**Title: Investigating the veracity of a sample of divergent published trial data in spinal pain.**

Open Science Framework Registration: https://osf.io/345vq

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**Abstract**

Evidence-based medicine is replete with studies assessing quality and bias, but few evaluating research integrity or trustworthiness. A recent Cochrane review of psychological interventions for chronic pain identified trials with a shared lead author with highly divergent results. We sought to systematically identify all similar trials from this author to explore their risk of bias, governance procedures, and trustworthiness.

We searched OVID MEDLINE, EMBASE, CENTRAL and PEDro to 22/12/2021 for trials. We contacted the authors requesting details of trial registration, ethical approval, protocol, and access to the trial data for verification. We used the Cochrane Risk of Bias tool and the Cochrane Pregnancy and Childbirth group's Trustworthiness Screening Tool to guide systematic exploration of trustworthiness.

Ten trials were included: nine compared cognitive behavioural therapy (CBT) and physical exercise to usual care, exercise alone, or physiotherapy, and one compared two brief CBT programmes. Eight trials reported results divergent from the evidence base. Assessment of risk of bias and participant characteristics identified no substantial concerns. Responses from the lead author did not satisfactorily explain this divergence. Trustworthiness screening identified concerns about research governance, data plausibility at baseline, the results, and apparent data duplication.

We discuss the findings within the context of methods for establishing the trustworthiness of research findings generally. Important concerns regarding the trustworthiness of these trials reduce our confidence in them. They should probably not be used to inform the results and conclusions of systematic reviews, in clinical training, policy documents, or any relevant instruction regarding adult chronic pain management.

**Introduction**

Trust is the foundation on which medicine is built. Patients trust that health professionals have based their practice on the best available evidence, and health professionals trust that researchers have accurately and honestly undertaken and reported their research according to best methods. Evidence-based medicine (EBM) has numerous tools and methods to assess and manage quality and bias in research but few addressing the important question of trust. Accordingly, while EBM is replete with studies assessing quality and bias, there are few examining the integrity or trustworthiness of research.

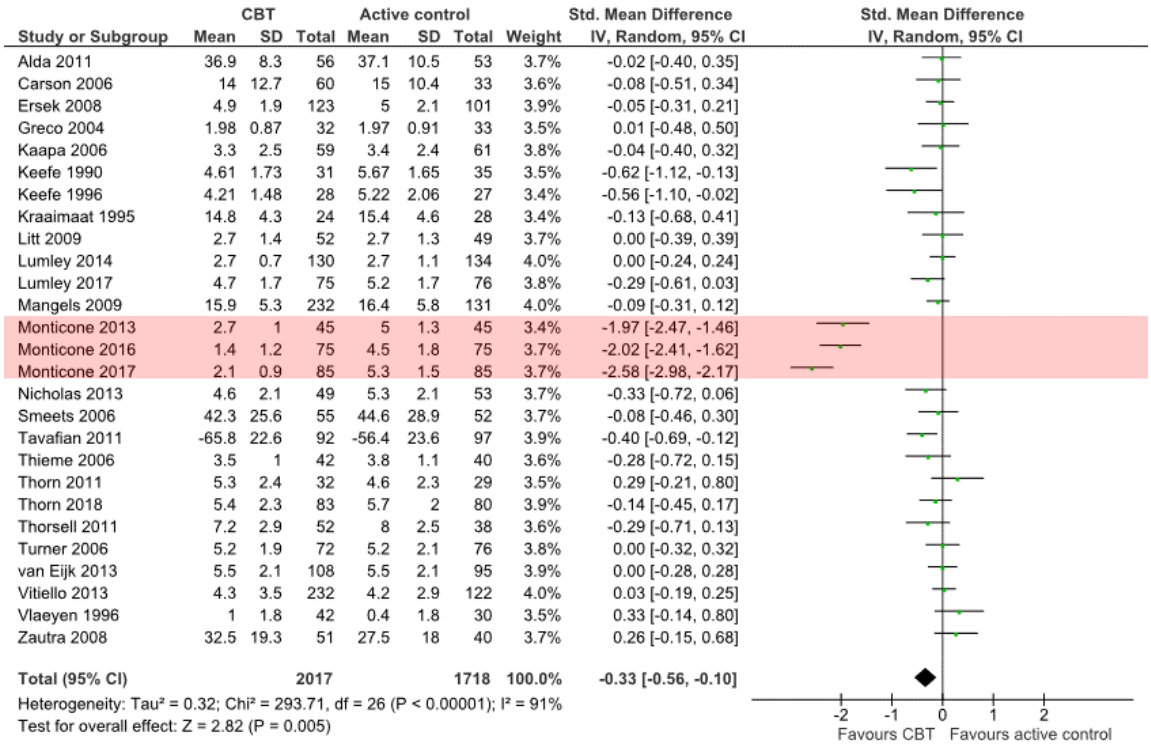
Trustworthiness incorporates research integrity, governance, and potential research misconduct. The latter might include fabrication or falsification of research results, or plagiarism [3], but, importantly, does not include error. We are aware of no consensus on the characteristics of studies that act as possible warning signs for untrustworthiness. Although a variety of methods have been used to assess research misconduct, there are few validated methods beyond the approaches that identify textual plagiarism [3]. Any single method is likely to be insufficient and investigators are recommended to use multiple methods considering aspects of research governance (pre-registration, ethical approval and quality of reporting), with close scrutiny of reported data and sight of the raw data, if deemed necessary.

Several tools have been proposed to formally explore the integrity and trustworthiness of research. The REAPPRAISED checklist [9], for example, was developed to identify possible problems with research integrity and includes items relating to research governance, ethics, authorship, productivity, plagiarism, research conduct, analyses and methods, possible image manipulation,

statistical considerations, errors, and data duplication. The Cochrane Pregnancy and Childbirth review group developed a Trustworthiness Screening Tool (CPC-TST) [6] specifically for clinical trials. This tool is applied to all trials eligible for inclusion in systematic reviews published by their group, exploring scientific integrity and trustworthiness with items relating to aspects of research governance, participant characteristics, feasibility, and study results.

Our research began with an attempt to determine the veracity and completeness of the Cochrane library entry on the effectiveness and safety of psychological interventions for the treatment of chronic pain in adults [34], conducted by some of the authors of this paper (EF, LH, CE, AW). The review included three trials [16,19,21], with a common lead author, whose results diverged substantially from the rest of the field, both at post-treatment and follow-up, with effect sizes and confidence intervals that did not overlap with outcome data from 24 other included trials (see Figure 1).

**Figure 1: Forest plot for the analysis "CBT vs active control" from Williams et al. [33] with the divergent trials highlighted.**




After assessment of error, and of uniqueness of treatment characteristics, the lead author (Dr M Monticone) was contacted for insight. Details of that correspondence can be found in Supplementary Information. The review author team concluded that these trials were unreliable and excluded them from their primary analyses, including them only in sensitivity analyses. Other similar publications from Dr Monticone's research group became the focus of this study. We determined to recover all recent published study reports, assessing their quality and bias, their governance procedures such as registration and ethical review, and finally their trustworthiness.

## Methods

We registered a protocol for this review on the Open Science Framework: https://osf.io/345vq

**Searches**

We conducted a search of the CENTRAL, PEDro, OVID MEDLINE and EMBASE databases from 2010 to 22/12/21 for all randomised clinical trials (RCTs) published since 2010 in subacute or persistent spinal pain in which Dr Monticone was lead author. We excluded non-randomised studies and studies that did not investigate the effectiveness of an intervention for subacute or persistent spinal pain. Three reviewers (NOC, AW, LH) independently screened the searches and any disagreements were resolved through discussion.

**Procedures to explore veracity**

We used the Cochrane Risk of Bias (RoB) tool [11] to evaluate the risk of bias for each included study. Two reviewers (NOC, EF) independently applied the screening tool to the included trials, with any disagreements resolved through discussion.

We used the following key domains and items of the Cochrane Pregnancy and Childbirth review group's TST (CPC-TST) [6] to guide our exploration of the included papers (Table 1). We chose this tool as it was specifically developed to evaluate RCTs. Three reviewers (NOC, AW, LH) independently applied the screening tool to each included study, with any disagreements resolved through discussion.

**Table 1. Key domains from the CPC-TST used to explore the sample of studies**

| |
|---|
| **Research Governance** |
| Are there any retraction notices or expressions of concern listed on the Retraction Watch Database relating to this study? |
| Was the study prospectively registered (for those studies published after 2010)? If not, have the authors provided a plausible reason? |
| When requested, did the trial authors provide/share the protocol and/or ethics approval letter? |
| Did the trial authors engage in communication with the Cochrane Review authors within the agreed timelines? |
| Did the trial authors provide Individual Patient Data (IPD) upon request? If not, was there a plausible reason? |
| **Baseline characteristics** |
| Is the study free from characteristics of the study participants that appear too similar? |
| **Feasibility** |
| Is the study free from characteristics that could be implausible? |
| In cases with (close to) zero losses to follow-up, is there a plausible explanation? |
| **Results** |
| Is the study free from results that could be implausible? |
| Do the numbers randomised to each group suggest that adequate randomisation methods were used? |

**Research Governance**

We reviewed the included trials for details of registration. Where details were provided, we checked the trial registry record to ascertain whether the trial was prospectively or retrospectively registered. We contacted the lead author of the included trials to request details of registration for all included trials, evidence of local ethical approval, full details of the intervention content and delivery, and full individual patient datasets for all included trials. We extracted any information regarding ethical approval processes from study reports. We searched Retraction Watch (https://retractionwatch.com/) for any retraction notices related to the included trials.

**Baseline Characteristics**

To explore the similarity of baseline data, we extracted these for treatment and control groups (means and standard deviations (SDs)) for all reported continuous variables and calculated p values with unpaired *t*-tests. For categorical variables, we used Fisher's exact test. We conducted separate tests for variables where there were multiple independent levels for which participants may have events in more than one level (e.g. use of different medications), and single multi-level tests (e.g. Fisher's exact test 2x3 or 2x4, $\chi^2$ test where n > 120) where there were multiple levels but participants could only be represented at a single level (e.g. highest level of education or employment status). For each trial, we plotted the distribution of p values and calculated the pooled p value using Stouffer's z-score method [32]. This method calculates a p value by summing the z-scores corresponding to each variable and dividing them by the square root of the number of variables [5]. The pooled p value represents the combined probability across multiple independent comparisons of observing a difference between groups as large as that observed where the null hypothesis is true.

We also used Stouffer's method to calculate a pooled p value using all p values of all included trials and plotted the distribution of all p values from all the included trials combined. In the case of simple randomisation, we might expect baseline p values to display a uniform distribution between 0 and 1. Combined p values close to 1.0 would indicate more similar baseline mean values and close to 0 would indicate more dissimilar means. We classified pooled p values of ≤ 5% from 0 or 1.0 as likely to be inconsistent with random allocation [3]. Distributions were plotted in Jamovi [33] and Microsoft Excel 2019.

**Feasibility**

To explore the feasibility of participant characteristics, we compared baseline data for pain intensity, disability and health-related quality of life (HRQoL) with published normative data from a clinical population of > 6000 people with persistent back and neck pain seen in a Pain Management and Research Centre [27], to identify unexplained divergence. We extracted and explored the amount of participant attrition for all groups in each study.

**Plausibility of results**

To enable combination and comparison of effect sizes, we calculated the standardised mean difference (SMD) (Hedge's g) using Revman 5.4 [30] for the outcome measures of pain and disability for all time points in all trials. We calculated pooled effect sizes for immediate, 3 months, 12 months and 24 months post-intervention time-points, using a random effects model. For the mean difference (MD), all pain scales were normalised to a 0-10 scale. We plotted the combined

distribution of both SMDs and p values for pain, disability and HRQoL outcomes for all subscales of the tools used in the trials (the 36-item short form survey (SF-36) or the Scoliosis Research Society-22 patient questionnaire (SRS-22)) for all trials.

We explored the plausibility of these results in several ways: by comparing pain and disability effect sizes with those of the other included trials in the Cochrane review of psychological therapies for persistent pain (Williams et al.) [34]; by examining the level of statistical significance in the results of the included trials; by comparing pain effect sizes for all included trials with other interventions for chronic pain; and by examining conversions of MD and SMD to number needed to treat (NNT) and comparing indicated NNTs with other interventions for chronic pain .

We formally examined the baseline and outcomes data across all included trials for the presence of duplicate or similar data, using an approach modified from that of Bordewijk et al. [2]. Identical data between trials were counted where the means and SDs matched for the same outcome. Similar data were counted where values for the same outcome differed by less than 1.

We explored potential concerns with the randomisation process by reviewing the description of the randomisation method and by scrutinising the number of participants allocated to each group. Identical numbers allocated to each group in the absence of a block approach to randomisation was considered as cause for concern. We extracted and examined the data relating to participant attrition. The observation of zero or nearly zero loss to follow-up, particularly in the longer term, was considered as cause for concern. In scrutinising data from the published records of included trials, we aimed to identify any further errors or apparent inconsistencies.

**Results**

Supplementary Figure 1 shows a flow diagram of the search process. Our searches identified 10 RCTs of interventions for subacute or persistent spinal pain, randomising 1100 participants [15-24]. Recruitment took place between December 2007 and December 2015, and the trials were published between 2012 and 2021. Trial sizes ranged from 20 to 170 participants randomised (mean (SD) 110 (53)); Table 2 provides a summary of study characteristics.

**Table 2. Characteristics of included trials.**

| Study ID | Journal of publication | Setting | Participants | N randomised | Details of experimental intervention | Details of control intervention |
|---|---|---|---|---|---|---|
| Monticone 2012 [15] | Eur Spine J | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Chronic non-specific neck pain | 80 | CBT Physiotherapy including exercise (posture, strength, stretching), ergonomic advice, manual therapy (≤ 12 sessions; x1-2 weekly) | Physiotherapy including exercise (posture, strength, stretching), ergonomic advice, manual therapy (≤ 12 sessions; x1-2 weekly) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Monticone 2013 [16] | Clin J Pain | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Chronic non-specific low back pain | 90 | CBT (x1 weekly; 5 weeks; then x1 monthly for 1 year)<br><br>Exercise (posture, strength, stretching), ergonomic advice, manual therapy (10 sessions; x2 weekly; telephone reminders to exercise for 1 year) | Exercise (posture, strength, stretching), ergonomic advice, manual therapy (10 sessions; x2 weekly; telephone reminders to exercise for 1 year) |
| Monticone 2014a [17] | Eur Spine J | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Chronic non-specific low back pain | 20 | CBT (x1 weekly; 8 weeks)<br><br>Exercise (motor control focused) (x2 weekly; 8 weeks) | Exercise (posture, strength, stretching), manual therapy. (x2 weekly; 8 weeks) |
| Monticone 2014b [18] | Eur Spine J | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Lumbar fusion for degenerative or isthmic spondylolisthesis | 130 | CBT (x2 weekly; 4 weeks)<br><br>Exercise (posture, strength, stretching, walking), ergonomic advice (x5 weekly; 4 weeks) | Exercise (posture, strength, stretching, walking), ergonomic advice (x5 weekly; 4 weeks) |
| Monticone 2016a [19] | Eur Spine J | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Chronic non-specific low back pain | 150 | CBT (x1 weekly; 5 weeks)<br><br>Task-based exercise (motor control training, task-oriented exercises, coordination/balance exercises) (x2 weekly; 5 weeks) | Exercise (posture, strength, stretching, walking), ergonomic advice (x2 weekly; 5 weeks) |
| Monticone 2016b [20] | Eur Spine J | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Adult idiopathic scoliosis | 130 | Active self-correction and scoliosis alignment exercises with cognitive-behavioural strategies and ergonomic advice (x1 weekly; 20 weeks) | Physiotherapy including exercise (postural, strength, stretching), manual therapy (x1 weekly; 20 weeks) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Monticone 2017 [21] | Clin Rehabil | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Chronic non-specific neck pain | 170 | CBT (x1 weekly; 10 weeks)<br><br>Exercises (graded exposure, mobility, postural, strength, stretching) (x1 weekly; 10 weeks) | Physiotherapy exercises (strength, stretching, mobilisation) (x1 weekly; 10 weeks) |
| Monticone 2018 [22] | Eur J Phys Rehabil Med | Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone | Chronic non-specific neck pain | 30 | NeckPix©* CBT (x4 weekly; 1 week)<br><br>Exercise (mobility, strength, stretching, motor control, task-oriented) (x2 weekly; 5 weeks) | CBT (x4 weekly; 1 week).<br><br>Exercise (mobility, strength, stretching, posture) (x2 weekly; 5 weeks) |
| Monticone 2020 [23] | Disabil Rehabil | Unclear | Failed back surgery syndrome | 150 | CBT (x1 weekly; 10 weeks)<br><br>Exercise (mobility, motor control, task-oriented, stretching, balance, proprioception), ergonomic advice (x2 weekly; 10 weeks) | Physiotherapy: exercise (mobility, stretching, strength, posture), manual therapy ergonomic advice (x2 weekly; 10 weeks). |
| Monticone 2021 [24] | Eur J Phys Rehabil Med | Unclear | Subacute low back pain | 150 | CBT (x1 weekly; 10 weeks)<br><br>Exercise (mobility, motor control, task-oriented, postural, proprioception) (x2 weekly; 10 weeks) | Physiotherapy: Exercise (strength, stretching, postural), manual therapy (x2 weekly;10 weeks) |

*Footnotes: * "a multi-image instrument developed to assess daily activities in the context of pain-related fear"*

Nine included trials compared a form of CBT and physical exercise to either usual care, exercise alone, or physiotherapy, and one trial [22] compared two different brief CBT programmes Eight trials were conducted in the same clinical centre in Lissone, Italy, while two trials did not specify the setting. There was some variation across trials in the description of the specific populations studied, with conditions including chronic low back pain [16,17,19], subacute low back pain [24], chronic

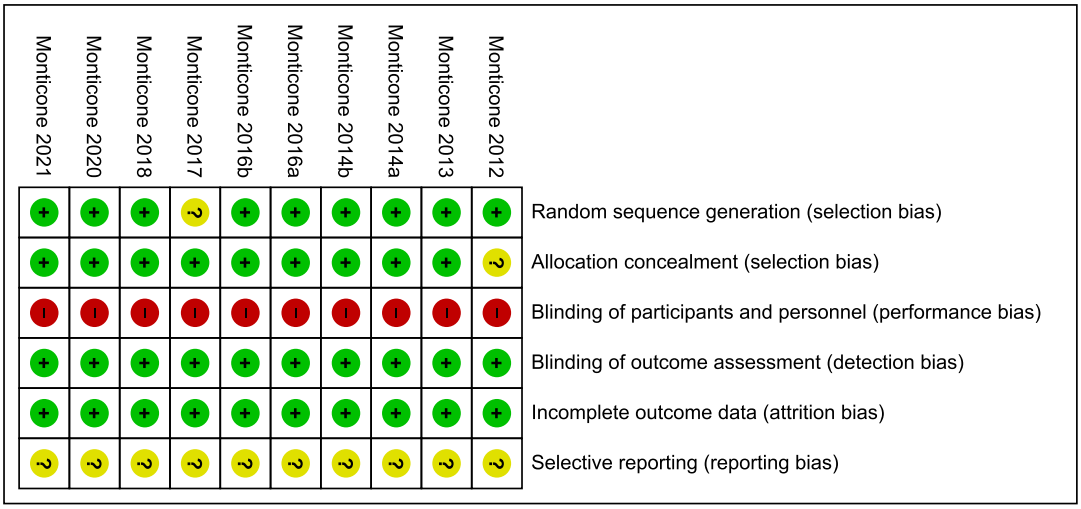
neck pain [15,21,22], persistent pain in adults with idiopathic scoliosis [20], failed back surgery syndrome [23] and pain after lumbar fusion surgery [18].

E-mail correspondence between members of the review [34] team and the lead author and two co-authors of these trials elicited data as requested that allowed their inclusion in the meta-analyses. However, the explanations of treatment content and process revealed nothing unusual, apart from monthly telephone reminders to participating patients which were offered as an explanation for zero attrition at two-year follow-up. At the time of that review, the team enquired further but received no information.

**Risk of bias**

The included trials were mostly rated as low RoB for randomisation, allocation concealment, blinding of outcome assessors and attrition, with one trial judged as unclear for randomisation and one for allocation concealment (due to lack of detail in the reported methods). All trials were rated as unclear RoB for selective outcome reporting due to the lack of pre-registration or available protocols. All trials were rated as high RoB for blinding of participants and personnel as it was not possible to blind clinicians or participants for these interventions and comparisons. This is the norm for most trials of psychological interventions. Figure 2 presents the RoB judgements on each domain for each study.

**Figure 2. Risk of bias summary: review authors' judgements about each RoB item for each included study.**




**Trustworthiness screening tool.**

Table 3 illustrates the results of the CPC-TST tool assessment. There follows a more detailed description of the findings of that screening process.

**Table 3. Results of the CPC-TST assessment**

| DOMAIN | 2012 | 2013 | 2014a | 2014b | 2016a | 2016b | 2017 | 2018 | 2020 | 2021 |
|---|---|---|---|---|---|---|---|---|---|---|
| Retraction notices? | | | | | | | | | | |
| Prospectively registered? | | | | | | | | | | |
| Did authors engage with requests for information? | | | | | | | | | | |
| Protocols or ethics approval shared on request | | | | | | | | | | |
| IPD shared on request? | | | | | | | | | | |
| Baseline similarity (continuous data only) | | | | | | | | | | |
| Baseline similarity all variables | | | | | | | | | | |
| Participant characteristics (feasibility) | | | | | | | | | | |
| Attrition feasibility | | | | | | | | | | |
| Randomisation concerns | | | | | | | | | | |
| Results plausibility | | | | | | | | | | |

*Footnotes: Red = Some concerns; Green = No concerns*

**Research governance**

We contacted the ethics committee of the Instituti Clinici Scientifici Maugeri on 7 January 2022 to request confirmation and evidence that ethical approval was sought and granted for the studies but, at the time of writing (5 April 2022), had not received a response. We contacted the lead author of the trials by email on 1 December 2021, with a reminder sent on 6 January 2022. For the 10 included trials, we asked: whether a clinical trial protocol was developed for the trials and for a copy of any such protocols; for information relating to trial registration or an explanation for non-registration; whether ethical approval was obtained for the included trials and for evidence of such; for access to IPD for each trial; and for an explanation of observed anomalies regarding randomisation, specific apparent errors in baseline p values and instances of duplicate and highly similar data between trials. We received an email response from Dr Monticone on 12 January 2022. Supplementary information has the full details of our enquiries and of Dr Monticone's responses. We also contacted co-author Dr Barbara Rocca on 14 January 2022 requesting this information but at the time of writing (5 April 2022) had not received a response.

None of the identified trials was pre-registered, though three [21,23,24] reported a trial registration number. These latter were registered retrospectively between 2 and 5 years after recruitment was reported to have ended. One trial was registered after the manuscript [21] had been submitted for

publication (ISRCTN14581536), while the other two were registered 12 and 16 months before submission. We identified no retraction notices for any of the included trials.

In his response, Dr Monticone confirmed that none of the trials had been pre-registered. The reasons given for this were that either they started before this issue was strictly required by journals or because the journals had not required it. In three cases [21,23,24], trials were retrospectively registered at the recommendation of the relevant journals.

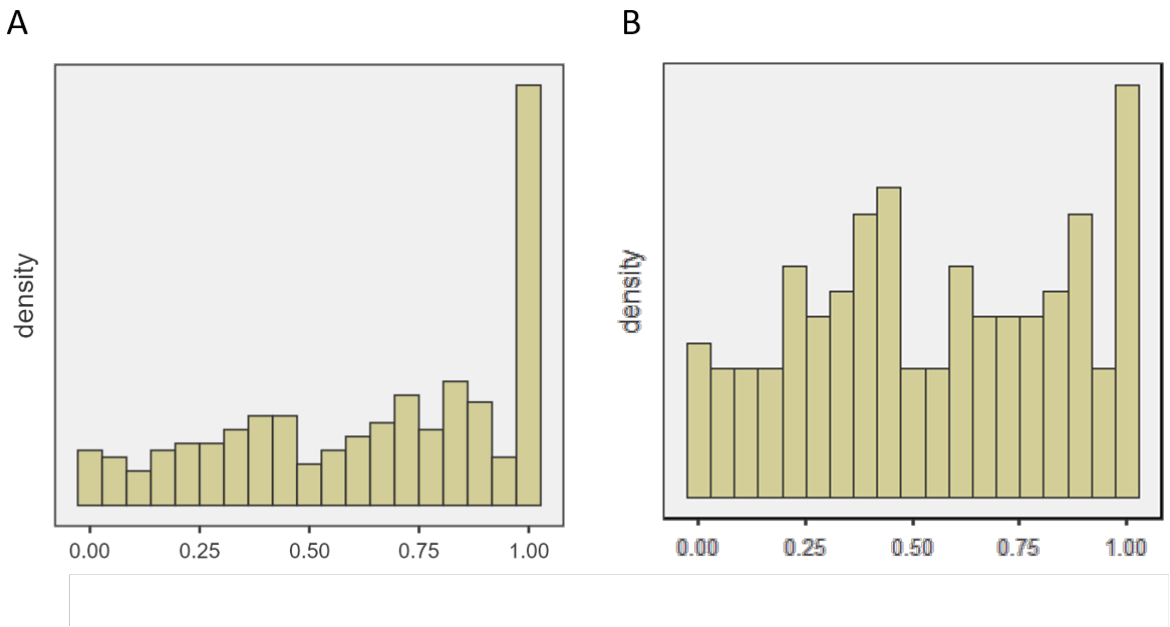
All trial reports included a statement that they had been approved by the Hospital's Institutional Review Board. Six stated that the trial was conducted in conformity with ethical and humane principles of research and one stated that the study was conducted in accordance with the principles of the Helsinki Declaration. In his response, Dr Monticone stated "There was the approval of our Institutional Review Board at the Hospital where the studies were performed. I would prefer to avoid sending these documents." Dr Monticone also responded that there were no trial protocols, giving as a reason that "*the intervention groups always belonged to our clinical practice*". It is therefore unclear what information was submitted to the ethics review board if there were no trial protocols. Dr Monticone also stated that he "*would prefer to avoid sending databases*" which we understood as a decision not to share full IPD sets for the included trials.

**Baseline Characteristics**

Reviewing the distribution of baseline p values for all variables across all included trials revealed a non-uniform distribution (see Figure 3). The median p value was 0.713 (interquartile range (IQR) 0.377 to 0.943). Stouffer's method revealed pooled baseline p values for each individual trial as within 5% of 0 or 1 for 9 of the 10 included trials.

The distribution of p values for each individual trial is presented in the Supplementary information (Supplementary Figure 2). Table 4 presents pooled p values for baseline comparisons for each trial.

**Figure 3. Distribution of p values across all trials.** A: for all baseline variables across all included trials. B: for continuous outcomes only



The baseline characteristics tables included several categorical variables with low numbers of events. We considered that this might skew our analysis and so conducted a sensitivity analysis including only continuous outcomes. In that analysis, the median p value was 0.623 (IQR 0.384 to 0.848). Stouffer's method resulted in pooled baseline p values for each trial as within 5% of 0 or 1 for 5 of the 10 included trials which we judged as likely to be inconsistent with random allocation. The distribution of p values remained non-uniform.

**Table 4: Pooled p values for baseline comparisons for each included study.**

| | Study ID | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Monticone 2012 | Monticone 2013 | Monticone 2014a | Monticone 2014b | Monticone 2016a | Monticone 2016b | Monticone 2017 | Monticone 2018 | Monticone 2020 | Monticone 2021 |
| All variables (continuous and categorical) | 0.0002 | 1.0000 | 1.0000 | 0.99787 | 0.9342 | 1.0000 | 1.0000 | 1.0000 | 0.9933 | 0.9972 |
| Continuous variables only | 0.0000 | 0.9999 | 1.0000 | 0.8538 | 0.0834 | 1.0000 | 0.9223 | 0.6461 | 0.8161 | 0.9917 |

**Feasibility of participant characteristics**

When comparing the baseline characteristics of participants in the trials of spinal pain with published norms [27], we observed that baseline pain intensity was frequently higher than norms, despite no study reporting a minimum threshold for pain intensity in their inclusion criteria. The median reported baseline intensity was 6/10 (range 4.8-7.0), compared to published norms of mean (SD) 4.1 (1.2) for persistent neck pain and 4.2 (1.0) for persistent low back pain. In some included trials, average baseline scores for HRQoL on the SF-36 subdomains of Role Function, Social Function and Vitality [14-19] and Physical Function [15,16,19] were notably higher than those observed in the published norms (Supplementary Table 1). However, we judged that these observations were not sufficiently remarkable to warrant a positive risk judgement on the CPC-TST for any trial.

**Randomisation concerns**

Treatment groups were of equal size after allocation in all studies. Four of the 10 trials [18,21,23,24] reported a block method for randomisation that might increase the chances of equal numbers emerging in treatment groups. Of these, one trial reported using random permuted blocks and random block length. The other three trials reported using a "*permuted block randomisation process*" but did not add further detail. In his response, Dr Monticone reported that "*the number of patients randomised was generated by chance based on the patients that were excluded*". We

judged that it was unlikely that equal group numbers in all 10 trials would result from a random process of allocation.

**Plausibility of results**

Effect sizes for all outcomes were large or extremely large in 8 of the 10 trials. All 8 of these trials compared a form of CBT and physical exercise with either usual care, exercise alone or physiotherapy. These large effect sizes were seen at both short- and long-term follow-up, with larger median effect sizes observed at long-term follow-up.

Figure 4 summarises the effect sizes for pain and disability for all trials. In addition, we present the distribution of effect sizes for pain, disability and all HRQoL subscales at both the short-term (immediate and 3 months post-intervention) and long-term (1 and 2 years post-intervention) follow-up time points. For this purpose, all were converted to positive values.

**Figure 4. A summary of effect sizes and the distribution of effect sizes across all trials and follow-up points.** *Effect sizes for A. Pain intensity; B. Disability; C/D. The distribution of effect sizes from the outcomes pain, disability, HRQoL subscales, combined at post-intervention (n = 81) and long-term follow-up (n = 80).*

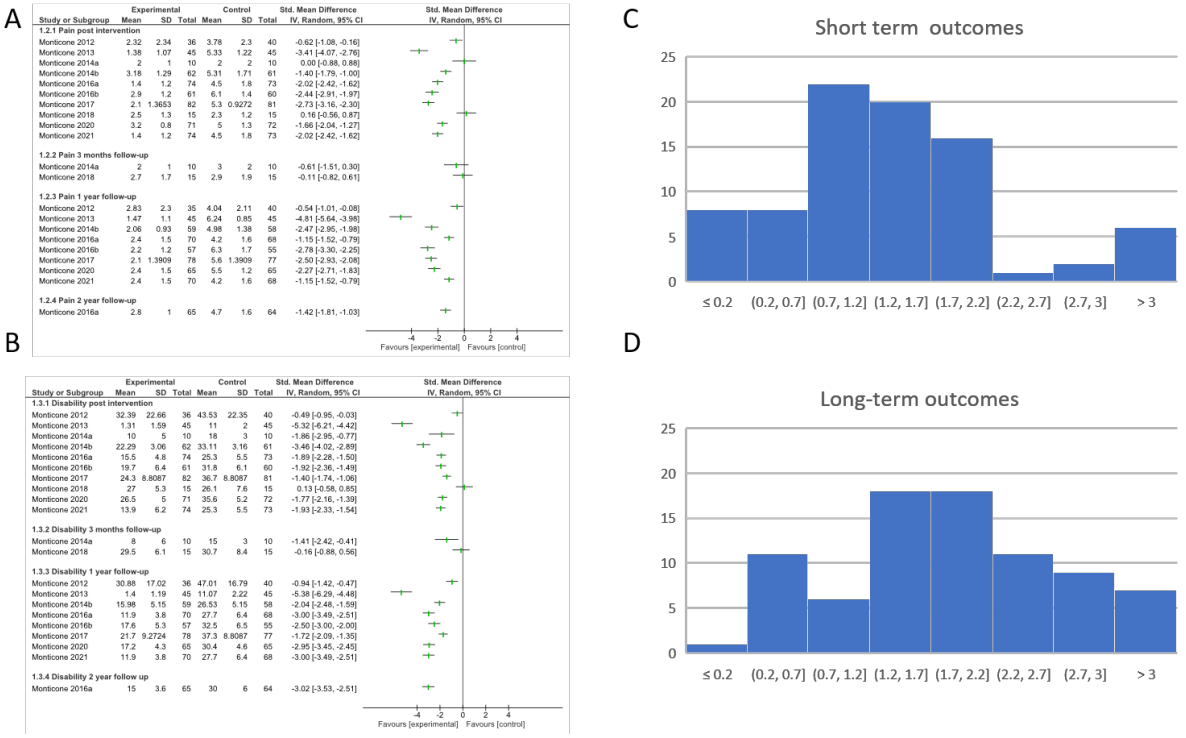



Table 5 presents the pooled effect sizes across the included trials for pain and disability for short- and long-term follow-up. In this sample of trials, the pooled effect size for pain intensity was SMD -1.65 (95% confidence interval (CI) -2.21, -1.09) at end of treatment and -2.17 (95% CI -2.89, -1.45) at long-term follow-up. This represents a six-fold difference between the lower confidence interval of the Monticone studies and the upper confidence interval of all others combined. Supplementary Figure 3 shows SMD values for pain and disability in Williams 2020 [34] excluding the three

previously included trials, and the SMD values for pain and disability from the 10 trials included in this analysis. There is little overlap.

On a 0-10 pain numerical rating scale (NRS), this equates to a pooled effect of -2.29 (95% CI -2.94, -1.65) at end of treatment and -2.93 (95% CI -3.73, -2.14) at one year follow-up. In comparison, a systematic review [29] comparing combined physical and psychological rehabilitation with physical rehabilitation alone reported a mean difference in pain intensity of -0.52 (95% CI 0.16-0.88) at short-term and -0.47 (95% CI 0.13, 0.81) at long-term follow-up.

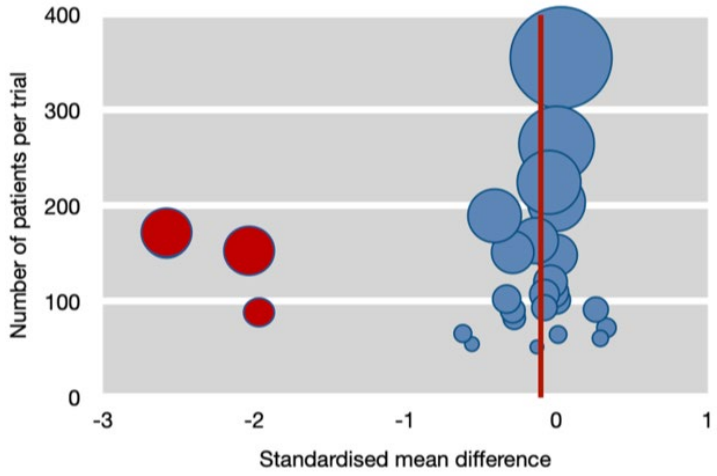
**Table 5: Comparison of effect sizes (all SMD with 95% confidence interval using random effects) for pain intensity and disability after treatment and at 1 year follow-up**

| | At end of treatment period | | | At 1 year follow-up | | |
|---|---|---|---|---|---|---|
| **Outcome** | **Number of studies** | **Results from studies currently examined** | **Results from the Cochrane review** | **Number of studies** | **Results from studies currently examined** | **Results from the Cochrane review** |
| **Pain intensity** | 10 | -1.65 (-2.21 to –1.09) | -0.09 (-0.17 to -0.01) | 8 | -2.17 (-2.89 to -1.45) | -0.08 (-0.19 to 0.04) |
| **Disability** | 10 | -1.96 (-2.60 to -1.32) | 0.12 (-0.20 to -0.04) | 8 | -2.64 (-3.32 to -1.95) | -0.12 (-0.26 to 0.02) |

**Comparisons within Williams 2020**

To place these results in context, in the most recent Cochrane systematic review of psychological interventions for persistent pain [34], the pooled effect size (SMD) for the comparison 'CBT vs active care', derived from 23 RCTs with 3235 participants, was -0.09 (95% CI -0.17, -0.01) for pain at the end of treatment. Figure 5 demonstrates the magnitude of the difference using the SMDs calculated for each of the included studies in the Williams et al. primary analysis [34], and the three Monticone trials [16,19,21] excluded from the primary analysis.

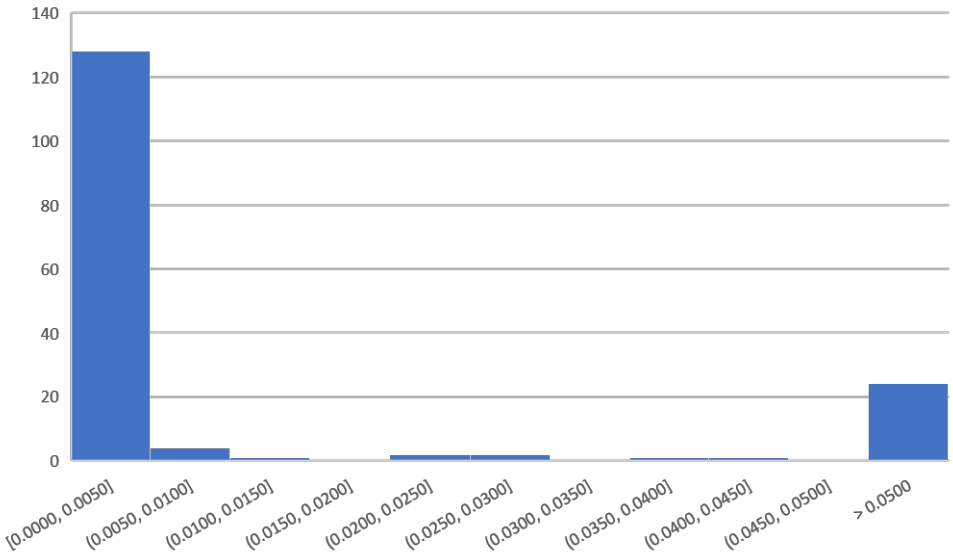
**Figure 5: Individual study pain reduction SMDs plotted against the total number of patients in trial (from Williams et al.) [33].** Symbol diameter is proportional to the total number of participants. Red filled circles represent studies by Monticone et al. Blue filled circles represent all other trials in that analysis.



**Examination of statistical significance**

Figure 6 displays the distribution of p values for all pain intensity, disability, and HRQoL subscales from all post-intervention and long-term follow-up comparisons, from all 10 included trials (n = 163 comparisons). Most had p values of < 0.001.

**Figure 6. Distribution of p values for pain, disability, and HRQoL comparisons from included spinal pain trials (from short-term and long-term follow-up): n=163 comparisons.**




The reported effect estimates in the 10 included Monticone trials in this analysis are both extreme in size and precise, as reflected by the extremely high rate of reported p values of < 0.001. The extent of the divergence is stark, illustrated by the six-fold difference between the lower confidence interval of the Monticone studies and the upper confidence interval of all others, and the more than 18-fold difference between point estimates of the SMD. Reflecting the MD in pain intensity as a proportion of baseline levels, results show median reductions in pain intensity of 40% (IQR 28-52) in the short term (ST) and 44% (IQR 28-53) in the long term (LT), attributable to the interventions. One trial [17] found no evidence for an effect and one trial [15] found medium size effects on pain and disability at short-term follow-up and a medium size effect on pain and a large effect on disability at long-term follow-up. Seven of the 8 included trials with long term (≥ 1 year) follow-up reported an average long-term mean difference for pain intensity greater than 1.5/10 (range 0-4.1). A similar pattern was also found for disability.

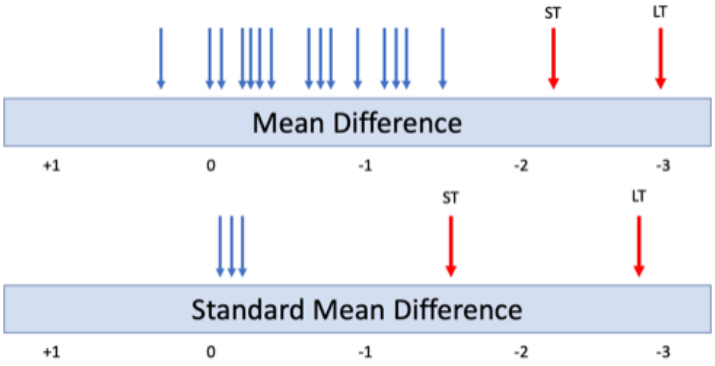
Dr Monticone responded that he would prefer not to provide us with access to full IPD. He stated that the large effect sizes "*were due to the specific characteristics of the CBT group. Indeed, relevant efforts were made in order to strongly improve patients 'health conditions. This is also demonstrated by the between-group clinical differences achieved as well as by the level of satisfaction found in CBT groups*." No further explanation was offered.

**Comparing effect sizes from included studies with those of other interventions for chronic pain, using SMD and MD**

Supplementary Table 2 shows 10 systematic reviews with 14 interventions, mainly reporting MDs using a 0-10 pain measure. Interventions include NSAIDs, antidepressants, anticonvulsants, cannabinoids, opioids, psychological therapies, acupuncture, magnetic stimulation, and therapeutic ultrasound. Pain conditions include chronic pain, low back pain, osteoarthritis and rheumatoid arthritis, fibromyalgia, and neuropathic pain. Most reported outcomes were compared with placebo at around three months, but some after shorter times.

Results are shown graphically in Figure 7. The pooled effect size for the included studies is considerably greater than for any other intervention. Few interventions have a greater average effect size than that often considered a clinically important difference, approximately equivalent to a mean difference of -1.

**Figure 7: MD and SMD for a range of interventions for chronic pain (blue), and the pooled analysis of all Monticone chronic pain studies (red) post-intervention (ST) and at follow-up (LT). The more negative, the larger the effect size.**




**Comparing effect sizes from included studies with those of other interventions for chronic pain, using NNT**

As stated above, the  included trials show median reductions in pain intensity of 40% (ST) and 44% (LT) (Supplementary Figure 4). For placebo, average initial pain intensity of about 5.9/10 fell to 4.7 post-intervention and 4.6 at long-term follow-up. For patients receiving experimental treatment, the values were 5.9, 2.4, and 2.2, respectively; this average LT reduction by 63% implies than most patients would experience pain reduction of more than 50%.

Using the method proposed by Faraone [8], we converted SMD to number needed to treat (NNT). When the SMD = 1, the NNT = 2, but as the SMD approaches zero the NNT becomes very large, so an SMD of 0.5 becomes an NNT of about 5, and an SMD of 0.25 is equivalent to an NNT of above 15. The average SMD for the Monticone studies produces a NNT **below** 2.

A linear relationship between MD and NNT can be shown up to a MD of about 1.5 for NSAIDs in OA, equivalent to an NNT of about 4.5 [26] (see Supplementary Figure 5). It is not possible to predict

accurately the shape of the curve beyond that, but the average MD of 2.7 for all 10 Monticone trials could plausibly imply NNTs of 2 or below. This level of effectiveness is highly unusual. There are almost no examples of NNT values for chronic pain interventions of any sort that are below 3 or even 4.

**Data duplication/ similarity**

There was no consistent evidence of large-scale data duplication across the included trials (see Supplementary Table 3). However, there were specific examples of identical or similar data, and Figure 8 shows tables from three publications with highlighted key examples of identical, or highly similar, data.

For baseline variables, most cases of similar or identical numbers arose from categorical variables with very low numbers (for example the number of participants taking specific types of medication) which might reasonably be expected to occur through chance. However, there were striking cases of similarity between outcome data in a trial (n = 150) published in 2016 in patients with chronic low back pain [19] and two trials published in 2020 and 2021 (both n = 150) in patients with failed back surgery syndrome and subacute low back pain, respectively [23,24]. In his response, Dr Monticone reported "*I checked the tables and you are right as for the NRS, the ODI and the TSK. I was surprised but these are the data the staff collected. I think that values on catastrophizing differ, because I used another scale in my 2021 paper (the CSQ-R).*"

**Figure 8. Examples of identical and highly similar data in the results of three included trials (table excerpts copied with permission).** *Footnotes: Red shading = identical data; orange shading = highly similar data*

Monticone 2016a

**Table 2** Changes over time within and between the control and experimental group ($n$ = 150)

| | Group | Pre-training* | Post-training* | 12M Follow-up* | 24M Follow-up* | |
|---|---|---|---|---|---|---|
| Primary outcome | | | | | | |
| ODI (0–100) | Experimental | 34.4 (4.6) | 15.5 (4.8) | 11.9 (3.8) | 15.0 (3.6) | |
| | Control | 32.4 (5.4) | 25.3 (5.5) | 27.7 (6.4) | 30.0 (6.0) | |
| Secondary outcomes | | | | | | |
| TSK (13–52) | Experimental | 27.5 (4.7) | 17.6 (5.3) | 15.5 (4.8) | 14.4 (4.1) | |
| | Control | 28.5 (5.5) | 26.8 (5.9) | 29.6 (5.3) | 29.9 (4.3) | |
| PCS (0–52) | Experimental | 27.8 (4.6) | 12.7 (5.3) | 10.0 (5.1) | 11.4 (3.7) | |
| | Control | 26.4 (5.4) | 25.1 (5.0) | 26.7 (4.9) | 27.1 (4.7) | |
| NRS (0–10) | Experimental | 6.4 (1.7) | 1.4 (1.2) | 2.4 (1.5) | 2.8 (1.0) | |
| | Control | 6.1 (1.6) | 4.5 (1.8) | 4.2 (1.6) | 4.7 (1.6) | |

ODI, Oswestry Disability Index; TSK, Tampa Scale of Kinesiophobia; PCS, Pain Catastrophizing S

Monticone 2020

Table 2. Changes over time within and between the experimental and the control group in terms c

| | Group | Pre-training* | Post-training* | 12M Follow-up* | |
|---|---|---|---|---|---|
| Primary outcome | | | | | |
| ODI (0–100) ↓ | Exp | 51.4 (10) | 26.5 (5) | 17.2 (4.3) | |
| | Control | 48.9 (10.3) | 35.6 (5.2) | 30.4 (4.6) | |
| Secondary outcomes | | | | | |
| TSK (13–52) ↓ | Exp | 36.5 (4.7) | 17.7 (5.4) | 15.3 (4.6) | |
| | Control | 35 (4.6) | 26.7 (5.9) | 29.5 (5.3) | |
| PCS (0–52) ↓ | Exp | 34.6 (3.9) | 12.6 (5.3) | 10.8 (4.5) | |
| | Control | 32.8 (4.2) | 25.1 (5) | 26.6 (4.9) | |
| NRS (0–10) ↓ | Exp | 6.6 (1.5) | 3.2 (0.8) | 2.4 (1.5) | |
| | Control | 6.5 (1.4) | 5 (1.3) | 5.5 (1.2) | |

*mean value (standard deviation).
†Between-group change (95% confidential interval).
ODI: Oswestry Disability Index; TSK: Tampa Scale of Kinesiophobia; PCS: Pain Catastrophising Scale; N

Monticone2021

| | Group | Pre-training[a] | Post-training[a] | 12M Follow-up[a] | Change at post-training[b] | |
|---|---|---|---|---|---|---|
| **Primary outcome** | | | | | | |
| ODI (0-100) ↓ | Experimental | 23.9 (12.1) | 13.9 (6.2) | 11.9 (3.8) | 11.5 (1.0) | |
| | Control | 23.7 (13.6) | 25.3 (5.5) | 27.7 (6.4) | | |
| **Secondary outcomes** | | | | | | |
| NRS (0-10) ↓ | Experimental | 5.5 (2.2) | 1.4 (1.2) | 2.4 (1.5) | 3.1 (0.3) | |
| | Control | 4.8 (2.5) | 4.5 (1.8) | 4.2 (1.6) | | |
| TSK | | | | | | |

**Data anomalies/ errors**

Beyond the apparent duplication of data, we identified examples of anomalous or erroneous data. Specifically, there were two instances of reported baseline p values that did not match the

presented means/SDs [17,20]. These were the variables step length, step time, single support time (left and right) in Monticone 2014a [17], and all SRS-22 subscales for Monticone 2016b [20]. In these instances, baseline mean values/SDs between the treatment groups were identical to or differed by a maximum of one decimal place unit but the presented p value ranged from 0.161 to 0.884. In his response, Dr Monticone stated that he had "*checked again the data and they are OK as presented*".

**Attrition**

Levels of attrition varied across the included studies (median (range) 9% (0-17)) at the end of follow-up, but three trials [16,17,22] reported no attrition at any follow-up point. Of these, two were small trials [17,22] but one [16] randomised 90 participants, with a 12-month intervention followed up for 24 months. A further three trials reported < 10% attrition at 1-year follow-up [15,21,24]. We considered the trial with zero attrition at 24-month follow-up [16] to be at high risk on this item of the CPC-TST. While we did not rate the other trials at high risk on this item, it should be noted that < 10% attrition at 1-year follow-up might be considered unusual.

**Discussion**

We wished to confirm the conclusions of the Cochrane review of psychological interventions for chronic pain [34]. Given the divergence identified in the results of three trials led by Dr Monticone [16,19,21], we assessed a total of 10 trials from the same research group examining chronic spinal pain. Eight reported very large effect sizes for pain, disability and HRQoL for comparisons of CBT and physical rehabilitation versus physical rehabilitation alone. In context, these are about 20 times the standard effect size of the comparison 'CBT vs active care'. This level of effectiveness is highly unusual in a single trial, let alone a group of trials. Expressed as an NNT of 2 or below, they are not only outliers in comparison to other CBT trials but, if treated separately as a specific treatment, they would give the best NNTs ever recorded, a 'best in class' treatment compared with any other psychological, physical, rehabilitative, or pharmacological treatment examined in any chronic pain condition.

There are no data in the 10 published reports to suggest that the treatments in these 8 trials are more potent than the norm. There is no indication of any aspects of the experimental treatment uniquely different to the CBT and rehabilitation provided in other trials: staff training and experience, treatment content, intensity, and mode of delivery were unremarkable. Similarly, there are no obvious reasons from the published reports for the excellent participant retention data. Using the Cochrane Risk of Bias tool, the trials have a normal (for this field) RoB profile.

By contrast, the analysis of trustworthiness, using the CPC-TST tool, revealed several anomalies. First, on governance: none of the trials was pre-registered, despite the International Committee of Medical Journal Editors (ICMJE) requirement for pre-registration, in place since 2005. Pre-registration protects integrity and increases trustworthiness by requiring a record of core methodological features of the trial, changes from which after study completion require justification. Second, on randomisation: the distribution of p values deviated from that expected with simple randomisation, with a skew towards higher p values, indicating that baseline average scores were broadly more similar than might be expected from simple randomisation. This is reflected across all trials combined, and, for many individual trials, combining p values for each trial produced p values that deviated substantially from 0.5. Third, all studies achieved groups of exactly equal size post-randomisation despite only four trials reporting a block method for randomisation. Fourth, there were identical or highly similar outcome data reported in trials presented as independent trials. Transposition error is possible within trials but hard to understand between

different trial reports. Errors in reporting p values raised further concern. In conclusion, data error, data similarity (or duplication), randomisation oddity, and p-value error, coupled with a failure to pre-register, are likely contributors to explaining the extreme positivity of these data. Dr Monticone has not shared evidence of ethical approval or IPD with us to allow independent scrutiny of these results. We did not consider that his responses to specific queries regarding randomisation, duplicate and highly similar data, or anomalous baseline p values adequately explained the issues raised. Overall, based on this analysis, we judge these trial data to be untrustworthy.

Our focus is on the reports of trials appearing in peer-reviewed scientific publications. We have no data on which to comment on the conduct or integrity of individual investigators. Data fabrication and alteration have occurred previously in pain research. In some cases, the evidence has been overwhelming, as in the cases of anaesthesia researchers Yoshitaka Fujii, Joachim Boldt, and others [1,4,14,35]. In other cases, the overall patterns of data put any natural explanation out of reach, leaving reasonable doubt about investigator conduct. None of the included trials were published in journals suspected or presumed to be "predatory" in nature (see Supplementary Table 4). Hayden et al. [10] recently explored aspects of publication integrity in a large cohort of clinical trials of exercise for low back pain. They found a growing number of trials published in presumed predatory journals. While publication in a predatory journal was not associated with reported outcomes, it was associated with a range of quality, reporting and integrity issues. Our results suggest that there is a need to carefully scrutinise trials in more trusted publications.

The scale of the problem of untrustworthy trials in pain is unknown. In a systematic review of surveys of researchers, 2% of researchers across scientific disciplines admitted to fabricating, falsifying or modifying data at least once themselves, and 14% believed that colleagues had falsified data [7]. In Norway, < 1% of researchers admit fabrication, falsification and plagiarism, but 40% admit questionable research practices [13]. As a community, we need to establish clearer routines of looking beyond bias to broader questions about the trustworthiness of evidence; one cofounder of the Committee on Publication Ethics and former BMJ editor, Richard Smith, suggested that we have reached the point where systematic reviewers should start by assuming that a study is fraudulent until they have evidence to the contrary [31]. "*A lot of what is published is incorrect*" (p1380) [12], and inclusion of untrustworthy studies in systematic reviews is not a trivial matter.

In current scientific editorial practice, where automatic integrity checks are not the norm, evaluating and raising concerns regarding the trustworthiness of studies lie in the hands of individual editors, peer reviewers, the broader research and clinical community, and initiatives such as Retraction Watch. Formal mechanisms and validated processes are currently lacking. Here we have used one of the developing approaches, strongly informed by the work of the Cochrane Pregnancy and Childbirth review group [6]. That group now applies its screening tool routinely to all trials identified in their systematic reviews, excluding from subsequent analyses trials considered to present any concerns. While there is some risk of losing potentially valuable evidence, such an approach would reduce the risk of reviews being distorted by untrustworthy data and should be actively considered. We might start by making pre-registration a prerequisite for the inclusion of trials in systematic reviews.

We conducted our review using a formal protocol published on the Open Science Framework [28]. It has some limitations. No available tools for exploring research integrity or trustworthiness have been formally validated and we selected the CPC-TST on the basis of face validity and perceived usability for the type of trials. In using Stouffer's method to combine p values, we acknowledge that the assumption of independence between pooled values is unlikely to be met for all variables and that this may have contributed to the observation of extreme combined p values. However, it does

not adequately explain the peak of p values of 1.0 in the observed distribution. We did not conduct further sensitivity analyses to explore correlations and exclude correlated variables. This is due to the lack of power in any such analyses and the issues it would raise as regards multiple testing. We focused on a sample of trials from a single author group evaluating similar interventions in similar patient groups. Our reasons for this were based on the prior observation of consistently extreme results in three trials from that group. This led us to consider whether this represented a broader pattern observable from other trials published from that group. We have not applied the same assessment to the broader evidence base on this topic or to other trials from this author group for conditions other than persistent spinal pain.

In summary, the results of eight of the included trials are highly divergent from norms in the evidence base for psychological therapies for persistent pain. Replication of these results outside a single institution would represent a substantial advance for pain medicine and very good news for patients living with pain. However, we have not found satisfactory plausible explanations for that divergence in either the details of the interventions themselves or how they were delivered, nor has reporting error been retrospectively declared. Our exploration of these studies has raised concerns in specific cases regarding trustworthiness, particularly relating to research governance and to the plausibility, integrity and accuracy of the data. Possible explanations for the latter include error, data manipulation, or data fabrication. Taken together or alone, we have no confidence in the veracity of these trial results and assert that these studies should be excluded from evidence syntheses on this topic and from clinical practice guidelines.

**Acknowledgements**

We would like to thank Professor Ben Mol for sharing early versions of the Cochrane Pregnancy and Childbirth TST**.**

**Declarations of interest**

NOC: None known.

RAM: None known.

AW: AW was an author on the most recent update of the Williams review [21]

EF: EF is funded by Versus Arthritis and was an author on the most recent update of the Williams review [21]. EF has no other declarations of interest in relation to this manuscript.

LH: None known; LH was an author on the most recent update of the Williams review [21]

GS: None known

AE: None known

CE: CE was an author on the most recent update of the Williams review [21]

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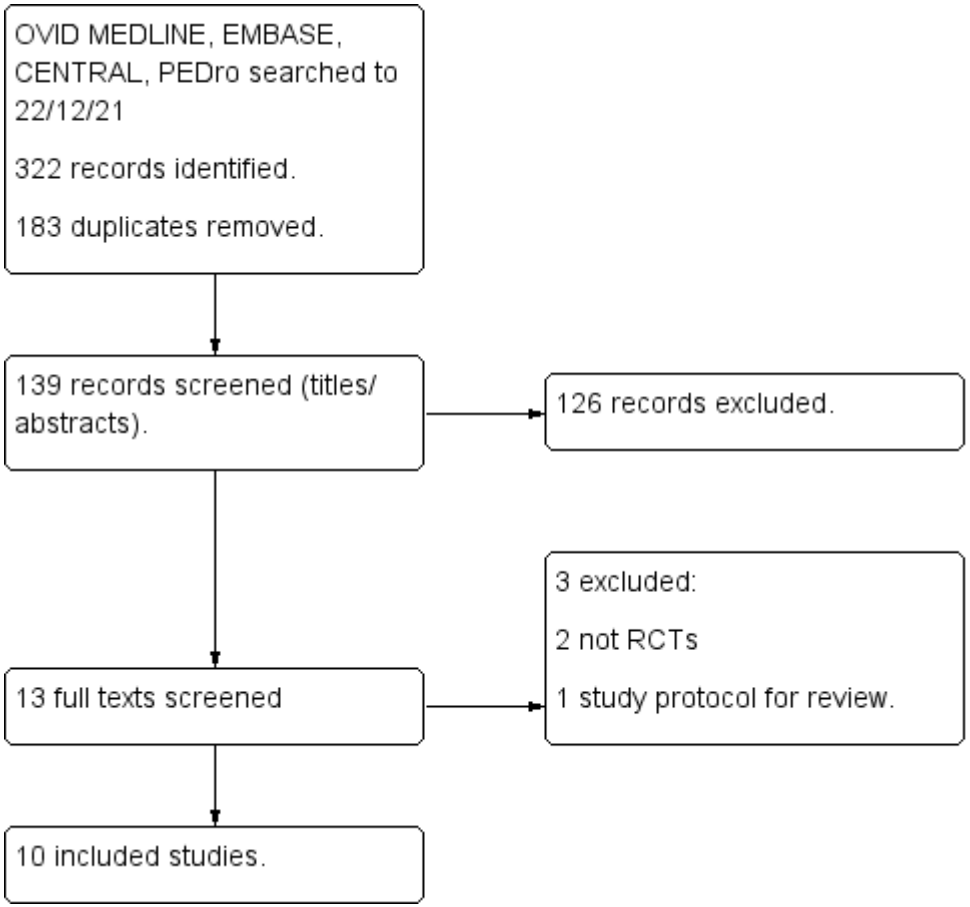
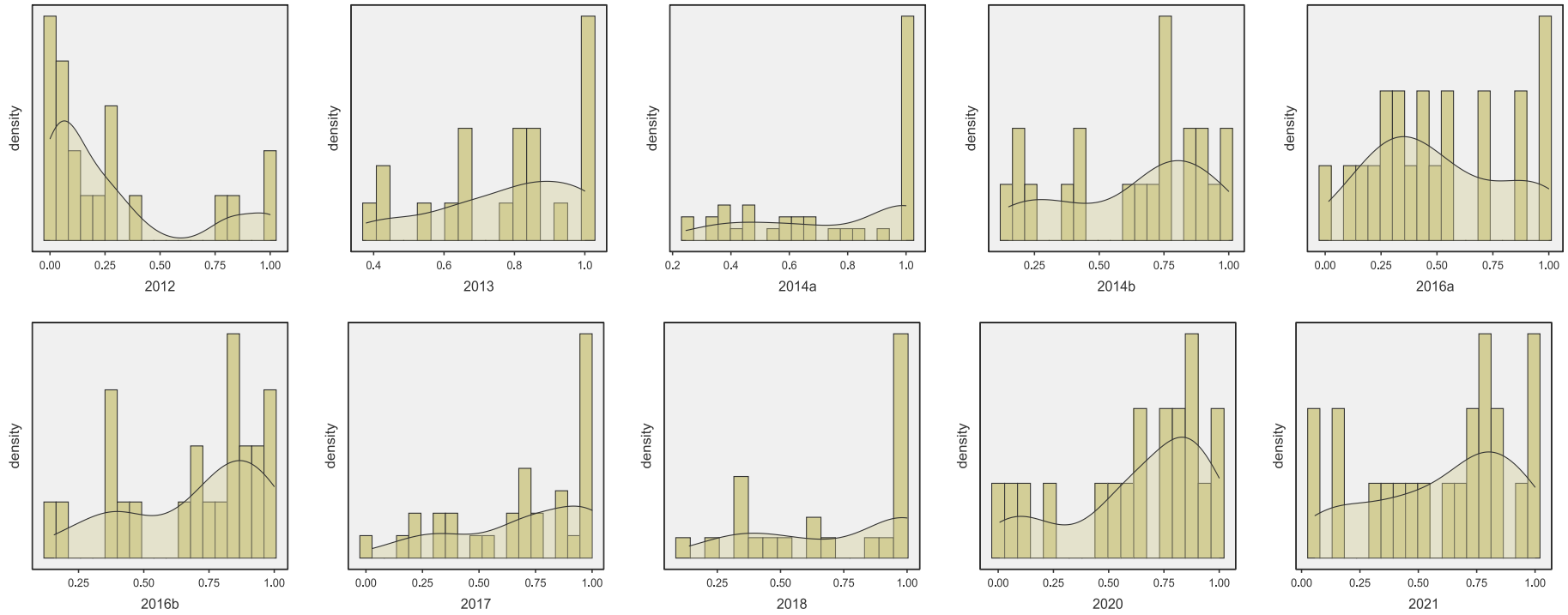
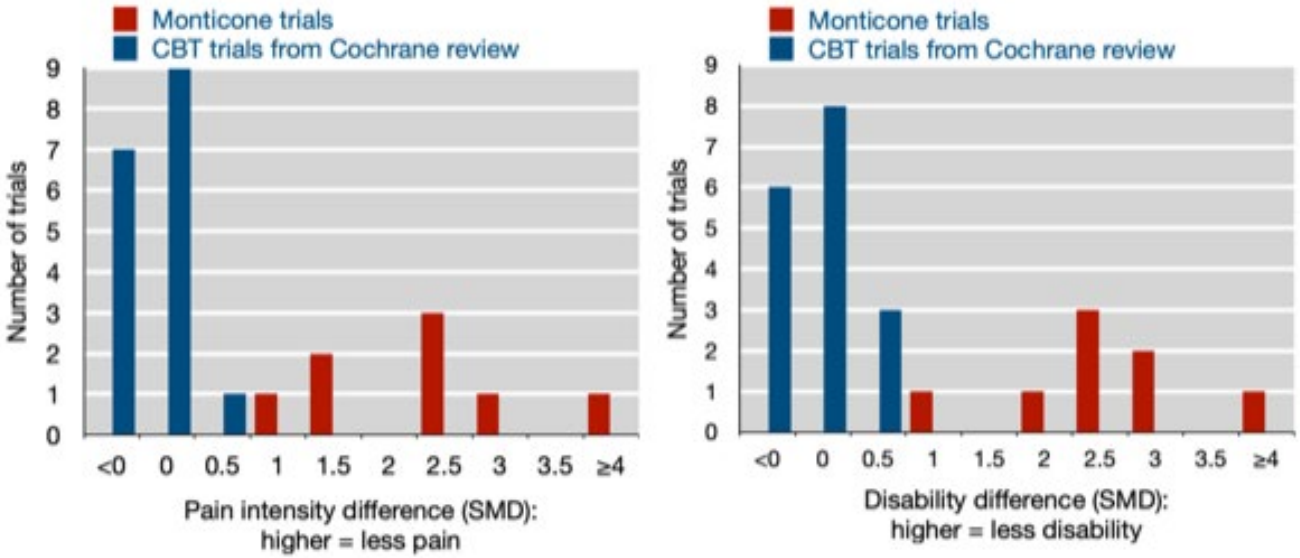
**Supplementary Figure 1: PRISMA flow diagram of the search process.**



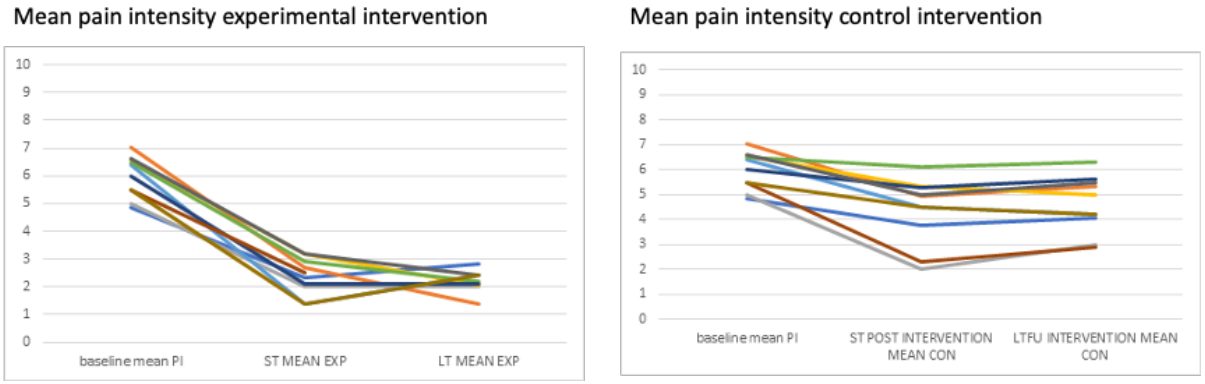
**Supplementary Figure 2: The distribution of baseline p values (continuous and categorical) for each included trial.**



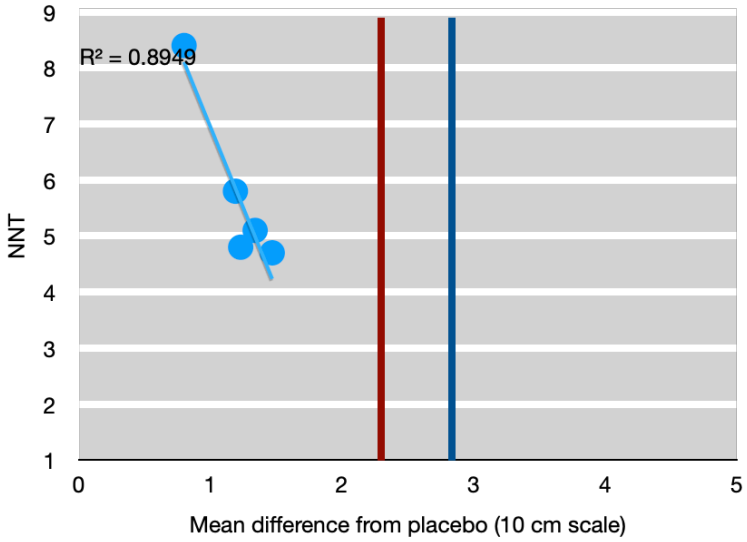
**Supplementary Figure 3: SMD values for pain and disability in from studies in the Cochrane review analysis "CBT vs Active care". The included studies are represented in red and all other studies in the analysis in blue.**



**Supplementary Figure 4. Mean pain intensity values from each trial, at baseline, at short term post intervention, and at long term follow up.**



**Supplementary Figure 5: The relationship between MD and NNT for NSAIDs in OA. Monticone short term follow up is shown as the red line, and the long term follow up as the blue line.**



**Supplementary Table 1. Baseline characteristics (mean (SD)) for pain intensity, disability and health related quality of life for each included spinal pain study contrasted with published norms (first column, from Nicholas 2008).**

| | LOW BACK NORMS | MONTICONE 2013 | MONTICONE 2014 | MONTICONE 2014D (fusion) | MONTICONE 2016a | MONTICONE 2016b | MONTICONE 2020 (FBSS) | MONTICONE 2021a |
|---|---|---|---|---|---|---|---|---|
| **PAIN NRS** | 4.2 (1) | 7.02 (1.07) | 5 (3) | 6.57 (1.67) | 6.4 (1.7) | 6.5 (1.2) | 6.6 (1.5) | 5.5 (2.2) |
| **DISABILITY RMDQ** | 13.5 (5.2) | 15.27 (2.94) | NA | NA | NA | NA | NA | NA |
| **PHYS FUNCTION SF-36** | 43.5 (25.7) | 47.22 (27.25) | 41 (7) | 32.31 (21.12) | 51.5 (10) | NA | 28.9 (12) | NA |
| **ROLE FUNCTION SF-36** | 13.6 (27.8) | 29.44 (35.47) | 38 (18) | 26.54 (34.48) | 42.3 (15.9) | NA | 19.3 (17.7) | NA |
| **SOCIAL FUNCTION SF-36** | 42 (27.3) | 50.83 (18.34) | 60 (10) | 50.58 (13.70) | 54.3 (11.5) | NA | 41 (19) | NA |
| **VITALITY SF-36** | 36.1 (20.7) | 52 (16.93) | 54 (12) | 47 (22.37) | 54.2 (15.6) | NA | 34.9 (17.8) | NA |
| **ROLE FUNCTION EMOTIONAL SF-36** | 43.7 (44) | 39.26 (25.02) | 47 (17) | 32.82 (33.06) | 44.9 (18.6) | NA | 43.1 (21.1) | NA |
| **MENTAL HEALTH SF-36** | 56.2 (20.5) | 50.13 (11.55) | 59 (10) | 48.35 (13.85) | 51.3 (11.6) | NA | 51.3 (11.6) | NA |
| **FEAR AVOIDANCE TSK** | 41.4 (8.8) | 41.67 (4.60) | 29 (7) | 29.63 (6.41) | 27.5 (4.7) | NA | 36.5 (4.7) | 29.7 (5.9) |
| | **NECK PAIN NORMS** | **MONTICONE 2012** | **MONTICONE 2017** | **MONTICONE 2018** | | | | |
| **PAIN NRS** | 4.1 (1.2) | 4.84 (2.72) | 6 (1) | 5.5 (1.6) | | | | |
| **DISABILITY RMDQ** | 10.4 (5.1) | NA | NA | NA | | | | |
| **PHYS FUNCTION SF-36** | 45.6 (23.7) | 73.80 (21.21) | 49.4 (10.2) | NA | | | | |
| **ROLE FUNCTION SF-36** | 15.8 (29.8) | 55.31 (36.42) | 41.2 (15.3) | NA | | | | |
| **SOCIAL FUNCTION SF-36** | 41.1 (25.1) | 65.08) (22.18) | 55.4 (12.7) | NA | | | | |
| **VITALITY SF-36** | 35.7 (20.5) | 52.43 (15.73) | 54.7 (15.8)) | NA | | | | |
| **ROLE FUNCTION EMOTIONAL SF-36** | 45.7 (43.3) | 65.17 (39.18) | 46.3 (16.3) | NA | | | | |
| MENTAL HEALTH SF-36 | 53.2 (21.3) | 64.13 (18.62) | 51.3 (11.8) | NA | | | | |
| FEAR AVOIDANCE TSK | 41.5 (10.1) | NA | 28 (7.6) | 27.9 (5.7) | | | | |
| | | | | | | | | |

**Supplementary Table 2. Effect sizes from selected systematic review of interventions for chronic pain.**

| | | | | |
|---|---|---|---|---|
| van Walsem A, Pandhi S, Nixon RM, Guyot P, Karabis A, Moore RA. Relative benefit-risk comparing diclofenac to other traditional non-steroidal anti-inflammatory drugs and cyclooxygenase-2 inhibitors in patients with osteoarthritis or rheumatoid arthritis: a network meta-analysis. Arthritis Res Ther. 2015 Mar 19;17(1):66. doi: 10.1186/s13075-015-0554-0. PMID: 25879879; PMCID: PMC4411793. | OA/RA | Diclofenac 150 mg vs placebo<br>12 weeks | -1.2<br>(-1.7 to -0.7) | |
| Moore RA, Moore OA, Derry S, Peloso PM, Gammaitoni AR, Wang H. Responder analysis for pain relief and numbers needed to treat in a meta-analysis of etoricoxib osteoarthritis trials: bridging a gap between clinical trials and clinical practice. Ann Rheum Dis. 2010 Feb;69(2):374-9. doi: 10.1136/ard.2009.107805. Epub 2009 Apr 12. PMID: 19364730; PMCID: PMC2800200. | OA | Etoricoxib 60 mg vs placebo<br>12 weeks | -1.5 | |
| | | Naproxen 1000 mg vs placebo<br>12 weeks | -1.2 | |
| | | Celecoxib 200 mg vs placebo<br>12 weeks | -1.2 | |
| | | Ibuprofen 2400 mg vs placebo<br>12 weeks | -0.8 | |
| Lunn MP, Hughes RA, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database Syst Rev. 2014 Jan 3;(1):CD007115. doi: 10.1002/14651858.CD007115.pub3. PMID: 24385423. | PDN | Duloxetine 120 mg vs placebo<br>12 weeks | -0.93<br>[-1.21, -0.65] | |
| | Fibromyalgia | Duloxetine 120 mg vs placebo<br>12 weeks | -0.80<br>[-1.35, -0.25] | |
| Williams ACC, Fisher E, Hearn L, Eccleston C. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev. 2020 Aug 12;8(8):CD007407. doi: 10.1002/14651858.CD007407.pub4. PMID: 32794606; PMCID: PMC7437545. | Chronic non cancer pain | Psychological therapies vs control<br>Post intervention | | -0.09<br>[-0.17 , -0.01] |
| | | At follow up | | -0.08<br>[-0.19, 0.04] |
| Mu J, Furlan AD, Lam WY, Hsu MY, Ning Z, Lao L. Acupuncture for chronic nonspecific low back pain. Cochrane Database Syst Rev. 2020 Dec 11;12(12):CD013814. doi: 10.1002/14651858.CD013814. PMID: 33306198; PMCID: PMC8095030. | Chronic low back pain | Acupuncture vs sham<br>4-12 months | -0.04<br>[-0.07, -0.01] | |
| Enke O, New HA, New CH, Mathieson S, McLachlan AJ, Latimer J, Maher CG, Lin CC. Anticonvulsants in the treatment of low back pain and lumbar radicular pain: a systematic review and meta-analysis. CMAJ. 2018 Jul 3;190(26):E786-E793. doi: 10.1503/cmaj.171333. PMID: 29970367; PMCID: PMC6028270. | Chronic low back and radicular pain | Gabapentinoids vs placebo<br>3-12 months | −0.1<br>(−1.4 to 1.2) | |
| Fisher E, Moore RA, Fogarty AE, Finn DP, Finnerup NB, Gilron I, Haroutounian S, Krane E, Rice ASC, Rowbotham M, Wallace M, Eccleston C. Cannabinoids, cannabis, and cannabis-based medicine for pain management: a systematic review of randomised controlled trials. | Neuropathic pain | Cannabinoids vs placebo<br>>4 weeks | -0.31<br>(-0.65 to 0.03) | |

| | | | | |
|---|---|---|---|---|
| Pain. 2021 Jul 1;162(Suppl 1):S45-S66. doi: 10.1097/j.pain.0000000000001929. PMID: 32804836. | | | | |
| Lange B, Kuperwasser B, Okamoto A, Steup A, Häufel T, Ashworth J, Etropolski M. Efficacy and safety of tapentadol prolonged release for chronic osteoarthritis pain and low back pain. Adv Ther. 2010 Jun;27(6):381-99. doi: 10.1007/s12325-010-0036-3. Epub 2010 Jun 11. Erratum in: Adv Ther. 2010 Dec;27(12):981. PMID: 20556560. | Chronic low back pain and OA | Tapentadol vs placebo<br>3 months | -0.31<br>(-0.7 to -0.1) | |
| | | Oxycodone vs placebo<br>3 months | 0.3<br>(0.1 to 0.5) | |
| O'Connell NE, Marston L, Spencer S, DeSouza LH, Wand BM. Non-invasive brain stimulation techniques for chronic pain. Cochrane Database Syst Rev. 2018 Apr 13;4(4):CD008208. doi: 10.1002/14651858.CD008208.pub5. PMID: 29652088; PMCID: PMC6494527. | Chronic pain | Transcranial magnetic stimulation vs sham<br>Up to 1 week | -0.40<br>(-0.5 to -0.3) | -0.22<br>(0.29 to -0.16) |
| Ebadi S, Henschke N, Forogh B, Nakhostin Ansari N, van Tulder MW, Babaei-Ghazani A, Fallah E. Therapeutic ultrasound for chronic low back pain. Cochrane Database Syst Rev. 2020 Jul 5;7(7):CD009169. doi: 10.1002/14651858.CD009169.pub3. PMID: 32623724; PMCID: PMC7390505. | Chronic low back pain | Therapeutic ultrasound vs placebo<br>Short term | −0.7,<br>(−1.8 to 0.4) | |

**Supplementary table 3. The number of identical or similar data in the baseline and outcomes data of all spinal pain trials.**

**Identical match (includes identical SDs)**

**≤1 whole number difference (means/ counts, not SDs)**

| | | | Baseline data | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Study ID | | | | | | | | | |
| | | | 2012 | 2013 | 2014a | 2014b | 2016a | 2016b | 2017 | 2018 | 2020 | 2021 |
| Outcome data | Study ID | 2012 | | 8 | 2 | 1, 1 | 2 | 4 | 4 | 4 | 5 | 3 |
| | | 2013 | 6 | | 2 | 5 | 3 | 7 | 7, 2 | 1 | 3 | 0 |
| | | 2014a | 4 | 2 | | 4, 1 | 5 | 1 | 10, 1 | 15, 11 | 2 | 6 |
| | | 2014b | 3 | 4 | 4 | | 2, 1 | 5 | 2 | 6, 8 | 5 | 3 |
| | | 2016a | 7 | 6 | 8 | 5 | | 4 | 12 | 3 | 4, 4 | 3 |
| | | 2016b | 2 | 2 | 2 | 3 | 1 | | 12, 3 | 2,1 | 1 | 1 |
| | | 2017 | 3 | 7 | 8 | 9 | 11 | 4 | | 6, 3 | 7, 1 | 5 |
| | | 2018 | 2 | 2 | 4 | 3 | 2 | 2 | 2 | | 0 | 2, 1 |
| | | 2020 | 6 | 5 | 4 | 6 | 15, 1 | 5 | 7, 1 | 4 | | 1 |
| | | 2021 | 4 | 1 | 3 | 5 | 2, 13 | 2 | 5 | 2 | 2, 2 | |

**Supplementary table 4. The journals and publishers for each included trial, and judgements on whether they are considered predatory.**

| Study ID | Journal | Publisher | Presumed Predatory? |
|---|---|---|---|
| Monticone 2012 [15] | European Spine Journal | Springer-Verlag | N |
| Monticone 2013 [16] | Clinical Journal of Pain | Lippincott-Williams and Wilkins | N |
| Monticone 2014a [17] | European Spine Journal | Springer-Verlag | N |
| Monticone 2014b [18] | European Spine Journal | Springer-Verlag | N |
| Monticone 2016a [19] | European Journal of Pain | Wiley Online | N |
| Monticone 2016b [20] | European Spine Journal | Springer-Verlag | N |
| Monticone 2017 [21] | Clinical Rehabilitation | Sage | N |
| Monticone 2018 [22] | European Journal of Physical and Rehabilitation Medicine | Minerva Medica | N |
| Monticone 2020 [23] | Disability and Rehabilitation | Taylor and Francis | N |
| Monticone 2021 [24] | European Journal of Physical and Rehabilitation Medicine | Minerva Medica | N |

**Supplementary data: correspondence with Dr Monticone and co-authors during Cochrane 2020 update review.**

**Date:** 17 May 2019

**From:** Amanda C de C Williams

**To:** Dr Rocca,

Dear Dr Rocca

Several colleagues and I are updating our systematic review and meta-analysis of psychologically-based treatments for pain. We are including three papers with the first author Marco Monticone, from 2013, 2016, and 2017. I believe that you were the psychologist delivering treatment in these trials: please tell me if this is not correct.

When we extracted data from all trials, we found that these three were extreme outliers: that the results are very substantially better than the other 76 trials in the meta-analysis. My colleague Professor Christopher Eccleston wrote to Dr Monticone to ask if he understood why this was the case.

He replied

*a) why the results were so very different than others?*
*--Concerning the paper published in the Clin J Pain (CLBP), the key factor was probably the psychological intervention, which may have cognitively modified the patients' subjective perception of being disabled. They became more comfortable with their usual activities after readjusting their beliefs about the possibility of performing them despite the pain, and this enhanced their positive attitude toward the exercises and increased physical performance. A further improvement in disability was observed at the end of the treatment period, and very satisfactory levels were maintained until the end of the 1-year follow-up: this was probably attributable to the monthly meetings that the patients had for a year with the psychologist; this trend also confirmed the positive effects of the telephone reminders from staff aimed at improving treatment adhesion during the reinforcement phase, as well as the close involvement of the psychologist, family doctors and relatives, who greatly supported patient compliance and clinical progress during the course of the study. Similar explanations for pain perception and quality of life can be done. Moreover, the presence of a well-integrated and coordinated multidisciplinary team of physiatrists, a psychologist, and physiotherapists (highly specialized in CLBP management), who concordantly contributed toward achieving treatment goals favored the goals.*

*--Concerning the paper published in the Eur J Pain (CLBP), the use of task-oriented exercises may have added value in enhancing functional outcomes as well as a faster return to usual activities. Moreover, adopting a CBT mainly aimed at addressing fear-avoidance beliefs proved to be a successful strategy even*

*when groupbased, additionally offering the opportunity for peer-group support and encouragement as well as for decentring and challenging beliefs and cognitions. Overall, multidisciplinary, deeply detailed and well-conducted functional and psychological interventions probably represented the key factor supporting our findings. Similar explanations for pain perception, psychological variables, and quality of life can be done. Evaluation of the perceived global effects also demonstrated higher levels of treatment satisfaction in the experimental group.*

*--Concerning the paper published in Clin Rehabil (NP), the study overcomes some of the methodological shortcomings of previous trials in this area. Furthermore, our programme was systematic and comprehensive, as well as being theory-driven: it was based on a precise and well-established model of change, including both physical and psychological components, linking specific cognitive modifications (fear avoidance) to definite outcomes (disability, kinesiophobia and catastrophizing); it included graded and very detailed task-oriented exercises in addition to CBT, which may have contributed to enhancing functional outcomes, as well as a faster return to usual activities. As well, it was characterized by a longer duration to increase the likelihood of long-lasting improvements. These strategies induced positive attitudes toward active exercises and graded recovery of physical performance. Similar explanations for pain perception, psychological variables, and quality of life can be done. Finally, the perceived global effects also demonstrated better levels of treatment satisfaction in the multidisciplinary group. This was favoured by the presence of a well-integrated multidisciplinary team who, concordantly, contributed towards treatment goals.*

*b) why no patient appeared to drop out of treatment?*
*This issue pertains only to the paper published in the Clin J Pain. Remarkably, there were no drop-outs from either group during the 2 years of the study, which suggests that the patients were highly motivated and determined to adhere to all of the phases of treatment. The key role of the psychologist, the monthly telephone reminders by the physiotherapists, and the support of family doctors and relatives probably played a crucial role in establishing a controlled and protected situation.*

This is helpful, but does not differ sufficiently from other high quality programmes to explain the very large changes in the intervention group, and the very low attrition.

I wondered if you had a protocol I could read, or a description of the programme, or whether we might speak on skype? It would really help us to interpret this difference in the published review.

Kind regards

Amanda

**Date:** 13 May 2019 at 16:50:31 BST

**From:** Marco Monticone
**To:** Chris Eccleston

**Subject: Re: Cochrane update of 'Psychological therapies for the management of chronic pain (excluding headache) in adults'**

Dear Prof. Eccleston,
please find below some explanations concerning your issues that can be used in order to explain our findings.
Thanks you, kind regards,
Marco Monticone

a) why the results were so very different than others?
Concerning the paper published in the Clin J Pain (CLBP), the key factor was probably the psychological intervention, which may have cognitively modified the patients' subjective perception of being disabled. They became more comfortable with their usual activities after readjusting their beliefs about the possibility of performing them despite the pain, and this enhanced their positive attitude toward the exercises and increased physical performance. A further improvement in disability was observed at the end of the treatment period, and very satisfactory levels were maintained until the end of the 1-year follow-up: this was probably attributable to the monthly meetings that the patients had for a year with the psychologist; this trend also confirmed the positive effects of the telephone reminders from staff aimed at improving treatment adhesion during the reinforcement phase, as well as the close involvement of the psychologist, family doctors and relatives, who greatly supported patient compliance and clinical progress during the course of the study. Similar explanations for pain perception and quality of life can be done. Moreover, the presence of a well-integrated and coordinated multidisciplinary team of physiatrists, a psychologist, and physiotherapists (highly specialized in CLBP management), who concordantly contributed toward achieving treatment goals favored the goals.

Concerning the paper published in the Eur J Pain (CLBP), the use of task-oriented exercises may have added value in enhancing functional outcomes as well as a faster return to usual activities. Moreover, adopting a CBT mainly aimed at addressing fear-avoidance beliefs proved to be a successful strategy even when groupbased, additionally offering the opportunity for peer-group support and encouragement as well as for decentring and challenging beliefs and cognitions. Overall, multidisciplinary, deeply detailed and well-conducted functional and psychological interventions probably represented the key factor supporting our findings. Similar explanations for pain perception, psychological variables, and quality of life can be done. Evaluation of the perceived global

effects also demonstrated higher levels of treatment satisfaction in the experimental group.
Concerning the paper published in Clin Rehabil (NP), the study overcomes some of the methodological shortcomings of previous trials in this area. Furthermore, our programme was systematic and comprehensive, as well as being theory-driven: it was based on a precise and well-established model of change, including both physical and psychological components, linking specific cognitive modifications (fear avoidance) to definite outcomes (disability, kinesiophobia and catastrophizing); it included graded and very detailed task-oriented exercises in addition to CBT, which may have contributed to enhancing functional outcomes, as well as a faster return to usual activities. As well, it was characterized by a longer duration to increase the likelihood of long-lasting improvements. These strategies induced positive attitudes toward active exercises and graded recovery of physical performance. Similar explanations for pain perception, psychological variables, and quality of life can be done. Finally, the perceived global effects also demonstrated better levels of treatment satisfaction in the multidisciplinary group. This was favoured by the presence of a well-integrated multidisciplinary team who, concordantly, contributed towards treatment goals.

b) why no patient appeared to drop out of treatment?
This issue pertains only to the paper published in the Clin J Pain. Remarkably, there were no drop-outs from either group during the 2 years of the study, which suggests that the patients were highly motivated and determined to adhere to all of the phases of treatment. The key role of the psychologist, the monthly telephone reminders by the physiotherapists, and the support of family doctors and relatives probably played a crucial role in establishing a controlled and protected situation.

---

**Date:** 8 May 2019

**From:** Chris Eccleston

**To:** Marco Monticone

Dear Professor Monticone

Thank you for your email in reply. We will, in the analyses, take account of variability (heterogeneity) in both sample and intervention. There do not appear to be any major differences from other approaches. Typically treatment description is poor in this field, hence the request for any information you might be able to add as to a) why the results were so very different than others, and b) why no patient appeared to drop out of treatment.

Cochrane reviews are 'live' documents, and when published you will have the opportunity to write comment on our approach in the feedback section.

However, any further rationale or explanation you can give as to the difference of your results from others in the field would be helpful.

Chris

**Date:** 7 May 2019

**From:** Marco Monticone

**To:** Christopher Eccleston

Sent: 07 May 2019 09:18

Subject: Re: Cochrane update of 'Psychological therapies for the management of chronic pain (excluding headache) in adults'

Dear Prof. Eccleston,

thanks for the message and the interest in our papers. We are happy to contribute to the Discussion, if needed. For instance, we wonder if there are differences in the treatment delivered as well as in the baseline characteristics of the subjects involved.

Kind regards,

Marco Monticone, MD, PhD

**Date:** 29 April 2019

**From:** Chris Eccleston:

**To:** Marco Monticone

Dear Professor Monticone

Re: Cochrane Systematic Review: “Psychological therapies for the management of chronic pain (excluding headache) in adults”. The protocol for the update can be found here:

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD007407/ful

We are currently updating this Cochrane systematic review. In the process we have identified three trials from your group that meet the inclusion criteria.

* Monticone M, Ferrante S, Rocca B, Baiardi P, Dal Farra F, Foti C. Effect of a long-lasting multidisciplinary program on disability and fear-avoidance behaviors in patients with chronic low back pain: results of a randomized controlled trial. Clinical Journal of Pain 2013;29(11):929-38.

* Monticone M, Ambrosini E, Rocca B, Cazzaniga D, Liquori V, Foti C. Group-based task-oriented exercises aimed at managing kinesiophobia improved disability in chronic low back pain. European Journal of Pain 2016;20:541-51.

* Monticone M, Ambrosini E, Rocca B, Cazzaniga D, Liquori V, Pedrocchi A, et al. Group-based multimodal exercises integrated with cognitive-behavioural therapy improve disability, pain and quality of life of subjects with chronic neck pain: a randomized controlled trial with one-year follow-up. Clinical Rehabilitation 2017;31(6):742-52.

We extracted data from papers and entered them into separate analyses with the endpoints: pain intensity, distress, and disability at different timepoints and with different comparisons.

In all analyses in which we included your studies, the data from your studies are extreme outliers, in that they were more than 3 standard deviations different from the means calculated in the other studies (n=14-22). We have discussed how to manage these data and decided that we will a) include the studies in our review, b) exclude the data from the main analyses and reporting of the findings, c) add a post-hoc analysis with the data from your studies included, to show the effect of their inclusion on the results.

It is unlikely that we will include an extensive discussion of your studies but if there is any contextual information you can give us as to why the data are such strong outliers, that would be very helpful to us, as we will need to give an explanation in the discussion.

Thank you for your consideration in this matter.

Yours sincerely

Christopher Eccleston

**Text of email sent to Dr Monticone on 1/12/21 from this review team (with reminder sent 6/1/22).**

Dear Dr Monticone,

We are a group of researchers based in the UK with an interest in the evidence-based management of spinal pain. You will remember that some of our team corresponded with you regarding three trials published by your team during the development of the Cochrane review “Psychological therapies for the management of chronic pain (excluding headache) in adults” (Cochrane Database of Systematic Reviews 2020, Issue 8. Art. No.: CD007407. DOI:10.1002/14651858.CD007407.pub4 (attached).

The results of those three studies diverged substantially from those of most studies in this field, as is clear from the analyses in the review. In order to understand why, we are currently taking a systematic approach to examining these studies and similar studies in persistent pain published by your group. It would be of enormous help if you were able to provide access to some key study data.

Our questions and requests relate to the following trials:

| Study identifier | Reference | DoI |
|---|---|---|
| 2013 | Monticone M, Ferrante S, Rocca B, Baiardi P, Dal Farra F, Foti C. Effect of a long-lasting multidisciplinary program on disability and fear-avoidance behaviors in patients with chronic low back pain: results of a randomized controlled trial. Clin J Pain. 2013 Nov;29(11):929-38 | 10.1097/AJP.0b013e31827fef7e |
| 2014a | Monticone M, Ambrosini E, Rocca B, Magni S, Brivio F, Ferrante S. A multidisciplinary rehabilitation programme improves disability, kinesiophobia and walking ability in subjects with chronic low back pain: results of a randomised controlled pilot study. Eur Spine J. 2014 Oct;23(10):2105-13 | 10.1007/s00586-014-3478-5 |

| | | |
|---|---|---|
| 2014b | Monticone M, Ferrante S, Teli M, Rocca B, Foti C, Lovi A, Brayda Bruno M.Management of catastrophising and kinesiophobia improves rehabilitation after fusion for lumbar spondylolisthesis and stenosis. A randomised controlled trial. Eur Spine J. 2014 Jan;23(1):87-95 | 10.1007/s00586-013-2889-z |
| 2016a | Monticone M, Ambrosini E, Rocca B, Cazzaniga D, Liquori V, Foti C. Group-based task-oriented exercises aimed at managing kinesiophobia improved disability in chronic low back pain. Eur J Pain. 2016 Apr;20(4):541-51 | 10.1002/ejp.756 |
| 2016b | Monticone M, Ambrosini E, Cazzaniga D, Rocca B, Motta L, Cerri C, Brayda-Bruno M, Lovi A. Adults with idiopathic scoliosis improve disability after motor and cognitive rehabilitation: results of a randomised controlled trial. Eur Spine J. 2016 Oct;25(10):3120-3129. | 10.1007/s00586-016-4528-y |
| 2017 | Monticone M, Ambrosini E, Rocca B, Cazzaniga D, Liquori V, Pedrocchi A, Vernon H.Group-based multimodal exercises integrated with cognitive- | 10.1177/0269215516651979 |

| | | |
|---|---|---|
| | behavioural therapy improve disability, pain and quality of life of subjects with chronic neck pain: a randomized controlled trial with one-year follow-up. Clinical Rehabilitation 2017; 1–11 | |
| 2020 | Monticone M, Ambrosini E, Rocca B, Cazzaniga D, Liquori V, Lovi A, Brayda-Bruno M. Multimodal exercises integrated with cognitive-behavioural therapy improve disability of patients with failed back surgery syndrome: a randomized controlled trial with one-year follow-up. Disabil Rehabil 2020 Dec 27;1-8 | 10.1080/09638288.2020.1863480 |
| 2021 | Monticone M, Ambrosini E, Portoghese I, Rocca B. Multidisciplinary program based on early management of psychological factors reduces disability of patients with subacute low back pain. Results of a randomised controlled study with one year follow-up. Eur J Phys Rehabil Med. 2021 May 5 | 10.23736/S1973-9087.21.06696-X |
| For completeness | | |

| | | |
|---|---|---|
| 2012 | Monticone M, Baiardi P, Vanti C, Ferrari S, Nava T, Montironi C, Rocca B, Foti C, Teli M. Chronic neck pain and treatment of cognitive and behavioural factors: results of a randomised controlled clinical trial. Eur Spine J. 2012 Aug;21(8):1558-66 | 10.1007/s00586-012-2287-y |
| 2018 | Monticone M, Ambrosini E, Vernon H, Rocca B, Finco G, Foti C, Ferrante S Efficacy of two brief cognitive-behavioral rehabilitation programs for chronic neck pain: results of a randomized controlled pilot study. European Journal of Physical and Rehabilitation Medicine 2018 ;54(6):890-9 | 10.23736/S1973-9087.18.05206-1 |

For each of these trials our questions are as follows:

1. **Clinical trial protocol**: was a clinical trial protocol developed prior to the trial being undertaken? If so, please can you provide us with a copy?
2. **Trial registration**: We noticed that the study reports either did not mention trial registration or provided registration numbers that on inspection appear to indicate retrospective registration. If there was a trial registration please can you provide the registration details? If no registration can you please explain the reason why the trials were not registered before enrolment of participants began?
3. **Ethics approval**: was ethical approval obtained prior to undertaking each trial? If so, please could you let us know from whom (i.e. National, Institutional; Hospital or University) and send us a copy of the approval letter or the full registration number and body to search online?
4. **Randomisation process**: there is an equal number of participants in both groups in all of these trials though most trials did not report a blocking method. Can you explain how this observation arose?

5. **Data**: For the majority of these trials (excepting 2012 and 2018) the observed effect sizes are large or very large and diverge from the findings of similar studies in this field. Please can you provide us with a copy of the full individual patient data set for each trial to allow further analysis?

We also have some specific questions relating to specific trials in this sample:

- In the studies labelled above 2016a and 2021 the outcomes data for pain (NRS) at the post training and 12 -follow up are identical in the treatment and control group (means and standard deviations). The 12-month Oswestry disability scores (means and standard deviations) are also identical between these two papers, despite them being reported as being from distinct populations. Similarly, there is a very high degree of similarity between the post-intervention and 12-month follow up scores for the TSK and PCS in the experimental and control groups in the studies labelled 2016a and 2021. Can you please explain these findings?
- In the studies labelled in the above table 2014a and 2016b there are a number of p values in the table of baseline characteristics that do not appear to match the data. In particular, could please you explain this observation for the following outcomes?
    - 2014a step length, step time, single support time (left and right)
    - 2016b All SRS-22 subscales

We recognise that this is an extensive list of requests that may require some time and preparation. We would be grateful if you could respond to this email within 2 weeks of receipt, and provide us with a timescale for a full response.

Many thanks for your assistance with these enquiries. We look forward to your reply,

Sincerely,

**Text of Dr Monticone's specific responses to enquiries (received 12/1/22)**

1. **Clinical trial protocol**: was a clinical trial protocol developed prior to the trial being undertaken? If so, please can you provide us with a copy?
No, there was not a protocol because the intervention groups always belonged to our clinical practice.
2. **Trial registration**: We noticed that the study reports either did not mention trial registration or provided registration numbers that on inspection appear to indicate retrospective registration. If there was a trial registration please can you provide the registration details? If no

registration can you please explain the reason why the trials were not registered before enrolment of participants began? Most studies did not have a registration either because they started before this issue was strictly required by Journals or because the Journals did not require it. In three cases (the 2017, 2020, 2021 papers) we retrospectively registered the studies based on Journal's recommendations.

3. **Ethics approval**: was ethical approval obtained prior to undertaking each trial? If so, please could you let us know from whom (i.e. National, Institutional; Hospital or University) and send us a copy of the approval letter or the full registration number and body to search online? There was the approval of our Institutional Review Board at the Hospital where the studies were performed. I would prefer to avoid sending these documents.
4. **Randomisation process**: there is an equal number of participants in both groups in all of these trials though most trials did not report a blocking method. Can you explain how this observation arose? I checked and you are right. However, the number of patients randomized was generated by chance based on the patients that were excluded.
5. **Data**: For the majority of these trials (excepting 2012 and 2018) the observed effect sizes are large or very large and diverge from the findings of similar studies in this field. Please can you provide us with a copy of the full individual patient data set for each trial to allow further analysis? I suppose that the large effect sizes were due to the specific characteristics of the CBT group. Indeed, relevant efforts were made in order to strongly improve patients' health conditions. This is also demonstrated by the between-group clinical differences achieved as well as by the level of satisfaction found in CBT groups. Again, I would prefer to avoid sending databases.

In the studies labelled above 2016a and 2021 the outcomes data for pain (NRS) at the post training and 12 -follow up are identical in the treatment and control group (means and standard deviations). The 12-month Oswestry disability scores (means and standard deviations) are also identical between these two papers, despite them being reported as being from distinct populations. Similarly, there is a very high degree of similarity between the post-intervention and 12-month follow up scores for the TSK and PCS in the experimental and control groups in the studies labelled 2016a and 2021. Can you please explain these findings?
I checked the tables and you are right as for the NRS, the ODI and the TSK. I was surprised but these are the data the staff collected. I think that values on catastrophizing differ, because I used another scale in my 2021 paper (the CSQ-R).

In the studies labelled in the above table 2014a and 2016b there are a number of p values in the table of baseline characteristics that do not appear to match the data. In particular, could please you explain this observation for the following outcomes?

1. 2014a step length, step time, single support time (left and right)
2. 2016b All SRS-22 subscales

I checked again the data and they are OK as presented.