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Targeting Musculoskeletal Pain with Digital Therapeutics: A Cross-Sectional Analysis of ClinicalTrials.gov

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ABSTRACT: Musculoskeletal pain is a leading cause of disability worldwide and remains challenging to manage. Conventional pharmacological therapies usually provide partial long-term benefit and are associated with adverse effects, including opioid-related risks. Digital therapeutics have emerged as innovative, software-driven interventions that target pain mechanisms, rehabilitation processes, and psychosocial contributors to musculoskeletal pain. **Methods:** A cross-sectional search was conducted using ClinicalTrials.gov to identify clinical trials evaluating digital therapeutics targeting musculoskeletal pain. A structured search was performed in December 2025. Eligible studies included interventional or observational trials assessing digital therapeutic interventions for musculoskeletal pain conditions. Data extracted included study design, recruitment status, intervention strategies, outcomes, funding sources, and reporting practices. Descriptive analyses were performed using frequencies and percentages. **Results:** A total of 52 Clinical registered trials met the inclusion criteria. Most studies were interventional (94.2%) and focused on adult populations. Digital therapeutic strategies included virtual reality–based interventions, digital physical therapy and tele-rehabilitation platforms, multidisciplinary digital therapeutics, digital cognitive behavioral and exposure-based therapies, and mobile application–based rehabilitation tools. Pain intensity was the most frequently assessed outcome ($\approx 96\%$ of trials), followed by psychological outcomes and functional disability measures. Only 13% of studies evaluated opioid or analgesic use. While 40.4% of trials were completed, results were publicly available for only 9.6%, highlighting limited reporting transparency. Considerable heterogeneity in study design, outcome measures, and follow-up duration precluded quantitative meta-analysis. **Conclusion:** Digital therapeutics represent a rapidly expanding and diverse therapeutic approach for targeting musculoskeletal pain, addressing nociceptive, nociplastic, and biopsychosocial pain mechanisms. However, substantial gaps remain in outcome standardization, medication-related assessments, long-term evaluation, and result reporting. Future research should focus on harmonized outcome frameworks, integration with pharmacological strategies, and improved transparency to support the clinical implementation of digital therapeutics in musculoskeletal pain management.

1. INTRODUCTION

Musculoskeletal pain represents one of the most prevalent and disabling health conditions worldwide, accounting for a substantial proportion of years lived with disability across all age groups [1]. Conditions such as low back pain, neck pain, osteoarthritis, shoulder disorders, and fibromyalgia contribute significantly to functional impairment, reduced quality of life, and increased healthcare utilization [2]. Despite advances in pharmacological and non-pharmacological management, the long-term control of musculoskeletal pain remains challenging, particularly in chronic and recurrent cases. Conventional pharmacological treatments, including nonsteroidal anti-inflammatory drugs, muscle relaxants, antidepressants, and opioids,

provide symptomatic relief for some patients but are frequently associated with limited efficacy, adverse effects, and poor long-term tolerability [3]. Opioid-based therapies have raised major concerns due to risks of dependence, tolerance, and misuse, highlighting the urgent need for alternative and adjunctive approaches to pain management [4]. Moreover, musculoskeletal pain is increasingly recognized as a complex condition involving peripheral nociceptive mechanisms and central sensitization, altered pain perception, psychological distress, and behavioral factors [5, 6].

In recent years, the concept of digital therapeutics has emerged as a novel strategy to address the complex and multidimensional nature of chronic pain [7]. Digital therapeutics include evidence-based software-driven interventions designed to prevent, manage, or treat medical conditions through mechanisms that extend beyond passive monitoring [8]. These interventions include virtual reality-based therapies, digital physical therapy and tele-rehabilitation platforms, mobile health applications, digital cognitive behavioral therapy, and multidisciplinary digital treatment programs [8, 9]. Unlike traditional digital health tools, digital therapeutics are intended to deliver active therapeutic effects by targeting pain processing pathways, motor function, psychological contributors, and patient engagement [10]. Digital interventions for musculoskeletal pain constitute a growing field that bridges pain research with a better understanding of chronic pain, including maladaptive neuroplasticity, fear avoidance behaviors, impaired motor control, and reduced adherence to rehabilitation programs [11]. Virtual reality interventions could modulate central pain processing, digital physical therapy can enhance biomechanical recovery and adherence, and cognitive-behavioral digital programs can address pain mechanisms such as catastrophizing and Kinesio phobia [12, 13]. Together, these approaches may complement pharmacological therapies and reduce dependence on long-term medication use. Therefore, this study explored the ClinicalTrials.gov-registered clinical trials and evaluated digital therapeutics targeting musculoskeletal pain. By characterizing study designs, intervention strategies, outcome domains, and reporting practices, this review provides a comprehensive overview of the current evidence landscape, identifies methodological gaps, and updates future research directions and clinical applications of digital therapeutics in musculoskeletal pain management.

2. MATERIALS AND METHODS

2.1 Study Design and Data Source

This study used a cross-sectional search to evaluate the landscape of clinical trials investigating digital therapeutics for musculoskeletal pain. The review used ClinicalTrials.gov, a publicly accessible database maintained by the U.S. National Library of Medicine, which provides comprehensive information on registered clinical studies across all phases and conditions. Clinical trials were identified through a structured search of ClinicalTrials.gov in December 2025. The initial screening included all registered clinical trials available at the time of data extraction. Filters were applied sequentially to identify studies relevant to musculoskeletal pain and digital therapeutic interventions. Search terms and registry filters included conditions related to musculoskeletal pain (e.g., low back pain, neck pain, shoulder pain, osteoarthritis, fibromyalgia, patellofemoral pain syndrome, and other musculoskeletal disorders) and interventions involving digital or technology-based therapeutic approaches, such as virtual reality, mobile health applications, digital physical therapy, rehabilitation platforms, digital cognitive behavioral therapy, and multidisciplinary digital therapeutic programs. Briefly, an initial pool of 563,845 registered studies was identified, from which non-relevant records were excluded. Studies reporting musculoskeletal pain conditions were retained, followed by screening for digital therapeutic interventions. After applying inclusion and exclusion criteria, 52 eligible clinical trials were included in the final analysis.

2.2 Eligibility Criteria

Trials were included if they were registered on ClinicalTrials.gov and focused on musculoskeletal pain conditions. Eligible studies evaluated a digital therapeutic intervention as a primary or adjunctive treatment and employed either an interventional or observational study design. Studies were considered regardless of recruitment status, including completed, recruiting, active but not recruiting, or not yet recruiting trials. No restrictions were applied based on participant age, sex, or geographic location. Trials were excluded if they were unrelated to musculoskeletal pain or if they evaluated non-therapeutic digital tools, such as administrative or monitoring-only platforms. Expanded access programs and individual patient protocols were also excluded. In addition, studies lacking a clearly defined digital therapeutic intervention component were not considered eligible for inclusion.

2.3 Data Extraction

Data were extracted directly from ClinicalTrials.gov using standardized registry fields for each included study. Extracted variables included study status, study phase, and study type, as well as participant eligibility characteristics such as age groups, sex, and acceptance of healthy volunteers. Information related to digital therapeutic interventions, outcome measures, and the availability of posted study results was also collected. In addition, the presence of supporting study documents, including study protocols, statistical analysis plans, and informed consent forms, was recorded. Funding sources were categorized according to registry-reported funder type. All extracted data were compiled into structured datasets to support descriptive and analytical synthesis.

2.4 Data Analysis

Descriptive statistics were used to summarize study characteristics. Categorical variables were reported as frequencies (n) and percentages (%). An integrated registry-based analysis was conducted to assess trends in study status, study phase, study type, result availability, and funding sources. Digital therapeutic interventions were further classified by therapeutic strategy and targeted pain mechanisms, including virtual reality-based interventions, digital physical therapy, multidisciplinary digital therapeutics, digital cognitive behavioral and exposure-based therapies, and mobile app-based rehabilitation tools. Outcome domains assessed across studies, including pain intensity, functional disability, psychological outcomes, quality of life, engagement, and opioid or analgesic use, were analyzed to evaluate the therapeutic focus of digital interventions. Methodological strengths, limitations, and evidence gaps were synthesized narratively.

3. RESULTS AND DISCUSSION

3.1 Study Selection

A cross-sectional search of ClinicalTrials.gov identified 563,845 registered studies. After excluding non-relevant records, 5,959 trials related to musculoskeletal pain conditions were retained for screening. Further filtering for digital therapeutic interventions yielded 52 eligible clinical trials, which were included in the final analysis.

3.2 Registry-Based Characteristics of Included Studies

Table 1 summarizes the registry-based characteristics of the included studies. Of the 52 trials, 21 (40.4%) were completed, 9 (17.3%) were recruiting, and 9 (17.3%) were active but not recruiting. An additional 5 trials (9.6%) were not yet recruiting, and 6 studies (11.5%) had an unknown recruitment status. Most trials were interventional (94.2%), with a smaller proportion observational (5.8%). Traditional drug development phases were largely not applicable, with 92.3% of studies categorized as “not applicable,” reflecting the non-pharmacological nature of digital therapeutics. Only one study (1.9%) was reported as Phase 4. Eligibility criteria across trials were broad, with all studies including female participants and most also including males (92.3%). Adult populations were predominantly represented, with 98.1% of studies enrolling adults aged 18–64 years and 88.5% including older adults. Only 11.5% of trials included pediatric populations. Most studies (86.5%) did not accept healthy volunteers. Analysis of funding sources revealed that academic and institutional funders were the most common, accounting for 86.5% of trials, while 26.9% involved industry sponsorship. Public funding was less frequent, with 3.8% of studies funded by the National Institutes of Health and 1.9% supported by other U.S. federal agencies (Table 1). Despite a substantial proportion of completed studies, only 5 trials (9.6%) had posted results available on ClinicalTrials.gov. Similarly, supporting study documents were limited: study protocols and statistical analysis plans were available for 13.5% of trials and informed consent forms for 11.5%, indicating ongoing challenges in transparency and result dissemination.

Table 1. Registry-Based Characteristics of ClinicalTrials.gov Studies Evaluating Digital Therapeutics for Musculoskeletal Pain (N = 52)

Domain	Category	n	%
Study Status	Recruiting	9	17.3
	Not yet recruiting	5	9.6
	Active, not recruiting	9	17.3

	Completed	21	40.4
	Enrolling by invitation	1	1.9
	Withdrawn	1	1.9
	Unknown	6	11.5
	Terminated	0	0.0
	Suspended	0	0.0
Eligibility – Sex	Female	52	100.0
	Male	48	92.3
	All sexes	52	100.0
Eligibility – Age	Children (0–17 years)	6	11.5
	Adults (18–64 years)	51	98.1
	Older adults (≥ 65 years)	46	88.5
Accepts Healthy Volunteers	Yes	7	13.5
	No	45	86.5
Study Phase	Phase 4	1	1.9
	Not applicable	48	92.3
	Early Phase 1 / Phase 1–3	0	0.0
Study Type	Interventional	49	94.2
	Observational	3	5.8
Study Results Availability	Results posted	5	9.6
	No results posted	47	90.4
Study Documents Available	Study protocols	7	13.5
	Statistical analysis plans (SAPs)	7	13.5
	Informed consent forms (ICFs)	6	11.5
Funder Type	Industry	14	26.9
	NIH	2	3.8
	Other U.S. federal agency	1	1.9
	Other funders (universities, organizations, individuals)	45	86.5

3.3 Classification of Digital Therapeutic Interventions

Digital therapeutic interventions were classified according to their therapeutic strategy and targeted pain mechanisms (Table 2). Virtual reality–based interventions were primarily designed to modulate central pain processing and neuroplasticity, targeting

conditions such as chronic shoulder pain and low back pain. Digital physical therapy and tele-rehabilitation interventions focused on mechanical dysfunction and motor control impairment, commonly addressing shoulder disorders, knee osteoarthritis, and patellofemoral pain syndrome. Multidisciplinary digital therapeutics integrated physical, cognitive, and behavioral components to target biopsychosocial pain mechanisms. In contrast, digital cognitive behavioral and exposure-based therapies primarily addressed pain mechanisms such as fear-avoidance and catastrophizing. Mobile application-based exercise and monitoring tools emphasized self-management, adherence, and functional recovery.

Table 2. Analytical Classification of Digital Therapeutics Targeting Musculoskeletal Pain

Digital Therapeutic Strategy	Targeted Pain Mechanism	Representative Conditions	Predominant Outcomes Targeted	Clinical Rationale
Virtual Reality–based interventions	Central sensitization, altered pain perception, neuroplasticity	Chronic shoulder pain, low back pain	Pain intensity, functional disability	VR modulates cortical pain processing and embodiment, acting as a non-pharmacological “neuromodulator”
Digital physical therapy / tele-rehabilitation	Mechanical dysfunction, motor control impairment	Shoulder pain, knee OA, patellofemoral pain	Function, ROM, disability scores	Remote delivery increases adherence while targeting biomechanical contributors to pain
Multidisciplinary digital therapeutics (MDT)	Biopsychosocial pain mechanisms	Patellofemoral pain syndrome, chronic MSK pain	Pain, function, QoL, psychological outcomes	Combines physical, cognitive, and behavioral components for holistic pain targeting
Digital CBT / exposure-based therapies	Nociplastic pain, fear-avoidance, catastrophizing	Fibromyalgia, chronic widespread pain	Pain intensity, psychological outcomes	Addresses maladaptive pain beliefs and central amplification
Mobile app–based exercise and monitoring tools	Physical inactivity, poor self-management	Knee OA, shoulder disorders	Function, adherence, symptom tracking	Enables personalized, adaptive rehabilitation pathways

3.4 Outcome Domains Assessed

Outcome domain coverage across included trials is summarized in Table 3. Pain intensity was the most frequently assessed outcome, reported in approximately 96% of studies, underscoring pain reduction as the primary therapeutic target. Psychological outcomes were evaluated in nearly three-quarters of trials, reflecting growing recognition of psychosocial contributors to chronic musculoskeletal pain. Functional disability measures were reported in about 70% of studies, while quality-of-life outcomes were assessed in 57%. Engagement and adherence metrics were reported in fewer than half of the trials, and outcomes related to opioid or analgesic use were evaluated in only 13% of studies, highlighting a notable gap in evidence regarding opioid-sparing effects of digital therapeutics.

Table 3. Outcome Domain Coverage and Therapeutic Focus Across Included Trials

Outcome Domain	No. of Trials (%)	Interpretation
Pain intensity (VAS/NRS)	22 (≈96%)	Primary endpoint across nearly all trials, reflecting pain as the central therapeutic target

Functional disability	16 ($\approx 70\%$)	Strong emphasis on function supports rehabilitation-focused digital strategies
Psychological outcomes	17 ($\approx 74\%$)	Highlights recognition of psychosocial contributors to chronic MSK pain
Quality of life (QoL)	13 ($\approx 57\%$)	Moderately assessed; often secondary rather than primary outcome
Engagement/adherence metrics	10 ($\approx 44\%$)	Reflects growing interest in real-world usability and digital compliance
Opioid/analgesic use	3 ($\approx 13\%$)	Underrepresented despite high clinical relevance

3.5 Methodological Characteristics and Evidence Gaps

Table 4 summarizes the methodological strengths and limitations identified across studies. Included trials demonstrated considerable heterogeneity in design, sample size, comparator selection, and outcome measures. At the same time, this reflects the innovative and evolving nature of digital therapeutics; such variability limited cross-study comparability and precluded quantitative meta-analysis. Table 5 presents key evidence gaps and future research priorities. Notably, trials consistently showed limited evaluation of medication-related outcomes, heterogeneity in outcome measures, a scarcity of head-to-head digital comparisons, and a lack of long-term follow-up data.

Table 4. Methodological Strengths and Limitations Identified Across Trials

Aspect	Observed Pattern	Analytical Interpretation
Study design	Mix of RCTs and single-arm studies	Field is transitioning from feasibility to confirmatory trials
Sample size	Wide variability (small pilots to >200 participants)	Early innovation phase with limited large-scale validation
Comparators	Usual care or conventional PT most common	Reflects real-world implementation focus
Follow-up duration	Mostly short to mid-term	Long-term durability of digital effects remains unclear
Standardization of endpoints	High variability	Limits meta-analysis and cross-trial comparison

Table 5. Knowledge Gaps and Future Research Priorities Identified

Gap	Implication for Clinical Practice	Research Priority
Limited opioid-related outcomes	Unclear opioid-sparing potential	Integrate medication use endpoints
Heterogeneous outcome measures	Reduced comparability	Standardize digital pain outcomes
Few head-to-head digital comparisons	Uncertain best-in-class tools	Comparative effectiveness trials
Limited integration with pharmacotherapy	Fragmented care pathways	Combined digital–drug protocols
Sparse long-term data	Sustainability unknown	Extended follow-up studies

3.4 Discussion

This study provides a comprehensive overview of registered clinical trials evaluating digital therapeutics for musculoskeletal pain. The growing role of digital interventions is evident as active therapeutic strategies aimed at addressing the complex, multidimensional nature of musculoskeletal pain. The findings show an expanding and increasingly diverse clinical trial field. A key finding is that most interventional study designs position digital therapeutics as active treatment modalities rather than passive monitoring tools. Most trials were designed to directly modify pain-related outcomes, including pain intensity, functional disability, and psychological variables. This aligns with current pain models that recognize musculoskeletal pain as a condition influenced by nociceptive, neuropathic, and nociplastic mechanisms, as well as behavioral and psychosocial factors [14]. The diversity of digital therapeutic strategies identified, ranging from virtual reality interventions to multidisciplinary digital programs, highlights the usefulness of digital approaches in targeting different pain pathways and rehabilitation needs.

Virtual reality interventions were frequently designed to modulate central pain processing and neuroplasticity, supporting their proposed role as non-pharmacological neuromodulator tools [15]. Digital physical therapy and rehabilitation platforms primarily targeted biomechanical dysfunction and motor control impairment, offering scalable solutions to improve access and adherence to rehabilitation programs [8]. Multidisciplinary digital therapeutics integrated physical, cognitive, and behavioral components, reflecting a biopsychosocial approach to pain management that is increasingly emphasized in clinical guidelines [16]. Together, these findings support conceptualizing digital therapeutics as complementary interventions that can be integrated into multimodal pain management strategies.

Using ClinicalTrials.gov registry data provides a comprehensive, transparent overview of ongoing and completed trials, minimizes publication bias, and captures emerging research trends. However, the analysis was limited to registry-level information, preventing assessment of detailed efficacy, safety, and trial quality. Substantial heterogeneity in study design, interventions, outcomes, and reporting limited comparability and prevented meta-analysis.

4. CONCLUSION

Digital therapeutics represent a rapidly expanding and innovative approach to targeting musculoskeletal pain, with the potential to complement existing pharmacological and rehabilitative strategies. While current clinical trials demonstrate broad interest and diverse therapeutic approaches, significant gaps remain in outcome standardization, long-term evaluation, medication-related outcomes, and reporting transparency. Addressing these challenges will be critical to advancing the evidence base and optimizing the clinical integration of digital therapeutics in musculoskeletal pain management.

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AUTHOR CONTRIBUTIONS

Not Applicable

CONFLICT OF INTEREST

The author declare that there is no conflict of interest.

ETHICS STATEMENT

This study did not require ethical approval.

DATA AVAILABILITY STATEMENT

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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