Supplementary material – Systematic review

This document describes the method and the results of the systematic review that were used for discussion in the main paper.

**METHOD OF THE SYSTEMATIC REVIEW**

A systematic review published in Spanish (8) was updated and improved with a modified protocol in order to include ongoing studies. The protocol was developed by consensus with physiotherapists and health technology assessment (HTA) specialists.

**Data Sources and Searches**

A systematic review of the literature was performed. The review protocol can be accessed upon request. The following electronic databases were systematically searched: MEDLINE and MEDLINE in process (OvidSP, 1950-current), EMBASE (Elsevier, 1980-current), CINAHL (EBSCO, 1982-current), Cochrane Central Register of Controlled Trials (OvidSP, 2010-current), Cochrane Database of Systematic Reviews (OvidSP, 2005-current), CRD (DARE, HTA, NHS-EED) (Centre for Reviews and Dissemination’s website, 1968-current) and Physiotherapy Evidence Database (PEDro) (PEDro website, 1929-current). The International Clinical Trials Registry Platform and ClinicalTrials.gov were searched as well. A documentalist designed the search strategies with the help of physiotherapists and HTA experts. This strategy combined Medical Subject Headings (MeSH) and text terms such as: osteoarthritis, knee/ or knee osteoarthritis, Exercise Therapy/, Physical Therapy Modalities/, Exercise Movement Techniques/, Musculoskeletal Manipulations/, Rehabilitation/, exercise, physiotherapy, physical therapy, training, thermotherapy, magnetic therapy, hydrotherapy, massage, mud therapy, and others. See Supplementary Table 1 for further details. Filters for economic evaluations were applied in MEDLINE, EMBASE and CINAHL (E1;E2). The searches were applied without language limits. The reference lists of the articles included were also reviewed. The original search was performed in May 2013 and updated in February 2015 in all the aforementioned databases (Supplementary Figure 1).

**Study Selection**

Studies were selected independently by two reviewers (economists). Compliance with the inclusion criteria was verified by physiotherapists. Disagreements between reviewers were resolved by consensus or by consulting a third reviewer. Ongoing studies without published results and studies with results published in peer-review journals in any language that fulfilled the predetermined criteria were selected (see paper).

**Data Extraction**

Data were extracted by a reviewer and verified by a second reviewer. Data were collated in spreadsheets designed ad hoc and piloted to obtain a standard format for each study. The extracted data were: aim, design, time horizon, perspective, subject’s characteristics, description of groups, data sources, analysis, costs, outcomes, ICER, and authors’ conclusions. Data from clinical trial papers were extracted to complete the information.

**Quality Assessment**

(See paper)

**Data Synthesis and Analysis**

The data collected were synthesized by means of narrative procedures and displayed in structured tables. Original costs and ratios were converted to 2012 international dollars (US$) according to the usual formulae in literature (E3) that includes purchasing power parity and gross domestic product deflator (E4).

**RESULTS OF THE SYSTEMATIC REVIEW**

The electronic search identified 957 references after discarding duplicates. Of these, 54 articles were retrieved for full review. Finally, seven papers related to six economic evaluation studies with published results were included in the systematic review (Supplementary Figure 1) (11-17). Results of one economic evaluation were reported in two papers (14,15). The search in clinical registries yielded 85 entries; eight ongoing studies were included in this review (Wang 2014; Allen 2013; Øiestad 2013; Bennell 2012; Bennell 2012) (E5-E9).

**Characteristics and Results of the Studies Included**

All economic evaluations were performed alongside RCTs (Supplementary Table 2). The main papers reporting the design and results of the clinical trials were retrieved to complete data (18-20). Different exercise programs at different settings and by different professionals were evaluated in four studies and described in five papers (11,12,14,15,17). The other two studies compared exercise programs before arthroplasty with no exercise before arthroplasty (13,16). The synthesis of results of the completed studies can be requested to the authors of this review.

**Ongoing studies**

Supplementary Table 3 reports the ongoing studies included in this review (E5-E9).

**LIMITATIONS OF THE REVIEW AND DISCCUSION**

Apart from possible publication and language bias, common types of bias in systematic reviews, one limitation of our study is related to the scope and the results we found. The interpretation of the results is conditioned by the studies themselves, their characteristics and limitations. For example, apart from WOMAC, used in five out of six studies, the studies used different measures and most of them were CCA so we had to report detailed results to be sufficiently informative. Only one study used QALYs as an outcome so it was not possible to draw conclusions over the cost-effectiveness of the interventions according to a willingness to pay threshold per QALY or to compare with other technologies or diseases. Partial economic evaluations or studies that hardly can be called economic evaluations given the absence of a method were excluded. Interesting studies were excluded because they did not fulfill the selection criteria; for example, a very good economic evaluation was excluded because the results for knee and hip osteoarthritis were not reported separately (E10) and a potential study was excluded because it was only published as a conference abstract at the time (E11). Other two studies identified through PubMed alerts were excluded because they included patients with varied joints affected (E12,E13).

Our review deals with the cost-effectiveness of physiotherapy, not its effectiveness, whereby we can only discuss the effectiveness notified in the studies included without drawing conclusions on the general effectiveness of physiotherapy for knee osteoarthritis. Regarding cost-effectiveness, we identified several papers as a review of cost-effectiveness of physiotherapy in general, not specifically physiotherapy for knee osteoarthritis (E14). Recently, Pinto et al. investigated the cost-effectiveness of non-pharmacologic, non-surgical interventions for the treatment of hip and/or knee osteoarthritis with review up until October 2010 (37). Our review reinforces previous conclusions, evidence is limited and more high-quality economic evaluations are required to further inform practice.

**REFERENCES**

References cited in the main paper appear in the Supplementary material with the same numeration.

Extra references only cited in the Supplementary material are the following:

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