Gynecological trials frequently exclude people based on their symptoms rather than their condition: a systematic review of Cochrane reviews and their component trials

Journal of Clinical Epidemiology 163 (2023) 29−36

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

Gynecological trials frequently exclude people based on their symptoms rather than their condition: a systematic review of Cochrane reviews and their component trials

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Accepted 25 September 2023; Published online 29 September 2023

Abstract

Objectives: To identify strategies used in recent randomized controlled trials (RCTs) and their associated Cochrane Reviews where patients with the same gynecological condition present with different symptoms but would plausibly benefit from a common intervention.

Study Design and Setting: We searched the Cochrane library (February 2022) for reviews in polycystic ovarian syndrome (PCOS) and endometriosis. Reviews were included if the intervention was intended to treat all condition-specific symptoms. For each trial we recorded the strategy used and the number of potentially eligible participants excluded as a direct result of the chosen strategy. For each review we recorded the numbers of RCTs and participants excluded on the basis of symptoms experienced.

Results: There were 89 distinct PCOS trials in 13 reviews, and 13 Endometriosis trials in 11 reviews. Most trials restricted their eligibility to participants with specific symptoms (55% PCOS, 46% endometriosis). The second most common strategy was to measure and analyze clinical outcomes that were not relevant to all participants (38% PCOS, 31% endometriosis). Reviews excluded 27% of trials in participants evaluating the same intervention in participants experiencing the same condition based on the outcomes measured in the trials.

Conclusion: Most gynecological trials exclude patients who could benefit from treatment or measure outcomes not relevant to all participants. We introduce a taxonomy to describe trial design strategies for conditions with heterogeneous symptoms.

Keywords: Research waste; Randomized clinical trial; Cochrane review; Gynecology; Outcome selection; Trial design

1. Introduction

The principal role of a randomized controlled trial (RCT) is to evaluate whether a medical intervention is safe and effective. In order for this to happen, it is imperative that researchers measure outcomes which are both appropriate and relevant to the population of interest. Although RCTs remain the gold standard tool for treatment evaluation, many, through poor design, contribute to the overwhelming problem of waste in research [1−4]. In the Lancet collection of papers on waste in medical research, it was estimated that $240 billion of annual research expenditure is wasted [3,5−8]. It is indeed true that much work is being done to reduce this figure; however, there is still much room for improvement [9,10]. Inefficient studies that fail to address questions that matter to both patients and stakeholders emphasize the importance that we need to do less, but better, research [11].

Often, in the case of gynecological conditions such as Polycystic Ovarian Syndrome (PCOS) and Endometriosis, patients require different things from their care, at different stages of their lifetime [12−15]. Not all patients with the same diagnosis will experience all of the associated complications, and, although their most bothersome symptom might differ, it is common to receive the same treatment.

Registration: PROSPERO (CRD42022334776).

Funding: Katie Stocking, Doctoral Research Fellow (NIHR301756), is funded by the National Institute for Health and Care Research (NIHR) for this research project. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR, NHS or the UK Department of Health and Social Care.

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https://doi.org/10.1016/j.jclinepi.2023.09.012

What is new?

Key findings

- Over a quarter of Cochrane reviews included in this review excluded trials based on the outcomes measured.
- Typically, recent randomized controlled trials in Polycystic Ovarian Syndrome and Endometriosis trials either exclude patients who have the same condition and could potentially benefit from the treatment given, or evaluate treatments using outcomes of no relevance to some participants.

What this adds to what was known?

- Strategies used in gynecological trials where patients experience heterogeneous symptoms were identified.
- There are multiple sources of waste in the current gynecological research landscape. Patients are often excluded based on the particular symptoms they experience, or alternatively, treatments are evaluated by assessing improvement in symptoms which are not experienced by all participants.

What is the implication and what should change now?

- There is a need to identify and use trial designs for incorporating patients with heterogeneous symptoms in a manner that is efficient and relevant to patients. Cochrane Reviews should include all trials of a treatment which have been undertaken in the population of interest, regardless of the particular symptoms the participants experience to improve efficiency and clarity.

If we take PCOS, for example, the Rotterdam criteria are the most widely used classification for diagnosis and proposes that PCOS is present if the patient has at least two of the three characteristics: oligo- and/or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovaries on ultrasound [16]. These criteria for the diagnosis of PCOS in itself has consequences, as by definition, not all patients with PCOS have all the possible manifestations of the disorder, and therefore do not experience the same symptoms [12]. Despite this, metformin might be beneficial for a variety of symptoms. For endometriosis, patients may have symptoms dominated by pelvic pain, infertility, or both. In the postreproductive era the reduction in quality-of-life from menstrual dysfunction may predominate. It is plausible that laparoscopic surgery could be beneficial in all cases. This prompts the question of how we should evaluate interventions in this scenario, where potential trial participants have no, or few, symptoms in common, but may nonetheless benefit from a common intervention, while avoiding research waste, as well as the implications for systematic reviews and meta-analyses. An understanding of the strategies currently used by researchers in this context is first required.

One of the most notable inclusions to the movement to reduce waste in research is the development of core outcome sets (COS). The Core Outcome Measures in Effectiveness Trials (COMET) Initiative encourages the application of agreed standardized sets of outcomes. These outcome sets represent the minimum that should be measured and reported in clinical trials in specific clinical areas [17−19]. Authors of the recently developed COS in both PCOS and endometriosis concluded that not all outcomes could be reported in all trials [20,21]. This is demonstrative of the fact that in the field of gynecology, it is not one-size-fits-all.

To this end, we conducted a systematic review to investigate how diverse symptoms and patient populations are currently handled in gynecological trials, in which the intervention could plausibly be used to treat all symptoms related to the diagnosis. We aimed to identify the methodological strategies applied within the design of RCTs and also in Cochrane Reviews, where an intervention is hypothesized to have potential benefit for patients with the index condition.

2. Methods

We undertook a systematic review of RCTs in Cochrane Reviews. Our overall approach was to identify Cochrane Reviews in two exemplar conditions, PCOS and endometriosis, and to examine the characteristics and methodological practice of their included and excluded trials. Protocol registration was with the Prospective Register of Systematic Reviews (registration number: CRD42022334776). Full details of methods are given there but summarized below.

In February 2022 searches were undertaken to identify systematic reviews contained in the Cochrane Library of interventions for PCOS or endometriosis.

2.1. Study inclusion criteria

To be eligible, the Review intervention under study had to be one intended to treat the underlying condition rather than simply to alleviate specific symptoms. For example, in vitro fertilization treatment would not be eligible as the intervention is intended only for fertility outcomes. Decisions regarding eligibility of interventions were made by AW, a consultant in gynecology.

Cochrane intervention reviews and RCTs were eligible for inclusion from 2012 onwards to give an overview of current practice. We examined trials listed under either

'included' or 'excluded' categories. We were interested in trials that were excluded from the associated Cochrane review only if exclusion was for reasons relating to the outcomes reported.

2.2. Data selection and extraction

Two reviewers (KS and AW) screened all titles and abstracts against the inclusion criteria. Any disagreements were resolved through discussion.

Outcomes were categorized into prespecified groupings (Appendix), along with whether each trial or Cochrane review specified the outcome as primary or secondary. The setting, intervention type, funding source, design, size (number of participants randomized), number of participants excluded for symptom/outcome-related reasons and the number of participants contributing to the primary outcome was extracted for the trials.

2.3. Strategy development and assessment

Seven different strategies were anticipated for the RCTs, as demonstrated in Table 1. We identified these strategies as part of an iterative process alongside input from a dedicated Public and Patient Involvement group with lived experience. As a pilot, we developed some potential strategies we had seen during our time as researchers, assessed several trials and determined if the strategy used by each trial was different to those we anticipated. We then discussed and re-evaluated until no new strategies were found. We note that this may not be an exhaustive list, and we considered whether any additional strategies not included in our list were used. Each trial was categorized according to the strategy used. Strategy allocation was completed in triplicate and agreed between KS, AV, and JJK.

For ease of context and reference, we named the strategies and will refer to them as such throughout. Table 1 contains descriptions of each strategy along with an example of each in a hypothetical trial of metformin in a PCOS population.

For each trial, where available, we recorded the number of potentially eligible participants excluded as a direct result of the Restricted Outcome strategy relative to the achieved sample size. That is, how much larger could the recruitment have been without a symptom-defined restriction on eligibility. Where available, the number of potentially eligible participants was taken from the CONSORT flow chart. This was taken to be the number of participants that were found to be ineligible for symptom-related reasons prerandomization. Similarly, for each Cochrane Review we recorded the numbers of identified RCTs excluded for reasons such as not measuring review-specific outcomes. To determine which trials were excluded from each Cochrane review and the reason for exclusion, we used the 'Characteristics of excluded studies' section of the review. We selected all excluded trials for assessment where the reason for exclusion was related to the strategy used in the trial. For example, trials might be excluded based on symptom-based eligibility and outcome measurement (Restricted Outcomes strategy) or simply for not measuring outcomes relating to particular symptoms (as could occur with several of the strategies described).

2.4. Data analysis

We calculated the frequency of each strategy in the RCTs. Descriptive analyses were undertaken. We summarized the numbers of participants excluded from trials, and the numbers of trials and total numbers of participants excluded from Cochrane Reviews.

We accepted the published risk of bias (RoB) assessment for the included studies. For the studies that were excluded from the Cochrane review, and therefore have no associated RoB assessment, these were independently assessed using Cochrane's RoB tool [22]. We aimed to analyze whether calendar year of publication and study-level factors (e.g., sample size, nature of intervention, RoB assessment) were associated with strategy used, using Fisher's Exact test as an exploratory analysis. For this, date of publication was divided into pre-2017 and 2017 or after; nature of intervention was medical, surgical or other; RoB was judged as either in the primary analysis or not if selection bias was deemed low using and strategy was compared as Universal Outcomes, Restricted Outcomes or Other strategy.

3. Results

3.1. Study selection and characteristics

For PCOS, there were 31 Cochrane reviews screened at the title and abstract stage, of which 13, containing 239 trials (including those that were excluded from the associated Cochrane Review), met the inclusion criteria. We excluded 136 trials from this review for reasons relating to design and access, information can be found in the PRISMA (Figure A1). Duplication occurred in two ways. Some trials appeared in multiple Cochrane Reviews. We removed these duplicate trials, including only the first time, chronologically, that the trial appears in a review (two trials appeared three times, seven appeared twice). The second form of duplication occurred on three instances where publications had re-analyzed original trial data, reporting different outcomes. In this case, all data were collected and considered as one trial. Therefore, a total of 89 trials in 13 Cochrane reviews contributed to the findings of this review. A list of included reviews can be found in the Appendix.

For endometriosis, 32 Cochrane reviews were screened at the title and abstract stage with 11, containing 19 trials, meeting the inclusion criteria. Six trials were excluded as they were abstract only ($n = 3$), inaccessible ($n = 1$) or had no locatable publication ($n = 2$); therefore, a total of 13 trials in 11 Cochrane reviews were included in our

Table 1. Description and examples of strategies in hypothetical trials of metformin in PCOS

Strategy	Description	Hypothetical example
Participant-specific outcome	Recruit participants with the condition of interest. Define patient-specific clinical outcome.	Participants with PCOS recruited; no symptom-related exclusion criteria. Primary outcome is most bothersome symptom as specified by each individual at baseline.
Composite outcome	Recruit participants with the condition of interest. Define composite clinical outcome.	Participants with PCOS recruited; no symptom-related exclusion criteria. Primary outcome is composite of resumption of menstruation or hirsutism improvement, even though some participants do not experience these symptoms.
Universal outcomes	Recruit participants with the condition of interest. Measure all clinical outcomes in all participants, regardless of symptoms/relevance.	Participants with PCOS recruited; no symptom-related exclusion criteria. Participants without hirsutism contribute to denominator of hirsutism outcome comparison, i.e., all participants are included in the analysis of the effect of the intervention on hirsutism.
Subgroup outcomes	Recruit participants with the condition of interest Measure clinical outcomes in subsets defined at baseline of participants with relevant symptom.	Participants with PCOS recruited; no symptom-related exclusion criteria. Participants without hirsutism do not contribute to denominator of outcome comparison, i.e., if they did not experience hirsutism at baseline, they are not included in the analysis of the effect of the intervention on hirsutism.
Restricted outcomes	Recruit only participants with specific symptoms, measure only clinical outcomes relevant to eligible symptoms.	Participants with PCOS only recruited if they experience hirsutism. Study outcomes do not include body weight or acne.
Downstream outcomes	Recruit participants with the condition of interest. Report only consequences of clinical outcomes.	Participants with PCOS recruited; no symptom-related exclusion criteria. No clinical outcomes, only quality-of-life measured.
Upstream outcomes	Recruit participants with the condition of interest. Report only immediate, physiological effects.	Participants with PCOS recruited; no symptom-related exclusion criteria. No clinical outcomes, only biomarkers measured.

systematic review (Figure A2). The trial characteristics are summarized in Table 2. Most commonly, PCOS patients were recruited from obstetrics and gynecology clinics (40%) and fertility clinics (35%), with very few research teams recruiting from the community (4%). Most endometriosis patients were recruited from obstetrics and gynecology clinics (85%).

3.2. Trial-level findings

Only seven trials included in this review reported the number of participants excluded prerandomization, for symptom-based reasons. These seven trials excluded a total of 990 participants (median 16, interquartile range [IQR]: 4-229, minimum: 3, maximum: 704). To give context to this, the total sample size accrued by these seven trials was 2,744 (median 172, IQR: 46-750, minimum: 45, maximum: 1,000).

Table 3 shows the trial strategies, by outcomes reported. The most common strategy used by researchers in PCOS and endometriosis was Restricted Outcomes (55% and 46%, respectively). In PCOS, we found that over half of the trials that used Restricted Outcomes focused solely on fertility-based symptoms (59%). For endometriosis there was more variation in the outcomes measured, with a third (33%) of Restricted Outcomes studies restricting to pain outcomes and a third (33%) to fertility outcomes.

Universal Outcomes was the second most used strategy, with 38% of PCOS trials using this approach. There were 31% of endometriosis trials that used this strategy. Combinations of outcomes measured are shown in Table 3.

No PCOS trials and only one endometriosis trial that used the Universal Outcomes strategy made note of the numbers of patients experiencing the primary outcome at baseline. Therefore, we were unable to calculate the ratio of patients not experiencing the primary outcome of interest in relation to the sample size randomized.

Subgroup Outcomes was used in 15% of identified endometriosis trials, and only 1% in PCOS trials. The Upstream Outcome strategy was used in 8% of endometriosis trials, and 6% of PCOS trials. There were no instances where the Patient-specific Outcome, Composite Outcome or Downstream Outcome strategies were used.

There was no significant difference in the strategies used in pre-2017 compared to 2017 and after in PCOS ($P = 0.76$) or endometriosis ($P = 0.63$). We did not find evidence that strategies varied according to the nature of the intervention in PCOS ($P = 0.05$) or endometriosis ($P = 0.27$). Only five out of the 102 possible PCOS and endometriosis trials were classified as low risk, and therefore could plausibly have been included in a primary analysis, using the RoB assessment.

Table 2. Characteristics of RCTs identified in PCOS and endometriosis

Demographics	PCOS (n = 89)	Endo (n = 13)
Included in Cochrane review		
Yes	62 (70%)	12 (92%)
No	27 (30%)	1 (8%)
Number randomized		
Median (IQR)	87 (50, 122)	130 (60, 159)
Minimum	15	40
Maximum	1,000	360
Type of trial		
Parallel	87 (98%)	13 (100%)
Crossover	1 (1%)	-
Factorial	1 (1%)	-
Intervention type		
Medical	54 (58%)	4 (31%)
Surgical	8 (9%)	5 (38%)
Lifestyle	7 (8%)	-
Alternative	10 (11%)	-
Medical & surgical	5 (5%)	4 (31%)
Medical & lifestyle	1 (1%)	-
Medical & alternative	5 (5%)	-
Lifestyle & alternative	7 (3%)	-
Funding source		
Noncommercial	28 (31%)	7 (54%)
Commercial	1 (1%)	2 (15%)
Mixed	3 (3%)	1 (8%)
None	21 (24%)	-
No info	36 (40%)	3 (23%)
Multicentre		
Yes	6 (7%)	4 (31%)
No	83 (93%)	9 (69%)
Setting		
Fertility clinic	31 (35%)	0
Obstetrics and gynecology	36 (40%)	11 (85%)
Community	5 (6%)	0
Other[a]	13 (15%)	2 (15%)

Abbreviation: IQR, interquartile range.
[a] Other = Acupuncture, Morphology, Nutrition, Physiopathology, Medical and Surgical sciences, Urology.

3.3. Review-level findings

Of the 27 trials excluded for symptom-related reasons from the Cochrane Reviews in PCOS, most were excluded as the authors of the review were interested in fertility symptoms: 74% (n = 20) because although they were studies of the same intervention and the same population, they did not measure fertility outcomes, 15% (n = 4) because some of the participants in the trials did not have infertility. The remaining trials were excluded for having no outcomes of interest (n = 2, 7%) and fertility outcomes only (n = 1, 4%). These 27 trials had a median number of 60 people randomized, (IQR: 45-88, minimum: 26, maximum: 233). Similarly, the trial excluded from the endometriosis reviews was on the basis of not measuring the review's outcome of interest. Overall, the exclusion of trials on the basis of the symptom-related reasons totaled 27% of available RCTs (28/102).

4. Discussion

We conducted a systematic review to examine the current strategies used for the design of and recruitment to RCTs in conditions with heterogeneous symptoms, using PCOS and endometriosis as exemplar conditions.

In the current research landscape, we are typically seeing two main strategies used in gynecological trials, which we refer to as Universal Outcomes and Restricted Outcomes. In the Universal Outcomes strategy, trialists include participants who are not experiencing a symptom at baseline, while using improvement in that symptom as a trial outcome. Because these participants do not experience the symptom, any benefit they experience is not captured by the trial. This means that treatment effects on these outcomes are attenuated, making it less likely that beneficial interventions will be identified. In the Restricted Outcomes strategy, trialists restrict eligibility to the subset of individuals experiencing a particular symptom. Consequently, some patients are excluded due to stringent inclusion criteria and are unable to be involved in a trial of treatment that may be of clinical benefit to them. This means that we do not learn about the effect of the intervention on different symptoms, unless a separate trial is undertaken in that group, which represents a waste of resources. Moreover, the restrictive eligibility criterion may hamper recruitment to the individual trials. In April 2022, the Royal College of Obstetricians and Gynecology reported that gynecological care waiting lists in England had grown the most substantially compared to any other medical specialty, seeing an over 60% increase on prepandemic levels [23]. There is no shortage of people seeking and requiring gynecological treatment. Neither the Universal Outcomes strategy nor the Restricted Outcomes strategy allow the potential population to usefully participate in research and both are potentially inefficient.

These findings prompt the question of how RCTs of heterogeneous conditions should be designed. Three of the strategies we anticipated: Participant-specific Outcome, Composite Outcome, and Downstream Outcome were not being used and require consideration. Each of these strategies would allow individuals with a given condition to participate regardless of their symptoms, using outcome measures which could potentially capture any benefit they experience from the intervention. The absence of these strategies may suggest they are not currently perceived as viable. Participant-specific outcomes, such as measuring a patient's most bothersome symptom or allowing a patient to set their own personalized goals, are relatively novel

Table 3. Proportion of outcome combinations in each trial-level strategy

	Strategy							
	Universal outcomes		Subgroup outcomes		Restricted outcomes		Upstream outcome	
Outcome combination	PCOS (n = 34)	Endo (n = 4)	PCOS (n = 1)	Endo (n = 2)	PCOS (n = 49)	Endo (n = 6)	PCOS (n = 5)	Endo (n = 1)
Fertility only	0	0	0	0	29 (59%)	2 (33%)	0	0
Pain only	0	0	0	0	0	2 (33%)	0	0
Fertility + QoL + other clinical outcome(s)	6 (18%)	0	0	0	0	0	0	0
Fertility + other clinical outcome(s)[a]	10 (29%)	2 (50%)	1 (100%)	0	13 (26%)	0	0	0
QoL + other clinical outcome(s)	4 (12%)	0	0	2 (100%)	0	1 (17%)	0	0
Clinical outcome(s) + treatment satisfaction	0	2 (50%)	0	0	0	1 (17%)	0	0
Other clinical outcome combinations	14 (41%)	0	0	0	7 (14%)	0	0	0
Biomarkers only	0	0	0	0	0	0	5 (100%)	1 (100%)

Percentage given is within condition. Note that there were no instances of the Patient-Specific Outcome, Composite Outcome or Downstream Outcome strategies being used, they are, therefore, not included in this table.

[a] Fertility + pain for endometriosis.

ideas [24,25]. The use of outcomes which allow patients to reflect and report on their own outcomes/experience is advantageous. However, although outcomes of this type have previously been used in gynecological trials, further consideration is needed of their advantages and limitations [24,26]. Composite outcomes allow research to address more than one aspect of a patient's health status, but their use is widely debated, with interpretation difficult [27–30]. Similarly, although a well-established instrument for providing evidence of an individual's physical, emotional and social health, interpretation of treatment effect can also be difficult when using a quality-of-life measurement. Cox et al. suggest that "in practice the main difficulty is likely to be in separating the real treatment-by-individual interaction from noise" [31]. Downstream Outcome strategies would allow all participants to be included and assessed using a common measure, such as Quality-of-life scales. However, Quality-of-life instruments also increase the participation burden compared to more direct and objective outcome measures, and may increase attrition.

Another solution might be to use novel trial designs, such as basket trials, in which participants are recruited into subtrials on the basis of their symptoms, and data are analyzed so as to allow borrowing of information across subtrials. These trials may have greater statistical and logistical efficiency compared to alternative solutions, while permitting the study of intervention effects on different symptoms. Further work is needed to elaborate the strengths and drawbacks of these potential solutions.

Systematic reviews are considered the gold standard of evidence for decision-making, used to collate, critique, and summarize evidence. The current review highlights potential inefficiencies in the conduct of Cochrane Reviews in heterogeneous populations. Many RCTs were excluded for reasons relating to patient symptoms. For example, if an RCT used a Restricted Outcomes strategy leading to the exclusion of participants experiencing a symptom of interest in the Review, the RCT was typically excluded. In some instances, the excluded RCTs were included in separate Cochrane Reviews of the same intervention and condition, but concerning a different symptom. This has potential implications for efficient use of resources (as conducted a single, somewhat broader review might require less duplication of effort compared to separate screening and assessment of RCTs in two Cochrane reviews) and clarity of communication to consumers (because it may be more useful to have all of the information about the effectiveness of an intervention for a given condition in one place). Dwan and colleagues have previously discussed the prevalence and impact of excluding studies from reviews on the basis of the relevance of outcome data in the context of outcome reporting bias [32,33]. The current view is that excluding RCTs which did not report a particular outcome will not lead to bias provided that the outcome was not measured in the trial (so there is no scope for selection). Our observation here is that excluding RCTs which did not measure a particular outcome may lead to different problems in the context of heterogeneous symptoms, including the somewhat arbitrary partitioning of RCTs answering very similar questions into separate Cochrane Reviews. For example, the use of metformin in PCOS patients was assessed by Sharpe et al. for ovulation induction (fertility-based outcomes) and by Fraison et al. for hirsutism, acne and menstrual pattern (nonfertility outcomes) [34,35]. Having one systematic review which assessed all of these outcomes together, could reduce waste from duplication of effort and make it easier for a consumer to find all relevant information about the intervention.

The current review has limitations. We considered PCOS and endometriosis only, and it remains to determine

whether the findings will be applicable to gynecological research in general, or in other conditions where patients experience varying symptoms. We restricted our review to trials within Cochrane Reviews, which limits the scope of our review. We also acknowledge that the list of strategies may not be exhaustive, although we identified more a priori than we found being used in practice.

5. Conclusions

We suggest that participants whose symptoms could potentially benefit from a treatment should have a chance to receive said treatment in research. This suggestion is motivated not only by equity but also by the desire to identify effective interventions in an efficient manner, with minimal research waste. We have shown that the population of patients available is often underused by excluding patients based on the symptoms they experience, or alternatively, by including patients regardless of symptoms but measuring outcomes in patients who do not experience the associated symptom(s). Cochrane Reviews could also be conducted in a more efficient manner if Review questions were broadened to incorporate the full spectrum of symptoms experienced by patients with a given condition which could plausibly be improved by the Review intervention.

Gynecological patients experience heterogeneity in their symptoms and strategies to efficiently evaluate interventions in this context must be identified. This may include the use of patient-specific outcome measures and innovative trial design, but the suitability of these approaches warrants further research.

CRediT authorship contribution statement

Katie Stocking: Conceptualization, Data curation, Formal analysis, Methodology, Writing − original draft. **Andrew Watson:** Conceptualization, Data curation, Validation, Writing − review & editing. **Jamie J. Kirkham:** Conceptualization, Methodology, Supervision, Writing − review & editing. **Jack Wilkinson:** Methodology, Supervision, Writing − review & editing. **Andy Vail:** Conceptualization, Methodology, Supervision, Writing − review & editing.

Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Katie Stocking reports financial support was provided by National Institute for Health and Care Research. Katie Stocking, Andrew Watson, Jack Wilkinson and Andy Vail report a relationship with Cochrane that includes: board membership.

Acknowledgments

The authors thank the Public Patient Involvement group that have given their time to help support this research and shape the strategies developed.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jclinepi.2023.09.012.

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