

Evaluating the design and reporting of pragmatic trials in osteoarthritis research

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TITLE: Evaluating the design and reporting of pragmatic trials in osteoarthritis research

RUNNING HEADER: Pragmatic trials in osteoarthritis research

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ABSTRACT

Objectives: Among challenges in health research is translating interventions from controlled experimental settings to clinical and community settings where chronic disease is managed daily. Pragmatic trials offer a method for testing interventions in real-world settings, but are seldom used in osteoarthritis research. We evaluate the literature on pragmatic trials in osteoarthritis research up to August 2016 in order to identify strengths and weaknesses in the design and reporting of these trials.

Methods: We used established guidelines to assess the degree to which 61 osteoarthritis studies complied with pragmatic trial design and reporting. We assessed design according to the pragmatic-explanatory continuum indicator summary (PRECIS), and reporting according to the pragmatic trials extension of the CONSORT (CONsolidated Standards of Reporting Trials) guidelines.

Results: None of the pragmatic trials met all 11 criteria evaluated, most of the trials met between 5 and 8 of the criteria. Criteria most often unmet pertained to practitioner expertise (by requiring specialists), and criteria most often met pertained to primary outcome analysis (by using intention-to-treat analysis).

Conclusion: Our results suggest a lack of highly pragmatic trials in osteoarthritis research. We identify this as a point of opportunity to improve research translation, since optimizing the design and reporting of pragmatic trials can facilitate implementation of evidence-based interventions for osteoarthritis care.

INTRODUCTION

The prevalence of osteoarthritis is expected to rise with population aging [1]. There is no cure for osteoarthritis, but there are strategies that can reduce progression and mitigate symptoms [2, 3]. The challenge lies in effective implementation of these interventions, particularly since there are demonstrated practice gaps in the delivery of osteoarthritis care [4]. Implementation research aims to reduce the gap between what is known to be clinically effective and what is actually delivered in clinical care [5]. Allen et al. provide an overview of the design and conduct of implementation trials of interventions for osteoarthritis [6]. The authors describe conceptual frameworks (e.g. knowledge-to-action), study designs (e.g. pragmatic trials), and evaluations (both process and formative) for implementation trials.

Pragmatic trials are particularly useful in implementation research, since they are designed to determine the generalizability of interventions to routine practice [6]. Whereas explanatory trials are used to test the *efficacy* of interventions in controlled settings, pragmatic trials are used to demonstrate the *effectiveness* of interventions in real-world settings [7, 8]. In theory, pragmatic trials test interventions that are evidence-based with flexibility for application across multiple settings with large and heterogeneous populations, looking at stakeholder-related outcomes over longer periods of time [9, 10]. In practice, this may not always be the case.

The objective of this study is to evaluate the degree to which existing pragmatic trials in osteoarthritis research comply with guidelines for the design and reporting of pragmatic trials [11, 12]. We identify strengths and weaknesses of pragmatic trials in osteoarthritis research,

and suggest ways in which pragmatic trial guidelines can be applied to osteoarthritis research to achieve highly pragmatic trials. By optimizing pragmatic trial methodology in osteoarthritis research, we can facilitate implementation of evidence-based interventions in routine practice, and reduce care gaps.

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METHODS

We searched PubMed and Web of Science using the terms “pragmatic AND trial AND osteoarthritis [All Fields]” to identify publications prior to August 2016. Our search identified 63 citations from PubMed and 93 citations from Web of Science, with 96 unique citations combined (**Supplementary Figure 1**). We included articles that explicitly stated that the study was “pragmatic” in the title (36%), abstract (59%), or methods/discussion (5%). We excluded articles that were not reports of primary research, were not available in full-text or English, and were not related to osteoarthritis. We excluded reports of trial results when reports of trial protocol for the same study were already included. For each study, we determined whether the intervention was clinician-based (oral drug, injections, acupuncture, surgery, or clinical pathways) or patient-based (diet, exercise, self-management programs, devices, topical therapies), and which joints were targeted (**Supplementary Table 1**).

We used the pragmatic-explanatory continuum indicator summary (PRECIS) [11] and the pragmatic trials extension of the CONSORT (CONsolidated Standards of Reporting Trials) [12] guidelines to determine the parameters of an ideal pragmatic trial in osteoarthritis research [13, 14]. Guidelines for optimal pragmatic trial design (PRECIS) and reporting (CONSORT) were consistent, with an additional guideline for reporting ‘Blinding’ in the CONSORT extension. We combined these guidelines into 11 criteria (**Table 1**) to evaluate each of the 61 studies reporting a pragmatic trial in osteoarthritis research. Determinations were made for each criterion using a simple binary system to indicate whether the study met pragmatic criteria (yes = 1) or not (no = 0), where a maximum score of 11 could be assigned per study (**Supplementary Table 2**). After

being trained to code [15], two independent raters (KL and KW) evaluated each study. Inter-rater agreement of coding for a random sample of studies (N=30) was determined to be 78%. A third reviewer (SAA) evaluated any discrepancies in coding (an average of 3 criteria per study).

For Peer Review

RESULTS

None of the 61 pragmatic trials we evaluated met all 11 criteria described in **Table 1**. Most of the trials, for both clinician- and patient-based interventions, met 5 to 8 of the criteria (**Supplementary Figure 2**). Few trials were at either extreme, meeting 9 or more criteria, or 4 or less criteria (**Supplementary Figure 2**). Of note, 5% of studies met 9 or more criteria, suggesting that it is possible, but rare, to have highly pragmatic trials in osteoarthritis research.

The criteria that most studies failed to meet were practitioner expertise for both experimental and comparison interventions. This requires the intervention be applied by practitioners ordinarily involved with the care of patients [11]. For osteoarthritis patients, this typically includes general practitioners, pharmacists, family, and friends. Only 10% of studies met this criterion for the experimental intervention and only 34% for the comparison intervention (**Table 2**). The majority of studies required additional training of practitioners delivering the intervention, or included experts that would require special referral in many health care systems (e.g. physiotherapists, orthopaedic surgeons).

Only 41% of studies met pragmatic trial guidelines for participant eligibility criteria (**Table 2**). As described by Thorpe et al., trials with minimal inclusion and exclusion criteria are considered pragmatic [11]. The majority of trials we evaluated imposed specific participant eligibility criteria relating to the severity or type of osteoarthritis (inclusion criteria), and the presence of co-morbidities (exclusion criteria), and seldom explained why. For example, 61% of studies recruited participants with knee osteoarthritis (16% knee and hip, 5% hip, 5% did not specify a

joint, 8% generalized osteoarthritis, 3% hand, 2% shoulder), and many studies excluded participants who had undergone joint replacement or other surgical interventions. These design decisions may be appropriate for trials examining interventions for specific populations, but do not capture the osteoarthritis population with multiple morbidities due to advanced age, and with persistent symptoms in the same or additional joints after surgery.

We found 48% of studies met criteria for flexibility of the comparison intervention (**Table 2**), where pragmatic trials use the existing standard of care as the comparison intervention [11]. This number may be inflated since many studies did not report the standard of care, so we assumed no changes were made. Many studies did change the standard of care, for example by offering the comparison group information pamphlets. Lack of reporting was also evident for blinding procedures. Traditional single- or double-blinding may not always be possible for pragmatic trials [10], but only 43% of studies provided an explanation for the blinding decisions (**Table 2**).

Pragmatic trials avoid monitoring participant compliance with the intervention [11]; we found 54% of the studies met this criterion (**Table 2**). Several studies required participants to keep track of a behaviour using diaries or logs over extended periods of time. While compliance measures may help researchers explain effect sizes, they may also introduce an observer effect. Truly pragmatic trials accept non-compliance as a reality [13]. This relates to flexibility of the experimental intervention, for which 51% of studies met the criterion (**Table 2**). Pragmatic trials

have interventions that are not closely monitored, that are flexible in delivery, and that accommodate variation across settings [13].

Strengths of pragmatic trials in osteoarthritis research include the choice of primary trial outcome, where 82% of studies used outcomes that were minimally invasive and clinically meaningful to participants (e.g. pain, quality of life, function), and analysis of primary outcome, where 87% of studies used intention-to-treat analysis. We found 79% of studies did not monitor practitioner adherence to the study protocol, although this number may reflect a common practice to refrain from monitoring practitioners rather than a research effort to comply with pragmatic trial guidelines. We found 77% of studies met the criterion for minimizing follow-up intensity, although we allowed for up to 2 follow-ups, and considered any follow-up by phone or mail to be pragmatic (**Table 2**).

DISCUSSION

In osteoarthritis research, studies that self-identify as pragmatic trials fail to meet many criteria for the design and reporting of pragmatic trials. While the PRECIS tool [11] is not intended as a method for classifying trials, it is useful for evaluating the degree to which pragmatic trials meet design recommendations [13, 15]. Our results show that most trials have both pragmatic and explanatory elements, supporting the idea of a pragmatic-explanatory continuum in trial design [11, 13].

Ideally, pragmatic trials should maximize external validity, and this requires moving away from the controlled conditions of traditional explanatory trials. In the 'real-world', populations are heterogeneous with different stages of osteoarthritis, practitioners apply protocols variably, and patients may not fully comply with interventions, particularly since osteoarthritis is deprioritized in clinical settings [4]. Yet for scientific rigor, trials must have some inclusion/exclusion criteria, practitioners must follow protocol to some degree, an appropriate comparison group is needed, and some type of follow-up is required to measure change in outcomes. As a result, there is considerable tension for some pragmatic trials criteria, between minimizing bias and maximizing generalizability [10]. How these tensions are reconciled will depend on the research question and parameters of individual studies [7].

Going forward, improved reporting of design decisions can reveal whether trials are more pragmatic, more explanatory, or potentially negligent in a particular domain of trial design. We did not evaluate overall quality of the studies included, but only what was reported, making it

difficult to distinguish shortcomings in design versus reporting. Although 75% of the studies included were published after the CONSORT extension for pragmatic trials was available in 2008 [12], it appears that there are still deficiencies in reporting of pragmatic trials.

To clarify what may constitute a pragmatic trial in osteoarthritis research, we identified common design decisions that are consistent with guidelines (**Table 1**). The list in **Table 1** is not exhaustive and was formulated based on the pragmatic trials we evaluated, of which 41% were clinician-based interventions and 59% were patient-based interventions. Existing guidelines for pragmatic trials had to be flexibly applied for trials with clinician-based interventions to qualify as pragmatic. We found eligibility criteria were more specific, experimental and comparison interventions were less flexible, practitioner adherence to protocol was stricter, and follow-up intensity was more frequent – out of necessity for surgical and pharmacologic interventions. Therefore, if the trial design captured as closely as possible the way in which the intervention would ultimately be delivered in usual clinical care, we considered it pragmatic.

We excluded articles that were not related to osteoarthritis or declared as pragmatic trials, making our search specific, but not necessarily sensitive. Other studies may have incorporated elements of pragmatic trial design without declaring the trial type as pragmatic, or may have tested interventions for joint pain without declaring an osteoarthritis diagnosis. This may have resulted in under-counting of pragmatic trials in osteoarthritis in our literature search. Other articles may have inappropriately declared the trial type as pragmatic, causing our results to reflect poor design and reporting and an overall lack of highly pragmatic trials. The underlying

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3 issue may be a lack of clarity and consensus in the field about what constitutes a pragmatic trial
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11 It remains unclear whether trials are not sufficiently pragmatic, or whether existing pragmatic
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13 trial guidelines are not appropriate. Ultimately, pragmatic trials test implementation of
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15 interventions in the real-world, and what constitutes 'real-world' will differ depending on the
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17 intervention type (in-home for many lifestyle interventions, hospital-based for surgical
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19 interventions), the end-users (patients, clinicians, policy-makers), and the social, political, and
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21 economic contexts in which the intervention will ultimately be delivered [16]. It is difficult to
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23 prove whether having more trials that are more pragmatic will improve implementation of
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25 evidence-based interventions [17]. Certainly without pragmatic trials and implementation
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27 research, practitioners may lack trial evidence that is amenable to their clinical context, and this
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29 may hinder their ability to operationalize clinical practice guidelines.
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39 In conclusion, there is a lack of highly pragmatic trials in osteoarthritis research, as defined by
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41 current guidelines for the design [11] and reporting [12] of pragmatic trials. Understanding
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43 existing pragmatic trial guidelines and how they can be applied to osteoarthritis research may
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45 improve use of this method in implementation research. Further efforts are needed to achieve
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47 a common understanding among researchers about what constitutes a pragmatic trial.
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KEY MESSAGES

- Only 61 self-identified pragmatic trials on osteoarthritis were published prior to August 2016.
- Existing pragmatic trials in osteoarthritis research show variable compliance with established guidelines.
- Most pragmatic trials met guidelines for ‘Analysis of primary outcome’, but not ‘Practitioner expertise’.

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Author Contributions: SAA conceptualized the study, interpreted results, and wrote the manuscript. Data collection and analyses were performed by SAA, KL, and KW. Revision of the manuscript was performed by MK, JCM and DF. All authors approved the final manuscript.

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Disclosure Statement: The authors declare no conflicts of interest.

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TABLE/FIGURE LEGENDS

Table 1. Summary of PRECIS (11) and CONSORT (12) guidelines, showing their overlap and application to pragmatic trials in osteoarthritis research.

Table 2. Evaluation of pragmatic trials in osteoarthritis research. Number (and percentage) of studies that met each criteria, separated by clinician- or patient-based intervention, and combined.

Supplementary Figure 1. Flowchart of literature search strategy.

Supplementary Figure 2. Distribution of summed scores for each pragmatic trial evaluated (N=61), with a maximum possible score of 11. Clinician-based intervention (black bars) = oral drug, injections, acupuncture, surgery, or clinical pathways. Patient-based intervention (grey bars) = diet, exercise, self-management programs, devices, topical therapies.

Supplementary Table 1. Summary of included studies.

Supplementary Table 2. Detailed evaluation of pragmatic trials in osteoarthritis research.

TITLE: Evaluating the design and reporting of pragmatic trials in osteoarthritis research

RUNNING HEADER: Pragmatic trials in osteoarthritis research

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ABSTRACT

Objectives: Among challenges in health research is translating interventions from controlled experimental settings to clinical and community settings where chronic disease is managed daily. Pragmatic trials offer a method for testing interventions in real-world settings, but are seldom used in osteoarthritis research. ~~Objective:~~ We evaluate the literature on pragmatic trials in osteoarthritis research up to August 2016 in order to identify strengths and weaknesses in the design and reporting of these trials.

Methods: We used established guidelines to assess the degree to which 61 osteoarthritis studies complied with pragmatic trial design ~~[pragmatic-explanatory continuum indicator summary (PRECIS)]~~ and reporting ~~[pragmatic trials extension of the CONSORT (CONsolidated Standards of Reporting Trials) guidelines]~~. We assessed design according to the pragmatic-explanatory continuum indicator summary (PRECIS), and reporting according to the pragmatic trials extension of the CONSORT (CONsolidated Standards of Reporting Trials) guidelines.

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INTRODUCTION

The prevalence of osteoarthritis is expected to rise with population aging [1]. There is no cure for osteoarthritis, but there are strategies that can reduce progression and mitigate symptoms [2, 3]. The challenge lies in effective implementation of these interventions, particularly since there are demonstrated practice gaps in the delivery of osteoarthritis care [4]. Implementation research aims to reduce the gap between what is known to be clinically effective and what is actually delivered in clinical care [5]. Allen et al. provide an overview of the design and conduct of implementation trials of interventions for osteoarthritis [6]. The authors describe conceptual frameworks (e.g. knowledge-to-action), study designs (e.g. pragmatic trials), and evaluations (both process and formative) for implementation trials.

Pragmatic trials are particularly useful in implementation research, since they are designed to determine the generalizability of interventions to routine practice [6]. Whereas explanatory trials are used to test the *efficacy* of interventions in controlled settings, pragmatic trials are used to demonstrate the *effectiveness* of interventions in real-world settings [7, 8]. In theory,

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RESULTS

None of the 61 pragmatic trials we evaluated met all 11 criteria described in **Table 1**. Most of the trials, for both ~~medical-clinician-~~ and ~~patient-based lifestyle-~~interventions, met 5 to 8 of the criteria (~~Figure 1A~~[Supplementary Figure 2](#)). Few trials were at either extreme, meeting 9 or

more criteria, or 4 or less criteria ([Figure 1A](#)[Supplementary Figure 2](#)). Of note, 5% of studies met 9 or more criteria, suggesting that it is possible, but rare, to have highly pragmatic trials in osteoarthritis research.

The criteria that most studies failed to meet were practitioner expertise for both experimental and comparison interventions. This requires the intervention be applied by practitioners ordinarily involved with the care of patients [11]. For osteoarthritis patients, this typically includes general practitioners, pharmacists, family, and friends. Only 10% of studies met this criterion for the experimental intervention and only 34% for the comparison intervention ([Figure 1B](#)[Table 2](#)). The majority of studies required additional training of practitioners delivering the intervention, or included experts that would require special referral in many health care systems (e.g. physiotherapists, orthopaedic surgeons).

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populations, but do not capture the osteoarthritis population with multiple morbidities due to advanced age, and with persistent symptoms in the same or additional joints after surgery.

We found 48% of studies met criteria for flexibility of the comparison intervention (**Figure 1B Table 2**), where pragmatic trials use the existing standard of care as the comparison intervention [11]. This number may be inflated since many studies did not report the standard of care, so we assumed no changes were made. Many studies did change the standard of care, for example by offering the comparison group information pamphlets. Lack of reporting was also evident for blinding procedures. Traditional single- or double-blinding may not always be possible for pragmatic trials [10], but only 43% of studies provided an explanation for the blinding decisions (**Figure 1B Table 2**).

Pragmatic trials avoid monitoring participant compliance with the intervention [11]; we found 54% of the studies met this criterion (**Figure 1B Table 2**). Several studies required participants to keep track of a behaviour using diaries or logs over extended periods of time. While compliance measures may help researchers explain effect sizes, they may also introduce an observer effect. Truly pragmatic trials accept non-compliance as a reality [13]. This relates to flexibility of the experimental intervention, for which 51% of studies met the criterion (**Figure 1B Table 2**). Pragmatic trials have interventions that are not closely monitored, that are flexible in delivery, and that accommodate variation across settings [13].

Strengths of pragmatic trials in osteoarthritis research include the choice of primary trial outcome, where 82% of studies used outcomes that were minimally invasive and clinically meaningful to participants (e.g. pain, quality of life, function), and analysis of primary outcome, where 87% of studies used intention-to-treat analysis. We found 79% of studies did not monitor practitioner adherence to the study protocol, although this number may reflect a common practice to refrain from monitoring practitioners rather than a research effort to comply with pragmatic trial guidelines. We found 77% of studies met the criterion for minimizing follow-up intensity, although we allowed for up to 2 follow-ups, and considered any follow-up by phone or mail to be pragmatic (~~Figure 1B~~ [Table 2](#)).

DISCUSSION

In osteoarthritis research, studies that self-identify as pragmatic trials fail to meet many criteria for the design and reporting of pragmatic trials. While the PRECIS tool [11] is not intended as a method for classifying trials, it is useful for evaluating the degree to which pragmatic trials meet design recommendations [13, 15]. Our results show that most trials have both pragmatic and explanatory elements, supporting the idea of a pragmatic-explanatory continuum in trial design [11, 13].

Ideally, pragmatic trials should maximize external validity, and this requires moving away from the controlled conditions of traditional explanatory trials. In the 'real-world', populations are heterogeneous with different stages of osteoarthritis, practitioners apply protocols variably, and patients may not fully comply with interventions, particularly since osteoarthritis is

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deprioritized in clinical settings [4]. Yet for scientific rigor, trials must have some inclusion/exclusion criteria, practitioners must follow protocol to some degree, an appropriate comparison group is needed, and some type of follow-up is required to measure change in outcomes. As a result, there is considerable tension for some pragmatic trials criteria, between minimizing bias and maximizing generalizability [10]. How these tensions are reconciled will depend on the research question and parameters of individual studies [7].

Going forward, improved reporting of design decisions can reveal whether trials are more pragmatic, more explanatory, or potentially negligent in a particular domain of trial design. ~~In this study, We did not evaluate overall quality of the studies included, but we could only evaluate what was reported, making it sometimes difficult to distinguish shortcomings in design versus reporting.~~ Although 75% of the studies included were published after the CONSORT extension for pragmatic trials was available in 2008 [12], it appears that there are still deficiencies in reporting of pragmatic trials.

To clarify what may constitute a pragmatic trial in osteoarthritis research, we identified common design decisions that are consistent with guidelines (**Table 1**). The list in **Table 1** is not exhaustive and was formulated based on the pragmatic trials we evaluated, of which 41% were ~~medical-clinician-based~~ interventions and 59% were ~~lifestyle-patient-based~~ interventions. Existing guidelines for pragmatic trials had to be flexibly applied for trials with ~~medical-clinician-based~~ interventions to qualify as pragmatic. We found eligibility criteria were more specific, experimental and comparison interventions were less flexible, practitioner adherence to

protocol was stricter, and follow-up intensity was more frequent – out of necessity for surgical and pharmacologic interventions. Therefore, if the trial design captured as closely as possible the way in which the intervention would ultimately be delivered in usual ~~medical~~-clinical care, we considered it pragmatic.

We excluded articles that were not related to osteoarthritis or declared as pragmatic trials, making our search specific, but not necessarily sensitive. ~~since~~ Other studies may have incorporated elements of pragmatic trial design without declaring the trial type as pragmatic, or may have tested interventions for joint pain without declaring an osteoarthritis diagnosis. This may have resulted in under-counting of pragmatic trials in osteoarthritis in our literature search. Other articles may have inappropriately declared the trial type as pragmatic, causing our results to reflect poor design and reporting and an overall lack of highly pragmatic trials. The underlying issue may be a lack of clarity and consensus in the field about what constitutes a pragmatic trial [7].

It remains unclear whether trials are not sufficiently pragmatic, or whether existing pragmatic trial guidelines are not appropriate. Ultimately, pragmatic trials test implementation of interventions in the real-world, and what constitutes ‘real-world’ will differ depending on the intervention type (in-home for many lifestyle interventions, hospital-based for surgical interventions), the end-users (patients, clinicians, policy-makers), and the social, political, and economic contexts in which the intervention will ultimately be delivered [16]. It is difficult to prove whether having more trials that are more pragmatic will improve implementation of

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evidence-based interventions [17]. Certainly without pragmatic trials and implementation research, practitioners may lack trial evidence that is amenable to their clinical context, and this may hinder their ability to operationalize clinical practice guidelines.

In conclusion, there is a lack of highly pragmatic trials in osteoarthritis research, as defined by current guidelines for the design [11] and reporting [12] of pragmatic trials. Understanding existing pragmatic trial guidelines and how they can be applied to osteoarthritis research may improve use of this method in implementation research. Further efforts are needed to achieve a common understanding among researchers about what constitutes a pragmatic trial.

KEY MESSAGES

- ~~• Pragmatic trials facilitate implementation of health research, but are seldom used in osteoarthritis research.~~
- Only 61 self-identified pragmatic trials on osteoarthritis were published prior to August 2016.
- Existing pragmatic trials in osteoarthritis research show variable compliance with established guidelines.

- Most pragmatic trials met guidelines for 'Analysis of primary outcome', but not 'Practitioner expertise'.

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TABLE/FIGURE LEGENDS

Table 1. Summary of PRECIS (119) and CONSORT (121) guidelines, showing their overlap and application to pragmatic trials in osteoarthritis research.

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Figure-Table 21. Evaluation of pragmatic trials in osteoarthritis research. ~~A) Distribution of summed scores for each pragmatic trial evaluated (N=61), with a maximum possible score of 11. Medical = oral drug, injections, acupuncture, surgery, or clinical pathways. Lifestyle = diet, exercise, self-management programs, devices, topical therapies.~~ B) Number (and percentage) of studies that met each criteria, separated by ~~medical-clinician-~~ or ~~patient-based lifestyle~~ intervention, and combined.

Supplementary Figure 1. Flowchart of literature search strategy.

Supplementary Figure 2. Distribution of summed scores for each pragmatic trial evaluated (N=61), with a maximum possible score of 11. Clinician-based intervention (black bars) = oral drug, injections, acupuncture, surgery, or clinical pathways. Patient-based intervention (grey bars) = diet, exercise, self-management programs, devices, topical therapies.

Supplementary Table 1. Summary of included studies.

Supplementary Table 2. Evaluation of included studies using 11 criteria for pragmatic trials.

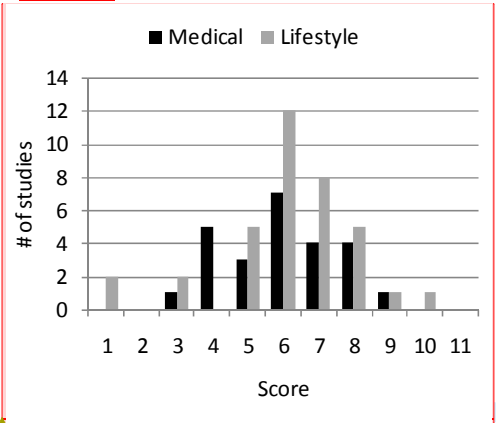
Table 1.

	<u>Design (PRECIS)</u>	<u>Reporting (CONSORT)</u>	<u>A pragmatic trial in osteoarthritis research:</u>
1	Participant eligibility criteria	Participants	Captures the target population (e.g. does not exclude people with co-morbidities)
	Experimental intervention	Interventions	
2	Flexibility	Generalizability	Implements an intervention that can be delivered after the study concludes
3	Practitioner expertise		Relies on a general practitioner or other typical OA care provider
	Comparison intervention	Background	
4	Flexibility		Describes current standard of care, does not alter it (e.g. by providing pamphlets)
5	Practitioner expertise		Relies on a general practitioner or other typical OA care provider
6	Follow-up intensity	Outcomes	Measures outcomes infrequently, and at least 6 months following the intervention
7	Primary trial outcome	Sample Size	Uses minimally invasive outcomes that are meaningful to the participant (e.g. function)
8	Participant compliance		Does not track participant compliance (e.g. with self-reports in diaries/logs)
9	Practitioner adherence		Does not monitor general practitioner/OA care provider adherence to study protocol
10	Analysis of primary outcome	Participant Flow	Includes all participants in an intention-to-treat analysis of the primary outcome
11		Blinding	Provides an explanation for blinding decisions

Table 2.

Criteria	Clinician-based intervention (N=25)	Patient-based intervention (N=36)	Combined (N=61)
Participant eligibility criteria	12 (48%)	13 (36%)	25 (41%)
Experimental intervention			
Flexibility	13 (52%)	18 (50%)	31 (51%)
Practitioner expertise	5 (20%)	1 (3%)	6 (10%)
Comparison intervention			
Flexibility	12 (48%)	17 (47%)	29 (48%)
Practitioner expertise	9 (36%)	12 (33%)	21 (34%)
Follow-up intensity	17 (68%)	30 (83%)	47 (77%)
Primary trial outcome	19 (76%)	31 (86%)	50 (82%)
Participant compliance	14 (56%)	19 (53%)	33 (54%)
Practitioner adherence	21 (84%)	27 (75%)	48 (79%)
Analysis of primary outcome	19 (76%)	34 (94%)	53 (87%)
Blinding	8 (32%)	18 (50%)	26 (43%)

Table 2.



Comment [AA1]: Edited to Supplementary Figure 2

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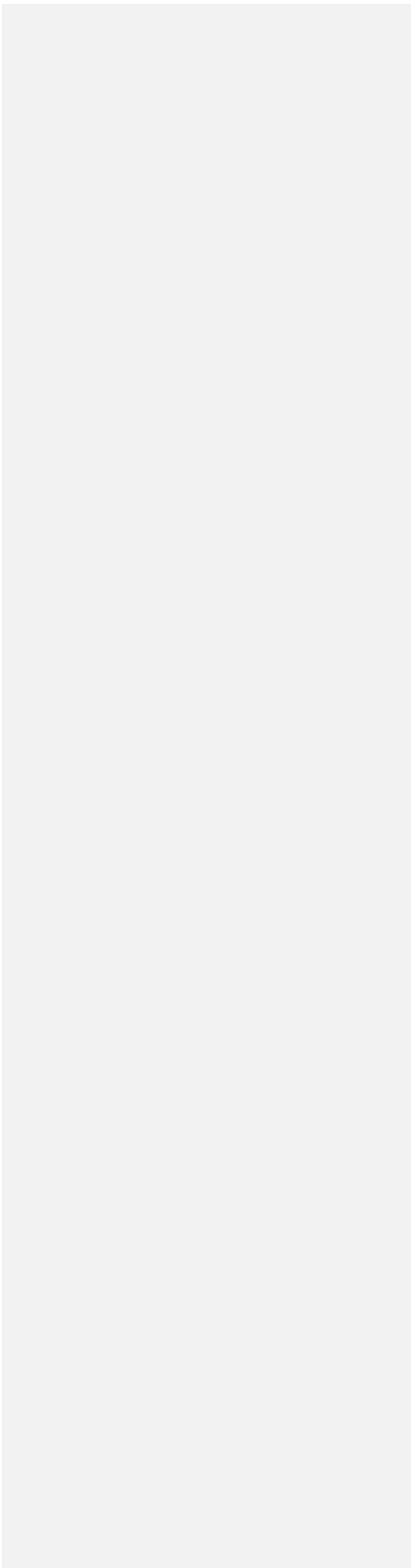
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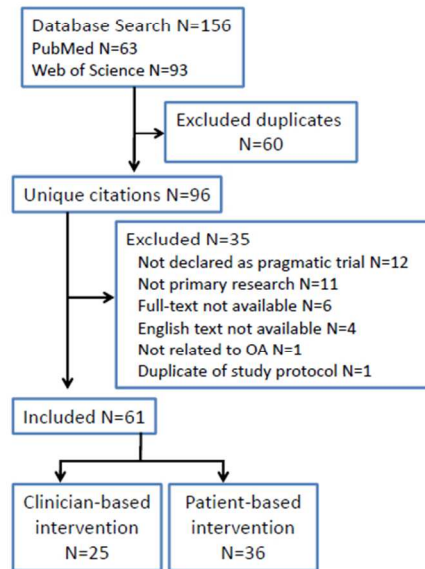
Criteria	Clinician-based intervention Medical (N=25)	Patient-based intervention Lifestyle (N=36)	Combined (N=61)
Participant eligibility criteria	12 (48%)	13 (36%)	25 (41%)
Experimental intervention			
Flexibility	13 (52%)	18 (50%)	31 (51%)
Practitioner expertise	5 (20%)	1 (3%)	6 (10%)
Comparison intervention			
Flexibility	12 (48%)	17 (47%)	29 (48%)
Practitioner expertise	9 (36%)	12 (33%)	21 (34%)
Follow-up intensity	17 (68%)	30 (83%)	47 (77%)
Primary trial outcome	19 (76%)	31 (86%)	50 (82%)
Participant compliance	14 (56%)	19 (53%)	33 (54%)
Practitioner adherence	21 (84%)	27 (75%)	48 (79%)
Analysis of primary outcome	19 (76%)	34 (94%)	53 (87%)
Blinding	8 (32%)	18 (50%)	26 (43%)

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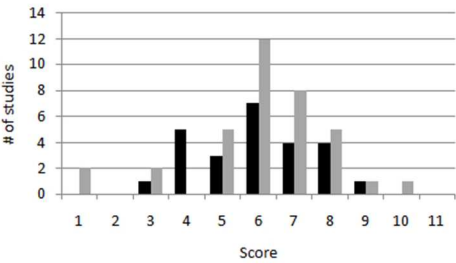
For Peer Review





Supplementary Figure 1.

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Supplementary Figure 2.

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Supplementary Table 1. Summary of included studies

Citation	Study question	Intervention	Protocol paper	Pragmatic score
Bilkman T, Rienstra W, Raaij T, Hagen A, Dijkstra B, Zijlstra W, et al. Duloxetine in OsteoArthritis (DOA) study: study protocol of a pragmatic open-label randomised controlled trial assessing the effect of preoperative pain treatment on postoperative outcome after total hip or knee arthroplasty. BMJ Open. 2016;6(3).	What are the effects of preoperative pain treatment on postoperative outcomes using duloxetine for hip or knee OA?	drug	protocol	7
Callahan LF, Callahan LF, Cleveland RJ, Altpeter M, Hackney B. Evaluation of Tai Chi Program Effectiveness for People with Arthritis in the Community: A Randomized Controlled Trial. Journal of aging and physical activity. 2016;24(1):101.	What is the effectiveness of the Arthritis Foundation Tai Chi Program for community participants with arthritis?	exercise		8
Deyle G, Gill N, Rhon D, Allen C, Allison S, Hando B, et al. A multicentre randomised, 1-year comparative effectiveness, parallel-group trial protocol of a physical therapy approach compared to corticosteroid injections. BMJ Open. 2016;6(3).	What is the effectiveness of physical therapy compared to corticosteroid injections alone for knee OA?	physiotherapy	protocol	4
Yu SP, Williams M, Eyles JP, Chen JS, Makovey J, Hunter DJ. Effectiveness of knee bracing in osteoarthritis: pragmatic trial in a multidisciplinary clinic. International Journal of Rheumatic Diseases. 2016;19(3):279-286.	What is the effectiveness of bracing treatment for tibiofemoral osteoarthritis (OA) and patellofemoral OA in patients with knee OA?	bracing		6
Beard D, Rees J, Rombach I, Cooper C. Trials: The CSAW Study (Can Shoulder Arthroscopy Work?) - a placebo-controlled surgical intervention trial assessing the clinical and cost effectiveness of arthroscopic subacromial decompression for shoulder pain: study protocol for a randomised controlled trial. Trials. 2015;16(5):210.	What is the efficacy and cost-effectiveness of ASAD (Arthroscopic subacromial decompression) in patients with subacromial pain?	surgery	protocol	5

1	Cuperus N, Hoogeboom T, Kersten C, et al. Randomized	How effective is non-	self-management	6
2	trial of the effectiveness of a non-pharmacological	pharmacological		
3	multidisciplinary face-to-face treatment program on	multidisciplinary face-to-face		
4	daily function compared to a telephone-based treatment	group-based treatment program		
5	program in patients with generalized osteoarthritis.	versus a telephone-delivered		
6	Osteoarthritis and Cartilage 2015. 23:1267–1275.	treatment program on daily		
7		function for patients with		
8		generalized OA?		
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11	Eymard F, Charles-Nelson A, Katsahian S, Chevalier X,	What is the prevalence of	surgery	4
12	Bercovy M. “Forgotten knee” after total knee	“forgotten knee” (FK) after TKR		
13	replacement: A pragmatic study from a single-centre	in a prospective pragmatic		
14	cohort. Joint Bone Spine. 2015;82(3):177-181.	cohort, with comparison to		
15		conventional scores?		
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18	Kingsbury SR, Tharmanathan P, Arden NK, Batley M,	How effective is oral	methotrexate	5
19	Birrell F, Cocks K, et al. Pain reduction with oral	methotraxate for reducing	protocol	
20	methotrexate in knee osteoarthritis, a pragmatic phase	synovitis (and pain) patients		
21	iii trial of treatment effectiveness (PROMOTE): study	with knee OA?		
22	protocol for a randomized controlled trial. Trials.			
23	2015;16:77.			
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26	Moonaz SH, Bingham CO, Wissow L, Bartlett SJ. Yoga in	Can integral-based hatha yoga	yoga	5
27	Sedentary Adults with Arthritis: Effects of a Randomized	improve fitnesss, mood, stress		
28	Controlled Pragmatic Trial. The Journal of Rheumatology.	and quality of life for people		
29	2015;42(7):1194–1202.	with knee RA or OA?		
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31	Teirlinck CH, Luijsterburg PA, Dekker J, Bohnen AM,	How effective is exercise at	exercise therapy	7
32	Verhaar JA, Koopmanschap MA, et al. Effectiveness of	improving function and pain for		
33	exercise therapy added to general practitioner care in	individuals with hip OA?		
34	patients with hip osteoarthritis: a pragmatic randomized			
35	controlled trial. Osteoarthritis and Cartilage.			
36	2015;24(1):82-90.			
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39	Bevers K, Zweers MC, Vriezekolk JE, Bijlsma JW, den	What is the predictive value of	glucocorticoid	6
40	Broeder AA. Are ultrasonographic signs of inflammation	ultrasound characteristics for	injection	
41	predictors for response to intra-articular glucocorticoids	the effect of intra-articular		
42	in knee osteoarthritis? Clinical and Experimental	glucocorticoids in knee OA?		
43	Rheumatology. 2014;32(6):930–934.			
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1 2 3 4 5 6	Broderick JE, Keefe FJ, Bruckenthal P, Junghaenel DU, Schneider S, Schwartz JE, et al. Nurse practitioners can effectively deliver pain coping skills training to osteoarthritis patients with chronic pain: A randomized, controlled trial. <i>Pain</i> . 2014;155(9):1743–1754.	How effectiveness are 10 education sessions about pain management facilitated by health nurses for patients with OA of knee or hip?	coping	7
7 8 9 10 11 12 13 14 15	Dobson F, Hinman RS, French S, Rini C, Keefe F, Nelligan R, et al. Internet-mediated physiotherapy and pain coping skills training for people with persistent knee pain (IMPACT – knee pain): a randomised controlled trial protocol. <i>BMC Musculoskelet Disorders</i> . 2014;15:279.	Is an internet-delivered intervention that combines PCST and physiotherapist-guided exercise more effective than online educational material in people with persistent knee pain?	coping/physio/exercise protocol	6
16 17 18 19 20 21 22 23 24 25	Foster NE, Healey EL, Holden MA, Nicholls E, Whitehurst DG, Jowett S, et al. A multicentre, pragmatic, parallel group, randomised controlled trial to compare the clinical and cost-effectiveness of three physiotherapy-led exercise interventions for knee osteoarthritis in older adults: the BEEP trial protocol (ISRCTN: 93634563). <i>BMC Musculoskelet Disorders</i> . 2014;15:254.	How effective are individually tailored exercise programs versus usual physiotherapy care for adherence?	physio/exercise protocol	6
26 27 28 29 30 31 32	Hermann M, Nilsen T, Eriksen CS, Slatkowsky-Christensen B, Haugen IK, Kjekshus I. Effects of a soft prefabricated thumb orthosis in carpometacarpal osteoarthritis. <i>Scandinavian Journal of Occupational Therapy</i> . 2014;21:31-39.	How does the use of a hand orthosis versus no orthosis affect pain?	orthosis	7
33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49	Janke E, Fritz M, Hopkins C, Haltzman B, Sautter J, Ramirez M. A randomized clinical trial of an integrated behavioral self-management intervention Simultaneously Targeting Obesity and Pain: the STOP trial. <i>BMC Public Health</i> . 2014;14:621.	What is the effectiveness of an integrated treatment (STOP) for weight loss and reduction in pain intensity?	behavioral self-management intervention protocol	3

1	Kjeken I, Berdal G, Bo I, Dager T, Dingsor A, Hagfors J, et	What is the clinical and cost-	goal planning and	protocol	5
2	al. Evaluation of a structured goal planning and tailored	effectiveness of a structured	tailored follow-up		
3	follow-up programme in rehabilitation for patients with	goal planning and tailored	programme		
4	rheumatic diseases: protocol for a pragmatic, stepped-	follow-up rehabilitation			
5	wedge cluster randomized trial. BMC Musculoskeletal	programme for patients with			
6	Disorders. 2014;15:153.	rheumatic diseases?			
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8	Martins F, Kaster T, Schützler L, Witt CM. Factors	How does immediate versus	acupuncture		6
9	Influencing Further Acupuncture Usage and a more	delayed acupuncture affect the			
10	positive outcome in patients with osteoarthritis of the	long term outcomes for people			
11	knee and the hip: a 3-year follow-up of a randomized	with OA?			
12	pragmatic trial. The Clinical Journal of Pain.				
13	2014;30(11):953–959.				
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16	Rabago D, Patterson JJ, Mundt M, Zgierska A, Fortney L,	Do scheduled hypertonic	dextrose & morrhuate		6
17	Grettie J, et al. Dextrose and Morrhuate Sodium	dextrose and morrhuate sodium	sodium		
18	Injections (Prolotherapy) for Knee Osteoarthritis: A	injections improved knee pain,			
19	prospective open-label trial. Journal of Alternative and	function and stiffness for knee			
20	Complementary Medicine. 2014;20(5):383–391.	osteoarthritis?			
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23	Beard D, Price A, Cook J, Fitzpatrick R, Carr A, Campbell	What is the clinical and cost	total vs.	protocol	4
24	M, et al. Total or Partial Knee Arthroplasty Trial -	effectiveness of total knee	unicompartement		
25	TOPKAT: study protocol for a randomised controlled	replacements versus	replacement		
26	trial. Trials. 2013;14:292.	unicompartmental			
27		replacements for patients with			
28		medial compartment			
29		osteoarthritis?			
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31					
32	Kim EJ, Lim CY, Lee EY, Lee SD, Kim KS. Comparing the	How efficient is meridian-based	acupunture	protocol	6
33	effects of individualized, standard, sham and no	syndrome differentiation and			
34	acupuncture in the treatment of knee osteoarthritis: a	Sa-am for reducing pain in knee			
35	multicenter randomized controlled trial. Trials.	OA?			
36	2013;14:129.				
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39	Lee S, Kim KH, Kim TH, Kim JE, Kim JH, Kang JW, et al.	Determined if moxibustin	moxibustion +	protocol	6
40	Moxibustion for treating knee osteoarthritis: study	(orietal therapy where herbs are	acupuncture		
41	protocol of a multicentre randomised controlled trial.	burned on certain areas of skin)			
42	BMC Complementary and Alternative Medicine.	could reduce pain and improve			
43	2013;13:59.	activity for knee OA.			
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1 2 3 4 5 6 7	Salisbury C, Montgomery AA, Hollinghurst S, Hopper C. Effectiveness of PhysioDirect telephone assessment and advice services for patients with musculoskeletal problems: pragmatic randomised controlled trial. British Medical Journal. 2013;346:f43.	What is the clinical effectiveness, effect on waiting times, and patient acceptability of PhysioDirect services in patients with musculoskeletal problems?	telephone assessment and advice service	3
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		2011	1	1	0	1	0	1	1	1	1	1	0	8
1	Breeman et al.	2011	0	0	0	0	0	0	0	0	0	1	0	1
2	Christensen et al.	2011	0	0	0	1	0	1	1	1	1	1	0	6
3	Juhakoski et al.	2011	0	1	0	1	0	1	1	0	1	1	1	7
4	Minns Lowe et al.	2011	0	1	0	1	0	1	1	0	1	1	1	7
5	Cadmus et al.	2010	0	1	0	1	1	1	1	1	1	1	0	8
6	Moe et al.	2010	0	1	0	1	0	1	1	0	1	1	1	7
7	Riecke et al.	2010	0	0	0	0	0	0	0	0	0	1	0	1
8	Gooch et al.	2009	1	0	0	1	1	1	0	1	1	1	1	8
9	Harmer et al.	2009	1	1	0	0	0	1	1	1	1	1	1	8
10	Jenkinson et al.	2009	0	1	0	0	1	1	1	1	1	1	0	7
11	Jessep et al.	2009	0	1	0	0	0	1	1	1	1	1	0	6
12	Lansdown et al.	2009	0	1	0	1	1	1	1	0	1	1	0	7
13	Lin et al.	2009	0	0	0	1	0	1	1	0	1	1	1	6
14	Rahmann et al.	2009	1	0	0	0	0	1	1	1	0	1	1	6
15	Ravaud et al.	2009	0	1	0	1	0	1	1	0	0	1	1	6
16	Itoh et al.	2008	0	0	0	0	0	0	1	1	1	0	1	4
17	Brealey et al.	2007	0	1	0	0	0	1	1	0	0	1	0	4
18	Brinks et al.	2007	0	0	0	1	1	1	1	1	0	1	0	6
19	Hurley et al.	2007	0	1	0	1	1	1	1	1	1	1	1	9
20	Rosemann et al.	2007	1	1	0	1	1	1	1	0	1	1	0	8
21	Hay et al.	2006	0	1	0	0	0	1	1	1	0	1	1	6
22	Rabenda et al.	2006	1	1	1	1	1	1	0	0	1	0	0	7
23	Mitchell et al.	2005	0	1	0	0	0	1	1	0	1	1	0	5
24	McCarthy et al.	2004	1	1	0	0	0	1	1	1	1	1	1	8
25	Raynauld et al.	2002	0	0	0	0	0	1	1	0	1	0	0	3
26	Thomas et al.	2002	0	0	0	1	1	1	1	0	1	1	1	7
27	Torrance et al.	2002	1	0	0	0	0	1	0	1	1	1	0	5
28	Barlow et al.	2000	1	1	1	1	1	1	1	1	1	1	0	10
29	van Haselen et al.	2000	0	1	0	0	0	1	1	1	1	1	1	7
30	Fagnani et al.	1998	1	0	0	1	0	1	1	0	1	1	0	6