CLINICAL TRIAL REPORT

Effectiveness of Hybrid Form Impulse Therapy (HFIT) Compared to Traditional Transcutaneous Electronic Nerve Stimulation (TENS) in Patients with Chronic Low Back and Knee Pain: A Randomized Controlled Trial

Mindy Hong [1], Jeffrey Krauss[1], Grace Wang[2], Ken Cohen[3], Christine E Chaisson[4], Amitabh Gulati [5]

[1]Hinge Health, San Francisco, CA, USA; [2]Weitzman Institute, Middletown, CT, USA; [3]Optum Care Center for Research and Innovation, Eden Prairie, MN, USA; [4]Yale University Center for Clinical Investigation, New Haven, CT, USA; [5]Memorial Sloan Kettering Cancer Center, New York, NY, USA

Correspondence: Mindy Hong, Email mindy.hong@hingehealth.com

Purpose: Physical therapy (PT) and conservative care are recommended first-line treatments for musculoskeletal (MSK) pain. While essential to high-quality care, these solutions often do not provide immediate or sufficient pain relief. Traditional transcutaneous electronic nerve stimulation (TENS) devices are often recommended; however, there is mixed evidence behind their effectiveness. A novel approach called hybrid form impulse therapy (HFIT) incorporates a priming pulse with a traditional TENS pulse width and frequency. This randomized controlled trial (RCT) aimed to compare the effectiveness of HFIT versus traditional TENS versus usual care among members of a digital MSK program.

Patients and Methods: A three-arm RCT comparing HFIT versus TENS versus usual care was conducted. A total of 325 people with chronic back or knee pain who were members of a digital MSK program consisting of PT-guided exercise therapy, education, and coaching were randomized. Outcomes including pain, function, anxiety, and depression were examined at 1, 2, and 4 weeks (primary endpoint). Engagement was measured through exercise therapy (ET) sessions completed. Unadjusted and adjusted logistic generalized estimating equations were conducted.

Results: Adjusted per-protocol results at 4 weeks showed significantly lower odds of achieving pain improvement for both TENS (OR: 0.42, 95% CI: [0.19, 0.92]) and usual care (OR: 0.35, 95% CI: [0.17, 0.72]) groups, compared to HFIT group. Both HFIT and usual care users had significantly higher engagement than the TENS users (p=0.026 and p=0.002, respectively). No adverse events were reported throughout the study.

Conclusion: More participants of a digital MSK program who were randomized to the HFIT group experienced meaningful pain improvement at 4 weeks than participants who used TENS and usual care. HFIT can be an effective, non-pharmaceutical solution for relief as a complement to first-line treatments for patients with chronic back and knee pain.

Keywords: HFIT, pain, chronic pain, neuromodulation, noninvasive treatment

Introduction

Musculoskeletal (MSK) pain is a prominent cause of disability and healthcare costs in the United States. In 2019, MSK disorders affected 127.4 million Americans, making it the third most prevalent disease or injury in the United States.[1–3] Some of the most prevalent forms of MSK pain are low back and knee pain. Chronic low back pain (CLBP) affects over 76 million people in the United States, costing over $100 billion per year.[4] Frequent knee pain affects almost 25% of adults, with osteoarthritis listed as the most common cause of knee pain in adults over 50 years old.[5] Furthermore, studies have shown that total knee arthroplasty (TKA) procedures in the United States cost $29,300 on average,[6] and project the incidence rate of TKA to increase 69% by 2050 compared to 2012.[7]

2417

Clinical guidelines often recommend physical therapy, education, behavioral support, non-steroidal anti-inflammatory drugs, and other conservative care as first-line treatment options.[8] Conservative treatment options include exercise and education due to both their safety and their impact on outcomes. Results from a meta-analysis of 3514 participants found that exercise and movement reduced lower back pain by an average of 10.7 points out of 100.[9] Additionally, studies have also shown the effectiveness of pain neuroscience education in improving pain, disability, and kinesiophobia in patients with chronic MSK pain.[10,11] Conservative care has traditionally been provided in-person, but has increasingly become more common through digital health in recent years following the COVID-19 pandemic.[12,13] However, while conservative care is effective, safe, and reduces costs, it is unable to provide immediate or sufficient pain relief for many patients. There is unclear consensus around the use of opioids and injections for chronic pain, which may also often carry harmful side effects.[14–16]

Pain physicians and physical therapists often treat MSK pain with transcutaneous electrical nerve stimulation (TENS). However, while traditional TENS devices can act as a temporary treatment for MSK pain, there is little evidence that indicates it to be an effective solution.[17,18] The high amplitudes required for an effective treatment can often be uncomfortable for users. While lower, tolerable amplitudes can provide more comfort due to the temporal summation induced by the wide pulse widths, the treatment effect is reduced. Due to the high impedance of the skin, it is often difficult for adequate electrical current to pass through.[19] Methods to overcome the impedance of the skin include delivering higher voltage to drive sufficient current or faster impulses to bypass the capacitive components of the impedance. A hybrid approach, called Hybrid Form Impulse Therapy (HFIT), combines a fast priming pulse to activate high-threshold nerves, followed by a lower amplitude pulse to achieve temporal summation on a larger group of nerves. By incorporating a short pulse followed by a longer and lower amplitude pulse, HFIT can potentially reduce the discomfort that often comes with traditional TENS.

A feasibility randomized controlled trial (RCT) found that HFIT provided a significant improvement in pain and function in comparison to a sham device among patients with chronic low back pain after four weeks.[20] However, little is known about how HFIT performs against traditional TENS. As a result, this study aimed to examine whether HFIT provided improvement in pain and function in comparison to traditional TENS and usual care among participants of a digital chronic MSK program with knee and low back pain. An exploratory objective was to compare engagement between the HFIT, TENS, and usual care groups in the form of number of exercise therapy (ET) sessions completed.

Methods
Study Design

A three-armed, parallel RCT comparing clinical outcomes of Hybrid Form Impulse Therapy (HFIT), traditional Transcutaneous Electronic Nerve Stimulation (TENS), and a comparison group of users who continued usual care in a digital MSK chronic program was conducted. Outcomes were compared at 1, 2, and 4 weeks.

Digital Chronic MSK Program

All study participants received a digital chronic MSK program, which was accessed remotely (Figure 1). The objective of the chronic MSK program was to address participants' chronic MSK pain through guided support and virtual consultations with health coaches and physical therapists, app-guided exercise therapy (ET) sessions, and educational articles. The program delivered ET and education through "playlists", which presented three to five exercises specific to back or knee pain. Exercise treatment plans were created by physical therapists following clinical guidelines for care for the indicated condition and focused on a curriculum of stretching, strengthening, balance, and mobility exercises. The curriculum incorporated over 60 distinct exercises, and playlists presented one to two sets of three to ten repetitions, depending on the difficulty level and type of exercise. Members of the chronic MSK app were encouraged to complete exercise playlists at least three times per week. As participants advanced throughout the program, the playlist incorporated more challenging exercises and/or added repetitions. Alongside the ETs, educational articles focused on MSK pain-related topics, including pain neuroscience, movement, treatment options, lifestyle changes, and social support, were delivered.
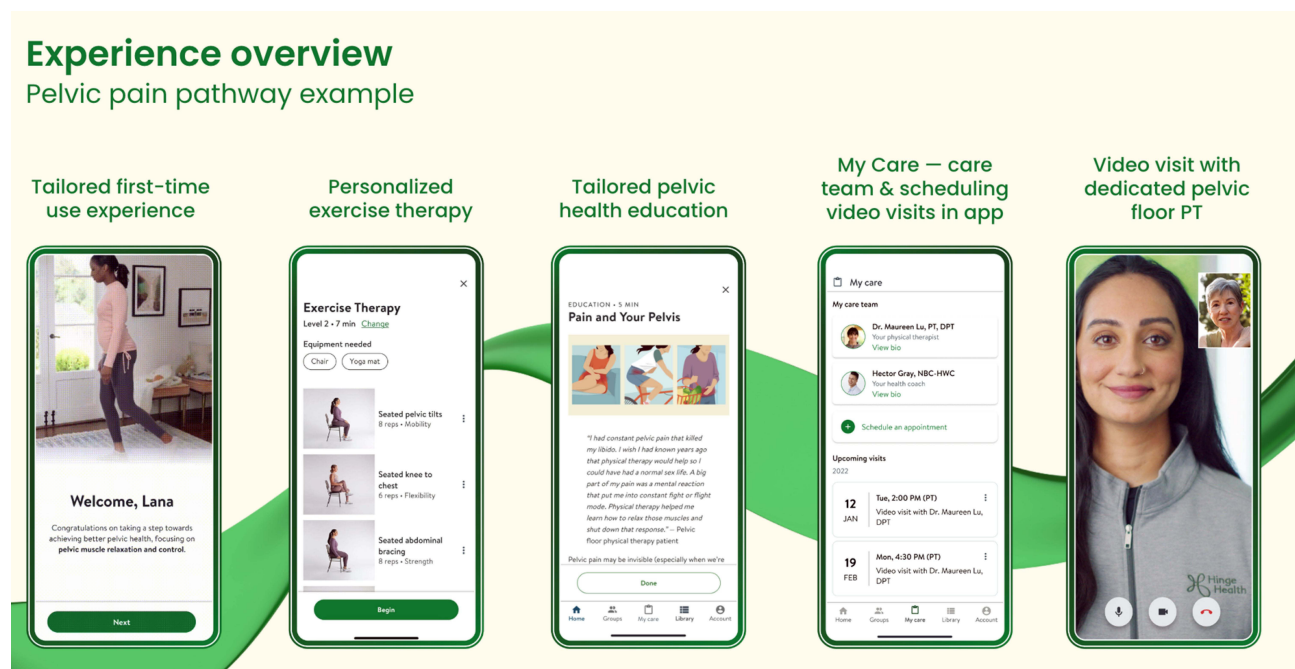
Figure 1 Digital MSK Application.
Abbreviation: MSK, musculoskeletal.

Participants were able to access the chronic MSK program app through smartphones or tablets. In addition to exercise and education, the digital MSK program provided personal support to adhere to the program. Each participant was paired with a personal, certified health coach and physical therapist. Coaches initiated contact with participants via text message and communicated with members asynchronously over time via text message, email, or in-app messaging. Physical therapists assisted participants with tailoring and designing their ET routines as well as providing direct support on exercise form. As an entirely virtual program, participants were able to choose when and where to access the app and its offerings.

Study Participants

In April 2023, individuals participating in the digital MSK program and meeting the inclusion and exclusion criteria based on self-reported information provided in the application were identified. Inclusion criteria were age between 18 and 65 years old; back or knee pain; experiencing pain for at least 12 weeks; Numeric Pain Rating Scale (NPRS) score ≥ 40 out of 100; joined the digital MSK program after January 1, 2023; completed an ET session or read an educational article every week in the last 3 weeks; provided research consent; and covered by employer's health plan. Exclusion criteria were diagnosis of cancer or malignant tumors in the last 5 years; back or knee surgery in the last 6 months; current use of a cardiac pacemaker, implanted defibrillator, spinal cord stimulator, pain pump, insulin pump, or any other implanted electronic device; history of opioid, alcohol, or drug use disorder in the last year; cognitive, behavioral, neurologic, or psychiatric disorder; pregnant or plan on becoming pregnant in the next year; epilepsy; or cardiovascular disease.

1853 individuals who met eligibility criteria based on responses to an applicant questionnaire were sent a screener questionnaire containing the exclusion criteria questions above. Of those, 772 (41.7%) responded and were fully assessed for eligibility and 325 (42.1%) were determined to be eligible. The participants deemed eligible for the study provided informed consent to participate in the trial.

Randomization and Blinding

Study participants were randomly assigned to one of three groups, two of which were intervention groups, the HFIT (n=109) or TENS (n=108), or a control group, who received usual care (n=108). Randomization allocation was 1:1:1 and

was stratified by pain location (back or knee) using random block sizes of 3, 6, or 9. A research scientist implemented the sequence and assigned the groups with letter codes in order to maintain allocation concealment from the statistician. Research staff enrolled participants and notified participants of their randomization assignment. All analyses were conducted by a statistician who was blinded to group assignment.

Participants randomized to the intervention groups, HFIT and TENS, were given an HFIT device (Enso) (Figure 2) or a traditional TENS (iTENS, LLC) device, respectively. The TENS device used in this study was chosen due to its similarity to the HFIT device, as both were wireless, controlled through an app, and could be attached to the skin through adhesive pads. Both HFIT and TENS group participants were asked to schedule an onboarding call with a study staff member, who provided instructions on how to install the software needed and set up the device. Study staff recommended that intervention participants use their device for at least one hour every day, or as often as needed. Individuals in the usual care group received routine care through the digital MSK program and no devices.

After randomization, all study participants were sent a baseline self-report questionnaire, which asked about demographics, clinical characteristics, and outcome variables (eg pain and function), as well as follow-up surveys 1, 2, and 4 weeks after baseline surveys were completed. In order to prevent overlap between surveys at each timepoint, participants were provided one week to respond to each survey before their survey link expired. To ensure participants in the HFIT and TENS groups received their devices in time, devices were shipped after the baseline survey link expired.

Ethical Considerations

The study was approved by the WIRB-Copernicus Group Institutional Review Board (OHRP/FDA IRB registration number IRB00000533) at WIRB-Copernicus Group, registered on ClinicalTrials.gov (NCT05821530), and conducted in accordance with the Declaration of Helsinki. All participants provided informed consent via an online consent form. CONSORT reporting guidelines were followed and are included (Supplementary Material 1).

Measures

The primary outcome was a dichotomous variable of minimal clinically important difference (MCID) in pain improvement (pain MCID), pain based on the response to a clinically validated patient-reported outcome measure: "Over the past 24 hours, how bad was your [back/knee] pain?" with a score from 0 (none) to 100 (worst imaginable). A person achieved a MCID in pain improvement if they showed at least a 23 point or 34% improvement from baseline.[21]

A secondary outcome was a dichotomous variable of MCID in functional improvement (function MCID), created from responses to the validated 11-item Roland Morris Disability Questionnaire (RMDQ-11, back only) and Knee Injury and Osteoarthritis Outcome Score Physical Function short-form (KOOS-PS, knee only). Change from baseline to follow-up was calculated, and function MCID was defined as at least 30% improvement on the RMDQ-11[22,23] or 8-point improvement on the KOOS-PS.[24–26]

Additional outcomes were anxiety and depression symptoms. These were measured through the Generalized Anxiety Disorder (GAD-2) and Patient Health Questionnaire (PHQ-2) scores, respectively. Both scales ranged from 0 (none at all)

Figure 2 HFIT Device.
Abbreviation: HFIT, hybrid form impulse therapy.

to 6 (most anxious/depressed). A score of 3 or higher was defined as having a positive screen for probable generalized anxiety or depressive disorder.[27,28] Self-reported opioid use was also collected, based on response to the questions: "Have you used any Vicodin®, OxyContin®, Norco®, Hydrocodone, Percocet®, Methadone, or other opioid painkillers for [back/knee] pain in the past three months?" at baseline.

Engagement outcomes among each group were compared by examining the number of program ET sessions completed, which were tracked through the app. Additionally, study participants were asked to report any adverse events or harms, such as burns, shocks or allergic reactions, to the digital MSK program's support staff.

Model covariates included age at baseline, gender, pain region (back/knee), education level (high school/some college or associate's degree/bachelor or advanced degree), general health status (poor/good/very good or excellent), number of comorbidities (hypertension, high cholesterol, asthma, prediabetes, diabetes, and/or osteoarthritis), conservative MSK-related healthcare service use at baseline (physical therapy or MSK-related physician office visits), nonconservative healthcare service use at baseline (MSK imaging or injections), and opioid use at baseline (no/yes).

Data Sources

Baseline data was acquired through the online application at program registration as well as the initial baseline survey. Education level, health status, and comorbidities were based on questions used by the National Health Interview Survey (NHIS). Follow-up surveys and up to two reminders were emailed at 1, 2, and 4 weeks. Respondents received gift cards for $5 at each timepoint for their participation.

Sample Size

Based on a previously conducted feasibility study among digital MSK members with low back and knee pain, differences of 50.8% and 47.0% were detected between the number of HFIT and TENS participants and the number of HFIT and usual care participants, respectively, who achieved pain MCID at Week 4. A more conservative estimate of a difference of 25.0% was used for this study's sample size calculations. Assuming 80% statistical power and 2.5% significance level to account for the two comparisons, a sample size of 72 per arm, or 216 total, was required to detect a 25.0% difference between groups in pain MCID. Allowing for 30% attrition, we aimed to recruit at least 281 participants.[29]

Statistical Analysis

Baseline demographic and clinical characteristics were presented as frequencies and percentages or means and standard deviations (SD). Descriptive statistics reported at 1, 2, and 4 weeks included the number and percentage of participants who achieved MCID in pain and function at follow-up compared to baseline. The percentage of participants who screened positive for anxiety and depression symptoms in each group were compared. To assess the differences among groups, chi-square tests were conducted, along with pairwise proportions tests, where Hochberg adjustments were used to adjust for multiple comparisons.

Unadjusted and adjusted logistic generalized estimating equations (GEE) methods were used to compare the effects of each treatment on primary and secondary outcomes. Covariates were controlled for by including baseline age, gender, pain region, education level, general health status, number of comorbidities, conservative healthcare service use (physical therapy or physician office visits), nonconservative healthcare service use (imaging or injections), and opioid use in the model. Between-group differences were assessed with a group × time interaction effect, with time as a categorical variable. Odds ratios (OR) and 95% confidence intervals (CIs) were estimated.

An exchangeable correlation structure was used to adjust for correlated observations. Missing data were addressed using multiple imputation analysis, assuming data were missing at random (MAR). The primary analysis employed study participants who adhered to the study protocol, defined as having used their device at least 3 days in the last week at all three follow-up timepoints, in a per-protocol analysis. Dropouts, non-compliant subjects, and protocol violations were included in an intention-to-treat analysis. All analysis was performed in R (version 4.0.5; R Foundation for Statistical Computing).

Results

Figure 3 reports the volume of subjects in the HFIT, TENS, and usual care groups at each stage throughout the study. Of the randomized participants, 100 (91.7%), 95 (88.0%), and 93 (86.1%) participants completed the initial baseline survey in the HFIT, TENS, and usual care arms, respectively, and 90 (82.6%), 86 (79.6%), and 87 (80.6%) participants completed the final follow-up survey in the HFIT, TENS, and usual care arms, respectively (Figure 3).

Sample Characteristics

Baseline characteristics of all randomized participants (n=325) are shown in Table 1. Baseline characteristics are comparable between participants in each group. Participants had a mean age of 50.0 (SD 9.8) years, with 75.7% enrolled in the digital MSK program for back pain and 24.3% for knee pain. At the time of program registration, study participants had a mean baseline pain score of 59.8 (SD 12.1), out of 100.

Baseline characteristics of participants who responded to the baseline questionnaire (n=288) are shown in Table 2. Participants who responded had a mean age of 50.3 (SD 9.8) years, with 75.7% enrolled in the program for back pain and 24.3% for knee pain. At the time of program registration, participants had a mean baseline pain score of 59.8 (SD 11.9), out of 100. 67.0% were White, 8.7% were Black or African American, 6.9% were Asian, 0.7% were American Indian or Alaska Native, and 15.3% were other single and multiple races.

Primary Outcome

The percentage of participants achieving MCID in pain improvement was 5.9% higher for the HFIT group versus the TENS group at 1 week, 12.8% at 2 weeks, and 14.1% at 4 weeks (Table 3). The percentage achieving MCID in pain
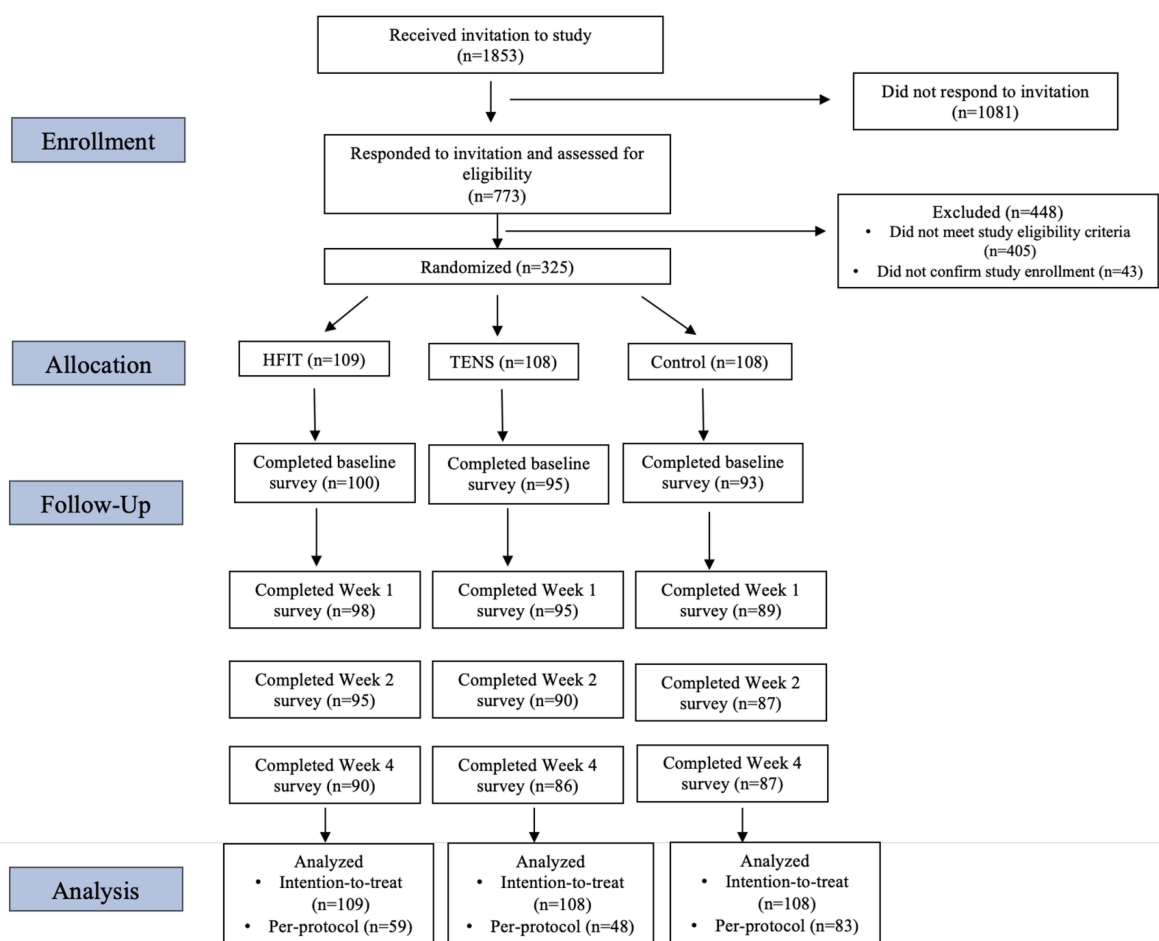

Figure 3 CONSORT Flowchart.

Table 1 Baseline Characteristics of Randomized Participants

	HFIT N=109	TENS N=108	Usual Care N=108	Total N=325
Age				
Mean (SD)	50.4 (9.0)	51.1 (9.2)	48.4 (10.9)	50.0 (9.8)
Median [Min, Max]	52.0 [25.0, 65.0]	53.0 [25.0, 65.0]	49.5 [24.0, 65.0]	52.0 [24.0, 65.0]
Gender				
Female	76 (69.7%)	68 (63.0%)	57 (52.8%)	201 (61.8%)
Male	33 (30.3%)	40 (37.0%)	50 (46.3%)	123 (37.8%)
Other	0 (0%)	0 (0%)	1 (0.9%)	1 (0.3%)
Pain Location				
Back	82 (75.2%)	82 (75.9%)	82 (75.9%)	246 (75.7%)
Knee	27 (24.8%)	26 (24.1%)	26 (24.1%)	79 (24.3%)
Baseline pain at time of program registration				
Mean (SD)	59.3 (12.6)	60.5 (12.2)	59.5 (11.6)	59.8 (12.1)
Median [Min, Max]	58.0 [40.0, 100]	60.0 [40.0, 94.0]	59.0 [40.0, 89.0]	59.0 [40.0, 100]

Abbreviations: HFIT, hybrid form impulse therapy; TENS, transcutaneous electrical nerve stimulator; SD, standard deviation.

Table 2 Baseline Characteristics of Randomized Participants Who Completed Baseline Questionnaire

	HFIT N=100	TENS N=93	Usual Care N=95	Total N=288
Age				
Mean (SD)	50.8 (9.0)	51.2 (9.5)	48.9 (10.8)	50.3 (9.8)
Median [Min, Max]	52.0 [29.0, 65.0]	53.0 [25.0, 65.0]	50.0 [24.0, 65.0]	52.0 [24.0, 65.0]
Gender				
Female	69 (69.0%)	62 (66.7%)	48 (50.5%)	179 (62.2%)
Male	31 (31.0%)	31 (33.3%)	46 (48.4%)	108 (37.5%)
Other	0 (0%)	0 (0%)	1 (1.1%)	1 (0.3%)
Pain Location				
Back	75 (75.0%)	72 (77.4%)	71 (74.7%)	218 (75.7%)
Knee	25 (25.0%)	21 (22.6%)	24 (25.3%)	70 (24.3%)
Baseline pain at time of program registration				
Mean (SD)	59.2 (12.1)	60.6 (12.2)	59.7 (11.5)	59.8 (11.9)
Median [Min, Max]	58.0 [40.0, 97.0]	60.0 [41.0, 94.0]	60.0 [40.0, 89.0]	59.0 [40.0, 97.0]
Pain (last 24 hours)				
Mean (SD)	54.3 (17.3)	52.0 (19.4)	48.4 (17.9)	51.6 (18.3)
Median [Min, Max]	59.5 [10.0, 86.0]	58.5 [0, 97.0]	49.0 [2.00, 82.0]	52.0 [0, 97.0]
Anxiety (GAD-2)				
Screened in	21 (21.0%)	13 (14.0%)	15 (15.8%)	49 (17.0%)
Screened out	77 (77.0%)	77 (82.8%)	74 (77.9%)	228 (79.2%)
Depression (PHQ-2)				
Screened in	9 (9.0%)	3 (3.2%)	8 (8.4%)	20 (6.9%)
Screened out	90 (90.0%)	90 (96.8%)	84 (88.4%)	264 (91.7%)
Opioid Use (last 3 months)				
No	90 (90.0%)	89 (95.7%)	86 (90.5%)	265 (92.0%)
Yes	9 (9.0%)	4 (4.3%)	6 (6.3%)	19 (6.6%)
General Health				
Poor	0 (0%)	0 (0%)	2 (2.1%)	2 (0.7%)
Fair	18 (18.0%)	9 (9.7%)	16 (16.8%)	43 (14.9%)
Good	44 (44.0%)	38 (40.9%)	47 (49.5%)	129 (44.8%)
Very good	31 (31.0%)	44 (47.3%)	26 (27.4%)	101 (35.1%)
Excellent	6 (6.0%)	2 (2.2%)	2 (2.1%)	10 (3.5%)

(*Continued*)

Table 2 (Continued).

	HFIT N=100	TENS N=93	Usual Care N=95	Total N=288
Race				
White only	66 (66.0%)	64 (68.8%)	63 (66.3%)	193 (67.0%)
Black or African American only	13 (13.0%)	5 (5.4%)	7 (7.4%)	25 (8.7%)
Asian only	5 (5.0%)	8 (8.6%)	7 (7.4%)	20 (6.9%)
American Indian or Alaska Native only	1 (1.0%)	0 (0%)	1 (1.1%)	2 (0.7%)
Other single and multiple races	14 (14.0%)	15 (16.1%)	15 (15.8%)	44 (15.3%)
Marriage Status				
Married	75 (75.0%)	67 (72.0%)	67 (70.5%)	209 (72.6%)
Living with partner	5 (5.0%)	5 (5.4%)	10 (10.5%)	20 (6.9%)
Widowed	3 (3.0%)	2 (2.2%)	1 (1.1%)	6 (2.1%)
Divorced	10 (10.0%)	12 (12.9%)	7 (7.4%)	29 (10.1%)
Separated	1 (1.0%)	1 (1.1%)	0 (0%)	2 (0.7%)
Never married	5 (5.0%)	5 (5.4%)	8 (8.4%)	18 (6.2%)
Employment Status				
Working for pay	89 (89.0%)	84 (90.3%)	77 (81.1%)	250 (86.8%)
Not working for pay	1 (1.0%)	0 (0%)	5 (5.3%)	6 (2.1%)
Student	0 (0%)	1 (1.1%)	0 (0%)	1 (0.3%)
Retired	4 (4.0%)	5 (5.4%)	5 (5.3%)	14 (4.9%)
Other	5 (5.0%)	2 (2.2%)	6 (6.3%)	13 (4.5%)
Education				
Less than high school	0 (0%)	1 (1.1%)	1 (1.1%)	2 (0.7%)
High school graduate	10 (10.0%)	5 (5.4%)	10 (10.5%)	25 (8.7%)
Some college	20 (20.0%)	13 (14.0%)	13 (13.7%)	46 (16.0%)
Associate	12 (12.0%)	15 (16.1%)	15 (15.8%)	42 (14.6%)
Bachelor	32 (32.0%)	38 (40.9%)	22 (23.2%)	92 (31.9%)
Master	18 (18.0%)	16 (17.2%)	27 (28.4%)	61 (21.2%)
Professional or Doctorate	7 (7.0%)	5 (5.4%)	5 (5.3%)	17 (5.9%)
Comorbidities				
Hypertension	38 (38.0%)	24 (25.8%)	27 (28.4%)	89 (30.9%)
High cholesterol	23 (23.0%)	32 (34.4%)	39 (41.1%)	94 (32.6%)
Asthma	18 (18.0%)	15 (16.1%)	18 (18.9%)	51 (17.7%)
Prediabetes or borderline diabetes	17 (17.0%)	13 (14.0)%	17 (17.9%)	47 (16.3%)
Diabetes	4 (4.0%)	4 (4.3%)	9 (9.5%)	17 (5.9%)
Osteoarthritis	19 (19.0%)	19 (20.4%)	13 (13.7%)	51 (17.7%)
None of these	34 (34.0%)	32 (34.4%)	24 (25.3%)	90 (32.1%)

Abbreviations: HFIT, hybrid form impulse therapy; TENS, transcutaneous electrical nerve stimulator; SD, standard deviation; GAD-2, Generalized Anxiety Disorder 2-item Questionnaire; PHQ-2, Patient Health Questionnaire 2-item.

improvement was 10.5% higher for the HFIT group versus the usual care group at 1 week, 20.3% at 2 weeks, and 12.9% at 4 weeks. At Week 4, there was no significant difference in the percentage of participants achieving MCID in pain (p=0.126) or functional (p=0.887) improvement among the groups.

Figure 4 shows results from unadjusted and adjusted models for the primary outcome from the per protocol analysis. In adjusted models, we observed significantly lower odds of achieving a MCID in pain improvement at 4 weeks for the TENS (OR: 0.42, 95% CI: [0.19, 0.92]) and usual care groups (OR: 0.35, 95% CI: [0.18, 0.72]), compared to the HFIT group. In intention-to-treat findings, the adjusted model showed significantly lower odds of achieving a MCID in pain improvement at 4 weeks for the usual care group (OR: 0.47, 95% CI: [0.26, 0.83]), compared to the HFIT group (Figure 5).

Table 3 Outcome Measures by Group Over Time

	Week 1 (n=286)	Week 2 (n=272)	Week 4 (n=263)
Pain MCID			
HFIT	26.74%	41.76%	48.81%
TENS	20.83%	28.95%	34.67%
Usual care	16.28%	21.43%	35.90%
Function MCID			
HFIT	25.56%	31.46%	37.65%
TENS	14.29%	25.97%	34.18%
Usual care	23.26%	31.76%	37.04%
Moderate/Severe Anxiety			
HFIT	11.46%	8.51%	7.95%
TENS	12.94%	5.88%	10.47%
Usual care	11.11%	12.50%	9.64%
Moderate/Severe Depression			
HFIT	7.14%	4.30%	6.90%
TENS	8.14%	2.35%	4.65%
Usual care	6.38%	11.11%	6.98%

Secondary Outcomes

The percentage of participants achieving MCID in functional improvement was higher for the HFIT group versus the TENS group by 11.3% at Week 1, 5.5% at Week 2, and 3.5% at Week 4. The percentage achieving MCID in functional improvement was higher for the HFIT group versus the usual care group by 2.3% at Week 1 and 0.6% at Week 4 (Table 3).

Adjusted model results from the per-protocol analyses showed lower odds of achieving MCID in functional improvement at 4 weeks for the TENS (OR: 0.49, 95% CI: [0.21, 1.12]) and usual care groups (OR: 0.76, 95% CI: [0.35, 1.7]), compared to the HFIT group. However, the findings were not significant in per-protocol (Figure 4) or intention-to-treat (Figure 5) analyses.

Of the participants who responded to the baseline survey, 21.0%, 14.0%, and 15.8% of HFIT, TENS, and usual care users screened positive for anxiety symptoms, respectively. About 9.0%, 3.2%, and 8.4% of HFIT, TENS, and usual care users screened positive for depression symptoms, respectively. At Week 4, fewer HFIT users screened positive for anxiety symptoms (8.0%) than TENS (10.5%) and usual care (9.6%) users. Fewer TENS users screened positive for depressive symptoms (4.7%) than HFIT (6.9%) and usual care (7.0%) users. No significant differences were detected among groups for anxiety or depression outcomes.

Exploratory Outcomes

Engagement was evaluated by collecting the number of ETs completed. Between May and October 2023, the HFIT, TENS, and usual care groups averaged 66.6 (SD: 58.9; range 1–277), 46.0 (SD: 45.9; range: 2–349), and 74.3 (SD: 56.8; range: 1–305) ET sessions, respectively. Both HFIT and usual care users completed significantly more ETs than TENS users (p=0.026 and p=0.002, respectively). No statistically significant difference was detected between the HFIT and usual care groups (p=0.586). Throughout the duration of the study, no adverse events were reported among study participants.

Discussion

To our knowledge, this is the first RCT to utilize a hybrid form impulse therapy for the treatment of chronic low back and knee pain. As first-line treatments, including exercise, education, and healthy behavior change, are essential to improving MSK pain, this study ensured that all study participants were enrolled and engaged in a digital MSK program providing these treatments. This study aimed to evaluate whether any additional treatments, such as HFIT or TENS, added value in addition to PT-guided exercise, education, and healthy behavior change coaching.
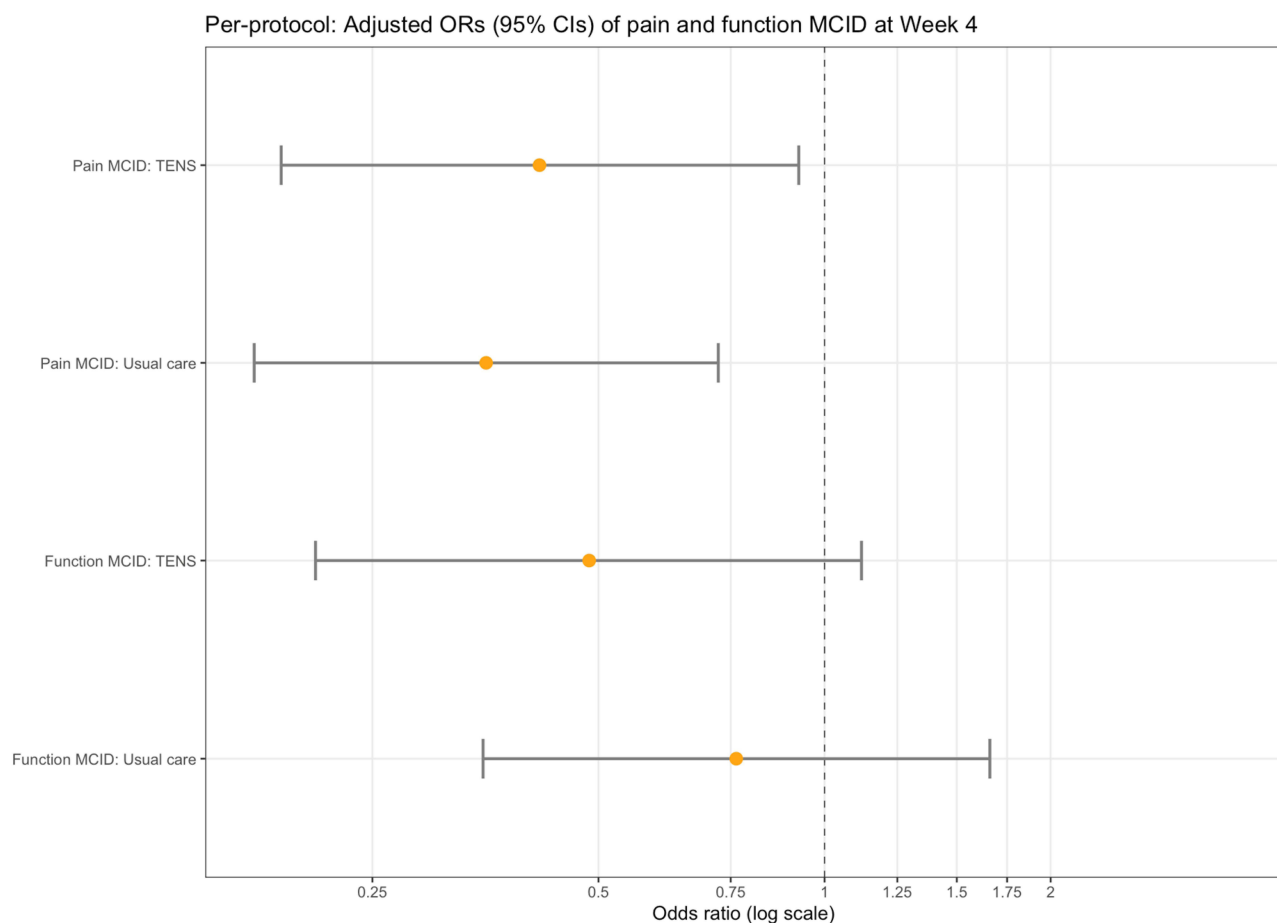
Per-protocol: Adjusted ORs (95% CIs) of pain and function MCID at Week 4

Figure 4 Per-protocol results: adjusted ORs (95% CI) of pain and function MCID at Week 4 (reference: HFIT).
Abbreviations: OR, odds ratio; MCID, minimal clinically important difference; TENS, transcutaneous electrical nerve stimulation; HFIT, hybrid form impulse therapy.

Results from this study suggest HFIT is more effective than traditional TENS and usual care in terms of achieving a clinically meaningful pain improvement. Analyses showed that more HFIT users achieved a minimal clinically important difference in pain than both TENS and usual care users as a trend over time. Primary analysis found that after adjusting for multiple covariates, among users who actively engaged with their devices, participants who were in the HFIT group had 2.3 times and 2.8 times the odds of achieving meaningful pain improvement compared to participants in the traditional TENS and usual care groups, respectively. While there is limited research around the use of HFIT in treating chronic pain, literature on the effectiveness of traditional TENS in pain management has been inconsistent. Results from a qualitative synthesis study of four RCTs found that TENS was unreliable in demonstrating benefits to chronic low back pain.[30] Several meta-analyses provided a similar conclusion, with results presenting little or no evidence to support the use of TENS among patients with chronic low back pain.[31,32] The results of this study are consistent with these findings, as traditional TENS users showed little difference in pain improvement compared to usual care users at Week 4 (34.7% versus 35.9%, respectively).

This study also found that both HFIT and usual care users had significantly higher engagement in exercise than traditional TENS users. We recruited members who were already actively engaged in the digital MSK program; however, we saw that members with HFIT continued to complete their exercises, while TENS users slowed down on their progress. Furthermore, no significant difference was detected between the number of ETs completed between HFIT and usual care users, suggesting that the difference in pain improvement between the two groups is due to the effects of the HFIT device rather than exercise alone.
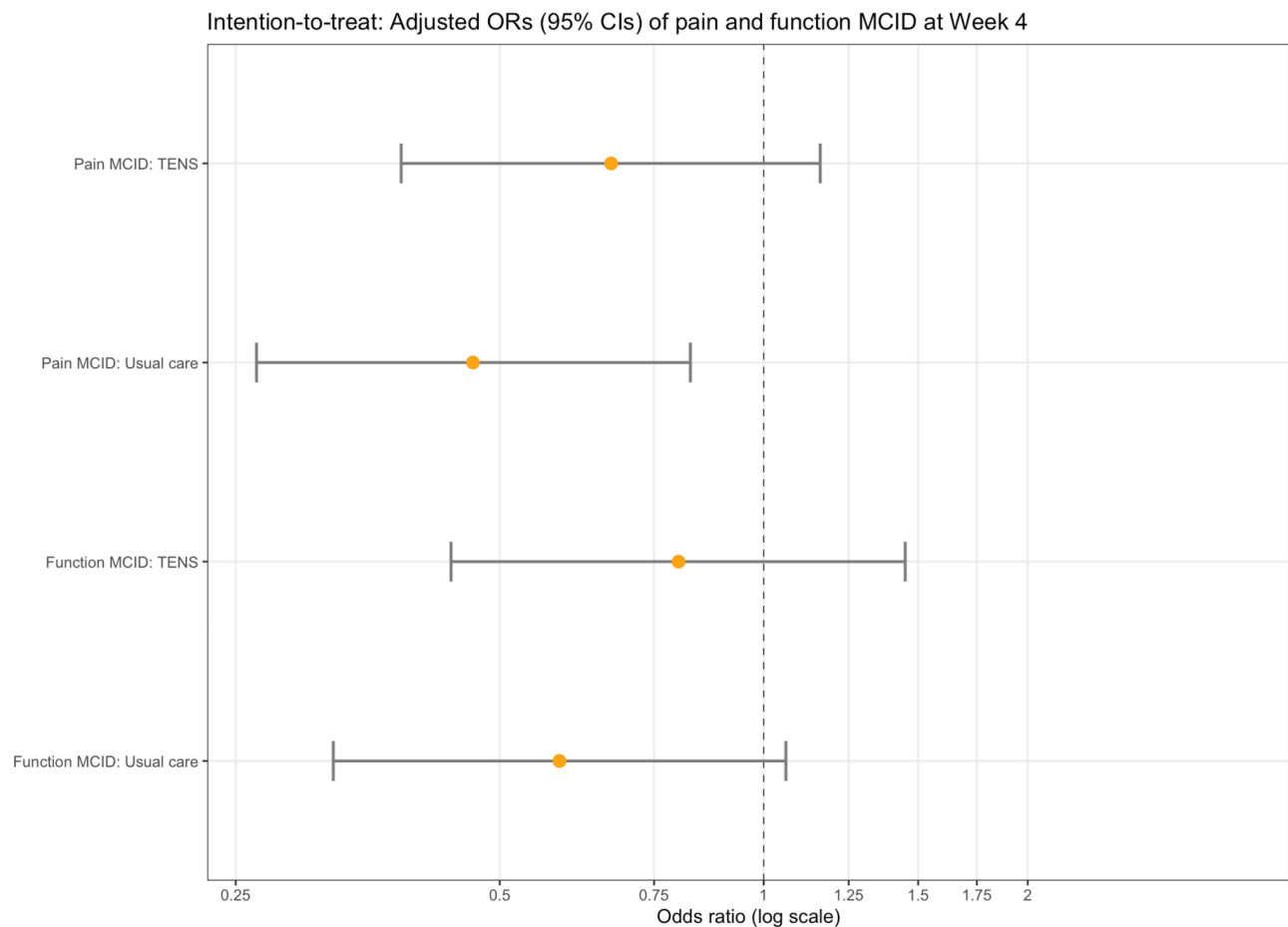
Intention-to-treat: Adjusted ORs (95% CIs) of pain and function MCID at Week 4

Figure 5 Intention-to-treat results: adjusted ORs (95% CI) of pain and function MCID at Week 4 (reference: HFIT).
Abbreviations: OR, odds ratio; MCID, minimal clinically important difference; TENS, transcutaneous electrical nerve stimulation; HFIT, hybrid form impulse therapy.

This study did not detect significant differences in function, anxiety, or depression symptoms. However, anxiety and depression were low among study participants at baseline and therefore may not have had room to improve substantially. Furthermore, as exercise has consistently been shown to have a positive impact on mental health among patients experiencing back pain,[9,33–35] it is possible that this study did not detect substantial differences in these outcomes from adding in a pain-relief device alone, as all participants in this study had access to exercise therapy. Lastly, the insignificant findings of secondary outcomes may also be due to the study being powered to detect differences only in the primary outcome, a clinically meaningful improvement in pain.

There are multiple inherent advantages to HFIT therapy, including its ability to provide local, immediate pain relief while being minimally invasive and portable. Additionally, as a non-drug-based therapy, HFIT avoids the adverse side effects that opioids can cause, such as drowsiness, addiction or dependence, constipation, and impairment in overall function.[36] Research evidence strongly supports conservative therapies, such as exercise and cognitive behavioral therapy, as a way to work towards sustained improvements in pain.[37,38] As a result, HFIT should not be a replacement for exercise therapy and other first-line treatments, but can be used to supplement and support them by providing patients with additional pain relief. This study confirmed that users who were assigned to the HFIT arm continued to complete their exercise sessions.

This study's strengths include its rigorous design as a three-arm, single-blinded RCT, where the analyst was blinded to treatment assignment. The study included participants experiencing both back or knee pain, which provides more generalizability. Additionally, the TENS unit selected for the study was similar in design to the HFIT device. Both devices were wireless, attached to the skin using an adhesive pad, and controlled through an app, which reinforces that

the difference in pain improvement between the two devices is due to the difference in the electrical stimulation rather than the usability of the device or sham effects of the device application. Lastly, this study imposed a strict definition of MCID in pain of at least a 23 point or 34% improvement from baseline, while several studies have considered 10–17 points to be a clinically meaningful difference in chronic musculoskeletal pain.[39,40]

Limitations of this study include the lack of blinding among the participants. However, this was not feasible given the packaging differences between devices. Given the variability in shipping times for the pain relief devices, the follow-up timepoints of 1, 2, and 4 weeks are approximate. The study was unable to control for whether participants' pain improved or worsened between the time they joined the digital MSK program and the start of the study. Lastly, to evaluate the effects of each treatment among users who adhered to the study protocol, the analysis employed a per-protocol analysis, which is underpowered, as the primary analysis. However, we also included the results of the intention-to-treat analysis, which is sufficiently powered and contains less bias.

Findings from this study suggest that HFIT improves pain and encourages more engagement with exercise therapy compared to both traditional TENS and usual care. Future studies will examine the effects of HFIT among patients experiencing pain in other locations, such as shoulder or hip. Future work will also evaluate clinical outcomes at longer follow-up time points to evaluate sustained relief.

Conclusion

More participants of a digital MSK program who were randomized to use the HFIT device experienced meaningful pain improvement at four weeks versus participants who used a traditional TENS device and participants who continued usual care. Among participants who adhered to the study protocol, study results found that HFIT users had significantly higher odds of achieving a minimal clinically important difference in pain at four weeks compared to traditional TENS and usual care users. Findings suggest that the efficacy and ease of use of HFIT can serve as an alternative solution to pharmaceutical treatments as well as a complement to first-line treatments to improve pain management among patients with chronic low back and knee pain.

Data Sharing Statement

De-identified data are available upon reasonable request from the corresponding author.

Acknowledgments

Funding

Disclosure

MH and JK are employed at Hinge Health and receive salary and equity compensation. GW was employed at Hinge Health during the conduct of the study. KC and CC receive salary and have ownership interest in UnitedHealth Group. AG is on the clinical advisory board of Hinge Health with nominal equity compensation. He is a consultant for Medtronic, AIS Healthcare, SPR Therapeutics, Nalu Medical, Tersera Medical, Bausch Health, Neurovasis, Modoscript and Smart MS3. The authors report no other conflicts of interest in this work.

References

1. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204–1222. doi:10.1016/S0140-6736(20)30925-9

2. Liu S, Wang B, Fan S, Wang Y, Zhan Y, Ye D. Global burden of musculoskeletal disorders and attributable factors in 204 countries and territories: a secondary analysis of the Global Burden of Disease 2019 study. *BMJ Open*. 2022;12(6):e062183. doi:10.1136/bmjopen-2022-062183

3. McConaghy K, Klika AK, Apte SS, Erdemir A, Derwin K, Piuzzi NS. A call to action for musculoskeletal research funding: the growing economic and disease burden of musculoskeletal conditions in the United States is not reflected in musculoskeletal research funding. *J Bone Jt Surg*. 2023;105 (6):492–498. doi:10.2106/JBJS.22.00693

4. Crow WT, Willis DR. Estimating cost of care for patients with acute low back pain: a retrospective review of patient records. *J Am Osteopath Assoc*. 2009;109(4):229–233.

5. Nguyen USDT, Zhang Y, Zhu Y, Niu J, Zhang B, Felson DT. Increasing prevalence of knee pain and symptomatic knee osteoarthritis: survey and cohort data. *Ann Intern Med*. 2011;155(11):725–732. doi:10.7326/0003-4819-155-11-201112060-00004

6. Ong KL, Niazi F, Lau E, et al. Knee OA cost comparison for hyaluronic acid and knee arthroplasty. *J Orthop Surg*. 2020;15(1):305. doi:10.1186/ s13018-020-01848-7

7. Inacio MCS, Paxton EW, Graves SE, Namba RS, Nemes S. Projected increase in total knee arthroplasty in the United States – an alternative projection model. *Osteoarthritis Cartilage*. 2017;25(11):1797–1803. doi:10.1016/j.joca.2017.07.022

8. Fullen BM, Wittink H, De Groef A, et al. Musculoskeletal pain: current and future directions of physical therapy practice. *Arch Rehabil Res Clin Transl*. 2023;5(1):100258. doi:10.1016/j.arrct.2023.100258

9. Hayden JA, Van Tulder MW, Malmivaara AV, Koes BW. Meta-analysis: exercise therapy for nonspecific low back pain. *Ann Intern Med*. 2005;142 (9):765. doi:10.7326/0003-4819-142-9-200505030-00013

10. Bridle C, Spanjers K, Patel S, Atherton NM, Lamb SE. Effect of exercise on depression severity in older people: systematic review and meta-analysis of randomised controlled trials. *Br J Psychiatry*. 2012;201(3):180–185. doi:10.1192/bjp.bp.111.095174

11. Siddall B, Ram A, Jones MD, Booth J, Perriman D, Summers SJ. Short-term impact of combining pain neuroscience education with exercise for chronic musculoskeletal pain: a systematic review and meta-analysis. *Pain*. 2022;163(1):e20–e30. doi:10.1097/j.pain.0000000000002308

12. Fagherazzi G, Goetzinger C, Rashid MA, Aguayo GA, Huiart L. Digital health strategies to fight COVID-19 worldwide: challenges, recommendations, and a call for papers. *J Med Internet Res*. 2020;22(6):e19284. doi:10.2196/19284

13. Koonin LM, Hoots B, Tsang CA, et al. Trends in the use of telehealth during the emergence of the COVID-19 pandemic — United States, January–March 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(43):1595–1599. doi:10.15585/mmwr.mm6943a3

14. Kolber MR, Ton J, Thomas B, et al. PEER systematic review of randomized controlled trials: management of chronic low back pain in primary care. *Can Fam Physician*. 2021;67(1):e20–e30. doi:10.46747/cfp.6701e20

15. Carassiti M, Pascarella G, Strumia A, et al. Epidural steroid injections for low back pain: a narrative review. *Int J Environ Res Public Health*. 2021;19(1):231. doi:10.3390/ijerph19010231

16. Cohen KR. Management of chronic low back pain. *JAMA Intern Med*. 2022;182(2):222. doi:10.1001/jamainternmed.2021.7359

17. Deyo RA, Walsh NE, Martin DC, Schoenfeld LS, Ramamurthy S. A Controlled Trial of Transcutaneous Electrical Nerve Stimulation (TENS) and exercise for chronic low back pain. *N Engl J Med*. 1990;322(23):1627–1634. doi:10.1056/NEJM199006073222303

18. Oosterhof J, Wilder-Smith OH, De Boo T, Oostendorp RAB, Crul BJP. The long-term outcome of transcutaneous electrical nerve stimulation in the treatment for patients with chronic pain: a randomized, placebo-controlled trial. *Pain Pract*. 2012;12(7):513–522. doi:10.1111/j.1533-2500.2012.00533.x

19. Hughes N, Bennett MI, Johnson MI. An investigation into the magnitude of the current window and perception of Transcutaneous Electrical Nerve Stimulation (TENS) sensation at various frequencies and body sites in healthy human participants. *Clin J Pain*. 2013;29(2):146–153. doi:10.1097/ AJP.0b013e3182579919

20. Amirdelfan K, Hong M, Tay B, et al. High-frequency impulse therapy for treatment of chronic back pain: a multicenter randomized controlled pilot study. *J Pain Res*. 2021;14:2991–2999. doi:10.2147/JPR.S325230

21. Olsen MF, Bjerre E, Hansen MD, Tendal B, Hilden J, Hróbjartsson A. Minimum clinically important differences in chronic pain vary considerably by baseline pain and methodological factors: systematic review of empirical studies. *J Clin Epidemiol*. 2018;101:87–106.e2. doi:10.1016/j. jclinepi.2018.05.007

22. Stroud MW, McKnight PE, Jensen MP. Assessment of self-reported physical activity in patients with chronic pain: development of an abbreviated Roland-Morris disability scale. *J Pain*. 2004;5(5):257–263. doi:10.1016/j.jpain.2004.04.002

23. Jordan K, Dunn KM, Lewis M, Croft P. A minimal clinically important difference was derived for the Roland-Morris Disability Questionnaire for low back pain. *J Clin Epidemiol*. 2006;59(1):45–52. doi:10.1016/j.jclinepi.2005.03.018

24. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: international Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (Tas). *Arthritis Care Res*. 2011;63:S11. doi:10.1002/acr.20632

25. White DK, Master H. Patient-reported measures of physical function in knee osteoarthritis. *Rheum Dis Clin N Am*. 2016;42(2):239–252. doi:10.1016/j.rdc.2016.01.005

26. Beletsky A, Gowd AK, Liu JN, et al. Time to achievement of clinically significant outcomes after isolated arthroscopic partial meniscectomy: a multivariate analysis. *Arthrosc Sports Med Rehabil*. 2020;2(6):e723–e733. doi:10.1016/j.asmr.2020.06.002

27. Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. *Gen Hosp Psychiatry*. 2016;39:24–31. doi:10.1016/j.genhosppsych.2015.11.005

28. Arroll B, Goodyear-Smith F, Crengle S, et al. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. *Ann Fam Med*. 2010;8(4):348–353. doi:10.1370/afm.1139

29. Juszczak E, Altman DG, Hopewell S, Schulz K. Reporting of multi-arm parallel-group randomized trials: extension of the CONSORT 2010 statement. *JAMA*. 2019;321(16):1610. doi:10.1001/jama.2019.3087

30. Khadilkar A, Odebiyi DO, Brosseau L, Wells GA. Transcutaneous electrical nerve stimulation (TENS) versus placebo for chronic low-back pain. *Cochrane Database Syst Rev.* 2008;2008(4). doi:10.1002/14651858.CD003008.pub3

31. Wu LC, Weng PW, Chen CH, Huang YY, Tsuang YH, Chiang CJ. Literature review and meta-analysis of transcutaneous electrical nerve stimulation in Treating Chronic Back Pain. *Reg Anesth Pain Med.* 2018;43(4):425–433. doi:10.1097/AAP.0000000000000740

32. Brosseau L, Milne S, Robinson V, et al. Efficacy of the transcutaneous electrical nerve stimulation for the Treatment of Chronic Low Back pain: a meta-analysis. *Spine.* 2002;27(6):596–603. doi:10.1097/00007632-200203150-00007

33. Amiri S. Exercise training and depression and anxiety in musculoskeletal pain patients: a meta-analysis of randomized control trials. *neuropsychiatrie.* 2023;37(2):88–100. doi:10.1007/s40211-022-00431-2

34. Sculco AD, Paup DC, Fernhall B, Sculco MJ. Effects of aerobic exercise on low back pain patients in treatment. *Spine J.* 2001;1(2):95–101. doi:10.1016/S1529-9430(01)00026-2

35. Wang G, Yang M, Hong M, et al. Clinical outcomes one year after a digital musculoskeletal (MSK) program: an observational, longitudinal study with nonparticipant comparison group. *BMC Musculoskelet Disord.* 2022;23(1):237. doi:10.1186/s12891-022-05188-x

36. Benyamin R, Trescot AM, Datta S, et al. Opioid complications and side effects. *Pain Physician.* 2008;11(2 Suppl):S105–120. doi:10.36076/ppj.2008/11/S105

37. Van Koulil S, Effting M, Kraaimaat FW, et al. Cognitive-behavioural therapies and exercise programmes for patients with fibromyalgia: state of the art and future directions. *Ann Rheum Dis.* 2007;66(5):571–581. doi:10.1136/ard.2006.054692

38. McBeth J, Prescott G, Scotland G, et al. Cognitive Behavior Therapy, Exercise, or Both for Treating Chronic Widespread Pain. *Arch Intern Med.* 2012;172(1):48. doi:10.1001/archinternmed.2011.555

39. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain.* 2004;8(4):283–291. doi:10.1016/j.ejpain.2003.09.004

40. Suzuki H, Aono S, Inoue S, et al. Clinically significant changes in pain along the Pain Intensity Numerical Rating Scale in patients with chronic low back pain. *PLoS One.* 2020;15(3):e0229228. doi:10.1371/journal.pone.0229228