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Lack of pragmatic attitude of self-labelled pragmatic trials on manual therapy: a methodological review

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Abstract

Background Pragmatic randomized controlled trials are getting more interest to improve trials' external validity. This study aimed to assess how pragmatic the design of the self-labelled pragmatic randomised controlled trials in the manual therapy field is.

Methods We searched MEDLINE and the Cochrane Central Register of Controlled Trials for self-labelled pragmatic randomised controlled trials in the manual therapy field until January 2024 were included. Two independent reviewers collected and extracted data related to the intention of the trial, the rationale for the intervention, and specific features of the trial and performed an assessment using the PRECIS-2 tool.

Results Of 39 self-labelled pragmatic trials, the mean PRECIS-2 score was 3.5 (SD: 0.6). Choice of outcome measures, how the interventions were performed, the follow-up of the participants and how all the available data were included in the statistical analysis were the domains rated as most 'pragmatic'. Participants' eligibility, recruitment, and setting obtained lower scores. Less than 25% of the trials claimed that the aim was to investigate an intervention under real-world conditions and to make clinical decisions about its effectiveness. In the 21% of the sample the authors described neither the proof-of-concept of the intervention nor the state of previous studies addressing related research questions.

Conclusions Self-labelled pragmatic randomised controlled trials showed a moderately pragmatic attitude. Beyond the label 'pragmatic', the description of the intention of the trial and the context of every PRECIS-2 domain is crucial to understanding the real pragmatism of a trial.

Keywords Pragmatic clinical trials, Musculoskeletal manipulations, Randomized controlled trials, Manual therapy, Generalizability, PRECIS-2

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Background

Medical research is often criticised for its low resemblance to real clinical settings [1, 2]. Moreover, there is a large gap between the amount of medical research available and that useful for healthcare practitioners [3]. In that sense, there is an increasing interest in trials designed with a pragmatic attitude to respond to the currently poor generalisability of many studies [1, 4, 5].

Pragmatic trials were introduced more than 50 years ago by Schwartz and Lellouch [6], who proposed classifying trials according to their "attitude" as (a) trials whose final goal is to examine the causal relationship between an intervention and a physiological effect (explanatory/efficacy) or (b) trials that aim to inform clinicians or health policy decision-making directly (pragmatic/effectiveness). Explanatory trials assess how a specific intervention impacts participants optimally, often using placebos or active comparators. They focus on measurable symptoms or markers and aim to minimise participant variability. In contrast, pragmatic trials evaluate interventions in real-world clinical settings to ensure broader applicability and effectiveness across diverse patient populations and treatment settings, requiring larger, more flexible designs [7]. It is essential to highlight that the pragmatic term refers to an attitude rather than a characteristic of the study and that a continuum exists from explanatory to pragmatic [7]. Therefore, some efficacy trials can have pragmatic features to increase their external validity, and pragmatic randomised controlled trials (pRCT) can use explanatory elements to ensure the trial's internal validity [6, 8]. The terms commonly used to show that a given study has a pragmatic attitude are "pragmatic", "naturalistic", and "effectiveness" (rather than "efficacy") [6, 9–11]. Pragmatic trials have been used in pharmacological research in phase IV trials [12]. However, the development of pharmacological and non-pharmacological interventions differs substantially because non-drug interventions are not as commonly regulated as drugs are (e.g. through the Food and Drug Administration or the European Medicines Agency). Arguably, this situation encourages trialists to attempt a pragmatic approach directly but using explanatory designs, concluding with recommendations of treatment (pragmatic attitude) regardless of the absence of high-quality efficacy trials (this was also observed by Zwarestein et al.) [13]. Although pragmatism is possible in both early and late-stage development trials, caution is required because, without efficacy evidence, results can be strongly biased toward a positive outcome [1, 14–16]. This is especially concerning for therapies not formally recognised and that lack high-quality efficacy trials [1, 16].

Various health professionals use manual therapy (MT) interventions to treat pain and disability [17–19]. Manual therapies are considered complex interventions (CI), and like many non-pharmacological interventions, it might be challenging to evaluate them scientifically [20–22]. Some frameworks have been proposed to assess CIs more adequately [23–25]. Within the proposals for improving the applicability of RCTs [1, 21, 26], pragmatic randomised controlled trials (pRCT) have been proposed as a suitable approach in the field of MTs [17, 21]; for example, using more heterogeneous populations with similar comorbidities to those patients seen habitually in practice or using non-protocolised interventions to respect the person-centred approach required in MT treatments [27]. However, a recent systematic review revealed that MT research lacks applicability to real practice [28]. Despite the increasing interest in designing pragmatic trials, some doubts arise about the real pragmatic attitude of those trials self-labelled "pragmatic" [9, 10, 29].

To date, it is unknown how pragmatic trials are used among MT researchers. Therefore, this review aims to assess, through the published article information, how pragmatic the design of the self-labelled pRCTs in the MT field is. Secondly, we aim to examine whether and how authors report the intention of the trial and how design choices are justified.

Methods

Protocol registration

We conducted a methodological review of pragmatic randomised controlled trials on manual therapy interventions and reported its findings according to PRISMA guidelines [30] (Supplementary file 1). We prospectively registered the protocol on the Open Science Framework (DOI https://doi.org/10.17605/OSF.IO/WKEPZ).

Eligibility criteria

To be eligible for inclusion in the review, RCTs had to meet specific criteria regarding the methods used and the experimental intervention. Concerning the methods, we included reports of RCTs that used the terms "pragmatic" or "naturalistic" (about the methodological design) either in the title or the abstract [10, 11]. Regarding the intervention used, we followed the criteria of previous research in this field [17], requiring eligible references to include either one manual technique or a combination of them. These techniques included soft tissue techniques, joint mobilisations or manipulations, massage, myofascial release, nerve manipulation, strain/counterstrain, and acupressure. We applied no restrictions regarding population, comparators or outcome measures. Exclusion criteria included experimental interventions delivered through tools, devices (electrotherapy, kinesiotaping, dry needling, acupuncture), drugs, active exercises or a combination of therapies without an MT intervention. We also excluded articles not written in English, protocols and poster/conference presentations.

Search strategy

We searched MEDLINE and the Cochrane Central Register of Controlled Trials from their inception to January 2024. The search strategy combined controlled vocabulary related to the field of MT and the design of interest (Supplementary file 2).

Study selection

The records retrieved from the search were imported to Rayyan software (www.rayyan.ai) [31]. After deduplication, two reviewers (SR, GA) independently screened the references based on title and abstract, resolving disagreements through discussion.

Data collection process

Two independent reviewers (SR and an additional reviewer among GA, RN, JB, DH, CF, and JP) collected data from the included studies, resolving disagreements by consensus. Data was collected from an extraction data form designed by 3 authors (SR, GA, GU). Before the pilot of the data extraction form, the reviewers discussed and received training from Dr Kirsty Loudon (developer of the PRECIS-2 tool [32]); note that PRECIS-2 tool will be explained below. After piloting five trials, the data extraction form incorporated all reviewers' suggestions to improve consistency. Finally, a guideline for reviewers was provided to the team (Supplementary file 3).

Data items

Recent literature has argued that a part of quantitatively assessing the degree of pragmatism of RCTs is important to understand the intent of the trial and how the design relates to this intent [4]. Authors typically use it to refer to the trial as a whole (instead of their intention) and often do not provide adequate supporting justification for its use [29]. For this reason, our data extraction form included the following:

1. Bibliometric identification elements and specific trial characteristics.
2. The intention of the trial given by the authors: assessed using the following three qualitative categories pre-established by the reviewer team, aimed at how authors reported if their aim was (I) examining the effectiveness of an intervention (only reporting how participants respond to treatment, examining and estimating effects/changes); (II) resemble clinical practice in terms of populations included, setting, or intervention delivery; and (III) resemble clinical practice and informing clinical decision-making [4, 29].
3. The rationale of the intervention given by the authors: This information was screened in the introduction section of the trials. It refers to the existence of any report of proof-of-concept information related to the intervention. Reviewers pre-established three types of rationale, reporting: (I) the existence of mechanistic experiments explaining the mechanisms of action of the intervention; (II) the existence of sham-controlled studies testing the intervention against a placebo; and (III) comparative effectiveness data about the intervention [33].
4. Experimental and control interventions: The research team used a categorisation process to distinguish between the experimental and control interventions. This was done to assess the extent to which the intervention differed from usual care. As a patient-centred intervention, a pragmatic approach to MT requires individual tailoring for each person and also adaptation of different techniques as the condition progresses [27]. Part of the research team were experts in MT and established a classification of the intervention according to its ability to resemble clinical practice. Box 1 refers to pre-established categories to classify the experimental and control interventions. Experimental interventions were divided into those that were protocolised due to the requirements of the study and those that led to the therapist's decisions depending on the patient's needs.
5. PRECIS-2 tool assessment: It consists of nine domains based on trial design decisions (Eligibility criteria, Recruitment, Setting, Organisation, Flexibility delivery, Flexibility adherence, Follow-up, Primary outcome and Primary analysis) [32]. Every domain is scored on a 5-point Likert-type scale, with a score of 1 being considered very explanatory and a score of 5 being considered very pragmatic. Scores for each domain are represented on a radar chart (PRECIS-2 wheel). Trials with more explanatory scores show a narrower wheel towards the centre, and trials containing more pragmatic scores have a wider wheel towards the periphery. Mean values were calculated, including all reported domains [32]. For this study, reviewers rated the non-reported domains "blank" and excluded them from the score.
6. Limitations reported by the authors: The extraction data was based on the 12 limitations categories proposed by Alvarez et al. [34]

Data analysis

We performed a descriptive analysis of the categorical variables, presenting the results as relative and absolute frequencies. Quantitative variables were described with means and standard deviations. Median and interquartile ranges defined ordinal variables. Each article's pragmatic attitude was graphically presented using the PRECIS-2

BOX 1 Pre-established experimental and control intervention categories

Experimental intervention categories	
Combination of non-protocolised *techniques*	The use of a combination of MT techniques already in use in clinical practice but chosen by the practitioner depending on the participant's needs.
Isolated non-protocolised *technique*	The practitioner chooses a single MT technique depending on the participant's needs.
Protocol of a combination of *techniques*	Use of a combination of MT techniques standardised by the trial protocol
Combination of non-protocolised *therapies*	Use of a combination of different modalities of treatment based on the needs of patients, i.e. MT combined with exercises
Isolated protocolised *technique*	Use of a single MT technique standardised by the trial protocol
Protocol of a combination of *therapies*	Use of a combination of therapies standardised to all patients by the trial protocol
Control intervention categories	
Active intervention	Use of another accepted or established intervention that is not considered beyond the label 'usual care.'
Placebo/sham	Use of a supposedly inactive intervention that looks like the drug or treatment being tested
Usual care	The intervention expected to be received as part of normal clinical care
No intervention	A group not receiving any intervention

wheel. Variables were compared using ANOVA for quantitative variables, Chi-square for categorical variables and Krustall Wallis for ordinal variables. According to previous literature [35–37], we used a scale ranging from 9 to 45 to assess the PRECIS-2 total score, a part of the PRECIS average. A score of 9–22 was considered slightly pragmatic, 23–34 moderately pragmatic, and ⩾35 very pragmatic. The significance level was 5% (alpha=0.05). All data were analysed using the software IBM-SPSS (V26.0).

Results

Study selection

After removing duplicated references, the search yielded 3553 unique references. Following the screening process, we included 39 self-labelled MT pRCTs [38–76]. Figure 1 provides the PRISMA diagram.

Study characteristics

Table 1 summarises the main characteristics of our sample. Three-quarters (27/39) of the pRCTs aimed to examine the effectiveness of an intervention, 8% (3/39) aimed at resembling clinical practice, and 23% (9/39) pursued both objectives. Two-thirds (25/39) of the studies provided the rationale for assessing the intervention with a pRCT in their introduction (of which 15 trials (60%) reported comparative effectiveness data, 11 trials (44%) reported mechanistic experiments, and one (4%) reported sham-controlled studies). In comparison, 21% (8/39) of the sample provided no rationale, and 15% (6/39) were unclear. Details and direct quotes from the authors about the intention, the rationale of the trial, and how authors justify them can be found in supplementary file 4.

Although this analysis was not pre-planned, our results showed no increase in MT pRCT publications over time (Fig. 2). Regarding the type of journal, 44% (17/39) of the studies were published in specialised journals in the MT field, and 56% (22/39) in journals non-specialised in MT. One-third (16/39) of the trials were reported according to the CONSORT statement, but only one study [44] reported their findings adhering to the CONSORT extension for pragmatic trials. Only one study reported using the PRECIS-2 tool in its design phase [50].

The primary outcome was a patient-reported outcome measure (PROM) in 72% of the sample (28/39). The intervention most frequently used was a combination of non-protocolised techniques (54%, 21/39). The modality of MT used was an unspecified combination of manual techniques (23%, 9/39), chiropractic treatment (18%, 7/39), spinal manipulation (18%, 7/39), osteopathy (10%, 4/39), Chuna treatment (10%, 4/39), reflexology (8%, 3/39), myofascial release (5%, 2/39), massage therapy (5%; 2/39), and acupressure (3%, 1/39). The most common control intervention was usual care (33%, 13/39) followed by an active intervention (31%, 12/39), whereas a placebo was used in only two studies (5%, 2/39). The most common self-reported limitation by the authors was lack of blinding of the participants (36%, 14/39), inadequate control (no-treatment control or a sham control group to assess the natural progression of the pathology) (33%, 13/39) and compromised generalisability (33%, 13/39), followed by sample size (28%, 11/39).

PRECIS assessment

The studies included in our sample scored an average of 3.5 (SD=0.6) across all PRECIS-2 domains (median 3.5; IQR: 3.1–3.9). Figure 3 shows the PRECIS-2 wheel representation of the pragmatic attitude from trials in our sample. We show PRECIS-2 wheels for each individual included trial in Supplementary file 5. Table 2 presents data for individual domains. The PRECIS-2 total score (ranging from 9 to 45) showed that 61% (24/39) of the studies were moderately pragmatic, 36% (14/39) highly pragmatic, and 3% (1/39) slightly pragmatic. The pragmatism score did not increase over time from a mean of 3.68 (SD=0.49) before 2012 to 3.67 (SD=0.57) after 2018 (Fig. 2). In general, there was a decrease in the mean score during the period 2012–2017; after that, they recovered but not significantly in 8 of 9 domains (D1 $p=0.250$; D2 $p=0.157$; D3 $p=0.729$; D4 $p=0.958$; D6 $p=0.654$: D7 $p=0.838$: D8 $p=0.271$ y D9 $p=0.480$). On

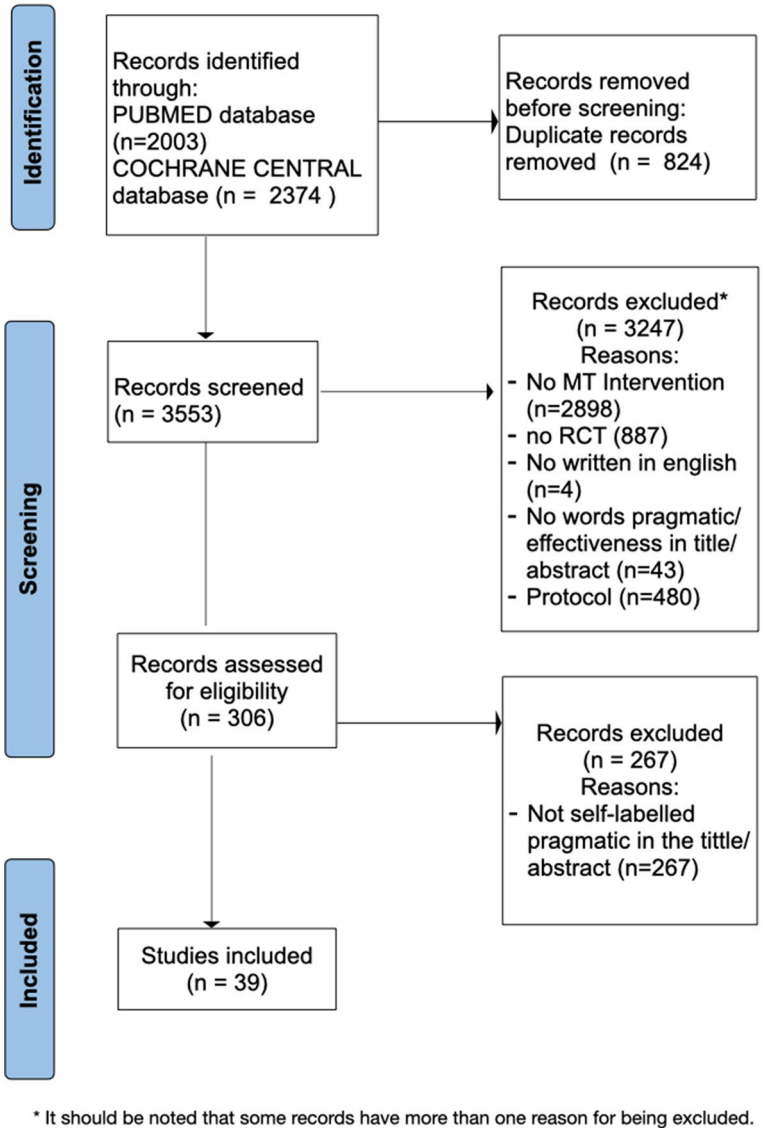

Fig. 1 PRISMA flow diagram [30]

the contrary, there was a statistically significant increase in Domain 5 ($p=0.002$). This value was confirmed with a non-parametric test showing the same statistical increase ($p=0.006$).

The number of studies rated for each domain was: Eligibility 39/39, Recruitment 37/39, Setting 38/39, Organisation 39/39, Flexibility delivery 39/39, Flexibility adherence 32/39, Follow-up 39/39, Primary Outcome 39/39, Primary analysis 38/39.

Figure 4 shows the PRECIS-2 scores for each domain. Domain 8 was rated as pragmatic (it means that they scored 4 or 5 in the PRECIS-2 score) by almost all the sample. Domains 5, 7 and 9 were considered pragmatic by 60% of the sample and Domains 1, 2, 3, and 4 were rated pragmatic only in half of the sample (54%, 51%, 54%,52%), (Fig. 5). The rest were explanatory or equally explanatory and pragmatic.

Discussion

We aimed to describe the characteristics related to the design of a cohort of self-labelled pRCTs in MT according to their pragmatic attitude. We obtained three main findings. First, MT pRCTs are not becoming more common despite the increased attention on this type of design. Second, our findings revealed that pRCTs in MT have a moderate pragmatic attitude. However, the label 'pragmatic' could be questioned in those trials using highly explanatory design features like blinding, unicentric setting, or a placebo as a control intervention. Lastly, the authors of our sample of pRCTs did not adequately

Table 1 Main characteristics of pRCTs in MT

Number of participants (Mean)		**169,23 (SD = 150.7)**
N of participants		Per cent (n**)
< 50		15% (6)
51–100		23% (9)
101–200		38% (15)
> 201		23% (9)
Experimental intervention		
Combination of non-protocolised *techniques*		54% (21)
Isolated non-protocolised *technique*		15% (6)
Protocol of a combination of *techniques*		13% (5)
Combination of non-protocolised *therapies*		10% (4)
Protocol of an isolated *technique*		5% (2)
Protocol of a combination of *therapies*		2% (1)
Control intervention		
2 arms	test treatment vs. other active intervention	31% (12)
	test treatment vs. placebo	2% (1)
	test treatment vs. usual care	33% (13)
	test treatment vs. no intervention	13% (5)
3 arms	test treatment vs. 2 other active interventions	5% (2)
	test treatment vs. 1 other intervention and 1 placebo	2% (1)
	test treatment vs. 1 intervention and 1 usual care	10% (4)
	test treatment vs. 1 other intervention and 1 no intervention	2% (1)
Blinding (Yes)		
Participants		10% (4)
Therapists		0% (0)
Outcome assessors		20% (8)
Statistician		26% (10)
Setting		
Multicentric		56% (22)
Unicentric		33% (13)
Unclear report		10% (4)
Follow-up		
No follow-up		18% (7)
< 2 weeks		0% (0)
2–4 weeks		2% (1)
4–12 weeks		10% (4)
3–6 months		18% (7)
6–12 months		20% (8)
>1 year		26% (10)
Individualised*		5% (2)

*Two studies used an individualised follow-up (trials assessing how many weeks patients remained pain-free)

** N of studies = 39

justify why the trial aimed to be pragmatic and which domains most contributed to this pragmatism.

Although research in the MT field has increased in the last decades [77–79], pRCTs are not so common. Only 39 papers assessing an MT intervention were identified as self-labelled pragmatic from inception to 2024. Our results indicate that the number of MT pRCTs has not increased in recent years, and the PRECIS-2 mean score has also not increased over time. Nevertheless, despite our comprehensive analysis of the available literature, the limited number of articles prevents us from drawing any definitive conclusions. These results are contrary to studies assessing pragmatism in critical care [80], pain [5] and cardiovascular interventions [81], wherein the mean PRECIS score increased over time. Only Domain 5 (flexibility intervention) increased after 2018, primarily due to the significant decrease in the mean PRECIS scores between 2012 and 2018. It might be interesting to explore the knowledge about non-pharmacological pRCTS among researchers to understand this lack of increase over time. It might be interesting to assess the necessity of including specific training on this topic in the academic stages.

The mean score of our sample in the retrospective PRECIS-2 tool assessment was 3.5 (SD = 0.6), indicating a moderate level of pragmatism of MT pRCTs. Those are similar ratings to a recent systematic review of nursing interventions and those found in pain interventions and other fields [5, 9, 10, 29, 35, 80, 81]. The moderate level of pragmatism found in our review was highly influenced by the domains "flexibility intervention", "follow-up", "outcome measure", and "primary analysis". Those domains were rated as pragmatic (4 or 5 on the Likert scale) in more than 60% of our assessed trials. Using an intention to treat analysis is a trait highly pragmatic, and most of the reviews assessing the pragmatism of trials in other fields found this item as the most pragmatic in their PRECIS-2 tool assessment [5, 35, 80, 81].

Considering the extensive debate about the appropriateness of self-labelled pragmatic trials using explanatory features such as blinding, unicentric setting and use of placebo controls [12, 13, 82–85, 90], we might exclude almost half of our sample (19/37). However, as there is no consensus on that matter, we decided to assess the whole sample and to further contribute to the debate as other authors did in other fields [5, 9, 29, 35].

Using a placebo as a comparator is considered a very explanatory feature. Some authors argue that it is hardly part of real-world care, and its use suggests an explanatory nature of the trial [12, 82–84]. PRECIS-2 authors defend that there are situations in which a trial could include a placebo control and still provide useful information to decision-making (e.g. to mitigate the subjectiveness of patient-reported outcomes in a comparative

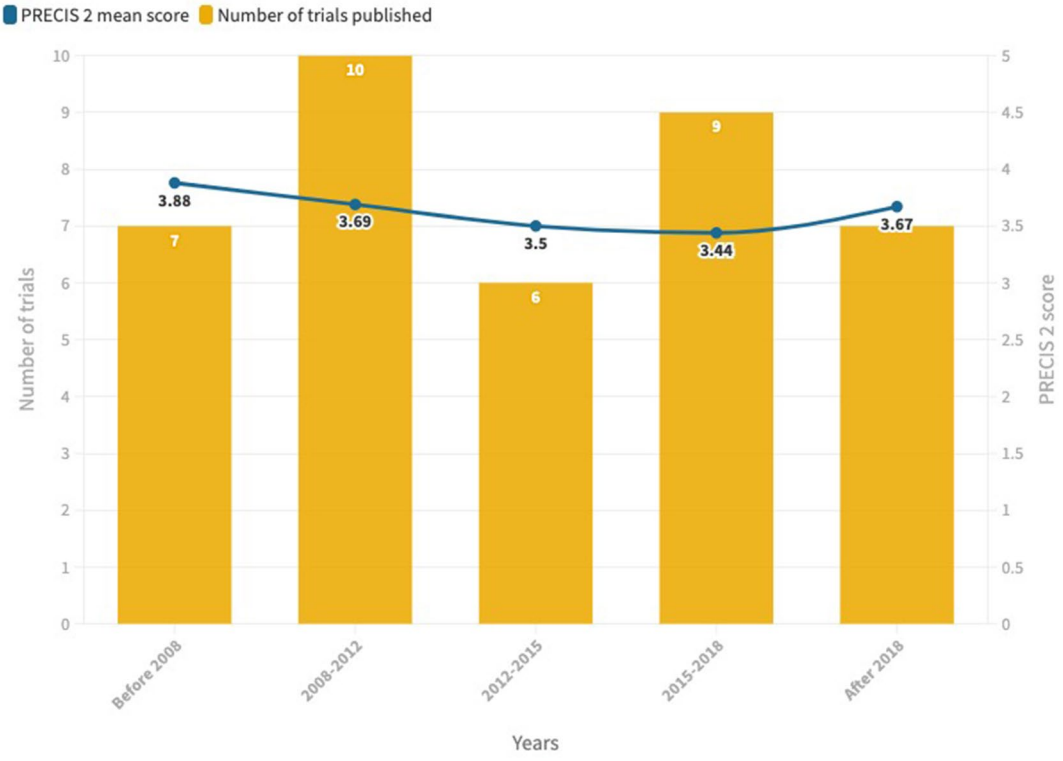

Fig. 2 The number of published pRCTs and mean PRECIS 2 score over time

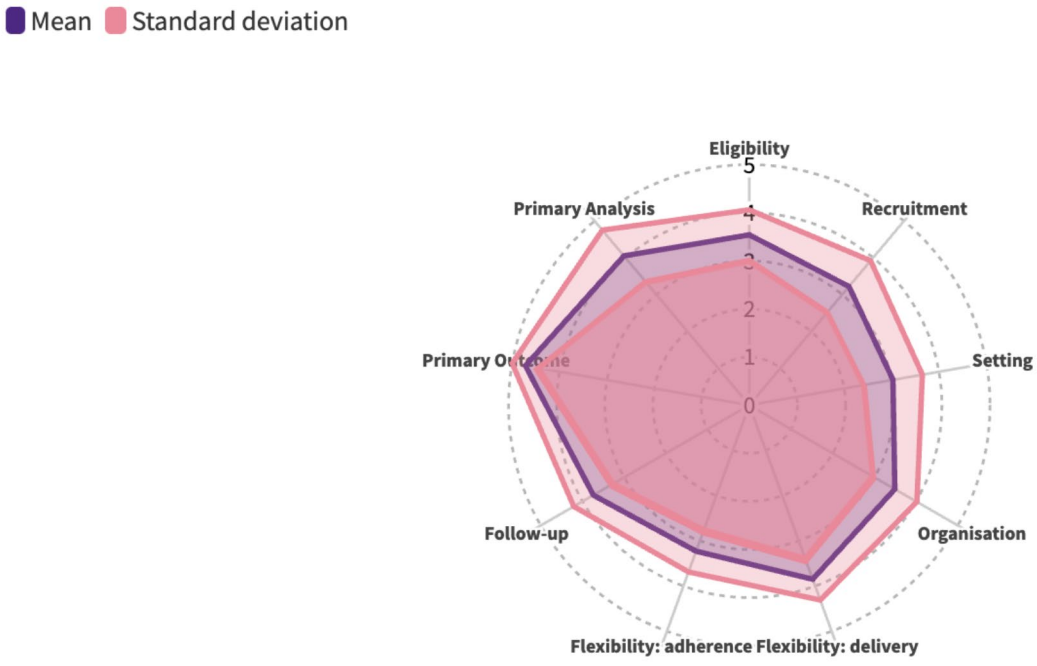

Fig. 3 Wheel diagram showing the mean PRECIS-2 score of the included studies

effectiveness trial of two accepted treatments) [7, 85]. We wonder if including an appropriate placebo/sham comparator could be interesting for understanding the real effect of the intervention, which is difficult to achieve in an efficacy study under non-real-world conditions (where all the contextual factors part of the patient-therapist encounter, are not present [86–89]). In our sample, only one study used a placebo control [39], and another

Table 2 Mean scores of each PRECIS-2 domain over time. For statistical reasons, years were divided into three periods (before 2012, 2012–2018, and after 2018)

	Mean (SD)			
	Overall *N* = 39/39	**Before 2012** *N* = 17	**2012–2018** *N* = 15	**After 2018** *N* = 7
Domain 1: Eligibility	3.54 (1.04)	3.82 (0.72)	3.33 (1.11)	3.29 (1.5)
Domain 2: Recruitment	3.22 (1.40)	3.65 (1.37)	2.79 (1.31)	3 (1.6)
Domain 3: Setting	3.03 (1.24)	3.06 (1.14)	3.07 (1.38)	2.83 (1.33)
Domain 4: Organization	3.49 (1.07)	3.53 (1.01)	3.47 (1.30)	3.43 (0.80)
Domain 5: Flexibility delivery	3.85 (0.93)	4.12 (0.70)	3.47 (1.06)	4.00 (1.00)
Domain 6: Flexibility adherence	3.23 (0.92)	3.15 (1.14)	3.23 (0.83)	3.40 (0.55)
Domain 7: Follow-up	3.74 (0.93)	3.82 (0.95)	3.73 (1.03)	3.57 (0.78)
Domain 8: Primary Outcome	4.72 (0.64)	3.82 (1.51)	4.36 (1.15)	4.00 (1.73)
Domain 9: Primary analysis	4.05(1.41)	3.82 (1.51)	4.30 (1.25)	4.44 (1.13)

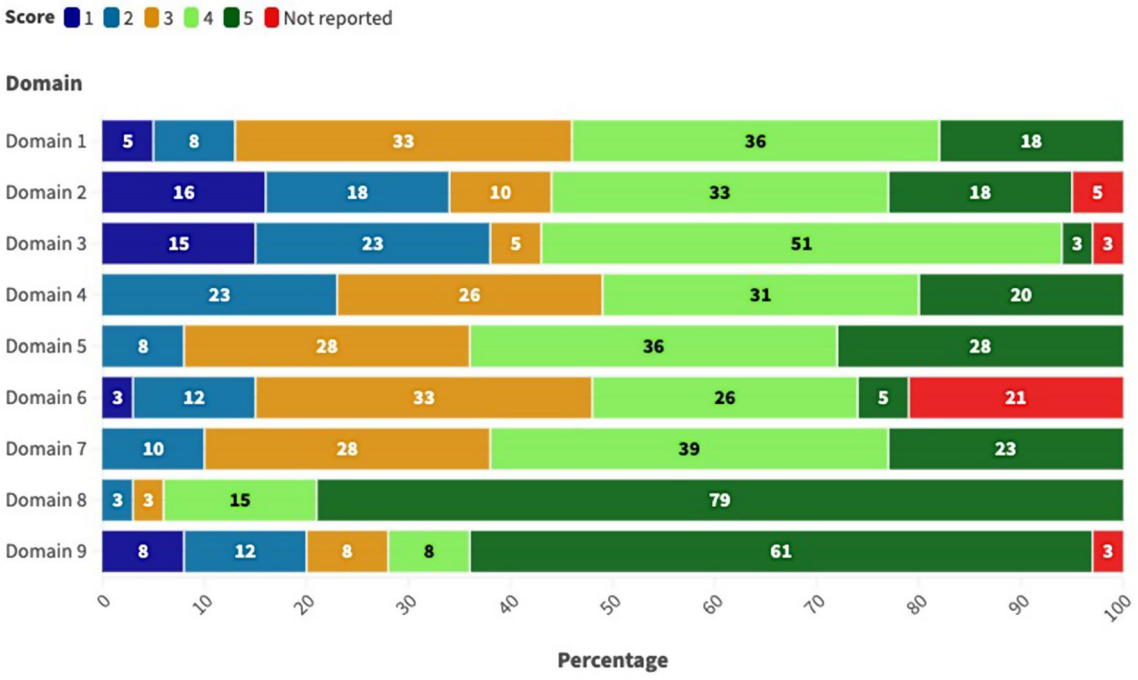

Fig. 4 PRECIS- 2 scores of the included studies

included a placebo control in a 3-armed trial [57]. In the latter, Mafetoni et al. showed that although the effect of the intervention was statistically larger than that in the control and placebo groups, the placebo group showed a larger effect than the control group [57]. Non-pharmacological interventions do not follow the same developing processes as pharmacological interventions do. This fact entails that effectiveness trials are often performed to assess interventions without performing previous efficacy trials. Further research should be conducted to contribute to this rich debate about using a placebo in pRCTs in the MT field [12, 84, 90].

Another controversial point is the use of single centres, as there is a debate about whether they should be considered pragmatic because of the arguably limited generalisability of their results [82, 84, 85, 90]. In our sample, 33% of the reports were performed in a single-centre setting.

Only one trial reported using the PRECIS-2 tool to guide where the trial falls in the explanatory-pragmatic continuum [50]. It is worth mentioning that this trial scored higher on average (4.1) than the rest. Other authors also noted this limited reporting of using a design tool [35, 80, 81].

Recently, it has been pointed out that, when assessing pragmatic attitude in a trial, special attention must be paid to detecting its intention besides awarding a quantitative score [4, 82]. By knowing the trial's intention, some domains can be expected to be more pragmatic than others. Some authors stated that the pragmatic attitude

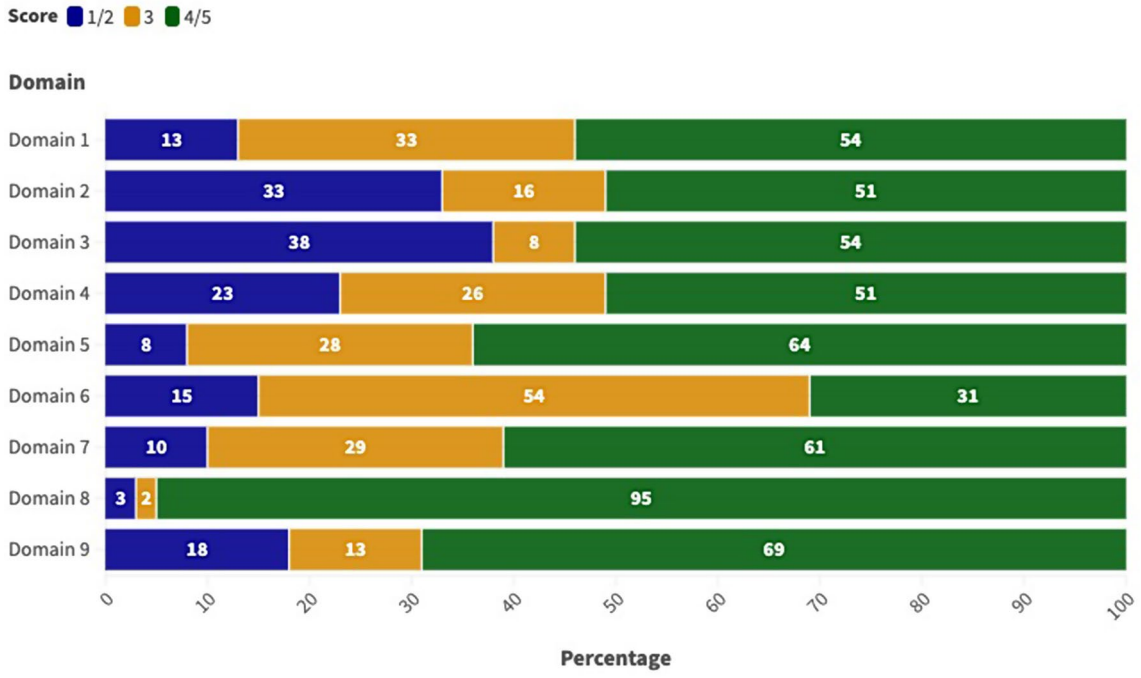

Fig. 5 Percentage of studies categorised as pragmatic (4/5) or explanatory (½)

is domain-specific and that PRECIS-2 ratings require context [5]. In fact, one of the fundamental principles of external validity is that context matters [3, 91]; it can help to understand the trial's attitude better, avoiding dichotomisation into pragmatic and explanatory [4]. In our sample, less than 25% of the trials reported that the aim was to investigate an intervention under real-world conditions and to make clinical decisions about its effectiveness, thus not identifying an intention aligned with a pragmatic attitude. So, almost 75% of our assessed trials did not adequately justify or discuss the claimed pragmatism. Likewise, Janiaud et al. assessed the pragmatic attitude of self-labelled trials in different fields, finding the same in 45% of the studies [9].

Both efficacy and effectiveness trials are necessary but address different research questions [28]. A potential question is whether there are already enough efficacy trials to explore further an intervention's effects in a more world-real setting. The authors should be expected to screen previous literature to appraise what is already known about a given intervention before attempting a pRCTs. Ultimately, a sound background should be provided alongside the rationale for attempting a pragmatic trial [92]. Such rationale might include existing mechanistic experiments and placebo- or sham-controlled efficacy trials, suggesting that the intervention has the desired physiological effects and efficacy [93]. Instead, in the 21% of the trials we reviewed, the authors described neither the proof-of-concept of the intervention nor the state of previous studies addressing related research questions (rationale of the intervention). Furthermore, when the rationale was given, it was mainly constructed from comparative effectiveness trials. These results align with a similar review assessing self-labelled trials' pragmatic attitudes [29]. It found that 71.3% of the sample did not justify why a pragmatic trial was selected instead of an explanatory one [29]. This should be considered fundamental when designing a pRCT [1].

Although some authors declared that pRCTs might be an option for non-regulated interventions in early and late development trials [1, 10], we argue that researchers need to appraise the research field as a whole and determine whether there is sufficient evidence of the efficacy of a given intervention before assessing it in a real clinical environment. When efficacy trials have not sufficiently demonstrated the effects of an intervention, spending resources on a more explanatory design might be preferable to pRCT [93].

Limitations

Our review has several potential limitations. Although the reviewer team included experts in the MT field and expert methodologists, providing a multidisciplinary approach to data extraction, this might introduce some heterogeneity to the data extraction process that could have affected the results. Also, a deep knowledge of each intervention assessed is required to properly assess the pragmatism of a given trial. Other authors have reported similar difficulties [4, 5, 10, 94]. To mitigate the impact of these limitations, we piloted the extraction data form

and extensively discussed the ratings beforehand. Also, we paired all reviewers with the IP to discuss the scores and minimise subjectivity. Although a third party was not required to solve discrepancies, frequent discussions between reviewers were needed to conclude a reliable score. The small sample in this review might not be considered relevant and may not represent all the MT modalities. However, it included all pRCTs published in the MT field from inception to January 2024. Finally, It is possible that pragmatic trials may not always label themselves as such, particularly in the title and abstract. This may result in the omission of potentially eligible trials. However, this review aimed to assess those studies self-labelled pragmatic in the title and/or abstract.

Conclusions

This study highlights how pragmatism is represented in self-labelled MT pRCTs. Overall, pRCTs showed a moderately pragmatic attitude that has not increased over time. Domains showing higher rates of pragmatism were "flexibility intervention", "follow-up", "outcome measure", and "primary analysis". Beyond the label 'pragmatic', the description of the intention of the trial and the context of every PRECIS-2 domain is crucial to understanding the genuine pragmatism of a trial.

Abbreviations

PRECIS	Pragmatic-explanatory continuum indicatory summary
pRCT	Pragmatic randomised controlled trials
MT	Manual therapy
PROM	Patient-reported outcome measure

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

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Author contributions

SR: Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing. GA: Conceptualization, Methodology, Investigation, Writing - review & editing. DHS: Investigation, Writing - review & editing. IS: Supervision, Investigation, Writing - review & editing. RNC: Methodology, Investigation, Writing - review & editing. JB: Methodology, Investigation, Writing - review & editing. CFJ: Investigation. Jules Phalip: Investigation. IG: Formal analysis, Writing - review & editing. MSR: Supervision, Writing - review & editing. GU: Conceptualization, Methodology, Supervision, Writing - review & editing.

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Data availability

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Ford I, Norrie J. Pragmatic trials. N Engl J Med. 2016;375:454–63.
2. Greenhalgh T, Howick J, Maskrey N. Evidence Based Medicine Renaissance Group. Evidence based medicine: a movement in crisis? BMJ. 2014;348:g3725.
3. Huebschmann AG, Leavitt IM, Glasgow RE. Making Health Research Matter: a call to increase attention to External Validity. Annu Rev Public Health. 2019;40:45–63.
4. Nicholls SG, Zwarenstein M, Hey SP, Giraudeau B, Campbell MK, Taljaard M. The importance of decision intent within descriptions of pragmatic trials. J Clin Epidemiol. 2020;125:30–7.
5. Hohenschurz-Schmidt D, Kleykamp BA, Draper-Rodi J, Vollert J, Chan J, Ferguson M et al. Pragmatic trials of pain therapies: a systematic review of methods. Pain. 2021.

6. Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. J Chronic Dis. 1967;20:637–48.
7. Thorpe KE, Zwarenstein M, Oxman AD, Treweek S, Furberg CD, Altman DG, et al. A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers. J Clin Epidemiol. 2009;62:464–75.
8. Treweek S, Zwarenstein M. Making trials matter: pragmatic and explanatory trials and the problem of applicability. Trials. 2009;10.
9. Janiaud P, Dal-Ré R, Ioannidis JPA. Assessment of Pragmatism in recently published randomized clinical trials. JAMA Intern Med. 2018;178:1278.
10. Dal-Ré R, Janiaud P, Ioannidis JPA. Real-world evidence: how pragmatic are randomized controlled trials labeled as pragmatic? BMC Med. 2018;16:49.
11. Sacristán JA, Dilla T. Pragmatic trials revisited: applicability is about individualization. J Clin Epidemiol. 2018;99:164–6.
12. Dal-Ré R. The PRECIS-2 tool seems not to be useful to discriminate the degree of pragmatism of medicine masked trials from that of open-label trials. Eur J Clin Pharmacol. 2021;77:539–46.
13. Zwarenstein M, Treweek S, Loudon K. PRECIS-2 helps researchers design more applicable RCTs while CONSORT Extension for pragmatic trials helps knowledge users decide whether to apply them. J Clin Epidemiol. 2017;84:27–9.
14. Patsopoulos NA. A pragmatic view on pragmatic trials. Dialogues Clin Neurosci. 2011;13:217–24.
15. Kent DM, Kitsios G. Against pragmatism: on efficacy, effectiveness and the real world. Trials. 2009;10:48.
16. Ernst E, Canter PH. Limitations of pragmatic trials. Postgrad Med J. 2005;81:203–203.
17. Alvarez G, Solà I, Sitjà-Rabert M, Fort-Vanmeerhaeghe A, Gich I, Fernández C, et al. A methodological review revealed that reporting of trials in manual therapy has not improved over time. J Clin Epidemiol. 2020;121:32–44.
18. Oliveira CB, Maher CG, Pinto RZ, Traeger AC, Lin C-WC, Chenot J-F, et al. Clinical practice guidelines for the management of non-specific low back pain in primary care: an updated overview. Eur Spine J. 2018;27:2791–803.
19. Qaseem A, Wilt TJ, McLean RM, Forciea MA, for the Clinical Guidelines Committee of the American College of Physicians. Noninvasive treatments for Acute, Subacute, and chronic low back Pain: a clinical practice Guideline from the American College of Physicians. Ann Intern Med. 2017;166:514.
20. Ninot G. Evaluation of non-pharmacological interventions. Non-Pharmacological Interventions. 2021;:221–38.
21. Dieppe P. Complex interventions. Musculoskelet Care. 2004;2:180–6.
22. Richards DA, Hallberg IR. Complex interventions in Health: an overview of research methods. Routledge; 2015.
23. Walach H, Falkenberg T, Fønnebø V, Lewith G, Jonas WB. Circular instead of hierarchical: methodological principles for the evaluation of complex interventions. BMC Med Res Methodol. 2006;6:29.
24. Minary L, Trompette J, Kivits J, Cambon L, Tarquinio C, Alla F. Which design to evaluate complex interventions? Toward a methodological framework through a systematic review. BMC Med Res Methodol. 2019;19:1–9.
25. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655.
26. Pinnock H, Epiphaniou E, Sheikh A, Griffiths C, Eldridge S, Craig P, et al. Developing standards for reporting implementation studies of complex interventions (StaRI): a systematic review and e-Delphi. Implement Sci. 2015;10:42.
27. Bishop MD, Torres-Cueco R, Gay CW, Lluch-Girbés E, Beneciuk JM, Bialosky JE. What effect can manual therapy have on a patient's pain experience? Pain Manag. 2015;5:455–64.
28. Daniel Maddox C, Subialka JA, Young JL, Rhon DI. TITLE: over half of clinical trials of mobilization and manipulation for patients with low back Pain May have Limited Real-World Applicability. A Systematic Review pf 132 Clinical Trials.
29. Taljaard M, Nicholls SG, Howie AH, Nix HP, Carroll K, Moon PM et al. An analysis of published trials found that current use of pragmatic trial labels is uninformative. J Clin Epidemiol. 2022.
30. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Rev Esp Cardiol. 2021;74:790–9.
31. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016;5:210.
32. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ. 2015;350:h2147.
33. Zhang Y-Q, Jiao R-M, Witt CM, Lao L, Liu J-P, Thabane L et al. How to design high quality acupuncture trials—a consensus informed by evidence. BMJ. 2022;376.
34. Alvarez G, Núñez-Cortés R, Solà I, Sitjà-Rabert M, Fort-Vanmeerhaeghe A, Fernández C, et al. Sample size, study length, and inadequate controls were the most common self-acknowledged limitations in manual therapy trials: a methodological review. J Clin Epidemiol. 2021;130:96–106.
35. Devos F, Foissac F, Bouazza N, Ancel P-Y, Tréluyer J-M, Chappuy H. Study characteristics impacted the pragmatism of randomized controlled trial published in nursing: a meta-epidemiological study. J Clin Epidemiol. 2019;116:18–25.
36. Elder WG, Munk N. Using the pragmatic-explanatory Continuum Indicator Summary (PRECIS) model in Clinical Research: application to refine a practice-based Research Network (PBRN) Study. J Am Board Family Med. 2014;27:846–54.
37. Rosas LG, Lv N, Azar K, Xiao L, Yank V, Ma J. Applying the pragmatic–explanatory Continuum Indicator Summary Model in a primary care–based lifestyle intervention trial. Am J Prev Med. 2015;49(3):S208–14.
38. Lee J, Cho J-H, Kim K-W, Lee J-H, Kim M-R, Kim J, et al. Chuna Manual Therapy vs Usual Care for patients with nonspecific chronic Neck Pain: a Randomized Clinical Trial. JAMA Netw Open. 2021;4:e2113757.
39. Nguyen AP, Pitance L, Mahaudens P, Detrembleur C, David Y, Hall T, et al. Effects of Mulligan Mobilization with Movement in Subacute lateral ankle sprains: a pragmatic Randomized Trial. J Man Manip Ther. 2021;29:341–52.
40. Groisman S, Malysz T, de Souza da Silva L, Rocha Ribeiro Sanches T, Camargo Bragante K, Locatelli F, et al. Osteopathic manipulative treatment combined with exercise improves pain and disability in individuals with non-specific chronic neck pain: a pragmatic randomized controlled trial. J Bodyw Mov Ther. 2019;24:189–95.
41. Wilkey A, Gregory M, Byfield D, McCarthy PW. A comparison between chiropractic management and pain clinic management for chronic low-back pain in a national health service outpatient clinic. J Altern Complement Med. 2008;14:465–73.
42. Finch P, Bessonnette S. A pragmatic investigation into the effects of massage therapy on the self efficacy of multiple sclerosis clients. J Bodyw Mov Ther. 2014;18:11–6.
43. Griswold D, Learman K, O'Halloran B, Cleland J. A preliminary study comparing the use of cervical/upper thoracic mobilization and manipulation for individuals with mechanical neck pain. J Man Manip Ther. 2015;23:75–83.
44. Cross J, Elender F, Barton G, Clark A, Shepstone L, Blyth A et al. A randomised controlled equivalence trial to determine the effectiveness and cost–utility of manual chest physiotherapy techniques in the management of exacerbations of chronic obstructive pulmonary disease (MATREX). Health Technol Assess. 2010;14.
45. Poole H, Glenn S, Murphy P. A randomised controlled study of reflexology for the management of chronic low back pain. Eur J Pain. 2007;11:878–87.
46. Sharp DM, Walker MB, Chaturvedi A, Upadhyay S, Hamid A, Walker AA, et al. A randomised, controlled trial of the psychological effects of reflexology in early breast cancer. Eur J Cancer. 2010;46:312–22.
47. Stochkendahl MJ, Christensen HW, Vach W, Høilund-Carlsen PF, Haghfelt T, Hartvigsen J. A randomized clinical trial of chiropractic treatment and self-management in patients with acute musculoskeletal chest pain: 1-year follow-up. J Manipulative Physiol Ther. 2012;35:254–62.
48. Goertz CM, Long CR, Hondras MA, Petri R, Delgado R, Lawrence DJ, et al. Adding chiropractic manipulative therapy to standard medical care for patients with acute low back pain: results of a pragmatic randomized comparative effectiveness study. Spine. 2013;38:627–34.
49. Attias S, Sivan K, Avneri O, Sagee A, Ben-Arye E, Grinberg O, et al. Analgesic effects of Reflexology in patients Undergoing Surgical procedures: a Randomized Controlled Trial. J Altern Complement Med. 2018;24:809–15.
50. Park S-Y, Hwang E-H, Cho J-H, Kim K-W, Ha I-H, Kim M-R et al. Comparative effectiveness of Chuna Manipulative Therapy for Non-acute Lower Back Pain: a Multi-center, pragmatic, randomized controlled trial. J Clin Med Res. 2020;9.
51. Hay EM, Mullis R, Lewis M, Vohora K, Main CJ, Watson P, et al. Comparison of physical treatments versus a brief pain-management programme for back pain in primary care: a randomised clinical trial in physiotherapy practice. Lancet. 2005;365:2024–30.
52. Dissing KB, Hartvigsen J, Wedderkopp N, Hestbæk L. Conservative care with or without manipulative therapy in the management of back and/or neck pain in Danish children aged 9–15: a randomised controlled trial nested in a school-based cohort. BMJ Open. 2018;8:e021358.
53. Wyatt K, Edwards V, Franck L, Britten N, Creanor S, Maddick A, et al. Cranial osteopathy for children with cerebral palsy: a randomised controlled trial. Arch Dis Child. 2011;96:505–12.

54. Goertz CM, Long CR, Vining RD, Pohlman KA, Walter J, Coulter I. Effect of Usual Medical Care Plus Chiropractic Care vs Usual Medical Care alone on Pain and Disability among US Service Members with Low Back Pain: a comparative effectiveness clinical trial. JAMA Netw Open. 2018;1:e180105.
55. Castien RF, van der Windt DAWM, Grooten A, Dekker J. Effectiveness of manual therapy for chronic tension-type headache: a pragmatic, randomised, clinical trial. Cephalalgia. 2011;31:133–43.
56. Dziedzic K, Hill J, Lewis M, Sim J, Daniels J, Hay EM. Effectiveness of manual therapy or pulsed shortwave diathermy in addition to advice and exercise for neck disorders: a pragmatic randomized controlled trial in physical therapy clinics. Arthr Rhuem. 2005;53:214–22.
57. Mafetoni RR, Shimo AKK. Effects of acupressure on progress of labor and cesarean section rate: randomized clinical trial. Rev Saude Publica. 2015;49:9.
58. Miller JE, Newell D, Bolton JE. Efficacy of chiropractic manual therapy on infant colic: a pragmatic single-blind, randomized controlled trial. J Manipulative Physiol Ther. 2012;35:600–7.
59. Walach H, Güthlin C, König M. Efficacy of massage therapy in chronic pain: a pragmatic randomized trial. J Altern Complement Med. 2003;9:837–46.
60. Harper B, Steinbeck L, Aron A. Fascial manipulation vs. standard physical therapy practice for low back pain diagnoses: a pragmatic study. J Bodyw Mov Ther. 2019;23:115–21.
61. Bergman GJ, Winters JC, Groenier KH, Meyboom-de Jong B, Postema K, van der Heijden GJ. Manipulative therapy in addition to usual care for patients with shoulder complaints: results of physical examination outcomes in a randomized controlled trial. J Manipulative Physiol Ther. 2010;33:96–101.
62. Groeneweg R, van Assen L, Kropman H, Leopold H, Mulder J, Smits-Engelsman BCM, et al. Manual therapy compared with physical therapy in patients with non-specific neck pain: a randomized controlled trial. Chiropr Man Th. 2017;25:12.
63. Hoving M, Therapy. Physical therapy, or continued care by the General Practitioner for patients with Neck Pain Long-Term results from a pragmatic Randomized Clinical Trial. 2006.
64. Lilje S, Friberg H, Wykman A, Skillgate E. Naprapathic manual therapy or conventional orthopedic care for outpatients on orthopedic waiting lists? A pragmatic randomized controlled trial. Clin J Pain. 2010;26:602–10.
65. Schwerla F, Rother K, Rother D, Ruetz M, Resch K-L. Osteopathic Manipulative Therapy in Women with Postpartum Low Back Pain and disability: a pragmatic randomized controlled trial. J Am Osteopath Assoc. 2015;115:416–25.
66. Williams NH, Wilkinson C, Russell I, Edwards RT, Hibbs R, Linck P, et al. Randomized osteopathic manipulation study (ROMANS): pragmatic trial for spinal pain in primary care. Fam Pract. 2003;20:662–9.
67. Gemmell H, Miller P. Relative effectiveness and adverse effects of cervical manipulation, mobilisation and the activator instrument in patients with sub-acute non-specific neck pain: results from a stopped randomised trial. Chiropr Osteopathy. 2010;18.
68. Castro-Sánchez AM, Lara-Palomo IC, Matarán-Peñarrocha GA, Fernández-de-las-Peñas C, Saavedra-Hernández M, Cleland J, et al. Short-term effectiveness of spinal manipulative therapy versus functional technique in patients with chronic nonspecific low back pain: a pragmatic randomized controlled trial. Spine J. 2016;16:302–12.
69. Bronfort G, Hondras MA, Schulz CA, Evans RL, Long CR, Grimm R. Spinal manipulation and home exercise with advice for subacute and chronic back-related leg pain: a trial with adaptive allocation. Ann Intern Med. 2014;161:381–91.
70. Evans R, Haas M, Schulz C, Leininger B, Hanson L, Bronfort G. Spinal manipulation and exercise for low back pain in adolescents: a randomized trial. Pain. 2018;159:1297–307.
71. Georgoudis G, Felah B, Nikolaidis P, Damigos D. The effect of myofascial release and microwave diathermy combined with acupuncture versus acupuncture therapy in tension-type headache patients: a pragmatic randomized controlled trial. Physiother Res Int. 2018;23:e1700.
72. Skillgate E, Bohman T, Holm LW, Vingård E, Alfredsson L. The long-term effects of naprapathic manual therapy on back and neck pain - results from a pragmatic randomized controlled trial. BMC Musculoskelet Disord. 2010;11:26.
73. Eklund A, Jensen I, Lohela-Karlsson M, Hagberg J, Leboeuf-Yde C, Kongsted A, et al. The Nordic Maintenance Care program: effectiveness of chiropractic maintenance care versus symptom-guided treatment for recurrent and persistent low back pain—A pragmatic randomized controlled trial. PLoS ONE. 2018;13:e0203029.
74. Lim K-T, Hwang E-H, Cho J-H, Jung J-Y, Kim K-W, Ha I-H, et al. Comparative effectiveness of Chuna manual therapy versus conventional usual care for non-acute low back pain: a pilot randomized controlled trial. Trials. 2019;20:216.
75. Kim B-J, Park A-L, Hwang M-S, Heo I, Park S-Y, Cho J-H et al. Comparative effectiveness and Safety of Concomitant Treatment with Chuna Manual Therapy and Usual Care for Whiplash injuries: a Multicenter Randomized Controlled Trial. Int J Environ Res Public Health. 2022;19.
76. Lynen A, Schömitz M, Vahle M, Jäkel A, Rütz M, Schwerla F. Osteopathic treatment in addition to standard care in patients with gastroesophageal reflux disease (GERD) - a pragmatic randomized controlled trial. J Bodyw Mov Ther. 2022;29:223–31.
77. Alvarez G, Cerritelli F, Urrutia G. Using the template for intervention description and replication (TIDieR) as a tool for improving the design and reporting of manual therapy interventions. Man Ther. 2016;24:85–9.
78. Cashin AG, Lee H, Bagg MK, O'Hagan E, Traeger AC, Kamper SJ, et al. A systematic review highlights the need to improve the quality and applicability of trials of physical therapy interventions for low back pain. J Clin Epidemiol. 2020;126:106–15.
79. Kamper SJ, Moseley AM, Herbert RD, Maher CG, Elkins MR, Sherrington C. 15 years of tracking physiotherapy evidence on PEDro, where are we now? Br J Sports Med. 2015;49:907–9.
80. Palakshappa JA, Gibbs KW, Lannan MT, Cranford AR, Taylor SP. Systematic review of the pragmatism of pragmatic critical care trials. Crit Care Explorations. 2022;4:e0738.
81. Sepehrvand N, Alemayehu W, Das D, Gupta AK, Gouda P, Ghimire A, et al. Trends in the explanatory or pragmatic nature of Cardiovascular clinical trials over 2 decades. JAMA Cardiol. 2019;4:1122–8.
82. Dal-Ré R, de Boer A, James SK. The design can limit PRECIS-2 retrospective assessment of the clinical trial explanatory/pragmatic features. J Clin Epidemiol. 2020;126:193–201.
83. Averitt AJ, Ryan PB, Weng C, Perotte A. A conceptual framework for external validity. J Biomed Inf. 2021;121:103870.
84. Dal-Ré R. Pragmatic trials, blinding, placebos, and the usefulness of the PRECIS-2 tool. Eur J Clin Pharmacol. 2021;77:1071–2.
85. Zwarenstein M, Thorpe K, Treweek S, Loudon K. PRECIS-2 for retrospective assessment of RCTs in systematic reviews. J Clin Epidemiol. 2020;126:202–6.
86. Rossettini G, Camerone EM, Carlino E, Benedetti F, Testa M. Context matters: the psychoneurobiological determinants of placebo, nocebo and context-related effects in physiotherapy. Arch Physiother. 2020;10:11.
87. Rossettini G, Carlino E, Testa M. Clinical relevance of contextual factors as triggers of placebo and nocebo effects in musculoskeletal pain. BMC Musculoskelet Disord. 2018;19:27.
88. Bialosky JE, Bishop MD, Penza CW. Placebo mechanisms of Manual Therapy: A Sheep in Wolf's Clothing? J Orthop Sports Phys Ther. 2017;47:301–4.
89. Bialosky JE, Beneciuk JM, Bishop MD, Coronado RA, Penza CW, Simon CB, et al. Unraveling the mechanisms of Manual Therapy: modeling an Approach. J Orthop Sports Phys Ther. 2018;48:8–18.
90. Zwarenstein M, Howie A. Blinding, pragmatism, and the PRECIS-2 tool for designing and assessing randomized trials. Eur J Clin Pharmacol. 2021;77:1069–70.
91. Leviton LC. Generalizing about Public Health Interventions: a mixed-methods Approach to External Validity. Annu Rev Public Health. 2017;38:371–91.
92. Hohenschurz-Schmidt DJ, Cherkin D, Rice ASC, Dworkin RH, Turk DC, McDermott MP et al. Research objectives and general considerations for pragmatic clinical trials of pain treatments: IMMPACT statement. Pain. 2023.
93. Zhang YQGG. How to design high quality acupuncture trials-a consensus informed by evidence. BMJ. 2022;377:o1046.
94. Neta G, Johnson KE. Informing real-world practice with real-world evidence: the value of PRECIS-2. BMC Med. 2018;16:76.

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