Pain Medicine, 2023, **00**, 1–11
https://doi.org/10.1093/pm/pnad049
Advance access publication 27 April 2023
Original Research Article

An artificial intelligence-powered, patient-centric digital tool for self-management of chronic pain: a prospective, multicenter clinical trial

Antje M. Barreveld, MD[1], Maria L Rosén Klement, PhD[2,3], Sophia Cheung, BA[4], Ulrika Axelsson, PhD[3], Jade I. Basem, BA[5], Anika S. Reddy, BA[5], Carl A. K. Borrebaeck, DSc[2,3], Neel Mehta, MD[5,*]

[1]Department of Anesthesiology, Tufts University School of Medicine, Newton-Wellesley Hospital, Newton, MA 02462, United States
[2]Department of Immunotechnology, Lund University, Lund 221 00, Sweden
[3]PainDrainer AB, Sheeletorget, Medicon Village, Lund 223 81, Sweden
[4]Office of Clinical Research, Newton-Wellesley Hospital, Newton, MA 02462, United States
[5]Department of Anesthesiology, Division of Pain Management, Weill Cornell Medicine, New York, NY 10065, USA

**Corresponding author:* Neel Mehta, MD, Division of Pain Management, Department of Anesthesiology, Weill Cornell Medicine, 525 East 68th Street, New York, NY 10065, USA. Email: nem9015@med.cornell.edu

Abstract

Objective: To investigate how a behavioral health, artificial intelligence (AI)-powered, digital self-management tool affects the daily functions in adults with chronic back and neck pain.

Design: Eligible subjects were enrolled in a 12-week prospective, multicenter, single-arm, open-label study and instructed to use the digital coach daily. Primary outcome was a change in Patient-Reported Outcomes Measurement Information Systems (PROMIS) scores for pain interference. Secondary outcomes were changes in PROMIS physical function, anxiety, depression, pain intensity scores and pain catastrophizing scale (PCS) scores.

Methods: Subjects logged daily activities, using PainDrainer^{TM}, and data analyzed by the AI engine. Questionnaire and web-based data were collected at 6 and 12 weeks and compared to subjects' baseline.

Results: Subjects completed the 6- (n = 41) and 12-week (n = 34) questionnaires. A statistically significant Minimal Important Difference (MID) for pain interference was demonstrated in 57.5% of the subjects. Similarly, MID for physical function was demonstrated in 72.5% of the subjects. A pre- to post-intervention improvement in depression score was also statistically significant, observed in 100% of subjects, as was the improvement in anxiety scores, evident in 81.3% of the subjects. PCS mean scores was also significantly decreased at 12 weeks.

Conclusion: Chronic pain self-management, using an AI-powered, digital coach anchored in behavioral health principles significantly improved subjects' pain interference, physical function, depression, anxiety, and pain catastrophizing over the 12-week study period.

Keywords: digital tool; chronic pain; self-management; ACT; patient-centric

Introduction

Chronic pain is a major health problem in both Europe and the United States, impacting an estimated 90 million people in Europe[1] and 100 million people in the United States.[2] Pain is one of the most common reasons patients see a physician[3] and a leading cause for suffering and disability,[4] with extraordinary economic impacts on individuals and society.[5] Despite the high prevalence of chronic pain, an unmet need for improved treatments remains.[2] Furthermore, concerns remain around long term chronic opioid usage push the need for more effective non-opioid treatments.[6] Only a small percentage of patients have access to interdisciplinary pain management centers due to geographic, insurance, and financial constraints.[7] Consequently, finding effective, safe, and accessible treatment options for chronic pain remains a global public health priority.[4]

Technological advancements in pain management strategies may provide more personalized, precision-based approaches to pain care[8] while addressing the multidimensional biopsychological nature of chronic pain.[8] Chronic pain is also impacted by psychological and cognitive effects, such as anxiety, depression, fatigue, as well as functional aspects of daily life. The multi-faceted nature of pain is thus immensely individual, interfering with normal daily activities, and has a large negative effect on health-related quality of life. Consequently, the individual's biopsychological parameters need to be considered, utilizing a patient-centric and individualized treatment modality optimal for improving daily functioning and quality of life.[2,9]

The fundamental goal of pain rehabilitation processes is to optimize a patient's self-rated quality of life through the ability to adapt and respond to changes, thereby minimizing pain and distress.[10] Programs addressing this include cognitive behavioral therapy (CBT) approaches, such as acceptance and commitment therapy (ACT).[11] A large proportion of patients with chronic pain focus on reducing or eliminating their pain, which leads to a fear avoidance behavior towards activity or rest.[12–14] Therefore, the aim with ACT is to increase psychological flexibility, ie, the ability to stay in the present moment, which is

Received: 9 January 2023. **Revised:** 13 March 2023. **Accepted:** 7 April 2023

achieved by avoiding difficult thoughts, feelings and sensations enabling change or promote behavior that serves a patient's values and goals.[15] Thus, ACT does not focus on symptoms, but rather on reducing the dominance of pain in daily life.[16] Improved daily function may also be observed with other CBT-based integrative approaches.[17] Today, CBT approaches are a common psychological intervention for chronic pain, although a recent systematic review concluded that the effects of CBT rapidly decreased with time after intervention.[17,18]

Novel approaches to self-management of pain care that promote long-lasting behavioral changes must therefore be tailored to each person's experience.[2] The Center for Disease Control and Prevention's (CDC's) Clinical Practice Guideline for Prescribing Opioids for Chronic Pain emphasizes an individualized, patient-centric approach for treating chronic pain.[19] However, most treatment options offered to patients today are based on population-based validations and are lacking this overall patient-centric approach. Core self-management skills, such as self-monitoring of symptoms, increased self-efficacy, that is, the ability to engage in behavioral changes to reach ones goals, are important in the pain rehabilitation process.[20–22] However, implementing new skills and behavioral changes can be difficult in daily self-care, partly since the human brain is incapable of handling more than four variables at the same time,[23] whereas everyday life consists of many more variables. The use of artificial intelligence (AI) may inform individualized and gradual behavioral changes when there are too many variables for the human brain to manage.[23] Thus, such AI-driven guidance is not based on population behavioral models, but rather on an individualized approach to improving function. A digital tool has the potential to increase the psychological flexibility, by guiding the user how to achieve personal goals and hence move toward a value based life despite their pain.[20–23]

Research studies on the impact of electronic tools to assist with day-to-day pain management skills are numerous, but a comprehensive daily tool that also guides patients with chronic pain in self-management strategies and lifestyle modifications would be desirable. A user-friendly, digital platform for patients suffering from chronic pain could provide patients with an individualized coaching to increase their control over their daily activities by identifying pain triggers, improving function, and decreasing pain. The AI-powered digital tool, PainDrainer™, based in part on the principles of ACT, aims to accomplish exactly this and uses a neural network that recognizes underlying relationships in the pain-activity axis through a process mimicking the way the human brain operates. The aim of the prospective, 12-week, multi-center, single-arm study, was to investigate if self-management with PainDrainer™, a medication-free, AI powered tool, improves daily functioning of patients with chronic back or neck pain. The outcome was evaluated by Patient-Reported Outcomes Measurement Information Systems (PROMIS) scores of pain interference (primary outcome). Secondary outcomes included improvements in PROMIS scores for physical function, anxiety, depression, and pain intensity, as well as pain catastrophizing.

Methods

Study design

The present study was a multicenter study performed at Newton-Wellesley Hospital (NWH) in Newton, Massachusetts, and New York-Presbyterian/Weill Cornell Medical Center Pain Management Division (WCMC) in New York, New York. The design was a single-arm, open label, prospective study. The studies were registered at www.clinicaltrials.gov (NCT04865263 at NWH and NCT04628650 at WCMC). The study was approved by the Institutional Review Boards at each study site (Massachusetts General Brigham protocol number 2020P000532, Boston, MA; and Weill Cornell Medicine protocol number 19–04020168).

Inclusion/exclusion criteria

Subject inclusion criteria were as follows: 1) age > 18; 2) > 3 months low back or neck pain; 3) average daily numeric rating scale (NRS) score $\geq$ of 4 in the lower back or neck; 4) back or neck pain as the primary area of pain (NRS scores < 4 in other areas of pain); 5) subject agreement to using the web-based application on a daily basis for 12 weeks; 6) no anticipated plans for back or neck surgery for at least 3 months; 7) subject knowledge, proficiency, and access to using a smart phone, tablet, or computer in the English language; 8) ability to engage in basic physical activity (eg, ambulation, light exercise, physical therapy exercises, etc.); 9) subject agreement to remain on stable doses of medication and a stable treatment regimen. Study exclusion criteria were as follows: 1) low back pain requiring anticipated surgical intervention within 3 months of enrollment; 2) severe or acute psychiatric illness, severe anxiety, or depression; 3) current history of substance use disorder; 4) serious illness in active treatment; 5) pain related to malignancy; 6) other areas of pain exceeding the level/intensity of low back or neck pain; 7) currently involved in a lawsuit or pending litigation in relation to the low back or neck pain.

Study procedure

Patients at the NWH ambulatory care center and WCMC center for comprehensive spine care were screened by study staff for eligibility. Patients were informed of the study by their treating providers or study staff who contacted potentially eligible participants virtually at NWH and in person at WCMC to describe the study in detail and assess initial eligibility. Written, informed consent was obtained by study staff prior to enrollment. Participants were free to withdraw from the study at any time without providing an explanation. The study was performed in accordance with the principles of the Declaration of Helsinki.

All subjects continued standard treatment and rehabilitation for their conditions, for example, physical therapy, medications, interventions, and education in pain management strategies, as applicable. Any changes to ongoing treatment modalities were recorded throughout the study. Patients logged and received digital information material daily, using a tablet, smart phone, or computer as well as login capabilities to the digital platform containing the cloud-based AI application for self-management of pain, PainDrainer™.

All baseline demographic and questionnaire data were recorded using secure email links, via REDCap, as detailed below. Data collected daily by the web-based tool in all subjects included, worst, least, and average pain scored by NRS through the digital web-based application. The subject was asked to spend a few minutes to log data at least every second day, such as sleep, work, physical activity, leisure time, housework, the intensity of the activity, as well as the feeling (satisfaction) when performing the activity. The logged activity

data were collected by the web application, and the AI engine used advanced algorithms to analyze the data. The AI engine was "educated" after approximately 8 times of logged activities (the learning period), and after this period the prognosis tool in PainDrainer™ had the power to suggest activities or combination of activities and to predict the resulting pain level. At 6 weeks and at the completion of the 12-week study period, repeat questionnaires were administered to all subjects. Participant engagement was measured by number of daily logs during the study, evaluated after 6 and 12 weeks. Participants not logging their daily activates for two weeks, or less than twice per week over the 12-week study time and not responding to reminders were considered lost to follow up and excluded from study analysis.

Assessment questionnaires

Questionnaires were administered at baseline, at 6 weeks, and at 12 weeks upon completion of the study, using REDCap secure email links. A demographics questionnaire was administered via REDCap email link upon study enrollment. Primary outcome measured: PROMIS scores for pain interference 6a (6 questions). Secondary outcomes measured included: PROMIS scores for physical function 10a (10 questions), anxiety (4 questions), depression (4 questions) and pain intensity (3 questions). Additional questionnaires administered at NWH at baseline, 6 weeks, and 12 weeks, included: 1) the Pain Catastrophizing Scale;[24] 2) the Chronic Pain Acceptance Questionnaire 8 (CPAQ-8);[25,26] 3) a brief medical history of ongoing treatment modalities and medications. Usability questionnaires were administered at WCMC at the study conclusion.

Statistical methods

A power calculation estimated that 24 patients were sufficient to achieve 80% power to detect a mean difference (delta T) of 0.5 points (assuming a standard deviation of 0.83 for the difference) as significant at the alpha-level of 0.05, using a two-sided paired *t* test. The power calculation was performed in Stata 15.1, StataCorp LLC, College Station, TX, USA. The overall treatment response was analyzed, using Wilcoxon nonparametric test for paired samples to calculate the statistical difference between T-scores, pre- and post-treatment for pain interference, physical function, depression, anxiety, pain intensity. A confidence level of 95% was used. The PROMIS questionnaire subscales were converted to T-scores by summing the scales and using the raw score to T-score conversion tables provided at HealthMeasures.net.[27,28] These are standardized scores with a mean of 50 and standard deviation of 10. The standardized T-scores facilitate comparison to the general population and to other study samples. The measured outcomes were the difference in mean change from baseline,[29] using the normalized T-score scale. Evaluating the change in anxiety (PROMIS anxiety 4a) and depression (PROMIS depression 4a), the PROMIS T-scores of 55, 60, 65, and 70 appeared to be sound thresholds for mild, moderate, moderately severe, and severe anxiety or depression.[30] The T-score was calculated from the PROMIS questionnaire at the start of the study and compared to post-treatment after 6 and 12 weeks of using the digital application. The T-score shows how many standard deviations the result is from the mean and a post-treatment reduction indicated a positive response and an improvement for the patient. The Minimally Important Difference (MID) was analyzed, where MID refers to the smallest meaningful difference in T-score that carries implications for the patient.[31] A clinically significant MID for PROMIS pain interference is an estimated reduction of 2.4, while for physical function it is an increase of 1.9. For anxiety it is a reduction of 2.3, and for depression a reduction of 3.0. Pain-related acceptance was assessed with the 8-item CPAQ-8 summary scores computed for two 4-item subscales, "Pain Willingness" and "Activity Engagement," and an overall total score for the eight items was calculated. Higher scores correspond to greater levels of acceptance. Cut off scores were set, according to Rovner et al.[32] The effect size for Wilcoxon signed-rank test was calculated and conventional classification was used, that is, 0.1 (small), 0.3 (moderate) and 0.5 and above (large effect).

Design of the digital tool

PainDrainer™, was developed by Lund University and PainDrainer AB, and is powered by an AI engine and uses machine learning to teach an individual model associating activities with average pain. Paindrainer is based on the principals of pain management, utilizing the core component of Acceptance and Commitment Therapy (ACT), that is, to move toward openness, awareness, and values-based life engagement. The model is based on artificial neural networks, specifically a multi-layer perceptron with a single hidden layer. During training (back-propagation), the weight factors are tuned for sleep, work, physical activity, leisure time, housework, the intensity of the activity, as well as the level of satisfaction, when performing the activity and the resulting level of pain, as recorded by the patient. The training is carried out to ensure that the model can generalize to unseen activity settings. A trained model can be queried in a reverse fashion to find appropriate activities for a desired average pain level. To test the engine prior to the study, we analyzed the convergence rate for each responding user. The AI engine showed convergence after approximately 8 daily logs. The PainDrainer™ converging AI engine demonstrated that the software adapted to the input data of each individual, which is the core of patient-centricity. The fundamental goal of the AI engine is to create an individualized activity balance that enables the user to increase their function and sustain the same pain level or alleviate the pain, and at the same time increase psychological flexibility. The user sets individual goals that the AI engine guides the subjects toward.

Results

This prospective study was performed from June 2021 to August 2022, to further investigate an AI-powered digital tool for pain management.[33] Ninety-four subjects consented, 28 (29.8%) chose not to enter the study, and 23 (24.5%) did not log data beyond the initial two weeks and were excluded from the analysis. 43/94 (45.7%) of subjects completed the 6-week questionnaire. On analysis, 2/43 patients did not comply with study requirements, that is, did not log activities and pain levels and were excluded from the study. One subject did not display any correlation between recorded activities and pain experience and was therefore not included in the analysis (Figure 1). In sum, 41 and 34 subjects were included in the final analysis.

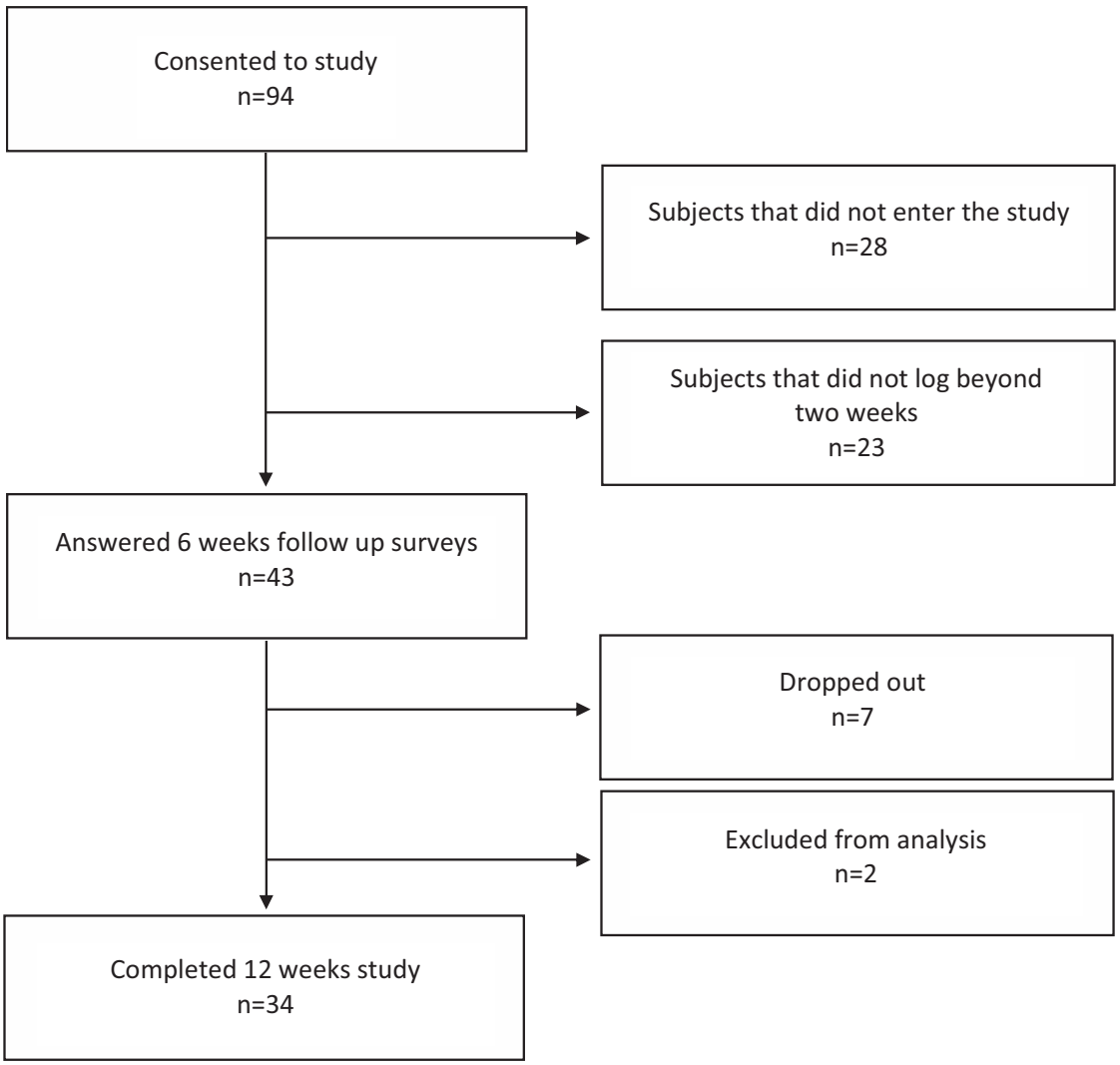

Figure 1. Study flow, showing the number of consented subject and the number that finished the 6- and 12-weeks questionnaires.

Primary outcome

The primary outcome was a decrease in pain interference, as measured by the PROMIS 6a pain interference scale. At 6 weeks the pain interference score had significantly decreased from baseline ($P < .0001$) and sustained at 12 weeks ($P = .020$) with a decrease in mean T-score from 61.5 to 57.6 at 6 weeks (n = 41) and to 59.1 at 12 weeks (n = 34) (Figure 2A). Overall, 73.8% of the subjects had an objective decrease in T-score. We then analyzed how many subjects reach MID during the study period, that is, the smallest meaningful difference that carries implications for the patient, in contrast to a statistically significance change.[31] The MID for pain interference, was calculated based on the delta T-score, pre- and post-treatment. An improvement in PROMIS pain interference, below the MID of −2.4,[29,34] was achieved by 57.5% of the patients during the study period. The responding group displayed a decrease in MID of −8.5 at 6 weeks (n = 19) and −7.4 at 12 weeks (n = 14) (Figure 2B).

Secondary outcomes

The secondary outcomes were improvement in the following scores: PROMIS physical function (Figure 3), PROMIS anxiety (Figure 4) and PROMIS depression (Figure 5) scores and PROMIS pain intensity scores (Figure 6), pain catastrophizing and Chronic Pain Acceptance Questionnaire. Delta T-score was calculated from pre- and posttreatment after 6 and 12 weeks. The use of the digital coach significantly improved physical function, measured by PROMIS physical function 10a, at 6 weeks ($P = .0008$) and at 12 weeks ($P = .0008$) with an increase in mean T-score from 39.9 to 41.9 at 6 weeks (n = 41) and to 41.8 at 12 weeks (n = 34) (Figure 3A). The MID for physical function, was calculated based on the delta T-score, pre- and post-treatment (Figure 3B). Improvement in physical function, above MID of 1.9)[34] was achieved by 72.5% of the subjects during the study period. The responding group displayed an increase in MID of 5.1 at 6 weeks (n = 20) and 4.7 at 12 weeks (n = 20).

A pre- to post-intervention improvement in depression and anxiety was also statistically significant, where the significance was calculated on the full data set, as well as for subjects with the more relevant baseline T-score >55, which is above the set limit for mild to severe depression (n = 17) or anxiety (n = 16). A significant decrease in anxiety was observed over the first 6 weeks ($P = .0001$) and sustained after 12 weeks ($P = .030$) with a decrease in mean T-score from 60.7 to 55.7 at 6 weeks (n = 17) and to 55.9 at 12 weeks

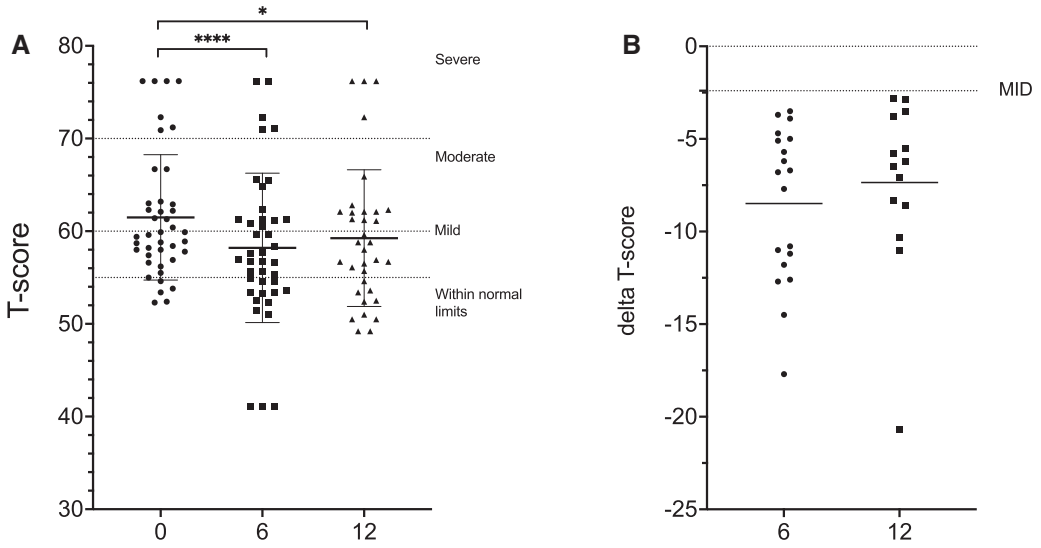

Figure 2. (**A**) T-score at baseline, 6, and 12w post-treatment in pain interference (PROMIS 6a) (n = 41 at 6w and n = 34 at 12w). Data for each patient shown and mean with standard deviation marked for each group. ****$P < .0001$, *.016. Pain interference effect thresholds on life marked. (**B**) Delta T-score change of MID, defined as 1.9 for PROMIS pain interference 6a. Mean change -8.50 and -7.36 at 6 and 12 weeks, respectively. SD ±4.16 and ±4.63 at 6 and 12 weeks, respectively. MID marked with dotted line in figure.

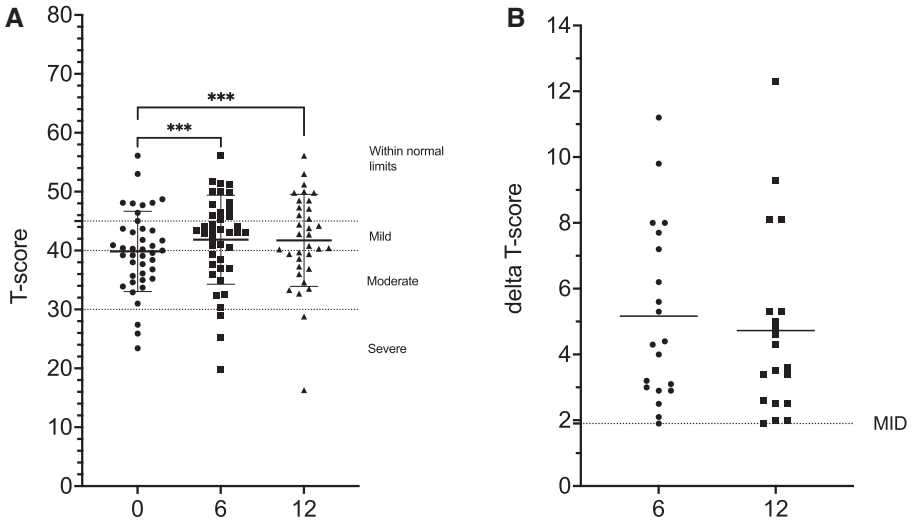

Figure 3. (**A**) T-score at baseline, 6 and 12w in PROMIS physical function 10 (n = 41 at 6 weeks and n = 34 at 12 weeks). Data for each patient shown with a dot, mean with standard deviation marked for each group. *** $P = .0008$, *** $P = .0008$. (**B**) Delta T-score change over MID, defined as 2.4 for PROMIS physical function 10a. Mean change +5.16 and 4.72 at 6 and 12 weeks, respectively. SD ±2.70 and ±2.77 at 6 and 12 weeks, respectively. MID marked with dotted line.

(n = 12) (Figure 4A). The MID for improvement in anxiety was calculated based on the delta T-score, pre- and posttreatment (Figure 4B). Improvement in anxiety, below the MID of −2.3,[34,35] was achieved by 81.3% of the subjects during the study period. The responding group displayed a decrease in MID of −6.4 at 6 weeks (n = 13) and −5.9 at 12 weeks (n = 5). A similar effect was seen for change in depression at 6 and 12 weeks ($P = .003$ and $P = .0001$) with a decrease in mean T-score from 59.7 to 54.6 at 6 weeks (n = 12) and to 52.3 at 12 weeks (n = 10) (Figure 5A). The MID for improvement in depression was calculated based on the delta T-score, pre- and posttreatment (Figure 5B). Improvement in depression, below the MID of −2.0,[35] was achieved in 100% of the subjects during the study period. The responding group displayed a decrease in MID of −6.9 at 6 weeks (n = 12) and −7.4 at 12 weeks (n = 10).

The effect on pain scores was measured differently at the two sites. At WCMC, measured by NRS, a significant difference was found at 6 weeks and 12 weeks ($P = .002$ and $P = .031$) with decrease in mean score from 5.6 to 4.4 at 6 weeks and to 4.1 at 12 weeks (n = 11) (Figure 6A), surpassing a MID score of 1.[36] At NWH, measured by PROMIS pain intensity 3a (Figure 6B), a significant difference was found at 6 weeks ($P = .022$), with a recorded decrease in mean score from 50.5 to 48.0 at 6 weeks (n = 30) and to 49.0 at 12 weeks (n = 27), ($P > .05$). Outcome data is summarized in **Table S1**.

PCS scores and CPAQ-8 summary scores were obtained at the NWH site only at 12 weeks. PCS mean scores decreased significantly from 12.9 to 8.2 ($P = .024$; n = 27) (Figure 7). A similar effect was also recorded on the activity engagement level measured by the CPAQ-8 summary scores, with a significant increase in mean score from 15.5 to 17.1 after 12 weeks

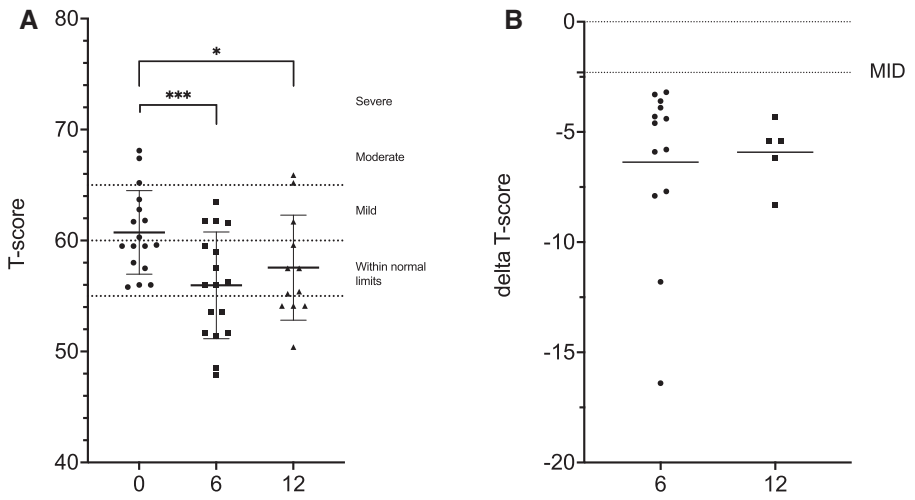

Figure 4. (**A**) PROMIS Anxiety 4a, T-score at baseline, 6 and 12 weeks for patients with a T-score above 55 at baseline (n = 17 at 6 weeks and n = 12 at 12 weeks). Data for each patient shown with a dot, mean with standard deviation marked for each group. ***P = .0001, *.032. (**B**) Delta T-score change over MID, defined as 2.3 for PROMIS anxiety 4a. Mean change −6.40 and −5.90 at 6 and 12 weeks, respectively. SD ±3.9 and ±1.5 at 6 and 12 weeks, respectively. MID marked with dotted line.

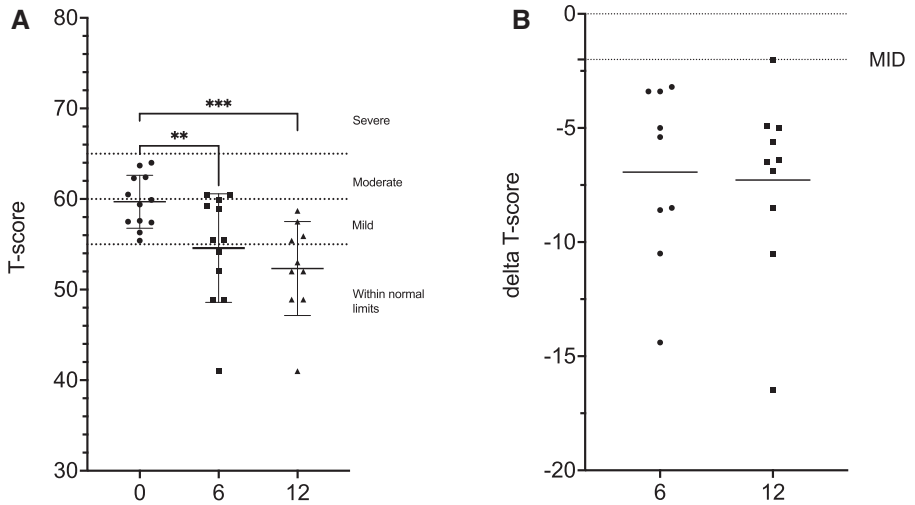

Figure 5. (**A**) PROMIS depression 4a, T-score at baseline, 6, and 12 weeks for patients with T-score above 55 at baseline (n = 13 at 6 weeks and n = 11 at 12 weeks). Data for each patient shown with a dot, mean with standard deviation marked for each group. *** P = .0010, **P = .003. T-score limits marked with dotted lines. **(B)** Delta T-score change over MID, defined as 2.3 for PROMIS depression 4a. Mean change -6.90 and -8.40 at 6 and 12 weeks, respectively. SD ±3.9 and ±14.0 at 6 and 12 weeks, respectively. MID marked with dotted line.

(P = .014; n = 27) (Figure 8A). No statistically significant effect was seen for pain willingness (Figure 8B).

To further investigate whether the digital tool had an impact on the daily work duration of working people, defined as the ability to work for more than 60 minutes per day (n = 32), their logged primary data was analyzed.

The average daily minutes of logged work was calculated at week 1, 6, and 12. The number of working days in a week was identified by analyzing work patterns and the average duration of up to 5 work loggings in a 7-day period. The same method was used to calculate logged work satisfaction and how intense the working day had been to the subject. The change in number of minutes of work per individual subjects was calculated (Figure 9), and around 50% of subjects showed an increase in daily capacity to work, 15% showed no change and 35% showed a decrease. A change of less than 15 minutes was considered as no change. In sum, 69% of the subjects increased their daily work period by over one hour (range 60–320 minutes) while having no major changes in clinical treatment program.

At WCMC, usability questions were obtained after the study period regarding the function of the device and what they had learned by using the device. All subjects (n = 6) confirmed that they now had a better understanding of what activities affect their pain, and 5 out of 6 had tried improving their pain level by changing activities. They majority (67%) found the application easy to use and would like to continue to use the application after the end of the study and 83% would recommend the tool to others living with chronic pain. The subjects stated that the time spent using the tool was 5–7 minutes per day.

Discussion

This prospective, multicenter study, single-arm, open-label study demonstrates that an AI-powered web-based tool

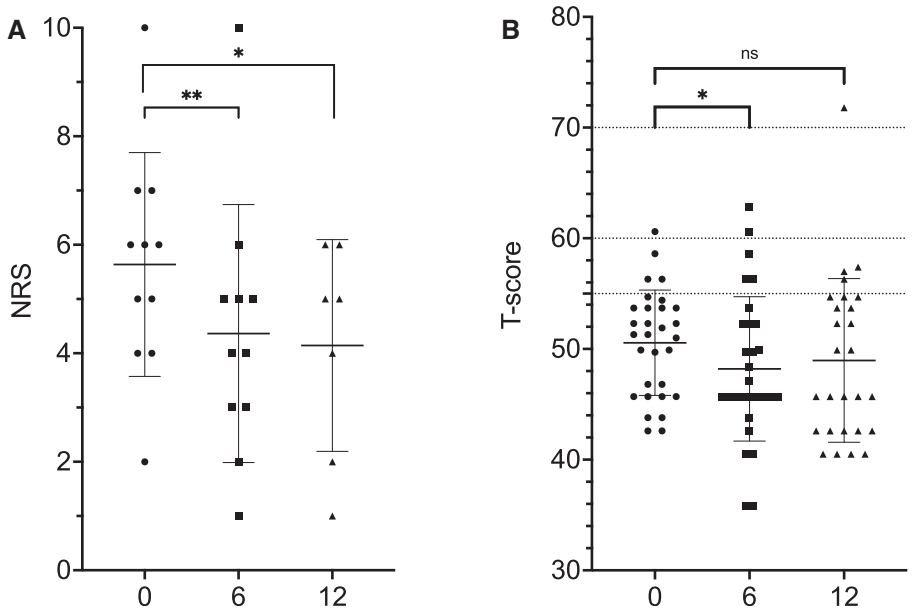

Figure 6. Pain intensity. **(A)** NRS pain score at pretreatment and 6, 12w posttreatment. Data for each patient shown, mean with standard deviation marked for each group. *$P = .03$; **$P = .0001$. **(B)** T-score at pretreatment and 6, 12w posttreatment, using PROMIS questionnaire Pain intensity 3a (n=30 and n=28 at 6 weeks and 12 weeks, respectively). Data for each patient shown, mean with standard deviation marked for each group. *$P = .022$.

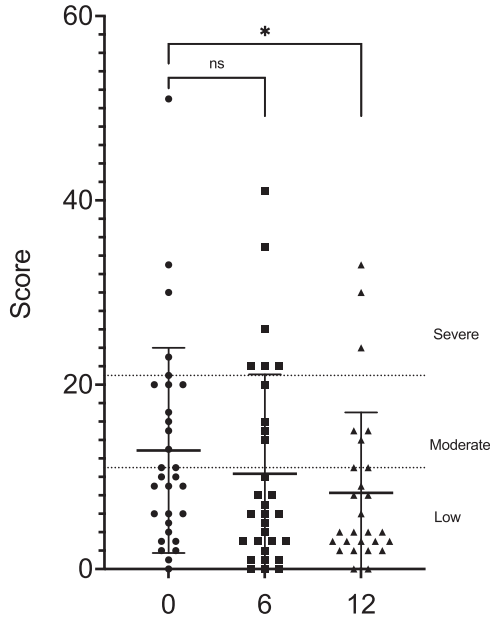

Figure 7. Pain catastrophizing, illustrated as significant change over time at pretreatment and 6, 12w posttreatment. * $P = .024$. Cut of scores are indicated with dotted lines.

anchored in ACT behavioral health principles to help guide daily activity significantly decreased chronic back and neck pain subjects' pain interference over a 12-week study period, evident by the recorded MID. Additional statistically significant improvements were observed in subjects' physical function, depression, anxiety, pain intensity, and pain catastrophizing with a high to medium positive effect on all parameters investigated other than pain willingness. The positive treatment effects superseded the MID in a large proportion of the subjects. Furthermore, of the subjects that improved their duration of daily work almost 70% increased by over an hour per day.

While previous studies utilizing machine learning have been able to find some patterns in retrospective data and suggest future pain levels, they have been very limited in their ability to provide real-time, individualized suggestions directly to patients and with multiple variables at a time.[37] Furthermore, other studies evaluating the usefulness of mobile applications did not find any suitable for clinical use, partly because of lack of evidenced based content,[38,39] while some reported a significant improvement in pain interference[40] and anxiety.[41] Although some digital tools use AI to improve physical function and decrease pain, their reference is based on population data and not on patient-centric, individually sourced data. For example, these tools analyze how generally recommended physical rehabilitation exercises are performed, give advice in real time and suggest new exercises to the patient.[42–44] Some of these digital tools for self-management of pain have been tested in clinical studies and a recent 2020 meta-analysis explored their effectiveness.[45] The primary outcome of efficacy was only pain intensity, since alternative outcomes were infrequently reported, and a small but significant effect was found when compared to baseline measures or control groups.[45] Despite the fact that some of these digital tools showed a statistical difference between intervention or control groups, they have not reported if the difference is clinically significant for the individual subjects. To the best of our knowledge, the present study is the first to demonstrate a clinically significant improvement for individual subjects with chronic pain, using a patient-centric and personalized AI-powered pain management digital tool.

This study demonstrates the clinical effectiveness of a digital AI tool that allows participants to self-manage their pain levels by adapting their daily activity to suit their needs. It does so by offering tools to synthesize, present, and project pain levels of the user, enabling discovery of the optimal, individualized, activity balance. This resulted in decreased pain interference, increased activity engagement, decreased pain catastrophizing, increased physical activity level, as well as

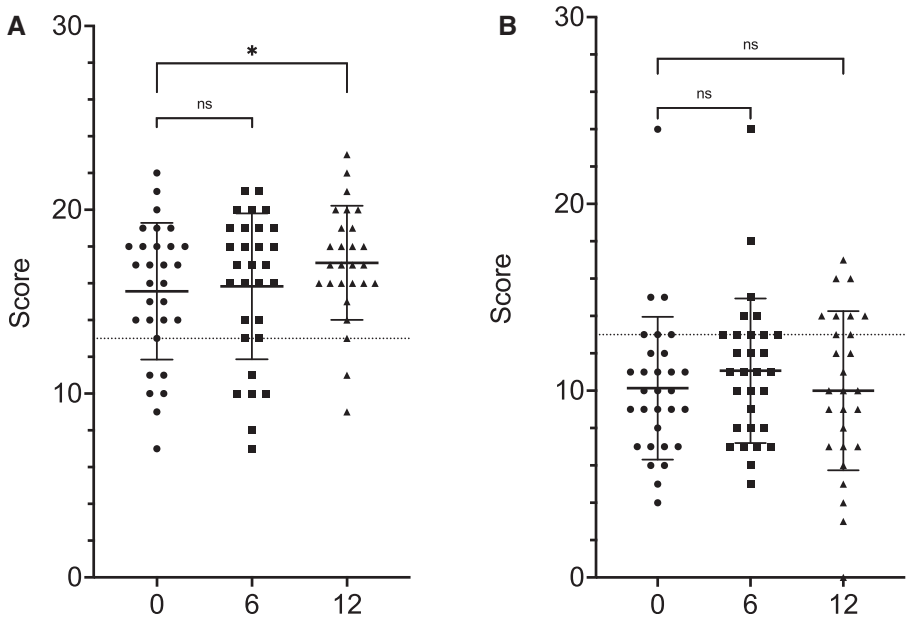

Figure 8. (**A**) Activity engagement (*$P = .014$) and (**B**) pain willingness are shown as significant change over time at pretreatment and 6, 12w posttreatment, measured by QPAC-8. Cut of scores for low activity engagement and pain willingness are indicated with dotted lines.

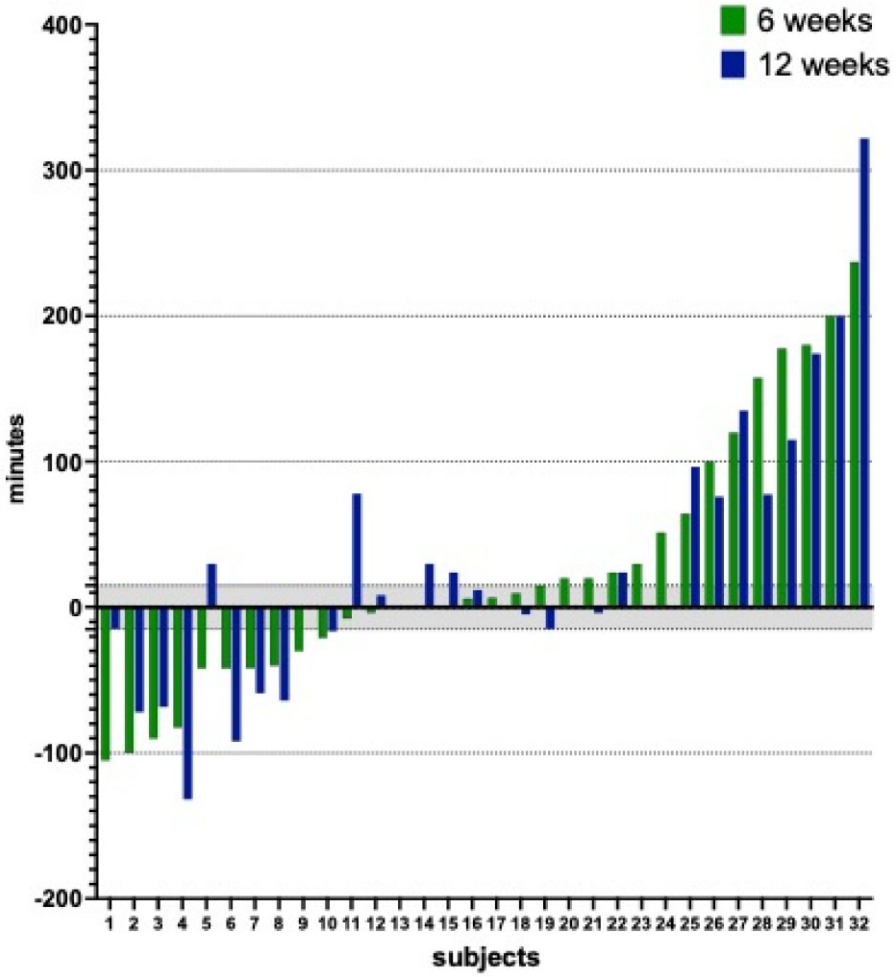

Figure 9. Change in the number of minutes of daily work duration, after 6 (green) and 12 (blue) weeks into the study period. A change of less than 15 minutes was considered as no change (grey).

decreased depression, anxiety, and pain intensity for most users, contributing to an increased health related quality of life.[46] The study demonstrates that the digital coach powered by AI affected multiple aspects of the pain experience.

Limitations of this present study include the following: 1) patients that participated were skewed toward subjects that were comfortable using web-based technology, which may impact the generalizability of PainDrainer™ as a treatment option; 2) there was a moderate loss-to-follow/drop-out rate after 2 weeks, likely due to initial setup in person versus 2 week follow up remote visitations at WCMC. Of note, the higher drop out cohort subjects (post hoc analysis) displayed higher scores in pain catastrophizing (data not shown); 3) there were minor differences in reported survey data, as the WCMC site did not collect pain catastrophizing or pain related acceptance data; 4) there were minor fluctuations in pain trends between the timepoints of baseline to six weeks, compared to 6 weeks to twelve weeks, as seen in pain interference scores. The latter is, however, common with pain treatments in that worsening and acclimation may occur in the absence of other interventions. We anticipate that this fluctuation would normalize if the study was of a longer duration.

While the dropout rate matches several other digital based studies[47,48] the following reasons could explain the phenomenon specifically in this study: 1) lack of payment to participants, 2) mostly virtual engagement with limited in office follow-up due to coronavirus disease 2019 (COVID-19) and clinic restrictions, 3) a web-based platform and expected technical challenges with user experience of the interface, 4) limited resources available to engage with patients due to it being an unfunded study and deployment of limited research assistants to focus on COVID-19 research efforts.

The magnitude of changes that a patient finds important or meaningful, rather than a statistically significant change, is essential for comparative digital effectiveness studies. Consequently, in understanding the full clinical impact of the present results, we adopted MID estimates of PROMIS measures.[31] In other studies, Substantial Clinical Benefit (SCB) thresholds are instead used to define the clinical relevance of changes in PROMIS scores, and these typically require a somewhat larger change in score compared to MID.[49–53] For example, in a study of patients receiving surgical spine surgery they found MID to be 4.9 and 4.5 for pain interference and physical function, respectively, while the SCB change was 6.9 and 6.8. In the present study the change in T-score was considerable, with four times of what was MID for pain interference and two times for physical function.

AI-based personalized pain treatment has significant potential for future pain care, providing an inexpensive, easily accessible, patient-centric and individualized treatment over time.[54] At a minimum, patients can predict and plan for activity modification for upcoming events to minimize pain. Furthermore, the technology could be applied in conjunction with other pain treatments where variable doses (pharmacotherapy), or programming (neuromodulation) could be adapted in closed-loop fashion with patient input and the AI input from PainDrainer™. Based on subject feedback and to further improve accessibility, user experience, and clinical outcome, an extensively upgraded version is now being developed that will be easier to utilize with a smart phone. This digital technology could be combined with coaching and CBT platforms to further enhance the offerings for pain treatment in a cost-effective personalized fashion. Future studies with the above applications should be undertaken to expand the horizon of personalized, AI-driven pain treatments.

Conclusion

Individualized, safe, and easily accessible pain management strategies are greatly needed to support the daily function of millions of people suffering from chronic pain today. In order to decrease pain and improve function, patients with chronic pain are frequently advised by healthcare professionals to keep a pain diary to track pain levels, triggers, and treatments in order to facilitate attempts to personalize treatment. Unfortunately, collection of this data is often incomplete, unanalyzed, and unactionable. As demonstrated in this multicenter study, an AI powered digital tool offers an individualized solution to these challenges by guiding patients to self-manage their daily pain for improved quality of life.

Acknowledgments

We thank Andrée Larsson for expert artificial intelligence support.

Supplementary material

Supplementary material is available at *Pain Medicine* online.

Funding

C.A.K. Borrebaeck received funding from Mats Paulsson Foundation, CREATE Health at Lund University and HealthTech Nordic. N. Mehta was supported by Weill Cornell Medicine Department of Anesthesiology.

Conflicts of interest: Antje M. Barreveld MD is an advisor for Lin Health. Carl A.K. Borrebaeck is cofounder of PainDrainer AB. Maria L Klement Rosén is advisor and cofounder of PainDrainer AB. N. Mehta, S. Cheung, U. Axelsson, J.I. Basem, and A.S. Reddy declare no conflict of interest.

References

1. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain. 2006;10(4):287–333.
2. Institute of Medicine (U.S.); Committee on Advancing Pain Research Care, and Education. Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, DC: National Academies Press; 2011.
3. Finley CR, Chan DS, Garrison S, et al. What are the most common conditions in primary care? Systematic review. Can Fam Physician. 2018;64(11):832–840.
4. Goldberg DS, McGee SJ. Pain as a global public health priority. BMC Public Health. 2011;11:770.
5. Gaskin DJ, Richard P. The economic costs of pain in the United States. J Pain. 2012;13(8):715–724.
6. Ballantyne JC. Opioids for the treatment of chronic pain: mistakes made, lessons learned, and future directions. Anesth Analg. 2017; 125(5):1769-1778.
7. Goucke CR, Chaudakshetrin P. Pain: a neglected problem in the low-resource setting. Anesth Analg. 2018;126(4):1283–1286.
8. Raja SN, Carr DB, Cohen M, et al. The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises. Pain. 2020;161(9):1976–1982.

9. Lotze M, Moseley GL. Theoretical considerations for chronic pain rehabilitation. Phys Ther. 2015;95(9):1316–1320.
10. Wade DT. What is rehabilitation? An empirical investigation leading to an evidence-based description. Clin Rehabil. 2020;34(5):571–s583.
11. Ruiz FJ. A review of Acceptance and Commitment Therapy (ACT) empirical evidence: Correlational, experimental psychopathology, component and outcome studies. Int J Psychol Psychol Ther. 2010;10(1):125–162.
12. Vlaeyen JWS, Kole-Snijders AMJ, Boeren RGB, van Eek H. Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. Pain. 1995;62(3):363–372.
13. Vlaeyen JWS, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain. 2000;85(3):317–332.
14. Hasenbring MI, Hallner D, Rusu AC. Fear-avoidance- and endurance-related responses to pain: development and validation of the Avoidance-Endurance Questionnaire (AEQ). Eur J Pain. 2009;13(6):620–628.
15. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and Commitment Therapy: model, processes and outcomes. Behav Res Ther. 2006;44(1):1–25.
16. Feliu-Soler A, Montesinos F, Gutiérrez-Martínez O, Scott W, McCracken LM, Luciano JV. Current status of acceptance and commitment therapy for chronic pain: a narrative review. J Pain Res. 2018;11:2145–2159.
17. Lumley MA, Schubiner H. Psychological therapy for centralized pain: an integrative assessment and treatment model. Psychosom Med. 2019;81(2):114–124.
18. Williams ACdC, Fisher E, Hearn L, Eccleston C. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev. 2020;8(8):CD007407.
19. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. Prescribing opioids for pain — the new CDC clinical practice guideline. N Engl J Med. 2022;387(22):2011–2013.
20. Keefe FJ, Rumble ME, Scipio CD, Giordano LA, Perri LCM. Psychological aspects of persistent pain: current state of the science. J Pain. 2004;5(4):195–211.
21. Devan H, Farmery D, Peebles L, Grainger R. Evaluation of self-management support functions in apps for people with persistent pain: systematic review. JMIR Mhealth Uhealth. 2019;7(2):e13080.
22. Jackson T, Wang Y, Wang Y, Fan H. Self-efficacy and chronic pain outcomes: a meta-analytic review. J Pain. 2014;15(8):800–814.
23. Halford GS, Baker R, McCredden JE, Bain JD. How many variables can humans process? Psychol Sci. 2005;16(1):70–76.
24. Sullivan MJL, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. Psychol Assess. 1995;7(4):524–532.
25. McCracken LM, Vowles KE, Eccleston C. Acceptance of chronic pain: component analysis and a revised assessment method. Pain. 2004;107(1-2):159–166.
26. McCracken LM, Vowles KE, Eccleston C. Acceptance-based treatment for persons with complex, long standing chronic pain: a preliminary analysis of treatment outcome in comparison to a waiting phase. Behav Res Ther. 2005;43(10):1335–1346.
27. Gershon RC, Rothrock N, Hanrahan R, Bass M, Cella D. The use of PROMIS and assessment center to deliver patient-reported outcome measures in clinical research. J Appl Meas. 2010;11(3):304–314.
28. Gershon R, Rothrock NE, Hanrahan RT, Jansky LJ, Harniss M, Riley W. The development of a clinical outcomes survey research application: assessment CenterSM. Qual Life Res. 2010;19(5):677–685.
29. Chen CX, Kroenke K, Stump TE, et al. Estimating minimally important differences for the PROMIS pain interference scales: results from 3 randomized clinical trials. Pain. 2018;159(4):775–782.
30. Kroenke K, Stump TE, Chen CX, et al. Minimally important differences and severity thresholds are estimated for the PROMIS depression scales from three randomized clinical trials. J Affect Disord. 2020;266:100–108.
31. Terwee CB, Peipert JD, Chapman R, et al. Minimal important change (MIC): A conceptual clarification and systematic review of MIC estimates of PROMIS measures. Qual Life Res. 2021;30(10):2729–2754.
32. Rovner G, Arestedt K, Gerdle B, Börsbo B, McCracken B. Psychometric properties of the 8-item Chronic Pain Acceptance Questionnaire (CPAQ-8) in a Swedish chronic pain cohort. J Rehabil Med. 2014;46(1):73–80.
33. Polston G, Klement M, Axelsson U, Olsson M, Barkfors G, Borrebaeck CAK. A drug-free, digital, self-management tool for chronic pain patients powered by artificial intelligence – a pilot trial. Ann Clin Case Rep. 2022;7:2226.
34. Lee AC, Driban JB, Price LL, Harvey WF, Rodday AM, Wang C. Responsiveness and minimally important differences for 4 patient-reported outcomes measurement information system short forms: physical function, pain interference, depression, and anxiety in knee osteoarthritis. J Pain. 2017;18(9):1096–1110.
35. Kroenke K, Yu Z, Wu J, Kean J, Monahan PO. Operating characteristics of PROMIS four-item depression and anxiety scales in primary care patients with chronic pain. Pain Med. 2014;15(11):1892–1901.
36. 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.
37. Nagireddi JN, Vyas AK, Sanapati MR, Soin A, Manchikanti L. The analysis of pain research through the lens of artificial intelligence and machine learning. Pain Physician. 2022;25(2):E211–E243.
38. Zhao P, Yoo I, Lancey R, Varghese E. Mobile applications for pain management: an app analysis for clinical usage. BMC Med Inform Decis Mak. 2019;19(1):106.
39. Salazar A, de Sola H, Failde I, Moral-Munoz JA. Measuring the quality of mobile apps for the management of pain: systematic search and evaluation using the mobile app rating scale. JMIR Mhealth Uhealth. 2018;6(10):e10718.
40. Gentili C, Zetterqvist V, Rickardsson J, Holmström L, Simons LE, Wicksell RK. ACTsmart: guided smartphone-delivered acceptance and commitment therapy for chronic pain: a pilot trial. Pain Med. 2021;22(2):315–328.
41. Leo AJ, Schuelke MJ, Hunt DM, et al. A digital mental health intervention in an orthopedic setting for patients with symptoms of depression and/or anxiety: feasibility prospective cohort study. JMIR Form Res. 2022;6(2):e34889.
42. Bailey JF, Agarwal V, Zheng P, et al. Digital care for chronic musculoskeletal pain: 10,000 participant longitudinal cohort study. J Med Internet Res. 2020;22(5):e18250.
43. Huber S, Priebe JA, Baumann K-M, Plidschun A, Schiessl C, Tölle TR. Treatment of low back pain with a digital multidisciplinary pain treatment app: short-term results. JMIR Rehabil Assist Technol. 2017;4(2):e11.
44. Anan T, Kajiki S, Oka H, et al. Effects of an artificial intelligence–assisted health program on workers with neck/shoulder pain/stiffness and low back pain: randomized controlled trial. JMIR Mhealth Uhealth. 2021;9(9):e27535.
45. Pfeifer A-C, Uddin R, Schröder-Pfeifer P, Holl F, Swoboda W, Schiltenwolf M. Mobile application-based interventions for chronic pain patients: a systematic review and meta-analysis of effectiveness. JCM. 2020;9(11):3557.
46. European European Medicines Agency. Reflection paper on the regulatory guidance for the use of health- related quality of life (HRQL) measures in the evaluation of medicinal products. 2006. Accessed December 16, 2022. https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-regulatory-guidance-use-health-related-quality-life-hrql-measures-evaluation_en.pdf.
47. Meyerowitz-Katz G, Ravi S, Arnolda L, Feng X, Maberly G, Astell-Burt T. Rates of attrition and dropout in app-based interventions for chronic disease: systematic review and meta-analysis. J Med Internet Res. 2020;22(9):e20283.

48. Selter A, Tsangouri C, Ali SB, et al. An mHealth app for self-management of chronic Lower Back Pain (Limbr): pilot study. JMIR Mhealth Uhealth. 2018;6(9):e179.
49. Park KB, Shin J-S, Lee J, et al. Minimum clinically important difference and substantial clinical benefit in pain, functional, and quality of life scales in failed back surgery syndrome patients. Spine (Phila Pa 1976). 2017;42(8):E474–E481.
50. Lu Y, Beletsky A, Chahla J, et al. How can we define clinically important improvement in pain scores after biceps tenodesis? J Shoulder Elbow Surg. 2021;30(2):430–438.
51. Gordon D, Pines Y, Ben-Ari E, et al. Minimal clinically important difference, substantial clinical benefit, and patient acceptable symptom state of PROMIS upper extremity after total shoulder arthroplasty. JSES Int. 2021;5(5):894–899.
52. Nwachukwu BU, Chang B, Rotter B-Z, Kelly BT, Ranawat AS, Nawabi DH. Minimal clinically important difference and substantial clinical benefit after revision hip arthroscopy. arthroscopy. Arthroscopy. 2018;34(6):1862–1868.
53. Steinhaus ME, Iyer S, Lovecchio F, et al. Minimal clinically important difference and substantial clinical benefit using PROMIS CAT in cervical spine surgery. Clin Spine Surg. 2019;32(9):392–397.
54. Cohen SP, Vase L, Hooten WM. Chronic pain: an update on burden, best practices, and new advances. Lancet. 2021;397 (10289):2082–2097.