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# Which Portion of Physiotherapy Treatments' Effect Is Not Attributable to the Specific Effects in People With Musculoskeletal Pain? A Meta-Analysis of Randomized Placebo-Controlled Trials

● **OBJECTIVE:** We aimed to quantify the proportion not attributable to the specific effects (PCE) of physical therapy interventions for musculoskeletal pain.

● **DESIGN:** Intervention systematic review with meta-analysis.

● **LITERATURE SEARCH:** We searched Ovid, MEDLINE, EMBASE, CINAHL, Scopus, PEDro, Cochrane Controlled Trials Registry, and SPORTDiscus databases from inception to April 2023.

● **STUDY SELECTION CRITERIA:** Randomized placebo-controlled trials evaluating the effect of physical therapy interventions on musculoskeletal pain.

● **DATA SYNTHESIS:** Risk of bias was evaluated using the Cochrane risk-of-bias tool for randomized trials (RoB 2). The proportion of physical therapy interventions effect that was not explained by the specific effect of the intervention was calculated, using the proportion not attributable to the specific effects (PCE) metric, and a quantitative summary of the data from the studies was conducted using the random-effects inverse-variance model (Hartung-Knapp-Sidik-Jonkman method).

● **RESULTS:** Sixty-eight studies were included in the systematic review (participants:  $n = 5238$ ), and 54 placebo-controlled trials informed our meta-analysis (participants:  $n = 3793$ ). Physical

therapy interventions included soft tissue techniques, mobilization, manipulation, taping, exercise therapy, and dry needling. Placebo interventions included manual, nonmanual interventions, or both. The proportion not attributable to the specific effects of mobilization accounted for 88% of the immediate overall treatment effect for pain intensity (PCE = 0.88, 95% confidence interval [CI]: 0.57, 1.20). In exercise therapy, this proportion accounted for 46% of the overall treatment effect for pain intensity (PCE = 0.46, 95% CI: 0.41, 0.52). The PCE in manipulation excelled in short-term pain relief (PCE = 0.81, 95% CI: 0.62, 1.01) and in mobilization in long-term effects (PCE = 0.86, 95% CI: 0.76, 0.96). In taping, the PCE accounted for 64% of disability improvement (PCE = 0.64, 95% CI: 0.48, 0.80).

● **CONCLUSION:** The outcomes of physical therapy interventions for musculoskeletal pain were significantly influenced by factors not attributable to the specific effects of the interventions. Boosting these factors consciously to enhance therapeutic outcomes represents an ethical opportunity that could benefit patients. *J Orthop Sports Phys Ther* 2024;54(6):391-399. Epub 11 April 2024. doi:10.2519/jospt.2024.12126

● **KEY WORDS:** contextual effects, musculoskeletal pain, physiotherapy, placebo

Physical therapists use different interventions when treating musculoskeletal pain disorders.<sup>44</sup> Although compelling evidence exists about the efficacy and cost-effectiveness of interventions such as joint mobilizations/manipulations, soft tissue techniques, neural mobilizations, exercise therapy, taping and dry needling,<sup>2,7,11,15,25,28,32,39</sup> and high-quality clinical practice guidelines recommend them for managing musculoskeletal pain,<sup>24</sup> the mechanisms of action are not well understood.<sup>3,5</sup> Understanding *how* physical therapy interventions work underscores the biological plausibility of physical therapy practice and provides evidence of its therapeutic value.<sup>4,17</sup>

The outcome of treatment (total or overall treatment effect) is the result of specific effects derived from the intervention itself, nonspecific effects, including the Hawthorne effect, natural history, regression to the mean, and contextual effects.<sup>3,4,6,8</sup> The

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effects that are not derived from the specific intervention itself are often termed placebo effects in clinical trials and placebo responses in clinical practice.<sup>18,46</sup> Contextual effects are embedded within a clinical encounter (eg, physical therapist's and patient's features, patient-physical therapist relationship, characteristics of the treatment and the healthcare setting),<sup>10,13</sup> and drive positive or negative therapeutic outcomes.<sup>29,30,38</sup> In research, the specific treatment effect can be isolated by comparing the average therapeutic outcomes of a treatment group versus a placebo group within a randomized controlled trial (RCT).<sup>8</sup> The RCT design allows for controlling both the nonspecific effects and contextual effects of an intervention.<sup>8</sup> The proportion not attributable to the specific effects (PCE) is a new metric designed to capture the therapeutic outcomes that are not attributable to the specific effects on an intervention.<sup>40</sup> The PCE ranges from 0 to 1, and a larger value indicates a smaller specific effect of an intervention.<sup>46</sup> Understanding how much nonspecific effects and contextual effects affect outcomes helps clinicians and patients make informed treatment decisions.<sup>42,45</sup>

The PCE of general medicine<sup>18,40</sup> and surgery in pain-related conditions<sup>22</sup> are generally large. In particular, the overall proportion not attributable to the specific effects of general medicine interventions is high (PCE = 65%), with higher values observed in semi-objective and objective outcomes (PCE = 78 and 94%, respectively) than in subjective outcomes (PCE = 50%).<sup>40</sup> More than half of the overall treatment effect observed in musculoskeletal pain conditions such as knee osteoarthritis,<sup>9,46</sup> neck pain,<sup>21</sup> low back pain,<sup>34,41</sup> and fibromyalgia<sup>43</sup> may be due to factors not related to the intended targets of treatment. It is time to disentangle the proportion not attributable to the specific effects of interventions in musculoskeletal rehabilitation practice.

We aimed to quantify the magnitude of the proportion not attributable to the specific effects of interventions commonly used by physical therapists when managing musculoskeletal pain. Our secondary aim was to study the variability of this

proportion by type of intervention (eg, manipulation, mobilization, taping, exercise therapy, dry needling) and type of placebo (eg, manual versus nonmanual).

## METHODS

**T**HE PREFERRED REPORTING ITEMS for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and recommendations<sup>27</sup> guided the conduct and reporting of our systematic review. We prospectively registered the review in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42022380322). Deviations from the protocol are reported in **SUPPLEMENTAL FILE 1**. As a systematic review with meta-analysis, this study did not directly involve patients in the research process.

### Data Sources and Search Strategy

The search was conducted by two authors (YE and LD), who independently searched in Ovid, MEDLINE, EMBASE, CINAHL, Scopus, Physiotherapy Evidence Database (PEDro), Cochrane Controlled Trials Registry, and SPORTDiscus databases for randomized placebo-controlled trials focused on evaluating the effect of physical therapy interventions on musculoskeletal pain published from inception to April 2023. Only studies written in Spanish, Italian, or English languages and published in peer-reviewed journals were considered. In addition, the reference lists of the selected articles were manually examined to retrieve additional potential eligible studies. The full search strategy for each database is reported in **SUPPLEMENTAL FILE 2**.

### Study Selection

To be included in the meta-analysis, studies needed to meet the following PICOS criteria: (1) participants: minimum age of 18 years presenting with musculoskeletal pain conditions (ie, pain that affects bones, muscles, ligaments, tendons, and/or nerves);<sup>14,36</sup> (2) intervention: physical therapy treatment (ie, manual therapy, therapeutic exercise therapy, taping or in-

vasive physical therapy techniques such as dry needling);<sup>44</sup> (3) comparator: a placebo-controlled group; (4) outcomes analyzed: pain intensity, disability; and (5) study design: randomized placebo-controlled trials.

Studies in which the treatment of the experimental group included nutritional supplementation, drugs, surgery, electrophysical agents (ie, laser therapy, electroanalgesia, microwaves), psychologically informed practice, a combination of various physical therapy techniques, education, or self-management were excluded. Studies whose participants experienced pain derived from neurological disorders, cancer-related pain, visceral pain, or post-surgical pain were also excluded. Both authors assessed the full-text articles for eligibility. Any disagreement was resolved by consensus with a third author (ELL). Interrater agreement was estimated by using Cohen's kappa statistic ( $\kappa$ ), considering that  $\kappa = 0.01-0.20$ ;  $\kappa = 0.21-0.40$ ;  $\kappa = 0.41-0.60$ ;  $\kappa = 0.61-0.80$ ;  $\kappa = 0.81-1.00$  indicate a slight, fair, moderate, substantial and almost perfect level of agreement among reviewers, respectively.<sup>23</sup>

### Data Extraction

Two authors independently extracted the following information from each included trial: (1) trial characteristics (first author's name, publication year, location, and sample size); (2) demographics (sex, age, condition and the number of participants of each group); (3) main outcomes and method of assessment; (4) intervention, placebo and/or control group characteristics (placebo and intervention type, session duration, sessions per week, intervention duration or type of control); and (5) statistical analysis plus outcome of interest and main results.

To categorize the effects of the placebo and treatment groups, three distinct time points were selected: immediate effects (immediately after the intervention), short-term effects (between 1 day and 30 days after the intervention), and long-term effects (beyond 1 month after the intervention). When relevant information from the studies was missing, it

was requested from the corresponding authors via e-mail.

### Risk of Bias

Two authors (LD and YE) independently assessed the risk of bias in eligible studies using version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2).<sup>37</sup> For each RCT and every domain, the judgments were “low risk of bias”, “some concerns”, or “high risk of bias”. Any discrepancies in quality ratings were solved by discussion. If consensus could not be reached, a third author (ELL) made the final decision. Interrater agreement was estimated using Cohen’s kappa statistic.<sup>23</sup> Sensitivity analyses were carried out, excluding studies with a high-risk bias to examine if these trials accounted for significant variance in the overall results. Additionally, the Grading of Recommendations Assessment Development and Evaluations (GRADE) approach was used to assess the certainty of evidence.

### Summary Measures

A quantitative summary of the data from all included studies was conducted using the random-effects inverse-variance model with the Hartung-Knapp-Sidik-Jonkman variance estimator based on DerSimonian-Laird estimate of tau. We used STATA software (version 17.0; StataCorp, College Station, TX, USA) to calculate the standardized mean difference, which was expressed as Hedges’ *g* with 95% confidence interval (CI). Changes in the outcomes of interest were calculated by subtracting change differences between the intervention and placebo groups using the pooled standard deviation (*SD*) of change in both groups. If change scores and *SD* were not available, they were calculated from 95% confidence interval (CI) for either change outcome or treatment effect differences as well as pre-*SD* and post-*SD* values.<sup>3</sup> The PCE was calculated using the mean change score of the placebo arm divided by the mean change score of the intervention arm.<sup>43,46</sup> Then, this value was log-transformed to normalize the distribution

for the analysis and transformed back for reporting. Its 95% CI was calculated using the Delta method, which allowed us to calculate the standard error estimator of the log(PCE).<sup>35</sup>

Trials were excluded from the analyses if they met any of the following conditions: (1) the intervention group and the placebo group had a different positive or negative direction of change; (2) studies in which the intervention elicited worse outcomes (ie, better mean scores at baseline than at post-intervention), as the calculation of the PCE entails a log transformation of ratios, not allowing for negative values. These values range from 0 to 1, indicating 0% contribution from factors not related to the specific intervention itself (PCE = 0) and 100% contribution from factors not related to the intervention itself (e.g. nonspecific effects and contextual effects) (PCE = 1), respectively. Since the PCE is intended to represent proportions and cannot exceed 1 (indicating 100% contribution), values higher than 1 were considered as the maximum limit and thus capped at 1 to maintain the integrity of the interpretation as a proportion.

In studies with more than one treatment group, we divided the “shared” group into two or more subsets with smaller sample sizes, thereby enabling the analysis of two or more reasonably independent comparisons, ensuring that the effects observed in one comparison were not influenced by the same participants or data points in another comparison. The PCE for each outcome and its 95% CI was pooled, and subgroup analyses were conducted when at least three trials were available. Subgroups included type of intervention (ie, dry needling, taping, exercise therapy, manipulation, mobilization, soft tissue technique), musculoskeletal condition, and type of placebo (ie, manual, nonmanual). Examples of manual placebos were sham manipulation, sham taping, superficial massage, sham dry needling (ie, simulation of dry needling without penetrating the skin), and nonmanual placebos include the use

of detuned devices like ultrasound, microwave, or laser.

Heterogeneity across RCTs was calculated using the inconsistency index (*I*<sup>2</sup>), considering *I*<sup>2</sup> values of 25%, 50%, and 75% as low, moderate, and high variability values due to between-study heterogeneity, respectively. Publication bias was assessed using doi plots and Luis Furuya-Kanamori (LFK) index.<sup>16</sup>

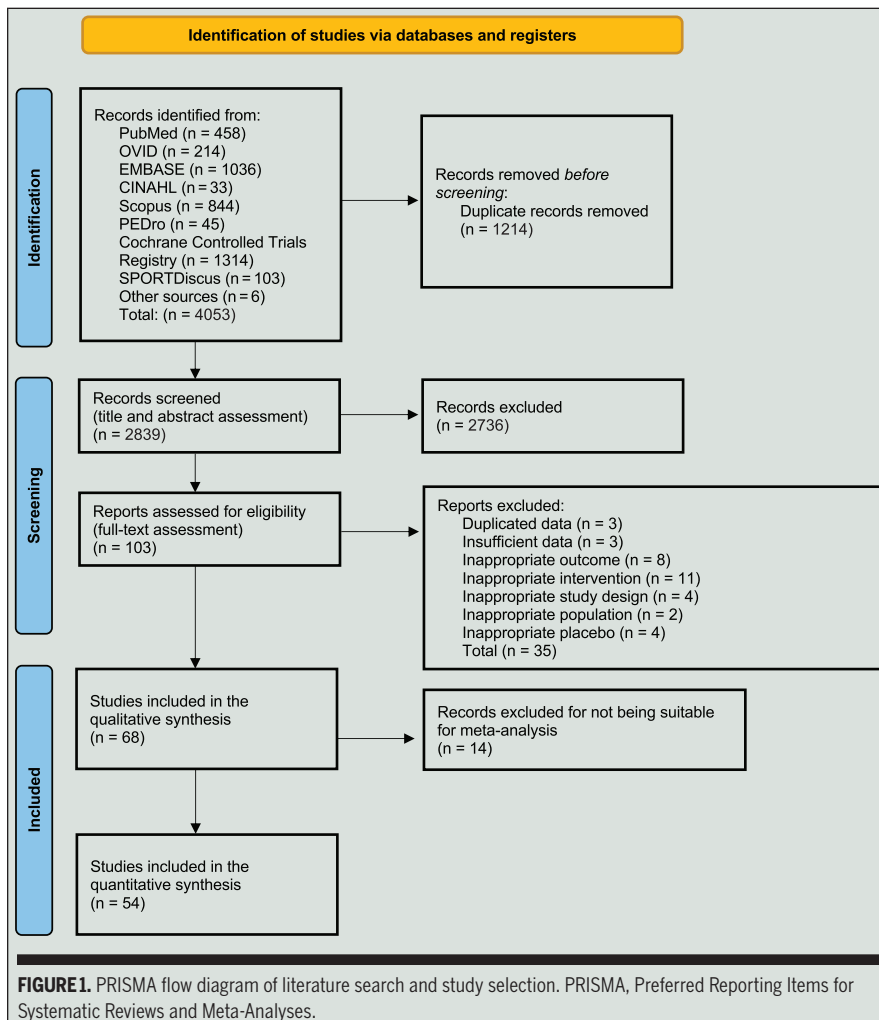
Sensitivity analysis was conducted to assess the robustness of the summary estimates to determine whether a particular study accounted for the heterogeneity. Thus, to examine the effects of each result from each study on the overall findings, results were analyzed with each study deleted from the model once. Finally, the potential moderating effect of age at baseline or number of intervention sessions was examined by performing metaregression analyses using the Hartung-Knapp-Sidik-Jonkman method.

## RESULTS

THE ELECTRONIC SEARCH STRATEGY yielded a total of 4051 studies, and 68 trials met the inclusion criteria (FIGURE 1; list of excluded studies and reasons for exclusion can be found in SUPPLEMENTAL FILE 3). Fourteen trials did not provide sufficient data for analysis; 54 placebo-controlled trials were included in the meta-analysis. Cohen’s kappa statistic for interrater reliability was  $\kappa = 0.81$  (95% CI: 0.678, 0.941), representing almost perfect agreement.

### Study Characteristics

The 68 studies included data from 5238 participants (mean age:  $36.9 \pm 11.2$  years; 59.7% female; SUPPLEMENTAL FILE 4). Sample sizes ranged from 23 to 394 individuals. Musculoskeletal conditions were predominantly chronic low back pain, chronic neck pain, myofascial pain syndrome, knee/hip osteoarthritis, temporomandibular disorders, and shoulder pain. Physical therapy interventions included dry needling, taping, manipulation, mobilization, soft tissue techniques, neural



techniques, and exercise therapy. Placebo interventions included manual interventions such as sham manipulation (ie, simulation of the procedure but without the rapid application of motion or without thrust), sham taping (ie, placebo neutral kinesiotaping without tension), superficial massage (ie, light touch), asking for nonrelated active movements, sham dry needling (ie, simulation of dry needling without penetrating the skin), and non-manual interventions (ie, detuned devices like ultrasound, microwave, laser), a combination of both. One study used unrelated movements as a placebo intervention.<sup>1</sup>

The number of treatment sessions ranged from 1 to 32 (mean:  $4.3 \pm 5.5$  sessions). The effect of physical therapy interventions on pain intensity was assessed

through different measurements, including the Visual Analogue Scale or Numeric Rating Pain Scale. Disability was evaluated using questionnaires, including Oswestry Disability Index, Neck Disability Index, Foot and Ankle Disability Index, Constant Shoulder Score, Headache Impact Test, Patient Specific Function Scale, Western Ontario and McMaster University, Quebec Pain Disability Index, or Roland-Morris Disability Questionnaire.

## Summary Measures

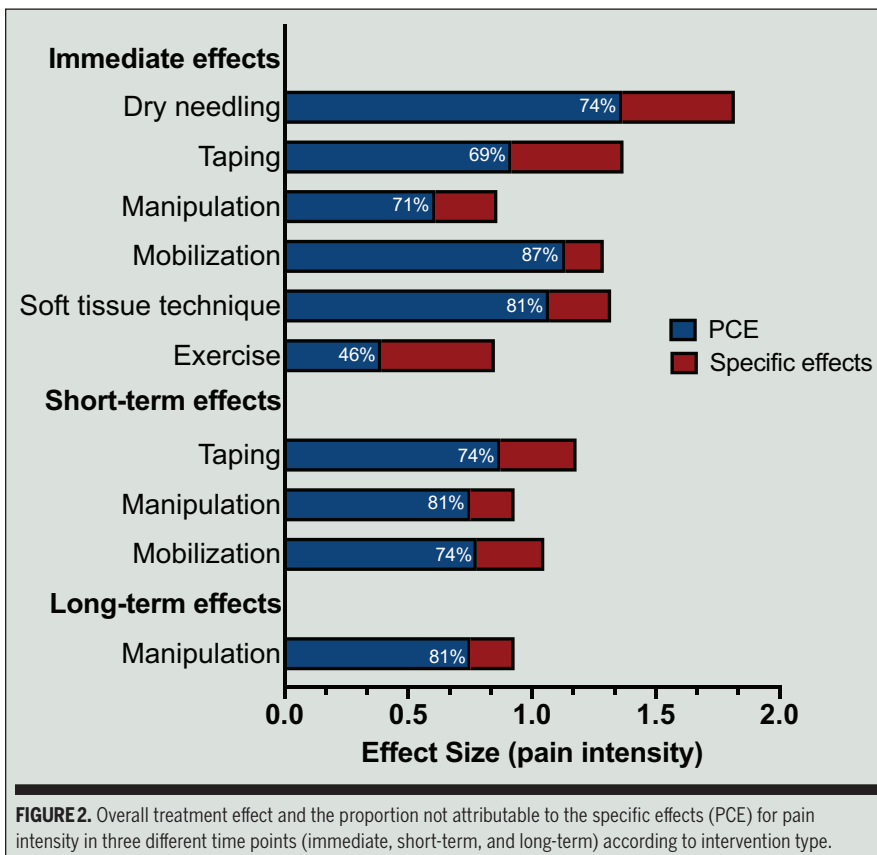
**PCE of Physical Therapy Interventions on Pain Intensity: Immediate Effects** We analyzed the proportion not attributable to the specific intervention itself for six techniques (soft tissue techniques, mobilization, manipulation, taping, exercise

therapy, and dry needling; **SUPPLEMENTAL FILE 5**). The type of treatment with the largest PCE for pain intensity assessed immediately after the intervention was mobilization, which represented 87% of the overall treatment effect (PCE = 0.87, 95% CI: 0.54, 1.19), followed by soft tissue techniques representing 81% of the overall treatment effect (PCE = 0.81, 95% CI: 0.64, 0.97), dry needling with 75% (PCE = 0.75, 95% CI: 0.36, 1.15), manipulation techniques with 74% (PCE = 0.74, 95% CI: 0.33, 1.14), taping with 69% of the overall treatment effect (PCE = 0.69, 95% CI: 0.48, 0.89), and the smallest proportion not attributable to the specific intervention itself for pain intensity was exercise therapy accounting for 46% of the overall treatment effect (PCE = 0.46, 95% CI: 0.41, 0.52).

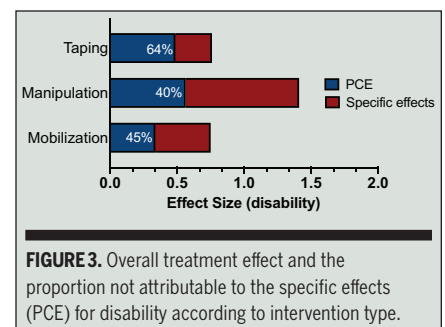
**PCE of Physical Therapy Interventions on Pain Intensity: Short-Term Effects** Three techniques were not included in the analysis (mobilization, manipulation, and taping; **SUPPLEMENTAL FILE 6**). Moreover, 81% of the overall treatment effects of manipulation techniques were not attributable to the intervention itself (PCE = 0.81, 95% CI: 0.61, 1.01), and 73 and 74% of the overall treatment effects were explained by factors not related to the intervention itself for mobilization techniques (PCE = 0.73, 95% CI: 0.29, 1.18) and taping (PCE = 0.74, 95% CI: 0.53, 0.95), respectively.

**PCE of Physical Therapy Interventions on Pain Intensity: Long-Term Effects** Only manipulation techniques could be included in the analysis (**SUPPLEMENTAL FILE 7**), finding that 86% of the overall treatment effects were not explained by the intervention itself in the long-term (PCE = 0.86, 95% CI: 0.76, 0.96). The overall effect size of both physical therapy and placebo interventions in the different time points is shown in **SUPPLEMENTAL FILES 8-13**. The immediate, short-term, and long-term treatment effects in combination with their PCE for pain intensity is shown in **FIGURE 2**.

**PCE of Physical Therapy Interventions on Pain Intensity by Musculoskeletal Condition** The analyzed conditions included



**FIGURE 2.** Overall treatment effect and the proportion not attributable to the specific effects (PCE) for pain intensity in three different time points (immediate, short-term, and long-term) according to intervention type.



**FIGURE 3.** Overall treatment effect and the proportion not attributable to the specific effects (PCE) for disability according to intervention type.

chronic low back pain, chronic neck pain, myofascial syndrome, knee/hip osteoarthritis, neck pain, shoulder pain, and tension-type headache. Further details are presented in **SUPPLEMENTAL FILE 14**.

**PCE of Physical Therapy Interventions on Pain Intensity by Placebo Type** Seventy percent of the overall treatment effect of trials that used a manual placebo were not attributable to the intervention itself (PCE = 0.70, 95% CI: 0.53, 0.88), and 83% of the overall treatment effects of the studies that used a nonmanual placebo were not explained by the specific effects of the intervention (PCE = 0.83, 95% CI: 0.54, 1.11; **SUPPLEMENTAL FILE 15**). Further details are presented in **SUPPLEMENTAL FILES 16-18**.

**PCE of Physical Therapy Interventions on Disability** Regarding disability, four techniques (mobilization, manipulation, soft tissue techniques, and taping) were included in the analysis (**FIGURE 3** and **SUPPLEMENTAL FIGURE 19**). The physical therapy intervention with the largest PCE for dis-

ability was taping, with 64% of the overall treatment effects not explained by the taping intervention itself (PCE = 0.64, 95% CI: 0.32, 0.96). Similarly, 47 and 40% of the overall treatment effect of mobilization techniques and manipulation techniques were not explained by the specific effects of those interventions (PCE = 0.47, 95% CI: -0.20, 1.13; PCE = 0.40, 95% CI: 0.01, 0.79, respectively).

**Meta Regression** The overall PCE was not affected either by the increase in age of the participants of the studies ( $p > .05$ ) or by the number of sessions of the different interventions ( $p > .05$ ; **SUPPLEMENTAL FILE 20**).

**Sensitivity Analysis and Publication Bias** No individual trial had an excessive impact on the pooled effect size of physical therapy interventions on pain or disability. Visual inspection of the doi plots and the LFK index revealed low levels of publication bias in terms of pain (**SUPPLEMENTAL FILE 21**). In terms of disability (**SUPPLEMENTAL FILE 22**),

manipulation techniques showed major asymmetry (LFK = 3.03) and mobilization and taping showed minor asymmetry (LFK = 1.05 and LFK = 1.02, respectively), suggesting that there might exist underrepresentation of studies with negative or small effects for these outcomes.

### Certainty Assessment and Risk of Bias

The risk of bias analysis is shown in **SUPPLEMENTAL FILE 23**. Thirteen studies were at low risk of bias, 22 were at high risk of bias, and the remaining 36 studies had some concerns regarding risk of bias. The Cohen's kappa statistic for interrater reliability was  $\kappa = 0.971$  (95% CI: 0.916, 1.000), representing almost perfect level of agreement. High risk of bias was mainly concentrated in domains of deviations from intended interventions, missing outcome data and measurement of the outcome. High risk of bias was found in studies applying taping techniques, and low risk of bias was found in studies using mobilization techniques. GRADE assessment showed the overall certainty of the evidence for pain was high and moderate, and for disability outcomes, it was moderate, low, and very low (**SUPPLEMENTAL FILE 24**).

## DISCUSSION

**O**UR FINDINGS, WHICH REMAINED robust after metaregression and sensitivity analysis, indicated that both nonspecific effects (e.g., natural history, regression to the mean) and contextual effects: (1) influenced pain and disability in patients with musculoskeletal pain following physical therapy treatments; (2)

had a magnitude dependent on the type of treatment considered; and (3) were also present in sham treatments.

## Comparison With Existing Literature

The subjective outcomes (pain and disability) of patients with musculoskeletal pain were influenced by different PCE depending on the physical therapy treatments considered. This finding is in line with several previous meta-analyses investigating the PCE of treatments in people with osteoarthritis<sup>9,46</sup> and fibromyalgia,<sup>34</sup> emphasizing that it is the subjective dimension of suffering experienced by the patient (“illness”) that is more influenced by factors not related to the specific interventions rather than the objective one (“disease”).<sup>30,38</sup> Despite the overall consistency reported in the literature, Tsutsumi et al.<sup>40</sup> reported that the PCE is larger for objective or semi-objective outcomes, deviating from the general trend. A potential explanation for this discrepancy could be the heterogeneity of the clinical conditions considered in general medicine (eg, cardiovascular and infectious disease) compared to musculoskeletal pain alone.

## The Influence of Factors Not Related to the Specific Intervention on Physical Therapy Treatments

Different physical therapy treatments presented distinct PCE, underlining that the overall outcome cannot be due only to the specific effects of the intervention.<sup>3–6</sup> The contextual effects represented, for example, by the ritual of the therapeutic touch of hands-on treatments (eg, mobilization), the use of external devices (eg, taping) and the invasiveness of some procedures (eg, dry needling), conveying a healing meaning,<sup>26</sup> can make patients aware of the therapy administration and influence the outcome itself.<sup>30</sup>

## The Role of Factors Not Related to the Specific Intervention in Manual and Nonmanual Placebos

Studies in chronic low back pain, chronic neck pain, and myofascial pain syndrome populations showed significantly higher

PCE values in nonmanual placebo interventions, such as detuned electrotherapy devices, compared to manual placebos, irrespective of the technique employed. A possible explanation is the potency of the treatment ritual associated with these interventions, which is likely more pronounced than in manual placebos. This phenomenon may also be attributed to the perception that nonmanual placebos are more technologically advanced and sophisticated, enhancing patients’ confidence in the treatment.<sup>29</sup> Consequently, patients develop higher expectations, leading to stronger placebo effects. Similarly, the non-predictable interaction between the specific and contextual effects of treatments along with the patient’s expectations, preferences and beliefs could explain the different impacts of treatments on outcomes (pain and disability),<sup>29</sup> thus shedding light on the complexity of the patient’s response to physical therapy interventions.

## The Challenge of Factors Not Related to the Specific Intervention in Physical Therapy Sham Treatments

Factors not related to the specific intervention itself were also involved in physical therapy sham treatments with different PCE magnitudes depending on the type of placebo comparator used. This finding indicates the nonexistence of inactive placebo treatments in physical therapy and highlights the challenge of eliminating contextual effects from sham physical therapy treatment adopted in the field of musculoskeletal pain.<sup>31</sup> The heterogeneity of placebo comparators (eg, manual vs instrumental) revealed by the included studies not only limits the comparison between the real and the sham treatments<sup>12</sup> but also suggests an urgent need to develop and conduct placebo-RCTs following international reporting guidelines.<sup>19,20</sup>

## Limitations

Although we extensively searched eight databases, we did not investigate pre-published registries, contact experts, or conduct gray literature searches, thus introducing a possible selection bias.<sup>42</sup> Like-

wise, the inclusion of studies published only in specific languages might have led us to exclude relevant research conducted in other languages, potentially skewing the overall findings.

The number of exercise therapy-based studies was small. This was due to the absence of placebo groups in exercise therapy studies and the frequent combination of exercise therapy with other interventions, preventing the isolated examination of exercise therapy effects. Thirdly, trials that included disability as an outcome were more likely to report positive or significant results rather than negative or inconclusive findings, thus introducing potential publication bias.<sup>19</sup> Moreover, our analysis was limited to subjective outcomes such as pain and disability due to the insufficient number of studies reporting objective outcomes.

There were a lack of data concerning quality-of-life outcomes in musculoskeletal pain interventions. Future research should incorporate these outcomes, enabling a broader assessment of interventions beyond physical symptoms like pain and disability. Lastly, accurately calculating contextual effects, as previously highlighted,<sup>33</sup> is a complex endeavor.

The PCE was calculated to assess the extent to which the placebo arm contributes to the treatment arm improvement response across different physical therapy interventions. However, the possible overestimation of effects not related to the intervention itself by excluding studies with no change or negative changes from baseline values might be considered when interpreting our results. Comparing a placebo versus a no treatment group allows to isolate contextual effects by controlling the nonspecific effects of an intervention.<sup>8</sup> Unfortunately, due to a scarcity of physical therapy RCTs with untreated control groups, we could not analyze the magnitude of the nonspecific effects (eg, regression to mean, natural history, and Hawthorne effect).<sup>8</sup>

Following the multiplicative model used for calculating the PCE in previous meta-analyses,<sup>9,43,46</sup> we assumed all the

improvements in the placebo group as the sum of nonspecific and contextual effects. In fact, despite the term PCE seems to refer only to contextual effects it refers in fact to the combination of nonspecific and contextual effects as reflected when calculating this metric (treatment versus placebo outcomes).

### Clinical Implications

Physical therapists should acknowledge the impact of factors not related to their specific treatments and harness their potential to benefit patients in clinical practice. Rather than ignoring or trying to control these effects not attributable to the intervention itself, physical therapists can limit them to their advantage when managing musculoskeletal pain.<sup>38</sup> During passive treatments, physical therapists might tap into contextual effects by considering the patients' expectations (whether positive or negative) of the therapy before choosing to administer a treatment. Specific language could amplify therapeutic benefits ("This mobilization will help to reduce your pain and disability"). Similarly, using a mirror or a video screen positioned in front of the patient.<sup>29</sup>

Consciously using contextual effects to enhance therapeutic outcomes is only ethical if it is offered within an evidence-based path that incorporates education and therapeutic exercises in addition to passive treatments (eg, soft tissue techniques, mobilization, manipulation, taping, and dry needling) to ensure the best available practice for musculoskeletal pain.<sup>24,29</sup> Accordingly, training programs for professionals treating musculoskeletal pain should incorporate these findings, emphasizing their integration into clinical practice.

To develop a full picture of the role of effects not related to the intended targets of treatment in the physical therapy field, future research embracing additional areas (eg, neurological, respiratory, urogynecological) are needed, especially studies reporting objective outcome measures (eg, electromyography), including the addition of no-

treatment control groups for comparison, and using standardized methodologies.

## CONCLUSIONS

**N**ONSPECIFIC AND CONTEXTUAL effects significantly contributed to the outcomes of physical therapy interventions for musculoskeletal pain. The magnitude of effects not related to the specific intervention itself varies across different physical therapy techniques. These results emphasize the pervasive influence of factors not related to the specific treatment across various physical therapy interventions, highlighting their critical role in impacting patient outcomes. ●

### KEY POINTS

**FINDINGS:** Nonspecific and contextual effects can explain a substantial proportion of the immediate, short-term, and long-term overall effects of physical therapy interventions for the treatment of musculoskeletal pain. The largest proportion not attributable to the specific effects of the intervention itself was found in mobilization techniques, followed by soft-tissue techniques, dry needling, manipulation, taping, and exercise therapy.

**IMPLICATIONS:** Harnessing the contextual effects to enhance therapeutic outcomes represents an ethical opportunity that physical therapists could use to benefit their patients.

**CAUTION:** The physical therapy interventions included in this study may represent only some of the therapeutic arsenal of physical therapists, thus limiting the generalization of our results.

### STUDY DETAILS

**AUTHOR CONTRIBUTIONS:** Yasmin Ezzatvar: Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Visualization, Writing - Original draft preparation. Lirios Dueñas: Data curation, Investigation, Formal analysis, Visualization, Writing - Reviewing and Editing. Mercè Balasch-Bernat: Data curation, Investigation, Formal analysis,

Visualization. Enrique Lluch-Girbés: Conceptualization, Methodology, Writing - Original draft preparation, Supervision. Giacomo Rossetini: Conceptualization, Methodology, Writing - Original draft preparation, Supervision.

**DATA SHARING:** Lirios Dueñas had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The data underlying this article will be shared on reasonable request to the corresponding author.

**PATIENT AND PUBLIC INVOLVEMENT:** As this meta-analysis involves the synthesis of existing data from previously conducted studies, direct involvement of patients was not applicable to the scope of this research.

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