# BMJ Open Effectiveness and characteristics of physical fitness training on aerobic fitness in vulnerable older adults: an umbrella review of systematic reviews

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#### ABSTRACT

**Objectives** To present an overview of effectiveness and training characteristics of physical training on aerobic fitness, compared with alternative or no training, in adults aged over 65 years with various health statuses, providing a basis for guidelines for aerobic training of vulnerable older adults that can be used in geriatric rehabilitation. **Design** An umbrella review of systematic reviews that included both randomised controlled trials and other types

Data sources MEDLINE, Embase, CINAHL and the Cochrane Library were searched on 9 September 2019. Eligibility criteria for selecting studies We included systematic reviews reporting on physical training interventions that are expected to improve aerobic fitness, presenting results for adults aged 65 years and older, describing at least one of the FITT-characteristics: Frequency, Intensity, Time or Type of exercise, and measuring aerobic fitness at least before and after the intervention.

Data extraction and synthesis Two independent reviewers extracted the data and assessed the risk of bias. A narrative synthesis was performed.

**Results** We included 51 papers on 49 reviews. Positive effect of training on aerobic fitness was reported by 33 reviews, 11 reviews remained inconclusive and 5 reviews reported no effect. Training characteristics varied largely. Frequency: 1-35 sessions/week, Intensity: light-vigorous, Time: <10-120 min/session and Types of exercise: many. The methodological quality was most often low. Subgroup analyses revealed positive effects for all health conditions except for trauma patients. Exercise characteristics from current existing guidelines are widely applicable. For vulnerable older adults, lower intensities and lower frequencies were beneficial. Some health conditions require specific adjustments. Information on adverse events was often lacking, but their occurrence seemed

**Conclusion** Physical fitness training can be effective for vulnerable older adults. Exercise characteristics from current existing guidelines are widely applicable, although lower frequencies and intensities are also beneficial. For some conditions, adjustments are advised.

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#### STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This review of systematic reviews provides a summary of the scientific literature on training of aerobic fitness in older adults with a wide variety of health statuses.
- ⇒ This review focuses on training characteristics, effects of aerobic fitness and adverse events.
- ⇒ The narrative analyses does justice to the diversity of vulnerabilities in older adults.
- An important challenge is the interpretation of the large variety of interventions, outcomes and description of the training characteristics within the studies.

#### INTRODUCTION

Geriatric rehabilitation can be defined as diagnostic and therapeutic interventions aimed at restoring functional ability or enhancing residual physical function in vulnerable older people with disabling impairments.<sup>1 2</sup> Patients in geriatric rehabilitation are vulnerable with regards to their health status, typically characterised by a wide range of frailty, comorbidity and disability. 1-3 Ageing is associated with physiological changes that result in reductions in functional capacity, such as a reduction in aerobic fitness and in muscle performance.<sup>3 4</sup> This deterioration can be a cause of disabling impairments, but hindering functional recovery. Therefore, the training of functional capacity can be considered an essential focus for geriatric rehabilitation.<sup>5</sup> An important element of functional capacity is aerobic fitness, that is, the ability of the circulatory and respiratory systems to supply oxygen during sustained physical activity. This can be improved through a number of therapeutic interventions such as walking, rowing and cycling.

There are several international guidelines that provide exercise recommendations for





improving aerobic fitness in healthy (older) adults or in adults with a specific disease or condition. <sup>47–12</sup> In general, these recommendations are based on the training principle of progressive overload. This principle implies that training should impose a greater load on the body than it is normally accustomed to and should increase throughout a training programme.<sup>7</sup> Exercise below a minimum training load will not challenge the body sufficiently enough to result in increased physical fitness.8 This relation between training load and gain in physical fitness is not linear. Training itself has a ceiling effect: the closer the patients' fitness approaches their personal ceiling, the greater the training intensity needed for improvement. Conversely, if the training load is too high, it can lead to adverse effects, for example, a decrease in training effect, myocardial infarction and in extreme cases, sudden cardiac death. 13–16 It is thus important to find the optimal equilibrium between under-training and over-training.

Training load is determined by the Frequency, Intensity and Time of training. <sup>17</sup> Together with the Type of exercise performed, these characteristics are referred to as the FITT-characteristics, which are used for exercise prescription. Exercise intensity, for example, expressed as the proportion of maximal oxygen uptake, is the most important of these four characteristics as it has the largest influence on the training load and, therefore, on the exercise dose. Frequency refers to how often the exercise is performed, usually represented in the number of sessions per week. Time is the length of the physical activity, typically expressed in minutes per session. The Type of exercise refers to the specific physical activity performed, such as walking or swimming. <sup>7</sup>

Although guidelines provide a multitude of exercise recommendations, they lack specific recommendations on aerobic exercise for the vulnerable group of patients in geriatric rehabilitation. These patients often face problems regarding frailty, comorbidity or disability, and their interaction.<sup>3</sup> Further, the underlying problems are wide-ranging. It is unclear whether and how the FITT-characteristics of, for example, the American College of Sports Medicine (ACSM), apply to this group. This is important as application of inappropriate FITTcharacteristics may lead to adverse events or to suboptimal training, resulting in the inadequate recovery of independence.<sup>8</sup> <sup>18</sup> As well as a lack of specific training guidelines for vulnerable older adults, an overview of the evidence with regards to physical fitness training in vulnerable older adults is also lacking. Currently, there are several reviews available reporting on the effect of physical fitness training on aerobic fitness in healthy older adults, 9 19 or in older patients with specific diagnoses.<sup>20–22</sup> The combination of the body of evidence of such systematic reviews regarding both healthy and impaired older adults might help to improve the exercise prescription in vulnerable older adults who are undergoing geriatric rehabilitation. Therefore, the research questions for this study are:

- 1. What is the effect of physical fitness training on aerobic fitness outcomes compared with alternative or no training in adults over 65 years old with various health statuses?
- 2. What are the training characteristics in studies that showed an improvement in aerobic fitness in adults over 65 years old?

# METHODS Design

An umbrella review was performed<sup>23</sup> and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>24</sup> Before the start of the study, a review protocol was created and registered at the PROSPERO International Prospective Register of Systematic Reviews, that is provided in online supplemental file A. Deviations from the protocol are reported in relevant parts of this methods section.

#### **Data sources**

We performed a systematic computerised search to identify systematic reviews reporting on the effect of physical fitness training on aerobic fitness in older adults. Four electronic databases were searched from their inception: MEDLINE, Embase, CINAHL and the Cochrane Library. The search strategy for MEDLINE is provided in online supplemental file B. We adapted the search strings accordingly for the other databases. The search was conducted on 9 September 2019.

### **Eligibility criteria**

We included reviews that met all of the following criteria: (1) the review was a systematic review, according to our minimal criteria that the search strategy and inclusion and exclusion criteria were described; (2) the reported intervention was physical training that was expected to improve aerobic fitness; (3) the review had to present results for adults aged 65 years and older; (4) the description of the intervention contained at least one of the FITT-characteristics: Frequency, Intensity, Time or Type of exercise; (5) aerobic fitness was measured at least before and after the intervention.

The design of the studies included in the systematic reviews could be either randomised controlled trials (RCTs) or other types of studies (non-RCTs), such as before–after studies, non-randomised or quasirandomised trials. We did this to ensure that we did not miss relevant studies on vulnerable patients for which RCT designs may not be feasible. We only included reviews published in English, with no restrictions on publication year.

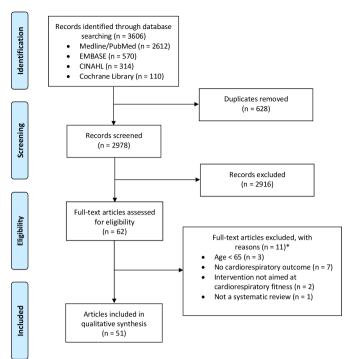
#### **Data extraction and synthesis**

Two investigators (DV and EBS) independently reviewed the titles and abstracts. Potentially relevant articles were identified and the full texts were retrieved for independent assessment using the inclusion criteria. Any disagreements were resolved by consensus or in consultation with a third reviewer (KHLG) when necessary. The validated Joanna Briggs Institute Data Extraction Form for Systematic Reviews and Research Syntheses was used and adapted for data extraction.<sup>23</sup> Data from each included systematic review were extracted independently by both reviewers (DV and EBS). Results were compared and any discrepancies were resolved through discussion. We tabulated review characteristics, such as participants, setting, number of included studies and review results, such as effect of training on aerobic fitness, and training characteristics using the FITT-characteristics. Our primary outcome was aerobic fitness by any measure, for example: VO<sub>9</sub>max and VO<sub>9</sub>peak, <sup>25</sup> 6-min walk test (6MWT), <sup>26</sup> endurance capacity with Graded Exercise Testing, 27 exercise tolerance with a BORG scale, 28 heart rate response during a graded or incremental exercise test and its recovery<sup>29</sup> and muscle fatigue measured as the decline in maximal power and electromyography activity after an incremental exercise test.<sup>30</sup>

The methodological quality of each included review was assessed independently by the two reviewers (DV and EBS), using the second version of 'A MeaSurement Tool to Assess systematic Reviews' (AMSTAR 2).<sup>31</sup> The results of the quality assessment were compared and any discrepancies were resolved through discussion.

A narrative synthesis was used to describe the characteristics of aerobic fitness training and the effect on aerobic fitness in older or frail patients. A narrative analysis enables us to handle the expected large variety in health statuses, interventions and outcomes. For the evaluation of the effect on aerobic fitness, reviews were classified into one of the following categories: 'positive effect', 'negative effect', 'inconclusive' or 'no effect', depending on the effect on aerobic fitness outcomes, such as VOomax or 6MWT. Reviews, both meta-analyses and narrative reviews, were classified as 'positive' if all of the comparisons, or at least all of the comparisons with non-exercise controls, had a statistically significant positive result. Reviews with narrative analyses were also classified as 'positive' if at least 75% of the included comparisons had a statistically significant positive result. The same criteria (in the other direction) were used for classifying reviews as 'negative'. Reviews, both with meta-analyses and with narrative analyses, were classified as having 'no effect' if none of the comparisons had a statistically significant effect. Further, reviews were classified as 'inconclusive' if the comparisons returned mixed results: some statistically significant positive results alongside not significant results. This classification of reviews was not described in-depth in the PROSPERO protocol.

In addition, two subgroup analyses were performed. The first focused on reviews that specifically reported on dose-response relationships of aerobic fitness interventions to explore optimal training characteristics of aerobic fitness. This was not explicitly stated in the PROSPERO protocol, but was added as further insights into dose effects are important for optimal exercise prescription. The second, predefined subgroup analysis explored the



PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) study flowchart. Full-text articles could be excluded for more than one reason, an overview per article can be found in online supplemental appendix 4. Adapted form Moher et al.84

effects of aerobic fitness training in groups with specific health statuses or diagnoses, such as trauma patients and patients with respiratory diseases. In this second analysis, only reviews with complete FITT-characteristics and with a risk of bias analysis were included. In the analyses of smaller subgroups, the reviews with incomplete reporting of FITT-characteristics could represent an inaccurate picture as it is unknown if the not-reported FITTcharacteristics are within the range of the other reviews in the same subgroup. Moreover, we exclude studies with an unknown risk of bias as it is impossible to judge the quality of these studies in the analyses.

#### Patient and public involvement

No patient involved.

### **Data sharing statement**

All data relevant to the study are included in the article or uploaded as supplementary information.

#### **RESULTS**

The PRISMA flowchart can be found in figure 1. It shows that 2978 records were screened and 62 articles were assessed for full-text analysis. We finally included 51 articles in the narrative synthesis, of which 3 were based on the same data, leaving 49 individual systematic reviews for analysis. 15 19-22 32-77 Online supplemental file C shows the characteristics of the included reviews, and online supplemental file D describes the interventions and a



summary of the evidence from the included reviews. A list of excluded reviews is presented in online supplemental file E.

#### **Quality assessment**

The quality of included reviews is presented in online supplemental file F. According to the AMSTAR 2 ratings, sources of bias were, for example, lacking a report of a Patient group, Intervention condition, Comparison condition and Outcome(s) (PICO) (14 reviews), no reported protocols prior to the start of the study (35 reviews) and no adequately explained decision to include RCTs, non-RCTs or their combination (44 reviews). Other sources of bias were: an incompletely described or incomprehensive literature search strategy (45 reviews) and the absence of a list of excluded studies in 41 reviews. A risk of bias analysis was performed in 40 reviews, but in only 13 did the authors take this risk of bias into account when discussing their results.

# **Participants**

The total number of participants was 28 085 with a median number of 399 and a range of 92-5230 participants per review. Only one review did not report the number of included patients. Due to large differences in reporting methods, we were not able to calculate a mean age for all of the participants. However, the mean age per review, at least for the subgroup of studies that reported on aerobic fitness outcomes, was at least 65 years. Gender was reported in only half of the included reviews. Reviews differed largely with respect to the health conditions of the studied population, varying from healthy participants to frail, hospitalised or institutionalised participants and many reviews focused on patients with specific diseases, such as heart failure or chronic obstructive pulmonary disease (COPD). The experimental setting was unclear in the majority of studies. The settings that were reported mainly concerned community-dwelling older adults and, to a lesser extent, institutionalised patients, hospitalised patients or a mixed group.

### **Characteristics of the interventions**

Of the included reviews, 30 reported on all of the FITTcharacteristics of the underlying intervention studies. The frequency of interventions ranged from one session per week to five sessions per day. The exercise intensity was measured in several ways, for example, via estimated heart rate value, a percentage of the maximum workload or walking speed or a predefined experienced exertion. The duration of training sessions lasted from several minutes to 120 min per session. The most common type of intervention was a mixed aerobics exercise programme. Mixed programmes were either combinations of different aerobic exercises or aerobic exercises combined with alternative forms of training, such as strength training. Walking and cycling were usually the major aerobic components in these mixed programmes. Both were also widely used as single interventions. Other interventions consisted of: dancing, Pilates, interactive gaming, Nordic walking and rowing. The total duration of programmes ranged from 4 days to 2 years.

#### **Outcome measures**

Twenty-three of the included reviews reported multiple outcome measures of aerobic fitness, mainly a combination of distance covered (in metres) on various walking tests and  $\mathrm{VO}_2$  max or  $\mathrm{VO}_2$ peak, which were both measured in different ways. The distance covered during walking tests was reported as the sole outcome measure of aerobic fitness for 16 reviews, and the  $\mathrm{VO}_2$ max or  $\mathrm{VO}_2$ peak was the sole outcome measure in 8 reviews. In the remaining two reviews, the outcome measure was not specified. Further, less commonly used outcome measures were time to reach a predefined rate of perceived exertion and the peg-and-ring test, among others.

# Effect of physical training on aerobic fitness

The effect of training on aerobic fitness is displayed in table 1. Twenty-nine reviews contained a meta-analysis. Twenty-two of these reviews were classified as having a 'positive effect', three were 'inconclusive' and four were classified as having 'no effect'. Of the narrative reviews, 11 reviews were classified as having a 'positive effect', 8 were 'inconclusive' and only 1 showed 'no effect'. None of the reviews was classified as having a 'negative effect'.

# Subgroup analysis: dose-response relationships

Four reviews reported that they could not draw conclusions about dose-response relationships. 36 37 41 48 One review found no dose-response relationships between physical training and aerobic capacity in older patients with heart failure.<sup>75</sup> Three publications, by the same authors and all based on the same 41 underlying studies, reported on dose-response relations of cardiorespiratory interventions in sedentary older adults. 51-53 In their most recent review, they concluded that a maximal gain in VO<sub>a</sub>max could be induced by aerobic training at a mean intensity of 66%-73% of heart rate reserve (HRR), when engaging in 40-50 min per session for 3-4 days per week for 30-40 weeks. The older adults began attaining VO<sub>o</sub>max improvements at lower training intensities of 35%-50% of HRR, and at a training length of at least 20-24 weeks. The studies in these reviews are 23 RCTs and 18 non-RCTs. The authors did not account for a risk of bias when interpreting the results.

# Subgroup analyses: categories with specific health status or diagnosis

The reviews with complete FITT-characteristics and with a risk of bias analysis could be divided into nine categories according to health status or diagnoses of their participants: (healthy) older adults (N=1), frail older adults (N=2), older adults hospitalised for an acute medical illness (N=1), cardiovascular disease (N=5), cognitive disorders (N=2), oncological disease (N=3), respiratory disease (N=7) and trauma (N=1). Three studies, reporting on participants with mixed conditions, were not included

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	(Health adults	(Healthy) older adults	Frail older adults	Hospitalised after critical illness		Cardiovascular disease	Cognitive impairment		Metabolic disease	Oncological disease	Respiratory disease	atory	Trauma	Mixed*	Total
MA: positive effect for all comparisons	ო	40 52 65			ιO	22 44 45 69 75	-	-	46	1 72	4	21 59 63 67		3 37 49 50	8
MA: positive effect, only for comparisons with non-exercise controls	<del>г</del>	6			-	42								2 4170	4
NAn: positive effect for all studies	8	38 54	1 47		-	09	2 38	36 48							9
NAn: positive effect, only for all studies with non- exercise controls	= 1 0										-	76			-
NAn: positive effect for >75% of all studies	of		33	1 22				-	39					17 1	4
Subtotal positive results	9		2	1	7		ဇာ	2		1	5		0	9	33
MA: inconclusive	4				-	99					2	43 61			က
NAn: inconclusive	Ф		2 3573	1 74	2	64 77				3 15 20 56					ω
Subtotal inconclusive results	0		0	1	ო		0	0		ಣ	2		0	0	11
MA: no effect	-	89			-	32					-	62	1 57		4
NAn: no effect			1 34												-
Subtotal not significant results	L 8		1	0	1		0	0		0	1		1	0	Ŋ
Total	7		5	6	Ŧ		ဗ	2		4	œ		-	9	49



in this analysis. For each review, the intervention and the summary of results is presented in online supplemental file D. In this file, the reviews that are included in this subgroup analysis are highlighted in italics.

# (Healthy) older adults

One review reported on (healthy) older adults. <sup>19</sup> This study showed positive effects on  $VO_2$ peak and 6MWT from combined aerobic and strength training, compared with non-exercise controls. Two to three sessions per week were given, with light-to-vigorous intensity for 30–90 min. Total duration of the programme varied from 6 to 52 weeks.

#### Frail older adults

Two reviews included frail older people,<sup>33</sup> <sup>73</sup> with one showing a positive effect,<sup>33</sup> while the other was inconclusive.<sup>73</sup>

#### Older adults hospitalised for acute medical illness

One review reported on older adults hospitalised for an acute medical illness and showed positive results. <sup>55</sup> Almost all of the FITT-characteristics showed broad ranges.

#### Cardiovascular diseases

The group of cardiovascular diseases consisted of patients after heart surgery, with peripheral arterial disease or with an abdominal aortic aneurysm. 45 64 66 69 77 Two reviews focused on patients after heart surgery. One found a positive effect on aerobic fitness after the training programme in an uncontrolled before–after study. 69 The other review on heart surgery patients showed inconclusive results from additional aerobic or resistance training added to standard aerobic cardiac rehabilitation. 66 Two reviews investigated peripheral artery disease, of which one reported a positive effect and the other inconclusive results. One review showed positive effects on (pain-free) walking distance after a training programme consisting of walking at an intensity that evoked severe claudication pain. 45 Another review demonstrated inconclusive results both in walking tests and in VO peak compared with non-exercise controls, and no effect when aerobic exercise was compared with other types or intensities of exercise.<sup>64</sup> Both the type and intensity of the training differed from the positive review: the types consisted of (treadmill) walking, lower limb aerobics, pole striding and arm cranking at a vigorous intensity or at an intensity that evoked moderate-to-maximum claudication pain.<sup>64</sup> One review reported on the effect of preoperative exercise for patients with an abdominal aortic aneurysm and showed inconclusive results.<sup>77</sup>

#### Cognitive disorders

Both reviews showed a positive effect on walking tests. <sup>36 58</sup> The severity of cognitive disorders varied from mild cognitive impairment to dementia. Blankevoort *et al* reported better outcomes for programmes with a longer duration, <sup>36</sup> and Lam *et al* showcased an effective increase in training

in studies with an intensity of 30%–60% of  ${\rm VO_2max}$  or 40% HRR that gradually progressed to 85%. <sup>58</sup>

### Oncological diseases

One review reported a positive effect in patients with prostate cancer.<sup>72</sup> The other two reviews had inconclusive findings for patients with colorectal cancer<sup>20</sup> and small-cell lung cancer.<sup>15</sup> The review showcasing a positive effect seemed to have a higher frequency and intensity than the inconclusive reviews.

#### Respiratory disease

The group concerning respiratory diseases consisted of patients with COPD, non-cystic fibrosis bronchiectasis or non-malignant, dust-related respiratory diseases. 21 43 59 61-63 76 Five reviews studied patients with moderate-to-severe COPD. Positive effects on aerobic fitness were found for aerobic training both in patients with stable COPD and in patients shortly after an exacerbation, and both for home-based and for outpatient rehabilitation. 21 63 76 The effect of (additional) resistance training is not clear; one review showed an inconclusive effect, <sup>61</sup> while another study showed no statistically significant effect.<sup>62</sup> The review on non-cystic fibrosis bronchiectasis was judged to be inconclusive, with positive effects on 6MWT but no effect on VO<sub>9</sub>max.<sup>59</sup> The review on patients with non-malignant, dust-related respiratory disease demonstrated positive effects.<sup>43</sup>

#### Trauma patients

The last category consisted of trauma patients with hip fractures in one review.<sup>57</sup> Low-frequency and moderate intensity programmes showed no effect on aerobic fitness.

#### **Adverse events**

Twenty reviews intended to report on adverse events, but they all concluded that there was a lack of information on adverse events in the underlying studies. Is 21 22 34–37 41 43–45 50 58 60 62 65 67 70 72 76 Of these 20 reviews, 9 reviews either found no adverse events I 34 36 43 60 62 72 or no difference in the presence of adverse events, compared with non-exercise controls. Seven reviews reported no serious 55 41 44 76 or very few 55 867 adverse events. One review reported serious adverse events that occasionally resulted in discontinuation of the exercise and even resulted in one death. The training programmes described in this review were for individuals with severe hypertension, mixed diagnoses or patients with heart failure, and had a frequency of three sessions per week, lasting 20–60 min for a duration of 12–24 weeks and were of light-to-vigorous intensity.

#### **Description of excluded studies**

Eleven of the 62 full-text papers were excluded after assessment (figure 1). The most important reasons for exclusion in this phase were the lack of aerobic outcomes, a participant mean age of under 65, or a lack of a subgroup analysis for this age criterion (see online supplemental file E).



#### **DISCUSSION**

This umbrella review was set up to study the effectiveness and characteristics of physical fitness training on aerobic fitness in vulnerable older adults and included 51 papers on 49 individual systematic reviews (N=28 085 participants). The majority of the included reviews found a statistically significant positive effect of physical fitness training on aerobic fitness. We found a large heterogeneity in the reported FITT-characteristics of the included interventions. Only one review found dose-effect relations for healthy older adults. For almost all categories of researched health statuses, studies with positive effects of physical fitness training were found with some variation in the FITT-characteristics reported between the categories.

#### **Comparison with current guidelines**

For older adults, the ACSM published general recommendations for physical activity (in conjunction with the American Heart Association (AHA)), and specific critical issues for exercise and training.<sup>4</sup> Guidelines for aerobic training in the position stand were derived from one of the papers based on the review of Huang et al that we included in this umbrella review. It states that 'aerobic exercise training programmes of sufficient intensity (>60% of pretraining VO<sub>9</sub>max), frequency, and length (>3 sessions per week for 16 weeks) can significantly increase VO<sub>9</sub>max in healthy middle-aged and older adults'. 4 52 Recently, expert guidelines were published for exercising in older adults, including slightly adjusted FITT-criteria and modality-specific adaptations. 12 Our review shows that for healthy older adults the guidelines of ACSM/AHA still apply to a great extent, although lower frequencies of two to three sessions per week are also beneficial. <sup>19</sup> Another finding from our review is that for most groups of older adults with impaired health, cardiorespiratory fitness can be improved with programmes that are offered less frequently and with less intensity than the ACSM/AHA guidelines prescribe. 19 21 33 36 45 58 63 69 76 This lower intensity is in line with the expert guidelines of Izquierdo et al. 12 Also in accordance with Izquierdo and colleagues, for the most vulnerable older adults, short sessions were most appropriate.<sup>33</sup> <sup>55</sup> The latter raises the question as to whether training load is best determined by separate FITT-characteristics or whether it should be merged in an overarching measure that is based on an interdependency between Frequency, Intensity and Time. In such an overarching measure, the underlying FITT-characteristics can be adjusted to a patient's needs as long as the combination of the characteristics meets the conditions of the overarching measure.<sup>78</sup>

### **Adverse events**

Due to a lack of information on adverse events in the reviews, no firm conclusions can be drawn about safety, although the available information indicates that serious adverse events rarely occur.

# Interpretation of results in the context of physiological principles of training

Aerobic fitness is the ability of the circulatory and respiratory systems to supply oxygen to the tissues. The transport of oxygen consists of several steps from ventilation of the alveoli to extraction of the oxygen from the blood at the tissue level.<sup>79</sup> In normal ageing, changes in the respiratory, cardiovascular and musculoskeletal systems lead to a decrease in aerobic fitness<sup>4</sup> that can be enhanced by specific health conditions. Impairment of one step in the aerobic pathway may be compensated by other steps. This means that the training of aerobic fitness in vulnerable older adults can focus on either improvement of impaired steps in the oxygen transport pathway, or on improvement of other, compensating steps. <sup>79</sup> An example of a mechanism of improvement of the impaired step is seen in the reviews concerning peripheral artery disease, where training at an intensity that induces severe claudication pain seems to be more beneficial for increasing (pain-free) walking distance than training at a moderate pain level or at a certain percentage of VO<sub>9</sub>max. 45 64 Intensity beyond the pain threshold may lead to an increase in the local production of collateral blood vessels.<sup>80</sup> An improved vascularisation of the lower limbs leads to an increase in the oxygen delivery and thus contributes to improved aerobic fitness. The mechanism in which training focuses on the improvement of compensating steps is also expected for patients with COPD, where the lung function decrease is irreversible. Therefore, it is likely that training which emphasises improvement of cardiovascular or muscle functioning will be successful in improving aerobic fitness in this patient group. 80 From this perspective, it seems surprising that we only found inconclusive results for resistance training, with no effect on VO<sub>o</sub>max and positive results on 6MWT and the peg-andring test. These results show that although the VO<sub>9</sub>max cannot improve (due to irreversible lung damage), submaximal performance (6MWT, peg-and-ring test) can improve through compensating mechanisms.<sup>81</sup>

Our review shows that for frail older adults, short session durations, from as little as 8 min, are beneficial when they include both aerobic and resistance training. Most programmes were progressive in time or intensity. This suggests that the programmes were fit to the abilities of the frail older adults, and thus able to provide a suitable stimulus for improvement of aerobic fitness. The combination of aerobic and resistance training suggests that multiple steps in the aerobic pathway are trained leading to a general improvement of the aerobic pathway.

Another finding of our review is the fact that many reviews included studies with short intervention durations. A deeper exploration of those studies revealed improvements in aerobic fitness for interventions with a duration of less than 6 weeks (not reported in the results section). Generally, the cardiovascular system is the major limiting factor in aerobic fitness, and adaptations to the cardiovascular system are expected after at least 6 weeks. The findings of the studies with short interventions in our



# Box 1 Summary of the evidence

# **Healthy older adults**

- ⇒ The guidelines of ACSM and AHA apply to a great extent, although lower frequencies of two to three sessions per week are also beneficial.
- ⇒ Optimal training programmes are three to four sessions per week, ranging from 40 to 50 min, for 32 to 36 weeks at a moderate-tovigorous intensity of 66%-73% of HRR.

# Vulnerable older adults: general

- ⇒ For almost all researched health conditions, aerobic fitness can improve through training.
- ⇒ High frequencies, short sessions and low intensity seem appropriate for the most vulnerable older adults. For example, after acute medical illness, heart surgery or exacerbation COPD.
- ⇒ For most patient groups, aerobic fitness can improve in programmes with a lower frequency and intensity than ACSM and AHA guidelines prescribe.

#### **Vulnerable older adults: specific health conditions**

- ⇒ For frail older adults aerobic fitness can improve in programmes with shorter sessions and programmes that consist of both aerobic and resistance training.
- ⇒ For patients after cardiovascular surgery and for patients with COPD there is no evidence that the addition of extra aerobic or resistance training to an aerobic training programme does improve cardiovascular fitness.
- ⇒ For patients with peripheral artery disease walking at an intensity that evokes severe claudication pain improves (pain-free) walking distance.
- ⇒ For patients with non-malignant, dust-related diseases low frequencies (two to three per week) and relatively short sessions (15–30 min) are advised.
- ⇒ For patients with non-small-cell lung cancer vigorous intensities are advised.
- ⇒ For patients after trauma training programmes with a low frequency, relatively short sessions and programme duration do not improve their cardiovascular fitness.
- ⇒ For *patients with abdominal aortic aneurysm* there is no evidence that exercise improves aerobic fitness.

ACSM, American College of Sports Medicine; AHA, American Heart Association; COPD, chronic obstructive pulmonary disease; HRR, heart rate reserve.

review suggest that in those patients the improvements in aerobic fitness are induced by capillary and/or mitochondrial adaptations that can be initiated within 14 days of endurance training.<sup>83</sup>

In box 1, we summarise our interpretation of the findings of this review, in comparison with the existing guidelines.

# Strengths and limitations

An important strength of our review is our conceptual approach to the 'geriatric rehabilitation population'. This population is characterised by a combination of older age and vulnerability, with a large degree of heterogeneity, which is difficult to operationalise within inclusion criteria. For that reason, we decided to use an age criterion (>65 years), and to include reviews with a large variety of health statuses, which may influence the degree

of vulnerability. A second strength is the use of a narrative approach which enabled us to make the variety in the evidence visible, instead of reducing the evidence to a simplified number that may not be applicable to a specific situation. Through these choices, we aimed to do justice to the heterogeneity of vulnerability in older adults.

Our review has several limitations. First, there is significant heterogeneity among the designs of the studies included in the reviews, ranging from RCTs to studies without a control group. This results in evidence of varying scientific quality, including a great variety in the risk of bias. Second, in the subgroup analyses on categories with specific health statuses, we excluded the reviews with incomplete FITT-characteristics and the reviews without a risk of bias. This decision had the disadvantage that not all of the available evidence was used for our final conclusions of these subgroup analyses. Nevertheless, this decision led to better justified evidence. A third limitation is the fact that the reported training prescription may not always reflect the actual performed training. Authors should make an effort to report on these measures as well. A last limitation is the large variation of the interventions, the outcomes and the description of the FITTcharacteristics across studies, in particular with regards to the intensity. Intensity is described with robust measures (such as percentage of VOopeak, and their derivative measures, such as percentage of maximal heart rate), with measures that depend on multiple body functions (for example, a percentage of the speed on a given walking test) and lastly with measures that are hard to interpret or compare, such as 'comfortable walking speed' or an unspecified 'moderate-to-high' intensity.

Due to this large heterogeneity in intensity measures, it is difficult to ascertain which measure is the best representation of intensity of aerobic fitness training. Training should be based on an intensity that enforces physiological adaptations. For this purpose, the so-called ventilatory thresholds have been proposed, which represent the extent to which the aerobic system is able to meet the energy demand. The aerobic thresholds are dependent on aerobic fitness and can be used for safe and personalised exercise prescription.<sup>79</sup> These thresholds are not so much determined by a fixed percentage of, for example VO<sub>o</sub>max, but require specialised equipment that is usually not available in exercise settings for vulnerable older adults. In just two of the reviews, were these thresholds used. 19 33 The development of easily accessible methods to establish the ventilatory thresholds could contribute to a more personalised prescription of exercise intensity.

#### **Recommendations**

Future research should focus on easily accessible methods that reflect relevant markers of aerobic exercise intensity more appropriately, such as based on the ventilatory thresholds, and on the feasibility of an overarching measure for training load that relates to the FITT-characteristics. The effect of aerobic training programmes with low frequencies combined with light intensities



should be further assessed, and finally, effective aerobic training programmes for trauma patients (eg, after hip fracture) should be developed and investigated.

#### CONCLUSIONS

In conclusion, physical fitness training can be an effective intervention to improve aerobic fitness in older adults in general, and also in the majority of categories of older adults with specific health statuses or diagnoses, including the most frail and vulnerable older adults. The effective training characteristics of Frequency, Intensity, Time and Type comply to a great extent to the guidelines of the ACSM and the AHA. For vulnerable older adults, we found evidence that lower frequencies of two to three sessions per week and lower intensities were most beneficial, for most categories. For some conditions, specific adjustments to the FITT-characteristics are advised. These findings can be used for better exercise prescription for vulnerable older adults in general, and thus the specific group of patients in geriatric rehabilitation.

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#### **REFERENCES**

- 1 Bachmann S, Finger C, Huss A, et al. Inpatient rehabilitation specifically designed for geriatric patients: systematic review and meta-analysis of randomised controlled trials. BMJ 2010;340:c1718.
- 2 Anon. Boston Working group on improving health care outcomes through geriatric rehabilitation. *Med Care* 1997;35:JS4–20.
- 3 Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 2004;59:255–63.
- 4 American College of Sports Medicine, Chodzko-Zajko WJ, Proctor DN, et al. American College of sports medicine position stand. exercise and physical activity for older adults. Med Sci Sports Exerc 2009;41:1510–30.
- 5 Pasanen T, Tolvanen S, Heinonen A, et al. Exercise therapy for functional capacity in chronic diseases: an overview of metaanalyses of randomised controlled trials. Br J Sports Med 2017;51:1459–65.
- 6 Spirduso WW, Cronin DL. Exercise dose-response effects on quality of life and independent living in older adults. *Med Sci Sports Exerc* 2001;33:S598–608.
- 7 Liguori G. ACSM's guidelines for exercise testing and prescription. Eleventh edition / ed. Philadelphia: Lippincott Williams & Wilkins, 2021
- 8 Garber CE, Blissmer B, Deschenes MR, et al. American College of sports medicine position stand. quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc 2011;43:1334–59.
- 9 Nelson ME, Rejeski WJ, Blair SN, et al. Physical activity and public health in older adults: recommendation from the American College of sports medicine and the American heart association. Med Sci Sports Exerc 2007;39:1435–45.
- 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.
- 11 Fletcher GF, Ades PA, Kligfield P, et al. Exercise standards for testing and training: a scientific statement from the American heart association. Circulation 2013;128:873–934.
- 12 Izquierdo M, Merchant RA, Morley JE, et al. International exercise recommendations in older adults (ICFSR): expert consensus guidelines. J Nutr Health Aging 2021;25:824–53.
- 13 O'Keefe JH, Patil HR, Lavie CJ, et al. Potential adverse cardiovascular effects from excessive endurance exercise. Mayo Clin Proc 2012;87:587–95.
- Mittleman MA, Maclure M, Tofler GH, et al. Triggering of acute myocardial infarction by heavy physical exertion. protection against triggering by regular exertion. determinants of myocardial infarction onset study Investigators. N Engl J Med 1993;329:1677–83.
- 15 Gardner JR, Livingston PM, Fraser SF. Effects of exercise on treatment-related adverse effects for patients with prostate cancer receiving androgen-deprivation therapy: a systematic review. J Clin Oncol 2014;32:335–46.
- 16 Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American heart association Council on nutrition, physical activity, and metabolism and the Council on clinical cardiology. Circulation 2007;115:2358–68.



- 17 Oberg E. Physical activity prescription: our best medicine. *Integr Med* 2007;6:18–22.
- 18 Portegijs E, Buurman BM, Essink-Bot M-L, et al. Failure to regain function at 3 months after acute hospital admission predicts institutionalization within 12 months in older patients. J Am Med Dir Assoc 2012;13:569.e1–7.
- Hurst C, Weston KL, McLaren SJ, et al. The effects of same-session combined exercise training on cardiorespiratory and functional fitness in older adults: a systematic review and meta-analysis. Aging Clin Exp Res 2019;31:1701–17.
- 20 Bruns ERJ, van den Heuvel B, Buskens CJ, et al. The effects of physical prehabilitation in elderly patients undergoing colorectal surgery: a systematic review. Colorectal Dis 2016;18:O267–77.
- 21 Ryrsø CK, Godtfredsen NS, Kofod LM, et al. Lower mortality after early supervised pulmonary rehabilitation following COPDexacerbations: a systematic review and meta-analysis. BMC Pulm Med 2018:18:154.
- 22 Doyle MP, Indraratna P, Tardo DT, et al. Safety and efficacy of aerobic exercise commenced early after cardiac surgery: a systematic review and meta-analysis. Eur J Prev Cardiol 2019;26:36–45.
- 23 Aromataris E, Fernandez R, Godfrey C. Chapter 10: Umbrella Reviews. In: Aromataris E, Munn Z, eds. JBI manual for evidence synthesis. Adelaide: JBI, 2020.
- 24 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Open Med 2009;3:e123–30.
- 25 Day JR, Rossiter HB, Coats EM, et al. The maximally attainable VO2 during exercise in humans: the peak vs. maximum issue. J Appl Physiol 2003:95:1901–7.
- 26 Guyatt GH, Sullivan MJ, Thompson PJ, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. Can Med Assoc J 1985;132:919–23.
- 27 Beltz NM, Gibson AL, Janot JM, et al. Graded Exercise Testing Protocols for the Determination of VO<sub>2</sub>max: Historical Perspectives, Progress, and Future Considerations. J Sports Med 2016;2016:3968393.
- 28 Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982;14:377–81.
- 29 Carvalho RC, Vigário PDS, Chachamovitz DSdeO, et al. Heart rate response to graded exercise test of elderly subjects in different ranges of TSH levels. Arch Endocrinol Metab 2018;62:591–6.
- 30 Cannon DT, Coelho AC, Cao R, et al. Skeletal muscle power and fatigue at the tolerable limit of ramp-incremental exercise in COPD. J Appl Physiol 2016;121:1365–73.
- 31 Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or nonrandomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
- 32 Ada L, Dean CM, Vargas J, et al. Mechanically assisted walking with body weight support results in more independent walking than assisted overground walking in non-ambulatory patients early after stroke: a systematic review. J Physiother 2010;56:153–61.
- 33 Angevaren M, Aufdemkampe G, Verhaar HJ. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. Cochrane Database Syst Rev 2008:CD005381.
- 34 Anthony K, Robinson K, Logan P, et al. Chair-based exercises for frail older people: a systematic review. Biomed Res Int 2013;2013:309506.
- Baker MK, Atlantis E, Fiatarone Singh MA. Multi-Modal exercise programs for older adults. *Age Ageing* 2007;36:375–81.
   Blankevoort CG, van Heuvelen MJG, Boersma F, *et al.* Review of
- 36 Blankevoort CG, van Heuvelen MJG, Boersma F, et al. Review of effects of physical activity on strength, balance, mobility and ADL performance in elderly subjects with dementia. Dement Geriatr Cogn Disord 2010:30:392–402.
- 37 Bouaziz W, Kanagaratnam L, Vogel T, et al. Effect of aerobic training on peak oxygen uptake among seniors aged 70 or older: a meta-analysis of randomized controlled trials. Rejuvenation Res 2018:21:341–9.
- 38 Bouaziz W, Lang PO, Schmitt E, et al. Health benefits of multicomponent training programmes in seniors: a systematic review. Int J Clin Pract 2016;70:520–36.
- 39 Bouaziz W, Schmitt E, Kaltenbach G, et al. Health benefits of endurance training alone or combined with diet for obese patients over 60: a review. Int J Clin Pract 2015;69:1032–49.
- 40 Bueno de Souza RO, Marcon LdeF, Arruda ASFde, et al. Effects of mat Pilates on physical functional performance of older adults: a meta-analysis of randomized controlled trials. Am J Phys Med Rehabil 2018;97:414–25.
- 41 Bullo V, Gobbo S, Vendramin B, et al. Nordic walking can be incorporated in the exercise prescription to increase aerobic

- capacity, strength, and quality of life for elderly: a systematic review and meta-analysis. *Rejuvenation Res* 2018;21:141–61.
- 42 Cugusi L, Manca A, Yeo TJ, et al. Nordic walking for individuals with cardiovascular disease: a systematic review and meta-analysis of randomized controlled trials. Eur J Prev Cardiol 2017;24:1938–55.
- 43 Dale MT, McKeough ZJ, Troosters T, et al. Exercise training to improve exercise capacity and quality of life in people with nonmalignant dust-related respiratory diseases. Cochrane Database Syst Rev 2015;11:CD009385.
- 44 Fukuta H, Goto T, Wakami K, et al. Effects of drug and exercise intervention on functional capacity and quality of life in heart failure with preserved ejection fraction: a meta-analysis of randomized controlled trials. Eur J Prev Cardiol 2016;23:78–85.
- 45 Golledge J, Singh TP, Alahakoon C, et al. Meta-Analysis of clinical trials examining the benefit of structured home exercise in patients with peripheral artery disease. Br J Surg 2019;106:319–31.
- 46 Gomes-Neto M, de Sá-Caputo DdaC, Paineiras-Domingos LL, et al. Effects of whole-body vibration in older adult patients with type 2 diabetes mellitus: a systematic review and meta-analysis. Can J Diabetes 2019;43:524–9.
- 47 Halloway S, Buchholz SW, Wilbur J, et al. Prehabilitation interventions for older adults: an integrative review. West J Nurs Res 2015;37:103–23.
- 48 Hernández SSS, Sandreschi PF, da Silva FC, et al. What are the benefits of exercise for Alzheimer's disease? A systematic review of the past 10 years. J Aging Phys Act 2015;23:659–68.
- 49 Heyn PC, Johnson KE, Kramer AF. Endurance and strength training outcomes on cognitively impaired and cognitively intact older adults: a meta-analysis. *J Nutr Health Aging* 2008;12:401–9.
- 50 Howes SC, Charles DK, Marley J, et al. Gaming for health: systematic review and meta-analysis of the physical and cognitive effects of active computer gaming in older adults. *Phys Ther* 2017;97:1122–37.
- 51 Huang G. Cardiorespiratory function changes response to controlled endurance exercise training in older adults: a meta-analysis. University of Kansas, 2002.
- 52 Huang G, Gibson CA, Tran ZV, et al. Controlled endurance exercise training and VO2max changes in older adults: a meta-analysis. Prev Cardiol 2005;8:217–25.
- 53 Huang G, Wang R, Chen P, et al. Dose-Response relationship of cardiorespiratory fitness adaptation to controlled endurance training in sedentary older adults. *Eur J Prev Cardiol* 2016;23:518–29.
- 54 Hwang PW-N, Braun KL. The effectiveness of dance interventions to improve older adults' health: a systematic literature review. Altern Ther Health Med 2015;21:64–70.
- 55 Kanach FA, Pastva AM, Hall KS, et al. Effects of structured exercise interventions for older adults hospitalized with acute medical illness: a systematic review. J Aging Phys Act 2018;26:284–303.
- 56 Keogh JWL, MacLeod RD. Body composition, physical fitness, functional performance, quality of life, and fatigue benefits of exercise for prostate cancer patients: a systematic review. J Pain Symptom Manage 2012;43:96–110.
- 57 Kuijlaars IAR, Sweerts L, Nijhuis-van der Sanden MWG, et al. Effectiveness of supervised home-based exercise therapy compared to a control intervention on functions, activities, and participation in older patients after hip fracture: a systematic review and metaanalysis. Arch Phys Med Rehabil 2019;100:101–14.
- 58 Lam FM, Huang M-Z, Liao L-R, et al. Physical exercise improves strength, balance, mobility, and endurance in people with cognitive impairment and dementia: a systematic review. J Physiother 2018;64:4–15.
- 59 Lee AL, Hill CJ, McDonald CF, et al. Pulmonary rehabilitation in individuals with non-cystic fibrosis bronchiectasis: a systematic review. Arch Phys Med Rehabil 2017;98:774–82.
- 60 Leggio M, Fusco A, Loreti C, et al. Effects of exercise training in heart failure with preserved ejection fraction: an updated systematic literature review. Heart Fail Rev 2020;25:703–11.
- 61 Li N, Li P, Lu Y, et al. Effects of resistance training on exercise capacity in elderly patients with chronic obstructive pulmonary disease: a meta-analysis and systematic review. Aging Clin Exp Res 2020;32:1911–22.
- 62 Liao W-H, Chen J-W, Chen X, et al. Impact of resistance training in subjects with COPD: a systematic review and meta-analysis. Respir Care 2015;60:1130–45.
- 63 Paneroni M, Simonelli C, Vitacca M, et al. Aerobic exercise training in very severe chronic obstructive pulmonary disease: a systematic review and meta-analysis. Am J Phys Med Rehabil 2017;96:541–8.
- 64 Parmenter BJ, Raymond J, Fiatarone Singh MA. The effect of exercise on fitness and performance-based tests of function in intermittent claudication: a systematic review. *Sports Med* 2013;43:513–24.



- 65 Patel NK, Newstead AH, Ferrer RL. The effects of yoga on physical functioning and health related quality of life in older adults: a systematic review and meta-analysis. J Altern Complement Med 2012;18:902–17.
- 66 Pengelly J, Pengelly M, Lin K-Y, et al. Exercise parameters and outcome measures used in cardiac rehabilitation programs following median sternotomy in the elderly: a systematic review and metaanalysis. Heart Lung Circ 2019;28:1560–70.
- 67 Puhan MA, Gimeno-Santos E, Cates CJ, et al. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2016;12:CD005305.
- 68 Rezende Barbosa MPdaCde, Oliveira VC, Silva AKFda, et al. Effectiveness of functional training on cardiorespiratory parameters: a systematic review and meta-analysis of randomized controlled trials. Clin Physiol Funct Imaging 2018;38:539–46.
- 69 Ribeiro GS, Melo RD, Deresz LF, et al. Cardiac rehabilitation programme after transcatheter aortic valve implantation versus surgical aortic valve replacement: systematic review and metaanalysis. Eur J Prev Cardiol 2017;24:688–97.
- 70 Rodrigues-Krause J, Farinha JB, Krause M, et al. Effects of dance interventions on cardiovascular risk with ageing: systematic review and meta-analysis. Complement Ther Med 2016;29:16–28.
- 71 Rodrigues-Krause J, Krause M, Reischak-Oliveira A. Dancing for healthy aging: functional and metabolic perspectives. *Altern Ther Health Med* 2019;25:44–63.
- 72 Rosero ID, Ramírez-Vélez R, Lucia A, et al. Systematic review and meta-analysis of randomized, controlled trials on preoperative physical exercise interventions in patients with non-small-cell lung cancer. Cancers 2019;11. doi:10.3390/cancers11070944. [Epub ahead of print: 05 07 2019].
- 73 Rydwik E, Frändin K, Akner G. Effects of physical training on physical performance in institutionalised elderly patients (70+) with multiple diagnoses. *Age Ageing* 2004;33:13–23.
- 74 Scheerman K, Raaijmakers K, Otten RHJ, et al. Effect of physical interventions on physical performance and physical activity in older

- patients during hospitalization: a systematic review. *BMC Geriatr* 2018:18:288.
- 75 Slimani M, Ramirez-Campillo R, Paravlic A, et al. The effects of physical training on quality of life, aerobic capacity, and cardiac function in older patients with heart failure: a meta-analysis. Front Physiol 2018;9:1564.
- 76 Vieira DSR, Maltais F, Bourbeau J. Home-Based pulmonary rehabilitation in chronic obstructive pulmonary disease patients. Curr Opin Pulm Med 2010;16:134–43.
- 77 Wee IJY, Choong AMTL. A systematic review of the impact of preoperative exercise for patients with abdominal aortic aneurysm. J Vasc Surg 2020;71:2123–31.
- 78 Borresen J, Lambert MI. The quantification of training load, the training response and the effect on performance. Sports Med 2009;39:779–95.
- 79 Wasserman K. Principles of exercise testing and interpretation: including pathophysiology and clinical applications. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins, 2012.
- 80 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.
- 81 Klijn P, van Keimpema A, Legemaat M, et al. Nonlinear exercise training in advanced chronic obstructive pulmonary disease is superior to traditional exercise training. A randomized trial. Am J Respir Crit Care Med 2013;188:193–200.
- 82 Bonne TC, Doucende G, Flück D, et al. Phlebotomy eliminates the maximal cardiac output response to six weeks of exercise training. Am J Physiol Regul Integr Comp Physiol 2014;306:R752–60.
- 83 Hoier B, Olsen K, Hanskov DJA, et al. Early time course of change in angiogenic proteins in human skeletal muscle and vascular cells with endurance training. Scand J Med Sci Sports 2020;30:1117–31.
- 84 Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta- analyses: the PRISMA statement. PLoS Med 2009:6:e1000097.