ORIGINAL ARTICLES

Understanding the applicability of results from primary care trials: lessons learned from applying PRECIS-2

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Abstract

Objective: To compare two approaches for trial teams to apply PRECIS-2 to pragmatic trials: independent scoring and scoring following a group discussion.

Study Design and Setting: We recruited multidisciplinary teams who were conducting or had conducted trials in primary care in collaboration with the Pragmatic Clinical Trials Unit, Queen Mary University of London. Each team carried out two rounds of scoring on the nine PRECIS-2 domains: first independently using an online version of PRECIS-2 and second following a discussion.

Results: Seven teams took part in the study. Before the discussion, within-team agreement in scores was generally poor and not all raters were able to score all domains; agreement improved after the discussion. The PRECIS-2 wheels suggested that the trials were pragmatic, although some domains were more pragmatic than others.

Conclusion: PRECIS-2 can facilitate information exchange within trial teams. To apply PRECIS-2 successfully, we recommend a discussion between those with detailed understanding of what usual care is for the intervention, the trial's design including operational and technical aspects, and the PRECIS-2 domains. For some cluster-randomized trials, greater insight may be gained by plotting two PRECIS-2 wheels, one at the individual participant level and another at the cluster level. © 2017 Elsevier Inc. All rights reserved.

Keywords: Randomized controlled trials; Clinical trial methodology; Pragmatic trial; Primary care; Trial design

1. Introduction

Many randomized controlled trials (RCTs) are carried out with the aim of informing health professionals, patients, and policy makers about whether an intervention should be adopted in practice. To facilitate this, it is recommended that trials taking a pragmatic design approach are carried out, testing the intervention under conditions as similar as possible to the conditions that would pertain if the intervention was rolled out in routine care [1−6]. It may be that the intervention itself alters or replaces some aspects of usual care, but the principle remains that if the purpose of the trial is to directly inform clinical practice, aside from the intervention itself, other aspects of care should be as they usually would be in the real world. For brevity, we refer to these types of conditions as "usual care." Recently, there has been a growing interest in the benefits from more pragmatic designs. This has led to the publication of literature on how to design and conduct pragmatic trials [7−11], the latest of these developments, PRECIS-2 allows researchers to plot a graph illustrating whether their design is more or less pragmatic across a number of domains.

PRECIS-2 is an updated version of PRECIS [9] with significant changes including revisions to the domains, the addition of a Likert scoring scale and a web site which can

be used to support use of the tool (https://precis-2.org). PRECIS-2 (Fig. 1) has nine domains covering different aspects of a trial: eligibility, recruitment, setting, organization, flexibility of delivery, flexibility of adherence, follow-up, primary outcome, and primary analysis [12]. To apply PRECIS-2, each domain is scored from one to five—a score of one indicates an explanatory design with highly controlled or ideal conditions for the intervention and a score of five indicates a very pragmatic design, replicating usual care conditions for that domain. The tool was developed to be used at the design stage so that if the tool highlights that a trial design does not match the investigators' aims, they may choose to modify the design or reasons for the design may become more transparent. The tool can, however, also used retrospectively as part as a critical appraisal of the generalizability of results from a trial or to illustrate a trial design to those using results.

Investigators who used the original PRECIS either discussed PRECIS wheels as a group to come to some consensus [13–18] or used independent scoring by different team members [19–21]. Challenges in applying the tool were reported both by investigators who discussed PRECIS

wheels and those that did not hold a discussion. The approach we used to apply PRECIS-2 was informed by this work [13–21]. In the earlier studies applying the original PRECIS, the tool was applied both in the design phase, as the authors intended PRECIS to be used, and also to trials which were already completed. Similarly, in the work described here, we consider trials at all stages in design.

Our primary aim in this work was to inform investigators how best to use the tool regardless of whether it was to be used for design or retrospectively. We were particularly interested in doing so for trials at the pragmatic end of the pragmatic–explanatory spectrum for which PRECIS-2 was designed and in exploring the difference between using the tool with and without discussion between group members.

2. Methods

We invited trial teams carrying out trials in collaboration with the Pragmatic Clinical Trials Unit (PCTU) at Queen Mary University of London to partake in this study. To identify trials at the pragmatic end of the pragmatic–explanatory spectrum, we focused on trials in primary care (generally considered more pragmatic than trials in other settings [22]). We invited all trial teams that had recently completed their trial, were in the process of running their trial, or were working toward submitting new proposals for funding.

Challenges encountered applying the original PRECIS tool came from a lack of information or difference in interpretation across three areas: what is happening or is being planned for a trial [15]; what usual care would be if the intervention were to be implemented in practice [16]; and how to interpret the PRECIS domains in the context of the trial [18]. Researchers also found a bias toward raters scoring their own trial as more pragmatic [18]. To overcome these problems, we selected different raters including the trial chief investigator, who had both clinical expertise of usual practice and the trial design, and the trial manager and statistician, who had detailed information about the technical and operational aspects of the trial design, conduct, and analysis. In addition, we sought two independent views of the design: a member of the relevant trial steering committee plus one of the authors of this study (G.F.). G.F. had understanding of the PRECIS-2 domains, gained from discussions with two of the authors of PRECIS-2 (K.L. and S.T.). For trials which were in the design stage, not all these positions had been appointed so we included instead coapplicants on the trial grants with appropriate experience.

For each trial, we asked the raters to independently score the trial using PRECIS-2 on two separate occasions: first before discussion using the online tool (www.PRECIS-2.org) and the information contained on the PRECIS-2 web site and, second, after discussion scoring following a group discussion of raters involved in the relevant trial. This discussion lasted up to 2 hours. PRECIS-2 scores were plotted using the median of the scores for all of the raters for each trial. The group discussion was based on prediscussion
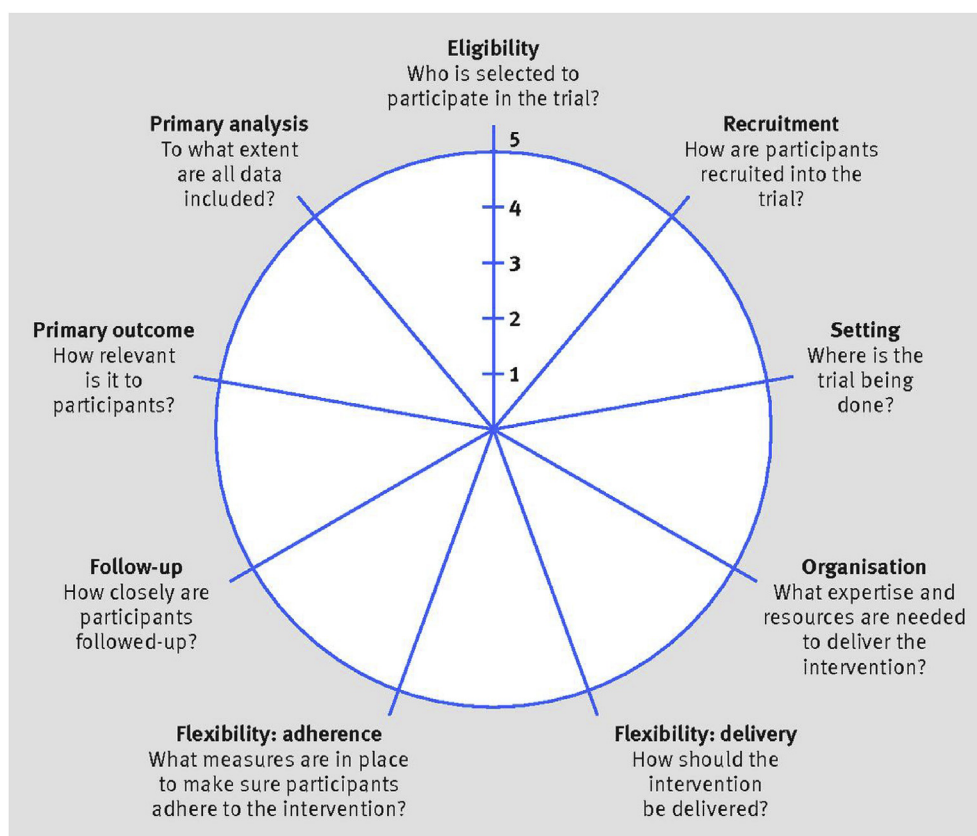
Fig. 1. A blank PRECIS-2 wheel. Reproduced with permission from [12].

scores and structured around the three key areas identified from work on PRECIS: the interpretation of each PRECIS-2 domain, what usual care was for the trial, and what was planned or had happened in the trial in relation to each domain; the discussion aimed achieve consensus on these three areas. However, the discussion would move on if there were areas of disagreement that could not be addressed within the time available. The postdiscussion scores were made independently at the end of the meeting.

We report the median of the prediscussion and postdiscussion scores for each domain and each trial as well as plotting PRECIS-2 wheels displaying the median prediscussion and postdiscussion scores. To assess the level of agreement within trial teams from the two sets of scores (prediscussion and postdiscussion), we compare the range of the scores for each domain across raters for each trial. For each domain, we report the median and interquartile range.

Ethical approval for this study was granted by the Queen Mary Research Ethics Committee (reference QMREC1360d). The members of the trials teams involved in this study provided informed consent.

3. Results

We invited 10 trial teams working on trials supported by the PCTU to participate in the study and seven agreed

to take part. The three trials that declined to take part all did so due to lack of availability of the trial team during the study period. The seven trials are described in Table 1. All seven trials aimed to answer the question of whether the intervention of interest would work in practice and the chief investigators considered their designs to be pragmatic.

The PRECIS-2 wheels (Fig. 2) indicate that trials being carried out by the PCTU are generally pragmatic. Domains for which trials were most often less pragmatic were recruitment where four trials had postdiscussion scores of three or less and organization where four trials had scores of three or less. All of the trials with less pragmatic scores for recruitment were individually randomized; the cluster-randomized trials were more pragmatic in their recruitment.

We produced eight PRECIS-2 wheels (Fig. 2) for the seven trials included in the study. For STOP, one of the cluster-randomized trials, during the discussion, the trial team thought that it would help them understand their design more if they produced two sets of scores, one set at the individual participant level and another at the cluster level for the pharmacy/pharmacist. For this trial, not all the domains were applicable at the individual level and this is reflected in the PRECIS-2 wheel by the domains with no score showing. This decision was consistent with

Table 1. Description of trials included in study

Short title	Full title	Intervention and setting	Unit of randomization	Status at time of study	No. in rating group
COPERS [23]	Effectiveness and cost-effectiveness of a novel, group self-management course for adults with chronic musculoskeletal pain	Group self-management course for chronic pain patients. Groups facilitated by a health care professional and lay person with experience of chronic pain. Trial set in local medical or community venues in urban and rural areas of the UK.	Individual	Complete	5 (chief investigator, trial manager, trial steering committee member, trial statistician, study author: GF).
HepFree	Chronic viral hepatitis in first and second generation immigrants from 'at risk' countries. A controlled randomised cross sectional cluster trial to assess the impact of identifying, screening and treating immigrants with viral hepatitis	Two interventions tested: (1) targeted screening for viral hepatitis for first- and second-generation immigrants from at-risk countries; (2) involvement of community therapy after diagnosis. Trial carried out across two cities in the UK with large immigrant populations (London & Bradford)	GP surgery	Recruiting	5 (chief investigator, trial manager, trial steering committee member, trial statistician, study author: GF).
Rhiva 2 [24]	Promotion of rapid testing for HIV in primary care: a cluster randomised trial	Intervention involved an education program promoting rapid HIV testing to adults newly registering at GP surgeries. Trial carried out in primary care settings in London, UK.	GP surgery	Complete	4 (chief investigator, trial manager, trial statistician, study author: GF).
STOP	Optimising pharmacist-based treatment from smoking cessation	Educational intervention package delivered to pharmacy staff. Pharmacies recruited to trial from those offering NHS smoking cessation services in two London boroughs.	Pharmacy	Protocol writing	4 (chief investigator, coapplicant, trial statistician, study author: GF).
SWAP	A peer-support weight action programme to supplement brief advice in general practice	Group health behavior modification intervention providing participants with the tools to lose weight and maintain a healthy lifestyle including pedometer use. Groups delivered by two trained advisors in community settings in London, UK.	Individual	Recruiting	5 (chief investigator, trial manager, trial steering committee member, trial statistician, study author: GF).
TANDEM	Tailored intervention for anxiety and depression management in chronic obstructive pulmonary disease	Psychological intervention based on cognitive behavioral approach to proceed routine pulmonary rehabilitation. Delivered 1-1 by respiratory nurses or allied health professionals. Intervention delivered in	Individual	Submitted for funding	4 (3× coapplicant, study author: GF).

(Continued)

Table 1. Continued

Short title	Full title	Intervention and setting	Unit of randomization	Status at time of study	No. in rating group
WAIT [25]	Intermittent montelukast in children aged 10 months to 5 years with wheeze: a multicentre, randomised, placebo-controlled trial	participant's home or convenient NHS facility. Trial run from sites across the UK. Intermittent montelukast given by parents at every viral cold or wheezing episode. Patients recruited via primary and secondary care sites across the UK and intervention delivered at participant's home.	Individual	Complete	5 (chief investigator, trial manager, trial steering committee member, trial statistician, study author: GF).

the purpose of PRECIS-2 and description of its use by those who developed it [12] but was not deemed necessary by the rating teams for the other two cluster-randomized trials.

Small differences between the prediscussion scores and postdiscussion scores were observed. Almost all the differences between the prediscussion scores and postdiscussion scores were one point or less (Fig. 2, Table 2). Thus, for most trials, design discussion led, at most, to a refinement in the extent a domain was considered pragmatic or explanatory rather than a change from a trial being rated as more pragmatic to more explanatory or visa versa. The one exception to this was the STOP trial which was at an earlier stage of development than the other trials. In this trial, larger changes between the prediscussion and postdiscussion scores were observed. This was in part due to greater understanding of how planned design related to the PRECIS-2 domains gained from plotting PRECIS-2 wheels at the individual and cluster levels, and in part due to some aspects of the design not being clear to all the raters before discussion.

The median range of the prediscussion scores was two or greater for five of nine domains: recruitment (median range 3), organization (median range 2), flexibility of delivery (median range 2), flexibility of adherence (median range 2), and follow-up (median range 2). This indicates poor agreement sometimes to the extent that raters disagreed about whether the trial was essentially pragmatic or essentially explanatory. Agreement in the postdiscussion scores was good; for all domains, the median range of scores was one or less: raters disagreed over the extent to which a domain was pragmatic or explanatory rather than whether the domain was pragmatic or explanatory.

Not all raters were able to score every domain using the online tool either due to insufficient information in the trial documents or due to insufficient knowledge of usual care. This was particularly an issue for flexibility of adherence (21% of raters unable to score), flexibility of delivery (14%), and organization (11%) (Table 3).

4. Discussion

We produced PRECIS-2 wheels for seven pragmatic trials of interventions in primary care. Most domains for each trial were scored by the teams as pragmatic indicating that the designs were appropriate to answer questions about the effectiveness of the interventions. Two domains, recruitment and organization stood out as being rated as less pragmatic across four of the seven trials. This indicated that steps to recruit in these trials could impact on the applicability of their results and that resources over and above those required for the intervention itself might be needed to ensure successful roll out of interventions.

Two of the trials included in the study were at the design stage, and there was the potential for changes to their design following the application of PRECIS-2. For one of these trials, TANDEM, the trial team made no changes following the application of the tool; the trial team were experienced in designing pragmatic trials and had already discussed the issues raised by applying PRECIS-2 before using the tool. The team commented that PRECIS-2 covered important areas of a trial's design that researchers should be aware of but that experienced teams may not need to go through the process of applying it fully. For the second trial, STOP, the design was yet to be finalized at the time of writing and the team found that PRECIS-2 helped clarify their thinking about their design. Of the completed trials, the researchers involved commented that the tool helped them think more about generalizability and had they applied it at the design stages could have pre-empted feedback they received from research funders on submitted applications.

The group discussions lead to a refinement rather than large change in median PRECIS-2 scores for each trial with the exception of one trial. Before the discussion, agreement in scores, as measured by the range in scores for each domain, was generally poor, and some raters were unable to rate all domains. The domains recruitment, flexibility of adherence, flexibility of delivery, and organization posed the greatest challenges to the raters when scoring the trials independently. Following the discussion, the agreement in
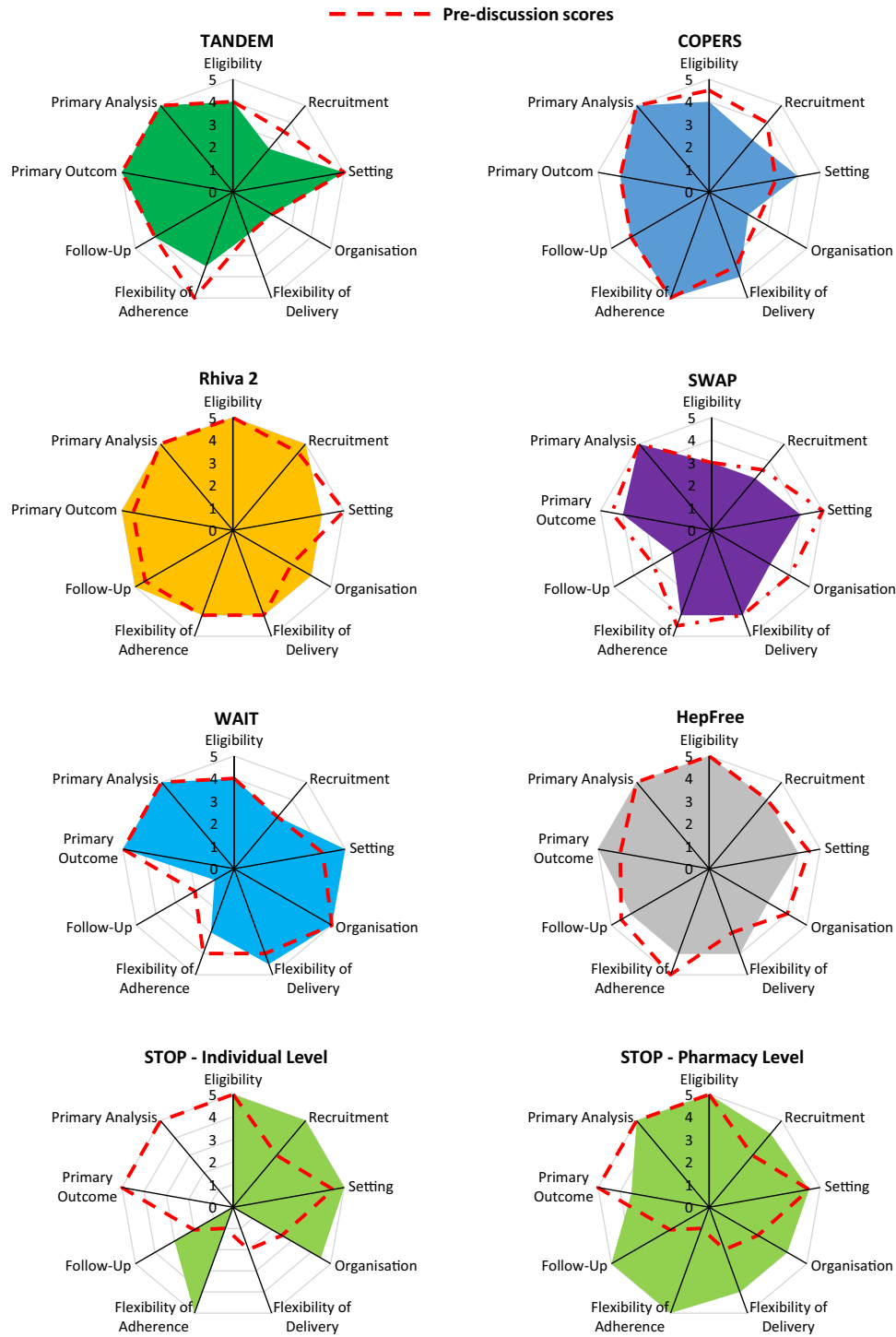
Fig. 2. PRECIS-2 wheels for trials included in the study. The solid shapes indicate the median postdiscussion scores. Dashed lines show the median prediscussion scores.

scores was improved and raters were able to score all domains. The challenges encountered by investigators applying the original PRECIS tool [9]: lack of information or understanding about the trial, usual care, or the PRECIS-2 domains, were mostly overcome. It was often the case that not one person in the trial team would have full

information to score all domains and good understanding came only through sharing information. This suggests that greater attention may need to be given to the reporting of operational aspects of trials if PRECIS-2 is to be applied by external groups. Updating the SPIRIT [26] and CONSORT [10,27] reporting guidelines for trial protocols and

Table 2. Median prediscussion scores and postdiscussion PRECIS-2 scores for each trial

PRECIS-2 domain	COPERS		HepFree		Rhiva 2		STOP cluster		STOP patient		SWAP		TANDEM		WAIT	
	Pre	Post	Pre	Post	Pre	Post	Pre[a]	Post	Pre[a]	Post	Pre	Post	Pre	Post	Pre	Post
Eligibility	4.5	4	5	5	5	5	5	5	5	5	3	3	4	4	4	4
Recruitment	4	3	4	4	4.5	5	3	4.3	3	5	3.5	3	3.5	2.5	3	3
Setting	3	4	4.5	4	5	4	4.5	4.5	4.5	5	5	4	5	5	4	5
Organization	2.5	2	4	3	3	4	2.5	4	2.5	4.5	4	3	2	2	5	5
Flexibility of delivery	3.5	4	3	4	4	4	2	4	2		4	4	2	2	4	4.5
Flexibility of adherence	5	5	5	4	4	4	1	5	1	5	4.5	4	5	3.5	4	3
Follow-up	4	4	4.5	4	4.5	5	2	5	2	3	3	2	4	4	2	1
Primary outcome	4	4	4	5	4.5	5	5	3.5	5		4.5	4	5	5	5	5
Primary analysis	5	5	5	5	5	5	5	5	5		5	5	5	5	5	5

[a] Only one set of prediscussion scores were made for STOP, combining both the cluster and patient levels of the trial.

RCTs, to include more focus on how interventions are delivered and the resources and expertise used, could help assessment of whether the results of trials are applicable to a particular setting.

We identified one further challenge when applying PRECIS-2 to pragmatic trials in primary care. When an intervention significantly changed the way in which patients were treated, it made comparisons with usual care difficult; especially for the organization domain, as it was not always clear what level of expertise or resourcing would be available to deliver the intervention if it were to be implemented in primary care after trial. For example, in the COPERS trial, the intervention was delivered partly by laypeople specifically recruited to deliver the intervention. This made judging the level of expertise and resources that would be available to deliver the intervention in usual care difficult as it was unclear what resources would be made available in primary care practice to recruit and train these individuals were the intervention to be rolled out after the trial.

At the time of writing, there has been one other published account of using PRECIS-2 in which Johnson et al. [28] applied PRECIS-2 to five pragmatic, cluster-randomized trials in health care systems research set in the United States producing one PRECIS-2 wheel for each trial. There are similarities with our findings in that there were challenges applying PRECIS-2 to interventions which changed usual care in a significant way and that not all the information required to apply PRECIS-2 was available in the trial documents. A notable difference in findings was that Johnson

et al. encountered more difficulties applying PRECIS-2 possibly because these authors did not report holding a discussion before scoring. Johnson et al. also did not have access to the full PRECIS-2 publication at the time of scoring [12] and had no involvement from the authors of PRECIS-2 in clarifying the definitions of the PRECIS-2 domains. Some of the trials in Johnson et al. [28] may also have benefited from producing two PRECIS-2 wheels, one at the cluster level and another at the individual level.

The results of this study are based on a sample of trials undertaken in a clinical trials unit that specializes in pragmatic trials, so different findings may arise from a unit with less of an expertise in pragmatic trials. In particular, there may be greater disagreement in scores made independently by researchers with less experience designing pragmatic trials as there could be greater scope for differences in the interpretation of the PRECIS-2 domains or what it means for a trial to be pragmatic. The focus of this study was pragmatic trials carried out in primary care; different challenges may present when applying PRECIS-2 to trials with more explanatory designs or in other health care settings.

5. Conclusions

Discussing PRECIS-2 wheels facilitated an exchange of information between different members of the trial team. It also highlighted two areas, recruitment and the level of resources used to deliver the intervention, where design

Table 3. Median and interquartile range of the range of prediscussion and postdiscussion scores

Domain	Range of prediscussion scores, median (interquartile range)	Range of postdiscussion scores, median (interquartile range)	Raters unable to score domain prediscussion, n (%)
Eligibility	1 (0, 2)	0 (0, 0.5)	1 (4)
Recruitment	3 (2, 4)	1 (0, 1)	0 (0)
Setting	1 (0, 2)	1 (.5, 1)	1 (4)
Organization	2 (2, 2)	1 (1, 1)	3 (11)
Flexibility of delivery	2 (1, 4)	1 (0, 1)	4 (14)
Flexibility of adherence	2 (0, 3)	0.5 (0, 1.5)	6 (21)
Follow-up	2 (1, 3)	0 (0, 1.5)	0 (0)
Primary outcome	1 (0, 2)	1 (0, 2)	0 (0)
Primary analysis	0 (0, 1)	0 (0, 0)	1 (4)

decisions may be impacting the applicability of results of trials from the PCTU, and it focused discussions around generalizability. When considering cluster-randomized trials or other more complex trial designs, greater insight may be gained from plotting more than one PRECIS-2 wheel. To apply PRECIS-2 successfully, we recommend holding a discussion between a group of people who between them have knowledge of what usual care is for the intervention, details of the trial's design including operational and technical aspects, and an understanding of the PRECIS-2 domains.

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