertension; Inter, intervention; JACC, Journal of the American College of Cardiology; JAMA, Journal of the American Medical Association; JAMA Int Med, JAMA Internal Medicine; JAMA Oncol, JAMA Oncology; JCO, Journal of Clinical Oncology; MDS, myelodisplastic syndrome; NEJM, New England Journal of Medicine; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; PAD, peripheral arterial disease; Resynch, resynchronization; T2DM, type 2 diabetes mellitus 

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Supplementary Table 3: Reporting Quality Differences Between Exercise and Pharmacological RCTs Matched on 50% to 100% of Criteria

Supplementary Table 3: Reporting Quality Differences Between Exercise and Pharmacological RCTs Matched on 50% to 100% of Criteria

Reporting Outcome	Criteria Matched	Number of Matched Studies	Difference Between Matched Studies	Standard Deviation	95% CI	p-value
CONSORT	100%	13	-14.8	17.4	-25.3 to -4.3	.97
	75%	18	-15.1	18.4	-24.2 to -5.9	
	50%	17	-13.7	19.3	-23.6 to -3.8	
CONSORT-Harms	100%	13	-19.7	29.0	-37.2 to -2.1	.85
	75%	18	-12.9	40.3	-32.9 to 7.2	
	50%	17	-17.7	32.7	-34.5 to -0.9	
Intervention	100%	13	-7.7	26.0	-23.4 to 8.0	.53
	75%	18	-14.8	22.1	-25.8 to -3.9	
	50%	17	-5.9	25.7	-19.1 to 7.3	

-23. 22.1 -25. -5.9 25.7 -19.1

# Supplementary Table 4: Pre vs. Post Author Contact

Outcomes		Exercise Studie	es (n=16)		Pharmacological Studies (n=7)			
		Pre	Post	Δ	Pre	Post	Δ	
Study Reporting Score	Median	30.5	43.0	12.5	33.0	39.0	5.0	
	IQR	27.8, 35.0	41.5, 45.8	10.0, 16.2	30.0, 37.0	35.5, 41.5	4.0, 6.5	
CONSORT	Median	24.5	36.5	10.5	24.0	27.0	4.0	
	IQR	24.0, 26.5	31.8, 38.2	8.8, 13.2	23.0, 27.5	27.0, 29.5	2.0, 4.0	
CONSORT-Harms	Median	1.0	2.0	1.0	6.0	6.0	0.0	
	IQR	0.0, 3.0	1.8, 5.0	0.0, 2.0	4.0, 6.5	4.0, 6.5	0.0, 0.0	
TIDieR	Median	9.5	12.5	3.0	NA	NA	NA	
	IQR	7.0, 10.2	10.0, 13.0	2.0, 4.0	NA	NA	NA	

Notes: Δ, change; CONSORT, Consolidated Standards for Reporting Trials; CONSORT-Harms, CONSORT Extension for Harms Reporting; IQR, interquartile range; Pre, original score (prior to author contact); Post, updated score (following author contact); TIDieR, Template for Intervention Description and Replication

# Supplementary Table 5: Exercise RCT Characteristics

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Beckers et al., (2008) <sup>18</sup>	Heart Failure	58	AET1: 30; CET1: 30	NR	16 (28)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Beer et al., $(2008)^{20}$	Dilated Cardiomyopathy	24	AET1: 12; UC: 12	56	NR	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Ligibel et al., (2008) <sup>22</sup>	Breast CA	101	CET1: 51; UC: 50	NR	101 (100)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Maltais et al. (2008) <sup>24</sup>	COPD	252	CET1: 126; CET2: 126	66	112 (44)	HTN: 112 (44); HCL: NR (NR) T2DM: 30 (12)
Adamsen et al., (2009) <sup>26</sup>	Mixed CA	269	CET1: 135; UC: 134	47.2	196 (73)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Courneya et al., $(2009)^{28}$	Lymphoma	122	AET1: 60; UC: 62	53	50 (41)	HTN: 35 (29); HCL: 36 (30); T2DM: NR (NR)
McDermott et al., (2009) <sup>30</sup>	PAD	156	AET1: 51; RET1: 52; UC: 53	73.7	81 (52)	HTN: NR (NR); HCL: NR (NR T2DM: 69 (44)
Monninkhof et al., $(2009)^{32}$	Postmenopausal Women	189	CET1: 96; UC: 93	NR	189 (100)	HTN: NR (NR); HCL: NR (NR T2DM: NA (NA)
O'Connor et al., (2009) <sup>34</sup>	Heart Failure	2331	AET1: 1159; UC: 1172	59.2 <sup>MED</sup>	661 (28)	HTN: 1388 (60); HCL: NR (NF T2DM: 748 (32)
Patwala et al., $(2009)^{36}$	Congestive Heart Failure	50	AET1: 25; UC: 25	64	4 (8)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Schmitz et al., (2009) <sup>38</sup>	Breast CA	141	RET1: 71; UC: 70	NR	NR	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Segal et al., (2009) <sup>40</sup>	Prostate CA	121	AET1: 40; CET1: 40; UC: 41	66	NA	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Church et al., $(2010)^{42}$	T2DM	262	AET1: 72; RET1: 73; CET1: 76; UC: 41	56	165 (63)	HTN: 208 (79); HCL: 168 (64) T2DM: 262 (100)
Friedenreich et al., (2010) <sup>44</sup>	Postmenopausal Women	320	AET1: 160; UC: 160	61	320 (100)	HTN: NR (NR); HCL: NA (NA T2DM: NR (NR)
Galvao et al., (2010) <sup>46</sup>	Prostate CA	57	CET1: 29; UC: 28	NR	NA	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Schmitz et al., (2010) <sup>48</sup>	Breast CA	154	RET1: 71; UC: 77	NR	154 (100)	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)
Edelmann et al., (2011) <sup>50</sup>	Heart Failure	64	CET1: 46; UC: 21	65	36 (56)	HTN: 55 (86); HCL: 30 (47); T2DM: 9 (14)
Hallsworth et al., $(2011)^{52}$	NAFLD	19	RET1: 11; UC: 10	NR	NR	HTN: NR (NR); HCL: NR (NR T2DM: NR (NR)

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Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Villareal et al., (2011) <sup>54</sup>	Obese Elderly	107	AET1: 26; CET1: 26; CET2: 28; UC: 27	70	67 (63)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Belardinelli et al., (2012) <sup>56</sup>	Heart Failure	123	AET1: 63; UC: 60	59	27 (22)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Campbell et al., (2012) <sup>58</sup>	Postmenopausal Women	439	AET1: 117; AET2: 117; RET1: 118; UC: 87	58	439 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
Duijts et al., (2012) <sup>60</sup>	Breast CA	422	AET1: 104; AET2: 106; RET1: 109; UC: 103	48	422 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Sandri et al., (2012) <sup>62</sup>	HFrEF	120	AET1: 60; UC: 60	NR	23 (19)	HTN: 90 (75); HCL: 72 (60); T2DM: 35 (29)
Winter et al., (2012) <sup>64</sup>	Systemic Right Ventricle	46	AET1: 28; UC: 26	32	23 (50)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Daumit et al., (2013) <sup>66</sup>	Serious Mental Illness	291	AET1: 144; UC: 147	45	146 (50)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Kitzman et al., (2013) <sup>68</sup>	HFpEF	63	AET1: 32; UC: 31	70	48 (76)	HTN: 56 (89); HCL: NA (NA); T2DM: 15 (24)
Messier et al., (2013) <sup>70</sup>	Overweight & Obese w Osteoarthritis	454	AET1: 152; CET1: 150; CET2: 152	66	325 (72)	HTN: 273 (60); HCL: NR (NR); T2DM: 59 (13)
Pitkala et al., (2013) <sup>72</sup>	Alzheimer's Diesase	210	AET1: 70; CET1: 70; UC: 70	78	81 (39	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Galvao et al., (2014) <sup>74</sup>	Prostate CA	100	CET1: 50; UC: 50	NR	NA	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Hollekim-Strand et al., (2014) <sup>76</sup>	T2DM w Diastolic Dysfunction	37	AET1: 23; AET2: 24	56	17 (46)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
Jones et al., (2014) <sup>78</sup>	Prostate CA	50	AET1: 25; UC: 25	59	NA	HTN: 27 (54); HCL: 30 (60); T2DM: 8 (16)
Pahor et al., (2014) <sup>80</sup>	Elderly	1635	CET1: 818; UC: 817	79	1098 (67)	HTN: 1151 (70); HCL: NR (NR); T2DM: 412 (25)
Fakhry et al., (2015) <sup>82</sup>	PAD	212	AET1: 106; AET2: 106	65	80 (38)	HTN: 128 (60); HCL: 91 (43); T2DM: 44 (21)
Friedenreich et al., (2015) <sup>84</sup>	Postmenopausal Women	400	AET1: 200; AET2: 200	59	400 (100)	HTN: NR (NR); HCL: NA (NA); T2DM: NA (NA)
Irwin et al., (2015) <sup>86</sup>	Breast CA	121	CET1: 61; UC: 60	61	121 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Murphy et al., (2015) <sup>88</sup>	PAD	111	AET1: 43; Stent: 46; UC: 22	64	42 (38)	HTN: 94 (85); HCL: 89 (80); T2DM: 26 (24)
Ross et al., (2015) <sup>90</sup>	Obese	300	AET1: 73; AET2: 76; CET1: 76; UC: 75	51	196 (65)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
van Waart et al., (2015) <sup>92</sup>	Breast CA	230	AET1: 77; CET1: 76; UC: 77	51	228 (99)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Ehlken et al., (2016) <sup>94</sup>	Pulmonary Artery HTN	87	CET1: 46; UC: 41	56	47 (54)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Kitzman et al., (2016) <sup>96</sup>	HFpEF	100	AET1: 26; AET2: 25; RET1: 24; UC: 25	67	81 (81)	HTN: 95 (95); HCL: NR (NR); T2DM: 32 (32)
Zhang et al., (2016) <sup>98</sup>	NAFLD	220	AET1: 73; AET2: 73; UC: 74	54	149 (68)	HTN: NA (NA); HCL: NR (NR); T2DM: NA (NA)
Johansen et al., (2017) <sup>100</sup>	T2DM	98	CET1: 64; UC: 34	55	47 (48)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
McDermott et al., (2017) <sup>102</sup>	PAD	210	AET1: 53; AET2: 53; RET1: 53; UC: 51	67	82 (39)	HTN: 175 (83); HCL: NR (NR); T2DM: 80 (38)
Saberi et al., (2017) <sup>104</sup>	Hypertrophic Cardiomyopathy	136	AET1: 67; UC: 69	50	57 (42)	HTN: 30 (22); HCL: NR (NR); T2DM: 9 (7)
Taaffe et al., (2017) <sup>106</sup>	Prostate CA	163	AET1: 51; RET1: 58; CET1: 54	NR	NA	HTN: 58 (36); HCL: 35 (21); T2DM: 20 (12)
Villareal et al., (2017) <sup>108</sup>	Obese Elderly	160	AET1: 40; RET1: 40; CET1: 40; UC: 40	70	103 (64)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Dieli-Conwright et al., (2018) <sup>110</sup>	Overweight & Obese Breast CA	100	CET1: 50; UC: 50	54	100 (100)	HTN: NA (NA); HCL: NR (NR); T2DM: NA (NA)
McDermott et al., (2018) <sup>112</sup>	PAD	200	AET1: 99; UC: 101	70	105 (53)	HTN: NR (NR); HCL: NR (NR); T2DM: 67 (34)

Notes: AET1, aerobic exercise training (group 1); AET2, aerobic exercise training (group 2); CA, cancer; CET1, combined aerobic and resistance exercise training (group 1); CET2, combined aerobic and resistance exercise training (group 2); COPD, chronic obstructive pulmonary disorder; CVD, cardiovascular disease; HCL, hypercholesterolemia; HFpEF, heart failure with preserved ejection fraction; HTN, hypertension; LTF, loss-to-follow up; PAD, peripheral arterial disease; n, number; NA, not applicable; NAFLD, non-alcoholic fatty liver disease; NR, not reported; RET1, resistance exercise training (group 1); RET2, resistance exercise training (group 2); T2DM, type 2 diabetes mellitus; UC, usual care

# Supplementary Table 6: Pharmacological RCT Characteristics

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Ahmed et al. (2008) <sup>113</sup>	Atrial Fibrillation	214	Grp1: 106; Grp2: 108	NR	73 (34.11)	HTN: 84 (39); HCL: NR (NR); T2DM: 21 (10)
Gheorghiade et al. (2008) <sup>97</sup>	Heart Failure	120	Grp1: 29; Grp2: 30; Grp3: 30; UC: 31	55	15 (12.5)	HTN: NA (NA); HCL: NR (NR); T2DM: 21 (18)
Greenspan et al. (2008) <sup>111</sup>	Breast CA	87	Grp1: 43; UC: 44	NR	87 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Grudell et al. (2008) <sup>109</sup>	Obese & Overweight	181	Grp1: 58; Grp2: 61; UC: 62	NR	161 (88.95)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Irani et al. (2008) <sup>75</sup>	Prostate CA	129	Grp1: 62; Grp2: 67	73	NA	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Nissen et al. (2008) <sup>43</sup>	T2DM	547	Grp1: 273; Grp2: 274	60	181 (33.09)	HTN: 475 (87); HCL: NR (NR); T2DM: NA (NA)
Ratziu et al. (2008) <sup>53</sup>	NASH	64	Grp1: 32; UC: 32	54	26 (40.63)	HTN: 22 (35); HCL: NR (NR); T2DM: 20 (32)
Caminiti et al. (2009) <sup>69</sup>	Heart Failure	70	Grp1: 35; UC: 35	$70^{\text{MED}}$	NA	HTN: 25 (36); HCL: 39 (56); T2DM: 20 (29)
Frustaci et al. (2009) <sup>63</sup>	Cardiomyopathy	85	Grp1: 43; UC: 42	NR	34 (40)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Lapperre et al. $(2009)^{25}$	COPD	114	Grp1: 26; Grp2: 31; Grp3: 28; UC: 29	NR	27 (23.68)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Pradhan et al. (2009) <sup>103</sup>	T2DM	500	Grp1: 126; Grp2: 126; Grp3: 124; UC: 124	54	281 (56.2)	HTN: 341 (68); HCL: 299 (60); T2DM: 500 (100)
Loprinzi et al. (2010) <sup>33</sup>	Women with Hot Flashes	207	Grp1: 69; Grp2: 69; UC: 69	NR	207 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Smith et al. (2010) <sup>55</sup>	Overweight & Obese	3182	Grp1: 1595; UC: 1587	44	2652 (83.34)	HTN: NA (NA); HCL: NR (NR) T2DM: NA (NA)
Ellis et al. (2011) <sup>59</sup>	Breast CA	377	Grp1: 124; Grp2: 128; Grp3: 125	NR	377 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Rosenheck et al. $(2011)^{67}$	Schizophrenia	382	Grp1: 190; UC: 192	51	32 (8.38)	HTN: NR (NR); HCL: NR (NR) T2DM: NR (NR)
Spitzer et al. (2012) <sup>71</sup>	Erectile Dysfunction	140	Grp1: 70; Grp2: 70	55	NA	HTN: 56 (40); HCL: NR (NR); T2DM: 27 (19)
Gheorghiade et al. (2013) <sup>35</sup>	Heart Failure	1639	Grp1: 821; UC: 818	65	368 (22.45)	HTN: 1225 (76); HCL: NR (NR) T2DM: 662 (41)

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Supplementary Table 6: Pharmacological RCT Characteristics

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
Hurvitz et al. (2013) <sup>49</sup>	Breast CA	137	Grp1: 67; Grp2: 70	NR	NR	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Klotz et al. (2013) <sup>107</sup>	Prostate CA	186	Grp1: 84; Grp2: 102	NR	NA	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Kosmala et al. (2013) <sup>51</sup>	HFpEF	61	Grp1: 30; UC: 31	67	50 (81.97)	HTN: 51 (84); HCL: NR (NR); T2DM: 22 (36)
Poole et al. $(2013)^{83}$	PAD	159	Grp1: 80; UC: 79	64	20 (12.58)	HTN: 153 (96); HCL: 134 (87) T2DM: 58 (37)
van der Bom et al. $(2013)^{65}$	Systemic Right Ventricle	88	Grp1: 44; UC: 44	33	31 (35.23)	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Yardley et al. (2013) <sup>87</sup>	Breast CA	130	Grp1: 64; Grp2: 66	NR	130 (100)	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Ford et al. $(2014)^{31}$	Cardiovascular Disease	171	Grp1: 86; UC: 85	65	26 (15.2)	HTN: 52 (30); HCL: NR (NR) T2DM: 14 (9)
Han et al. (2014) <sup>77</sup>	T2DM & Chronic Kidney Disease	3082	Grp1: 1543; UC: 1539	61	1044 (33.87)	HTN: 2156 (70); HCL: 256 (8) T2DM: 3082 (100)
Harman et al. (2014) <sup>85</sup>	Menopausal	727	Grp1: 230; Grp2: 222; UC: 275	53	727 (100)	HTN: NA (NÀ); HCL: NA (NA T2DM: NA (NA)
Taplin et al. (2014) <sup>47</sup>	Prostate CA	58	Grp1: 28; Grp2: 30	58 <sup>MED</sup>	NA	HTN: NR (NR); HCL: NR (NF T2DM: NR (NR)
Cummings et al. (2015) <sup>73</sup>	Alzheimer's	220	Grp1: 93; UC: 127	78	126 (57.27)	HTN: NR (NR); HCL: NR (NI T2DM: NR (NR)
Hamshere et al. $(2015)^{21}$	Dilated Cardiomyopathy	60	Grp1: 15; Grp2: 15; Grp3: 15; UC: 15	55	17 (28.33)	HTN: 6 (10); HCL: 6 (10); T2DM: 6 (10)
Hoendermis et al. (2015) <sup>19</sup>	HFpEF	52	Grp1: 26; UC: 26	74	37 (71.15)	HTN: 47 (90); HCL: 27 (52); T2DM: 18 (35)
Krankenberg et al. (2015) <sup>89</sup>	PAD	119	Grp1: 62; Grp2: 57	NR	37 (31.09)	HTN: 105 (88); HCL: 93 (78); T2DM: 45 (38)
Tsujita et al. (2015) <sup>37</sup>	Coronary Artery Disease	246	Grp1: 122; Grp2: 124	NR	44 (17.89)	HTN: 142 (58); HCL: 142 (58) T2DM: 60 (24)
Ulrich et al. (2015) <sup>95</sup>	Pulmonary Artery HTN	23	Grp1: 23; Grp2: 23; UC: 23	66	15 (65.22)	HTN: NR (NR); HCL: NR (NI T2DM: NR (NR)
Cortelazzo et al. (2016) <sup>29</sup>	Lymphoma	246	Grp1: 126; Grp2: 120	51 <sup>MED</sup>	99 (40.24)	HTN: NR (NR); HCL: NR (NI T2DM: NR (NR)
Cusi et al. (2016) <sup>99</sup>	NASH & Prediabetes or T2DM	101	Grp1: 50; UC: 51	NR	30 (29.7)	HTN: NR (NR); HCL: NR (NI T2DM: 52 (52)
Kosmala et al. (2016) <sup>105</sup>	HFpEF	150	Grp1: 75; UC: 75	67	110 (73.33)	HTN: 120 (80); HCL: NR (NR T2DM: 52 (35)

Study	Population	Participants [n]	Participants per Arm [n]	Age [mean]	Female Sex [n (%)]	CVD Comorbidity [Condition: n (%)]
McKay et al. (2016) <sup>41</sup>	Prostate CA	102	Grp1: 66; Grp2: 36; UC: NA	65 <sup>MED</sup>	NA	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Schmid et al. (2016) <sup>23</sup>	Breast CA	75	Grp1: 26; Grp2: 49	NR	75 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
Yoshimura et al. (2016) <sup>79</sup>	Prostate CA	73	Grp1: 36; Grp2: 37	NR	NA	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Goebel et al. (2017) <sup>57</sup>	Complex Regional Pain Syndrome	111	Grp1: 55; UC: 56	NR	75 (67.57)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Soiffer et al. (2017) <sup>93</sup>	Acute Leukemia or MDS w HSCT	260	Grp1: 128; UC: 132	NR	115 (44.23)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Urruticoechea et al. (2017) <sup>61</sup>	Breast CA	452	Grp1: 224; Grp2: 228	NR	452 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NA (NA)
Wysham et al. (2017) <sup>101</sup>	T2DM	721	Grp1: 361; Grp2: 360	61	338 (46.88)	HTN: NR (NR); HCL: NR (NR); T2DM: 721 (100)
Devereux et al. $(2018)^{81}$	COPD	1578	Grp1: 791; UC: 787	68	724 (45.88)	HTN: 594 (38); HCL: NR (NR); T2DM: 176 (11)
Johnson et al. $(2018)^{45}$	Breast CA	355	Grp1: 120; Grp2: 117; Grp3: 118	NR	355 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Kim et al. (2018) <sup>91</sup>	Depression & Acute Coronary Syndrome	300	Grp1: 149; UC: 151	60	119 (39.67)	HTN: 184 (61); HCL: 144 (48); T2DM: 85 (28)
Rimawi et al. (2018) <sup>27</sup>	Breast CA	258	Grp1: 129; Grp2: 129	60	258 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)
Wapnir et al. (2018) <sup>39</sup>	Breast CA	162	Grp1: 85; UC: 77	56 <sup>MED</sup>	162 (100)	HTN: NR (NR); HCL: NR (NR); T2DM: NR (NR)

**Notes**: CA, cancer; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; Grp, group; HCL, hypercholesterolemia; HFpEF, heart failure with preserved ejection fraction; HSCT, hematopoietic stem cell transplantation; HTN, hypertension; kg, kilogram; LTF, loss to follow up; MDS, myelodisplastic syndrome; MED, median; PAD, peripheral arterial disease; n, number; NA, not applicable; NASH, non-alcoholic steatohepatitis; NR, not reported; T2DM, type 2 diabetes mellitus; UC, usual care

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Supplementary Table 7: Exercise Intervention Characteristics

# Supplementary Table 7: Exercise Intervention Characteristics

	Length			<b>Exercise Dose</b>			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]
Beckers et al., (2008) <sup>18</sup>	MC	Total (single-phase): 26 wks	AET1: CE, TM CAET1: NR CRET1: MW	AET1: 3 CAET1: 3 CRET1: 3	AET1: 40-45 CAET1: 10-45 CRET1: 10-40	AET1: 90% HR at AT CAET1: 90% HR at AT CRET1: 50-60% 1RM; 10-15 reps, 1-2 sets	NA
Beer et al., (2008) <sup>20</sup>	NR	Total (single-phase): 36 wks	AET1: CE, NR	AET1: 5	AET1: 45	AET1: 60-80% VO2 <sup>max</sup> ; 13-15 RPE	NA
Ligibel et al., (2008) <sup>22</sup>	PG, HM	Total (single-phase): 16 wks	CAET1: NR CRET1: MW, BW	CAET1: NR CRET1: 2	CAET1: NR CRET1: 35	CAET1: 55-80% HR <sup>max</sup> CRET1: 80% 1RM; 10 reps, 4 sets	NA
Maltais et al. (2008) <sup>24</sup>	MC, HM, Other	Total: 52 wks Lead-in: 4 wks Phase 1: 8 wks	Lead-in: NA <u>Phase 1</u> CAET1: CE CRET1: RB, BW, NR CAET2: CE CRET2: RB, BW, NR	Lead-in: NA <u>Phase 1</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	Lead-in: NA <u>Phase 1</u> CAET1: 25-30 CRET1: 30 CAET2: 40 CRET2: 30	Lead-in: NA <u>Phase 1</u> CAET1: 80% peak work CRET1: NR; 10 reps, 1-3 sets CAET2: 60% maximum work capacity CRET2: NR; 10 reps, 1-3 sets	Lead-in: 4 wk education progr
		Phase 2: 40 wks	<u>Phase 2</u> CRET1: NR CAET1: NR CAET2: NR CRET2: NR	<u>Phase 2</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	Phase 2 CAET1: NR CRET1: NR CAET2: NR CRET2: NR	<u>Phase 2</u> CAET1: NR (NR) CRET1: NR (NR) CAET2: NR (NR) CRET2: NR (NR)	
Adamsen et al., (2009) <sup>26</sup>	MC	Total (single-phase): 6 wks	CAET1: CE CRET1: MW	CAET1: 3 CRET1: 3	CAET1: 15 CRET1: 45	CAET1: 85-95% HR <sup>max</sup> CRET1: 70-100% 1RM; 5-8 reps, 3 sets	Body awareness restoration; rela ation; massage
Courneya et al., (2009) <sup>28</sup>	NR	Total (single-phase): 12 wks	AET1: CE	AET1: 3	AET1: 15-45	AET1: 60-75% PPO at VO <sub>2</sub> <sup>peak</sup>	NA
McDermott et al., (2009) <sup>30</sup>	UNI, Other	• Total (single-phase): 24 wks	AET1: TM RET1: MW, BW	AET1: 3 RET1: 3	AET1: 15-40 RET1: NR	AET1: 12-14 RPE RET1: 50-80% 1RM, 12-14 RPE; 8 reps, 3 sets	NA
	PG, HM	Total (single-phase): 52 wks	CAET1: CE, WK, NR CRET1: NR	CAET1: 3 CRET1: 2	CAET1: 20-30 CRET1: 25	CAET1: 60-85% HR <sup>max</sup> CRET1: NR; NR; NR	NA

Supplementary Table 7: Exercise Intervention Characteristics

		Length		<b>Exercise Dose</b>			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-interventior [Group: Details]
O'Connor et al., (2009) <sup>34</sup>	Other	Total: 130 wks <sup>MED</sup> Phase 1: 12 wks	Phase 1 AET1: CE, TM, WK	Phase 1 AET1: 3	<u>Phase 1</u> AET1: 15-35	<u>Phase 1</u> AET1: 60-70% HRR	NA
		Phase 2: 118 wks <sup>MED</sup>	Phase 2 AET1: CE, TM, WK	<u>Phase 2</u> AET1: 5	<u>Phase 2</u> AET1: 40	<u>Phase 2</u> AET1: 60-70% HRR	
Patwala et al., (2009) <sup>36</sup>	UNI	Total (single-phase): 12 wks	AET1: CE, TM	AET1: 3	AET1: 30	AET1: 80-90% HR <sup>peak</sup>	NA
Schmitz et al., (2009) <sup>38</sup>	PG	Total: 52 wks Phase 1: 13 wks	<u>Phase 1</u> RET1: MW, FW	<u>Phase 1</u> RET1: 2	<u>Phase 1</u> RET1: 90	<u>Phase 1</u> RET: NR; 10 reps, 2-3 sets	NA
		Phase 2: 39 wks	Phase 2 RET1: NR	<u>Phase 2</u> RET1: 2	<u>Phase 2</u> RET1: NR	<u>Phase 2</u> RET1: NR; NR, NR	
Segal et al., (2009) <sup>40</sup>	RC	Total (single-phase): 24 wks	AET1: CE, TM, EE RET1: MW, FW	AET1: 3 RET1: 3	AET1: 15-45 RET1: NR	AET1: 50-75% VO <sub>2</sub> <sup>peak</sup> RET1: 60-70% 1RM; 8-12 reps, 2 sets	NA
Church et al., (2010) <sup>42</sup>	MC	Total (single-phase): 40 wks	AET1: NR RET1: MW, BW CAET1: NR CRET1: MW, BW	AET1: NR RET1: 3 CAET1: NR CRET1: 2	AET1: NR RET1: NR CAET1: NR CRET1: NR	AET1: 50-80% VO <sub>2</sub> <sup>peak</sup> RET1: NR; 10-12 reps, 2-3 sets CAET1: 50-80% VO <sub>2</sub> <sup>peak</sup> CRET1: NR, 10-12 reps, 1 set	NA
Friedenreich et al., (2010) <sup>44</sup>	UNI, PG, HM	Total (single-phase): 52 wks	AET1: NR	AET1: 3-5	AET1: 15-45	AET1: 50- 80% HRR	NA
Galvao et al., (2010) <sup>46</sup>	RC, HM	Total (single-phase): 12 wks	CAET1: CE, WK, JG CRET1: MW, FW	CAET1: 2 CRET1: 2	CAET1: 15-20 CRET1: NR	CAET1: 65-80% HR <sup>max</sup> ; 11-13 RPE CRET1: 6-12 RM; NR, 2-4 sets	NA
Schmitz et al., (2010) <sup>48</sup>	PG	Total: 52 wks Phase 1: 13 wks	<u>Phase 1</u> RET1: MW, FW	<u>Phase 1</u> RET1: 2	<u>Phase 1</u> RET1: 60-90	Phase 1 RET1: NR; 10 reps, 3 sets	NA
		Phase 2: 39 wks	<u>Phase 2</u> RET1: MW, FW	<u>Phase 2</u> RET1: 2	<u>Phase 2</u> RET1: NR	<u>Phase 2</u> RET1: NR; NR, NR	
Edelmann et al., (2011) <sup>50</sup>	Other (Facility Based)	Total: 12 wks Phase 1: 4 wks	<u>Phase 1</u> CAET1: CE CRET1: NR	<u>Phase 1</u> CAET1: 2 CRET1: NR	<u>Phase 1</u> CAET1: 20-40 CRET1: NR	Phase 1 CAET1: 50-60% VO <sub>2</sub> <sup>peak</sup> CRET1: NR	NA

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Supplementary Table 7: Exercise Intervention Characteristics

Study Edelmann cont'd	Location	Length [Total; Phase 1 & Phase 2 (when applicable)] Phase 2: 8 wks	Phase 2	Frequency [days / week] Phase 2	Duration [Grp: mins] Phase 2	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]
		Phase 2: 8 wks		Phase 2	Dhasa 2	51 .	
			CAET1: CE CRET1: MW	CAET1: 3 CRET1: 2	CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: 70% VO <sub>2</sub> <sup>peak</sup> CRET1: 60-65% 1RM; 15 reps, NR	
Hallsworth et al., (2011) <sup>52</sup>	NR	Total (single-phase): 8 wks	RET1: MW	RET1: 3	RET1: 25-40	RET1: 50% 1RM; 8-12 reps, 2-4 sets	NA
Villareal et al., (2011) <sup>54</sup>	UNI	Total (single-phase): 52 wks	CAET1: CE, TM, SC CRET1: MW, FW CAET2: CE, TM CRET2: MW, FW	CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	CAET1: 30 CRET1: 30 CAET2: 30 CRET2: 30	CAET1: 65-85% VO <sub>2</sub> <sup>peak</sup> CRET1: 65-85% 1RM; 6-12 reps, 1-3 sets CAET2: 65-85% VO <sub>2</sub> <sup>peak</sup> CRET2: 65-85% 1RM; 6-12 reps, 1-3 sets	CET1: Diet CET2: NA
Belardinelli et al., (2012) <sup>56</sup>	МС	Total: 120 mo Phase 1: 8 wks	Phase 1 AET1: CE, TM	<u>Phase 1</u> AET1: 3	<u>Phase 1</u> AET1: 40	Phase 1 AET1: 60% VO <sub>2</sub> <sup>peak</sup>	Phase 1 & Phase 2 Counselling (smoking, stress
		Phase 2: 118 mo	Phase 2 AET1: CE, TM	<u>Phase 2</u> AET1: 3	<u>Phase 2</u> AET1: 40	Phase 2 AET1: 70% VO2 peak	& diet)
Campbell et al., (2012) <sup>58</sup>	МС, НМ	Total (single-phase): 52 wks	AET1: WK AET2: WK	AET1: 5 AET2: 5	AET1: 45 AET2: 45	AET1: 70-85% HR <sup>max</sup> AET2: 70-85% HR <sup>max</sup>	AET1 & AET2: Diet
Duijts et al., (2012) <sup>60</sup>	HM	Total (single-phase): 12 wks	AET1: NR AET2: NR	AET1: NR AET2: NR	AET1: NR AET2: NR	AET1: 60-80% HR - Karvonen AET2: 60-80% HR - Karvonen	AET1 & AET 2: CBT
Sandri et al., (2012) <sup>62</sup>	NR	Total (single-phase): 4 days	AET1: NR CAET1: CE, WK CRET1: BW	AET1: NR CAET1: 5 CRET1: 1	AET1: NR CAET1: CE: 20 4x/day; WK: NR CRET1: NR	AET1: NR CAET1: 70% VO <sub>2</sub> <sup>max</sup> CRET1: NR; NR, NR	NA
Winter et al., (2012) <sup>64</sup>	HM	Total (single-phase): 10 wks	AET11: NR	AET1: 3	AET1: 32	AET1: 60-90% HR <sup>max</sup>	NA
Daumit et al., (2013) <sup>66</sup>	HM	Total: 78 wks Phase 1: 26 wks	Phase 1 AET1: WK	<u>Phase 1</u> AET1: 3	<u>Phase 1</u> AET1: 10-30	Phase 1 AET1: 50-69% HR <sup>max</sup>	Phase 1 & Phase AET1: Ind & grp weight manage
		Phase 2: 52 wks	<u>Phase 2</u> AET1: WK	<u>Phase 2</u> AET1: 3	<u>Phase 2</u> AET1: NR	<u>Phase 2</u> AET1: NR	ment

Supplementary Table 7: Exercise Intervention Characteristics

		Length		<b>Exercise Dose</b>			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-interventior [Group: Details]
Kitzman et al., (2013) <sup>68</sup>	NR	Total (single-phase): 16 wks	AET1: CE, WK	AET1: 3	AET1: 10-40	AET1: 40-70% HRR	NA
Messier et al., (2013) <sup>70</sup>	MC, UNI	Total: 78 wks Phase 1: 26 wks	<u>Phase 1</u> CAET1: CE, WK CRET1: MW CAET2: CE, WK CRET2: MW	<u>Phase 1</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	<u>Phase 1</u> CAET1: 30 CRET1: 20 CAET2: 30 CRET2: 20	<u>Phase 1</u> CAET1: 50-75% HRR CRET1: NR; 10-12 reps, 1-2 sets CAET2: 50-75% HRR CRET2: NR; 10-12 reps, 1-2 sets	Phase 1 & Phase CET1: Diet CET2: NA
		Phase 2: 52 wks	<u>Phase 2</u> CAET1: CE, WK CRET1: MW, RB CAET2: CE, WK, NR CRET2: MW, RB	<u>Phase 2</u> CAET1: 3 CRET1: 3 CAET2: 3 CRET2: 3	<u>Phase 2</u> CAET1: 30 CRET1: 20 CAET2: 30 CRET2: 20	Phase 2 CAET1: 50-75% HRR CRET1: NR; 10-12 reps, 1-2 sets CAET2: 50-75% HRR CRET2: NR; 10-12 reps, 1-2 sets	
Pitkala et al., (2013) <sup>72</sup>	RC, HM	Total (single-phase): 52 wks	AET1: NR CAET1: CE CRET1: MW	AET1: 2 CAET1: 2 CRET1: 2	AET1: 60 CAET1: NR CRET1: NR	AET1: NR CAET1: NR CRET1: NR; NR, NR	NA
Galvao et al., (2014) <sup>74</sup>	NR	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> CAET1: CE, WK/JG CRET1: MW, FW, BW	<u>Phase 1</u> CAET1: 4 CRET1: 2	<u>Phase 1</u> CAET1: 20-30 CRET1: NR	<u>Phase 1</u> CAET1: 70-85% HR <sup>max</sup> , 11-13 RPE CRET1: 6-12RM; NR, 2-4 sets	NA
		Phase 2: 26 wks	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR; NR, NR	
Hollekim-Strand et al., (2014) <sup>76</sup>	HM, Other	Total: 52 wks Phase 1: 12 wks Phase 2: 40 wks	Phase 1 AET1: CE, WK, SW AET2: TM Phase 2 AET1: CE, WK, SW AET2: TM, CE, SW	Phase 1 AET1: NR AET2: 3 Phase 2 AET1: NR AET2: NR	<u>Phase 1</u> AET1: 10-NR AET2: 40 <u>Phase 2</u> AET1: NR AET2: NR	Phase 1           AET1: 70% HR <sup>max</sup> AET2: 90-95% HR <sup>max</sup> Phase 2           AET1: NR           AET2: NR	NA
Jones et al., (2014) <sup>78</sup>	HM, Other	Total (single-phase): 26 wks	AET1: TM	AET1: 5	AET1: 30-45	AET1: 55-100% VO <sub>2</sub> <sup>peak</sup>	NA
Pahor et al., (2014) <sup>80</sup>	MC	Total: 135 wks Phase 1: 52 wks	<u>Phase 1</u> CAET1: WK CRET1: FW	<u>Phase 1</u> CAET1: 3-6 CRET1: 3	<u>Phase 1</u> CAET1: NR CRET1: 10	<u>Phase 1</u> CAET1: 13 RPE (Borg) CRET1: 15-16 RPE (Borg); 10 reps, 2 sets	NA

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Supplementary Table 7: Exercise Intervention Characteristics

		Length		<b>Exercise Dose</b>		~ • •	
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]
		Phase 2: 83 wks	<u>Phase 2</u> CAET1: WK CRET1: FW	<u>Phase 2</u> CAET1: 5-6 CRET1: 3	<u>Phase 2</u> CAET1: NR CRET1: 10	<u>Phase 2</u> CAET1: 13 RPE (Borg) CRET1: 15-16 RPE (Borg); 10 reps, 2 sets	
Fakhry et al., (2015) <sup>82</sup>	RC	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> AET1: TM AET2: TM	<u>Phase 1</u> AET1: 2-3 AET2: 2-3	<u>Phase 1</u> AET1: 30-45 AET2: 30-45	<u>Phase 1</u> AET1: NR AET2: NR	Phase 1 & Phase AET1: NA AET2: Endovase revascularizatio
		Phase 2: 26 wks	<u>Phase 2</u> AET1: TM AET2: TM	<u>Phase 2</u> AET1: 1 AET2: 1	<u>Phase 2</u> AET1: 30-45 AET2: 30-45	<u>Phase 2</u> AET1: NR AET2: NR	
Friedenreich et al., (2015) <sup>84</sup>	PG, HM	Total: 52 wks Phase 1: 12 wks	Phase 1 AET1: NR AET2: NR	<u>Phase 1</u> AET1: 3-5 AET2: 3-5	<u>Phase 1</u> AET1: 15-60 AET2: 10-30	<u>Phase 1</u> AET1: 50-75% HRR AET2: 50-75% HRR	NA
		Phase 2: 40 wks	<u>Phase 2</u> AET1: WK, EG, CE, RG, NR AET2: NR	<u>Phase 2</u> AET1: 5 AET2: 5	Phase 2 AET1: 60 AET2: 30	<u>Phase 2</u> AET1: 65-75% HRR AET2: 65-75% HRR	
Irwin et al., (2015) <sup>86</sup>	PG, HM	Total (single-phase): 52 wks	CAET1: CE, TM, WK, NR CRET1: MW	CAET1: NR CRET1: 2	CAET1: NR CRET1: NR	CAET1: 50-80% HR <sup>max</sup> CRET1: NR; NR, NR	NA
Murphy et al., (2015) <sup>88</sup>	RC	Total: 78 wks Phase 1: 26 wks Phase 2: 52 wks	<u>Phase 1</u> AET1: TM <u>Phase 2</u> AET1: NR	Phase 1 AET1: 5 Phase 2 AET1: NR	Phase 1           AET1: 15-50           Phase 2           AET1: NR	Phase 1 AET1: 2-4 claudication pain scale Phase 2 AET1: NR	Phase 1 Cilostazol, EX counselling Phase 2 EX counselling
Ross et al., (2015) <sup>90</sup>	NR	Total (single-phase): 24 wks	AET1: TM AET2: TM CAET1: TM	AET1: 5 AET2: 5 CAET1: 5	AET1: 31.2 AET2: 58.4 CAET1: 40	AET1: 50% $VO_2^{peak}$ AET2: 50% $VO_2^{peak}$ CAET1: 75% $VO_2^{peak}$	NA
van Waart et al., (2015) <sup>92</sup>	RC, HM	Total (single-phase): NR	AET1: NR CAET1: NR CRET1: MW, FW, BW	AET1: 5 CAET1: 2 CRET1: 2	AET1: 30-NR CAET1: 30 CRET1: 20	AET1: 12-14 RPE CAET1: 50-80% workload max CRET1: 70-80% 1RM; 8-12 reps, NR	NA

Supplementary Table 7: Exercise Intervention Characteristics

		Length		Exercise Dose				
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]	
Ehlken et al., (2016) <sup>94</sup>	MC	Total: 15 wks Phase 1: 3 wks	<u>Phase 1</u> CAET1: CE, WK CRET1: FW	<u>Phase 1</u> CAET1: 7 CRET1: 5	<u>Phase 1</u> CAET1: 70-85 CRET1: 30	$\frac{Phase 1}{CAET1: 60-80\% HR at VO_2^{max}}$ CRET: NR; NR, 1-3 sets	<u>Phase 1</u> Respiratory & "mental" training	
		Phase 2: 12 wks	<u>Phase 2</u> CAET1: CE CRET1: FW	<u>Phase 2</u> CAET1: 5 CRET1: 3-4	<u>Phase 2</u> CAET1: 15-30 CRET1: 15-30	<u>Phase 2</u> CAET1: NR CRET1: NR; NR, 1-2 sets	<u>Phase 2</u> Respiratory training	
Kitzman et al., (2016) <sup>96</sup>	MC	Total (single-phase): 20 wks	AET1: WK AET2: WK	AET1: 3 AET2: 3	AET1: 18-48 AET2: 19-50	AET1: HRR (NR) AET2: HRR (NR)	AET1 & AET2: Diet	
Zhang et al., (2016) <sup>98</sup>	PG, HM	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> AET1: TM AET2: WK	<u>Phase 1</u> AET1: 5 AET2: 5	<u>Phase 1</u> AET1: 15-30 AET2: 30	<u>Phase 1</u> AET1: 45-50%; 65-80% HR <sup>max</sup> AET2: 45-55% HR <sup>max</sup>	Phase 1 & Phase 2 AET1 & AET2: Health education	
		Phase 2: 26 wks	<u>Phase 2</u> AET1: WK AET2: WK	<u>Phase 2</u> AET1: 5 AET2: 5	Phase 2 AET1: 30 AET2: 30	Phase 2 AET1: 45-55% HR <sup>max</sup> AET2: 45-55% HR <sup>max</sup>	w EX behaviora support	
Johansen et al., (2017) <sup>100</sup>	REC, Other	Total: 52 wks Phase 1: 16 wks	<u>Phase 1</u> CAET1: NR CRET1: NR	<u>Phase 1</u> CAET1: 6 CRET1: 2	<u>Phase 1</u> CAET1: 30-60 CRET1: 30	<u>Phase 1</u> CAET1: 62-80% HRR CRET1: NR; NR, NR	<u>Phase 1 &amp; Phase</u> Diet & sleep	
		Phase 2: 36 wks	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: NR CRET1: NR	<u>Phase 2</u> CAET1: 45-60 CRET1: 30	<u>Phase 2</u> CAET1: 68-88% HRR CRET1: NR; NR, NR		
McDermott et al., (2017) <sup>102</sup>	MC	Total (single-phase): 26 wks	AET1: TM AET2: TM	AET1: 3 AET2: 3	AET1: 15-50 AET2: 15-50	AET1: 12-14 RPE AET2: 12-14 RPE	AET1: GM-CSF injections AET2: NA	
Saberi et al., (2017) <sup>104</sup>	HM	Total (single-phase): 16 wks	AET1: EE, WK	AET1: 3-7	AET1: 20-60	AET1: 60-70% HRR, 11-14 RPE	NA	
Taaffe et al., (2017) <sup>106</sup>	UNI	Total: 52 wks Phase 1: 26 wks	<u>Phase 1</u> RET1: MW CAET1: CE, TM, RE; MW CRET1: MW	<u>Phase 1</u> RET1: 2 CAET1: 2 CRET1: 2	<u>Phase 1</u> RET1: NR CAET1: 20-30 CRET1: NR	<u>Phase 1</u> RET1: 6-12 RM CAET1: 60-75% HR <sup>max</sup> CRET1: 6-12 RM; NR, 2-4 sets	<u>Phase 1</u> RET1: Impact- loading activitie CET1: NA	

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Supplementary Table 7: Exercise Intervention Characteristics

		Length		<b>Exercise Dose</b>			
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [days / week]	Duration [Grp: mins]	Intensity [AET Grp: % tested value] [RET Grp: % tested value; reps, sets]	Co-intervention [Group: Details]
Taaffe cont'd		Phase 2: 26 wks	Phase 2 AET1: CE	Phase 2 AET1: 2	<u>Phase 2</u> AET1: NR	Phase 2 AET1: 70% HR <sup>max</sup>	<u>Phase 2</u> AET1: NA
Villareal et al., (2017) <sup>108</sup>	МС	Total (single-phase): 26 wks	AET1: CE, TM RET1: MW, FW CAET1: CE, TM, SC CRET1: MW, FW	AET1: 3 RET1: 3 CAET1: 3 CRET1: 3	AET1: 40 RET1: 40 CAET1: 30-40 CRET1: 30-40	AET1: 65-85% VO <sub>2</sub> <sup>max</sup> RET1: 65-85% 1RM; 8-12 reps, 1-3 sets CAET1: 65-85% VO <sub>2</sub> <sup>max</sup> CRET1: 65-85% 1RM	AET1, RET1 & CET1: Diet & dieticia support thera
Dieli-Conwright et al., (2018) <sup>110</sup>	UNI	Total (single-phase): 16 wks	CAET1: CE, TM, WK, RE CRET1: MW	CAET1: 3 CRET1: 2	CAET1: 30-50 CRET1: NR	CAET1: 65-80% HR <sup>max</sup> CRET1: 60% 1RM (upper); 10-15 reps, 3 sets; 80% 1RM (lower); 10-15 reps, 3 sets	NA
McDermott et al., (2018) <sup>112</sup>	HM	Total: 40 wks Phase 1: 4 wks	Phase 1 AET1: WK	<u>Phase 1</u> AET1: 1	<u>Phase 1</u> AET1: NR	<u>Phase 1</u> AET1: NR	NA
		Phase 2: 36 wks	<u>Phase 2</u> AET1: WK	Phase 2 AET1: 5	<u>Phase 2</u> AET1: 10-50	<u>Phase 2</u> AET1: 12-14 RPE	

combined aerobic and resistance exercise training (group 1); CAET2: aerobic component of combined aerobic and resistance exercise training (group 2); CE: cycle ergometer; CET1: combined aerobic and resistance exercise training (group 1); CET2: combined aerobic and resistance exercise training (group 2); CRET1: resistance component of combined aerobic and resistance exercise training (group 1); CRET2: resistance component of combined aerobic and resistance exercise training (group 2); d/wk: days per week; EE: elliptical ergometer; EX: exercise; FW: free weights; HM: home; HR: heart rate; HR<sup>max</sup>: maximal heart rate; HRP<sup>eak</sup>: peak heart rate; HRR: heart rate reserve; JG: jogging; MC: medical center; min: minutes; MW: machine weights; NA: not applicable; n: number; NR: not reported; PG: public gym; RB: resistance bands; RC: rehabilitation center; RE: rowing ergometer; REC: recreational center; reps: repetitions; RET1: resistance exercise training (group 1); RET2: resistance exercise training (group 2); RM: repetition maximum; RPE: rate of perceived exertion; SC: stair climb; SW: swimming; TM: treadmill; UC: usual care; UNI: university; VO2max: maximal oxygen uptake; VO2peak: peak oxygen uptake; WK: walking; wk(s): week(s)

## Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose	rmaceutical Dose			
Study	Location		Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]		
Ahmed et al. (2008) <sup>113</sup>	NR	Total (single-phase): 109.2 wks	Grp1: NR Grp2: NR	Grp1: 1x/day Grp2: 1x/day	Grp1: Amiodarone 200mg, 600mg Grp2: Amiodarone 200mg	NA		
Gheorghiade et al. (2008) <sup>97</sup>	HSP	Total (single-phase): 1 day	Grp1: IV Grp2: IN Grp3: IN	Grp1: 1x dose Grp2: 1x dose Grp3: 1x dose	Grp1: Istaroxime 0.5ug/kg/min Grp2: Istaroxime 1.0ug/kg/min Grp3: Istaroxime 1.5ug/kg/min	NA		
Greenspan et al. (2008) <sup>111</sup>	NR	Total (single-phase): 104 wks	Grp1: PO	Grp1: 1x/wk	Grp1: Risendronate 35 mg	Calcium & Vitamin needed		
Grudell et al. (2008) <sup>109</sup>	OMC	Total (single-phase): 12 wks	Grp1: NR Grp2: NR	Grp1: 1x/day Grp2: 1x/day	Grp1: Sibutramine 10mg Grp2: Sibutramine 15mg	Grp1 & Grp2: Writt psychologist-base weight manageme behavioral therapy		
Irani et al. (2008) <sup>75</sup>	NR	Total (single-phase): 193.5 wks	Grp1: PO, IN Grp2: PO, IN	Grp1: 1x/3mo (Goserelin) Grp1: 3x/day (Flutamide) Grp2: 1x/3mo (Goserelin) Grp2: 3x/day (Flutamide) 6 mths, no drugs 6mths, repeat	Grp1: Goserelin 10.8mg Grp1: Flutamide 250mg Grp2: Goserelin 10.8mg Grp2: Flutamide 250mg	NA		
Nissen et al. (2008) <sup>43</sup>	NR	Total (single-phase): 52 wks	Grp1: PO Grp2: PO	Grp1: 1x/day Grp2: 1x/day	Grp1: Glimepiride 2.9 mg (1-4mg) Grp2: Pioglitazone 37.4 mg (15-45mg)	Grp1 & Grp2: Insul Metformin, or bot needed		
Ratziu et al. (2008) <sup>53</sup>	NR	Total: 51.3 wks Phase 1: 4 wks	<u>Phase 1</u> Grp1: NR	<u>Phase 1</u> Grp1: 1x/day	<u>Phase 1</u> Grp1: Rosiglitazone 4mg	NA		
		Phase 2: 47.3 wks	<u>Phase 2</u> Grp1: NR	<u>Phase 2</u> Grp1: 1x/day	<u>Phase 2</u> Grp1: Rosiglitazone 8mg			
Caminiti et al. (2009) <sup>69</sup>	NR	Total (single-phase): 12 wks	Grp1: IN	Grp1: 1x/6wks	Grp1: Testosterone undecanoate 1000mg	NA		
Frustaci et al. (2009) <sup>63</sup>	NR	Total (single-phase): 26 wks	Grp1: PO	Grp1: 2x/day	Grp1: Prednisone 0.33mg/kg/day, 1mg/kg/day Grp1: Azathioprine 2mg/kg/day	NA		

Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		- C
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Lapperre et al. (2009) <sup>25</sup>	NR	Total: 130 wks Phase 1: 26 wks	<u>Phase 1</u> Grp1: INH Grp2: INH Grp3: INH	Phase 1 Grp1: 2x/day Grp2: 2x/day Grp3: 2x/day	<u>Phase 1</u> Grp1: Fluticasone propionate 500ug Grp2: Fluticasone propionate 500ug Grp3: Fluticasone propionate 500ug Grp3: Salmeterol 50ug	NA
		Phase 2: 104 wks	Phase 2 Grp1: INH Grp2: INH Grp3: INH	Phase 2 Grp1: 2x/day Grp2: 2x/day Grp3: 2x/day	Phase 2 Grp1: Fluticasone propionate 500ug Grp2: Placebo 0mg Grp3: Fluticasone propionate 500ug Grp3: Salmeterol 50ug	
Pradhan et al. (2009) <sup>103</sup>	HSP	Total (single-phase): 14 wks	Grp1: IN Grp2: PO Grp3: PO, IN	Grp1: 1x/day Grp2: 2x/day Grp3: 1x/day (Insulin) Grp3: 1-2x/day (Metformin)	Grp1: Insulin glargine 5U starting Grp2: Metformin 500mg, 1000mg Grp3: Insulin glargine 5U starting Grp3: Metformin 500mg, 1000mg	NA
Loprinzi et al. (2010) <sup>33</sup>	NR	Total (single-phase): 6 wks	Grp1: PO Grp2: PO	Grp1: 1x/day; 2x/day Grp2: 1x/day; 2x/day	Grp1: Pregabalin 50mg, 75mg Grp2: Pregabalin 50mg, 75mg, 150mg	NA
Smith et al. (2010) <sup>55</sup>	NR	Total (single-phase): 52 wks	Grp1: PO	Grp1: 2x/day	Grp1: Lorcaserin 10mg	NA
Ellis et al. (2011) <sup>59</sup>	NR	Total (single-phase): 3-4 wks	Grp1: PO Grp2: PO Grp3: PO	Grp1: 1x/day Grp2: 1x/day GrGrp3: 1x/day	Grp1: Exemestane 25mg Grp2: Letrozole 2.5mg Grp3: Anastrozole 1mg	NA
Rosenheck et al. $(2011)^{67}$	HSP	Total (single-phase): 104 wks	Grp1: IN	Grp1: 1x/2wk	Grp1: Risperidone 25mg, 37.5mg, 50mg	NA
Spitzer et al. (2012) <sup>71</sup>	NR	Total (single-phase): 14 wks	Grp1: PO, TD Grp2: PO	Grp1: 2.7 x/wk (Sildenafil) Grp1: 3 x/day (Testosterone) Grp2: 2.7 x/wk (Sildenafil)	Grp1: Sildenafil 25mg, 50mg, 100mg Grp1: Testosterone 5g, 10g, 15g Grp2: Sildenafil 25mg, 50mg, 100mg	NA
Gheorghiade et al. $(2013)^{35}$	NR	Total (single-phase): 48.6 wks <sup>MED</sup>	Grp1: PO	Grp1: 1x/day	Grp1: Aliskiren 150mg or 300mg	NA
Hurvitz et al. (2013) <sup>49</sup>	NR	Total (single-phase): 43.9 wks <sup>MED</sup>	Grp1: IV Grp2: Other, IV	Grp1: 1x/3wks Grp2: 1x/3wks	Grp1: Trastuzumab emtansine 3.6 mg/kg Grp2: Trastuzumab 8mg/kg load, 6mg/kg Grp2: Docetaxel 75mg/m <sup>2</sup> or 100mg/m <sup>2</sup>	NA
		I	For peer review only	/ - http://bmjopen.bmj.com/site/a	about/guidelines.xhtml	

Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		~
Study	Location		Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Klotz et al. (2013) <sup>107</sup>	NR	Total (single-phase): 52 wks	Grp1: PO, IN Grp2: PO, IN	Grp1: 1x/4mo (Leuoprolide) Grp1: 1x/wk (Alendonrate) Grp1: 1x/day (Calcium) Grp1: 1x/day (Vitamin D) Grp2: 1x/4mo (Leuoprolide) Grp2: 1x/day (Calcium) Grp2: 1x/day (Vitamin D)	Grp1: Leuoprolide 30mg Grp1: Alendonrate 70mg Grp1: Calcium 500mg Grp1: Vitamin D 500lu Grp2: Leuoprolide 30mg Grp2: Calcium 500mg Grp2: Vitamin D 500lu	NA
Kosmala et al. (2013) <sup>51</sup>	HSP	Total (single-phase): 1 wk	Grp1: PO	Grp1: 2x/day	Grp1: Ivabradine 5mg	NA
Poole et al. (2013) <sup>83</sup>	HSP	Total (single-phase): 4 wks	Grp1: IN	Grp1: 3x/wk	Grp1: Granulocyte-macrophage-colony stimulating factor 500ug	NA
van der Bom et al. $(2013)^{65}$	NR	Total (single-phase): 166.4 wks	Grp1: PO	Grp1: 2x/day	Grp1: Valsartan 160mg	NA
Yardley et al. (2013) <sup>87</sup>	HSP	Total (single-phase): Grp1: 18.5 wks <sup>MED</sup> Grp2: 9.89 wks <sup>MED</sup>	Grp1: PO Grp2: PO	Grp1: 1x/day (Exemestane) Grp1: 1x/wk (Entinostat) Grp2: 1x/day	Grp1: Exemestane 25mg; Grp1: Entinostat 5mg Grp2: Exemestane 25mg	NA
Ford et al. (2014) <sup>31</sup>	NR	Total (single-phase): 30 days	Grp1: PO	Grp1: 1x/day	Grp1: Clopidogrel 75mg	NA
Han et al. (2014) <sup>77</sup>	NR	Total (single-phase): 5 days	Grp1: PO	Grp1: 1x/day	Grp1: Rosuvastatin 10mg	Isotonic saline (0.9 NaCl at 1ml/kg/h) as needed
Harman et al. (2014) <sup>85</sup>	NR	Total (single-phase): 208 wks	Grp1: PO Grp2: TD	Grp1: 1x/day Grp2: 1x/wk	Grp1: Equine estrogen 0.45mg Grp2: Transdermal 17B-estradiol 50ug/d	Grp1& Grp2: Progest- erone (200 mg/d; first 12 days / mth)
Taplin et al. (2014) <sup>47</sup>	NR	Total: 24 wks Phase 1: 12 wks	<u>Phase 1</u> Grp1: IN Grp2: IN, NR	Phase 1 Grp1: 1x/4wk Grp2: 1x/4wk (LHRH agonist) Grp2: 1x/day (Abiraterone acetate) Grp2: 1x/day (Prednisone)	Phase 1 Grp1: Leuprolide acetate 7.5mg Grp2: LHRH agonist 7.5 mg Grp2: Abiraterone acetate 1000 mg Grp2: Prednisone 5 mg	Phase 1 & Phase 2: Radical prostatectomy at end of Phase 2

Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		
Study	Location		Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Taplin cont'd		Phase 2: 12 wks	<u>Phase 2</u> Grp1: IN, NR Grp2: IN, NR	Phase 2 Grp1: 1x/day (Abiraterone acetate) Grp1: 1x/4wk (Leuprolide acetate) Grp1: 1x/day (Prednisone) Grp2: 1x/day (Abiraterone acetate) Grp2: 1x/4wk (Leuprolide acetate) Grp2: 1x/day (Prednisone)	Grp1: Leuprolide acetate 7.5mg Grp1: Prednisone 5mg	
Cummings et al. (2015) <sup>73</sup>	HSP, OMC	Total (single-phase): 5 wks	Grp1: PO	Grp1: 1x/day (active drug) & 1x/day placebo (wk 1) Grp1: 2x/day active drug (wks 2-5)	Grp1: Dextromethorphan 20mg, 30mg Grp1: Quinidine 10mg	NA
Hamshere et al. (2015) <sup>21</sup>	HSP	Total (single-phase): 5 days	Grp1: IN Grp2: IN Grp3: IN	Grp1: 1x/day Grp2: 1x/day Grp3: 1x/day	Grp1: GCSF 10 ug/kg/day Grp2: GCSF 10 ug/kg/day Grp3: GCSF 10 ug/kg/day	Grp1: NA Grp2: BM harvest of intracoronary injection of bom marrow-derived Grp3: BM harvest of intracoronary se injection
Hoendermis et al. (2015) <sup>19</sup>	NR	Total (single-phase): 10 wks	Grp1: PO	Grp1: 3x/day	Grp1: Sildenafil 60 mg	NA
Krankenberg et al. (2015) <sup>89</sup>	OMC	Total (single-phase): 1 day	Grp1: Intra-lesion via coated balloon Grp2: NR	Grp1: 1x dose (Paclitaxel); Grp1: 1x/day (Aspirin); Grp1: 1x/day (Clopidogrel) Grp2: 1x/day (Aspirin); Grp2: 1x/day (Clopidogrel)	Grp1: Paclitaxel 3.5ug/mm <sup>2</sup> of balloon; Grp1: Aspirin 100mg; Grp1: Clopidogrel 75mg Grp2: Aspirin 100mg; Grp2: Clopidogrel 75mg	Grp1 & Grp2: Hep (5,000 - 10,000 based on body weight during S
Tsujita et al. (2015) <sup>37</sup>	NR	Total (single-phase): Grp1: 43.4 wks Grp2: 41.7 wks	Grp1: NR Grp2: NR	Grp1: 1x/day Grp2: NR	Grp1: Atorvastatin NR Grp1: Ezemtimibe 10mg Grp2: Atorvastatin NR	NA
Ulrich et al. (2015) <sup>95</sup>	HSP	Total (single-phase): 1 wk	Grp1: PO Grp2: PO	Grp1: 2x/day Grp2: 2x/day	Grp1: Acetazolamide 250mg Grp2: Placebo 0mg	Grp1: Sham noctur oxygen therapy Grp2: Real nocturn oxygen therapy

Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		
Study	Location	[Total; Phase 1 & Phase 2 (when applicable)]	Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Cortelazzo et al. (2016) <sup>29</sup>	NR	Total: Grp1: 4 wks Grp2: 4.6 wks Phase 1: Grp1: 2 wks Grp2: 3 wks	Phase 1 Grp1: PO, IN, IV Grp2: PO, IN, IV	Phase 1           Grp1: 1x/2wk RCHOP (w 1x/d P; days 1-5 per cycle)           Grp1: 1x/d Filgrastim; days 7-11 per cycle)           Grp2: 1x/d R; days 52, 60, 78, 86           Grp2: 1x/C; day 50           Grp2: 1x/2wk H; days 1, 15, 29           Grp2: 1x/2wk O; days 1, 15, 29           Grp2: 1x/d P; days 1-28           Grp2: 1x/d Filgrastim; days 51-60           Grp2: 2x/d Cytarabine; days 71-76	H (50mg/m <sup>2</sup> ); O (1.4 mg/m <sup>2</sup> ); P (100mg); Filgrastim (5ug/kg) Grp2: R (375mg/m <sup>2</sup> ); C (7g/m <sup>2</sup> ); H (50mg/m <sup>2</sup> ; 75mg/m <sup>2</sup> ); O (1.4 mg/m <sup>2</sup> ); P (40mg/m <sup>2</sup> ); Filgrastim (5ug/kg and 10ug/kg); Cytarabine (2g/m <sup>2</sup> )	Phase 1 & Phase 2 Grp1: CNS prophylax (high risk patients) Grp1: PCP prophylaxi Grp1: HSV prophylax Grp2: Peripheral blood progenitor cell reinfusion (day 77 Grp2: CNS prophylax (high risk patients) Grp2: PCP prophylaxi Grp2: HSV prophylax
		Phase 2: Grp1: 2 wks Grp2: 1.6 wks	<u>Phase 2</u> Grp1: PO, IN, IV Grp2: IV	Phase 2 Grp1: 1x/2wk RCHOP (w 1x/d P; days 1-5 per cycle) Grp1: 1x/d Filgrastim; days 7-11 per cycle) Grp2: 1x/d Etoposide; day 112 Grp2: 1x/d Cisplatin; day 113 Grp2: 1x/d Filgrastim; day 114	<u>Phase 2</u> Grp1: <b>R</b> (375mg/m <sup>2</sup> ); <b>C</b> (750 mg/m <sup>2</sup> ); <b>H</b> (50mg/m <sup>2</sup> ); <b>O</b> (1.4 mg/m <sup>2</sup> ); <b>P</b> (100 mg/m <sup>2</sup> ); Filgrastim (5ug/kg) Grp2: Etoposide 2.4 g/ m <sup>2</sup> Grp2: Cisplatin 100mg/ m <sup>2</sup> Grp2: Filgrastim 5ug/kg	
				Conditional Grp2: 1x/d Mitoxantrone; day 133 Grp2: 1x/day Melphalan; day 135 or 137 OR Grp2: 1x/d Carmustine; day 133 Grp2: 1x/d Etoposide; day 134- 137 Grp2: 12hr Cytarabine; day 134- 137 Grp2: 1x/d Melphalan; day 138	Conditional Grp2: Mitoxantrone 60mg/ m <sup>2</sup> Grp2: Melphalan 180mg/ m <sup>2</sup> OR Grp2: Carmustine 300mg/m <sup>2</sup> Grp2: Etoposide 200mg/m <sup>2</sup> Grp2: Cytarabine 200mg/m <sup>2</sup> Grp2: Melphalen 140mg/m <sup>2</sup>	
Cusi et al. (2016) <sup>99</sup>	NR	Total: 77 wks Phase 1: 8 wks Phase 2: 69 wks	<u>Phase 1</u> Grp1: PO <u>Phase 2</u> Grp1: PO	Phase 1 Grp1: 1x/day Phase 2 Grp1: 1x/day	Phase 1 Grp1: Pioglitazone 30mg Phase 2 Grp1: Pioglitazone 45mg	Phase 1 & Phase 2 Hypocaloric diet
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Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		<u> </u>
Study	Location		Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
Kosmala et al. (2016) <sup>105</sup>	NR	Total (single-phase): 26 wks	Grp1: PO	Grp1: 1x/day	Grp1: Spironolactone 25mg	NA
McKay et al. (2016) <sup>41</sup>	NR	Total (single-phase): 26 wks	Grp1: PO, IN, IV Grp2: PO, IN	Grp1: 1x/3mo (Leuprolide OR Goserelin); Grp1: 1x/day (Bicalutamide) Grp1: 1x/3wk (Bevacizumab) Grp2: 1x/3mo (Leuprolide OR Goserelin) Grp2: 1x/day (Bicalutamide)	Grp1: Leuprolide acetate 22.5mg or Goserelin acetate 10.8mg Grp1: Bicalutamide 10mg Grp1: Bevacizumab 15mg/kg Grp2: Leuprolide acetate 22.5mg or Goserelin acetate 10.8mg Grp2: Bicalutamide 50mg	NA
Schmid et al. (2016) <sup>23</sup>	NR	Total (single-phase): 2 wks	Grp1: PO Grp2: PO	Grp1: 1x/day Grp2: 1x/day	Grp1: Anastrazole 1mg Grp2: Anaztrazole 1mg Grp2: Pictilisib 260mg, 340mg	NA
Yoshimura et al. (2016) <sup>79</sup>	NR	Total (single-phase): Grp1: 30 wks <sup>MED</sup> Grp2: 94.6 wks <sup>MED</sup>	Grp1: NR Grp2: IN, NR	Grp1: 1x/day Grp2: 1x/day (Dexamethasone) Grp2: 1x/2wk (Peptide vaccine)	Grp1: Dexamethasone 1mg Grp2: Dexamethasone 1mg Grp2: Peptide vaccine 3mg	NA
Goebel et al. (2017) <sup>57</sup>	NR	Total (single-phase): 6 wks	Grp1: IV	Grp1: 2x/6wks	Grp1: Intratectivig 0.5g/kg	NA
Soiffer et al. (2017) <sup>93</sup>	NR	Total (single-phase): 3 days	Grp1: IV	Grp1: 1x/day Anti-T- lymphocyte globulin (3 days) Grp1: Antihistamine (NR) Grp1: 1x/day Methylprednisolone (3 days) Grp1: 1x/day Methotrexate (4 days)	Grp1: Anti–T- lymphocyte globulin Grp1: Antihistamine 20mg/kg Grp1: Methylprednisolone 2mg/kg, 1mg/kg Grp1: Methotrexate 10-15 mg/m <sup>2</sup>	NA
Urruticoechea et al. (2017) <sup>61</sup>	NR	Total (single-phase): Grp1: 36 wks (Trastuzumab) 30 wks (Capecitabine) Grp2: 45 wks (Trastuzumab) 36 wks (Capecitabine) 45 wks (Pertuzumab)	Grp1: PO, IV Grp2: PO, IV	Grp1: 1x/3wk Trastuzumab Grp1: 2x/day Capecitabine (2 wks on / 1wk off) Grp2: 1x/3wk Pertuzumab Grp2: 1x/3wk Trastuzumab Grp2: 2x/day Capecitabine (2 wks on / 1wk off)	<ul> <li>Grp1: Trastuzumab (8mg/kg loading; 6mg/kg maintenance)</li> <li>Grp1: Capecitabine 1250 mg/m<sup>2</sup></li> <li>Grp2: Pertuzumab (840mg loading; 420mg maintenance)</li> <li>Grp2: Trastuzumab (8mg/kg loading; 6mg/kg maintenance)</li> <li>Grp2: Capecitabine 1000 mg/m<sup>2</sup></li> </ul>	NA
Wysham et al. (2017) <sup>101</sup>	NR	Total: 64 wks Phase 1: 32 wks	<u>Phase 1</u> Grp1: IN Grp2: IN	<u>Phase 1</u> Grp1: 1x/day Grp2: 1x/day	<u>Phase 1</u> Grp1: Insulin degludec 70U Grp2: Insulin glargine 74U	NA

Supplementary Table 8: Pharmacological Intervention Characteristics

		Length		Pharmaceutical Dose		<u> </u>
Study	Location		Modalities	Frequency [x/time]	Medication [Grp#: Med 1 dose; med 2 dose, etc.]	Co-intervention [Group: Details]
		Phase 2: 32 wks	<u>Phase 2</u> Grp1: IN Grp2: IN	<u>Phase 2</u> Grp1: 1x/day Grp2: 1x/day	<u>Phase 2</u> Grp1: Insulin glargine 83U Grp2: Insulin degludec 83U	
Devereux et al. (2018) <sup>81</sup>	NR	Total (single-phase): 52 wks	Grp1: PO	Grp1: 1-2x/day	Grp1: Theophylline 200mg	NA
Johnson et al. (2018) <sup>45</sup>	NR	Total (single-phase): 53.6 wks	Grp1: PO, IV Grp2: IV Grp3: PO	Grp1: 1x/day (Lapatinib) Grp1: 1x/3wk (Trastuzumab) Grp2: 1x/3wk Trastuzumab GrGrp3: 1x/day Lapatinib	Grp1: Lapatinib 1000mg; Grp1: Trastuzumab (8mg/kg loading, 6mg/kg maintenance) Grp2: Trastuzumab (8mg/kg loading, 6mg/kg maintenance) Grp3: Lapatinib 1500 mg	Grp1, Grp2 & GrGrp3 Aromatase inhibitor (as needed): Letroz 2.5mg/day, Anas- trozole 1mg/day, or Exemestane 25mg/d
Kim et al. (2018) <sup>91</sup>	NR	Total (single-phase): 24 wks	Grp1: PO	Grp1: 1x/day	Grp1: Escitalopram 7.6mg (5mg, 10mg, 15mg or 20mg)	NA
Rimawi et al. (2018) <sup>27</sup>	OMC	Total (single-phase): 52 wks	Grp1: PO, IV Grp2: PO, IN	Grp1: 1x/3wk (Pertuzumab or Trastuzumab); Grp1: 1x/day (Letrozole) Grp2: 1x/3wk (Trastuzumab); Grp2: 1x/day (Anastrozole or Letrozole)	<ul> <li>Grp1: Pertuzumab (840mg loading, 420mg maintenance)</li> <li>Grp1: Trastuzumab (8mg/kg loading, 6mg/kg maintenance)</li> <li>Grp1: Anastrozole 1mg or Letrozole 2.5mg</li> <li>Grp2: Trastuzumab (8mg/kg loading, 6mg/kg maintenance)</li> <li>Grp2: Anastrozole 1mg or Letrozole 2.5mg</li> </ul>	Grp1 & Grp2: Induct IV Docetaxel q3wk Paclitaxel q1wk for 18-24wk as needed (decided prior to random assignment
Wapnir et al. (2018) <sup>39</sup>	NR	Total (single-phase): 12-26 wks	Grp1: NR	Grp1: NR	Grp1: NR	Grp1: Radiotherapy & endocrine therapy required by surgica margins & tumor hormone markers.

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# Supplementary Table 9: Exercise RCT CONSORT-NPT Data Extraction Summary

## Supplementary Table 9: Exercise RCT CONSORT-NPT Data Extraction Summary

ication as a randomized trial in the title. ired summary of trial design, methods, results, and conclusions. fic background and explanation of rationale. ic objectives or hypothesis. ption of trial design (such as parallel, factorial) including allocation ratio. applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers. as and locations where the data were collected.	Yes           No. (%)           36 (75.0%)           46 (95.8%)           48 (100.0%)           44 (91.7%)           13 (27.1%)           0 (0.0%)           9 (18.8%)           38 (79.2%)           3 (6.3%)	Unclear No. (%) 0 (0.0%) 0 (0.0%) 0 (0.0%) 4 (8.3%) 20 (41.7%) 0 (0.0%) 0 (0.0%) 10 (20.8%) 16 (33.3%)	2 (4.2%) 0 (0.0%) 0 (0.0%) 15 (31.3%) 46 (95.8%) 6 (12.5%) 0 (0.0%)	NA           No. (%)           0 (0.0%)           0 (0.0%)           0 (0.0%)           0 (0.0%)           0 (0.0%)           2 (4.2%)           33 (68.8%)           0 (0.0%)
red summary of trial design, methods, results, and conclusions. fic background and explanation of rationale. ic objectives or hypothesis. ption of trial design (such as parallel, factorial) including allocation ratio. applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	36 (75.0%) 46 (95.8%) 48 (100.0%) 44 (91.7%) 13 (27.1%) 0 (0.0%) 9 (18.8%) 38 (79.2%) 3 (6.3%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 4 (8.3%) 20 (41.7%) 0 (0.0%) 0 (0.0%) 10 (20.8%)	12 (25.0%) 2 (4.2%) 0 (0.0%) 0 (0.0%) 15 (31.3%) 46 (95.8%) 6 (12.5%) 0 (0.0%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%) 2 (4.2%) 33 (68.8%
red summary of trial design, methods, results, and conclusions. fic background and explanation of rationale. ic objectives or hypothesis. ption of trial design (such as parallel, factorial) including allocation ratio. applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	46 (95.8%) 48 (100.0%) 44 (91.7%) 13 (27.1%) 0 (0.0%) 9 (18.8%) 38 (79.2%) 3 (6.3%)	0 (0.0%) 0 (0.0%) 4 (8.3%) 20 (41.7%) 0 (0.0%) 0 (0.0%) 10 (20.8%)	2 (4.2%) 0 (0.0%) 0 (0.0%) 15 (31.3%) 46 (95.8%) 6 (12.5%) 0 (0.0%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 0 (0.0%) 2 (4.2%) 33 (68.8%
fic background and explanation of rationale. Ic objectives or hypothesis. ption of trial design (such as parallel, factorial) including allocation ratio. applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	48 (100.0%) 44 (91.7%) 13 (27.1%) 0 (0.0%) 9 (18.8%) 38 (79.2%) 3 (6.3%)	0 (0.0%) 4 (8.3%) 20 (41.7%) 0 (0.0%) 0 (0.0%) 10 (20.8%)	0 (0.0%) 0 (0.0%) 15 (31.3%) 46 (95.8%) 6 (12.5%) 0 (0.0%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 2 (4.2%) 33 (68.8
ic objectives or hypothesis. ption of trial design (such as parallel, factorial) including allocation ratio. applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	44 (91.7%) 13 (27.1%) 0 (0.0%) 9 (18.8%) 38 (79.2%) 3 (6.3%)	4 (8.3%) 20 (41.7%) 0 (0.0%) 0 (0.0%) 10 (20.8%)	0 (0.0%) 15 (31.3%) 46 (95.8%) 6 (12.5%) 0 (0.0%)	0 (0.0%) 0 (0.0%) 2 (4.2%) 33 (68.8
ption of trial design (such as parallel, factorial) including allocation ratio. applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	13 (27.1%)         0 (0.0%)         9 (18.8%)         38 (79.2%)         3 (6.3%)	20 (41.7%) 0 (0.0%) 0 (0.0%) 10 (20.8%)	15 (31.3%) 46 (95.8%) 6 (12.5%) 0 (0.0%)	0 (0.0%) 2 (4.2%) 33 (68.8
applicable, how care providers were allocated to each trial group. ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	0 (0.0%) 9 (18.8%) 38 (79.2%) 3 (6.3%)	0 (0.0%) 0 (0.0%) 10 (20.8%)	46 (95.8%) 6 (12.5%) 0 (0.0%)	2 (4.2%) 33 (68.8
ant changes to methods after trial commencement (such as eligibility criteria), with reasons. lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	9 (18.8%) 38 (79.2%) 3 (6.3%)	0 (0.0%) 10 (20.8%)	6 (12.5%) 0 (0.0%)	33 (68.8
lity criteria for participants. applicable, eligibility criteria for centers and for care providers.	38 (79.2%) 3 (6.3%)	10 (20.8%)	0 (0.0%)	
applicable, eligibility criteria for centers and for care providers.	3 (6.3%)	<b>`</b>	~ /	0 (0.0%)
		16 (33.3%)	29 (60 4%)	
s and locations where the data were collected.	10 (27 50/)		29 (00.470)	0 (0.0%)
	18 (37.5%)	3 (6.3%)	27 (56.3%)	0 (0.0%)
terventions for each group with sufficient details to allow replication, including how and when they ctually administered.	0 (0.0%)	0 (0.0%)	48 (100.0%)	0 (0.0%)
e details of both the experimental treatment and comparator.	47 (97.9%)	0 (0.0%)	1 (2.1%)	0 (0.0%)
ption of the different components of the interventions and, when applicable, description of the ure for tailoring the interventions to individual participants.	8 (16.7%)	16 (33.3%)	24 (50.0%)	0 (0.0%)
of whether and how the interventions were standardized.	5 (10.4%)	2 (4.2%)	41 (85.4%)	0 (0.0%)
of whether and how adherence of care providers to the protocol was assessed or enhanced.	2 (4.2%)	3 (6.3%)	43 (89.6%)	0 (0.0%)
of whether and how adherence of participants to interventions was assessed or enhanced.	2 (4.2%)	3 (6.3%)	43 (89.6%)	0 (0.0%)
etely defined pre-specified primary and secondary outcome measures, including how and when they ssessed.	40 (83.3%)	2 (4.2%)	6 (12.5%)	0 (0.0%)
of of	f whether and how adherence of care providers to the protocol was assessed or enhanced. f whether and how adherence of participants to interventions was assessed or enhanced.	f whether and how adherence of care providers to the protocol was assessed or enhanced. 2 (4.2%) f whether and how adherence of participants to interventions was assessed or enhanced. 2 (4.2%) ely defined pre-specified primary and secondary outcome measures, including how and when they 40 (83.3%)	f whether and how adherence of care providers to the protocol was assessed or enhanced. 2 (4.2%) 3 (6.3%) f whether and how adherence of participants to interventions was assessed or enhanced. 2 (4.2%) 3 (6.3%) ely defined pre-specified primary and secondary outcome measures, including how and when they 40 (83.3%) 2 (4.2%)	f whether and how adherence of care providers to the protocol was assessed or enhanced. 2 (4.2%) 3 (6.3%) 43 (89.6%) f whether and how adherence of participants to interventions was assessed or enhanced. 2 (4.2%) 3 (6.3%) 43 (89.6%) ely defined pre-specified primary and secondary outcome measures, including how and when they 40 (83.3%) 2 (4.2%) 6 (12.5%)

Supplementary Table 9: Exercise RCT CONSORT-NPT Data Extraction Summary

ltem No.		<b>Evaluation</b>	<u>Outcomes</u>		
10.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)
6b	Any changes to trial outcomes after the trial commenced, with reasons.	2 (4.2%)	0 (0.0%)	1 (2.1%)	45 (93.8
7ai	How sample size was determined.	42 (87.5%)	0 (0.0%)	6 (12.5%)	0 (0.0%)
7aii	When applicable, details of whether and how the clustering by care providers or centers was addressed.	0 (0.0%)	0 (0.0%)	30 (62.5%)	18 (37.5
7b	When applicable, explanation of any interim analyses and stopping guidelines.	5 (10.4%)	0 (0.0%)	0 (0.0%)	43 (89.6
8a -	Method used to generate random allocation sequence.	33 (68.8%)	0 (0.0%)	15 (31.3%)	0 (0.0%)
8b	Type of randomization; details of any restriction (such as blocking and block size).	39 (81.3%)	0 (0.0%)	9 (18.8%)	0 (0.0%)
	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.	15 (31.3%)	0 (0.0%)	33 (68.8%)	0 (0.0%)
	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.	3 (6.3%)	7 (14.6%)	38 (79.2%)	0 (0.0%)
	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	18 (37.5%)	0 (0.0%)	30 (62.5%)	0 (0.0%
11b	If relevant, description of the similarity of interventions.	12 (25.0%)	0 (0.0%)	0 (0.0%)	36 (75.0
11c	If blinding was not possible, description of any attempts to limit bias.	12 (25.0%)	1 (2.1%)	22 (45.8%)	13 (27.1
12ai	Statistical methods used to compare groups for primary and secondary outcomes.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%
12aii	When applicable, details of whether and how the clustering by care providers or centers was addressed.	5 (10.4%)	0 (0.0%)	21 (43.8%)	22 (45.8
12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses.	27 (56.3%)	0 (0.0%)	0 (0.0%)	21 (43.8
13a	Participant flow diagram.	42 (87.5%)	0 (0.0%)	6 (12.5%)	0 (0.0%
	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome.	41 (85.4%)	0 (0.0%)	7 (14.6%)	0 (0.0%)
	The number of care providers or centers performing the intervention in each group and the number of patients treated by each care provider or in each center.	7 (14.6%)	0 (0.0%)	41 (85.4%)	0 (0.0%)
	For each group, losses and exclusions after randomization, together with reasons.	43 (89.6%)	2 (4 2%)	3 (6.3%)	0 (0.0%)

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Supplementary Table 9: Exercise RCT CONSORT-NPT Data Extraction Summary

		<b>Evaluation</b>	Outcomes		
Item No.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)
13c	For each group, the delay between randomization and the initiation of the intervention.	1 (2.1%)	0 (0.0%)	47 (97.9%)	0 (0.0%)
13d	Details of the experimental treatment and comparator as they were implemented.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
14a	Dates defining the periods of recruitment and follow-up.	18 (37.5%)	22 (45.8%)	8 (16.7%)	0 (0.0%)
14b	Why the trial ended or was stopped.	7 (14.6%)	0 (0.0%)	3 (6.3%)	38 (79.2
15i	A table showing baseline demographic and clinical characteristics for each group.	45 (93.8%)	0 (0.0%)	3 (6.3%)	0 (0.0%
15ii	When applicable, a description of care providers (case volume, qualification, expertise, etc.) and centers (volume) in each group.	13 (27.1%)	0 (0.0%)	35 (72.9%)	0 (0.0%
16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.	37 (77.1%)	9 (18.8%)	2 (4.2%)	0 (0.0%
17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval).	36 (75.0%)	0 (0.0%)	12 (25.0%)	0 (0.0%
17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended.	13 (27.1%)	0 (0.0%)	3 (6.3%)	32 (66.7
18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory.	29 (60.4%)	0 (0.0%)	1 (2.1%)	18 (37.5
19	See CONSORT-Harms				
20i	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.	33 (68.8%)	8 (16.7%)	7 (14.6%)	0 (0.0%
20ii	In addition, take into account the choice of the comparator, lack of or partial blinding, and unequal expertise of care providers or centers in each group.	9 (18.8%)	7 (14.6%)	32 (66.7%)	0 (0.0%
21	Generalizability (external validity) of the trial findings according to the intervention, comparators, patients, and care providers and centers involved in the trial.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%
22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%
23	Registration number and name of trial registry.	39 (81.3%)	0 (0.0%)	9 (18.8%)	0 (0.0%
	Where the full trial protocol can be accessed, if available.	10 (20.8%)	0 (0.0%)	38 (79.2%)	0 (0.0%
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## Supplementary Table 10: Pharmacological RCT CONSORT Data Extraction Summary

## Supplementary Table 10: Pharmacological RCT CONSORT Data Extraction Summary

		<b>Evaluation</b>	<u>Outcomes</u>		
Item No.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)
1a	Identification as a randomized trial in the title.	43 (89.6%)	0 (0.0%)	5 (10.4%)	0 (0.0%)
1b	Structured summary of trial design, methods, results, and conclusions.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2a	Scientific background and explanation of rationale.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2b	Specific objectives or hypothesis.	37 (77.1%)	11 (22.9%)	0 (0.0%)	0 (0.0%)
3a	Description of trial design (such as parallel, factorial) including allocation ratio.	30 (62.5%)	9 (18.8%)	9 (18.8%)	0 (0.0%)
3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons.	10 (20.8%)	0 (0.0%)	5 (10.4%)	33 (68.8
4a	Eligibility criteria for participants.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4b	Settings and locations where the data were collected.	10 (20.8%)	7 (14.6%)	31 (64.6%)	0 (0.0%)
	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered.	32 (66.7%)	0 (0.0%)	16 (33.3%)	0 (0.0%)
	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.	42 (87.5%)	5 (10.4%)	1 (2.1%)	0 (0.0%)
6b	Any changes to trial outcomes after the trial commenced, with reasons.	1 (2.1%)	0 (0.0%)	0 (0.0%)	47 (97.9
7a	How sample size was determined.	46 (95.8%)	0 (0.0%)	2 (4.2%)	0 (0.0%)
7b	When applicable, explanation of any interim analyses and stopping guidelines.	10 (20.8%)	0 (0.0%)	1 (2.1%)	37 (77.1
8a	Method used to generate random allocation sequence.	26 (54.2%)	0 (0.0%)	22 (45.8%)	0 (0.0%)
	Type of randomization; details of any restriction (such as blocking and block size).	38 (79.2%)	0 (0.0%)	10 (20.8%)	0 (0.0%)

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Supplementary Table 10: Pharmacological RCT CONSORT Data Extraction Summary

Item		<b>Evaluation</b>	Outcomes		
No.	Criterion	Yes	Unclear	No	NA
		No. (%)	No. (%)	No. (%)	No. (%)
9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned.	21 (43.8%)	0 (0.0%)	27 (56.3%)	0 (0.0%)
10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions.	4 (8.3%)	10 (20.8%)	34 (70.8%)	0 (0.0%)
11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	47 (97.9%)	0 (0.0%)	1 (2.1%)	0 (0.0%)
11b	If relevant, description of the similarity of interventions.	22 (45.8%)	0 (0.0%)	0 (0.0%)	26 (54.2)
12a	Statistical methods used to compare groups for primary and secondary outcomes.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses.	30 (62.5%)	0 (0.0%)	11 (22.9%)	7 (14.6%
13	Participant flow diagram.	43 (89.6%)	0 (0.0%)	5 (10.4%)	0 (0.0%)
13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome.	46 (95.8%)	0 (0.0%)	2 (4.2%)	0 (0.0%)
13b	For each group, the delay between randomization and the initiation of the intervention.	39 (81.3%)	6 (12.5%)	1 (2.1%)	2 (4.2%)
14a	Dates defining the periods of recruitment and follow-up.	32 (66.7%)	14 (29.2%)	2 (4.2%)	0 (0.0%)
14b	Why the trial ended or was stopped.	7 (14.6%)	0 (0.0%)	6 (12.5%)	35 (72.9
15	A table showing baseline demographic and clinical characteristics for each group.	47 (97.9%)	0 (0.0%)	1 (2.1%)	0 (0.0%)
16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups.	36 (75.0%)	11 (22.9%)	1 (2.1%)	0 (0.0%)
17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval).	39 (81.3%)	0 (0.0%)	9 (18.8%)	0 (0.0%)
17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended.	34 (70.8%)	0 (0.0%)	3 (6.3%)	11 (22.9
18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory.	41 (85.4%)	0 (0.0%)	1 (2.1%)	6 (12.5%
	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.x	html			

Supplementary Table 10: Pharmacological RCT CONSORT Data Extraction Summary

Itom		<b>Evaluation</b>	Outcomes		
Item No.	Criterion	Yes No. (%)	Unclear No. (%)	No No. (%)	NA No. (%)
19	See CONSORT-Harms				<u> </u>
20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.	29 (60.4%)	9 (18.8%)	10 (20.8%)	0 (0.0%)
21	Generalizability (external validity) of the trial findings.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.	48 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
23	Registration number and name of trial registry.	40 (83.3%)	0 (0.0%)	8 (16.7%)	0 (0.0%)
24	Where the full trial protocol can be accessed, if available.	12 (25.0%)	0 (0.0%)	36 (75.0%)	0 (0.0%)
25	Sources of funding and other support (such as supply of drugs), role of funders.	23 (47.9%)	23 (47.9%)	2 (4.2%)	0 (0.0%)
	: NA, not applicable; No., number				

Supplementary Table 11: Exercise & Pharmacological RCT CONSORT-Harms Data Extraction Summary

Item No.	Criterion	Evaluation Outcomes	Exercise No. (%)	Pharma No. (%)
1	If the study collected data on harms and benefits, the title or	Yes	17 (35.4%)	34 (70.8%)
	abstract should so state.	Unclear	0 (0.0%)	0 (0.0%)
		No	31 (64.6%)	14 (29.2%)
		NA	0 (0.0%)	0 (0.0%)
2	If the trial addresses both harms and benefits, the introduction	Yes	10 (20.8%)	16 (33.3%)
	should so state.	Unclear	0 (0.0%)	0 (0.0%)
		No	38 (79.2%)	32 (66.7%)
		NA	0 (0.0%)	0 (0.0%)
3	List addressed adverse events with definitions for each (with	Yes	31 (64.6%)	41 (85.4%)
	attention, when relevant, to grading, expected vs. unexpected	Unclear	1 (2.1%)	3 (6.3%)
	events, reference to standardized and validated definitions, and	No	16 (33.3%)	4 (8.3%)
	description of new definitions).	NA	0 (0.0%)	0 (0.0%)
4	Clarify how harms-related information was collected (mode of	Yes	12 (25.0%)	17 (35.4%)
	data collection, timing, attribution methods, intensity of	Unclear	5 (10.4%)	12 (25.0%)
	ascertainment, and harms-related monitoring and stopping rules,	No	31 (64.6%)	19 (39.6%)
	if pertinent).	NA	0 (0.0%)	0 (0.0%)
5	Describe plans for presenting and analyzing information on	Yes	8 (16.7%)	27 (56.3%)
	harms (including coding, handling of recurrent events,	Unclear	0 (0.0%)	1 (2.1%)
	specification of timing issues, handling of continuous measures,	No	39 (81.3%)	20 (41.7%)
	and any statistical analyses).	NA	1 (2.1%)	0 (0.0%)
6	Describe for each arm the participant withdrawals that are due to	Yes	26 (54.2%)	31 (64.6%)
	harms and their experiences with the allocated treatment.	Unclear	0 (0.0%)	0 (0.0%)
	1	No	16 (33.3%)	12 (25.0%)
		NA	6 (12.5%)	5 (10.4%)
7	Provide the denominators for analyses on harms.	Yes	22 (45.8%)	39 (81.3%)
	,	Unclear	0 (0.0%)	0 (0.0%)
		No	18 (37.5%)	8 (16.7%)
		NA	8 (16.7%)	1 (2.1%)
8	Present the absolute risk per arm and per adverse event type,	Yes	13 (27.1%)	33 (68.8%)
-	grade, and seriousness, and present appropriate metrics for	Unclear	0 (0.0%)	0 (0.0%)
	recurrent events, continuous variables, and scale variables,	No	29 (60.4%)	14 (29.2%)
	whenever pertinent.	NA	6 (12.5%)	1 (2.1%)
9	Describe any subgroup analyses and exploratory analyses for	Yes	3 (6.3%)	3 (6.3%)
-	harms.	Unclear	0 (0.0%)	0 (0.0%)
		No	24 (50.0%)	44 (91.7%)
		NA	21 (43.8%)	1 (2.1%)
10	Provide a balanced discussion of benefits and harms with	Yes	15 (31.3%)	31 (64.6%)
-	emphasis on study limitations, generalizability, and other	Unclear	0 (0.0%)	0 (0.0%)
	sources of information on harms.	No	25 (52.1%)	16 (33.3%)
		NA	8 (16.7%)	1 (2.1%)

Supplementary Table 11: Exercise & Pharmacological RCT CONSORT-Harms Data Extraction Summary

Notes: NA, not applicable; No., number

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### Supplementary Table 12: Exercise & Pharmacological Intervention Data Extraction Summary

Item No.	Criterion	Evaluation Outcomes	Exercise No. (%)	Pharma No. (%)
1	Intervention Modality	Yes	22 (45.8%)	40 (83.3%)
1	inter vention woodunty	Unclear	17 (35.4%)	0 (0.0%)
		No	9 (18.8%)	8 (16.7%)
		NA	0 (0.0%)	0 (0.0%)
2	Intervention Setting	Yes	36 (75.0%)	10 (20.8%)
-		Unclear	5 (10.4%)	2 (4.2%)
		No	7 (14.6%)	36 (75.0%)
		NA	0 (0.0%)	0 (0.0%)
3	Intervention Frequency	Yes	40 (83.3%)	46 (95.8%)
5	inter ( entren i requency	Unclear	0 (0.0%)	0 (0.0%)
		No	8 (16.7%)	2 (4.2%)
		NA	0 (0.0%)	0(0.0%)
4	Total Intervention Time	Yes	48 (100.0%)	47 (97.9%)
•		Unclear	0 (0.0%)	0 (0.0%)
		No	0 (0.0%)	1 (2.1%)
		NA	0 (0.0%)	0 (0.0%)
5	Intervention Dose <sup>*</sup>	Yes	22 (45.8%)	46 (95.8%)
		Unclear	0 (0.0%)	0 (0.0%)
		No	26 (54.2%)	2 (4.2%)
		NA	0 (0.0%)	0 (0.0%)
6	Intervention Compliance & Adherence	Yes	2 (4.2%)	8 (16.7%)
		Unclear	3 (6.3%)	0 (0.0%)
		No	43 (89.6%)	40 (83.3%)
		NA	0 (0.0%)	0 (0.0%)

\*Complete reporting of exercise therapy dose required complete reporting of:

- Exercise session intensity (aerobic and resistance training interventions) •
- Exercise session duration (aerobic and resistance training interventions) •
- Number of sets (resistance training interventions only) •
- ly) Number of repetitions (resistance training interventions only) •

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Online Supplement References

1 2 3	Onlin	e Supplement References
4 5	1.	Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols
6 7		(PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.
8 9	2.	Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological
10 11		quality of systematic reviews. Bmc Med Res Methodol. 2007;7:10.
12 13	3.	Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, Group C. Extending the CONSORT statement to randomized trials
14 15		of nonpharmacologic treatment: explanation and elaboration. Ann Intern Med. 2008;148(4):295-309.
15 16 17	4.	Kunath F, Grobe HR, Rücker G, et al. Do journals publishing in the field of urology endorse reporting guidelines? A survey
18		of author instructions. Urologia Internationalis. 2012;88(1):54-59.
19 20	5.	Samaan Z, Mbuagbaw L, Kosa D, et al. A systematic scoping review of adherence to reporting guidelines in health care
21 22		literature. J Multidiscip Healthc. 2013;6:169-188.
23 24	6.	Mills E, Wu P, Gagnier J, Heels-Ansdell D, Montori VM. An analysis of general medical and specialist journals that endorse
25 26		CONSORT found that reporting was not enforced consistently. Journal of clinical epidemiology. 2005;58(7):662-667.
27 28	7.	Hoffmann TC, Erueti C, Glasziou PP. Poor description of non-pharmacological interventions: analysis of consecutive sample
29 30		of randomised trials. BMJ. 2013;347:f3755.
31 32	8.	Mills E, Loke YK, Wu P, et al. Determining the reporting quality of RCTs in clinical pharmacology. Br J Clin Pharmacol.
33 34		2004;58(1):61-65.
35 36	9.	Mills EJ, Wu P, Gagnier J, Devereaux PJ. The quality of randomized trial reporting in leading medical journals since the
37 38		revised CONSORT statement. Contemp Clin Trials. 2005;26(4):480-487.
39	10.	Khan MS, Lateef N, Siddiqi TJ, et al. Level and Prevalence of Spin in Published Cardiovascular Randomized Clinical Trial
40 41		Reports With Statistically Nonsignificant Primary Outcomes: A Systematic Review. JAMA Netw Open. 2019;2(5):e192622.
42 43	11.	Pandis N, Polychronopoulou A, Eliades T. An assessment of quality characteristics of randomised control trials published in
44 45		dental journals. J Dent. 2010;38(9):713-721.
46 47	12.	Grant SP, Mayo-Wilson E, Melendez-Torres GJ, Montgomery P. Reporting quality of social and psychological intervention
48 49 50 51 52 53		trials: a systematic review of reporting guidelines and trial publications. PLoS One. 2013;8(5):e65442.
	13.	Ghimire S, Kyung E, Kang W, Kim E. Assessment of adherence to the CONSORT statement for quality of reports on
		randomized controlled trial abstracts from four high-impact general medical journals. Trials. 2012;13(1):77.
54 55	14.	American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. Wolters Kluwer; 2018.
56 57		
57 58 59		127
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Online Supplement References** 

#### **BMJ** Open

1 15. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for 2 3 health-related research. Public Health Rep. 1985;100(2):126-131. 4 5 16. Fleming PS, Koletsi D, Seehra J, Pandis N. Systematic reviews published in higher impact clinical journals were of higher 6 7 quality. Journal of clinical epidemiology. 2014;67(7):754-759. 8 9 17. Gluud LL, Sørensen TIA, Gøtzsche PC, Gluud C. The Journal Impact Factor as a Predictor of Trial Quality and Outcomes: 10 11 Cohort Study of Hepatobiliary Randomized Clinical Trials. American Journal of Gastroenterology. 2005;100(11):2431-2435. 12 13 18. Beckers PJ, Denollet J, Possemiers NM, Wuyts FL, Vrints CJ, Conraads VM. Combined endurance-resistance training vs. 14 endurance training in patients with chronic heart failure: a prospective randomized study. Eur Heart J. 2008;29(15):1858-15 16 1866. 17 18 Hoendermis ES, Liu LC, Hummel YM, et al. Effects of sildenafil on invasive haemodynamics and exercise capacity in heart 19. 19 20 failure patients with preserved ejection fraction and pulmonary hypertension: a randomized controlled trial. Eur Heart J. 21 22 2015;36(38):2565-2573. 23 24 20. Beer M, Wagner D, Myers J, et al. Effects of exercise training on myocardial energy metabolism and ventricular function 25 26 assessed by quantitative phosphorus-31 magnetic resonance spectroscopy and magnetic resonance imaging in dilated 27 28 cardiomyopathy. J Am Coll Cardiol. 2008;51(19):1883-1891. 29 30 21. Hamshere S, Arnous S, Choudhury T, et al. Randomized trial of combination cytokine and adult autologous bone marrow 31 32 progenitor cell administration in patients with non-ischaemic dilated cardiomyopathy: the REGENERATE-DCM clinical 33 34 trial. Eur Heart J. 2015;36(44):3061-3069. 35 Ligibel JA, Campbell N, Partridge A, et al. Impact of a mixed strength and endurance exercise intervention on insulin levels 36 22. 37 in breast cancer survivors. J Clin Oncol. 2008;26(6):907-912. 38 39 23. Schmid P, Pinder SE, Wheatley D, et al. Phase II Randomized Preoperative Window-of-Opportunity Study of the PI3K 40 41 Inhibitor Pictilisib Plus Anastrozole Compared With Anastrozole Alone in Patients With Estrogen Receptor-Positive Breast 42 43 Cancer. J Clin Oncol. 2016;34(17):1987-1994. 44 45 24. Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive 46 47 pulmonary disease: a randomized trial. Ann Intern Med. 2008;149(12):869-878. 48 49 25. Lapperre TS, Snoeck-Stroband JB, Gosman MM, et al. Effect of fluticasone with and without salmeterol on pulmonary 50 51 outcomes in chronic obstructive pulmonary disease: a randomized trial. Ann Intern Med. 2009;151(8):517-527. 52 53 26. Adamsen L, Ouist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients 54 55 undergoing chemotherapy: randomised controlled trial. BMJ. 2009;339(7726):b3410. 56 57 58 128 59 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml 60

Page 173 of 179

# BMJ Open

Online Supplement References

	0	
1 2	27.	Rimawi M, Ferrero JM, de la Haba-Rodriguez J, et al. First-Line Trastuzumab Plus an Aromatase Inhibitor, With or Without
3 4		Pertuzumab, in Human Epidermal Growth Factor Receptor 2-Positive and Hormone Receptor-Positive Metastatic or Locally
5 6		Advanced Breast Cancer (PERTAIN): A Randomized, Open-Label Phase II Trial. J Clin Oncol. 2018;36(28):2826-2835.
7 8	28.	Courneya KS, Sellar CM, Stevinson C, et al. Randomized controlled trial of the effects of aerobic exercise on physical
9		functioning and quality of life in lymphoma patients. J Clin Oncol. 2009;27(27):4605-4612.
10 11	29.	Cortelazzo S, Tarella C, Gianni AM, et al. Randomized Trial Comparing R-CHOP Versus High-Dose Sequential
12 13		Chemotherapy in High-Risk Patients With Diffuse Large B-Cell Lymphomas. J Clin Oncol. 2016;34(33):4015-4022.
14 15	30.	McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial
16 17		disease with and without intermittent claudication: a randomized controlled trial. JAMA. 2009;301(2):165-174.
18 19	31.	Ford I, Scott NW, Herd V, Mitchell LR, Williams DJ, Brittenden J. A randomized controlled trial of platelet activity before
20		and after cessation of clopidogrel therapy in patients with stable cardiovascular disease. J Am Coll Cardiol. 2014;63(3):233-
21 22		239.
23 24		
25	32.	Monninkhof EM, Velthuis MJ, Peeters PH, Twisk JW, Schuit AJ. Effect of exercise on postmenopausal sex hormone levels
26 27		and role of body fat: a randomized controlled trial. J Clin Oncol. 2009;27(27):4492-4499.
28 29	33.	Loprinzi CL, Qin R, Balcueva EP, et al. Phase III, randomized, double-blind, placebo-controlled evaluation of pregabalin for
30 31		alleviating hot flashes, N07C1. J Clin Oncol. 2010;28(4):641-647.
32 33	34.	O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-
34		ACTION randomized controlled trial. JAMA. 2009;301(14):1439-1450.
35 36	35.	Gheorghiade M, Bohm M, Greene SJ, et al. Effect of aliskiren on postdischarge mortality and heart failure readmissions
37 38		among patients hospitalized for heart failure: the ASTRONAUT randomized trial. JAMA. 2013;309(11):1125-1135.
39 40	36.	Patwala AY, Woods PR, Sharp L, Goldspink DF, Tan LB, Wright DJ. Maximizing patient benefit from cardiac
41 42		resynchronization therapy with the addition of structured exercise training: a randomized controlled study. J Am Coll
43 44		Cardiol. 2009;53(25):2332-2339.
45 46	37.	Tsujita K, Sugiyama S, Sumida H, et al. Impact of Dual Lipid-Lowering Strategy With Ezetimibe and Atorvastatin on
47 48		Coronary Plaque Regression in Patients With Percutaneous Coronary Intervention: The Multicenter Randomized Controlled
49 50		PRECISE-IVUS Trial. J Am Coll Cardiol. 2015;66(5):495-507.
51	38.	Schmitz KH, Ahmed RL, Troxel A, et al. Weight lifting in women with breast-cancer-related lymphedema. N Engl J Med.
52 53		2009;361(7):664-673.
54 55	39.	Wapnir IL, Price KN, Anderson SJ, et al. Efficacy of Chemotherapy for ER-Negative and ER-Positive Isolated Locoregional
56 57		Recurrence of Breast Cancer: Final Analysis of the CALOR Trial. J Clin Oncol. 2018;36(11):1073-1079.
58 59		129
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Online Supplement References

2	40.	Segal RJ, Reid RD, Courneya KS, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving
3 4		radiation therapy for prostate cancer. J Clin Oncol. 2009;27(3):344-351.
5 6	41.	McKay RR, Zurita AJ, Werner L, et al. A Randomized Phase II Trial of Short-Course Androgen Deprivation Therapy With
7 8		or Without Bevacizumab for Patients With Recurrent Prostate Cancer After Definitive Local Therapy. J Clin Oncol.
9 10		2016;34(16):1913-1920.
11	42.	Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with
12 13		type 2 diabetes: a randomized controlled trial. JAMA. 2010;304(20):2253-2262.
14 15	43.	Nissen SE, Nicholls SJ, Wolski K, et al. Comparison of pioglitazone vs glimepiride on progression of coronary
16 17		atherosclerosis in patients with type 2 diabetes: the PERISCOPE randomized controlled trial. JAMA. 2008;299(13):1561-
18 19		1573.
20 21	44.	Friedenreich CM, Woolcott CG, McTiernan A, et al. Alberta physical activity and breast cancer prevention trial: sex hormone
22 23		changes in a year-long exercise intervention among postmenopausal women. Journal of Clinical Oncology. 2010;28(9):1458.
24 25	45.	Johnston SRD, Hegg R, Im SA, et al. Phase III, Randomized Study of Dual Human Epidermal Growth Factor Receptor 2
26 27		(HER2) Blockade With Lapatinib Plus Trastuzumab in Combination With an Aromatase Inhibitor in Postmenopausal
28 29		Women With HER2-Positive, Hormone Receptor-Positive Metastatic Breast Cancer: ALTERNATIVE. J Clin Oncol.
30 31		2018;36(8):741-748.
32 33	46.	Galvao DA, Taaffe DR, Spry N, Joseph D, Newton RU. Combined resistance and aerobic exercise program reverses muscle
34		loss in men undergoing androgen suppression therapy for prostate cancer without bone metastases: a randomized controlled
35 36		trial. Journal of clinical oncology. 2010;28(2):340-347.
37 38	47.	Taplin ME, Montgomery B, Logothetis CJ, et al. Intense androgen-deprivation therapy with abiraterone acetate plus
39 40		leuprolide acetate in patients with localized high-risk prostate cancer: results of a randomized phase II neoadjuvant study. J
41 42		<i>Clin Oncol.</i> 2014;32(33):3705-3715.
43 44	48.	Schmitz KH, Ahmed RL, Troxel AB, et al. Weight lifting for women at risk for breast cancer-related lymphedema: a
45 46		randomized trial. JAMA. 2010;304(24):2699-2705.
47 48	49.	Hurvitz SA, Dirix L, Kocsis J, et al. Phase II randomized study of trastuzumab emtansine versus trastuzumab plus docetaxel
49 50		in patients with human epidermal growth factor receptor 2-positive metastatic breast cancer. J Clin Oncol. 2013;31(9):1157-
51 52		1163.
53 54	50.	Edelmann F, Gelbrich G, Dungen HD, et al. Exercise training improves exercise capacity and diastolic function in patients
55		with heart failure with preserved ejection fraction: results of the Ex-DHF (Exercise training in Diastolic Heart Failure) pilot
56 57		study. J Am Coll Cardiol. 2011;58(17):1780-1791.
58 59		130
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Online Supplement References

# BMJ Open

1 2	51.	Kosmala W, Holland DJ, Rojek A, Wright L, Przewlocka-Kosmala M, Marwick TH. Effect of If-channel inhibition on
3 4		hemodynamic status and exercise tolerance in heart failure with preserved ejection fraction: a randomized trial. J Am Coll
5 6		Cardiol. 2013;62(15):1330-1338.
7 8	52.	Hallsworth K, Fattakhova G, Hollingsworth KG, et al. Resistance exercise reduces liver fat and its mediators in non-alcoholic
9		fatty liver disease independent of weight loss. Gut. 2011;60(9):1278-1283.
10 11	53.	Ratziu V, Giral P, Jacqueminet S, et al. Rosiglitazone for nonalcoholic steatohepatitis: one-year results of the randomized
12 13		placebo-controlled Fatty Liver Improvement with Rosiglitazone Therapy (FLIRT) Trial. Gastroenterology. 2008;135(1):100-
14 15		110.
16 17	54.	Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J
18 19		Med. 2011;364(13):1218-1229.
20 21	55.	Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. N
22 23		Engl J Med. 2010;363(3):245-256.
24 25	56.	Belardinelli R, Georgiou D, Cianci G, Purcaro A. 10-year exercise training in chronic heart failure: a randomized controlled
26		trial. J Am Coll Cardiol. 2012;60(16):1521-1528.
27 28	57.	Goebel A, Bisla J, Carganillo R, et al. Low-Dose Intravenous Immunoglobulin Treatment for Long-Standing Complex
29 30		Regional Pain Syndrome. Annals of Internal Medicine. 2017;167(7):476-483.
31 32	58.	Campbell KL, Foster-Schubert KE, Alfano CM, et al. Reduced-calorie dietary weight loss, exercise, and sex hormones in
33 34		postmenopausal women: randomized controlled trial. J Clin Oncol. 2012;30(19):2314-2326.
35 36	59.	Ellis MJ, Suman VJ, Hoog J, et al. Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and
37 38		exemestane for postmenopausal women with estrogen receptor-rich stage 2 to 3 breast cancer: clinical and biomarker
39 40		outcomes and predictive value of the baseline PAM50-based intrinsic subtypeACOSOG Z1031. J Clin Oncol.
41 42		2011;29(17):2342-2349.
43 44	60.	Duijts SF, van Beurden M, Oldenburg HS, et al. Efficacy of cognitive behavioral therapy and physical exercise in alleviating
45		treatment-induced menopausal symptoms in patients with breast cancer: results of a randomized, controlled, multicenter trial.
46 47		J Clin Oncol. 2012;30(33):4124-4133.
48 49	61.	Urruticoechea A, Rizwanullah M, Im SA, et al. Randomized Phase III Trial of Trastuzumab Plus Capecitabine With or
50 51	-	Without Pertuzumab in Patients With Human Epidermal Growth Factor Receptor 2-Positive Metastatic Breast Cancer Who
52 53		Experienced Disease Progression During or After Trastuzumab-Based Therapy. J Clin Oncol. 2017;35(26):3030-3038.
54 55		
56 57		
57 58 59		131
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Online Supplement References** 

60

1 62. Sandri M, Kozarez I, Adams V, et al. Age-related effects of exercise training on diastolic function in heart failure with 2 3 reduced ejection fraction: the Leipzig Exercise Intervention in Chronic Heart Failure and Aging (LEICA) Diastolic 4 5 Dysfunction Study. Eur Heart J. 2012;33(14):1758-1768. 6 7 Frustaci A, Russo MA, Chimenti C. Randomized study on the efficacy of immunosuppressive therapy in patients with virus-63. 8 9 negative inflammatory cardiomyopathy: the TIMIC study. Eur Heart J. 2009;30(16):1995-2002. 10 11 64. Winter MM, van der Bom T, de Vries LC, et al. Exercise training improves exercise capacity in adult patients with a 12 13 systemic right ventricle: a randomized clinical trial. Eur Heart J. 2012;33(11):1378-1385. 14 15 65. van der Bom T, Winter MM, Bouma BJ, et al. Effect of valsartan on systemic right ventricular function: a double-blind, 16 randomized, placebo-controlled pilot trial. Circulation. 2013;127(3):322-330. 17 18 Daumit GL, Dickerson FB, Wang NY, et al. A behavioral weight-loss intervention in persons with serious mental illness. N 66. 19 20 Engl J Med. 2013;368(17):1594-1602. 21 22 67. Rosenheck RA, Krystal JH, Lew R, et al. Long-acting risperidone and oral antipsychotics in unstable schizophrenia. N Engl J 23 24 Med. 2011;364(9):842-851. 25 26 68. Kitzman DW, Brubaker PH, Herrington DM, et al. Effect of endurance exercise training on endothelial function and arterial 27 28 stiffness in older patients with heart failure and preserved ejection fraction: a randomized, controlled, single-blind trial. J Am 29 30 Coll Cardiol. 2013;62(7):584-592. 31 32 69. Caminiti G, Volterrani M, Iellamo F, et al. Effect of long-acting testosterone treatment on functional exercise capacity, 33 34 skeletal muscle performance, insulin resistance, and baroreflex sensitivity in elderly patients with chronic heart failure a 35 double-blind, placebo-controlled, randomized study. J Am Coll Cardiol. 2009;54(10):919-927. 36 37 Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and 70. 38 39 clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA. 40 41 2013;310(12):1263-1273. 42 43 71. Spitzer M, Basaria S, Travison TG, et al. Effect of testosterone replacement on response to sildenafil citrate in men with 44 45 erectile dysfunction: a parallel, randomized trial. Ann Intern Med. 2012;157(10):681-691. 46 47 Pitkälä KH, Pöysti MM, Laakkonen M, et al. Effects of the Finnish Alzheimer disease exercise trial (FINALEX): a 72. 48 49 randomized controlled trial. JAMA internal medicine. 2013;173(10):894-901. 50 51 73. Cummings JL, Lyketsos CG, Peskind ER, et al. Effect of Dextromethorphan-Quinidine on Agitation in Patients With 52 53 Alzheimer Disease Dementia: A Randomized Clinical Trial. JAMA. 2015;314(12):1242-1254. 54 55 56 57 58 132 59

Page 177 of 179

1

Online Supplement References

# BMJ Open

2	74.	Galvao DA, Spry N, Denham J, et al. A multicentre year-long randomised controlled trial of exercise training targeting
3 4		physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG
5 6		03.04 RADAR. Eur Urol. 2014;65(5):856-864.
7 8	75.	Irani J, Celhay O, Hubert J, et al. Continuous versus six months a year maximal androgen blockade in the management of
9		prostate cancer: a randomised study. Eur Urol. 2008;54(2):382-391.
10 11 12	76.	Hollekim-Strand SM, Bjorgaas MR, Albrektsen G, Tjonna AE, Wisloff U, Ingul CB. High-intensity interval exercise
12 13 14		effectively improves cardiac function in patients with type 2 diabetes mellitus and diastolic dysfunction: a randomized
15		controlled trial. J Am Coll Cardiol. 2014;64(16):1758-1760.
16 17	77.	Han Y, Zhu G, Han L, et al. Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in
18 19		patients with diabetes and chronic kidney disease. J Am Coll Cardiol. 2014;63(1):62-70.
20 21	78.	Jones LW, Hornsby WE, Freedland SJ, et al. Effects of nonlinear aerobic training on erectile dysfunction and cardiovascular
22 23		function following radical prostatectomy for clinically localized prostate cancer. Eur Urol. 2014;65(5):852-855.
24 25	79.	Yoshimura K, Minami T, Nozawa M, et al. A Phase 2 Randomized Controlled Trial of Personalized Peptide Vaccine
26 27		Immunotherapy with Low-dose Dexamethasone Versus Dexamethasone Alone in Chemotherapy-naive Castration-resistant
28 29		Prostate Cancer. Eur Urol. 2016;70(1):35-41.
30 31	80.	Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability
32 33		in older adults: the LIFE study randomized clinical trial. JAMA. 2014;311(23):2387-2396.
34	81.	Devereux G, Cotton S, Fielding S, et al. Effect of theophylline as adjunct to inhaled corticosteroids on exacerbations in
35 36		patients with COPD: a randomized clinical trial. JAMA. 2018;320(15):1548-1559.
37 38	82.	Fakhry F, Spronk S, van der Laan L, et al. Endovascular Revascularization and Supervised Exercise for Peripheral Artery
39 40		Disease and Intermittent Claudication: A Randomized Clinical Trial. JAMA. 2015;314(18):1936-1944.
41 42	83.	Poole J, Mavromatis K, Binongo JN, et al. Effect of progenitor cell mobilization with granulocyte-macrophage colony-
43 44		stimulating factor in patients with peripheral artery disease: a randomized clinical trial. JAMA. 2013;310(24):2631-2639.
45 46	84.	Friedenreich CM, Neilson HK, O'Reilly R, et al. Effects of a High vs Moderate Volume of Aerobic Exercise on Adiposity
47 48		Outcomes in Postmenopausal Women: A Randomized Clinical Trial. JAMA Oncol. 2015;1(6):766-776.
49 50	85.	Harman SM, Black DM, Naftolin F, et al. Arterial imaging outcomes and cardiovascular risk factors in recently menopausal
51 52		women: a randomized trial. Ann Intern Med. 2014;161(4):249-260.
53 54	86.	Irwin ML, Cartmel B, Gross CP, et al. Randomized exercise trial of aromatase inhibitor-induced arthralgia in breast cancer
55 56		survivors. Journal of Clinical Oncology. 2015;33(10):1104.
57 58		
59		133 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
60		for peer renerron y integr/bingopeniong.com/site/about/guidelines.kitini

**Online Supplement References** 

1 87. Yardley DA, Ismail-Khan RR, Melichar B, et al. Randomized phase II, double-blind, placebo-controlled study of exemestane 2 3 with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptor-positive breast 4 5 cancer progressing on treatment with a nonsteroidal aromatase inhibitor. J Clin Oncol. 2013;31(17):2128-2135. 6 7 88. Murphy TP, Cutlip DE, Regensteiner JG, et al. Supervised exercise, stent revascularization, or medical therapy for 8 9 claudication due to aortoiliac peripheral artery disease: the CLEVER study. Journal of the American College of Cardiology. 10 11 2015;65(10):999-1009. 12 13 89. Krankenberg H, Tubler T, Ingwersen M, et al. Drug-Coated Balloon Versus Standard Balloon for Superficial Femoral Artery 14 In-Stent Restenosis: The Randomized Femoral Artery In-Stent Restenosis (FAIR) Trial. Circulation. 2015;132(23):2230-15 16 2236. 17 18 90. Ross R, Hudson R, Stotz PJ, Lam M. Effects of exercise amount and intensity on abdominal obesity and glucose tolerance in 19 20 obese adults: a randomized trial. Ann Intern Med. 2015;162(5):325-334. 21 22 91. Kim JM, Stewart R, Lee YS, et al. Effect of Escitalopram vs Placebo Treatment for Depression on Long-term Cardiac 23 24 Outcomes in Patients With Acute Coronary Syndrome: A Randomized Clinical Trial. JAMA. 2018;320(4):350-358. 25 26 92. van Waart H, Stuiver MM, van Harten WH, et al. Effect of Low-Intensity Physical Activity and Moderate- to High-Intensity 27 28 Physical Exercise During Adjuvant Chemotherapy on Physical Fitness, Fatigue, and Chemotherapy Completion Rates: 29 30 Results of the PACES Randomized Clinical Trial. J Clin Oncol. 2015;33(17):1918-1927. 31 32 93. Soiffer RJ, Kim HT, McGuirk J, et al. Prospective, Randomized, Double-Blind, Phase III Clinical Trial of Anti-T-33 34 Lymphocyte Globulin to Assess Impact on Chronic Graft-Versus-Host Disease-Free Survival in Patients Undergoing HLA-35 36 Matched Unrelated Myeloablative Hematopoietic Cell Transplantation. J Clin Oncol. 2017;35(36):4003-4011. 37 94. Ehlken N, Lichtblau M, Klose H, et al. Exercise training improves peak oxygen consumption and haemodynamics in patients 38 39 with severe pulmonary arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, 40 41 randomized, controlled trial. Eur Heart J. 2016;37(1):35-44. 42 43 95. Ulrich S, Keusch S, Hildenbrand FF, et al. Effect of nocturnal oxygen and acetazolamide on exercise performance in patients 44 45 with pre-capillary pulmonary hypertension and sleep-disturbed breathing: randomized, double-blind, cross-over trial. Eur 46 47 Heart J. 2015;36(10):615-623. 48 49 Kitzman DW, Brubaker P, Morgan T, et al. Effect of Caloric Restriction or Aerobic Exercise Training on Peak Oxygen 96. 50 51 Consumption and Quality of Life in Obese Older Patients With Heart Failure With Preserved Ejection Fraction: A 52 53 Randomized Clinical Trial. JAMA. 2016;315(1):36-46. 54 55 56 57 58 134 59 60

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1

2 3

4 5

6

14

33

#### **BMJ** Open

Online Supplement References
------------------------------

- 97. Gheorghiade M, Blair JE, Filippatos GS, et al. Hemodynamic, echocardiographic, and neurohormonal effects of istaroxime, a novel intravenous inotropic and lusitropic agent: a randomized controlled trial in patients hospitalized with heart failure. *J Am Coll Cardiol.* 2008;51(23):2276-2285.
- 7 98. Zhang HJ, He J, Pan LL, et al. Effects of Moderate and Vigorous Exercise on Nonalcoholic Fatty Liver Disease: A
   9 Randomized Clinical Trial. *JAMA Intern Med.* 2016;176(8):1074-1082.
- 99. Cusi K, Orsak B, Bril F, et al. Long-Term Pioglitazone Treatment for Patients With Nonalcoholic Steatohepatitis and
   Prediabetes or Type 2 Diabetes Mellitus: A Randomized Trial. *Ann Intern Med.* 2016;165(5):305-315.
- Johansen MY, MacDonald CS, Hansen KB, et al. Effect of an Intensive Lifestyle Intervention on Glycemic Control in
   Patients With Type 2 Diabetes: A Randomized Clinical Trial. *JAMA*. 2017;318(7):637-646.
- 18
   101. Wysham C, Bhargava A, Chaykin L, et al. Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients
   20
   21 With Type 2 Diabetes: The SWITCH 2 Randomized Clinical Trial. JAMA. 2017;318(1):45-56.
- McDermott MM, Ferrucci L, Tian L, et al. Effect of Granulocyte-Macrophage Colony-Stimulating Factor With or Without
   Supervised Exercise on Walking Performance in Patients With Peripheral Artery Disease: The PROPEL Randomized
   Clinical Trial. JAMA. 2017;318(21):2089-2098.
- Pradhan AD, Everett BM, Cook NR, Rifai N, Ridker PM. Effects of initiating insulin and metformin on glycemic control and
   inflammatory biomarkers among patients with type 2 diabetes: the LANCET randomized trial. *JAMA*. 2009;302(11):1186 1194.
- Saberi S, Wheeler M, Bragg-Gresham J, et al. Effect of Moderate-Intensity Exercise Training on Peak Oxygen Consumption
   in Patients With Hypertrophic Cardiomyopathy: A Randomized Clinical Trial. *JAMA*. 2017;317(13):1349-1357.
- Kosmala W, Rojek A, Przewlocka-Kosmala M, Wright L, Mysiak A, Marwick TH. Effect of Aldosterone Antagonism on
  Exercise Tolerance in Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol. 2016;68(17):1823-1834.
- 41
  42 106. Taaffe DR, Newton RU, Spry N, et al. Effects of Different Exercise Modalities on Fatigue in Prostate Cancer Patients
  43
  44 Undergoing Androgen Deprivation Therapy: A Year-long Randomised Controlled Trial. *Eur Urol.* 2017;72(2):293-299.
- Klotz LH, McNeill IY, Kebabdjian M, Zhang L, Chin JL, Canadian Urology Research C. A phase 3, double-blind,
  randomised, parallel-group, placebo-controlled study of oral weekly alendronate for the prevention of androgen deprivation
  bone loss in nonmetastatic prostate cancer: the Cancer and Osteoporosis Research with Alendronate and Leuprolide
  (CORAL) study. *Eur Urol.* 2013;63(5):927-935.
- Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or Resistance Exercise, or Both, in Dieting Obese Older Adults. *N Engl J Med.* 2017;376(20):1943-1955.
- 57 58 59 60

Online Supplement References

- 109. Grudell AB, Sweetser S, Camilleri M, et al. A controlled pharmacogenetic trial of sibutramine on weight loss and body composition in obese or overweight adults. Gastroenterology. 2008;135(4):1142-1154. 110. Dieli-Conwright CM, Courneya KS, Demark-Wahnefried W, et al. Effects of Aerobic and Resistance Exercise on Metabolic Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in Overweight or Obese Survivors of Breast Cancer: A Randomized Controlled Trial. J Clin Oncol. 2018;36(9):875-883. 111. Greenspan SL, Brufsky A, Lembersky BC, et al. Risedronate prevents bone loss in breast cancer survivors: a 2-year, randomized, double-blind, placebo-controlled clinical trial. J Clin Oncol. 2008;26(16):2644-2652. McDermott MM, Spring B, Berger JS, et al. Effect of a Home-Based Exercise Intervention of Wearable Technology and 112. Telephone Coaching on Walking Performance in Peripheral Artery Disease: The HONOR Randomized Clinical Trial. JAMA. 2018;319(16):1665-1676. Ahmed S, Rienstra M, Crijns HJ, et al. Continuous vs episodic prophylactic treatment with amiodarone for the prevention of 113. atrial fibrillation: a randomized trial. JAMA. 2008;300(15):1784-1792.
  - For peer review only http://bmjopen.bmj.com/site/about/guidelines.xhtml