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LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

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Corresponding author:

Linda Fernandes
Address: Postboks 23, Vinderen, 0319 Oslo, NORWAY
E-mail: linda.fernandes1@gmail.com
Phone: 0045-88335330
Mobile: 0045-42661006
Fax: 0045-63183226

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Author affiliations
Linda Fernandes, National Resource Center for Rehabilitation in Rheumatology, Diakonhjemmet Hospital, Oslo, Norway.
Kåre B. Hagen, National Resource Center for Rehabilitation in Rheumatology, Diakonhjemmet Hospital, Oslo, Norway.
Johannes W.J. Bijlsma, Department of Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, The Netherlands.
Oyvor Andreassen, Patient representative, Patient panel, Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway.
Pia Christensen, The Parker Institute, Department of Rheumatology, Copenhagen; and Copenhagen University Hospital, Frederiksberg, Denmark.
Philip G. Conaghan, Division of Musculoskeletal Disease, University of Leeds, & NIHR Leeds Musculoskeletal Biomedical Research Unit, UK
Michael Doherty, Academic Rheumatology, University of Nottingham, Nottingham, UK
Rinie Geenen, Department of Clinical and Health Psychology, Utrecht University, Utrecht, The Netherlands.
Alison Hammond, Centre for Health Sciences Research, University of Salford, Salford, UK.
Ingvild Kjeken, National Resource Center for Rehabilitation in Rheumatology, Diakonhjemmet Hospital, Oslo, Norway
L. Stefan Lohmander, Department of Orthopaedics, Clinical Sciences Lund, University of Lund, Sweden; and Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Denmark; and Department of Orthopaedics and Traumatology, University of Southern Denmark, Denmark
Hans Lund, Research Unit for Musculoskeletal Function and Physiotherapy, Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Denmark
Christian D. Mallen, Arthritis Research UK Primary Care Centre, Keele University, Keele, UK
Tiziana Nava, Faculty of Physiotherapy, University of Studies of Milan, Milan, Italy
Susan Oliver, Nurse Consultant Rheumatology, Minerva Health Centre, Preston, UK.
Karel Pavelka, Institute of Rheumatology and Clinic of Rheumatology Charles University, Prague, Czech Republic
Irene Pitsillidou, Patient representative, Cyprus League Against Rheumatism, Cyprus.

José Antonio da Silva, Department of Rheumatology, Centro Hospitalar Universitário de Coimbra, Coimbra, Portugal

Jenny de la Torre-Aboki, Rheumatology Department, Alicante General and University Hospital, Alicante, Spain

Gustavo Zanoli, Università degli Studi di Ferrara Casa di Cura SM Maddalena, Ferrara, Italy

Theodora P.M. Vliet Vlieland, Department of Orthopaedics, Leiden University Medical Center, Leiden, The Netherlands.

List of competing interests

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ABSTRACT

Objective: To develop evidence-based recommendations and a research and educational agenda for the non-pharmacological management of hip and knee osteoarthritis (OA).

Methods: The multidisciplinary task force comprised 21 experts; nurses, occupational therapists, physiotherapists, rheumatologists, orthopaedic surgeons, general practitioner, psychologist, dietician, clinical epidemiologist and patient representatives. After a preliminary literature review, a first task force meeting and five Delphi rounds provisional recommendations were formulated in order to perform a systematic review. A literature search of Medline and 8 other databases was performed until February, 2012. Evidence was graded in categories I-IV and agreement with the recommendations was determined through scorings from 0 (total disagreement) to 10 (total agreement).

Results: Eleven evidence-based recommendations for the non-pharmacological core management of hip and knee OA were developed, concerning the following 9 topics: assessment, general approach, patient information and education, life style changes, exercise, weight loss, assistive technology and adaptations, footwear, and work. The average level of agreement ranged between 8.0 and 9.1. The proposed research agenda included an overall need for more research into non-pharmacological interventions for hip OA, moderators to optimise individualised treatment, healthy lifestyle behaviour with economic evaluation and long-term follow-up, and the prevention and reduction of work disability. Proposed educational activities include the required skills to teach, initiate and establish life style changes.

Conclusion: The 11 recommendations for non-pharmacological management provide guidance on the delivery of non-pharmacological interventions to people with hip or knee OA. More research and educational activities are needed, in particular in the area of life style changes.

INTRODUCTION

Osteoarthritis (OA) is one of the most common chronic diseases, with an estimated overall prevalence in the general adult population of 11% and 24% for hip and knee OA, respectively.[1] OA is an age-related condition, with manifestations often not occurring until middle age. In elderly people, OA is the most common cause of disability, including pain and limitations of activities and participation.[2-4] As life expectancy is increasing the number of people living for prolonged periods with severe OA is expected to grow.

The need for high quality care for such a prevalent condition with major personal and societal impact is generally recognized and several guidelines for the care and management of people with hip and knee OA are currently available.[5-9] International recommendations for management of OA are often divided into three main categories: non-pharmacological, pharmacological and surgical.[6] During the past decade, much emphasis has been put on non-pharmacological management. Current recommendations, though, are not sufficiently specific about the content, timing, intensity, frequency, duration and mode of delivery of each non-pharmacological option. This lack of detailed guidance may be one of the reasons why the quality of care for people with hip or knee OA is found to be suboptimal in many studies.[10;11]

In order to address this problem, the European League Against Rheumatism (EULAR) convened a group of experts to produce evidence-based recommendations for the non-pharmacological management of people with hip or knee OA, in accordance with the EULAR standard operating procedures,[12] and to develop a research and educational agenda for future activities. These recommendations would provide more detail and would therefore be an addition to the already available management guidelines and would be easier to implement. The target groups for these recommendations are all health care providers involved in the delivery of non-pharmacological interventions, researchers in the field of OA, officials in health care governance, reimbursement agencies, and policy makers. In addition, persons with hip or knee OA can use the recommendations for information on current non-pharmacological management strategies.

METHODS

The task force aimed to aggregate available information on non-pharmacological management of hip and knee OA into practical recommendations, using EULAR standardised

operational procedures.[12] These involved the assembly of an expert committee to develop consensus, based both on research evidence provided by a systematic literature review and expert opinion.

The task force comprised 21 individuals with particular knowledge of OA from 10 European countries, specifically: two nurses (SO, JT); one psychologist (RG); one dietician (PC); two occupational therapists (AH, IK); three physiotherapists (KH, HL, TN); five rheumatologists (JB, PC, MD, KP, JS); two orthopaedic surgeons (SL, GZ); one general practitioner (CM); two persons representing people with hip and/or knee OA (OA, IP); a clinical epidemiologist (TV); and a research fellow (LF).

The process was both research evidence and consensus based (online supplementary Appendix, Table S1-2 and Figures S1-12), and included, between June 2011 and May 2012, two task force meetings, systematic literature reviews (SLR) and extensive discussions. If a recommendation showed to be inaccurate, based on data from the SLR, it could be rejected. Research evidence was graded in categories I-IV (Table 1).[12] During the second task force meeting, votes for level of agreement (LOA) was were performed anonymously, by giving a score on a numeric rating scale from 0 (total disagreement) to 10 (total agreement) for each recommendation; mean and 95% confidence interval of scores were calculated. Topics to the research and educational agenda were formulated based on discussions of the lack of evidence to substantiate the recommendations and weaknesses in current health care delivery.

Table 1 Categories of levels of evidence

Category	Level of evidence
Ia	Meta-analysis of randomised controlled trials
Ib	At least one randomised controlled trial
IIa	At least one controlled trial without randomisation
IIb	At least one type of quasi-experimental study
III	Descriptive studies, such as comparative studies, correlation studies, or case-control studies
IV	Expert committee reports or opinions and/or clinical experience of respected authorities

RESULTS

Development of the recommendations

After the first meeting, a total of 168 propositions were suggested by the experts. Propositions that were identical were merged and propositions containing one word only were excluded. The second Delphi round comprised 140 propositions, with topics being very broad and including far more non-pharmacological interventions than currently included in these recommendations. After five Delphi rounds, consensus on 11 recommendations was achieved, which are presented with complete formulation in Table 2 with the accompanying level of evidence and LOA. The 11 recommendations are ordered in a logical sequence or procedural and chronological hierarchy rather than by any considered importance.
The terms “non-pharmacological” and “non-surgical” management were discussed by the expert group. The terms were found to be negative as to their prefix “non” and were therefore not considered optimal; finding a new terminology was included in the research agenda (Table 3). In addition, the hip OA specific research evidence was very sparse and, in general, recommendations for the management of people with hip OA was derived largely from trials including both people with hip and knee OA or with knee OA only.

Table 2 EULAR recommendations for the non-pharmacological core management of hip and knee OA, with levels of evidence (LOE) and level of agreement (LOA). The propositions are ordered by topic.

No.	Recommendation	LOE I-IV	LOA (95% CI)
1	In people with hip or knee OA, initial assessments should use a biopsychosocial approach including: a physical status (including: pain; fatigue; sleep quality; lower limb joint status (foot, knee, hip), mobility, strength, joint alignment, proprioception and posture; co-morbidities, weight); b activities of daily living; c participation (work/ education, leisure, social roles); d mood; e health education needs, health beliefs and motivation to self-manage.	Ib, mixed.	8.6 (7.9 to 9.2)
2	Treatment of hip and/or knee OA should be individualised according to the wishes and expectations of the individual, localisation of OA, risk factors (such as age, sex, comorbidity, obesity, and adverse mechanical factors), presence of inflammation, severity of structural change, level of pain, and restriction of daily activities, societal participation and quality of life.	Ib, mixed. Ib, knee.	8.7 (8.2 to 9.2)
3	All people with knee/hip OA should receive an individualised management plan (a package of care) that includes the core non-pharmacological approaches, specifically: a information and education regarding OA; b addressing maintenance and pacing of activity; c addressing a regular individualised exercise regimen; d addressing weight loss if overweight or obese; e* reduction of adverse mechanical factors (for example appropriate footwear); f* consideration of walking aids and assistive technology.	Ib, hip. Ib, knee.	8.7 (8.2 to 9.3)
4	When life style changes are recommended, people with hip or knee OA should receive an individually tailored programme, including long and short-term goals, intervention or action plans, and regular evaluation and follow-up with possibilities for adjustment of the programme.	Ib, mixed. Ib, knee.	8.0 (7.1 to 9.0)
5	To be effective, information and education for the person with hip or knee OA should: a* be individualised according to the person's illness perceptions and educational capability; b* be included in every aspect of management; c† specifically address the nature of OA (a repair process triggered by a range of insults), its causes (especially those pertaining to the individual), its consequences and prognosis; d† be reinforced and developed at subsequent clinical encounters; e† be supported by written and/or other types of information (for example DVD, website, group meeting) selected by the individual; f† include partners or carers of the individual, if appropriate.	Ia, mixed.	8.4 (7.7 to 9.1)
6	The mode of delivery of exercise education (for example individual 1:1 sessions, group classes etc.) and use of pools or other facilities should be selected according both to the preference of the person with hip or knee OA and local availability. Important principles of all exercise include: a† "small amounts often" (pacing, as with other activities); b† linking exercise regimens to other daily activities (for example just prior to morning shower or meals) so they become part of lifestyle rather than additional events; and	Ia, knee, delivery mode. Ia, mixed, water-based exercise.	8.9 (8.5 to 9.3)

	c* starting with levels of exercise that are within the individual's capability, but building up the "dose" sensibly over several months.		
7	People with hip and/or knee OA should be taught a regular individualised (daily) exercise regimen that includes: a strengthening (sustained isometric) exercise to both legs, including the quadriceps and proximal hip girdle muscles (irrespective of site or number of large joints affected); b aerobic activity and exercise; and c adjunctive range of movement/stretching exercises. * Although initial instruction is required, the aim is for people with hip or knee OA to learn to undertake these regularly on their own in their own environment	Ia, hip, overall exercise. Ia, knee, overall exercise. Ia, knee, strength. Ia, knee, aerobic. Ia, mixed, mixed programmes.	8.5 (7.7 to 9.3)
8	Education on weight loss should incorporate individualised strategies that are recognised to effect successful weight loss and maintenance*, for example: a† regular self-monitoring, recording monthly weight; b† regular support meetings to review/discuss progress; c† increasing physical activity; d† follow a structured meal plan that starts with breakfast; e† reduce fat (especially saturated) intake; reduce sugar; limit salt; increase intake of fruit and vegetables (at least "5 portions" per day); f† limit portion size; g† addressing eating behaviours and triggers to eating (e.g. stress); h† nutrition education; i† relapse prediction and management (for example with alternative coping strategies)	III, hip. Ia, knee.	9.1 (8.6 to 9.5)
9	a‡ The use of appropriate and comfortable shoes is recommended.	Ib, knee.	8.7 (8.2 to 9.2)
	b Recommendation rejected: A lateral-wedged insole could reduce symptoms in medial knee pain.	Ib, knee.	8.0 (7.0 to 9.1)
10	Walking aids, assistive technology and adaptations at home and/or at work should be considered, to reduce pain and increase participation, for example: a† a walking stick used on the contralateral side, walking frames and wheeled "walkers"; b* increasing the height of chairs, beds and toilet seats; c* hand-rails for stairs; d* replacement of a bath with a walk-in shower; e* change to car with high seat level, easy access and automatic gear change.	III, hip. III, knee.	8.9 (8.5 to 9.3)
11	People with hip or knee OA at risk of work disability or who want to start/return to work should have rapid access to vocational rehabilitation, including counselling concerning modifiable work-related factors such as altering work behaviour, changing work tasks or altering work hours, use of assistive technology, workplace modification, commuting to/from work, and support from management, colleagues and family towards employment.	III, hip III, knee. Ib, mixed, sick-leave.	8.9 (8.3 to 9.5)

LOE, level of evidence; LOA, level of agreement; OA, osteoarthritis; mixed, the evidence is extracted from studies including a mixed population, i.e. people with hip and/or knee OA.

Recommendations with different LOE within the recommendation are listed below. In the absence of grading of evidence for hip OA populations, the LOE equals IV. LOA was computed as a 0 to 10 scale, based on 17 votes of agreement with the recommendation.

* The specific element was not included in composite interventions and LOE for the inclusion of this specific element could not be graded. †The specific element was included in composite interventions and LOE for the inclusion of this specific element was graded to Ib (i.e. no. 5 *c* to *f*, mixed populations; no. 6 *a* and *b*, mixed or knee populations; no. 8, knee populations; no. 10, knee population). ‡Comparisons between different pairs of comfortable shoes.

Table 3 Research and educational agenda for non-pharmacological management of hip and knee OA

Research	
Theme	*Research questions*
Terminology	Defining non-pharmacological management
	Finding an appropriate terminology for non-pharmacological management
General	Evaluating effectiveness and safety of non-pharmacological management strategies specifically in hip OA
Individualised treatment	Assessing moderators of the outcome of hip and knee OA to optimize individualised treatment
Delivery of care	Defining to whom and in what stage the package of care needs to be delivered
	Assessing by which professionals the package of care can best be delivered
Lifestyle changes	Assessing the long term outcomes (≥ 2 years) of exercise, physical activity, and weight reduction with outcomes including adherence and cardiovascular morbidity
Footwear	Assessing the effectiveness and costs of various forms of footwear
Assistive technology	Assessing the use of and satisfaction with assistive technology
Work ability	Assessing the effectiveness and costs of interventions aiming to prevent or reduce work disability and/or increase return to or entering the workforce
Research methodology	Developing and including measures of societal participation
	Developing and including measures of adherence
	Including economic analyses in studies on non-pharmacological management
	Conducting studies with appropriate sample sizes
Education	
	Need for training courses regarding the required skills to initiate and establish life style changes; this education should be aimed at professionals, people with arthritis and public.

1. Initial assessment

To date, research data on how a comprehensive assessment of people with hip or knee OA should best be executed are scarce. Since initial assessment will always be a part of the management in any individual with hip or knee OA, controlled trials evaluating assessment will have difficulties in selecting the most appropriate comparator. One randomised, controlled trial (RCT) comparing a comprehensive assessment and management approach with usual care could not demonstrate a difference with respect to pain or physical function.[13] However, in that study, both approaches comprised initial assessments, but with different content and were executed by different professionals.[13]

The group considered a comprehensive initial assessment a prerequisite for the individualised management strategy described in recommendation 2. The recommendation on the initial assessment included the following elements: the person's physical status, activities of daily living, participation, mood and health education needs, health beliefs and motivation to self-manage. In the absence of evidence from studies on the effectiveness of

various forms of assessment, the group based the recommended content of the initial assessment mainly on the main areas of disease consequences, including potentially interacting personal and environmental factors described in the literature. [14-22] Evaluation of cardiovascular disease, people's expectations and self-efficacy were also discussed as important aspects in a biopsychosocial approach.[14;17] Moreover, the group found that a comprehensive assessment is not only applicable to the initial consultation; a comprehensive evaluation should be repeated during regular follow-up of the person.

2. Individualised treatment

The task force was unanimous in the overarching principle that treatment of a person with hip or knee OA should be individualised, which is in line with previous guidelines.[7-9;23] Individualised treatment does not imply that every treatment should be individually provided, it rather means that treatment is personalised, or tailored. RCTs on individualised non-pharmacological management are scant. The available studies showed reduced pain [mean difference, 95% CI (0 to 20 point scale): -1.19, -2.1 to -0.3 and -1.10, -1.84 to -0.19; and (0-100 scale): -17.0, -23.6 to -10.4] and improved physical function [mean difference, 95% CI (0 to 68 point scale): 3.65, 1.0 to 6.3 and 3.33, 0.78 to 5.88] compared to usual care,[24-26] but not compared to group-based rehabilitation[25;27;28] or information on healthy lifestyle[29;30]. Follow-ups at 9, 18 or 30 months showed no effect on pain.[31;32]

As the data underpinning this recommendation are limited the factors to be considered for the tailoring of management were mainly based on prognostic factors shown in the literature. An important and modifiable risk factor for knee OA is weight,[20;33;34] implying individualised targeting at weight reduction in people who are overweight or obese. Moreover, individualised treatment being the standard of care in OA and chronic disease in general [7;35;36] was considered to imply informed, shared decision making, taking into account the person's wishes and preferences. The group noted that with the conduct of an RCT to study the impact of individualisation, the patient's view cannot be wholly taken into account and that some element of individualisation will always be incorporated in any treatment. To better understand individualised treatment, the group found that future research should focus on factors that impact outcome, i.e. moderators, not at individualisation as such.

3. Comprehensive package of care

This recommendation addresses the provision of an integrated package of care rather than single treatment modalities alone or in succession. The group recommended five core interventions to be considered comprehensively in every patient with hip or knee OA. The recommendation specifically implies that a person with hip or knee OA should not only receive education about her/his condition (3a), but also be managed according to these (3b-e).

With the exception of walking aids and assistive technology and addressing adverse mechanical factors, the literature supports the delivery of combined interventions concerning information and education, exercise and/or weight reduction.

In patients with hip and/or knee OA the combination of a patient education or self-management intervention plus exercise was found to have a significant effect on pain, but a less marked effect on function.[26;31;37-40] In people with hip OA the effect of such combinations was mainly seen on function (0 to 100 point scale) at 3 and 6 months post-intervention (mean difference, 95% CI: -7.5, -13.9 to -1.0; and, -8.4, -15.1 to -1.7).[41;42] In people with knee OA effects on pain and/or function were observed in eight studies,[24;25;43-48] whereas no effect was observed in four studies.[32;49-51] The addition of advice from a dietician in overweight or obese patients to the combination of patient education or self management intervention plus exercise was found to improve both pain and function in patients with hip or knee OA.[52-55]

4. Principles of life style changes

Recommendation 4 deals with key elements of the delivery of interventions aimed to initiate and maintain life style changes. It is known that behavioural changes are difficult to achieve and maintain, and the effect of advice and counselling practices of health care providers is disappointing.[56] The literature search for this recommendation was limited to life style changes considered most relevant for hip and knee OA, i.e. exercise and weight loss.

The common attribute in the trials supporting this recommendation was to teach and encourage behavioural change strategies through goal-setting of physical activity and weight changes, action plans to maintain changes, and regular follow-up over at least one year to re-evaluate and discuss goals and action plans.[28;39;40;53;57-62]

Overall, the literature addressing the effectiveness of specific elements to be included in interventions aiming to initiate behavioural changes in people with hip or knee OA is scarce. With respect to exercise, the literature suggests that individual exercise, graded activity, individualisation according to the person's exercise goals, feedback on progress made toward the goals, iterative problem solving with emphasis on skills that will improve adherence, reinforcements of maintaining exercise such as additional motivational programmes, exercise plans and log-books, written information and audio- or videotape, and booster sessions improve adherence to exercise or physical activity in patients with hip or knee OA.[28;39;40;61-63] In addition, some studies found an effect on pain[39;40] or function[59] from lifestyle interventions that integrate such elements. A systematic review including a mixed population of people with OA and/or rheumatoid arthritis found effect-sizes of 0.21 (95% CI 0.08 to 0.34) for pain and 0.69 (95% CI 0.49 to 0.88) for increased physical activity from life style interventions aiming at increased physical activity.[64] Over 40% of these included lifestyle interventions which prompted problem-solving, self-monitoring, goal-setting, and provided regular feed-back.[64]

Concerning weight loss, in people with knee OA or knee pain positive effects were seen on pain, function and weight loss from diet interventions that included individual weight loss goals, problem-solving on how to reach the weight loss goal, and follow-up visits to re-evaluate and discuss goals in combination with exercise.[53;60] In obese patients, weight loss programmes with explicit weight loss goals showed a higher mean change in weight than programmes without explicit goals.[65] This indicates that the elements in recommendation 4 are important for the change of behaviour and maintenance on long-term. The group discussed the importance of regular follow-up that includes feed-back on the progress towards explicit goals and extends over a long time to achieve long-term effects of healthy lifestyle.

5. Principles of information and education

Recommendation 5 is concerned with the content and delivery mode of various forms of educational programmes to best benefit the person with hip or knee OA. It is grounded in the general recognition that appropriate information and education are indispensible elements in the process of prompting adequate self-management in chronic diseases. The recommendation is underpinned by the majority of studies on education interventions

provided to patients with hip and/or knee OA. In general, small, but statistically significant effect sizes on pain (0.06, 95% CI 0.02 to 0.10) and physical function (0.06, 95% CI 0.02 to 0.10) have been reported from attending education or self-management programmes.[6;66] From a health economic perspective, lower costs of community-based care and medication up to 12 months from attending a combined self-management and exercise programme and a reduced number of medical consultations from attending self-management programmes in patients with hip and/or knee OA have been reported.[32;67;68]

The literature review included trials that compared education or self-management programmes to usual care, attention controls, or no intervention. The included trials described one or several elements from *c* to *f* (Table 2) in their interventions.[69-85] The literature did not support the additional value of spouse-assisted coping skills training,[79] and no trials were found for individualisation according to illness perception and educational capability, or that education should be included in every aspect of management. The group, however, considered the inclusion of spouses in the intervention to be a question of individualisation and appropriate in some cases. One systematic review found that, in people with OA, effective self-management interventions were protocolised, included elements of cognitive behavioural theory or social cognitive theory, and were led by trained health-professionals.[86] These elements are not specifically addressed in the recommendation yet they were supported by the group.

6. Principles of exercise education

Recommendation 6 deals with the principles of the delivery of education on exercise and physical activity in persons with hip or knee OA. The basis for education on exercise and physical activity is found in the convincing evidence for the overall effectiveness of exercises on pain (ES, 95% CI: 0.40, 0.30 to 0.50) and function (ES , 95% CI: 0.37, 0.25 to 0.49) in people with knee OA,[87] and to a lesser extent in people with hip OA (ES, 95% CI, pain 0.38, 0.08 to 0.68).[88]

Very few studies have directly compared different exercise 'dosage' (frequency, intensity, and duration) and progression approaches in people with OA.[87;89;90] One RCT reported reduced pain from attending a progressive functional strengthening programme compared to a non-progressive programme in people with knee OA,[90] and two trials could not

demonstrate any differences from attending various intensity levels of aerobic or resistance exercise programmes.[89;91] Hence, the optimal exercise 'dosage' and rate of progression remain uncertain.

With respect to the delivery of exercise as an individual treatment or as group-based programmes, in patients with knee OA different delivery modes (individual, group-based, or home programmes) have all been demonstrated to be effective in terms of reducing pain (Individual, ES, 95% CI: 0.55, 0.29 to 0.81; Group-based, ES, 95% CI: 0.37, 0.24 to 0.51; and, Home, ES, 95% CI: 0.28, 0.16 to 0.39) and improving function (Individual, ES, 95% CI: 0.52, 0.19 to 0.86; Group-based, ES, 95% CI: 0.35, 0.19 to 0.50; and, Home, ES, 95% CI: 0.28, 0.17 to 0.38) compared to education, telephone calls, waiting list, relaxation, ultrasound, hot-packs, or no treatment.[87] In patients with hip and/or knee OA, water-based exercise was found to significantly reduce pain (ES, 95% CI: 0.19, 0.04 to 0.35) and improve function (ES, 95% CI: 0.26, 0.11 to 0.42) compared to education, telephone calls, or no intervention.[92] Home-based exercise was found to be as effective as water-based exercise in one small RCT in people with hip OA.[93] Water-based exercise can include swimming and/or different types of exercise programmes. Since the different modes of delivery are equally effective, the person's preference, findings of the initial assessment and local availability should determine the choice regarding the mode of delivery in clinical practice.

Concerning activity pacing and/or integrating physical activity into daily living as part of a comprehensive exercise regimen the literature suggests their effectiveness in people with hip or knee OA or with knee pain as compared to usual care or written information, but not compared to standardised exercise or pharmacy review. [24-26;29;31;38;46;57;58;77-79;94]

This recommendation includes the increase of the intensity and/or duration of exercise over time. This is based on the literature, where most strength training exercise programmes evaluated in people with knee OA included dynamic exercises with progression over time.[95] Moreover, one study has compared a progressive and a non-progressive approach in people with knee OA, where the former was found to be more effective in reducing pain.[90] General recommendations for dosage and progression of exercise in older people and people with chronic disease are aerobic moderate-intensity training at least 30 minutes/day or up to 60 minutes for greater benefit and progressive strength training involving the major muscle groups at least 2 days/week at a level of moderate to vigorous intensity (60-80% of 1 repetition maximum) for 8-12 repetitions.[96;97] These recommendations emphasise that in

people with chronic disease who do not reach the recommended level, they should be as physically active as their abilities and condition allows.[97]

7. Exercise regimen

Regarding the evidence for specific exercises in hip and knee OA, it should first be noted that although a favourable effect of exercises on pain in patients with hip OA has been reported,[88] overall there is a lack of information to support treatment effects of exercise in hip OA.[8;88;98-103] The LOE for the recommendation of different types of exercise in people with hip OA therefore could not be graded. For knee OA, however, high-quality research evidence has reported that exercise reduces pain and improves physical function.[6;87;104] There are inconsistent results for the effect exercise on quality of life. [90;92;95;99;102;104;105]

Concerning strengthening exercises in knee OA, both specific quadriceps strengthening exercises or strength training for the lower limb are effective in reducing pain (ES, 95% CI: 0.29, 0.06 to 0.51 and 0.53, 0.27 to 0.79, respectively) and improving physical function (ES, 95% CI: 0.24, 0.06 to 0.42 and 0.58, 0.27 to 0.88, respectively).[87] The literature on strength training in people with knee OA included in most cases dynamic exercises, whereas research on isometric exercises is sparse.[95] Hip strengthening exercises have been poorly evaluated in people with hip OA.[103] In people with medial tibio-femoral knee OA, though, hip strengthening exercises reduced knee pain and improved physical function.[106]

Aerobic training (walking) is effective in reducing pain (ES, 95% CI: 0.48, 0.13 to 0.43) and improving physical function (ES, 95% CI: 0.35, 0.11 to 0.58) in patients with knee OA.[87]

The evidence for mixed exercise programmes including strengthening, aerobic and flexibility components in patients with knee OA is conflicting.[107;108] One type of exercise has not been demonstrated to be superior to another (strength, aerobic, or mixed exercises).[87;107;108]

The group reached consensus that mixed programmes should be recommended. However, it was noted that with mixed programmes the minimal requirements to improve or maintain muscle strength, aerobic capacity and/or joint range of motion need to be met[97] as some literature suggests that mixed programmes may be less effective then focussed programmes.[108]

This recommendation says that initial instruction is required, but that in the longer term the person should integrate exercise into daily life. This part of the recommendation is substantiated by studies showing that the number of supervised sessions influences

outcome in people with knee OA.[87] Twelve or more directly supervised sessions has shown to be more effective than less than 12 sessions on pain (ES 0.46, 95% CI 0.32 to 0.60 versus ES 0.28, 95% CI 0.16 to 0.40, p=0.03) and physical function (ES 0.45, 95% CI 0.29 to 0.62 versus ES 0.23, 95% CI 0.09 to 0.37, p=0.02).[87]

In addition, it was noted that research evidence is growing for Tai Chi and yoga. Though not included in the literature review, Tai Chi has been found to be effective for the reduction of pain in patients with hip or knee OA with ES ranging from 0.28 to 1.67.[108]

8. Education on weight loss

In recommendation 8, the principles of education on weight management are included. The recommendation is mainly supported by the literature in knee OA, as the evidence to support the effect of weight loss in patients with hip OA is absent. Being overweight or obese, though, has been shown to be associated with hip OA (OR 1.11, 95% CI 1.07 to 1.16).[33]

In patients with knee OA, the effectiveness of weight loss programmes on body weight, pain and/or physical function was demonstrated in programmes typically delivered weekly as supervised sessions for a range of 8 weeks to two years.[54;60;109-113] The effects on pain, function and weight loss from attending weight loss programmes were small but significant (ES, 95% CI, pain 0.20, 0.00 to 0.39; physical function 0.23, 0.04 to 0.42; mean difference, 95% CI, 6.1 kg, 4.7 to 7.6).[109] The interventions included strategies on how to reduce the calorie intake by meal plans, reduce fat and sugar, reduce portion size, meal-replacements and they comprised behavioural modifications, self-monitoring, weight loss goals, and maintaining body weight in participants who had reached their goals and/or exercises in some of them.[54;60;109-112] Overall, the evidence from RCTs for the maintenance of achieved weight loss after the interventions have ended is absent in people with hip and knee OA.

In general, in overweight or obese populations, healthy eating, limiting fat and salt intake, eating at least 5 portions of fruit and vegetables a day, being physically active for at least 30 minutes/day and elements such as self-monitoring, explicit weight loss goals, and motivational interviewing have all been suggested to be active elements for weight loss and that regular follow-up over 4 years is an active element for maintenance.[65;114-118] With respect to goal setting, weight loss programmes in older obese people that included explicit weight loss goals showed mean changes in weight of -4.0 kg (95% CI, -7.3 to -0.7), which was

significantly more than programmes without explicit weight loss goals (mean change, 95% CI, -1.3 Kg, -2.9 to 0.3).[65] In the strive for a structured meal plan with a balanced combinations of low calorie and sufficient vitamin and mineral intake, meal replacement bars or powders can be an addition to healthy eating.[54;60;109;110] Though not included in the literature review, it has been suggested that bariatric surgery should be part of a comprehensive weight management in people with hip or knee OA who are morbidly obese, which could help reduce weight and joint pain.[119;120]

9. Footwear

Although the evidence in the literature is scant, the group was unanimous in its view that the use of appropriate footwear should be recommended in patients with hip or knee OA. Shoes may help through different mechanisms, such as acting as shock absorbers or control of foot pronation.[121;122] Appropriate shoes implies no raised heel, thick, shock absorbing soles, support for the arches of the foot, and shoe size big enough to give a comfortable space for the toes.[121-123]

In patients with hip OA there is no evidence to support the effect of specific shoes or insoles on pain or function. In patients with knee OA, the use of shoes with shock-absorbing insoles for one month reduced pain and improved physical function in a pre-post test design.[124] No differences in knee pain by the use of specialised shoes (unstable Masai technology shoe or variable-stiffness shoe) compared to conventional athletic shoes have been seen, but reduced pain was observed in both groups over time.[125;126] In addition, decreased knee joint loads were found by the use of specialised mobility shoes.[121]

The literature on the effectiveness of the use of lateral wedged insoles in patients with medial knee OA found no significant effect on pain or function.[121;127;128] There is no support for which type of insole would be superior to another[129] and adverse effects including foot sole pain, low-back pain, and popliteal pain have been reported.[121;128;129] In light of evidence for no clinical effects, and the report of adverse effects, the group rejected the recommendation on laterally wedged insoles (Table 2, 9 b).

10. Assistive technology and adaptations at home and/or at work

The frequent use of assistive technology and the high satisfaction rates with the use of it indicate that walking aids, assistive technology and adaptations are important and useful to

people with hip or knee OA.[130-133] There are, however, no clinical trials to substantiate elements in this proposition except for the use of a cane in patients with knee OA.[134] However, the group was unanimous in its view that in all patients with hip or knee OA walking aids, assistive technology and adaptations at home and/or at work should be considered systematically and recurrently. The group noted that the value of some of these interventions is so obvious and has an immediate effect in individual cases that further research into the effectiveness of specific devices or adaptations can hardly be expected. Cross-sectional studies describe that walking aids, assistive technology and adaptations at home and/or work are important and frequently used by people with hip or knee OA. The majority of people with severe hip (63%) or knee pain (90%) report that they used walking aids.[130;131] In people with arthritis, a mean of 9.9-10.8 devices have been reported to be in use and the satisfaction rate for all categories of devices was above 87%.[132] Moreover, unmet needs for new assistive technology to help perform activities that individuals were unable to do were identified.[132] Having access to a walking aid or other assistive technologies can be a help and provide security for individuals both with constant and fluctuating symptoms. The group found that future observational studies on the use, satisfaction and suggestions for new technology or improvements of existing technology are needed.

11. Management of work ability

Recommendation 11 deals with the effectiveness of work related interventions. The proportion of employed people who have work disability due to OA is substantial. Although there are known occupational risk factors for knee OA and its progression, e.g. heavy work, knee squatting or bending, lifting, and specific sports,[18] there are no studies to support the effect of vocational rehabilitation on pain, physical function, or quality of life specifically in patients with hip or knee OA. One study in patients with peripheral OA found that a specialist-run, protocol-based early intervention significantly decreased number of days of sick-leave compared to standard primary care.[135] The intervention was administered by a rheumatologist and comprised three main elements; education, protocol-based clinical management, and administrative duties. The educational part included information of the condition, reassurance that serious disease was not present, self-management, exercises, ergonomic care, booklets, optimal level of physical activity, and early return to work.

Descriptive studies have found that environmental factors, such as having access to public transport or a car for mobility outside home are facilitators and that the absence of these is associated with daily activity limitations.[136;137] Some elements in this recommendation may have to be adapted to the country in which it is executed, since availability and accessibility of services in the health care and social security system may vary greatly. The group concluded that there is a clear paucity of research evidence for work related interventions in people with hip and knee OA.

DISCUSSION

Eleven recommendations for the core non-pharmacological management of people with hip and knee OA were developed based on research evidence and expert consensus. While the 11 evidence-based recommendations are not exhaustive and do not include all existing non-pharmacological treatment modalities, they cover the main principles of non-pharmacological management. The selected recommendations support a patient-centred, multidisciplinary approach rather than a discipline specific approach.

There was a considerable body of evidence underlying the recommendations, with systematic reviews and/or randomised controlled trials available for the majority. It is worth noting, however, that overall the research evidence for hip OA was found to be poorer than for knee OA, limiting the conclusion on the effectiveness of non-pharmacological interventions in this patient group. Moreover the majority of trials found in the literature review used pain or physical function as the primary outcome and surprisingly few included quality of life outcome measures. Mental health, physical independence, autonomy, and social participation have been reported as important domains by people with OA and older adults.[138;139] Given these observations, the task force recommends that future research should include well-powered studies to evaluate the effect of core non-pharmacological treatments specifically in people with hip OA, moderators of effect and the inclusion of quality of life measurements that reflect physical, mental, and social health in their evaluation.

Several RCTs found in the systematic literature review compared two non-pharmacological interventions and found no significant differences on pain or physical function between the

two. This does not mean that the interventions were ineffective, but that neither was superior to the other. For example, a well-powered RCT compared a behavioural graded activity intervention to education and exercise following the Dutch physiotherapy guideline for patients with hip and/or knee OA and found no differences between groups.[57] Nevertheless, both groups showed improvements in pain and physical function over time. Moreover, it was found that non-pharmacological interventions often consisted of combinations of different treatment modalities, with the combinations varying largely between studies. This not only hampered comparisons between studies, but also the ability to define the effect of the individual components, so that the underpinning of every specific element in some of the recommendations proved to be difficult. Hence, the aim of developing detailed recommendations could not always be fulfilled. However, compared to previous recommendations[5-9] the current recommendations are more specific. They provide substantiated and more detailed recommendations concerning content (for patient education, exercise, weight reduction, and combined treatment), frequency (at least 12 sessions, activity pacing and follow-ups), and mode of delivery (1:1, group based or home exercise) than previously published recommendations. In addition, principles for optimizing long-term adherence and effect are described. The optimal exercise volume ('dose') could not be substantiated. Exercise volume is difficult to investigate as exercise volume not only include the exercises performed at a gym or the at the physiotherapy clinic, but would be the total amount of exercise performed in daily life. Exercise volume would therefore vary widely between individuals. The matter of timing lacks research evidence and the topic was included in the research agenda. Furthermore, the effect sizes for several non-pharmacological interventions reported in the literature were generally relatively low. It should be noted however that the costs associated with these interventions are generally limited, and the occurrence of adverse effects is low. The results of the LOA in addition to the traditional determination of the level of evidence are therefore very important, as this reflects the experts' interpretation of all the abovementioned aspects.

Limitations concerning the methodological quality of the systematic literature review were that only one person (LF) extracted data from the literature. According to the Assessment of Multiple Systematic Reviews,[140] at least two independent data extractors are recommended. However, the research fellow (LF) presented and discussed all results with the convenors

(JWB, KBH, TVV) and the extracted data were, thereafter, reviewed by experts in the committee. Another limitation was that, due to limited time and resources, no scoring of the methodological quality of the systematic reviews or individual trials included in the literature review was done. Also, due to limited resources, some potential health care providers playing a role in the management of hip and knee OA, such as the podiatrist or rehabilitation specialist, were not represented in the task force.

To obtain a broad consensus and practical applicability of the recommendations, the task force had an inclusive and multidisciplinary approach. Nine different professional disciplines and people with OA were included in the committee. The task force followed a similar procedure as for other management recommendations, such as for the general management of OA, rheumatoid arthritis and ankylosing spondylitis,[8;9;141;142] but is the first with such an inclusive approach. It has been strongly recommended that a minimum of two patient research partners with the relevant disease are included in development of recommendations.[143] The participation of the persons with OA in this task force was successful, with their experiential knowledge to ensure clinical relevance being integrated throughout the process.

Finally, the task force reached consensus on a research and educational agenda, with general topics including the definition and nomenclature for non-pharmacological and non-surgical management and the need for more knowledge on their effectiveness in hip OA. Specific needs for additional research and/or education included the optimization of tailoring of treatment and the mode of delivery, the long term effects of life style interventions, vocational rehabilitation and footwear, the measurement of adherence and participation and the conduct of studies with a sufficient sample size. An important subject regarding education pertained to life style interventions, highlighting the need for educational activities not only for health care provided, but also for people with OA and the public.

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Appendix

Expert consensus on propositions

Before the first task force meeting, a general literature search of practice guidelines, overviews of systematic reviews and evidence-based recommendations was undertaken to obtain an overview of current recommendations and addressed treatment modalities in people with hip or knee OA. For this purpose, the databases Medline, Embase, Pedro, CINAHL, OTseekers, PsychInfo, AMED, G-I-N and The Cochrane Database of systematic reviews were searched until March 2011. After removing duplicates, 984 hits were retrieved and after excluding recommendations on pharmacological or surgical treatment or other diagnoses than OA, 31 studies remained. The 31 studies addressed 30 different non-pharmacological treatment modalities. The results were presented at the first task force meeting. All addressed treatment modalities and potential topics for propositions were discussed. After the first meeting, the experts were asked to contribute independently with 10 propositions concerning non-pharmacological management and its content. Experts' consensus was achieved using the Delphi technique. In total, five Delphi rounds, facilitated by the convenor, were performed by e-mail. All members of the task force, except for the convenor and the research fellow, responded during each round. The preliminary literature review as well as the first Delphi rounds included propositions covering different aspects of non-pharmacological treatment, for example thermal modalities, Transcutaneous Electric Nerve Stimulation, acupuncture, manual therapy and traction. Consensus on 11 propositions was reached in the 5th Delphi round concerning the topics; initial assessment, individualised treatment, comprehensive care, principles of life style changes, patient education, exercise, and weight loss, footwear, assistive technology, and vocational rehabilitation.

Systematic literature search

A systematic literature search was undertaken by the research fellow (LF) supported by her mentors (JB, KH and TV), using Medline (In-Process & Other Non-Indexed Citations 1948-), Embase (1980-), AMED (1985-), PsychINFO (1806-), CINAHL (1981-), Cochrane Database of Systematic Reviews (2005-), Database of Abstracts of Reviews of Effects (1994-), Cochrane Central Register of Controlled Trials (1898-), and PEDro (1929-). The search comprised a general and proposition-specific searches and were all performed until February 2012. The

general search combined a search query for hip or knee OA with a search query for study design. Study designs of interest were; systematic review/meta-analysis, randomised controlled trial (RCT)/ controlled trial (CT), or observational studies. Systematic reviews were included if they had undertaken a literature search of at least two databases, were of a time frame of more than one year and presented at least one meta-analysis of RCTs. Effect-sizes presented in the results derived from the latest systematic review containing the largest number of studies. Propositions that were not substantiated by at least one meta-analysis of RCT's were followed by a proposition-specific search for RCT/CT's. If the propositions still was not substantiated, a proposition-specific search for observational studies was performed. RCTs were included if they described a random allocation procedure and presented between group comparisons. The general search queries and proposition-specific search queries for Medline are included in Table S1-2; these were adapted for the other databases. Part I, II and III (Table S1-2) were combined with "and" as appropriate. The extraction procedures are presented in Figures S1-12. Studies were included if they: a. evaluated the effect of non-pharmacological treatment related to the propositions; b. used clinical outcomes (pain, physical function, quality of life) or other outcomes relevant to the proposition (adherence, activity level, weight, sick-leave); c. concerned persons diagnosed with hip or knee OA or with persisting knee pain, if 45 years or older. In case of a mixed sample, studies were included if they provided a separate analysis for persons with hip and/or knee OA or if the majority of included persons were diagnosed with hip or knee OA. Reviews, dissertations, case-reports, editorials, commentaries, meeting abstracts, and protocols were excluded.

For every recommendation, all results obtained by the research fellow were discussed with the convenor and co-applicants. If needed, the extracted data were then reviewed by a committee member and any additional data known by the member could be included.

Table S1 General search queries for Medline. These were adapted for other databases.

General search query Part I, Osteoarthritis		General search query Part II, Study design	
OA	1. Osteoarthritis/ 2. osteoarthrit$.tw. 3. osteoarthros$.tw. 4. degenerative arthrit$.tw. 5. arthrosis.tw. 6. arthroses.tw. 7. or/1-6 8. Hip/ 9. Hip Joint/ 10. hip$.tw. 11. or/8-10 12. Knee/ 13. knee$.tw. 14. exp Knee joint/ 15. or/12-14 16. 11 or 15 17. 7 and 16 18. Osteoarthritis, hip/ 19. Osteoarthritis, Knee/ 20. coxitis.tw. 21. gonarthritis.tw. 22. or/17-21	SR/ MA	1. exp Meta-Analysis as Topic/ 2. Meta-Analysis.pt. 3. quantitative review$.tw. 4. quantitative overview$.tw. 5.statistical pool$.tw. 6. data pool$.tw. 7. (meta analy$ or metaanaly$ or meta?analy$).tw. 8. exp "Review Literature as Topic"/ 9. Review.pt. 10. Systematic review$.tw. 11. or/1-10
		RCT/ CT	1. randomized controlled trial.pt. 2. controlled clinical trial.pt. 3. randomized.ab. 4. placebo.ab. 5. drug therapy.fs. 6. randomly.ab. 7. trial.ab. 8. groups.ab. 9. or/1-8 10. (animals not (humans and animals)).sh. 11. 9 not 10
		Obs.	1. exp Cohort Studies/ 2. cohort stud$.tw. 3. exp Prospective Studies/ 4. prospective stud$.tw. 5. exp Risk/ 6. risk.tw. 7. relative risk$.tw. 8. exp Incidence/ 9. incidence.tw. 10. exp Longitudinal Studies/ 11. longitudinal studies.tw. 12. or/1-11 13. exp Case-Control Studies/ 14. case-control stud$.tw. 15. exp Retrospective Studies/ 16. retrospective stud$.tw. 17. exp Odds Ratio/ 18. odds ratio$.tw. 19. or/13-18 20. exp Cross-Sectional Studies/ 21. cross-sectional stud$.tw. 22. exp Prevalence/ 23. prevalence.tw. 24. disease frequenc$.tw. 25. or/20-24 26. 12 or 19 or 25

OA, osteoarthritis; SR, systematic review; MA, meta-analysis; RCT/CT, randomised controlled trial/controlled trial; Obs., observational studies.

Table S2 Proposition-specific search queries for Medline (proposition 1-11). These were adapted for other databases.

1	1. Medical History Taking/ 2. medical history.tw. 3. exp Physical examination/ 4. examination.tw. 5. assessment$.tw. 6. measurement$.tw. 7. or/1-6 8. biopsychosocial.tw. 9. psychosocial.tw. 10. exp Holistic Health/ 11. exp Holistic Nursing/ 12. holistic.tw. 13. (comprehensive or thorough or full or complete).tw. 14. or/8-13 15. exp "Activities of Daily Living"/ 16. activit$ of daily living.tw. 17. exp Disability Evaluation/ 18. disabilit$.tw. 19. ((limitation$ or reduc$ or restrict$) and activit$).tw. 20. ((limitation$ or reduc$ or restrict$) and physical function).mp. 21. or/15-20 22. social behavior/ or exp social adjustment/ or exp social isolation/ or exp social environment/ 23. (social function$ or social behavior or social adjustment or social isolation or social environment).tw. 24. participation.tw. 25. exp Work/ 26. work.tw. 27. exp Education/ 28. education.tw. 29. societal participation.tw. 30. exp Leisure Activities/ 31. (leisure or recreation).tw. 32. or/22-31 33. pain.tw. 34. exp Pain Measurement/ 35. exp Fatigue/ 36. fatigue.tw. 37. exp Sleep Disorders/ 38. sleep.tw. 39. exp Foot Joints/ 40. (foot or feet).tw. 41. exp "Range of Motion, Articular"/ 42. range of motion.tw. 43. Muscle Strength/ 44. (muscle strength or muscular strength).tw. 45. Joint Instability/ 6. (joint$ adj2 instability).tw. 47. alignement.tw. 48. exp Proprioception/ 49. proprioception.tw. 50. joint position sense.tw. 51. Posture/ 52. posture.tw. 53. Comorbidity/ 54. comorbidity.tw. 55. exp Body Weight/ 56. body weight.tw. 57. body mass index/
4	1. exp Life Style/ or exp Health Behavior/ or exp Adaptation, psychological 2. lifestyle$.tw. 3. exp goals/ 4. (goal or action plan).tw. 5. (re adj2 (evaluation or examination)).tw. 6. (reinforcement or booster or adjustment or adherence).tw. 7. (individual$ adj4 (treatment$ or therap$ or prorgram$ ro management$)).tw. 8. (tailor$ adj4 (treatment$ or therap$ or prorgram$ ro management$)).tw. 9. (target$ adj4 (treatment$ or therap$ or prorgram$ ro management$)).tw. 10. or/1-9
5	1. exp Health Education/ 2. exp Patient Education as Topic/ 3. exp Self Care/ 4. (health education or patient education or self care).tw. 5. (self adj2 manage$).tw. 6. (information or advice or counsel$).tw. 7. or/1-6
6	1. exp Exercise Tolerance/ or exp Exercise/ or exp Exercise Therapy/ 2. exercise.tw. 3. physical activity.tw. 4. or/1-3 5. (pacing or dose or progression or link$ or integrate or adhere$).tw. 6. 4 and 5
7	Covered by the general search for SR / MA
8	1. exp Weight Loss/ 2. weight loss$.tw. 3. (los$ adj2 weight).tw. 4. weight reduction$.tw. 5. (reduc$ adj2 weight).tw. 6. weight decreas$.tw. 7. (decreas$ adj2 weight).tw. 8. weight control$.tw. 9. (control$ adj2 weight).tw. 10. or/1-9 11. exp Maintenance/ 12. (maint$).tw. 13. (retention$ or preserv$ or sustain$ or continu$ or keep).tw. 14. or/11-13 15. 10 and 14 16. exp Diet/ 17. diet.tw. 18. exp Health Promotion/ 19. (nutrition adj2 education).tw. 20. ((meal or activity or individual or patient) adj2 (plan or goal)).tw. 21. (eating adj2 (behavio$ or trigger$)).tw. 22. ((self adj3 (monitor$ or record$ or assess$))

58. body mass index.tw.
59. or/33-58
60. exp Emotions/
61. exp Depressive Disorder/
62. (emotion$ or depression or mood or fear or anxiety or affect or frustration or anger or loneliness or sadness).tw.
63. or/60-62
64. exp Motivation/
65. motivation$.tw.
66. exp Attitude to Health/
67. exp Health Behavior/
68. (health belief$ or health behavior or attitude to health).tw.
69. or/64-68
70. 21 or 32 or 63 or 69
71. 14 or 70

2
1. Individualized medicine/
2. individual$.tw.
3. (individual$ adj4 (treatment$ or therap$ or prorgram$ or management$)).tw.
4. (tailor$ adj4 (treatment$ or therap$ or prorgram$ or management$)).tw.
5. (target$ adj4 (treatment$ or therap$ or prorgram$ or management$)).tw.
6. exp Classification/
7. classif$.tw.
8. stratif$.tw.
9. categor$.tw.
10. or/1-9

3
1. exp health services/ or exp patient care/ or exp preventive health services/ or exp rehabilitation/
2. exp Patient Care Management/
3. (multidisciplinary or rehabilitation or complex intervention or package of care).tw.
4. ((multifaceted or multimodal or integrated or complex or combined) adj2 management).tw.
5. (education or information or advise).tw.
6. or/1-5

and weight).tw.
23. (portion size or (reduc$ adj2 (fat or sugar or salt)) or vegetables).tw.
24. (((relapse adj2 prediciton) or booster session$ or support) and adj2 weight).tw.
25. or/16-24
26. 10 or 15 or 25

9
1.exp Shoes/
2.insole$.tw.
3.lateral wedge$.tw.
4.shoe$.tw.
or/1-4

10
1. Walkers/
2. walker$.tw.
3. (walking adj3 aids).tw.
4. (walking adj3 stick$).tw.
5. (walking adj3 frame$).tw.
6. self-help devices/ or wheelchairs/
7. assistive device$.tw.
8. crutch$.tw.
9. (environmental adj3 modification$).tw.
10. (height adj3 (bed$ or chair$ or seat$)).tw.
11. (adaptation$ adj3 home).tw.
12. (adaptation$ adj3 work).tw.
13. (cane or canes).tw.
14. (rail$ adj4 stair$).tw.
15. (handrail$ or (hand adj rail$)).tw.
16. (walk adj3 shower).tw.
17. (automatic adj gear).tw.
18. (car or cars or driving).tw.
19. occupational therapy/
20. or/1-20

11
1. exp Rehabilitation, Vocational/
2. vocation$.tw.
3. (occupational adj3 rehabilitation).tw.
4. exp Work/
5. work$.tw.
6. job$.tw.
7. career.tw.
8. exp Employment/
9. employment.tw.
10. exp Disability Evaluation/
11. or/1-10

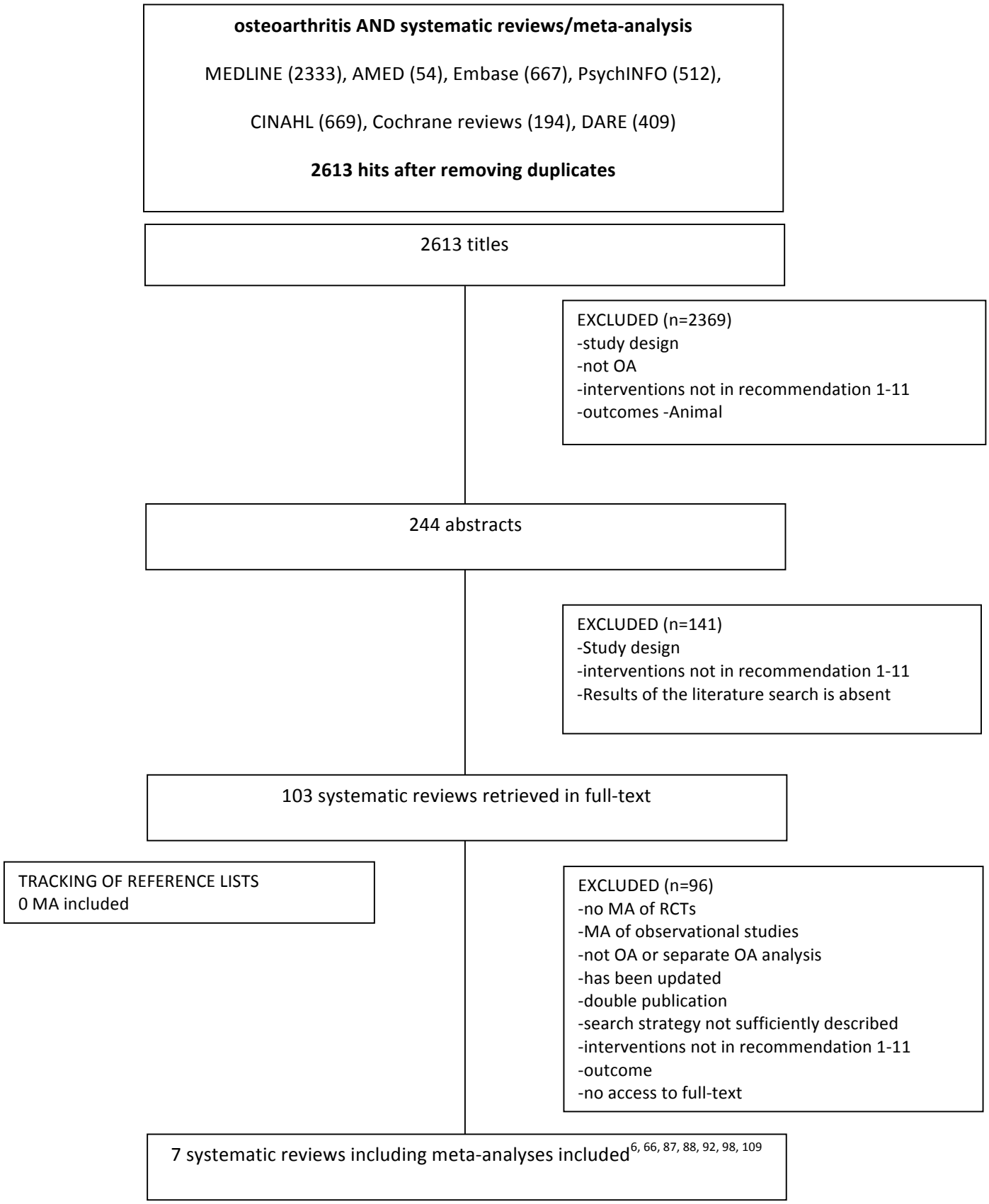
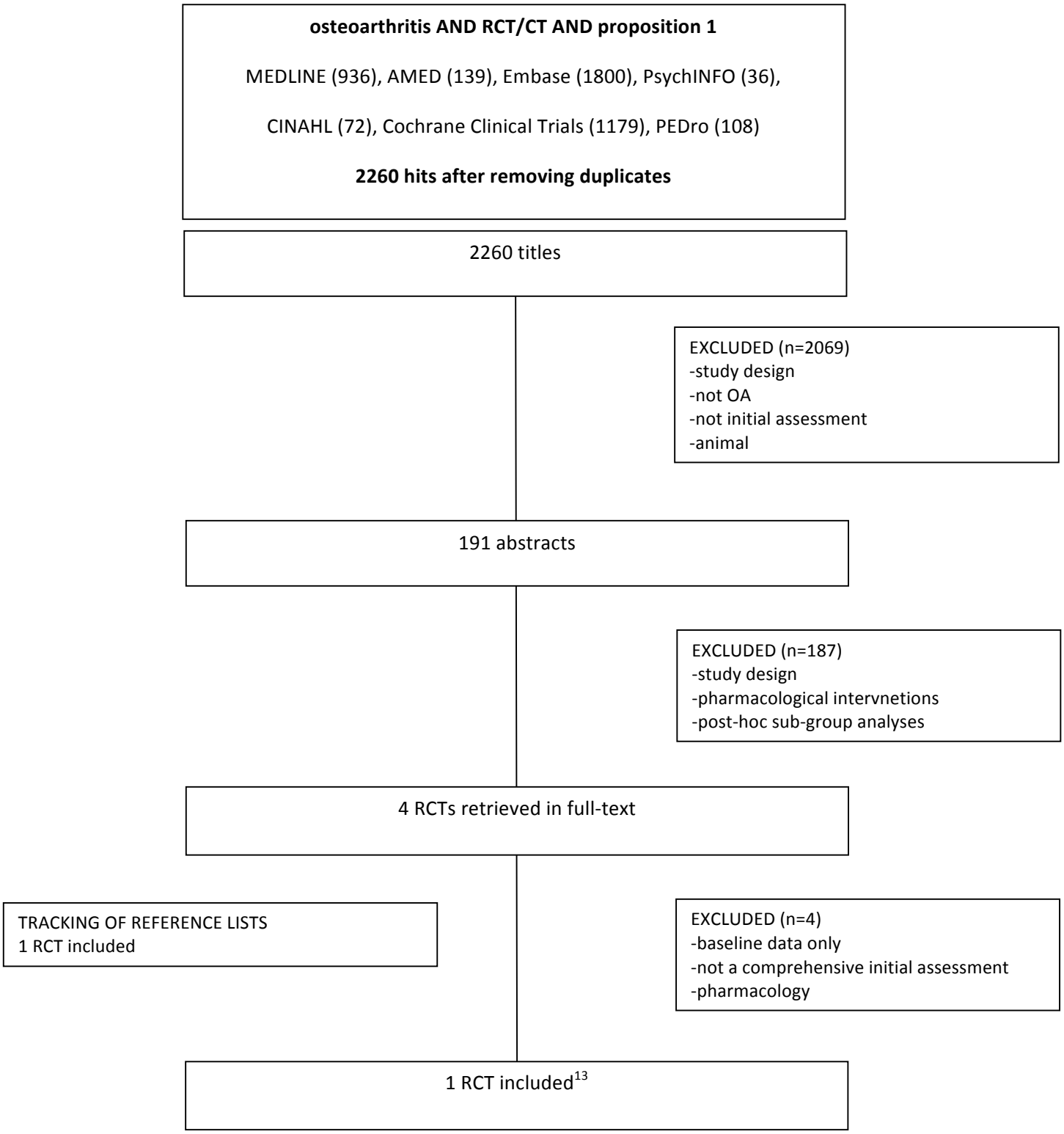


Figure S1 General literature search combining the search query for osteoarthritis and meta-analysis.



gure S2 Proposition-specific search literature search for proposition 1.

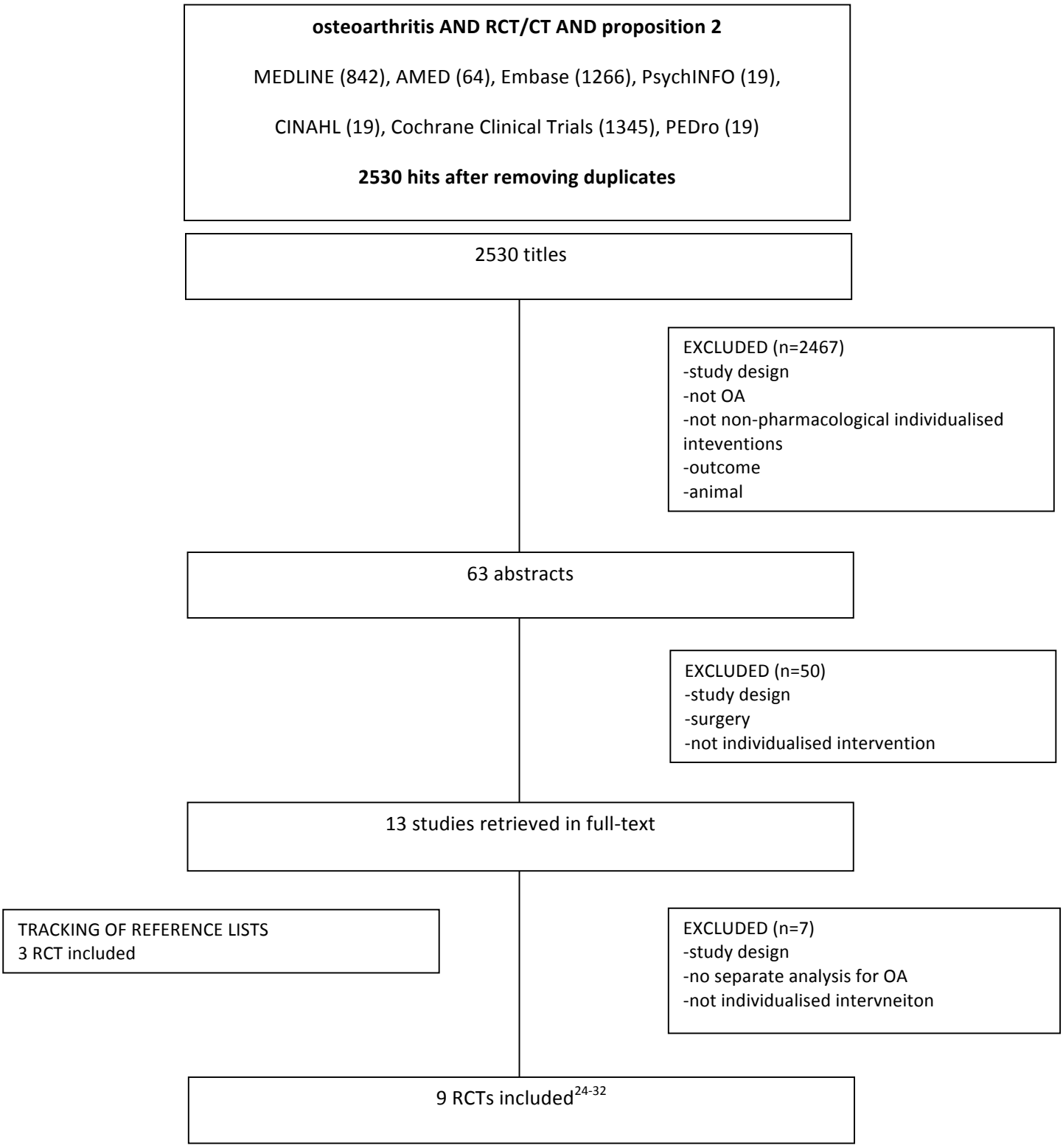


Figure S3 Proposition-specific literature search for proposition 2

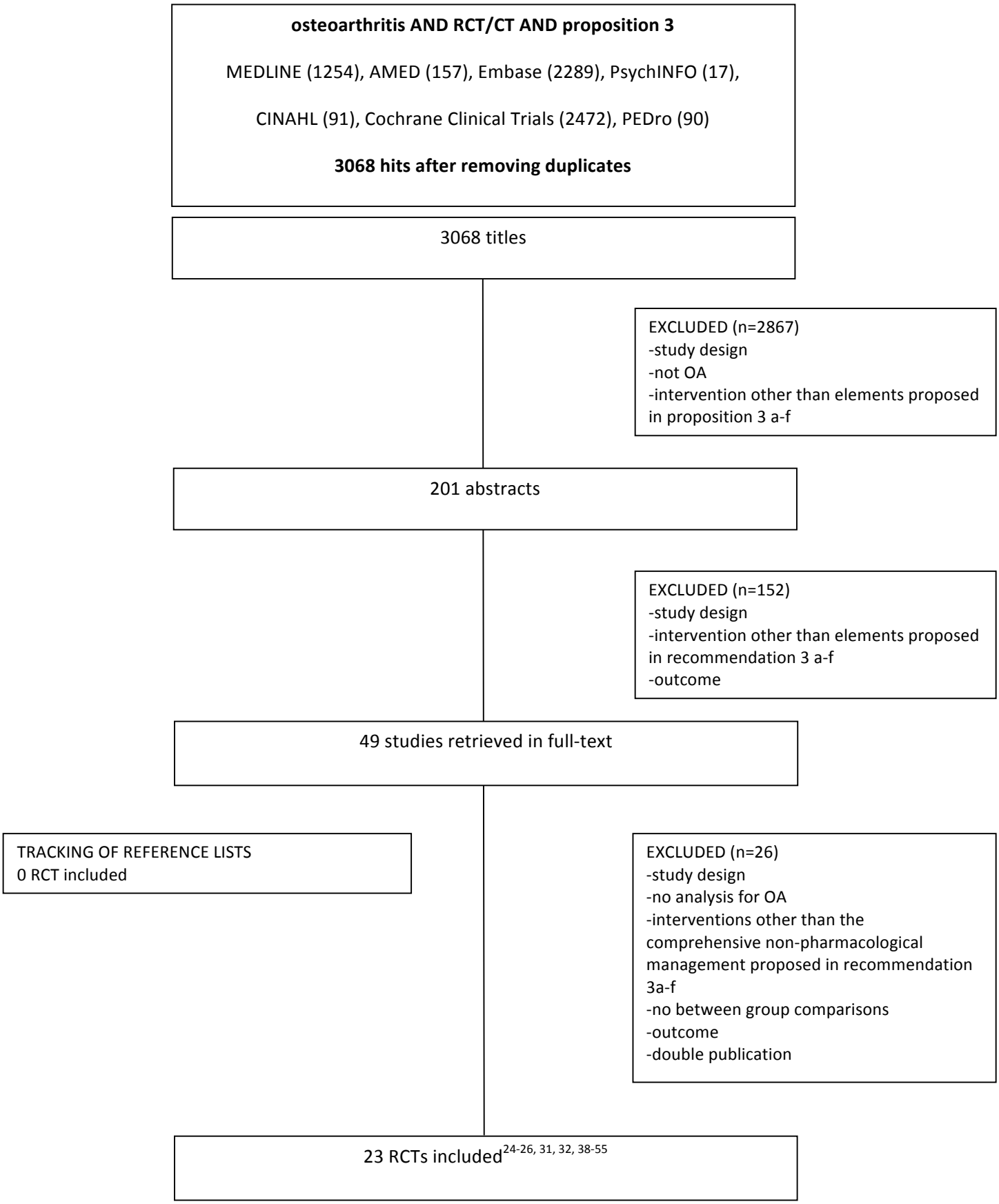


Figure S4 Proposition-specific literature search for proposition 3.

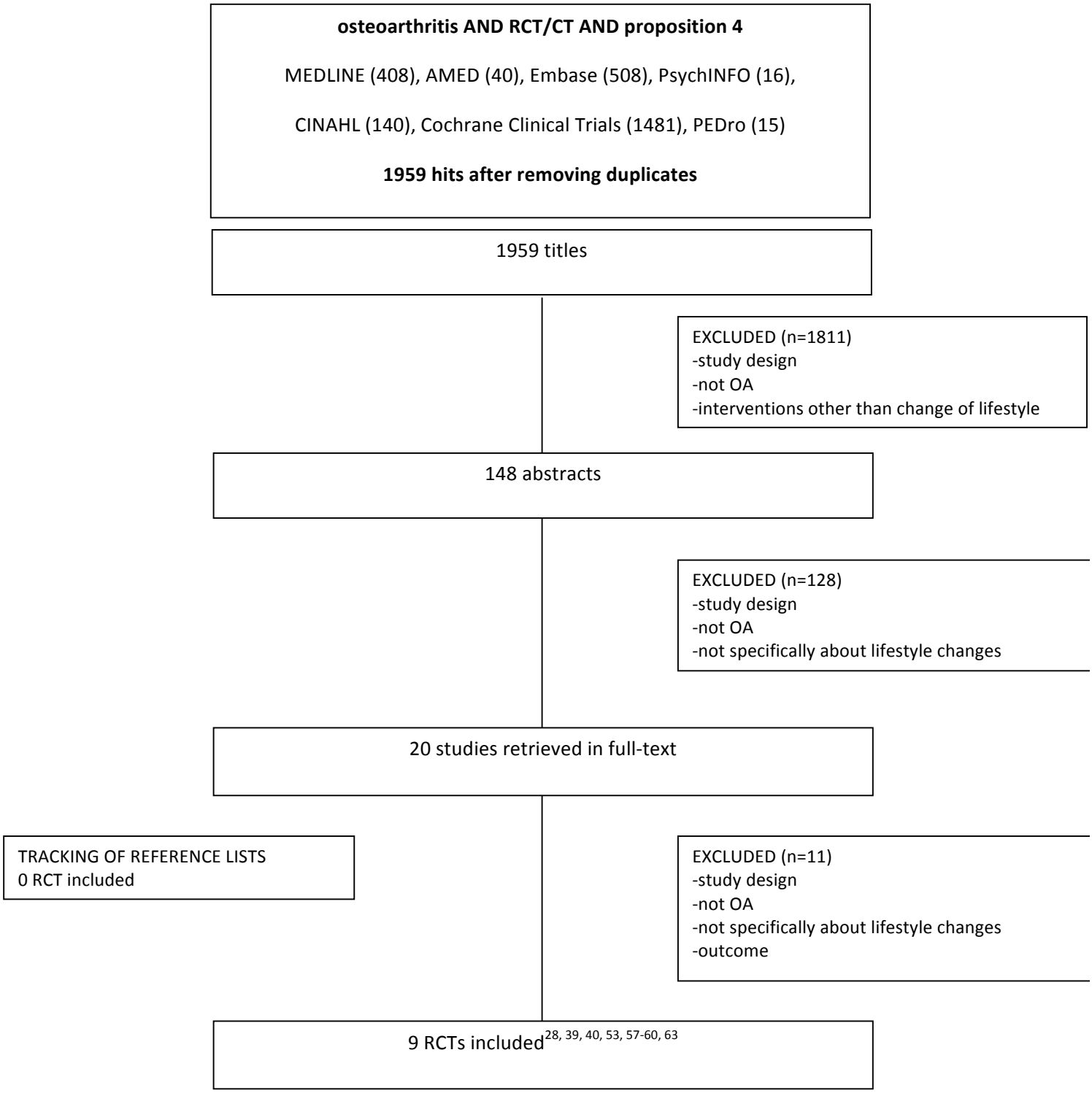


Figure S5 Proposition-specific literature search for proposition 4.

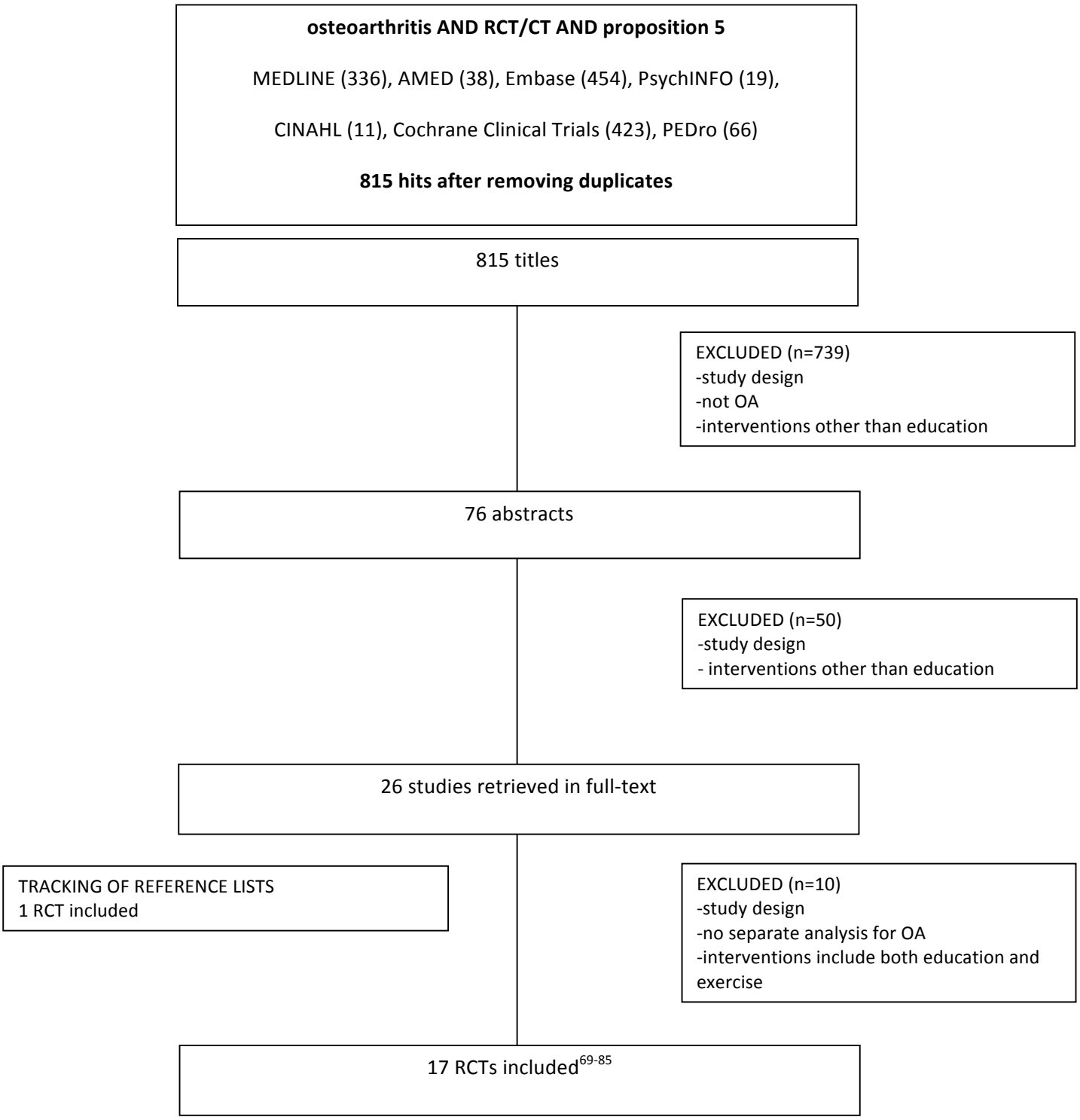


Figure S6 Proposition-specific literature search for proposition 5.

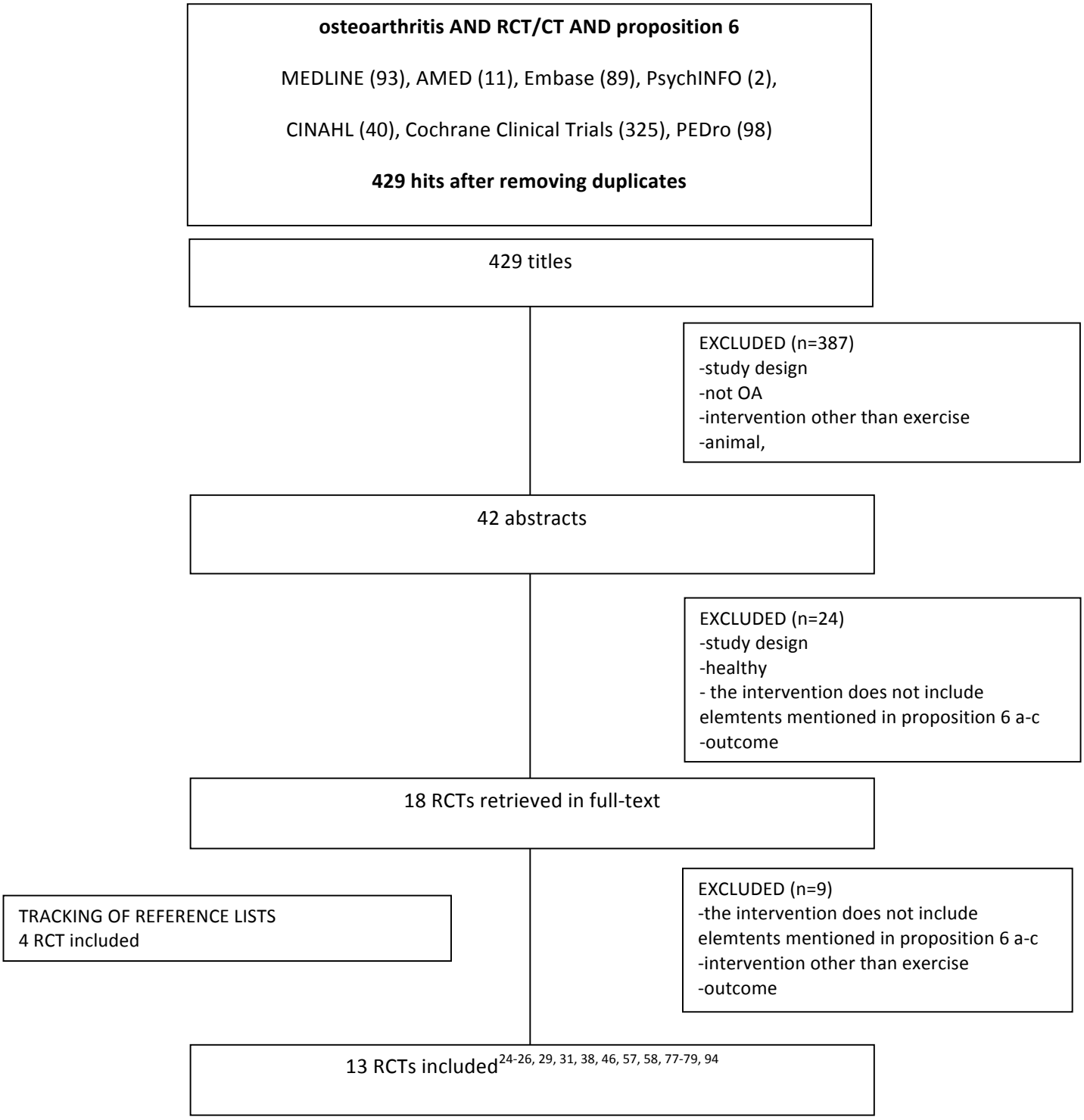


Figure S7 Proposition-specific literature search for proposition 6.

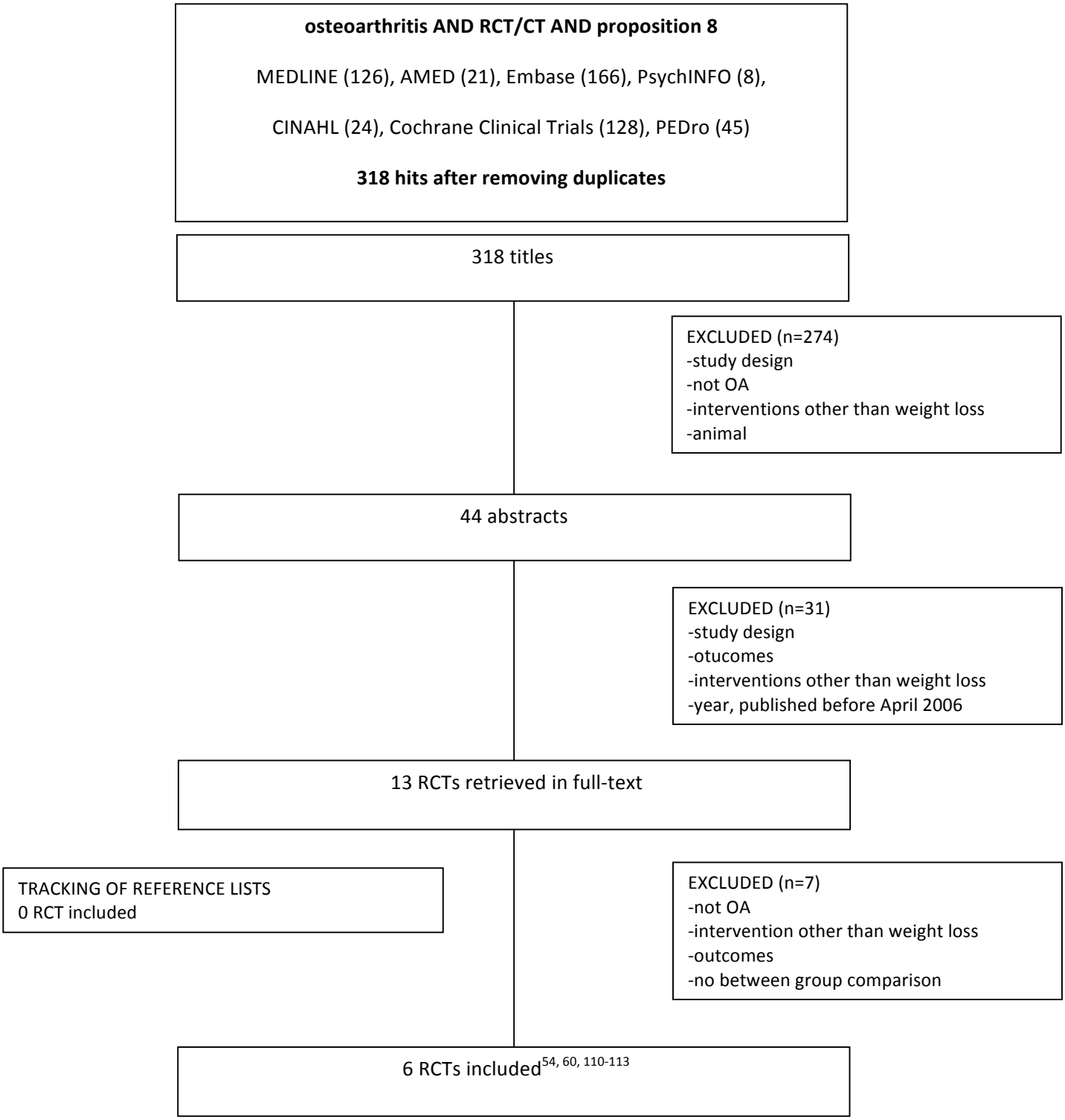


Figure S8 Proposition-specific literature search for proposition 8. Time limit April 2006 to February 2012.

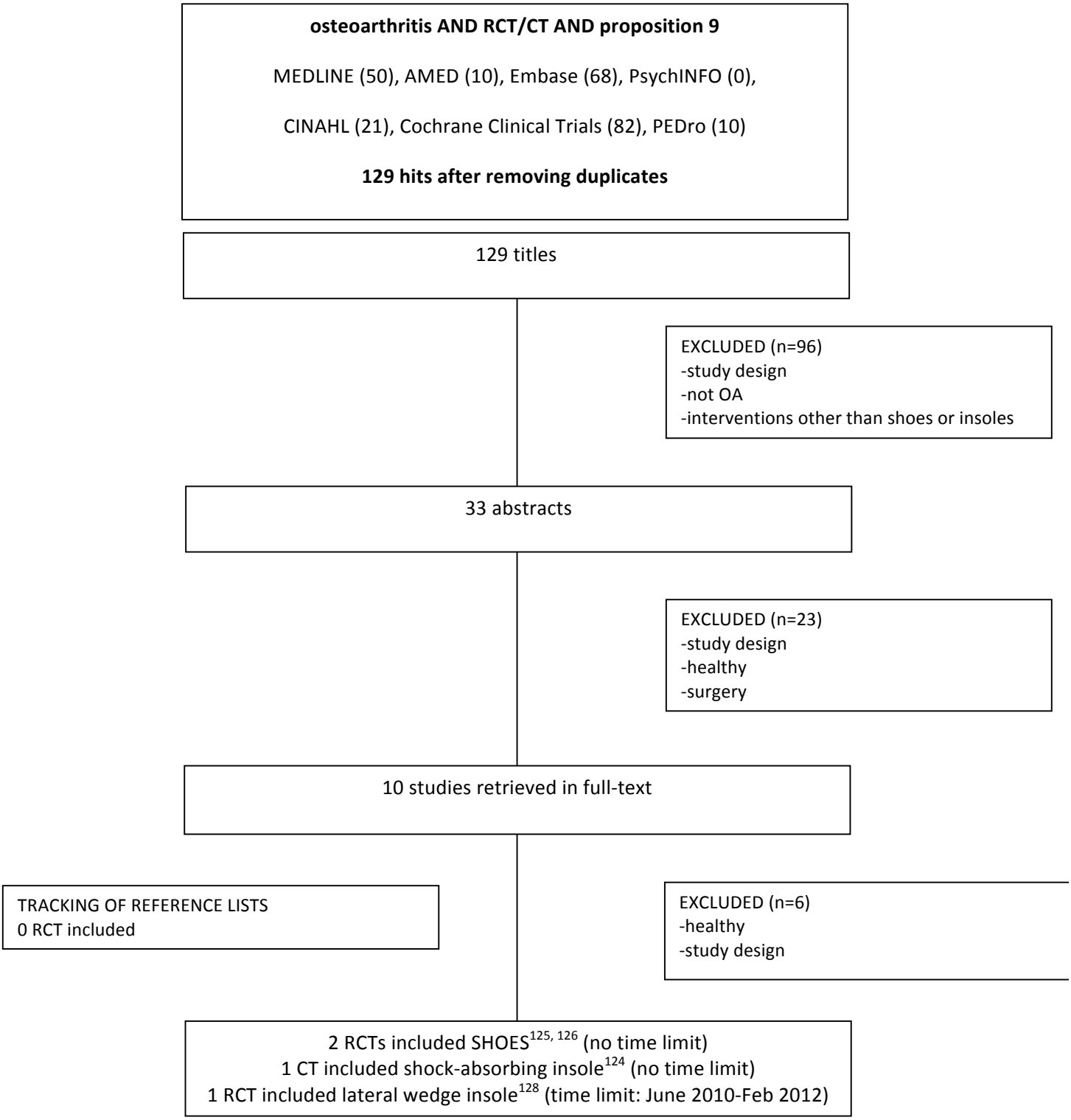


Figure S9 Proposition-specific search for proposition 9.

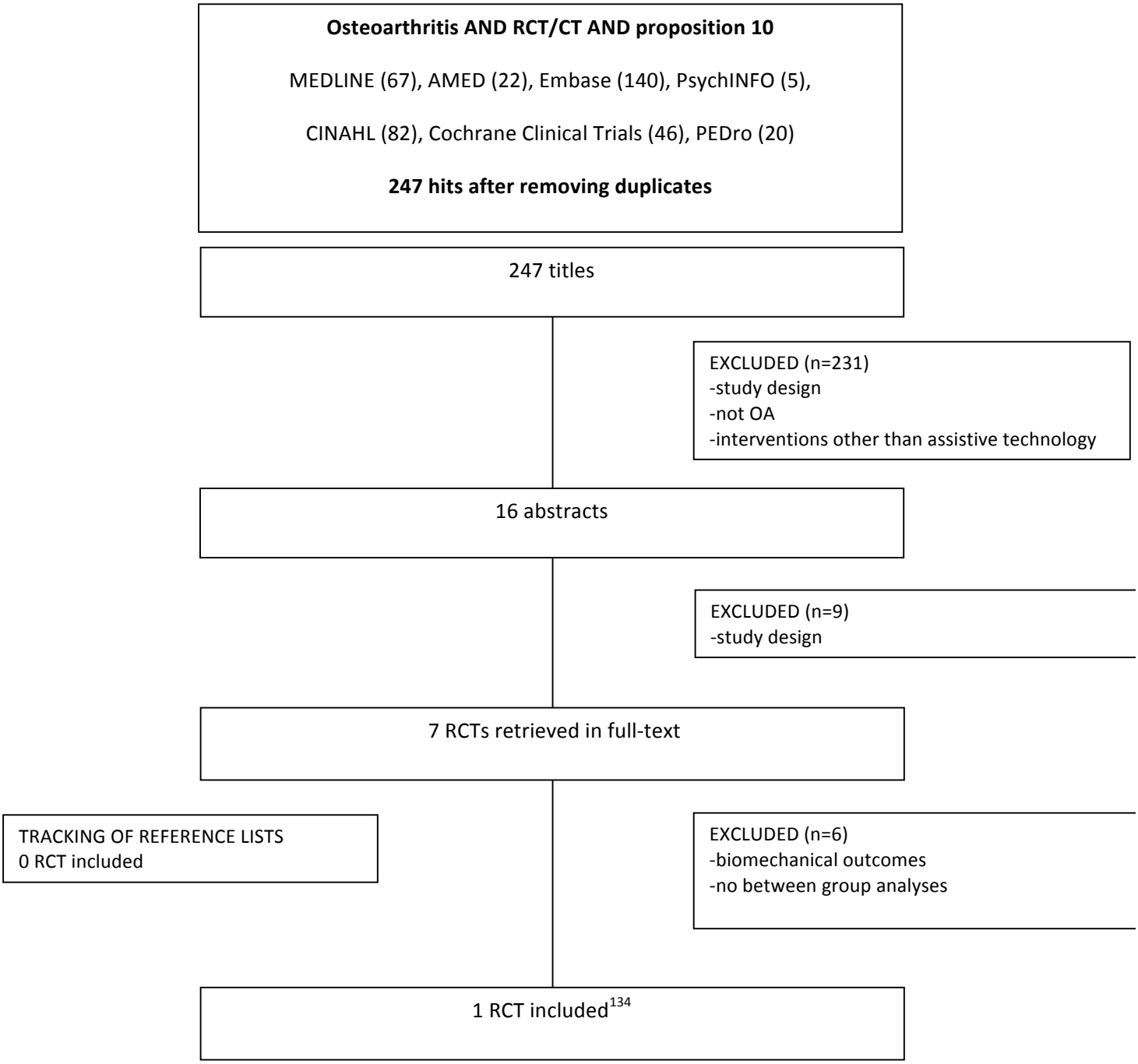


Figure S10. Proposition-specific literature search for proposition 10.

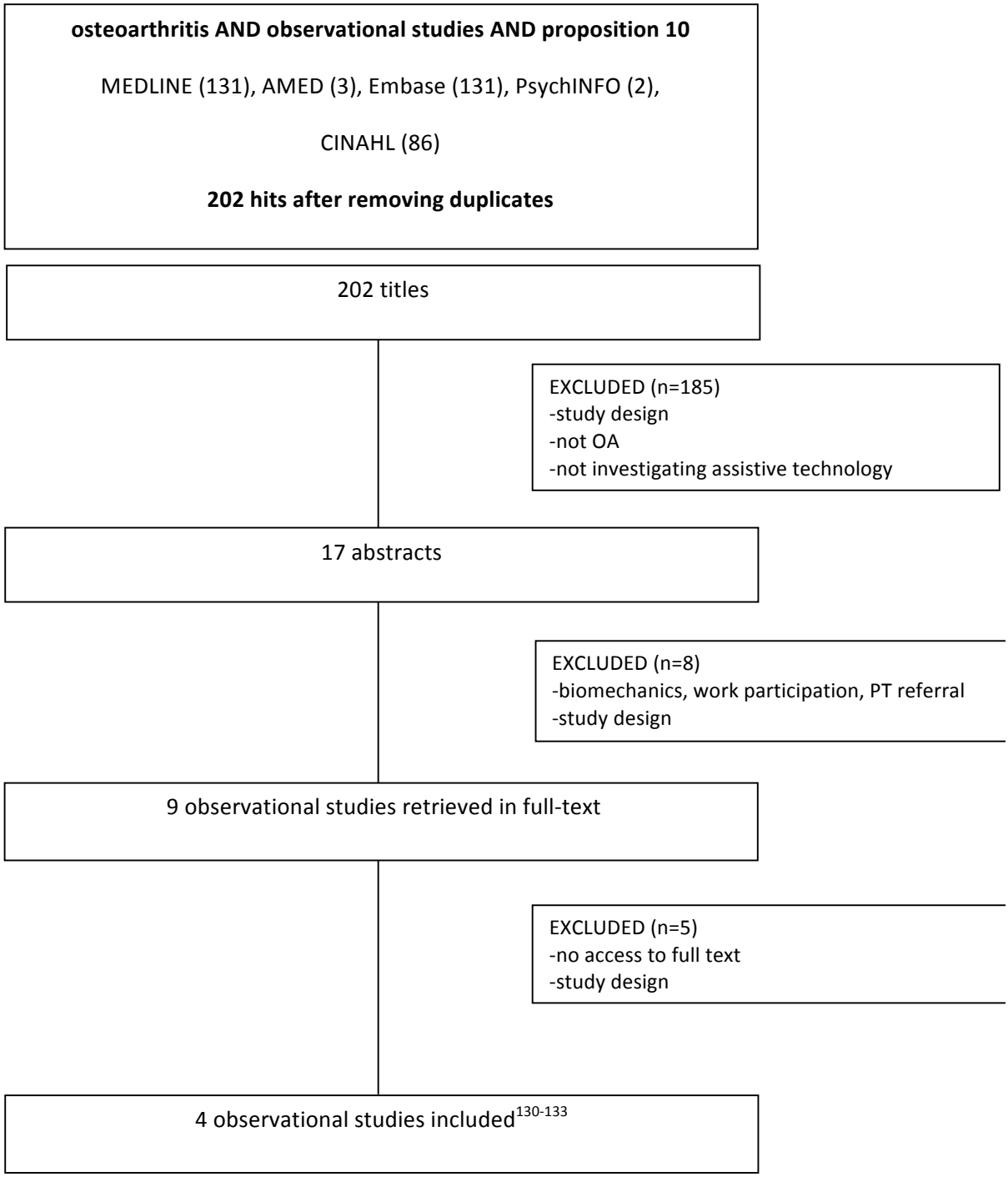


Figure S11 Proposition-specific literature search for proposition 10.

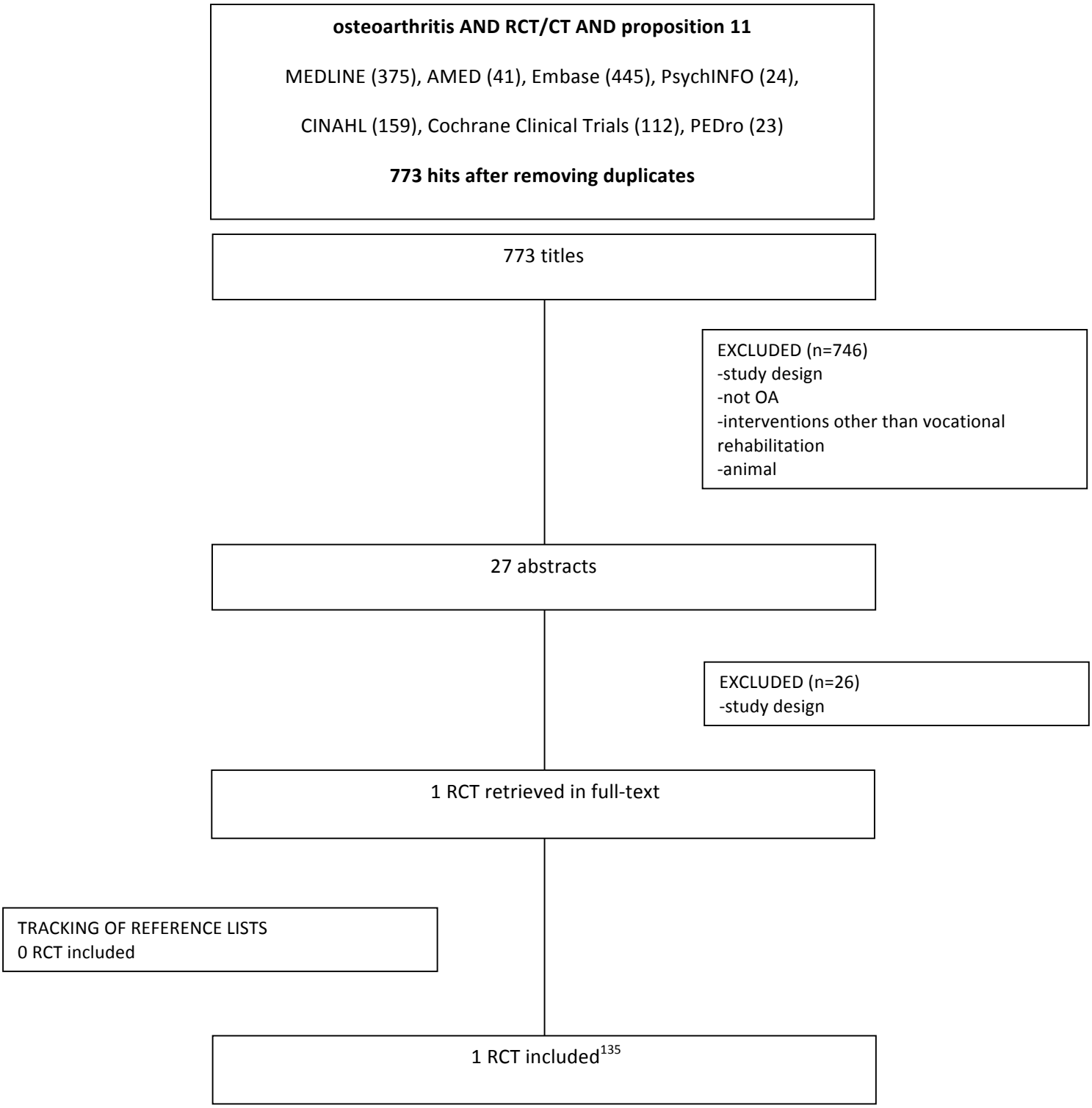


Figure S12. Proposition-specific search for proposition 11.