

BMJ Open Effect of differentiating exercise guidance based on a patient's level of low back pain in primary care: a mixed-methods systematic review protocol

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To cite: Jorgensen JE, Afzali T, Riis A. Effect of differentiating exercise guidance based on a patient's level of low back pain in primary care: a mixed-methods systematic review protocol. *BMJ Open* 2018;**8**:e019742. doi:10.1136/bmjopen-2017-019742

► Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2017-019742>).

Received 22 September 2017
Revised 9 November 2017
Accepted 29 November 2017



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ABSTRACT

Introduction Low back pain (LBP) is one of the health conditions that lead to the most disability worldwide. Guidelines aimed at management of LBP recommend non-invasive and non-pharmacological management, including patient education, advice to stay active and exercise therapy; however, the guidelines offer no recommendation as to the allowable level of pain during exercise or how specific levels of pain should be reflected in the stage and progression of exercises or activities. The purpose of this review is to study the effect of differentiation of exercise guidance based on the level of LBP in patients in primary care.

Methods and analysis A systematic search will be performed on PubMed, EMBASE, The Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, Physiotherapy Evidence Database (PEDRO), Cochrane and PROSPERO from their inception until September 2017. Published peer-reviewed human experimental and observational studies with quantitative or qualitative designs will be included. Two independent reviewers will identify papers by reviewing titles and abstracts. Papers passing the initial selection will be appraised by two reviewers, based on their full texts. Furthermore, the reference lists of included studies will be snowballed for identification of other relevant studies. Data will be extracted using a standard extraction sheet by two independent reviewers. Disagreements will be resolved by discussion and consensus with a third reviewer. The methodological quality of studies will be assessed using the Grading of Recommendations, Assessment, Development and Evaluation risk of bias tool, or the Critical Appraisal Skills Programme. Results will be reported narratively. Search histories will be documented on EndNote X8 (Clarivate Analytics).

Ethics and dissemination Ethical approval for this review was not required as primary data will not be collected. The results will be disseminated through a peer-reviewed international journal and conference presentations.

PROSPERO registration number CRD42017074880.

INTRODUCTION

Low back pain (LBP) is one of the most common pain conditions worldwide, with a lifetime prevalence of 80%.¹ The prevalence of LBP is highest among women and

Strengths and limitations of this study

- To our knowledge, this will be the first review to synthesise evidence for differentiation of advice given by healthcare professionals for exercise treatment of low back pain, based on the pain levels of patients.
- Patients with a broad range of pain intensity levels are treated in primary care; therefore, the findings of this study will be applicable to the heterogeneous group of patients with low back pain seen in clinical practice.
- Patients participating in exercise therapy for low back pain often experience pain; this review could uncover how different levels of pain can be addressed in this context.
- We expect studies included in the review to be heterogeneous in design and to exhibit varying methodological quality, which is a limitation of this review.

individuals aged 40–80 years.¹ In the literature, LBP is traditionally defined accordingly to the duration of symptoms, where symptoms lasting less than 12 weeks are defined as acute or subacute LBP, and symptoms lasting more than 12 weeks as chronic LBP.^{2,3} In the majority of cases, the cause of LBP is unknown, and only 1%–5% of patients have a serious underlying condition, such as cancer, osteoporosis, fractures, systematic inflammatory disease or other serious condition (red flags) causing the LBP.⁴ The first-line management of LBP comprises a non-invasive and non-pharmacological treatment approach, including patient education, advice to stay active, exercise therapy and manual therapy.^{4–7} A Danish study showed that 35% of the adult population have had transient or continuous pain in the lower back in the last year. Furthermore, 21% indicated that they have had disabling LBP during the last 14 days.⁸ LBP often develops into a chronic health condition, with an unpredictable

pattern of acute episodes, remission and recurrence. In Denmark with an estimated population of approximately 5.7 million, LBP is a socioeconomic burden to society.^{8 9} The cost of treatment of LBP is estimated at €457 million, and the costs of production loss due to short-term and long-term LBP amount to an estimated €1 billion annually in Denmark.¹⁰ As LBP is the condition for which there are the most frequent consultations for professional advice in primary care,¹¹ there is a strong case for increased efforts to improve healthcare for patients with this condition.

Regardless of the duration of LBP, guidelines consistently recommend staying active and exercise therapy. However, guidelines offer no recommendation on how a specific level of pain should be reflected in the level and progression of exercises or activities; consequently, there is a substantial interpatient variation in clinician recommendations for LBP management.¹² A recent review found that protocols using painful exercises offer a small but significant benefit over pain-free exercises in the short term, with moderate quality of evidence.¹³ In the medium and long terms, there is no clear superiority of one treatment over another.¹³ Therefore, pain during therapeutic exercise to treat chronic musculoskeletal pain need not be a barrier to exercise treatment participation.¹³ Considering patients in two groups, those with and without pain, may be impractical, whereas considering patients as experiencing a continuum of different pain levels may better reflect the clinical situation.

It is possible that therapeutic exercise can modify the concentration of pain-relieving peptides and change cerebral neurological activities linked with pain processing in patients with musculoskeletal pain; however, the level of neurophysiological evidence supporting this relationship is very low.¹⁴ Accepting pain during exercise can also be an important therapeutic approach to addressing fear avoidance, since accepting pain can support physical recovery and diminish psychological fear of movement, which can worsen the physical condition.^{14 15}

An approach to targeting exercise advice based on a pain monitoring model, aligning the fluctuation of pain levels with the advice given, was effective for patients with Achilles tendinopathy.¹⁶ The model included six levels of exercise therapy, ranging from 'hardly any physical activity' to 'hard or very hard exercise regularly'. Choice of level was based on pain experienced during and after exercise. According to this model, pain was permitted to be between levels 0 and 5 on a scale from 0 to 10 during exercise, where 0 was no pain and 10 indicated the worst imaginable pain. Pain was allowed to reach 5 during exercise, but should subside by the next day to the pain level before exercise. If it did not, the patient was advised to shift to an easier exercise level.¹⁶

There is no evidence that one particular type of exercise therapy for LBP is clearly more effective than others.¹⁷ Moreover, we were unable to identify any systematic reviews evaluating the effect of guiding activity based on the level of LBP of patients in primary care. Thus, it

remains unclear if the level of pain should be reflected in the treatment approach for this condition, or whether patients with different levels of pain will benefit from different exercise approaches.^{6 17–20}

Aim

The aim of this review is to identify studies evaluating the effect of differentiating exercise guidance for patients with LBP based on the patient's level of pain in primary care. The primary outcomes considered in this review will be pain and functional outcome measurements in LBP.

The review will address the following question: What is the effect and potential cost-effectiveness of exercises for patients with LBP based on their specific levels of pain, in primary healthcare?

METHODS AND ANALYSIS

Study registration

This study is registered in PROSPERO (trial registration number: CRD42017074880).

Study conduct and reporting

This review will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols 2015 statement.²¹

Data sources

A pilot search has been conducted with the assistance of a librarian at Aalborg University Library with experience in searching for articles for systematic reviews. The pilot search was performed to qualify our search strategy. We will carry out systematic searches of PubMed (see online supplementary file 1), EMBASE, The Cumulative Index to Nursing and Allied Health Literature (CINAHL), PsycINFO, Physiotherapy Evidence Database (PEDRO), Cochrane and PROSPERO from their inception until September 2017. The search strategy will be conducted using Medical Subject Headings (MeSH)/Emtree headings, combined with free text words. We will include the following MeSH/Emtree/free text terms: 'low back pain', 'rehabilitation', 'physical therapy/medicine' and 'exercise therapy'. This will be followed by snowballing of the reference lists of included studies to identify possible articles that may not have been found in the initial search. Authors of included articles will be contacted if complete articles, or certain data such as data presented only in graphs, are not available. Studies published in English, Danish, Swedish, Norwegian and German will be considered for inclusion in this review, and there will be no limitation on the time of publication.

Types of study

The review will include studies evaluating differential guidance for exercise and physical interventions for adults above the age of 18 in primary care, where differentiation was based on the pain levels of patients. Exercise and physical therapy are broadly defined as a regimen, or a plan, of physical activities designed and prescribed for

specific therapeutic goals, with the purpose of restoring normal musculoskeletal function or reducing pain caused by disease or injury.^{22 23}

Data selection

We will include all published peer-reviewed human investigations, including both quantitative and qualitative studies, related to differential guidance on choice of exercise, based on the level of pain. We will consider both experimental and observational quantitative study designs, including randomised controlled trials (RCTs), non-RCTs, quasi-experimental, before and after studies, and prospective and retrospective cohort studies, and economic evaluations. We will include qualitative studies based on interviews and/or workshops. Studies of adults (≥ 18 years) treated in primary healthcare settings with non-specific LBP or nerve root LBP (including sciatica and/or radiculopathy) for any duration will be included.

We will exclude studies with a primary focus on pharmacological intervention of LBP, studies including patients with red flags (cancer, osteoporosis, fractures, systematic inflammatory disease or other serious conditions causing the LBP); studies performed outside primary healthcare; studies with pregnant women, children and adolescents (< 18 years); reviews, audits or service reports; conference posters or abstracts; and studies that were not peer-reviewed.

Selection of studies

Search results will be imported into Mendeley bibliographic software (Elsevier) and duplicates removed with the help of the 'check for duplicates' tool. After removing duplicates, two identical libraries will be created for the two reviewers to select relevant articles independently.

A two-stage process will be undertaken. The initial search will identify papers by review of their titles and abstracts against the inclusion and exclusion criteria, and will be conducted by two members of the review team (JEJ and TA). Any disagreement will be resolved by team discussion and consensus with a third review member (AR). Papers passing the initial selection stage will be critically appraised by two team members (JEJ and TA) based on their full texts for final eligibility. Again, disagreements will be resolved through team discussion and consensus. If further disagreement is an issue, a third team member will be involved (AR). The reference lists of the included studies will be snowballed for identification of further relevant papers. The search history will be documented in EndNote X8 (Clarivate Analytics).

Data extraction

We will tabulate the characteristics of the included studies, including date of publication, country where the study was conducted, study design, study aim, setting, condition (acute/subacute or chronic LBP), intervention(s), number of participants, follow-up periods short term (≤ 12 weeks), medium term (> 12 to < 52 weeks) and

long term (≥ 52 weeks), outcomes, author conclusions, and other (see online supplementary file 2). Data from the included studies will be extracted by two independent reviewers (JEJ and TA) using a standardised form to identify the above-mentioned characteristics of the included studies. Disagreements will be resolved through team discussion and consensus. If further disagreement is an issue, a third team member will be involved (AR). In the case of missing methodological information, the corresponding authors of the studies will be contacted. Based on current literature, when possible, outcomes will be rescaled to scales of 0–100 points. For example, a Visual Analogue Scale (VAS) score (0–10) of 4.5 (SD 1.2) will be rescaled to 45 (SD 12). For studies to be appropriate for inclusion in a meta-analysis on exercise therapy for LBP, we consider a 20-point scale for improvement in pain and a 10-point improvement scale for changes in functional outcomes to be clinically relevant. Statistical significance will be set at the 5% level.^{24–26}

Outcome(s)

The primary outcomes will be the commonly applied domains—pain and function.^{27 28} Other outcome domains will be regarded as secondary in this review.

We will measure the effect of exercise therapy guided by the participants pain levels where it is incorporated as either a primary or secondary outcome in the included studies. Outcomes may include, but will not be limited to, the following:

1. self-reported methods of pain level assessment, such as the VAS or numerical pain rating
2. LBP disability scores, such as the Roland-Morris Disability Questionnaire or the Oswestry Disability Index
3. patient pain-related fear, such as the Pain Anxiety Symptoms Scale or the Tampa Scale of Kinesiophobia
4. health-related quality of life, such as the Short Form Survey (SF-36) (as measured by the general health subscale) or EuroQol
5. employment status
6. satisfaction with treatment received
7. fear avoidance due to LBP
8. pain self-efficacy
9. self-esteem because of LBP
10. self-management of LBP.

Risk of bias (quality) assessment

As we expect this review to include studies with both quantitative and qualitative designs, it will be necessary to apply more than one quality appraisal tool to review identified studies across different types of research design.

The quality of final evidence (QoE) in quantitative studies will be determined according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE).²⁹ In the GRADE system, evaluating the QoE for each outcome of interest begins with determining the study design (eg, randomised trial or observational study) and then assessing eight additional domains:

risk of bias,³⁰ indirectness of evidence,³¹ inconsistency of evidence,³² imprecision of the estimated effect,³³ likelihood of publication bias,³⁴ the presence of a dose-response effect, magnitude of the estimated effect and issues around residual confounding.³⁵ After assessing all the mentioned domains, QoE per outcome is categorised as high, moderate, low or very low.³⁶ The overall QoE will be determined by the QoE for each of the critical outcomes, and in most instances the overall QoE will be based on the lowest QoE for any of the critical outcomes.

Appraisal of qualitative studies

Assessment of qualitative studies will be conducted using the worksheets provided by the Critical Appraisal Skills Programme (CASP).³⁷ CASP provides a checklist of questions for assessing the clarity and appropriateness of the research question; the description and appropriateness of sampling, data collection and data analysis; levels of support and evidence for claims; coherence between data, interpretation and conclusions; and, finally, level of contribution of the paper.³⁷

The process for assessment of methodological bias in individual studies will be performed on Microsoft Word, and the results will be presented as a risk of bias summary (review of the author's judgements about each risk of bias item for each study included).

Strategy for data synthesis

Qualitative research findings will be presented in a narrative form. Quantitative data will be synthesised based on ranges, descriptive analysis and interpretations of results. As heterogeneity is expected, we anticipate describing quantitative findings narratively. Meta-analysis will be conducted if a group of studies is sufficiently homogeneous, in terms of the subjects involved, interventions and outcomes, to provide a meaningful summary.³⁸ Meta-analyses will then be conducted to summarise data and produce more precise estimates of outcomes for studies considered sufficiently homogeneous to provide a meaningful combined estimate. The choice of whether to conduct a meta-analysis will depend on the number of studies, the completeness of the reported outcomes and judgement of the homogeneity among the results. Specifically, if a meta-analysis is based on a small number of studies, the estimate of between-studies variance may be substantially in error.³⁹

Ethics and dissemination

The results will be disseminated through a peer-reviewed international journal and conference presentations.

DISCUSSION

To our knowledge, this will be the first systematic review of the effect of basing exercise advice on the level of LBP of patients in primary care. A pain monitoring method often used in clinical practice is that suggested by Silbernagel *et al*¹⁶ and Thomee.^{16 40} This pain monitoring system documents

pain and discomfort during the rehabilitation period using the VAS from 0 to 10. Pain reported up to a level of 2 was accepted as 'safe', and pain levels from 3 to 5 were considered 'acceptable', whereas pain above 5 was considered to involve a 'high risk'. Pain should have subsided by the next morning. If pain did not subside, the level of the exercise programme was lowered one step. Normal participation in physical activities during the treatment period using the pain monitoring system was accepted.^{16 40} However, these studies investigated Achilles and patellofemoral pain, and it will be of interest to see if the model is also useful in LBP.

We will probably not be able to make pooled estimations of effects; therefore, the findings will likely be reported in a narrative form. However, we believe that the findings of this review will be both relevant and easily implemented in clinical practice. Results from this review will provide information that can support clinicians in decision-making regarding exercise therapy for patients with LBP. Furthermore, the review will suggest practical solutions for provision of the most effective exercise therapy for the treatment of LBP.

There is no consensus on the assessment of the validity and reliability of qualitative research; consequently, critical appraisal instruments differ.^{41 42} The Cochrane Collaboration recommends specific tools to assess the risk of bias in each included study in an intervention review, a process that is facilitated by the use of appraisal instruments that address the specific features of the study design, and focusing on the extent to which results of included studies should be believed. Study quality assessment should focus on the quality of reporting, methodological rigour, and conceptual depth and breadth of studies. Filtering, technical appraisal and theoretical appraisal are the three main stages in a critical appraisal assessment.⁴³ Online appraisal instruments are available and easily accessible, and clearly define what is meant by each individual criterion listed.^{41 43} One of these tools is the CASP, consisting of 10 questions for qualitative studies.^{37 44} The checklist provides some decision rules and instructions on how to interpret the criteria and reach a consensus, helping the reviewer to assess the rigour, credibility and relevance of a study: rigour, referring to whether the approach to the study is thorough and appropriate; credibility, referring to whether the findings are well presented and meaningful; and relevance, indicating the usefulness of the study's findings to the review.⁴⁴

Contributors This study was conceptualised by JEJ and AR. JEJ drafted the manuscript. All authors contributed equally to the design of the study. The search strategy was developed by all authors. JEJ and TA will contribute to data collection. All the authors will contribute equally to the data analysis and interpretation for the review. All the authors will critically revise the review. All authors will read and approve the final manuscript.

Funding This work is supported by the Novo Nordisk Foundation grant number NNF170C0024422. The funder has no role in the study design, collection of data, management, analysis, interpretation of data, writing of the review or the decision to submit this paper for publication.

Competing interests None declared.

Patient consent Not required.

Ethics approval Ethical approval for this review was not sought as primary data will not be collected.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

- Hoy D, March L, Brooks P, *et al.* The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;73:968–74.
- Koes BW, van Tulder M, Lin CW, *et al.* An updated overview of clinical guidelines for the management of non-specific low back pain in primary care. *Eur Spine J* 2010;19:2075–94.
- Ladeira CE. Evidence based practice guidelines for management of low back pain: physical therapy implications. *Rev Bras Fisioter* 2011;15:190–9.
- National Institute for Health and Care Excellence. Low back pain and sciatica in over 16s: assessment and management, 2016. <https://www.nice.org.uk/guidance/ng59> (accessed Aug 2017).
- Wong JJ, Côté P, Sutton DA, *et al.* Clinical practice guidelines for the noninvasive management of low back pain: A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMA) Collaboration. *Eur J Pain* 2017;21:201–16.
- Chou R, Deyo R, Friedly J, *et al.* Nonpharmacologic therapies for low back pain: a systematic review for an American College of Physicians clinical practice guideline. *Ann Intern Med* 2017;166:493–506.
- Chou R, Huffman LH. American Pain Society, American College of Physicians. Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/ American College of Physicians clinical practice guideline. *Ann Intern Med* 2007;147:492–504.
- The Danish Health Authority. Statens Institut for Medicinsk Teknologivurdering: Ondt i ryggen: Forekomst, behandling og forebyggelse i et MTV-perspektiv. *Medicinsk Teknologivurdering Serie B* 1999;1. <https://www.sst.dk/da/udgivelses/1999/ondt-i-ryggen>
- The Danish Health Authority. Sundhedsstyrelsen, Center for Evaluering og Medicinsk Teknologivurdering. Evaluering af udviklingen på rygområdet i Danmark 1999-2004 København: Sundhedsstyrelsen, Center for Evaluering og Medicinsk Teknologivurdering. 2006. <https://www.sst.dk/da/udgivelses/2006/evaluering-af-udvikling-paa-rygomraadet-i-danmark-1999-2004> (accessed Aug 2017).
- Koch MB, Davidsen M, Juel K. De samfundsmæssige omkostninger ved rygsygdomme og rygsmerter i Danmark. Statens Institut for Folkesundhed (SIF), Syddansk Universitet. National Institute of Public Health University of Southern Denmark, 2011. <http://www.si-folkesundhed.dk/udgivelses/B%C3%B8ger%20og%20rapporter/2011/De%20samfundsm%C3%A6ssige%20omkostninger%20ved%20rygsygdomme%20og%20rygsmerter%20i%20Danmark.aspx> (accessed Aug 2017).
- Della Mora LS, Perruccio AV, Badley EM, *et al.* Differences among primary care patients with different mechanical patterns of low back pain: a cross-sectional investigation. *BMJ Open* 2016;6:e013060.
- Knaggs R. Low back pain clinical guidelines: similarities and divergent views across the pond. *Br J Pain* 2017;11:70.
- Smith BE, Hendrick P, Smith TO, *et al.* Should exercises be painful in the management of chronic musculoskeletal pain? A systematic review and meta-analysis. *Br J Sport Med* 2017;1:1–10.
- Fuentes C JP, Armijo-Olivo S, Magee DJ, *et al.* Effects of exercise therapy on endogenous pain-relieving peptides in musculoskeletal pain: a systematic review. *Clin J Pain* 2011;27:365–74.
- Pincus T, Smeets RJ, Simmonds MJ, *et al.* The fear avoidance model disentangled: improving the clinical utility of the fear avoidance model. *Clin J Pain* 2010;26:739–46.
- Silbernagel KG, Thomeé R, Eriksson BI, *et al.* Continued sports activity, using a pain-monitoring model, during rehabilitation in patients with Achilles tendinopathy: a randomized controlled study. *Am J Sports Med* 2007;35:897–906.
- van Middelkoop M, Rubinstein SM, Kuijpers T, *et al.* A systematic review on the effectiveness of physical and rehabilitation interventions for chronic non-specific low back pain. *Eur Spine J* 2011;20:19–39.
- Hayden JA, van Tulder MW, Tomlinson G. Systematic review: strategies for using exercise therapy to improve outcomes in chronic low back pain. *Ann Intern Med* 2005;142:776–85.
- Pillastrini P, Gardenghi I, Bonetti F, *et al.* An updated overview of clinical guidelines for chronic low back pain management in primary care. *Joint Bone Spine* 2012;79:176–85.
- Stochkendahl MJ, Kjaer P, Hartvigsen J, *et al.* National Clinical Guidelines for non-surgical treatment of patients with recent onset low back pain or lumbar radiculopathy. *Eur Spine J* 2017;1:1–16.
- 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;4:1–9.
- Carlson H, Carlson N. An overview of the management of persistent musculoskeletal pain. *Ther Adv Musculoskelet Dis* 2011;3:91–9.
- Bernstein IA, Malik Q, Carville S, *et al.* Low back pain and sciatica: summary of NICE guidance. *BMJ* 2017;356:i6748.
- Hayden J, van Tulder MW, Malmivaara A, *et al.* Exercise therapy for treatment of non-specific low back pain (review) summary. *Cochrane Database Syst Rev* 2005;20:2–4.
- Hayden JA, Cartwright J, van Tulder MW, *et al.* Exercise therapy for chronic low back pain (protocol). *Cochrane Database Syst Rev* 2012;4:1–20.
- Hayden JA, Cartwright JL, Riley RD, *et al.* Exercise therapy for chronic low back pain: protocol for an individual participant data meta-analysis. *Syst Rev* 2012;1:64.
- Froud R, Patel S, Rajendran D, *et al.* A systematic review of outcome measures use, analytical approaches, reporting methods, and publication volume by year in low back pain trials published between 1980 and 2012: Respite, adspice, et prospice. *PLoS One* 2016;11:e0164573.
- Bombardier C. Outcome assessments in the evaluation of treatment of spinal disorders: summary and general recommendations. *Spine* 2000;25:3100–3.
- Mustafa RA, Santesso N, Brozek J, *et al.* The GRADE approach is reproducible in assessing the quality of evidence of quantitative evidence syntheses. *J Clin Epidemiol* 2013;66:736–42.
- Guyatt GH, Oxman AD, Vist G, *et al.* GRADE guidelines: 4. Rating the quality of evidence—study limitations (risk of bias). *J Clin Epidemiol* 2011;64:407–15.
- Guyatt GH, Oxman AD, Kunz R, *et al.* GRADE guidelines: 8. Rating the quality of evidence—indirectness. *J Clin Epidemiol* 2011;64:1303–10.
- Guyatt GH, Oxman AD, Kunz R, *et al.* GRADE guidelines: 7. Rating the quality of evidence—inconsistency. *J Clin Epidemiol* 2011;64:1294–302.
- Guyatt GH, Oxman AD, Kunz R, *et al.* GRADE guidelines 6. Rating the quality of evidence—imprecision. *J Clin Epidemiol* 2011;64:1283–93.
- Guyatt GH, Oxman AD, Montori V, *et al.* GRADE guidelines: 5. Rating the quality of evidence—publication bias. *J Clin Epidemiol* 2011;64:1277–82.
- Guyatt GH, Oxman AD, Sultan S, *et al.* GRADE guidelines: 9. Rating up the quality of evidence. *J Clin Epidemiol* 2011;64:1311–6.
- Balshem H, Helfand M, Schünemann HJ, *et al.* GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.
- Critical Appraisal Skills Programme (CASP) Checklists. 2017. <http://www.casp-uk.net/casp-tools-checklists> (accessed Aug 2017).
- Haidich AB. Meta-analysis in medical research. *Hippokratia* 2010;14:29–37.
- Borenstein M, Hedges LV, Higgins JPT, *et al.* When does it make sense to perform a meta-analysis? Introduction to meta-analysis. 2009:357–64.
- Thomeé R. A comprehensive treatment approach for patellofemoral pain syndrome in young women. *Phys Ther* 1997;77:1690–703.
- Hannes K. Critical appraisal of qualitative research. *Supplementary Guidance for Inclusion of Qualitative Research in Cochrane Systematic Reviews of Interventions*, 2011:1–14.
- Leung L. Validity, reliability, and generalizability in qualitative research. *J Family Med Prim Care* 2015;4:324–7.
- Zeng X, Zhang Y, Kwong JS, *et al.* The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. *J Evid Based Med* 2015;8:2–10.
- Dixon-Woods M, Shaw RL, Agarwal S, *et al.* The problem of appraising qualitative research. *Qual Saf Health Care* 2004;13:223–5.