Ali, SA, Kloseck, M, Lee, K, Walsh, KE, MacDermid, JC and Fitzsimmons, DA

Evaluating the design and reporting of pragmatic trials in osteoarthritis research

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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

Shabana Amanda Ali, PhD¹*, Marita Kloseck, PhD¹, Karen Lee¹, Kathleen Ellen Walsh², Joy C MacDermid, BScPT, PhD¹,³, Deborah Fitzsimmons, PhD¹,⁴,⁵

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KEY WORDS: pragmatic trials, osteoarthritis, PRECIS, CONSORT, implementation
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.
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).
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
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 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

• 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’.
ACKNOWLEDGEMENTS

SAA was supported by a Transdisciplinary Bone & Joint Training Award from the Collaborative Training Program in Musculoskeletal Health Research and the Sam Katz Community Health and Aging Research Unit at The University of Western Ontario. JCM is funded by a CIHR Chair in Gender, Work and Health; and Dr. James Roth Research Chair in Musculoskeletal Measurement and Knowledge Translation. DF is supported by the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care for Yorkshire and The Humber (NIHR CLAHRC YH). The views and opinions expressed are those of the author, and not necessarily those of the NHS, the NIHR or the Department of Health. CLAHRC YH would also like to acknowledge the participation and resources of our partner organisations. Further details can be found at http://clahrc-yh.nihr.ac.uk/.

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.
REFERENCES

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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KEY WORDS:

pragmatic trials, osteoarthritis, PRECIS, CONSORT, implementation
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. 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.
design and reporting of pragmatic trials can facilitate implementation of evidence-based interventions for osteoarthritis care.

**KEY WORDS**

pragmatic trials, osteoarthritis, PRECIS, CONSORT, implementation

**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 apply interventions flexibility for application across y-in multiple settings with large and heterogeneous populations, and 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.

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 medical-clinician-based (administered by a health professional: oral drug, injections, acupuncture, surgery, or clinical pathways) or lifestyle patient-based (administered by the individual: 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).

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 1ASupplementary 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 1BTable 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 (Figure 1BTable 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 (Figure 1BTable 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 1BTable 2).

Pragmatic trials avoid monitoring participant compliance with the intervention [11]; we found 54% of the studies met this criterion (Figure 1BTable 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 1BTable 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...
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. 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 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
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’.

ACKNOWLEDGEMENTS

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CLAHRC YH would also like to acknowledge the participation and resources of our partner organisations. Further details can be found at http://clahrc-yh.nihr.ac.uk/.

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.

REFERENCES


TABLE/FIGURE LEGENDS

Table 1. Summary of PRECIS (110) and CONSORT (121) guidelines, showing their overlap and application to pragmatic trials in osteoarthritis research.
**Figure 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.

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

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Supplementary Figure 1.
Supplementary Figure 2.
**Supplementary Table 1. Summary of included studies**

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<td>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.</td>
<td>What is the effectiveness of the Arthritis Foundation Tai Chi Program for community participants with arthritis?</td>
<td>exercise</td>
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How effective is non-pharmacological multidisciplinary face-to-face group-based treatment program versus a telephone-delivered treatment program on daily function for patients with generalized OA?


What is the prevalence of “forgotten knee” (FK) after TKR in a prospective pragmatic cohort, with comparison to conventional scores?


How effective is oral methotrexate for reducing synovitis (and pain) patients with knee OA?


Can integral-based hatha yoga improve fitness, mood, stress and quality of life for people with knee RA or OA?


How effective is exercise at improving function and pain for individuals with hip OA?


What is the predictive value of ultrasound characteristics for the effect of intra-articular glucocorticoids in knee OA?


How effectiveness are 10 education sessions about pain management facilitated by health nurses for patients with OA of knee or hip?

Is an internet-delivered intervention that combines PCST and physiotherapist-guided exercise more effective than online educational material in people with persistent knee pain?

How effective are individually tailored exercise programs versus usual physiotherapy care for adherence?

How does the use of a hand orthosis versus no orthosis affect pain?

What is the effectiveness of an integrated treatment (STOP) for weight loss and reduction in pain intensity?

What is the clinical and cost-effectiveness of a structured goal planning and tailored follow-up rehabilitation programme for patients with rheumatic diseases?

group planning and tailored follow-up programme


How does immediate versus delayed acupuncture affect the long term outcomes for people with OA?

acupuncture


Do scheduled hypertonic dextrose and morrhuate sodium injections improved knee pain, function and stiffness for knee osteoarthritis?

dextrose & morrhuate sodium


What is the clinical and cost effectiveness of total knee replacements versus unicompartmental replacements for patients with medial compartment osteoarthritis?

total vs. unicompartment replacement


How efficient is meridian-based syndrome differentiation and Sa-am for reducing pain in knee OA?

acupuncture


Determined if moxibustion (oriental therapy where herbs are burned on certain areas of skin) could reduce pain and improve activity for knee OA.

moxibustion + acupuncture
<table>
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<th>Page</th>
<th>Reference</th>
<th>Title</th>
<th>Abstract</th>
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What is the cost-effectiveness and efficiency for needle and laser acupuncture for relieving chronic knee pain?


What is the long-term (up to 30 months) clinical and cost effectiveness of a rehabilitation program combining self-management and exercise?


What is the short- and long-term effectiveness of patient education compared with patient education and physiotherapy for patellofemoral pain syndrome in adolescents?


What are the advantages and disadvantages of patellar resurfacing and selective resurfacing?


Does a very low-energy formula diet cause greater weight loss than a formula 810 kcal d-1LED in older sedentary individuals?


What is the short- and long-term effectiveness of exercise training in relation to pain, function and direct costs to health care systems attributable to hip OA?

What is the effectiveness of a postdischarge physiotherapy intervention in improving patient function after total knee arthroplasty for OA? blinding (physio)


What is the effectiveness of a community-based aquatic exercise program to improve quality of life among persons with osteoarthritis? aquatic exercise


What are the effects of a multidisciplinary outpatient clinic with a brief group-based educational programme, versus a traditional individual outpatient clinic for patients with hip, knee, hand or generalized OA? self-management protocol


What is the symptom response for patients assigned a very low energy diet versus a low energy diet, for patients who are obese and have knee OA? diet


Can the Alberta Hip and Knee Replacement Project be used as a model for health technology assessment based on comparative effectiveness of alternative clinical pathways? study effectiveness of clinical pathway


What are the outcomes for land-based and water-based exercise programs after total knee replacement (TKR)?

How do dietary intervention plus quadriceps strengthening exercises; dietary intervention alone; quadriceps strengthening exercises alone; advice leaflet only (control group) effect knee pain in obese patients?

What is the feasibility of ESCAPE-knee pain, clinical effectiveness and costs versus outpatient physiotherapy?

How effective is acupuncture versus usual care to reduce knee OA pain?

What is the clinical and cost effectiveness of an initial home exercise programme followed by higher intensity outpatient exercise classes after knee replacement?

What is the effect of inpatient aquatic physiotherapy versus regular physiotherapy to recover of strength, function, and gait speed after total hip or knee replacement surgery due to OA?

What is the impact of standardized consultations on patients with osteoarthritis of the knee?


What is the effect of trigger point acupuncture on pain and quality-of-life in knee osteoarthritis patients, compared with acupuncture at standard points, and sham acupuncture?


What is the effect of early access to MRI, compared with referral to an orthopaedic specialist for knee problems?


What is the efficacy of local corticosteroid injections in the trochanter syndrome in the general practice?


Is a rehabilitation program integrating exercise, self-management, and active coping strategies effective for OA?

Does providing information on arthritis self-management through general practitioners (GPs) increase quality of life and does additional case management provided by practice nurses shows better results?


What is the effectiveness of enhanced pharmacy review and community physiotherapy for knee pain?


What is the effectiveness of gastro-protective drugs (GPDs) during treatment with nonselective NSAIDs?


What is the effectiveness of pre- and post-operative physiotherapy at home for unilateral total knee replacement (TKR)?


What is the effectiveness of a home-based exercise programme with a class-based programme for OA?

What is the clinical and cost effectiveness of hylan G-F 20 for knee OA?

hylan G-F 20


Can home-based exercise programme improve outcomes in patients with knee pain?

home-based exercise programme


What is the effectiveness of viscosupplementation of hylan G-F 20 for OA?

hylan G-F 20


Does Arthritis Self-Management Programmes (ASMP) improve perceptions of control, health behaviours and health status, and change the use of health care resources?

arthritis self-management programme


What is the effectiveness of a homeopathic gel vs an NSAID (piroxicam) gel in the treatment of osteoarthritis of the knee?

homeopathic piroxicam gel


What is the effectiveness of diacerein with or without standard therapy in knee and hip OA?

diacerein
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