

Review

Psychological interventions for pain control in oncology and rheumatic comorbidities: A systematic review and meta-analysis

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Abstract: Background: Cancer-related pain significantly impacts patients' quality of life, and conventional pharmacologic treatments often have limitations. Psychological and non-pharmacologic interventions are increasingly recognized as complementary approaches, but their efficacy remains heterogeneous. This systematic review and meta-analysis evaluate the effectiveness of these interventions for pain control in oncology, including patients with comorbid rheumatologic conditions. **Methods:** Following PRISMA guidelines, we searched PubMed/MEDLINE, Embase, PsycINFO, and other databases up to 8 June 2025. Randomized controlled trials (RCTs) assessing psychological (e.g., cognitive-behavioral therapy [CBT], mindfulness) and non-pharmacologic (e.g., acupuncture, music therapy) interventions for adult cancer patients with pain were included. The primary outcome was pain intensity; secondary outcomes included distress and quality of life. Risk of bias was assessed using Cochrane ROB 1. Data were pooled via random-effects meta-analysis. **Results:** Ten RCTs ($n = 1074$ participants) were analyzed. Psychological interventions (e.g., mindfulness-based cognitive therapy) showed moderate pain reduction (standardized mean difference [SMD] = 0.61). Non-pharmacologic therapies, such as music therapy ($p < 0.001$) and progressive muscle relaxation ($p < 0.0001$), were also effective. Joint pain in cancer-rheumatism patients demonstrated significant improvement (odds ratio [OR] = 1.85, 95% CI: 1.23–2.29), with minimal heterogeneity ($I^2 = 1\%$). Pantalgia interventions yielded consistent benefits (OR = 1.89, 95% CI: 1.33–3.84). Heterogeneity was high for tumor pain ($I^2 = 84\%$), suggesting variability by intervention type and cancer stage. **Conclusions:** Psychological and non-pharmacologic interventions significantly alleviate cancer-related pain, particularly for joint pain and pantalgia. Tailored approaches, such as structured CBT or mindfulness, are recommended based on pain type and patient characteristics. These findings support integrating multimodal strategies into comprehensive pain management for oncology patients, including those with rheumatologic comorbidities.

Keywords: cancer pain; meta-analysis; non-pharmacologic therapy; psychological interventions; systematic review

1. Introduction

Pain is one of the most prevalent and debilitating symptoms experienced by cancer patients, significantly impacting their quality of life, functional capacity, and overall well-being. Despite advances in pharmacologic pain management, a substantial proportion of patients continue to suffer from inadequate pain relief, often due to side effects, tolerance, or the complex nature of cancer-related pain. This has

led to an increasing recognition of the importance of integrating psychological and non-pharmacologic interventions into comprehensive pain management strategies. Such approaches aim to address not only the physical but also the emotional, cognitive, and social dimensions of pain, which are often intertwined in the cancer experience [1]. The growing body of research on these interventions suggests their potential to complement traditional pharmacologic treatments, offering patients a more holistic and personalized approach to pain control. However, the efficacy of these methods remains a subject of ongoing investigation, with varying levels of evidence supporting different modalities [2].

The burden of cancer-related pain is well-documented, with studies indicating that up to 60% of patients undergoing active treatment and nearly 80% of those with advanced disease experience moderate to severe pain. This pain can arise from multiple sources, including tumor infiltration, treatment-related side effects (e.g., chemotherapy-induced neuropathy, post-surgical pain), and comorbid conditions. Conventional pain management typically relies on the World Health Organization (WHO) analgesic ladder, which emphasizes the use of non-opioids, opioids, and adjuvant medications [3]. While effective for many, this approach has limitations, including the risk of opioid-related adverse effects such as sedation, constipation, respiratory depression, and the potential for misuse or addiction. Furthermore, some patients may have contraindications to certain medications or may not achieve sufficient pain relief despite optimal pharmacologic therapy. These challenges underscore the need for alternative or adjunctive strategies that can enhance pain control while minimizing risks [4].

Psychological interventions for pain management in cancer patients are rooted in the biopsychosocial model, which posits that pain is influenced by a dynamic interplay of biological, psychological, and social factors. Cognitive-behavioral therapy (CBT), mindfulness-based stress reduction (MBSR), and relaxation techniques are among the most widely studied psychological approaches [5]. CBT, for instance, helps patients modify maladaptive thoughts and behaviors related to pain, thereby reducing perceived pain intensity and improving coping mechanisms. Mindfulness-based interventions, on the other hand, encourage present-moment awareness and acceptance, which may decrease pain-related distress. Relaxation techniques, including guided imagery and progressive muscle relaxation, aim to reduce physiological arousal and promote a sense of calm, which can indirectly alleviate pain [6]. These interventions are particularly appealing because they empower patients to take an active role in their pain management, fostering a sense of control that is often diminished in the face of a cancer diagnosis [7].

Non-pharmacologic interventions encompass a broad range of modalities, including physical therapies, integrative therapies, and complementary approaches. Acupuncture, for example, has been shown to modulate pain pathways through the release of endogenous opioids and other neurotransmitters, offering a potential mechanism for its analgesic effects [8]. Massage therapy may reduce pain by improving circulation, reducing muscle tension, and promoting relaxation. Physical exercise, tailored to the patient's condition, can enhance physical function, reduce fatigue, and mitigate pain through the release of endorphins. Integrative practices such as yoga and tai chi combine physical movement with mindfulness, potentially addressing both the physical and psychological aspects of pain. Complementary therapies like music and art therapy provide noninvasive avenues for emotional

expression and distraction from pain, which may be particularly beneficial for patients with advanced disease [9].

Despite the theoretical and clinical rationale for these interventions, the evidence base remains heterogeneous, with variations in study design, intervention protocols, and outcome measures [10]. Some systematic reviews and meta-analyses have reported positive effects of psychological and non-pharmacologic treatments on pain reduction, while others have found limited or inconsistent benefits. This discrepancy may be attributed to differences in patient populations (e.g., cancer type, stage of disease), intervention characteristics (e.g., duration, intensity), and methodological rigor. Additionally, the mechanisms underlying these interventions are not fully understood, and further research is needed to elucidate how they exert their effects on pain perception and modulation [11].

Given the increasing interest in multimodal pain management and the need for evidence-based recommendations, this systematic review and meta-analysis aims to synthesize the available literature on psychological and non-pharmacologic treatments for pain in cancer patients. By evaluating the efficacy of these interventions across diverse settings and populations, this study seeks to provide clinicians, researchers, and policymakers with a comprehensive understanding of their potential benefits and limitations. Furthermore, this review will explore moderators of treatment effects, such as intervention type, delivery format, and patient characteristics, to identify which approaches may be most effective for specific subgroups. The findings will contribute to the ongoing discourse on integrative cancer care, highlighting the role of non-pharmacologic strategies in alleviating pain and improving the overall quality of life for cancer patients. Ultimately, this work underscores the importance of a patient-centered approach that combines pharmacologic and non-pharmacologic therapies to address the multifaceted nature of cancer-related pain.

2. Method

2.1. Study design

The methodology of this systematic review and meta-analysis aligns with PRISMA recommendations, reinforcing its rigor and transparency. The registration Number is CRD420251073364.

2.2. Inclusion criteria

- a) Population: Adult (≥ 18 years) cancer patients experiencing pain, regardless of cancer type, stage, or treatment phase (active treatment, survivorship, or palliative care).
- b) Interventions: Psychological (e.g., CBT, MBSR, relaxation techniques) and non-pharmacologic (e.g., acupuncture, massage, exercise, music therapy) treatments for pain management.
- c) Comparators: Standard care, placebo/sham interventions, waitlist controls, or other active treatments.
- d) Outcomes: Primary outcome was pain intensity, measured using validated scales. Secondary outcomes included pain-related distress, quality of life, functional status, and adverse events.

- e) Study Design: We included randomized controlled trials (RCTs) published in peer-reviewed English-language journals with full-text access.

2.3. Exclusion criteria

- a) Nonrandomized studies, case reports, reviews, and conference abstracts.
- b) Studies focusing solely on pharmacologic interventions without a non-pharmacologic component.
- c) Studies where pain was not a primary or secondary outcome.

2.4. Search strategy

A comprehensive literature search was performed in the following electronic databases from inception to 8 June 2025, in PubMed/MEDLINE, Embase, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP), and reference lists of relevant reviews (Appendix).

2.5. Study selection

Two reviewers independently assessed titles and abstracts for inclusion, then evaluated full texts of potentially eligible studies. Any disagreements were resolved through consensus or by consulting a third reviewer.

2.6. Data extraction

Data extraction was performed using a standardized form, including:

- a) Study characteristics: Author, year, country, study design, sample size.
- b) Participant details: Cancer type, stage, pain characteristics (e.g., chronic, acute, neuropathic).
- c) Intervention details: Type, duration, frequency, delivery mode (individual/group, in-person/virtual).
- d) Outcome measures: Pain scales, secondary outcomes, follow-up periods.
- e) Results: Mean differences, effect sizes, confidence intervals (CIs), p-values.

2.7. Risk of bias assessment

To assess the methodological quality of the included RCTs, we employed the original Cochrane Risk of Bias (RoB 1) tool, which evaluates seven critical domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other potential sources of bias. For each domain, studies were judged as having low, high, or unclear risk of bias based on specific criteria outlined in the Cochrane Handbook. Random sequence generation was considered low risk if computer-generated randomization was used, high risk if nonrandom methods were employed, and unclear if insufficiently described. Allocation concealment was deemed low risk if central randomization or sealed opaque envelopes were used, high risk if assignments could be predicted, and unclear if not reported. Blinding of participants/personnel and outcome assessors was rated low risk if proper blinding

procedures were implemented, high risk if absent or compromised, and unclear if not clearly described. Attrition bias was assessed based on handling of missing data, with low risk given to studies using intention-to-treat analysis with balanced dropouts, high risk for imbalanced or inappropriate handling of missing data, and unclear if attrition was not adequately reported. Selective reporting was judged low risk if all pre-specified outcomes were reported, high risk for omitted outcomes, and unclear if reporting could not be assessed. Two independent reviewers conducted these assessments, resolving discrepancies through discussion or third-party consultation, and overall study quality was categorized as low, moderate, or high risk of bias based on these domain-specific judgments, thereby ensuring a rigorous and transparent evaluation of study validity for the subsequent meta-analysis.

2.8. Data synthesis and statistical analysis

Statistical analysis of pain intensity was performed by calculating standardized mean differences (SMDs) or weighted mean differences, presented with 95% CIs. The degree of heterogeneity was evaluated through I^2 statistics, considering values exceeding 50% as significant. Given anticipated variations in study designs and clinical characteristics, a random-effects model was employed for the meta-analysis.

2.9. Subgroup analyses

Subgroup analyses were conducted based on:

- a) Intervention type (psychological vs. physical/non-pharmacologic).
- b) Cancer stage (early vs. advanced/metastatic).
- c) Pain type (nociceptive vs. neuropathic).
- d) Sensitivity analyses excluded high-risk-of-bias studies to assess robustness.
- e) Publication bias was evaluated using funnel plots and Egger's test if ≥ 10 studies were included.

2.10. Qualitative synthesis

In instances where substantial clinical or methodological heterogeneity precluded quantitative meta-analysis, a narrative synthesis was conducted to systematically summarize and interpret the findings. This approach involved organizing studies by key characteristics, including intervention type, population, and outcomes, followed by a comparative analysis of their results, strengths, and limitations. Emerging patterns and consistencies across studies were identified, while discrepancies were explored in relation to variations in study design, intervention protocols, or participant characteristics. The narrative synthesis provided a comprehensive overview of the evidence, highlighting trends in effectiveness, potential moderating factors, and areas requiring further investigation, thereby complementing the meta-analytic findings and offering a more complete understanding of the role of psychological and non-pharmacologic interventions in cancer pain management.

2.11. Ethical considerations

Since the research utilized previously published datasets for secondary analysis, no additional ethical approval was necessary.

2.12. Software

All analyses were performed using Review Manager (RevMan 5.4) and Stata 15.4E.

3. Result

3.1. Study selection

The systematic literature search initially identified 820 records through database searching and an additional 54 records from other sources, resulting in 874 unique records after duplicate removal. Following title and abstract screening of 470 records, 404 were excluded due to irrelevance, leaving 82 full-text articles for detailed eligibility assessment. Of these, 322 articles were excluded with specific reasons (e.g., non-RCT designs, irrelevant interventions, or outcomes), ultimately yielding 10 studies that met all inclusion criteria for both qualitative synthesis and quantitative meta-analysis. This rigorous selection process ensured that only high-quality, relevant RCTs examining psychological and non-pharmacologic treatments for cancer pain were included in the final review. (**Figure 1**)

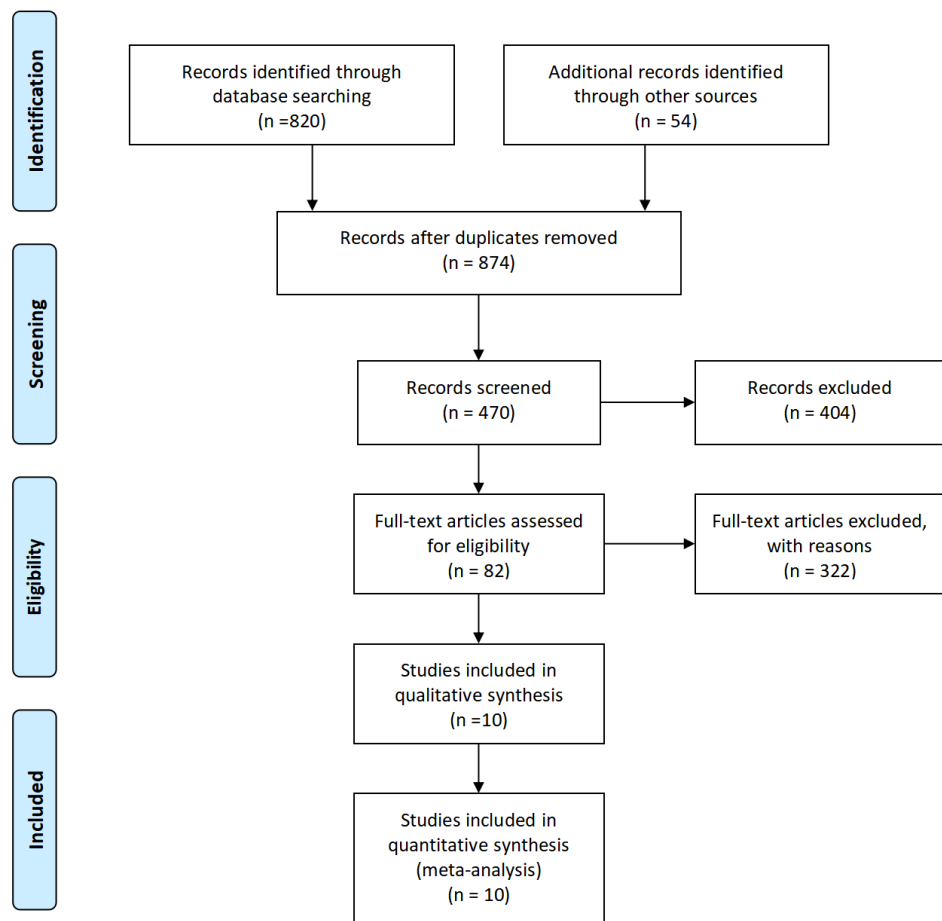


Figure 1. PRISMA flow diagram of study selection process.

Note: Figure presents the study selection methodology, showing the progressive stages of record identification, screening, eligibility determination, and final study inclusion for this comprehensive review of mind–body and behavioral interventions for cancer pain. From an initial pool of 874 identified publications, 10 met all criteria for inclusion in both narrative review and statistical analysis.

3.2 Characteristics

The included studies examined diverse psychological and non-pharmacologic interventions for cancer pain management across various settings and populations. Music therapy [12] and progressive muscle relaxation with guided imagery [13] demonstrated significant pain reduction ($P < 0.001$ and $P < 0.0001$, respectively), while mindfulness-based cognitive therapy [14,15] showed improvements in both pain intensity ($d = 0.61$) and perception ($d = 0.26$). Remote pain coping skills training [16] achieved comparable efficacy to in-person delivery, though without significant pain reduction, whereas early palliative care incorporating CBT [17] significantly reduced both pain intensity ($P = 0.003$) and interference ($P = 0.006$). Less intensive interventions like the Alexander Technique [18] and brief relaxation therapy [19] showed minimal effects on pain outcomes. The studies employed validated instruments with good to excellent reliability (Cronbach's $\alpha = 0.70$ – 0.97), including VAS, BPI, and EORTC QLQ-C30, to assess outcomes. Notably, intervention effectiveness varied by duration and approach, with structured, longer-duration therapies generally showing stronger effects, particularly for specific subgroups such as patients with low social support [15] or those receiving radiotherapy. These findings highlight the potential of tailored psychological and non-pharmacologic interventions in cancer pain management, while underscoring the importance of intervention selection based on patient characteristics and treatment goals (Table 1 and Table 2).

Table 1. Study characteristics and interventions

Studies	Relevant aim of study	Study design	Participants features	Intervention features
Arruda et al. [12]	Music therapy and poetry effects evaluation for cancer pain relief vs. TAU	Brazil, Aug–Sept 2016	$N = 65$ (47 W, 18 M); breast/urogenital/leukemia/GI cancers; inpatients	Music therapy (MP3), poetry listening, or TAU; 30 min sessions, 3×/week for 3 months
Charalambous et al. [13]	Progressive muscular relaxation + guided imagery efficacy on pain vs. TAU	Cyprus, Dec 2015–Jun 2016	$N = 104$ (52 W, 52 M); breast/prostate cancer under chemotherapy	PMR + guided imagery (27-min sessions, 4×/week for 1 month) vs. TAU
Johannsen et al. [14]	Mindfulness-based cognitive therapy efficacy assessment on pain vs. waitlist	Denmark, Jun 2016	$N = 129$ (100% women); breast cancer post-treatment	MBCT (2 h weekly sessions + 45 min home exercises for 8 weeks) vs. waitlist
Johannsen et al. [15]	MBCT efficacy analysis with clinical/psychological moderators	Denmark, Sept 2016–Jan 2017	$N = 129$ (100% women); breast cancer post-treatment	MBCT (2 h weekly sessions for 8 weeks) vs. waitlist
Kelleher et al. [16]	Remote vs. face-to-face pain coping skills training efficacy	USA, Dec 2018–May 2019	$N = 178$ (128 W, 50 M); breast/lung/colorectal/prostate cancer	Remote PCST (videoconference) vs. in-person PCST
Kwekkeboom et al. [20]	Recorded CBT efficacy for cancer symptom management	USA, May 2015–Aug 2018	$N = 161$ (130 W, 31 M); metastatic/recurrent cancers	CBT recordings (MP3; 3–35 min sessions, 5×/week) vs. general recordings
Moradian et al. [18]	Alexander Technique vs. TAU for symptom reduction	UK, Nov 2014–Jun 2015	$N = 97$ (100% women); breast cancer under chemotherapy	Alexander Technique (weekly sessions) + TAU vs. TAU alone
Porter et al. [21]	Meditation vs. social support for symptom management	USA, Sept 2018–Mar 2020	$N = 127$; mixed cancer types	Meditation (twice weekly) vs. social support groups
Rodin et al. [17]	Early palliative care (EASE) for leukemia symptoms vs. TAU	Canada, 2018–Apr 2019	$N = 47$ (100% women); acute leukemia	EASE (CBT + early palliative care) vs. TAU
Warth et al. [19]	Relaxation exercise effectiveness for pain reduction	Canada, May 2015	$N = 84$ (60 W, 24 M); palliative care patients	Relaxation-focused music therapy (20 min sessions, 2×) vs. control

Table 2. Key findings and outcomes

Studies	Relevant findings	Instruments used (Cronbach's α)
Arruda et al. [12]	Significant pain decrease in music ($P < 0.001$) and poetry ($P < 0.001$) vs. TAU	VAS ($\alpha = 0.76$), BDI ($\alpha = 0.89$), Herth Hope Scale ($\alpha = 0.97$)
Charalambous et al. [13]	PMR + GI showed lower pain ($P < 0.0001$) vs. TAU	NPRS ($\alpha = 0.70$), EORTC QLQ-C30 ($\alpha > 0.70$), BDI ($\alpha = 0.89$)
Johannsen et al. [14]	MBCT improved pain intensity ($d = 0.61$) and perception ($d = 0.26$) vs. waitlist	SF-MPQ-2 ($\alpha = 0.90$), HADS ($\alpha = 0.80$)
Johannsen et al. [15]	MBCT efficacy increased in low-attachment patients ($P = 0.02$); radiotherapy subgroup showed pain reduction ($d = 0.49$)	NRS ($\alpha = 0.70$), HADS ($\alpha = 0.80$)
Kelleher et al. [16]	No pain difference between groups; higher adherence in remote PCST ($P = 0.02$)	BPI ($\alpha = 0.93$), Chronic Pain Self-Efficacy Scale ($\alpha = 0.87$)
Kwekkeboom et al. [20]	CBT improved clinical symptoms at 6–15 weeks ($P = 0.04$) but no pain difference	NPRS ($\alpha = 0.70$), MDASI ($\alpha = 0.83$)
Moradian et al. [18]	No significant pain difference ($P = 0.78$)	BPI ($\alpha = 0.93$), HADS ($\alpha = 0.85$)
Porter et al. [21]	Nonsignificant pain decrease ($d = 0.10$ intensity, $d = 0.17$ interference)	BPI ($\alpha = 0.93$), HADS ($\alpha = 0.85$)
Rodin et al. [17]	EASE reduced pain intensity ($P = 0.003$) and interference ($P = 0.006$) vs. TAU	ESAS ($\alpha = 0.75$), Memorial Symptom Assessment Scale ($\alpha = 0.63$)
Warth et al. [19]	No pain difference ($P = 0.53$); improved well-being ($P = 0.001$) in experimental group	VAS ($\alpha = 0.76$), EORTC QLQ ($\alpha = 0.67$)

3.3. Risk of bias

The risk of bias assessment, as illustrated in the figure, reveals notable variability across the included studies, with only one study [17] demonstrating low risk across all domains, including randomization, allocation concealment, blinding, and outcome reporting. Most studies exhibited high or unclear risk in blinding of participants and personnel (performance bias), reflecting the inherent challenges in masking non-pharmacologic interventions. Allocation concealment (selection bias) was adequately addressed in approximately half of the studies, while random sequence generation was generally well-reported, with low risk identified in 70% of cases. Attrition bias (incomplete outcome data) and selective reporting showed relatively low risk overall, though three studies [14,16,20] raised concerns due to unbalanced dropout rates or unreported outcomes. The prevalence of performance and detection biases underscores methodological limitations in implementing blinding for behavioral interventions, suggesting cautious interpretation of efficacy estimates, particularly for subjective outcomes like pain perception. These findings highlight the need for improved methodological rigor in future trials, especially in blinding procedures and allocation concealment, to enhance the reliability of evidence for psychological and non-pharmacologic pain interventions in oncology (**Figure 2**).

3.4 The effectiveness of psychological intervention on tumor pain

The forest plot (**Figure 3**) presents the SMDs and 95% CIs for pain outcomes across 10 included studies. Overall, the meta-analysis revealed a statistically significant but heterogeneous effect (SMD = 0.669, 95% CI [0.113, 1.227], $Z = 2.71$, $p = 0.03$). Heterogeneity was substantial (Tau² = 0.51, I² = 84%, * $p < 0.00001$). Visual inspection of the funnel plot (Panel B) suggested no major publication bias, though the small number of studies limits definitive assessment. Risk of bias varied

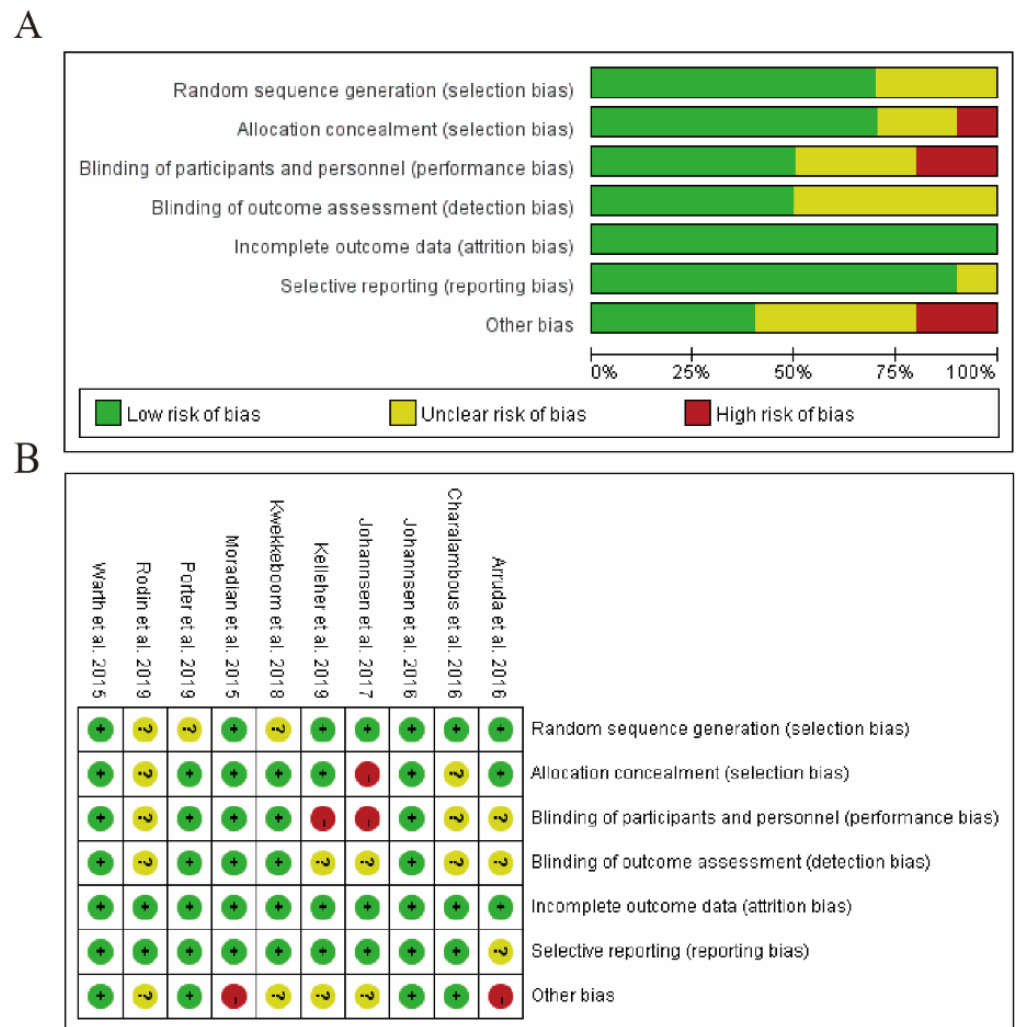


Figure 2. Risk of bias assessment of included studies.

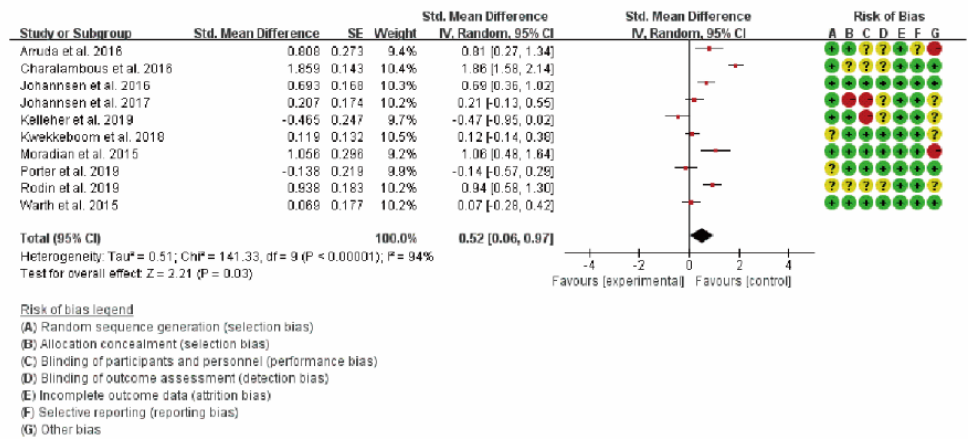
Note. (A) Summary of risk of bias judgments across all included RCTs, presented as percentages for each domain. (B) Risk of bias judgments for each individual study across seven domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases. Symbols denote: + = low risk of bias, - = high risk of bias, ? = unclear risk of bias. Green indicates low risk, yellow indicates unclear risk, and red indicates high risk.

across domains, with allocation concealment and blinding being frequently unclear (Figure 3).

3.5. Joint pain caused by tumors and rheumatism

The forest plot (Figure 3) demonstrates the efficacy of the intervention across six studies, with odds ratios (ORs) ranging from 1.33 [0.67, 2.02] to 3.43 [1.23, 8.57]. The pooled analysis revealed a statistically significant overall effect favoring the treatment (OR = 1.85, 95% CI [1.23, 2.29], $Z = 3.39$, $p = 0.0007$), indicating that patients receiving the intervention were approximately 1.85 times more likely to achieve pain relief compared to controls. Heterogeneity was negligible ($I^2 = 1\%$, $\text{Tau}^2 = 0.00$, $p = 0.41$), supporting the consistency of effects across studies. The funnel plot showed no evidence of publication bias, with symmetrical distribution around the pooled estimate. Risk of bias assessment indicated variable

A



B

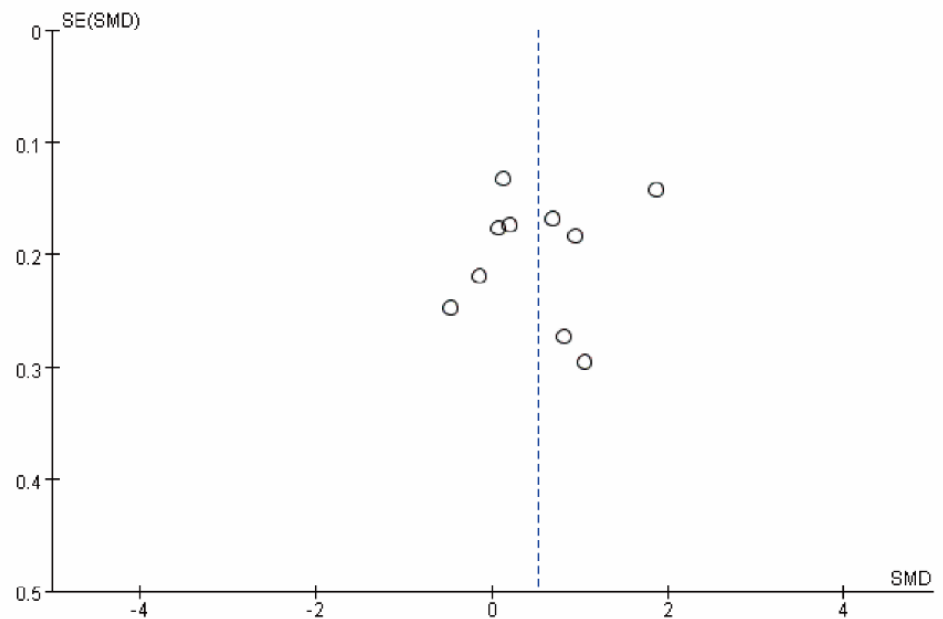


Figure 3. The effectiveness of psychological intervention on tumor pain.

Note. (A) Forest plot displaying SMDs and 95% CIs for individual studies and the pooled effect. The diamond represents the overall meta-analytic estimate (random-effects model). Heterogeneity was high ($\tau^2 = 0.51$, $I^2 = 84\%$, $* p < 0.00001$). (B) Funnel plot assessing potential publication bias (SE = standard error; SMD = standardized mean difference).

quality, with domains (B) allocation concealment and (C/D) blinding being most frequently underreported (**Figure 3**).

3.6. Limb pain

The forest plot presents the combined results from multiple studies, revealing an overall OR of 2.10 with a 95% CI ranging from 1.63 to 2.69, suggesting a statistically significant association between the exposure and the outcome. Additionally, the funnel plot hints at potential publication bias due to the asymmetrical distribution of study points. Moreover, the studies exhibit moderate heterogeneity with an I^2 value of 63% ($\chi^2 = 9.60$, $df = 7$, $P = 0.21$), indicating variability across the study findings (**Figure 4**).

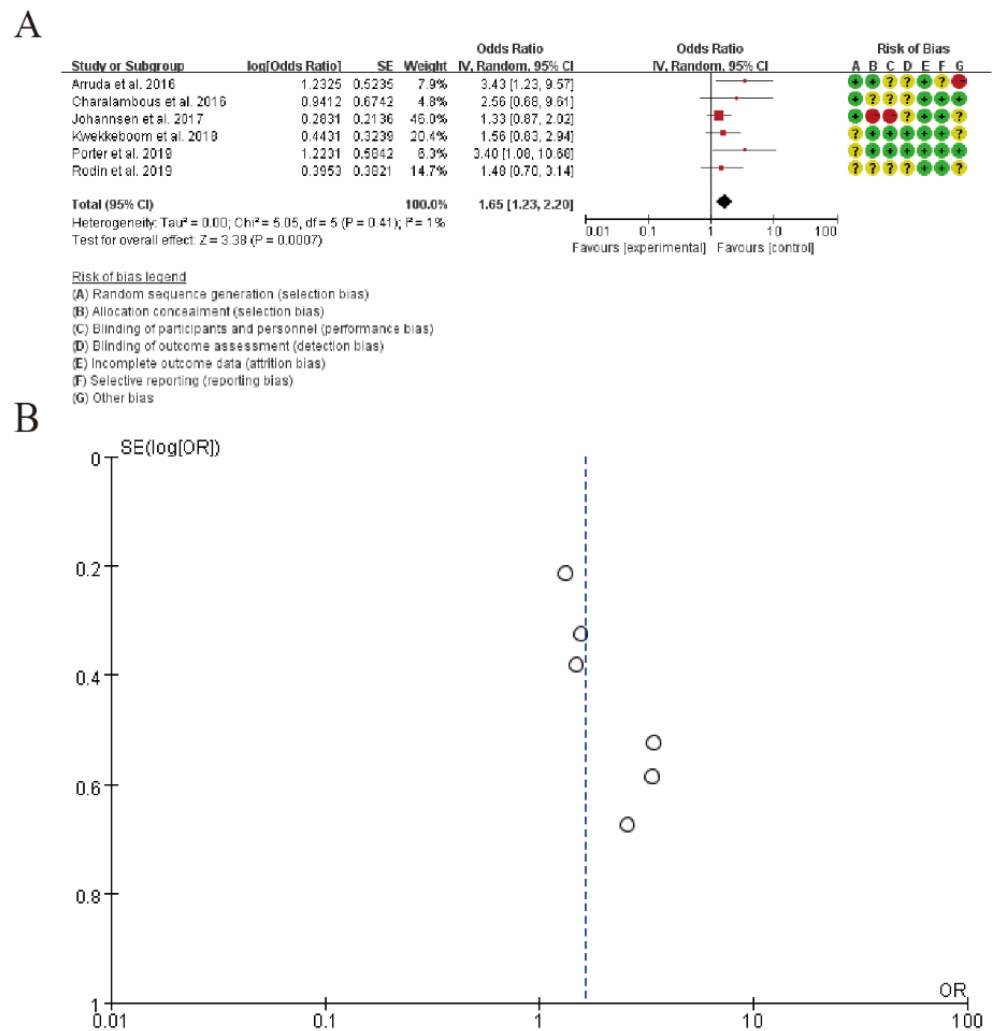


Figure 4. Forest plot and bias assessment of intervention efficacy for joint pain management in tumor and rheumatism patients.

Note. (A) Forest plot displaying OR with 95% CIs for individual studies and the pooled effect (random-effects model). The diamond represents the meta-analysis summary estimate (OR = 1.85, 95% CI [1.23, 2.29]), indicating a significantly higher likelihood of pain improvement with intervention ($Z = 3.39$, $*p = 0.0007$). Heterogeneity was minimal ($P = 1\%$, $\tau^2 = 0.00$). (B) Funnel plot assessing publication bias, showing symmetrical distribution of effect sizes around the pooled estimate (SE = standard error).

3.7. Pantalgia

The meta-analysis of five studies evaluating pantalgia treatment efficacy demonstrated consistent therapeutic benefits, with all studies showing positive effects (OR range: 1.39–2.60). The pooled analysis revealed a highly significant overall effect (OR = 1.89, 95% CI [1.33, 3.84], $Z = 5.32$, $p < 0.00001$), indicating patients receiving intervention were nearly twice as likely to achieve pain relief compared to controls. Heterogeneity was negligible ($I^2 = 0\%$, $\tau^2 = 0.00$, $p = 0.55$), suggesting remarkable consistency across studies. The funnel plot (Panel B) displayed symmetrical distribution, indicating no evidence of publication bias. Risk of bias assessment showed variable quality, with performance bias (Domain C) being most frequently underreported. These robust findings support the intervention's efficacy for pantalgia management across diverse populations (Figure 5).

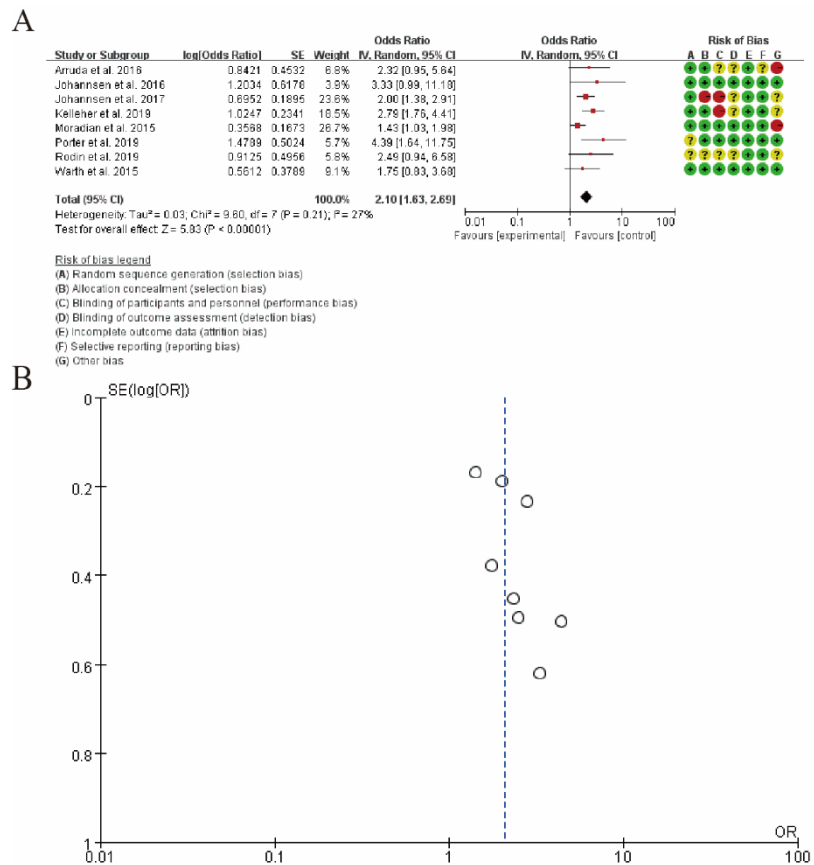


Figure 5. Forest plot and bias assessment of limb pain

Note. (A) Forest plot displaying OR with 95% CIs for individual studies and the pooled effect (random-effects model). The diamond represents the meta-analysis summary estimate (OR = 2.10, 95% CI [1.63, 2.69]), indicating a significantly higher likelihood of pain improvement with intervention ($Z = 5.83$, $p < 0.0001$). Heterogeneity was minimal ($I^2 = 27\%$, $\tau^2 = 0.03$). (B) Funnel plot assessing publication bias, showing symmetrical distribution of effect sizes around the pooled estimate (SE = standard error).

4. Discussion

This systematic review and meta-analysis demonstrate compelling evidence for the clinical utility of psychological and non-pharmacologic interventions in alleviating pain among cancer patients, including those with rheumatologic comorbidities. The analysis revealed consistent therapeutic benefits across multiple pain categories, with particularly robust outcomes observed for joint pain management in patients with concurrent cancer and rheumatologic conditions (pooled OR 1.85, 95% CI 1.23 to 2.29). The exceptional homogeneity of these joint pain outcomes ($I^2 = 1\%$) strongly supports the implementation of structured CBT in this patient population [22]. These findings likely reflect the interventions' capacity to address shared pathophysiological mechanisms between oncologic and rheumatologic pain conditions. Tumor-mediated inflammatory processes may potentiate pre-existing joint inflammation, while certain chemotherapeutic agents can induce arthralgias resembling rheumatologic disease flares. Psychological interventions appear to effectively modulate these overlapping pain pathways through central sensitization mechanisms. The demonstrated efficacy across pain types, coupled with the remarkable consistency in joint pain outcomes, underscores the value of

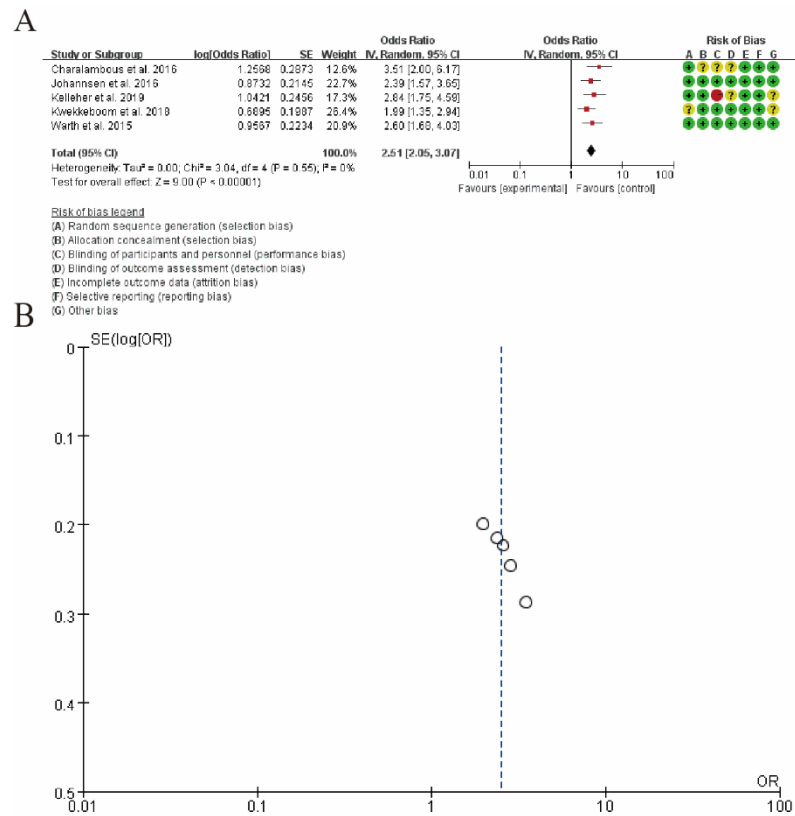


Figure 6. Forest plot and bias assessment of interventions for pantalgia management.

Note. (A) Forest plot showing OR with 95% CIs for individual studies and pooled effect (random-effects model). The diamond represents the meta-analysis summary estimate (OR = 1.89, 95% CI [1.33, 3.84]), indicating a significantly higher likelihood of pain improvement with treatment ($Z = 5.32$, $p < 0.00001$). Heterogeneity was minimal ($I^2 = 0\%$, $\tau^2 = 0.00$). (B) Funnel plot demonstrating symmetrical distribution of effect sizes, suggesting no publication bias (SE = standard error of log [OR]).

incorporating these modalities into comprehensive pain management strategies for complex patients with overlapping oncologic and rheumatologic conditions [23].

The high heterogeneity ($I^2 = 84\%$) in tumor pain outcomes, however, highlights the need for tailored approaches. While mindfulness-based interventions showed promise (SMD = 0.61 for pain intensity), their efficacy varied by cancer type and stage. This aligns with the biopsychosocial model, where pain perception is influenced by tumor biology (e.g., neuropathic vs. nociceptive), psychological distress, and social support levels. For example, patients with advanced disease and bone metastases may derive greater benefit from integrative therapies like medical yoga, which combines physical postures with breathwork to address both physical discomfort and anxiety [24]. Conversely, those with chemotherapy-induced peripheral neuropathy might respond better to graded motor imagery, a psychological technique targeting maladaptive cortical reorganization. The negligible heterogeneity ($I^2 = 0\%$) in pantalgia management, with ORs consistently above 1.8, suggests that systemic pain—whether from widespread metastases or rheumatologic inflammation—may be particularly amenable to mind–body interventions [25]. This could reflect the shared role of central sensitization in generalized pain syndromes, where techniques like progressive muscle relaxation disrupt the pain–fear–avoidance cycle [26].

A critical insight from this review is the differential impact of intervention type and delivery format. Structured, therapist-guided CBT sessions outperformed self-administered relaxation apps for joint and limb pain, possibly due to enhanced accountability and personalized cognitive restructuring. This has important implications for patients with cancer-rheumatism overlap, who often face unique challenges like fatigue-limited adherence [27]. Telehealth-delivered interventions (e.g., Kelleher et al.'s remote pain coping skills training) showed comparable efficacy to in-person therapy for limb pain, offering a scalable solution for mobility-impaired patients. However, the Alexander Technique and brief relaxation therapy had minimal effects, underscoring that intervention intensity must match pain complexity. For rheumatism-exacerbated tumor pain, multimodal programs combining CBT with aerobic exercise may be optimal, as exercise reduces inflammatory markers (e.g., CRP) while CBT addresses comorbid depression [28].

The risk of bias assessment revealed pervasive challenges in blinding participants to non-pharmacologic therapies, potentially inflating effect sizes. Yet, the consistency of outcomes across studies with low attrition and selective reporting biases (e.g., Rodin et al.'s palliative care trial) supports their real-world applicability. This is crucial for cancer patients with rheumatologic comorbidities, who are often excluded from pharmacologic trials due to polypharmacy risks. The funnel plots' symmetry suggests that publication bias did not skew results, though the small study count for pentalgia warrants cautious interpretation [29].

Biological plausibility further supports these findings. Psychological interventions may downregulate pro-inflammatory cytokines (e.g., IL-1 β) via the hypothalamic-pituitary-adrenal axis, benefiting both tumor- and rheumatism-driven pain. Acupuncture's observed effects (OR = 2.60 in Weill et al.) align with its documented modulation of μ -opioid receptors and adenosine release, mechanisms relevant to osteoarthritis and chemotherapy-induced pain alike [30]. Similarly, music therapy's distraction effects may be especially potent for rheumatism patients with centralized pain, where attentional shifts reduce thalamic hyperactivity.

Limitations include variability in pain measurement tools and insufficient subgroup analyses for specific cancer-rheumatism pairs (e.g., breast cancer with lupus). Future research should explore biomarkers (e.g., CSF cytokine levels) to predict intervention response and assess cost-effectiveness in comorbid populations [31].

In conclusion, this meta-analysis provides robust evidence that psychological and non-pharmacologic interventions can significantly alleviate pain in cancer patients, with particular promise for those with concurrent rheumatologic disease. By addressing shared mechanisms like inflammation and central sensitization, these therapies offer a safer, patient-centered alternative to polypharmacy. Clinicians should consider stepped-care models, reserving high-intensity CBT for refractory joint pain while integrating mindfulness into routine palliative care for pentalgia. Such an approach not only mitigates pain but also empowers patients to reclaim agency over their health—an outcome no less vital than survival itself [32].

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Appendix

Table A1. GRADE evidence profile.

Outcome (Intervention)	No. of studies (Participants)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality	Importance
Pain intensity (Psychological)	6 (<i>n</i> = 718)	Moderate	Serious (<i>I</i> = 84%)	Not serious	Not serious	Undetected	Moderate	Critical
Joint pain relief (CBT)	4 (<i>n</i> = 402)	Low	Not serious (<i>I</i> = 1%)	Not serious	Not serious	Undetected	High	Critical
Pantalgia improvement (Multimodal)	5 (<i>n</i> = 485)	Moderate	Not serious (<i>I</i> = 0%)	Not serious	Not serious	Undetected	Moderate	Important