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Systematic Review

Exploring Factors Associated with Changes in Pain and Function Following mHealth-Based Exercise Therapy for Chronic Musculoskeletal Pain: A Systematic Review with Meta-Analysis and Meta-Regression

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Abstract: Exercise therapy is the first-line intervention recommended for those with chronic musculoskeletal pain (CMP). Smartphone technologies (mHealth) represent a feasible means for exercise prescription and individualization. This systematic review with meta-analysis aimed to identify factors associated with changes in pain and function following mHealth-based exercise therapy in patients with CMP. CINAHL (via EBSCOhost), Embase, PubMed, Scopus, and SPORTdiscus were searched from inception to February 2023. Observational and controlled clinical trials with correlation or regression analysis of factors associated with the effect of mHealth exercise interventions on pain and function were included. The risk of bias, completeness of interventions, spin of information, and certainty in the evidence were evaluated. Eight studies with 51,755 participants were included. Reduced pain intensity after intervention was associated with higher physical function: r (95% CI) = −0.55 (−0.67 to −0.41); I^2 = 86%, Tau^2 = 0.02; $p < 0.01$. Meta-regression identified the Body Mass Index (BMI), exercise dose, and completion rate as potential moderators between changes in pain and physical function following mHealth exercise therapy. No association was found between pain and anxiety: r (95% CI) = 0.15 (−0.08 to 0.37); I^2 = 87%, Tau^2 = 0.02; $p = 0.19$. Very low certainty in the evidence was observed due to serious concerns regarding the risk of bias, inconsistency, and indirectness. The limited available evidence detracts from the clinical interpretation of the findings.

Keywords: chronic pain; exercise; mHealth; meta-analysis; systematic review; telehealth

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1. Introduction

Two out of three adults may require rehabilitation at some point during the course of a musculoskeletal disorder [1], and this figure is expected to increase [1,2]. Spinal pain, together with knee and hip osteoarthritis (OA), ranks among the most prevalent and limiting musculoskeletal conditions [3] for which exercise is usually recommended as a first-line care approach [4,5]. Exercise-based interventions have been shown to enhance symptoms and decrease disability in individuals with chronic musculoskeletal pain [6–9]. However, exercise therapy is often omitted or sub-optimally prescribed [5,10]; thus, the impact of exercise on patients with knee OA, low back pain, or neck pain tends to be small to moderate [7,11,12] and not clinically relevant [8,11]. Indeed, more than 50%

of patients may not respond positively to exercise [13] aiming to reduce pain [14,15] or improve function [14]. Exercise therapy is not a "one-size-fit-all" solution, and many clinical, contextual, and psychosocial factors can modulate its effects. Previous research suggests that aspects such as age, pain intensity, treatment expectations, and employment status [16,17] can have an impact on the effect of exercise. For example, higher levels of pain and disability at baseline have been correlated with better outcomes following exercise-based interventions [18].

Exercise programs need to be both meaningful and achievable [19] to increase treatment adherence [20,21] and facilitate successful rehabilitation [19]. Exercise should be tailored to the individual's characteristics, preferences, and capabilities [19,22]. In this context, new technologies offer opportunities to enhance prescription in the form of telerehabilitation [5,23]. Current evidence supports telerehabilitation as a cost-saving resource for the management of chronic musculoskeletal pain [24,25]. It represents a good alternative to simplify access to clinical care [26], adapt exercise regimes, and monitor patients' progression and engagement with the intervention [7,27,28]. The widespread use of mobile devices [29] makes mobile apps easily accessible across healthcare [30,31]. mHealth, defined as 'health practice supported by mobile devices' [32], is showing an increasing trend in providing self-management strategies for people with musculoskeletal pain [30,33]. Specifically, digital interventions include motivating and enjoyable interventions through treatment gamification. These features applied gaming elements to maintain patient adherence and engagement with therapy, which can improve clinical outcomes [28,34]. mHealth is clinically feasible and effective in implementing exercise therapy [1,35,36], and it has proven beneficial in enhancing recovery [35–38] and saving healthcare resources [27] among different musculoskeletal disorders. The impact of mHealth on improving pain and function in those with chronic pain may vary based on the particular condition, the specific mHealth modality, and the individuals' characteristics [35,36]. A better understanding of the factors associated with the outcome following exercise therapy in patients with chronic pain is warranted to identify potential responders [13]. Exploratory analyses suggest that psychological [39], racial, and ethnic factors [40] can influence the effect of digitally delivered exercise interventions in adults with musculoskeletal pain. This systematic review aims to gather evidence on factors associated with changes in pain and function following mHealth-based exercise therapy in individuals diagnosed with chronic musculoskeletal pain. Possible associations between changes in pain and physical function will be also explored.

2. Materials and Methods

The study protocol was prospectively registered at Open Science Framework https://osf.io/fywhc (accessed on 25 February 2023) and has followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and the PRISMA for abstracts [41,42].

2.1. Deviations from the Review Protocol

There were some minor deviations from the intended protocol. The construct 'quality of life' was omitted from the analysis, as it was assessed in a single study [43]. The severity of anxiety or depressive symptoms was included among possible factors associated with the effect of mHealth [40,43–46]. In addition, the quality of mHealth reporting was assessed using the mHealth evidence reporting and assessment (mERA) checklist [47] in order to improve clarity and completeness in how mHealth interventions were described.

2.2. Data Sources and Search Strategies

A reviewer (PRSL) searched CINAHL (via EBSCOhost), Embase, PubMed, SPORTdiscus (via EBSCOhost), and Scopus from inception to February 2023. Filters for document type, source type, and language were imposed. Manual searches were conducted in reviews related to the topic of interest to search for eligible records not retrieved from electronic databases. The complete search strategies are detailed in Supplementary File S1.

2.3. Eligibility Criteria

The PECOs (Population, Exposure, Comparator, Outcomes, Study design) framework was followed to establish the eligibility criteria [48].

Inclusion criteria:

- P (population): adults (>18 years) diagnosed with chronic musculoskeletal pain or chronic spine pain according to the ACTTION-APS Pain Taxonomy [49]. This includes individuals with chronic low back pain, lumbosacral radiculopathy, fibromyalgia and myofascial widespread pain, gout, osteoarthritis, rheumatoid arthritis, and spondyloarthropathies.
- E (exposure): participants underwent an mHealth-based exercise program, alone or within a multimodal intervention. mHealth was defined as 'health practice supported by mobile devices such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices' [32].
- C (comparator): any control group, with no restriction, or no control group.
- O (outcomes): pain-related measures (e.g., pain intensity) and physical function.
- S (study design): observational studies and controlled clinical trials that provide results from a correlation or regression analysis between clinical or demographic variables and the impact of mHealth exercise-based therapy on pain and function.

Exclusion criteria:

- Patients with chronic pain were analyzed together with participants with other chronic disorders.
- Studies where exercise was provided using a digitally delivered modality other than mHealth, e.g., web-based tools.
- Participants with cancer-related pain or with pain associated with the central or peripheral nervous systems.
- Cluster analysis.
- Outcome measures were evaluated before and after surgery, e.g., knee arthroplasty.
- Studies written in a language other than English or Spanish.
- Reviews, editorials, letters, commentaries, thesis dissertations, grey literature, and conference abstracts.

2.4. Study Selection

One researcher (PRSL) conducted the selection process using the Mendeley desktop software, v2.72.0 (Elsevier Inc., New York, NY, USA). Duplicate records were automatically removed and manually checked. The remaining studies were screened based on the title and abstract. Then, two independent reviewers (PRSL and JSG) revised the full text of eligible records and those without an abstract. A consensus with a third reviewer (AMHR) was needed in seven studies to solve disagreements. A manual search was conducted in the list of references of systematic reviews on the topic of interest.

2.5. Data Extraction and Synthesis

Three reviewers (PRSL, AMHR, and LMFS) independently extracted the following information using a standardized form: first author, year of publication, and country; study design; number of participants, including sex distribution, mean age, body mass index, and race/ethnicity; educational stage; employment, family, and financial status; medical diagnosis; duration of symptoms and previous history of chronic pain; type of

mHealth intervention; characteristics of mHealth and control groups; outcome measures; mHealth completion rate (number of participants who completed the intervention vs. those initially recruited); and main findings (e.g., correlation analysis). For a detailed description of the mHealth intervention, additional information was collected: the type of devices used; professional monitoring system; software company; study setting; financial support; format of exercise presentation; type of exercises; adjusting program; weekly doses; and engagement intervention rate, which was estimated as the number of completed sessions vs. expected sessions. One researcher (CGM) contacted two corresponding authors via email [40,45] when information was not reported or needed clarification. Both corresponding authors replied.

2.6. Risk of Bias Appraisal

Two independent reviewers (JSG and FPP) evaluated the methodological quality of the studies using the Quality in Prognosis Studies (QUIPS) tool [50] for observational cohort studies. The revised Cochrane Risk of Bias tool for randomized trials version 2 (RoB-2) [51] and the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) tool [52] were used for controlled clinical trials. The QUIPS includes six domains that can be categorized as a 'low', 'moderate', or 'high' risk of bias [50]. The RoB-2 tool includes five domains, with the overall score ranked as 'low', 'some concerns', or 'high' risk of bias [51]. The ROBINS-I tool consists of seven domains that can be judged as having a 'low', 'moderate', 'serious', or 'critical' risk of bias [52].

2.7. Description of Interventions

One researcher (JSG) used the Template for Intervention Description and Replication (TIDieR) 12-item checklist [53], and another researcher (PRSL) employed the mERA 16-item checklist [47] to determine the quality of reporting of mHealth interventions.

2.8. Spin of Information

Two researchers (JSG and FPP) independently evaluated the quality and consistency of the information provided in the abstracts of the included studies. A seven-item checklist was used to quantify the amount of misleading information ('yes' or 'no') [54]. The spin overall score (after adding up the number of positive answers in each study) and the most prevalent items with some form of spin are reported [54].

2.9. Certainty in the Evidence

The certainty in the evidence was judged by two independent reviewers (PRSL and CGM) following the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach [55]. The GRADE includes five domains, risk of bias, imprecision, inconsistency, indirectness, and publication bias, and can be used in systematic reviews of both interventions and observational studies [55]. Randomized controlled trials start with high evidence, non-randomized clinical trials start with high evidence but should automatically be downgraded for limitations in design, and observational studies start with low evidence [55].

2.10. Meta-Analysis

Meta-analyses assessed those factors associated with changes in pain and physical function following mHealth exercise therapy for participants with chronic musculoskeletal pain. Possible direct associations between changes in pain and function after the intervention were also explored. Meta-analyses were performed when at least two studies evaluated the same bivariate association and could be only conducted for the association between pain and physical function (where a negative correlation indicates that lower pain intensity after the intervention is associated with higher function) and between anxiety and pain (where a positive correlation indicates that fewer anxiety symptoms following the intervention are associated with lower pain intensity). We used the

R Studio software, v. 4.1.1 (Posit PBC, Boston, MA, USA) with the packages of meta (v.5.1-1) [56], metafor (v.3.0-2) [57], and dmetar (v.0.0.9000) [58]. When necessary, data were transformed into correlation coefficients (r) before the analysis. For example, the formula $r = \beta + 0.05\lambda$ (when β is nonnegative, λ is equal to 1; when β is negative, λ is equal to zero) was used to transform regression data [59]. Also, if necessary, the direction of the correlation data was adjusted based on the scoring interpretation of the assessment tool. For instance, an improvement in function can be represented by a lower score in the Australian/Canadian Hand Osteoarthritis Index (AUSCAN) or a higher score in the Hip Disability and Osteoarthritis Outcome Score (HOOS). Data were pooled using a random effect model. Correlation coefficients were transformed using Fisher's Z and then back-transformed to correlation coefficients denoting 'low' (r = 0.10), 'moderate' (r = 0.30), and 'high' (r = 0.50) correlations [56]. Heterogeneity among the studies was explored using I2 statistics (high heterogeneity when $I^2 > 50\%$) [60]. The Tau2 test and Q-test were also used to explore heterogeneity. Forest plots were generated to report the results of the meta-analyses.

2.11. Meta-Regression and Sensitivity Analyses

A sensitivity exploratory analysis was conducted to identify outliers and potential sources of heterogeneity using influence analysis, the leave-one-out method, or Baujat plots. Outliers were excluded from the meta-analyses. We included prediction intervals in each forest plot as a measure of heterogeneity. These intervals provide 95% confidence for how likely future results may fall within their range. In addition, subgroup analyses were performed when at least two studies included the same covariate. These analyses were illustrated using forest plots with their prediction intervals. Q-tests within and between subgroups were carried out. In addition, mixed-model effect meta-regressions were performed to explore sources of heterogeneity and potential predictors of the treatment effects. Meta-regression analyses were developed when one of these predictors was included in at least three trials: age, body mass index, number of female or male participants, sample size, control comparator, duration of symptoms, number and frequency of sessions in the mHealth and control groups, type of mHealth, completion rate, and outcome measure for pain and physical function. Bubble plots were generated to visually represent the results of meta-regressions involving continuous variables.

2.12. Publication Bias

Publication bias was explored using funnel plots and the Egger's test (a p value < 0.05 indicates the presence of publication bias) when there were at least three studies in the same meta-analysis [61].

3. Results

3.1. Study Selection

A total of 1462 citations were retrieved from databases and manual search strategies. From these potentially eligible records, eight studies were finally included in the systematic review (Figure 1). A list of the records excluded after full-text reading (n = 124), with the reasons for exclusion, can be found in Supplementary File S2.

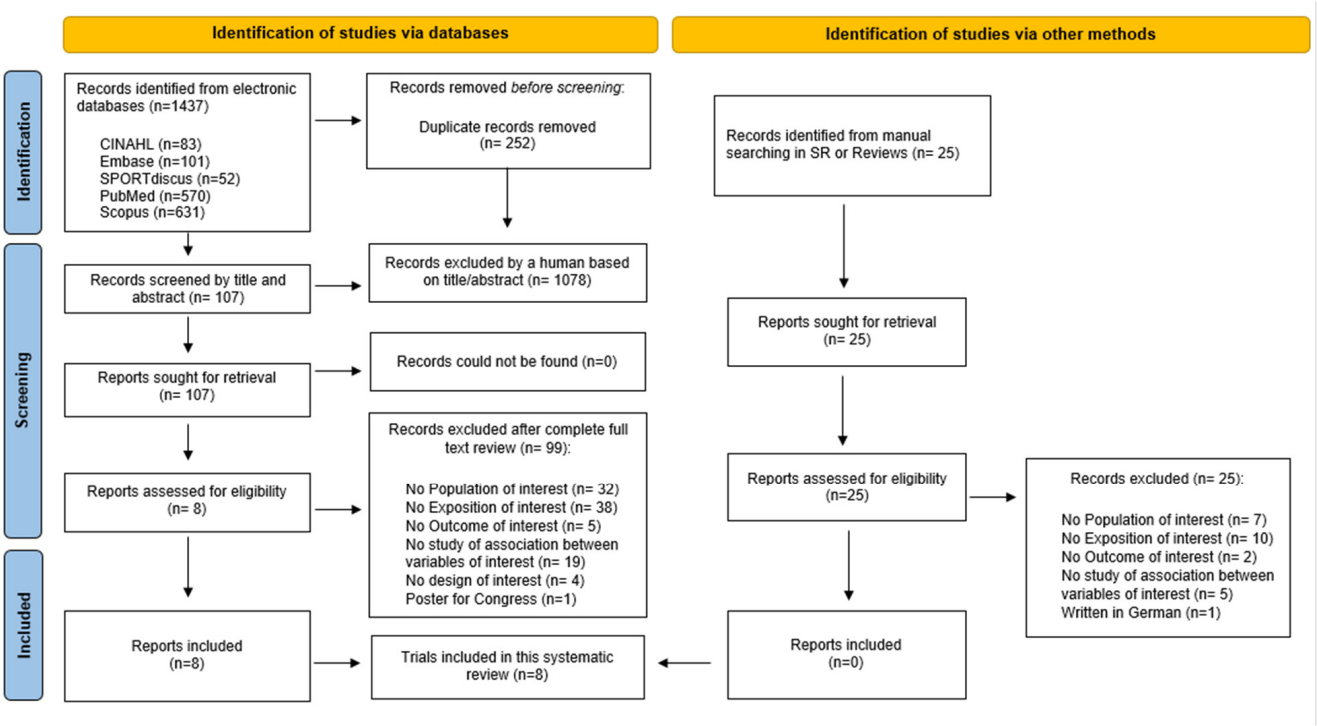


Figure 1. Flow diagram of studies through the review.

3.2. Description of Clinical Trials

One randomized controlled trial (RCT) [37], two non-RCTs [45,62], and five observational cohort studies [40,43,44,46,63] were included. The total number of participants was 51,755 (27,127 females, 51.41%); they were diagnosed with chronic musculoskeletal pain in the lower back (four studies) [40,45,46,63], shoulder (three studies) [40,46,62], and wrist–hand (three studies) [37,40,44] as the most frequent pain locations. mHealth interventions lasted from 4 to 12 weeks, were delivered using a mobile [37,45,62,63] or a Tablet app [40,43,44,46], and involved wearable devices in three studies: BoostFix (COMPAL Electronics Inc., Taipei, Taiwan) [62], Hinge Health (Hinge Health Inc., San Francisco, CA, USA) [46], and SWORD health (SWORD Health Inc., New York, NY, USA) [40,43,44]. The comparator groups included home-based [37,62] or face-to-face exercise programs [45], combined with educational material [45,62] or regular medical visits [37]. A follow-up evaluation was conducted by a single study [37] at 12 weeks after the intervention. Table 1 shows the characteristics of the included studies. A detailed description of the mHealth interventions in primary studies is reported in Supplementary File S3.

Table 1. Characteristics of the included studies.

Author(s), Year, and Country	Study Design	Participants (Sex, Mean Age), BMI, and Race/Ethnicity	Educational Stage, Employment, Family, and Financial Status	Diagnosis	mHealth Type	Symptom Duration; Previous History	mHealth Intervention Group	Comparison Group	Outcomes of Interest; Assessment Points	Treatment Completion Rate [a]	Main Findings of Interest
Chen et al., 2020 Taiwan [62]	Two-arm parallel non-RCT	*N* = 15 (5 females) [b]: EG = 8, CG = 7. Mean age, EG: 53(6.2), CG: 56.1(13.3) BMI: UR Ethnicity: UR	Educational stage: senior high (EG, *n* = 2; CG, *n* = 4); bachelor's degree or higher (EG, *n* = 5; CG, *n* = 3). Employment status: UR Family status: UR Financial status: UR	Adhesive capsulitis of the shoulder > 12 wks.	Mobile app and wearable inertial sensors	Symptom duration: 3 to 6 mo. (*n* = 7); 26 to 52 mo. (*n* = 7) Previous history: UR	Motion sensor-assisted home-based shoulder exercise program via the Patient App. Daily, 12 wks.	Home-based shoulder exercise program, with advices on sleep, posture, and pain relief. Daily (10 times per exercise per day), 12 wks.	Pain intensity (worst pain last week): VAS Function: QDASH Shoulder ROM (active and passive): motion sensor T0, T1 (week 4), T2 (week 8), T3 (week 12)	Overall: 93.3% (14/15) EG: 87.5% CG: 100%	**Correlations:** Significant correlation between passive internal rotation and changes in QDASH at T1 ($r = -0.539$, $p < 0.05$)
Costa et al., 2022 USA [44]	Single-arm cohort study	*N* = 189 (115 females): Mean age, 47.3(11.1) BMI: 28.7(6.8) Ethnicity: UR	Educational stage: UR Employment status: Full- or part-time (*n* = 174) Family status: UR Financial status: UR	Wrist or hand pain: CTS (*n* = 50), tendinopathy (*n* = 45), non-specific wrist pain (*n* = 28), DeQuervain tenosynovitis (*n* = 16), wrist/hand OA (*n* = 16), sprain or fracture (*n* = 14), systemic disease (*n* = 11), other (*n* = 9)	Tablet App, Inertial motion trackers and Cloud-based portal.	Symptom duration: <3 mo. (*n* = 69); >3 mo. (*n* = 120) Previous history: UR	SWORD Health's digital treatment (CBT, exercise program, and education). Three times per week, 8 wks.	N/A	Anxiety: GAD-7 Depression: PHQ-9 Pain intensity (average pain last week): NRS Function: QDASH T0, T1 (week 4), T2 (week 8)	Overall: 78.8% (149/189)	**OR (95% CI), *p* value** Considering an MCID (30% change) in pain intensity at T2: Age, 1.03 (0.97 to 1.10), 0.34 BMI, 1.08 (0.96 to 1.26), 0.24 Female, 0.94 (0.25 to 3.58), 0.92 GAD-7, 0.99 (0.67 to 1.53), 0.96 PHQ-9, 1.04 (0.78 to 1.38), 0.80 **Correlations**: Significant ($p < 0.001$) between ↓ pain and ↑ function: r = 0.659, **Latent growth curve model**: Female sex was associated with faster-paced recovery for QDASH = −0.85 per week, $p = 0.029$

Table 1. *Cont.*

Author(s), Year, and Country	Study Design	Participants (Sex, Mean Age), BMI, and Race/Ethnicity	Educational Stage, Employment, Family, and Financial Status	Diagnosis	mHealth Type	Symptom Duration; Previous History	mHealth Intervention Group	Comparison Group	Outcomes of Interest; Assessment Points	Treatment Completion Rate [a]	Main Findings of Interest
Janela et al., 2022 USA [43]	Single-arm cohort study	*N* = 534 (363 females): Mean age, 50.2(11.3) BMI: 29.1(6.4) Ethnicity: UR	Educational stage: UR Employment status: Full or part time (*n* = 480) Family status: UR Financial status: UR	Hip pain > 12 wks.: hip OA (*n* = 106), other conditions, e.g., non-specific pain, bursitis, sprain/strain, tendinopathy (*n* = 428)	Tablet App, Inertial motion trackers, and Cloud-based portal.	Symptom duration: UR Previous history: UR	SWORD Health's digital treatment: (CBT, exercise program, and education). Three times per week, 12 wks.	N/A	Anxiety: GAD-7 Pain intensity (average pain last week): NRS Pain: HOOS-pain Function: HOOS-function T0, T1 (week 4), T2 (week 8), T3 (week 12)	Overall: 74.2% (396/534)	**Correlations:** Significant ($p < 0.001$) between ↓ pain and positive change in HOOS-function, r = −0.404 HOOS-pain, r = −0.556 HOOS-QoL, r = −0.357 GAD-7, r = 0.265 Significant between change in surgery intent and ↓ Pain, r = 0.155, $p = 0.033$ ↑ HOOS-function, r = −0.28, $p = 0.004$ **Latent growth curve model:** Older age was associated with ↓ pain (NRS) = −0.01, $p = 0.012$. Female sex was associated with change in HOOS-pain = −1.00, $p = 0.016$. ↑ BMI was associated with ↓ in HOOS-function = 0.14, $p = 0.003$

Table 1. *Cont.*

Author(s), Year, and Country	Study Design	Participants (Sex, Mean Age), BMI, and Race/Ethnicity	Educational Stage, Employment, Family, and Financial Status	Diagnosis	mHealth Type	Symptom Duration; Previous History	mHealth Intervention Group	Comparison Group	Outcomes of Interest; Assessment Points	Treatment Completion Rate [a]	Main Findings of Interest
Rodríguez-Sánchez-Laulhé et al., 2023 Spain [37]	Two-arm parallel RCT	*N* = 74 (50 females): EG = 34, CG = 40. Mean age, EG: 62.2(8.8) CG: 64.3(7.7) BMI: UR Ethnicity: UR	Educational stage: UR Employment status: UR Family status: UR Financial status: UR	Unilateral or bilateral hand OA > 6 mo.	Mobile App	Symptom duration: UR Previous history: UR	CareHand app: exercise (15 to 20 min.), info about the disease, joint protection, and self-management advice. Four times per week, 12 wks.	Written home exercise program and regular medical visits (info about the disease). Four times per week, 12 wks.	Pain intensity: NRS, AUSCAN Function: AUSCAN, QDASH Overall status: AUSCAN total Pinch and grip strength: pinch gauge, dynamometer. T0, T1 (week 4), T2 (week 12), T3 (week 24)	Overall: 85.1% (63/74) EG: 85.3% CG: 85%	**Regression β (95% CI), *p* value:** Change AUSCAN function at T2: AUSCAN pain at T0: 0.995 (0.788 to 2.639), $p = 0.001$ AUSCAN total at T0: −1.054 (−1.060 to −0.206), $p = 0.005$ Change in AUSCAN pain at T2: 0.592 (0.406 to 1.431), $p = 0.001$. Change NRS at T2: AUSCAN pain at T0: −0.603 (−0.997 to −0.334), $p = 0.001$ QDASH at T0: 0.433 (0.008 to 0.106), $p = 0.023$ Change in QDASH at T2: 0.469 (0.016 to 0.112), $p = 0.010$
Scheer et al., 2022 USA [40]	Single-arm cohort study	*N* = 9550 (5589 females): Mean age, 49.4 (12.9) BMI: 29.2 (6.7) Ethnicity: Asian (*n* = 910); Black (*n* = 1025); Hispanic (*n* = 913); non-Hispanic white (*n* = 6240); other (*n* = 462)	Educational stage: middle, elementary, high school, or college (*n* = 3649); bachelor or higher (*n* = 5763). Employment status: Full- or part-time (*n* = 8080); not employed (*n* = 414) Family status: UR Financial status: UR	Chronic pain > 12 wks.: ankle (*n* = 352), hip (*n* = 817), knee (*n* = 1275), low back (*n* = 4097), neck (*n* = 882), wrist and hand (*n* = 335), elbow (*n* = 191), shoulder (*n* = 1431).	Tablet App, Inertial motion trackers, and Cloud-based portal.	Symptom duration: UR Previous history: UR	SWORD tablet app: exercise program, education, and CBT (60 min total). Three times per week, 12 wks.	N/A	Anxiety: GAD-7 Depression: PHQ-9 Pain intensity (average pain last week): NRS T0, T1 (week 4), T2 (week 8), T3 (week 12)	Overall: 72.8% (6949/9550)	**Logistic regression OR (95% CI), *p* value** Clinically meaningful change in pain intensity at T3: Hispanic vs. non-Hispanic: 1.74 (1.24 to 2.45), $p = 0.001$ Men vs. women: N/S, $p = 0.007$ Prior upper limb pain vs. no prior: N/S, $p < 0.001$

Table 1. *Cont.*

Author(s), Year, and Country	Study Design	Participants (Sex, Mean Age), BMI, and Race/Ethnicity	Educational Stage, Employment, Family, and Financial Status	Diagnosis	mHealth Type	Symptom Duration; Previous History	mHealth Intervention Group	Comparison Group	Outcomes of Interest; Assessment Points	Treatment Completion Rate [a]	Main Findings of Interest
Selter et al., 2018 USA [63]	Single-arm cohort study	*N* = 35 (22 females) [b] : Mean age, 46(16). BMI: 25.4(4.0) Ethnicity: UR	Educational stage: UR Employment status: UR Family status: UR Financial statu: UR	LBP (discogenic) > 12 wks. with axial symptoms	Mobile app	Symptom duration: 19.6 (7.4) mo. Previous history: UR	Limbr app: self-report system of pain, medica-tion/coping, and affect, self-exercise program via coach and Force Therapeutics app. Three times a week, 12 wks.	N/A	Function: ODI, YADL Visual report. T0, T1 (week 2), T2 (week 6), T3 (week 12)	Overall: 37.6% (35/93)	**Correlations:** Significant correlations between ODI and YADL visual report at T0 (r = 0.551, $p < 0.001$) **Hierarchical linear modeling:** ODI increased by 0.33 for every one-unit increase in YADL visual report.
Sitges et al., 2022 Spain [45]	Two-arm parallel non-RCT	*N* = 59 (33 females): EG = 27, CG = 32. Mean age, EG: 45(9.1); CG: 48.6(7.5) BMI: EG, *n* = 0.41(0.07); CG, *n* = 0.43(0.09) Ethnicity: UR	Educational stage: UR Employment status: UR Family status: UR Financial status: UR	LBP > 12 wks. Diagnoses: hernia or protrusion (*n* = 13), degenerative pathology (*n* = 2), anterolisthe- sis (*n* = 3), others (*n* = 12)	Mobile app	Symptom duration (yrs.): EG = 8.1(8.7); CG = 11.8 (7.5). Previous history: >3 LBP episo-des > 1 wk. prior yr.	BackFit App: self-managed home-based exercise sessions (50 min.), pain education video (4 min.). Two times per week, 4 wks. (approx. 50 min).	Face-to-face group exercise program (50 min), pain education video (4 min.) Two times per week, 4 wks. (approx. 50 min).	Anxiety: STAI Pain intensity (current): VAS Pain sensitivity: PPT at spinal erector muscle Function: ODI T0, T1 (week 4)	Overall: 84.7% (50/59) EG: 85.2% CG: 84.4%	**Correlations:** No significant correlations between changes in ODI at T1 and EEG-resting state data

Table 1. *Cont.*

Author(s), Year, and Country	Study Design	Participants (Sex, Mean Age), BMI, and Race/Ethnicity	Educational Stage, Employment, Family, and Financial Status	Diagnosis	mHealth Type	Symptom Duration; Previous History	mHealth Intervention Group	Comparison Group	Outcomes of Interest; Assessment Points	Treatment Completion Rate [a]	Main Findings of Interest
Wang et al., 2021 United States [46]	Single-arm retrospective cohort study	*N* = 41,241 (50.8% females): gen Z, *n* = 13,535; gen X, *n* = 16,982; baby boomers, *n* = 9262; silent gen, *n* = 1462. Mean age, Gen Z: 31.3(4.3); Gen X: 46.1(4.7); baby boomers: 58.7 (2.9); silent gen: 68.5(4.2) BMI: overweight/obese (76.3%), normal/underweight (23.7%) Ethnicity: UR	Educational stage: UR Employment status: UR Family status: UR Financial status: UR	Low back, knee, hip, shoulder, or neck pain > 12 wks. Back pain (56.6%), knee (34.3%), hip (7.7%)	Tablet App	Symptom duration: UR Previous history: UR	Tablet app with wearable motion sensors: guided exercise therapy sessions (animations and videos), health coaching, and education for chronic pain. Three sensor-guided exercise sessions and two education papers per week, 12 wks.	NA	Anxiety: GAD-7 Depression: PHQ-9 Pain intensity (average last 24 h): NRS T0, T1 (week 12)	Overall: 84.7% (36,142/41,241) Gen Z: 66.9% Gen X: 75.5% Baby boomer: 81.5% Silent Gen: 83.0%	**Regression β (95% CI), *p* value (adjusted or unadjusted model):** No association of age with change in pain score (all, $p > 0.05$) **OR (95% CI), *p* value (adjusted model):** Association between age and change in anxiety (all, $p < 0.05$) Baby boomer vs. Gen Z and Millennial: 2.05 (1.56 to 2.69) Baby boomer and Silent generation vs. Gen Z and Millennial: 2.71 (1.19 to 6.20) Association between age and change in depression ($p < 0.05$) Baby boomer vs. Gen Z and Millennial: 1.31 (1.01 to 1.71)

Abbreviations: AUSCAN = Australian/Canadian Hand Osteoarthritis Index; BMI = body mass index; CBT = Cognitive Behavioral Therapy; CG = control group; CI = confidence interval; CTS = carpal tunnel syndrome; EEG = electroencephalography; EG = experimental group; GAD-7 = Generalized Anxiety Disorder; gen = generation; HOOS = Hip Disability and Osteoarthritis Outcome Score; LBP = low-back pain; MCID = minimum clinically important difference; mo. = months; N/A = Not Applicable; NRS = Numerical Rating Scale; OA = osteoarthritis; ODI = Oswestry Disability Index; OR = Odds ratio; PDI = pain disability index; PHQ-9 = Patient Health Questionnaire; PPT = pressure pain threshold; QDASH = Disabilities of the Arm, Shoulder, and Hand questionnaire (quick form); r = correlation coefficient; RCT = randomized controlled trial; ROM = range of motion; QoL = quality of life: STAI = State-Trait Anxiety Inventory; UR = unreported; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; wks. = weeks; YADL = Your Activities of Daily Living; β = standardized beta coefficient. [a] Treatment completion rate refers to the number of participants who completed the intervention. [b] Participants characteristics are reported based on those who completed the intervention. ↑ Higher score. ↓ Lower score.

3.3. Risk of Bias Assessment

None of the included studies were judged with an overall low risk of bias (interrater reliability, 62.38%). Bias due to attrition and confounding were the most common among observational cohort studies (Supplementary File S4). In the included RCT [35], some concerns arose due to deviations from the intended intervention and the selection of the reported results (Supplementary File S5), while bias due to the confounding and measurement of outcomes was the most prevalent among the non-RCTs (Supplementary File S6).

3.4. Completeness of Intervention Descriptions

None of the studies completed all of the items of the TIDieR checklist. Item 5, 'who provided the intervention' ($n = 2$, 25%), and item 10 'modifications of the intervention' ($n = 1$, 12.5%), were the most poorly reported (Supplementary File S7 and Figure 2). Regarding the mERA checklist, six of the items, 'technology platform', 'interoperability', 'cost assessment', 'limitations for delivery at scale', 'replicability', and 'data security', were not reported in any of the included studies (Supplementary File S8).

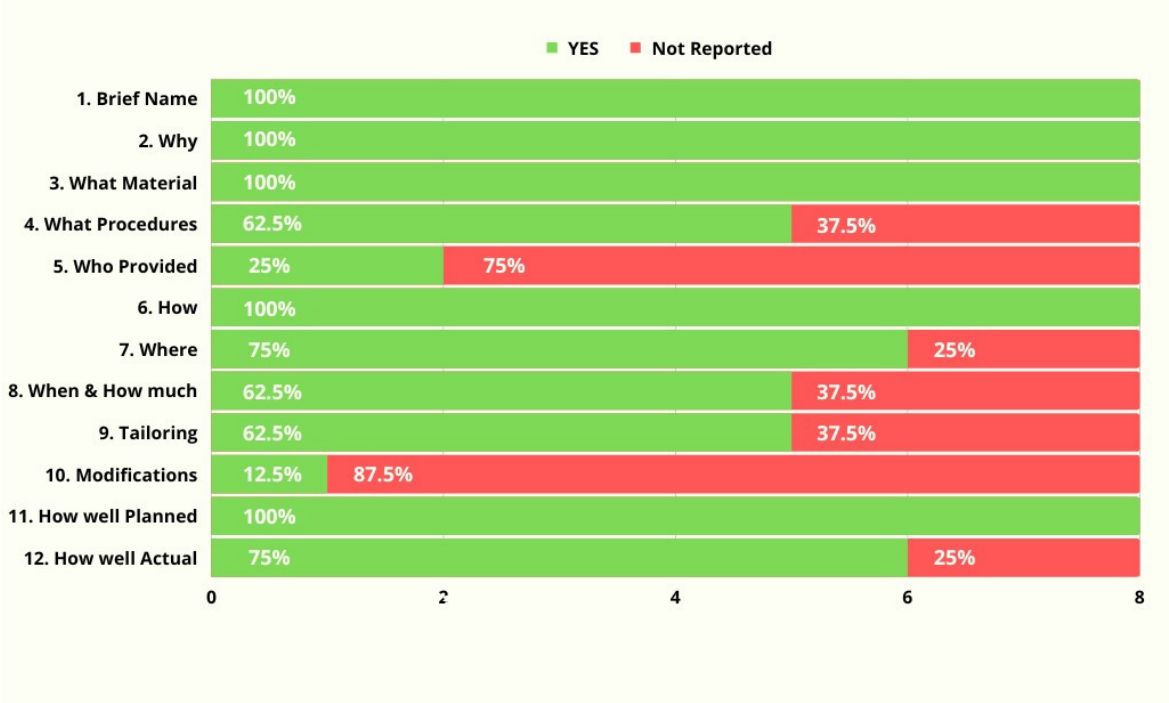


Figure 2. The TIDieR Checklist Overall Vision.

3.5. Spin of Information

The overall spin-abstract score was 24, with a mean value of 3.0 (SD 1.8) (Supplementary File S9) and an interrater reliability of 78.57%. All abstracts showed some form of spin of information. The most common types were 'failure to mention adverse events of interventions' ($n = 7$, 87.5%) and 'recommendation of a treatment without a clinically important effect on primary outcomes' ($n = 6$, 75%).

3.6. Certainty in the Evidence (GRADE)

Serious and very serious concerns regarding the risk of bias, inconsistency, and indirectness of the evidence were identified (Table 2, interrater reliability, 88.9%). This caused the certainty in the evidence to be judged as very low for both the associations between pain and physical function and between anxiety and pain.

Table 2. Certainty in the evidence in the included studies: GRADE.

Summary of Findings				Certainty in the Evidence Based on the GRADE Approach					
Outcome	**Studies (k)**	**Participants (N)**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication Bias**	**Certainty in the Evidence**	**Importance**
Pain–Function	5	871	−1: Serious [a]	−1: Serious [c]	−2: Very Serious [d]	No [f]	Undetected	Very Low ⊕◯◯◯ [h]	Critical
Pain–Anxiety	2	723	−1: Serious [b]	−1: Serious [c]	−2: Very Serious [e]	No [f]	Not possible [g]	Very Low ⊕◯◯◯ [h]	Critical

[a] Risk of bias: More than 75% of the included studies included important risk of bias. [b] Risk of bias: More than 75% of the included studies presented at least one item with high risk of bias item in the QUIPS. [c] Inconsistency: One level downloaded due to high heterogeneity. No possible sensibility analysis. [d] Indirectness: two levels downloaded due to differences in populations, interventions, assessment tools, and timelines. [e] Indirectness: two levels downloaded due to differences in populations and assessment tools. [f] Imprecision: Sample size was more than 400 participants. [g] Publication Bias: No possible Egger Test. [h] Certainty in the Evidence: A very low level of certainty due to results in previous domains.

3.7. Meta-Analysis of the Association between Pain and Physical Function (GRADE: Very Low)

After excluding three records that did not report physical function [40,46] or pain [62,63] in their analysis, the meta-analysis included four studies [37,43–45]. Pain intensity was measured with a Numeric Rating Scale (NRS) [37,43,44] or a Visual Analogue Scale (VAS) [45], while physical function was evaluated with the Disabilities of the Arm, Shoulder, and Hand (QDASH) questionnaire [37,44], the AUSCAN [37], the Oswestry Disability Index [45], and the HOOS [43]. Considering the heterogeneity among the tools used to assess function, the signs of the correlation data from Rodriguez Sanchez-Laulhé et al., 2023 [37], Costa et al., 2022 [44], and Sitges et al., 2022 [45] were adjusted to align with the correlation between lower pain and higher function. The pooled results showed that lower pain intensity after intervention was associated with higher physical function, with a marked heterogeneity (r (95% CI) = −0.41 (−0.68 to −0.05); I2 = 94%, Tau2 = 0.19 (0.04 to 1.32); p = 0.03) (Figure 3). This heterogeneity remained high in the sensitivity analysis that showed a similar association between pain and physical function after excluding one outlier [45] (r (95% CI) = −0.55 (−0.67 to −0.41); I^2 = 86%, Tau^2 = 0.02 (0.005 to 0.55); $p < 0.01$) (Supplementary File S10). Graphical representations are listed in Supplementary Files S11–S13. No publication bias was detected (Egger test, p = 0.86, Supplementary File S14). Meta-regression analyses identified various factors that can modulate this association: (a) Using an NRS for measuring pain intensity; (b) the participants' BMI; (c) the completion rate and frequency of sessions in both mHealth and control intervention groups; and (d) the number of sessions in the control group (Supplementary File S15). Subgroup analyses revealed a significant heterogeneity between subgroups (Q-test < 0.05), based on the tools used to assess pain or function, study design, and pain location, and a significant heterogeneity within subgroups (Q-test < 0.05), based on the tools used to assess pain or function, the comparator group, study design, duration of symptoms, and type of mHealth (Supplementary Files S16–S23).

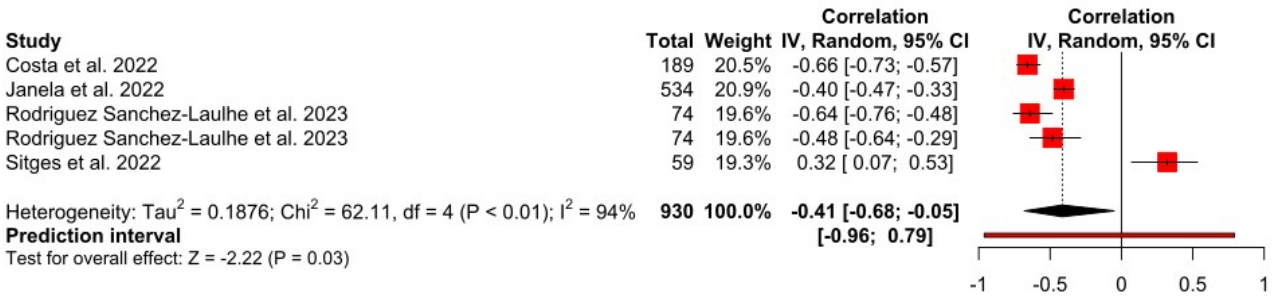


Figure 3. Pooled Effect of Pain and Physical Function [37,43–45].

3.8. Meta-Analysis of the Association between Pain and Anxiety (GRADE: Very Low)

The meta-analysis included two studies [43,44] showing no association between changes in the severity of anxiety symptoms after the intervention and pain intensity: r (95% CI) = 0.15 (−0.08 to 0.37); p = 0.19; I^2 = 87%, Tau^2 = 0.02 (Figure 4). Anxiety was measured with the 7-item Generalized Anxiety Disorder (GAD-7), and pain intensity was measured with an NRS. The funnel plot detected no publication bias (Supplementary File S24). No sensitivity, prediction interval, meta-regression, subgroup analyses, or Egger test could be performed due to the limited number of studies.

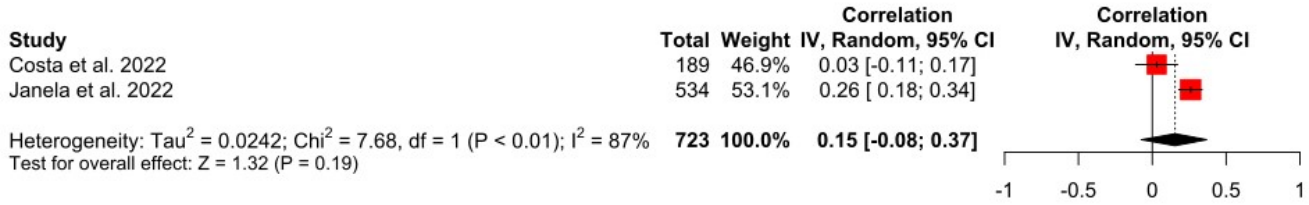


Figure 4. Pooled Effect of Pain and Anxiety [43,44].

4. Discussion

The findings from this systematic review suggest that a decrease in pain intensity following mHealth-based exercise therapy is associated with an improvement in physical function in patients with chronic musculoskeletal pain. This association was modulated by several factors, including individual characteristics (BMI), the mHealth intervention dose (frequency of sessions), and the completion rate. On the contrary, we found no association between changes in pain intensity and anxiety symptoms. This contradicts previous findings on the role of mental well-being as a functional outcome predictor in musculoskeletal care [64], but it is line with a recent systematic review concluding that there is not enough evidence to suggest that mental health moderates the effect of exercise on pain and physical function in patients with hip or knee OA [18]. In contrast, a previous study reported how psychosocial factors can moderate the effect of exercise interventions on pain and disability in patients with chronic low back pain [65]. This study raised an important dilemma as to whether psychosocial factors truly function as moderators (where the psychosocial state influences the effect of exercise) or as mediators (where exercise influences the psychosocial state, which subsequently impacts pain), as suggested with the present results [65].

Stratified care entails tailoring treatment to specific subgroups of patients based on key characteristics, such as prognostic factors [66]. Among the observed variables that can modulate the association between pain and physical function, BMI has already been considered, with a strong level of evidence, as a predictor of functional outcomes in musculoskeletal care [64]. Specifically, obesity has been associated with increased pain following exercise in patients with knee OA [67] and, therefore, could influence the effect of exercise on pain and function in people with hip or knee OA [68]. However, a recent systematic review and individual participant data meta-analysis concluded the opposite [18]. Despite the contradictory evidence, clinicians seem to perceive patients with obesity as the most difficult to manage to implement exercise therapy in individuals with OA [68]. In this context, how physiotherapists should discuss obesity with patients and the need for interprofessional collaboration, e.g., with a dietitian, have been reported as the main barriers to overcome in the clinical setting [68]. As opposed to obesity, age did not seem to influence the association between changes in pain and physical function after the intervention. The role of age as a moderator of the effect of exercise is still a matter of debate [16,18,69] and could be especially relevant considering mHealth technologies. An older age is often cited as a barrier to the adoption of mHealth [70]. However, this may not be only attributed to age per se but rather to other contextual aspects, such as the device's ease of use and cognitive challenges [70].

mHealth technologies may help to enhance a more personalized treatment [71]. Our findings support the importance of the mHealth intervention dose and completion rate, which reinforces the crucial role of treatment adherence. The loss of motivation and lack of adherence to exercise is a real problem, as it compromises its effectiveness for chronic musculoskeletal pain [72]. The individualization of exercise programs and the use of self-monitoring tools, e.g., mobile devices, could lead to more adherent behavior [21]. However, users' adherence to mHealth programs is also an issue [73]. Although adherence to mHealth should be automatically recorded [73], it is frequently poorly reported, as shown with the mERA checklist. In addition, providing training to clinicians in technical aspects, such as digital literacy, could ensure a more effective use of the technology and, consequently, yield better outcomes [23]. Future studies should adhere to the recommendations of the mERA checklist and provide a comprehensive and detailed training process for both professionals and patients.

4.1. Methodological and Clinical Considerations

We were able to conduct meta-analyses on how changes in pain intensity and severity of anxiety symptoms after interventions could be associated with improvements in function and pain, respectively. Correlation analyses can be used as a measure of association, but they are not sufficient to infer causality [74]. In fact, observational studies should not be used to claim causation [75]. Ultimately, the longitudinal design of the included studies adds robustness to the observed association between pain and function. More RCTs with high methodological quality and a control of confounding variables would be needed to test causal hypotheses [74].

Using the GRADE framework, serious concerns were identified from the risk of bias, inconsistency among studies, and indirectness of the evidence. Bias due to uncontrolled confounding was common, and this represents an important source of error in the health literature [76]. Studies with various methodological designs were meta-analyzed together, which added more heterogeneity. The differences in populations, interventions, and assessment tools limit the generalizability of the findings.

To our knowledge, this systematic review is the first to explore factors associated with changes in pain and function after mHealth exercise therapy for chronic musculoskeletal pain. We aimed to investigate the distinct effects of mHealth rather than those of digital health in general [35]. Studies used several types of mobile apps (with or without wearable devices), which included different monitoring systems, exercise presentation formats, and adjustment programs. Despite this possibly reflecting the existing variability within mHealth technology [36], it also detracts from the external validity of the findings. This review included patients with musculoskeletal disorders under the same diagnostic taxonomy [49]. However, participants reported a wide range of conditions and pain locations; thus, the results may not be specific to a particular disorder. Finally, one way to support the clinical applicability and future replication of interventions is to improve how these are reported. For this purpose, we used both the TIDieR and mERA checklists. In the TIDieR checklist, common concerns arose related to the lack of descriptions of who provided the intervention and the modifications implemented during the course of the study. Similarly, most studies did not meet the essential guidelines of reporting according to the mERA checklist, with especial attention to items of the technology platform, interoperability, data security, replicability, or limitations for scaling-up. Some of these shortcomings have already been mentioned by the 2020 WHO Digital Health Guideline for decision-makers and politicians [77] to facilitate the incorporation of mHealth systems in the clinical settings. Another important aspect is how accurate the information reported in the abstracts of the included studies was. The spin of information was mostly related to inaccuracies in reporting adverse events and the recommendation of the intervention when this failed to achieve a clinically important effect. This situation can have a detrimental influence on clinical decision-making for both healthcare professionals and the broader audience. More

effort is needed for editors, reviewers, and authors to improve the quality of abstracts to provide transparent and accurate information.

mHealth technology offers great opportunities for musculoskeletal research [35] and practice [77]. Mobile devices facilitate data collection and increase the statistical power of studies to find associations. They also represent an easy-to-use approach to influence patients' behavior, i.e., the delivery of follow-up educational information [78]. However, there are still significant barriers to overcome [78]. For instance, high participant attrition is a prevalent issue in the mHealth literature [79,80]. We identified a moderate or high risk of bias due to attrition in 50% of the studies [40,43,46,63]. Also, the accessibility of mHealth for all sociodemographic groups remains questionable. In this systematic review, aspects such as the educational level and the financial status of participants were not reported in most studies. Indeed, it is worth noting that all the studies included were conducted in high-income countries; thus, we must be cautious to extrapolate the results to broader population groups. Overall, the limited number of studies and the substantial heterogeneity among them, along with serious methodological concerns and a very low certainty in the evidence, prevent us from making strong clinical recommendations.

4.2. Study Limitations

Although many citations were initially reviewed, few studies fulfilled the eligibility criteria. The Cochrane Handbook recommends a minimum of 10 studies for each examined covariate in a meta-regression [60], although this remains controversial, with other studies suggesting that a lower number of observations may be sufficient [81]. All in all, conducting meta-analyses and meta-regressions with a limited number of studies limits the generalizability of the results and does not allow for establishing definite conclusions. In addition, most studies showed an overall high risk of bias and high heterogeneity in patients' characteristics, mHealth interventions, and outcome measures. This heterogeneity remained high even after the sensitivity analyses. Finally, no study assessed outcomes in the long term, which detracts from their clinical applicability. More longitudinal cohort studies and RCTs with high methodological quality and long-term follow-ups are warranted to understand the possible moderators of the effect of digitally based exercise programs for chronic pain.

5. Conclusions

The present systematic review suggests that a decrease in pain intensity after mHealth-based exercise therapy is associated with higher physical function in patients with chronic musculoskeletal pain. However, no association was found between changes in the severity of anxiety symptoms and pain intensity. Potential factors modulate the association between pain and function, such as the BMI and the mHealth intervention dose and completion rate. Given the low certainty in the evidence and the presence of serious methodological concerns in primary studies, no clinical recommendations are warranted at this time.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app14156632/s1, Supplementary File S1: Search strategies; Supplementary File S2: List of studies excluded after full text reading, including the specific reasons for exclusion (n = 124); Supplementary File S3: Characteristics of the mHealth interventions; Supplementary File S4: Risk of Bias Assessment QUIPS; Supplementary File S5: Risk of Bias Assessment RoB-2; Supplementary File S6: Risk of Bias Assessment ROBIN-I; Supplementary File S7: The Template for Intervention Description and Replication (TIDieR) Checklist Results; Supplementary File S8: mHealth evidence reporting and assessment (mERA) checklist; Supplementary File S9: Spin of Information in the abstracts; Supplementary File S10: Forest Plot Sensitivity Analysis Pain and Function; Supplementary File S11: Baujat Plots Analysis Pain and Function; Supplementary File S12: Influence Analysis Pain and Function; Supplementary File S13: Leave one out method analysis Pain and Function; Supplementary File S14: Funnel Plot for Publication Bias for Pain and Function; Supplementary File S15: Univariate meta-regression analysis of covariates that could moderate the correlation between pain and function in patients with chronic musculoskeletal pain; Supplemen-

tary File S16: Subgroup meta-analyses for the correlation between pain and function in patients with chronic musculoskeletal pain; Supplementary File S17: Forest Plot subgroup analysis on Pain Assessment tools in Pain and Function association; Supplementary File S18: Forest Plot subgroup analysis on Function Assessment tools in Pain and Function association; Supplementary File S19: Forest Plot subgroup analysis on Comparators in Pain and Function association; Supplementary File S20: Forest Plot subgroup analysis on study design in Pain and Function association; Supplementary File S21: Forest Plot subgroup analysis on duration of symptoms in Pain and Function association; Supplementary File S22: Forest Plot subgroup analysis on type of mHealth in Pain and Function association; Supplementary File S23: Forest Plot subgroup analysis on location of the lesion in Pain and Function association; Supplementary File S24. Funnel Plot for Publication Bias for Pain and Anxiety.

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