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Editorial

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Pragmatic trials in osteoarthritis—Are we ready?

Analysing delivery in clinical care

This editorial refers to Evaluating the design and reporting of pragmatic trials in osteoarthritis research, Shabana Amanda Ali *et al.*, doi: 10.1093/rheumatology/kex050.

Implementation research has emerged to reduce the gap between what is known to be clinically effective and what is actually delivered in clinical care [1], as is the case in OA. One of the study designs used in implementation research is the pragmatic trial. While the traditional explanatory trial is designed to test a physiological or clinical hypothesis, pragmatic trials aim to get a real-world sense of how an intervention works compared with usual care [2]. In this issue of *Rheumatology*, Ali *et al.* [3] review the design and reporting of pragmatic trials in OA. The authors conducted a search of the PubMed and Web of Science databases using the terms 'pragmatic trial' and 'osteoarthritis'; 96 unique citations and 61 studies were identified. Guidelines for optimal pragmatic trial design [Pragmatic–Explanatory Continuum Indicator Summary (PRECIS) [4]] and reporting (Consolidated Standards of Reporting Trials [5]) were combined to create 11 criteria against which each study was evaluated using a yes/no response; a higher score indicated a more pragmatic trial.

The main finding of their study was that few of the studies reviewed met criteria for a truly pragmatic trial; only 5% scored $\geqslant$9/11. A potential explanation is that dichotomizing the evaluation of each trial criterion (yes or no) underestimated the degree to which the criterion was met. Since PRECIS was first developed, it has become clear that there is a spectrum of trial design from one that is highly explanatory to one that is highly pragmatic. The modified and validated PRECIS-2 has incorporated this variability, requiring each trial domain to be evaluated on a 5-point Likert scale from 1 = very explanatory ideal conditions to 5 = very pragmatic usual care conditions [6] (Fig. 1).

The criterion least often met was that the intervention be applied by practitioners ordinarily involved with the care of (OA) patients. General practitioners, pharmacists, family and friends were considered typical OA care providers. Yet, current guidelines for OA care indicate the need for an interdisciplinary team approach that may also require occupational and physical therapists, dieticians and even specialists [7]. Thus it is not surprising that many of the interventions assessed required either additional practitioner training or inclusion of experts such as physiotherapists. As the field of implementation research advances in OA, it will be important to clarify which practitioners—or perhaps clinical skills—are ordinarily required in the care of patients with OA and the degree to which these people/skills are available in different geographic and health care system settings.

Inherent in a pragmatic trial is the desire to assess evidence-based OA therapies in the typical person with OA. Pragmatic trials have minimal inclusion and exclusion criteria so as to maximize the external validity of findings. Fewer than half of the studies reviewed by Ali *et al*. were deemed to have met this criterion; most failed due to exclusion of individuals with comorbidities. Currently the typical OA patient has multijoint involvement and is living with at least one other chronic condition [8]. Despite this, most OA clinical trials have been conducted in individuals with a single affected joint, most often the knee, and without comorbidities [7]. As a result, it might be said that we have few evidence-based OA therapies that have been adequately tested in the typical OA patient. There is also a paucity of data regarding subsets of OA patients (OA phenotypes) that may experience a greater or lesser response to a specific therapy, for example, corticosteroid injection with or without synovitis. Thus the pros and cons of an all-in approach to trials in OA must be considered.

Although pragmatic trials are intended to compare an intervention with usual care, Ali *et al*. found that fewer than half of the studies examined used the existing standard of care as the comparison. Studies of the quality of OA care indicate both underdiagnosis and undertreatment, with major barriers to OA care at the patient, provider and health system levels [1]. Thus pragmatic trials will only be useful in OA if there is a clear understanding of what usual care entails. For example, in a primary care context where patients are not routinely assessed for joint complaints, and thus OA may be underdiagnosed, an intervention focused on initiation of a specific educational or therapeutic approach in individuals with an OA diagnosis may miss the mark.

Approximately half the pragmatic trials reviewed met the criteria that the intervention is flexible in its delivery and in ensuring provider/patient adherence, which is necessary to assess whether the intervention works in the real world. The downside of minimal monitoring of outcomes and adherence is that, in the end, investigators will know whether or not the intervention worked, but not why. OA interventions are frequently complex, with multiple components. Understanding the element(s) of the intervention responsible for the result may be very helpful in determining future directions. As a means of addressing this limitation, a rigorous process of intervention development is recommended [1]. In this

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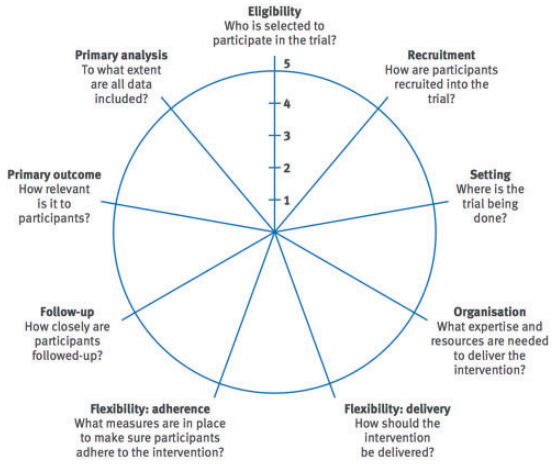
Fig. 1 The Pragmatic–Explanatory Continuum Indicator Summary 2 wheel



The Pragmatic–Explanatory Continuum Indicator Summary 2 (PRECIS-2) tool is a modified and validated version of PRECIS that is intended as a guide in clinical trial design decisions. Each trial domain is scored on a 5-point Likert continuum (from 1 = very explanatory ideal conditions to 5 = very pragmatic usual care conditions). Available online at https://www.precis-2.org/. Adapted by permission of the BMJ Publishing Group Limited. Loudon K, Treweek S, Sullivan F et al. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ 2015;350: h2147.

development phase, the intervention and its components are ideally co-developed with key stakeholders in the usual care environment and tested for feasibility and acceptability to these stakeholders in an iterative plan–do–study–act manner prior to launching the trial.

Pragmatic trials should choose primary outcomes that are meaningful to participants and, ideally, minimally invasive, ideally relying on routinely collected data. The majority of trials reviewed (>80%) met this criterion; most focused on patient-reported OA symptoms. The extent to which these outcomes are routinely assessed in usual care is likely highly variable. The incorporation of patient-reported outcome and experience measures into routine primary care practice will facilitate the conduct of future OA pragmatic trials.

In summary, more implementation research is needed in OA to shift evidence gleaned from traditional clinical trials into routine clinical practice. As this field moves forward it behoves us to increase our understanding of the continuum of explanatory–pragmatic trials, including the relative strengths and weaknesses of each implementation trial design, in advancing the care of people with OA.

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