Research Paper

PAIN®

OPEN

Opioid dose and pain effects of an online pain self-management program to augment usual care in adults with chronic pain: a multisite randomized clinical trial

Marian Wilson[a,*], Rowena J. Dolor[b], Daniel Lewis[c,d], Saundra L. Regan[e], Mary Beth Vonder Meulen[e], T. John Winhusen[c,d]

Abstract

Readily accessible nonpharmacological interventions that can assist in opioid dose reduction while managing pain is a priority for adults receiving long-term opioid therapy (LOT). Few large-scale evaluations of online pain self-management programs exist that capture effects on reducing morphine equivalent dose (MED) simultaneously with pain outcomes. An open-label, intent-to-treat, randomized clinical trial recruited adults (n = 402) with mixed chronic pain conditions from primary care and pain clinics of 2 U.S. academic healthcare systems. All participants received LOT-prescriber-provided treatment of MED ≥ 20 mg while receiving either E-health (a 4-month subscription to the online Goalistics Chronic Pain Management Program), or treatment as usual (TAU). Among 402 participants (279 women [69.4%]; mean [SD] age, 56.7 [11.0] years), 200 were randomized to E-health and 202 to TAU. Of 196 E-heath participants, 105 (53.6%) achieved a ≥15% reduction in daily MED compared with 85 (42.3%) of 201 TAU participants (odds ratio, 1.6 [95% CI, 1.1-2.3]; $P = 0.02$); number-needed-to-treat was 8.9 (95% CI, 4.8, 66.0). Of 166 E-health participants, 24 (14.5%) achieved a ≥2 point decrease in pain intensity vs 13 (6.8%) of 192 TAU participants (odds ratio, 2.4 [95% CI, 1.2-4.9]; $P = 0.02$). Benefits were also observed in pain knowledge, pain self-efficacy, and pain coping. The findings suggest that for adults on LOT for chronic pain, use of E-health, compared with TAU, significantly increased participants' likelihood of clinically meaningful decreases in MED and pain. This low-burden online intervention could assist adults on LOT in reducing daily opioid use while self-managing pain symptom burdens.

Keywords: Chronic pain, Opioids, Web-based intervention, Self-management, Randomized trial

1. Introduction

Approximately 18 million Americans receive long-term opioid therapy (LOT) for chronic pain.[9] Expert panels and authorities, such as the Centers for Disease Control and Prevention (CDC), warn of potential risks of LOT and emphasize nonpharmacological chronic pain therapies.[11] The CDC's guidelines for opioid tapering emphasize person-centered decision-making in the use of nonopioid therapies and inclusion of patient education, cognitive behavioral therapy (CBT), and interdisciplinary rehabilitation.[6] These guidelines align with the U.S. National Pain Strategy's recommendation for developing individualized, pain self-management strategies to provide consistent pain education and coping skills training.[22] Globally, equitable access to high-quality pain care is a recognized problem.[38] Still lacking is consensus on standardized self-management materials or methods for clinicians to deliver on recommendations to ensure safe, effective opioid dose reduction.

Substantial research supports self-management programs to improve pain intensity and minimize disability with similar outcomes obtained using face-to-face or internet-based programs.[15] Internet-based programs could, potentially, allow for increased ability to standardize and replicate effective programs, making them accessible and affordable to people with chronic pain. Lacking from most efficacy studies of internet-based, self-management chronic pain interventions is an evaluation of their impact on opioid dose reduction.[13,26] This study sought to address this gap by testing the Goalistics Chronic Pain Management Program (referred to here as E-health) for its impact on LOT dose.

Two prior randomized controlled trials (RCTs) found reductions in both self-reported pain and medication use with this E-

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

[a] College of Nursing, Washington State University, Spokane, WA, United States, [b] Division of General Internal Medicine, Department of Medicine, Duke University School of Medicine, Durham, NC, United States, [c] Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, Cincinnati, OH, United States, [d] Center for Addiction Research, University of Cincinnati College of Medicine, Cincinnati, OH, United States, [e] Department of Family & Community Medicine, University of Cincinnati College of Medicine, Cincinnati, OH, United States

**Corresponding author. Address: College of Nursing, Washington State University, 103 E. Spokane Falls Blvd, Spokane, WA 99210. Tel.: 509-324-7443; fax: 509-324-7341. E-mail address: marian.wilson@wsu.edu (M. Wilson).*

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.painjournalonline.com).

PAIN 00 (2022) 1–9

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the International Association for the Study of Pain. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

http://dx.doi.org/10.1097/j.pain.0000000000002785

health program.[25,36] To build upon these findings, the EMPOWER trial reported here (NCT03308188) included an objective measure of morphine equivalent dose (MED) using electronic health record (EHR) data. The study's primary objective was to evaluate the impact of treatment as usual (TAU) vs TAU plus E-health (E-health) with the hypothesis that the E-health, relative to TAU, group would have a significantly greater proportion of participants with ≥15% reduction in daily MED and clinically significant decrease in pain intensity 6 months after treatment. Secondary outcomes to evaluate multidimensional aspects of pain were selected based on recommendations from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) guidelines and included pain interference on sleep, function, and mood, pain coping, and pain self-efficacy.[16]

2. Methods

2.1. Trial design and oversight

EMPOWER was a two-site intent-to-treat (ITT), two-arm, open-label, RCT approved by the single IRB of record (University of Cincinnati). Innovative design features that allowed for fully remote study activities and data capture have been described in detail previously.[37] The protocol provided in Supplement 1 (available at http://links.lww.com/PAIN/B721) was designed by the research team and registered before participant enrollment at ClinicalTrials.gov (NCT03308188). Written informed consent was secured electronically. A stipend of up to $110 was provided to participants for completing 4 scheduled research assessments ($20 for 1 and $30 each for 3); participants were not reimbursed for completing E-health modules. A Data and Safety Monitoring Board composed of pain management professionals and researchers external to the study team met annually to review and advise on collected data and adverse events (AEs).

2.1.1. Participants

Outpatients receiving treatment at one of the 2 participating U.S. university-based healthcare systems were included. Adults (age 25-80 years) were eligible for the trial if they had been prescribed LOT of ≥20 MED over the prior 90 days at the time of EHR query (conducted between February 2018 and October 2020), had ≥1 chronic pain-related diagnosis, were able to provide informed consent, self-reported current use of opioid medication(s) to treat chronic pain, had a Brief Pain Inventory (BPI) intensity score ≥3, and had internet access and a working email account. The ≥20 MED cutoff was chosen because, although a single dosage threshold for safe opioid use has not been identified, experts note that dosages <20 mg/day MED are safer than doses 20 to 50 mg/day MED.[12] Excluded were patients who were pregnant, incarcerated, unwilling to complete a web-based neurological assessment, or who, in the judgement of study staff, would be unlikely to complete the study (eg, terminal illness).

2.1.2. Randomization

Participants were recruited using an "opt in" process using EHRs at the sites. Patients flagged as potentially eligible received an IRB-approved recruitment letter and brochure describing the study sent via the U.S. Postal Service. The letter explained that the recipient may be eligible for the EMPOWER study that would test an online pain self-management program and that they would be called by research staff to discuss the study; instructions on how to opt-out from further study contact were included. Participants were randomized in a 1:1 ratio to TAU or E-health, stratified by site. Treatment group sizes never differed by more than a factor of $b/2$ where b is the block size to help ensure treatment balance. To ensure unpredictability, block size randomly alternated between $b = 2$ and $b = 4$. Research Electronic Data Capture performed the randomization process with the randomization sequence unknown to research staff.[18] EMPOWER enrollment was listed in the EHR at one site, but treatment condition was not provided; thus, the prescribers were, in effect, blinded.

2.2. Intervention

Participants were notified of their randomized group assignment. All participants received TAU; the most common non-LOT treatment received during study participation was physical therapy sessions based on both self-report (33.1% of E-health and 34.0% of TAU participants) and EHR pain-related referrals (34.0% of E-health and 32.7% of TAU participants) with no significant group differences. E-health participants received a free 4-month subscription to the Goalistics Chronic Pain Management Program (estimated cost $30 per month), which was developed from evidence-based cognitive, behavioral, interpersonal, and self-management strategies.[29] Input from people with chronic pain and chronic pain professionals was used in its development, and it has been tested and found efficacious for self-reported opioid dose-reduction and pain in several RCTs.[29,35,36] The program was created by pain psychologists Drs. Linda Ruehlman and Paul Karoly with funding from U.S. National Institutes of Health in 2010. It is presently owned by their company Goalistics, a limited liability company, and available with limited use agreements (http://www.mood.goalistics.com/). Program content is delivered via 5 learning centers and uses a combination of online and offline activities including videos, symptom-tracking tools, and downloadable worksheets that can be accessed with personal computers, tablets, and smartphones. Supplement 1 Appendix (available at http://links.lww.com/PAIN/B721) provides more details on program content. Additional content was added to the program since its initial testing that includes information on opioid tolerance, dependence, and nonopioid pain management options. The program can be understood through the lens of self-management theories, which hold common concepts recognizing pain self-management as an ongoing process involving (1) an individual's active role in pain management, (2) adoption of self-management skills (eg, planning, self-monitoring, and attention focus) and targets for change (eg, exercise level, negative emotions, and dysfunctional thoughts), and (3) the achievement of pain-related outcomes (eg, increased fitness, decreased suffering, and reduced pain-related interference).[30]

E-health program activities can be completed within 8 weeks by spending approximately 1 to 2 hours per week. E-health participants received weekly emails with program instructions and goals for weekly activity completion. Fidelity in intervention delivery was addressed by giving specific directions regarding what program modules to complete with each weekly communication. Research staff attempted to make phone contact with participants not significantly engaged with the program; they also troubleshot technical problems. Staff were bachelor's-prepared research assistants and had no special training in pain management other than the content included in the E-health program. All intervention activities took place within the

participants' home environment and with no special equipment required beyond a phone and internet connection. Additional time was spent in phone contact for any participants requesting assistance or not completing assigned modules; this generally involved only encouragement and direction on how and where to access the program activities.

2.3. Dependent variables and measurements

Participants completed self-report measures at baseline, the end of the 4-month active treatment phase, and 6 months after active treatment (ie, month-10) using Research Electronic Data Capture to collect data from March 2018 to September 2021.[18] Baseline information, such as age, sex, and health history, were collected per trial protocol (Supplement 1, available at http://links.lww.com/PAIN/B721).

2.3.1. Assessment of opioid use

Opioid prescription information was collected from the participants' EHR through Month-10. It is important to note that while some EHR data can have significant shortcomings, medication prescription data are generally of high quality.[14,24] The primary outcome was whether there was a ≥15% decrease (yes/no) in MED, based on EHR opioid prescribing information between baseline and month-10. Morphine equivalent dose calculation used the Opioid Morphine Equivalent Conversion Factors table created by the CDC.[5] A ≥15% MED decrease has been defined as a meaningful change in past research and recognized as an "opioid taper."[1,7] The effect of treatment on this binary outcome was tested using a logistic regression as described in the analysis section below. As a secondary numeric outcome, the raw baseline-month-10 difference in MED was also tested for a treatment effect using a linear regression. Morphine equivalent dose calculations using EHR are limited in that they cannot account for how much of a prescription a person is using or whether additional opioid prescriptions are received outside of one's primary healthcare system. However, this study sought to add evidence by building upon the prior RCTs testing this intervention that only captured opioid use with self-report measures.

2.3.2. Assessment of pain

The key secondary outcome was whether there was a clinically meaningful baseline-to-month-10 decrease (≥2 points; yes/no) in pain intensity.[15] The BPI was used as a well-validated, reliable instrument that includes a 4-item pain intensity subscale (Likert scales; range 0-10, with lower scores indicating less pain).[8] Additional secondary outcomes were investigated using the BPI interference subscale that measures on Likert scales (range 0-10) the level of pain interference on life (eg, mood, activity, sleep, and relationships). Treatment effects were examined for both pain intensity and interference with binary outcomes (≥2 points; yes/no) using a logistic regression. In addition, the raw baseline-posttreatment differences in both BPI intensity and BPI interference scales were tested for treatment effects.

2.3.3. Assessment of pain-related outcomes

Pain-related secondary measurements of pain knowledge, pain self-efficacy, and pain coping were included and expected to improve from E-health.[30] The Pain Knowledge Questionnaire included 15 true/false items about opioid medications and nonopioid treatment alternatives covering content specific to the E-health program (eg, When in pain, it is best to limit activities). This instrument was developed and used in a prior RCT of E-health and measured significantly increased pain knowledge.[29] The Pain Self-Efficacy Questionnaire (PSEQ) is a 10-item measure to assess confidence in managing pain that has good construct validity and reliability (Cronbach's $\alpha = 0.92$).[32] Pain coping was measured by using the Coping Strategies Questionnaire (CSQ-R), which is a 27-item Likert-scale questionnaire assessing the use of 6 pain-coping strategies: (1) catastrophizing; (2) coping self-statements; (3) ignoring sensation; (4) distancing; (5) distraction; and (6) praying. Participants rate their utilization of each strategy on a 7-point scale (from 0-"Never do that" to 6-"Always do that"). The CSQ-R has been found to have adequate internal consistency and validity in several patient populations.[19,33]

2.3.4. Assessment of global health

Global health, which is a quality-of-life measure, was assessed as a secondary outcome with the Patient-Reported Outcomes Measurement Information System (PROMIS) 10-item measure for global health, which briefly but comprehensively assesses physical and mental health; this is a reliable (Cronbach's $\alpha > 0.80$) measure with demonstrated construct validity.[20] Raw sum scores are converted to T-scores, where a T-score of 50 is equivalent to the U.S. general population average and ±10 points is equivalent to the standard deviation.[28]

2.3.5. Assessment of opioid misuse

The Current Opioid Misuse Measure (COMM) was used to assess opioid misuse. The COMM is a 17-item self-assessment used to monitor patients on opioid therapy and to assess whether they are currently exhibiting behaviors indicative of substance misuse. The COMM has good predictive validity and reliability (Cronbach's $\alpha > 0.82$). Test-retest reliability has been established and construct validity demonstrated with positive correlations with urine toxicology results.[3,4,34]

2.3.6. Assessment of program adherence

E-health program adherence was assessed by the presence of participant satisfaction ratings that participants were prompted to complete after each online activity. Data on the number of ratings were captured by the Goalistics software program and sent in a report to the research team. Similar to past research, an adherence score (range 0-6) was used with higher scores representing greater adherence.[35] An adherence score ≥2 was defined as substantive program exposure; this cutoff reflects, at minimum, completion of: (1) three "understanding pain" activities, which include information about opioid medications (eg, potential problems, reducing reliance, etc), and nonmedicine treatments (eg, relaxation, CBT, hypnosis); and (2) the "profile of chronic pain" assessment, or at least one other learning module activity. The content participants would be exposed to at this level of adherence has been shown in past studies to be sufficient to achieve measurable benefits.[36]

2.3.7. Adverse events

Adverse events were assessed using the BPI intensity and interference scores[8] and the Depression, Anxiety, and Stress Scales (DASS-21).[2,10] The DASS-21 has established validity and

reliability and assesses 3 constructs with 21 Likert-scale items of past-week ratings: (1) depression; (2) anxiety; and (3) stress.[2,10] Adverse events were defined as ≥30% symptom deterioration from baseline indicated by the BPI intensity, BPI interference, or DASS-21 subscales with a ≥ "moderate" severity score. Research staff attempted to contact participants experiencing an AE to obtain additional information and to assess for potential serious AEs.

2.4. Statistical analysis

The sample size calculation assumed an α level of 0.05 (2-tail). A pilot RCT, which had a 79% completion rate, found that 21% of E-health, compared with 7% of wait-list control, participants reported decreasing their opioid medication[36]; this difference equates to an odds ratio (OR) of 3.6. Although EMPOWER used a different MED reduction outcome (≥15%) than the pilot (any reduction), the pilot data were the most pertinent available for estimating power. EMPOWER had a target sample size of 400 (200/arm) participants—using a conservative estimated completion rate of 75% yielded 300 total completers (150/arm). Having 300 completers provides 80% power to detect an E-health treatment effect if ≥18% participants had a ≥15% MED reduction against 7% of TAU; this equates to an OR of ≥2.77.

Outcome measures were analyzed for the ITT population. All statistical tests were conducted at the 5% type I error rate (2-sided). Each binary outcome was tested for unadjusted treatment group differences using the Pearson χ^2 test and odds ratios with 95% confidence intervals. All reported regressions used outcome as the response variable, treatment (E-health vs TAU) as the covariate of interest, and baseline outcome as a supporting covariate. Site and site-by-treatment were initially included as supporting covariates and dropped if they were not significant. Binary outcomes such as the primary outcome (change in MED ≥ 15%) and key secondary outcome (change in BPI intensity ≥ 2) were tested using a logistic generalized linear regression. Baseline-month-10 continuous outcomes such as raw difference in MED and BPI intensity were tested using linear regressions.

The Pearson χ^2 test was used to test for treatment group differences in AEs. Number-needed-to-treat (NNT) was calculated for the primary outcome and the number-needed-to-harm (NNH) was calculated for the AEs.[31]

As a rule of thumb, an analysis can be completed with observed data, without imputation, if the missing data are ≤5%.[23] For the primary and MED outcomes, 98.8% of the data (98% for E-health and 99.5% for TAU) were obtained. Month-10 was chosen a priori as the desired end point, in part, to allow time for participants to digest the E-health content and follow-up with their prescriber. For TAU, the month-10 survey data were obtained for 95% of participants. However, while the month-10 survey completion rate was still relatively high for the E-health participants (83%), it was significantly lower than that for the TAU participants ($X^2(1) = 5.98$, $P < 0.05$) and exceeded the 5% rule of thumb for missing data. The main set of analyses in which observed data were analyzed without imputation was supplemented with analyses using multiple imputation. Specifically, SAS MI and MIANALYZE procedures were used to perform a multiple imputation regression on each month-10 survey outcome measure; the results (see Supplement 2, available at http://links.lww.com/PAIN/B721) were very similar to the observed data analysis results and were in complete agreement vis-à-vis statistical significance.

3. Results

3.1. Participant characteristics

Demographic and baseline characteristics did not differ significantly between groups. The sample was approximately 70% female and 75% Caucasian; the average age of the participants was 57 years (**Table 1**). The total number of practices from which participants were recruited were 38 primary care clinics (16 from UC Health and 22 from Duke) and 5 pain clinics (3 from UC Health and 2 from Duke). The final sample included 152 (37.8%) participants from pain clinics and 250 (62.2%) from primary care. Participants reported an average of 3.8 (1.8) pain diagnoses, with the most common diagnoses including arthritis (248 [61.7%]), back (312 [77.6%]), and joint (234 [58.2%]) pain. The mean BPI intensity score was 5.9 (1.6). The mean MED was 48.0 (58.6) milligrams.

Research staff completed a short prescreen with patients receiving a recruitment letter, with 208 patients failing prescreen. The majority of prescreen failures (N = 116; 55.8%) failed because of not having internet access, with the next most common reason for pre-screen failure being not currently taking opioids for pain (N = 30; 14.4%). As shown in **Figure 1**, 589 potential participants were consented and screened, and 402 were randomized to E-health (n = 200) or TAU (n = 202). Approximately 98.8% of participants were included in the primary analysis. Of the 5 participants not included in the primary analysis, 3 withdrew consent (E-health), one died (E-health), and one had an unusable baseline value (TAU, baseline included prescriptions for 190 pills per day for 190 days with MED of 12,040). Approximately 89% of participants completed the month-10 follow-up survey. Approximately 90.9% of participants not completing the month-10 survey were unable to be contacted (88.2% of the E-health and 100% of the TAU participants). Additional reasons for noncompletion in the E-health group were withdrawing consent (n = 3; 8.8%) and death (n = 1; 2.9%). No participant discontinued the study because of an AE.

3.2. Primary and secondary outcomes

3.2.1. Morphine equivalent dose

Of 196 E-health participants, 105 (53.6%) achieved a ≥15% reduction in daily MED compared with 85 (42.3%) of 201 TAU participants (odds ratio, 1.6 [95% CI, 1.1-2.3]; $P = 0.02$); NNT was 8.9 (95% CI, 4.8, 66.0). Regression results revealed a significant beneficial E-health treatment effect for both the proportion meeting the target reduction ($X^2(1) = 5.1$, $P = 0.02$) and the continuous MED ($X^2(1) = 4.50$, $P = 0.03$) outcomes. A visual depiction of regression treatment effects for primary and key secondary outcomes is provided in **Figure 2**. **Table 2** details the results of regression on all measured outcomes with effect sizes.

3.2.2. Pain

Of 166 E-health participants, 24 (14.5%) achieved a ≥2 point decrease in BPI intensity vs 13 (6.8%) of 192 TAU participants (odds ratio, 2.3 [95% CI, 1.1-4.7]; $P = 0.02$). Regression results revealed a significant beneficial E-health treatment effect for the key secondary outcome ($X^2(1) = 5.6$, $P = 0.02$) and no significant group difference for the continuous BPI intensity outcome ($X^2(1) = 0.8$, $P = 0.39$). Pain intensity on average was in the moderate range (5-6) at baseline and month-10 posttest for the full sample.

Table 1

Participant demographic and clinical characteristics as a function of treatment group.

Characteristic	No. (%)	
	E-health	Treatment as usual
Participants, no.	200	202
Age, mean (SD)	56.4 (11.1)	56.9 (10.9)
Sex		
Female	139 (69.5)	140 (69.3)
Male	61 (30.5)	62 (30.7)
Race and ethnicity		
African American/Black	43 (21.5)	29 (14.4)
Caucasian	147 (73.5)	154 (76.2)
Other*	10 (5.0)	19 (9.4)
Hispanic or Latinx	3 (1.5)	2 (1.0)
Pain diagnosis		
Arthritis	124 (62.0)	124 (61.4)
Back	150 (75.0)	162 (80.2)
Fibromyalgia	45 (22.5)	46 (22.8)
Joint	120 (60.0)	114 (56.4)
Migraines	50 (25.0)	52 (25.7)
Neck	73 (36.5)	78 (38.6)
Nerve pain/Neuropathy	96 (48.0)	96 (47.5)
Other	84 (42.0)	101 (50.0)
No. of pain diagnoses, mean (SD)	3.7 (1.8)	3.8 (1.9)
MED, mean (SD)	48.1 (63.6)	47.8 (53.4)
MED, range	20.0-660.0	20.0-548.0
Pain: BPI intensity, mean (SD)	5.9 (1.5)	5.9 (1.6)
Education		
<High school	5 (2.5)	13 (6.4)
High school	124 (62.0)	113 (55.9)
Bachelor's degree	35 (17.5)	50 (24.8)
>Bachelor's degree	36 (18.0)	26 (12.9)
Employment		
Full-time	45 (22.5)	46 (22.8)
Part-time	13 (6.5)	12 (5.9)
Disabled	85 (42.5)	86 (42.6)
Retired	49 (24.5)	44 (21.8)
Other	8 (4.0)	14 (6.9)

* Six participants were American Indian, 1 was Asian, 1 was Pacific Islander, 8 were more than one race, and 13 did not specify.

BPI, Brief Pain Inventory; MED, morphine equivalent dose.

A greater proportion of E-health participants, 42 (25.3%), relative to TAU, 32 (16.7%), had a ≥2 point decrease in BPI interference (odds ratio, 1.7 [95% CI, 1.0-2.8]; $P = 0.04$). Regression results revealed no significant beneficial E-health treatment effect for the ≥2 point decrease in BPI-interference outcomes ($X^2(1) = 3.4$, $P = 0.07$) and no significant group difference for the continuous BPI-interference outcome ($X^2(1) = 1.5$, $P = 0.23$).

3.2.3. Pain-related outcomes

The change in percentage of correct answers on the Pain Knowledge Questionnaire was significantly greater in the E-health relative to the TAU group ($X^2(1) = 11.05$, $P = 0.0009$). Pain self-efficacy as measured by the PSEQ also increased on average by approximately twice as much in the E-health group compared with TAU, yielding a significant treatment effect ($X^2(1) = 7.35$, $P = 0.007$). Pain coping was significantly improved on several CSQ-R subscales in the E-health group relative to TAU (catastrophizing $X^2(1) = 4.50$, $P = 0.03$; distraction $X^2(1) = 9.22$, $P = 0.002$; passive coping $X^2(1) = 4.86$, $P = 0.03$). The largest effect size was observed on the subscale of catastrophizing ($d = 0.30$).

3.2.4. Global health

On average, the PROMIS global physical and mental health scores of participants were poorer than the average healthy adult (<50). Neither variable showed a significant treatment effect from baseline to 10-month posttest (physical health $X^2(1) = 1.18$, $P = 0.28$; mental health $X^2(1) = 0.02$, $P = 0.90$).

3.2.5. Opioid misuse

At baseline, approximately 40% of all participants exhibited a COMM score ≥ 9, indicative of opioid misuse (E-health n = 79 [39.5%] vs TAU 84 [41.6%]). No significant treatment effect was noted from baseline to 10-month posttest for the continuous COMM outcome ($X^2(1) = 0.01$, $P = 0.94$) or for the binary COMM indicator ($X^2(1) = 0.01$, $P = 0.91$).

3.2.6. Program adherence

Based on adherence scores, a total of 136 of the 200 E-health participants (68.0%) had a score of at least 2, indicating that they had received substantive exposure to the program. The mean adherence score was 2.5 (SD = 2.0). The range was 0 to 6, with a median of 2.0.

3.2.7. Adverse events

An AE occurred for 42.5% of E-health and 47.0% of TAU participants with no significant group differences ($X^2(1) = 0.8$, $P = 0.36$); because AEs were less prevalent in E-health, the NNH was a negative (−22.1) and thus, the NNH was, effectively, 0. An AE for the BPI was reported for 20.5% of E-health and 23.3% of TAU participants with no significant treatment group difference ($X^2(1) = 0.5$, $P > 0.05$). An AE for the DASS-21 was reported for 31.5% of E-health and 32.7% of TAU participants with no significant treatment group difference ($X^2(1) = 0.1$, $P > 0.05$). No serious AEs were reported.

4. Discussion

The present RCT evaluated the ability of an online chronic pain program (E-health), relative to TAU only, to decrease daily MED (primary) and pain intensity (key secondary) in adults with chronic pain receiving LOT. The ITT analyses revealed a statistically significant beneficial impact of E-health, relative to TAU, on both the primary outcome of ≥ 15% MED reduction and the key secondary outcome of a ≥2-point decrease in pain intensity. A significant treatment effect was also found for MED, but not BPI intensity, as continuous measures. Secondary outcomes with significant treatment effects included pain knowledge, pain self-efficacy, and pain coping subscales of catastrophizing, distraction, and passive coping.

The significant E-health effect on the primary outcome measure and MED is consistent with the findings from 2 prior RCTs, which found that E-health significantly decreased prescription-pain medication use. In an RCT with patients heterogeneous for LOT use (N = 305), E-health participants reported significantly greater decreases in prescription medication use compared with wait-list control.[25] The second RCT, conducted with 92 adults with chronic pain with a current opioid

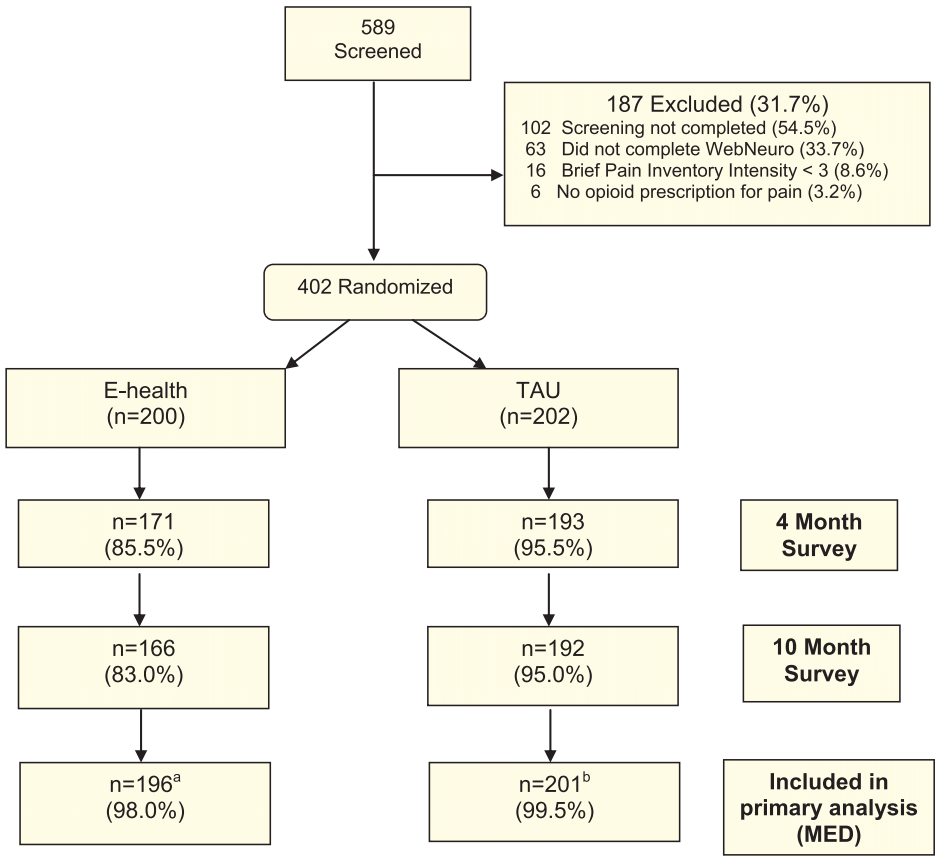

Figure 1. CONSORT diagram. [a]Three participants withdrew consent. One participant died. [b]The baseline morphine equivalent dose for one participant was an unusable outlier. MED, morphine equivalent dose; TAU, treatment as usual.

Table 2

Changes from baseline to posttest in average primary and secondary outcome measurements for treatment and control groups.

	Baseline*		Month-10 posttest*				
	E-health	TAU	E-health	TAU	Test†	*P*†	d (95% CI)‡
MED	48.1 (63.6)	47.8 (53.4)	49.8 (87.2)	61.1 (98.4)	**4.50**	**0.0339**	−0.20 (−0.40, −0.00)
BPI pain intensity	5.9 (1.5)	5.9 (1.6)	5.5 (1.8)	5.7 (1.8)	0.75	0.3855	−0.09 (−0.29, 0.12)
BPI pain interference	5.8 (2.2)	5.6 (2.3)	5.0 (2.5)	5.2 (2.5)	1.46	0.2274	−0.14 (−0.34, 0.07)
PROMIS global physical health	36.0 (6.5)	36.8 (6.2)	37.7 (6.6)	37.7 (7.1)	1.18	0.2781	0.14 (−0.06, 0.35)
PROMIS global mental health	43.2 (8.3)	43.2 (8.7)	44.4 (9.1)	44.1 (9.1)	0.02	0.9017	0.00 (−0.20, 0.21)
Current opioid misuse measure	8.7 (6.5)	8.7 (6.1)	7.5 (6.7)	7.4 (6.2)	0.01	0.9416	0.00 (−0.20, 0.21)
Pain knowledge (% right)	72.6% (14.1%)	74.2% (14.1%)	81.6% (13.3%)	78.4% (12.5%)	**11.05**	**0.0009**	0.34 (0.13, 0.55)
Pain self-efficacy	24.6 (12.5)	25.2 (12.8)	31.6 (13.3)	28.6 (13.7)	**7.35**	**0.0067**	0.27 (0.06, 0.48)
Coping strategies							
Catastrophizing	2.2 (1.2)	2.0 (1.3)	1.9 (1.1)	1.9 (1.3)	**4.50**	**0.0339**	−0.30 (−0.51, −0.09)
Coping self statements	3.8 (1.3)	3.6 (1.2)	3.9 (1.2)	3.7 (1.1)	1.60	0.2057	0.06 (−0.15, 0.27)
Distance from pain	1.5 (1.3)	1.2 (1.4)	2.1 (1.4)	1.7 (1.5)	3.78	0.0518	0.12 (−0.09, 0.33)
Distraction	3.3 (1.3)	3.1 (1.4)	3.7 (1.1)	3.3 (1.3)	**9.22**	**0.0024**	0.19 (−0.01, 0.40)
Ignoring pain	2.2 (1.2)	2.1 (1.3)	2.5 (1.2)	2.3 (1.4)	1.34	0.2467	0.07 (−0.13, 0.28)
Praying	3.5 (1.7)	3.4 (2.0)	3.4 (1.7)	3.4 (2.0)	1.52	0.2176	−0.16 (−0.37, 0.05)
Passive coping§	5.7 (2.2)	5.3 (2.6)	5.3 (2.2)	5.3 (2.7)	**4.86**	**0.0275**	−0.29 (−0.50, −0.08)

* All measures summarized as mean (SD).
† Linear regression type-III Wald χ^2 (df = 1) test for treatment effect for baseline-posttest difference (bold text indicates $P < 0.05$).
‡ Cohen's d for baseline-posttest difference.
§ Passive coping includes catastrophizing and/or praying.
BPI, Brief Pain Inventory; MED, morphine equivalent dose; PROMIS, Patient-Reported Outcomes Measurement Information System; TAU, treatment as usual.

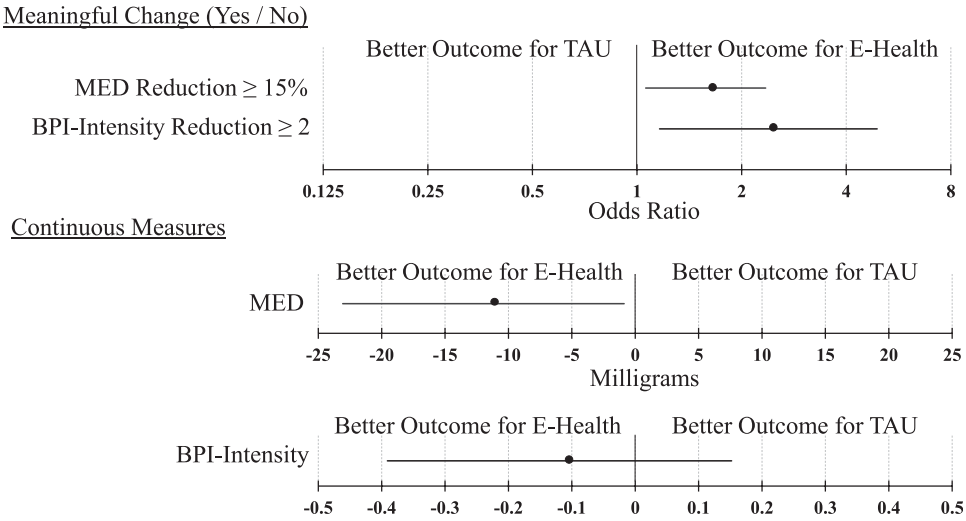

Figure 2. Treatment effects for opioid dose and pain intensity outcomes. The chart shows regression treatment effect estimates for MED and BPI pain intensity with 95% CIs (represented by horizontal line lengths). BPI, Brief Pain Inventory; MED, morphine equivalent dose; TAU, treatment as usual.

prescription, found that significantly more E-health, relative to wait-list control, participants reported decreasing or discontinuing their opioid medication.[36] This study contributes to the evidence base by capturing MED from clinical records vs self-report, which increases confidence that the program can be beneficial in reducing opioid use.

The key secondary measure of a ≥2 point decrease in BPI intensity was defined a priori and selected to be a clinically meaningful outcome.[37] The significant E-health effect on this key secondary outcome measure is consistent with the findings from 2 prior RCTs, which found significant reductions in pain intensity after E-health relative to a control group[29] and a greater percentage of participants reducing pain intensity by ≥ 2 points after 8 weeks of E-health relative to controls.[36] Secondary outcomes affected in this study also align with prior research on E-health and other self-management programs that often improve self-efficacy and knowledge.[29,30,36] Although pain interference was not significantly improved here, E-health has shown positive results in prior studies.[29,32] This study also did not reveal significant improvements in opioid misuse via COMM scores, yet E-health has yielded improvements when tested with adults in opioid use disorder treatment who have comorbid chronic pain.[35] Variability in scores may account for these differences; the COMM score was nearly twice as high on average among those in opioid use disorder treatment as among the present study population.[35] Global health scores were not affected in this study, and no comparison data have been published with this E-health program. Although E-health did not improve global physical or mental health, it also was not worsened in response to lowering MED.

E-health's potential impact on clinical practice is reflected not only in the relative size of its effect on MED and pain but also in terms of reach and effectiveness, which are the RE-AIM framework components pertinent for the present trial.[17] In terms of reach, we were able to recruit and retain a heterogeneous population of participants with chronic pain prescribed opioids with a broad range of pain conditions from primary care and pain medicine practices, lending strength to external validity. Hence, unlike research conducted with more highly selected patients and/or those with a specific pain diagnosis, the present results should be applicable to the majority of the 18 million Americans receiving LOT. Of importance, because the trial did not require that participants be interested in decreasing their opioid dose, the results are pertinent to the large number of patients who similarly have not expressed an interest in dose reduction. Of note, our sample consisted of predominantly White and female participants; therefore, future outreach and adaptations may be required to meet the needs of more diverse populations. Effectiveness includes both the benefits and adverse impacts on an intervention.[17] E-health demonstrated a significant positive impact on the clinically meaningful primary and key secondary outcomes with the analyses of AEs revealing no significant difference between E-health and TAU; the NNT for the primary outcome was 8.9 (95% CI, 4.8, 66.0) and the NNH was 0. Although the precise mechanism for MED reduction cannot be ascertained with this study design, several possibilities are likely. The E-health program provided information on opioid tolerance, dependency, and overdose risks along with suggestions for nonopioid alternatives. This content may have increased receptivity to shared decision-making conversations about opioids that are already underway in many clinics along with the boost to pain self-efficacy and coping to manage symptoms, which are well-established mechanisms of pain self-management programs.[10]

Pain self-management education has been a recommended foundation of chronic pain care since 2011.[21] More recently, the U.S. Federal Pain Research Strategy outlined a vision where "people with pain would have access to educational materials and learn effective approaches for pain self-management programs to prevent, cope with, and reduce pain and its disability."[22] Absent from recommendations to date is how pain self-management should be integrated into clinical practice, how it is best delivered, and precisely what content should be included. The E-health intervention used in this study demonstrates one possible way to deliver well-vetted pain self-management content that can, potentially, be influential in reducing opioid dose while meeting national objectives to improve pain care. Specifically, the program studied cost approximately $120 for a 4-month subscription, could be done from home, and could be completed at a pace and schedule suited to an individual's preferences. Of note, approximately 43% of our participants reported they were disabled. Transportation

and scheduling have been noted as significant barriers to accessing nonpharmacological pain management options.[27] An online E-health option could help reduce pain care disparities for people who have disabilities or are homebound. The program, although designed to be self-administered, required some facilitation by research staff who provided guidance on program features, troubleshot technical issues (eg, problems with the participant's web browser, forgotten login information, etc), and encouraged program completion. Based on adherence scores, approximately 68% of the 200 randomized E-health participants received substantive exposure to the program. For clinical practice implementation, program facilitation by professionals or community health workers with behavioral health or pain management proficiency may result in improved engagement and outcomes along with more detailed information about how people engage. Because the adherence scores only credit participants if they complete a postlearning module satisfaction survey, it is possible participants viewed or engaged in more modules and materials, but did not record their satisfaction. Because the program can be accessed from home, billing a session with a professional to help work through the program activities could be done on a separate day than primary care visits, removing barriers to billing that presently exist in the United States because primary care and behavioral health cannot be billed on the same day for some health plans.

4.1. Limitations

This study had several limitations. First, although the EHR-derived primary outcome of MED was available for 98.8% of participants, with no significant difference between the treatment groups, there was a significant treatment group difference in the month-10 self-assessment completion rates, with higher completion for the TAU (95%) relative to E-health (83%) participants. The results from multiple imputation analyses were consistent with the results from the completers analyses, and the 17% E-health attrition rate is comparable with that of other online pain self-management studies (ie, ranging from 0.9% to 69.8%),[30] but an impact of differential completion rate on the self-report outcomes cannot be entirely ruled out. Another limitation was the inability to conduct a double-blinded trial, given the nature of the intervention, although this would not have had an impact on the primary outcome, given that most of the prescribers would have been unaware of the patient's participation in the trial. It is also possible participants informed their providers about their study enrollment. Although an attention control group could have provided greater confidence that this specific intervention was efficacious, the amount of attention provided to E-health participants was minimal and equivalent to attention provided to TAU members who received phone calls when needed to complete their scheduled assessments. The majority of participants had relatively low MED, which may indicate some selection bias. Finally, although the sample size was relatively large (N = 402), we recruited participants from 2 health systems in 2 geographic regions of the United States (Ohio and North Carolina). Selection bias could have occurred whereby those with computers, higher education, or more receptivity to online interventions were more willing to join the study. The results, therefore, may not generalize to other regions or countries.

5. Conclusion

This trial demonstrates the significant and beneficial impact of an E-health self-management chronic pain program for reducing opioid medication dose while improving pain along with other outcomes important to pain management. Research on optimal implementation approaches for providing access to, and encouraging use of, pain education and self-management tools seems warranted. Augmenting usual care with pain self-management content may aid in opioid dose reduction, even when opioid use is not explicitly targeted.

Conflict of interest statement

All authors have no potential conflicts of interest to report. This study was preregistered on ClinicalTrials.gov, and design details including analysis plan were published before enrollment completion in Winhusen T, Wilson M, Dolor RJ, et al. Design considerations for a remote randomized multi-site clinical trial evaluating an E-health self-management program for chronic pain patients receiving opioid therapy. Contemporary Clinical Trials. 2021;101:106245. doi:10.1016/j.cct.2020.106245. Data and program codes used in analysis will be made available to researchers for purposes of reproducing the results, replicating the procedures, or any preapproved use. Data will be available after approval of a proposal, additional IRB approval (if necessary), and signing of a data access agreement. Data will be available by email to winhust@ucmail.uc.edu.

Previous presentation of this research includes 1) a published paper focused on our trial design without regard for outcomes: Winhusen T, Wilson M, Dolor RJ, et al. Design considerations for a remote randomized multi-site clinical trial evaluating an E-health self-management program for chronic pain patients receiving opioid therapy. *Contemporary Clinical Trials*. 2021;101:106245. doi:10.1016/j.cct.2020.106245; 2) an abstract focused on baseline data only accepted to be presented at the American Society for Pain Management Nursing conference in Indian Wells, CA, September 2022, and to be published in *Pain Management Nursing*: Wilson M, Mazumder S, Vonder Meulen MB, Winhusen TJ. Disparities in non-pharmacological therapy use among adults prescribed opioids for persistent pain. Podium presentation, American Society for Pain Management Nursing's 32nd National Conference, September 14-17, 2022. Indian Wells, CA.

Acknowledgments

Supported by the National Institute on Drug Abuse, National Institutes of Health, by grant R01DA044248 (Winhusen). The funding source had no further involvement in the study design, the writing of the report, or the decision to submit this manuscript.

Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/B721.

Article history:
Received 7 July 2022
Received in revised form 26 August 2022
Accepted 6 September 2022
Available online 15 September 2022

References

[1] Agnoli A, Xing G, Tancredi DJ, Magnan E, Jerant A, Fenton JJ. Association of dose tapering with overdose or mental health crisis among patients prescribed long-term opioids. JAMA 2021;326:411–19.
[2] Antony MM, Bieling PJ, Cox BJ, Enns MW, Swinson RP. Psychometric properties of the 42-item and 21-item versions of the Depression Anxiety

Stress Scales in clinical groups and a community sample. Psychol Assess 1998;10:176–81.
[3] Butler SF, Budman SH, Fanciullo GJ, Jamison RN. Cross validation of the current opioid misuse measure to monitor chronic pain patients on opioid therapy. Clin J Pain 2010;26:770–6.
[4] Butler SF, Budman SH, Fernandez KC, Houle B, Benoit C, Katz N, Jamison RN. Development and validation of the current opioid misuse measure. PAIN 2007;130:144–56.
[5] Centers for Disease Control and Prevention (CDC). About CDC's opioid prescribing guideline, 2021. Available at: https://www.cdc.gov/opioids/providers/prescribing/guideline.html#anchor_1561563251. Accessed April 4, 2022.
[6] Centers for Disease Control and Prevention. Nonopioid treatments for chronic pain, 2016. Available at: https://www.cdc.gov/drugoverdose/pdf/nonopioid_treatments-a.pdf. Accessed April 3, 2022.
[7] Chen L, Vo T, Seefeld L, Malarick C, Houghton M, Ahmed S, Zhang Y, Cohen A, Retamozo C, St Hilaire K, Zhang V, Mao J. Lack of correlation between opioid dose adjustment and pain score change in a group of chronic pain patients. J Pain 2013;14:384–92.
[8] Cleeland CS, Ryan KM. Pain assessment: global use of the brief pain inventory. Ann Acad Med Singap 1994;23:129–38.
[9] Darnall BD, Juurlink D, Kerns RD, Mackey S, Van Dorsten B, Humphreys K, Gonzalez-Sotomayor JA, Furlan A, Gordon AJ, Gordon DB, Hoffman DE, Katz J, Kertesz SG, Satel S, Lawhern RA, Nicholson KM, Polomano RC, Williamson OD, McAnally H, Kao MC, Schug S, Twillman R, Lewis TA, Stieg RL, Lorig K, Mallick-Searle T, West RW, Gray S, Ariens SR, Sharpe Potter J, Cowan P, Kollas CD, Laird D, Ingle B, Julian Grove J, Wilson M, Lockman K, Hodson F, Palackdharry CS, Fillingim RB, Fudin J, Barnhouse J, Manhapra A, Henson SR, Singer B, Ljosenvoor M, Griffith M, Doctor JN, Hardin K, London C, Mankowski J, Anderson A, Ellsworth L, Davis Budzinski L, Brandt B, Hartley G, Nickels Heck D, Zobrosky MJ, Cheek C, Wilson M, Laux CE, Datz G, Dunaway J, Schonfeld E, Cady M, LeDantec-Boswell T, Craigie M, Sturgeon J, Flood P, Giummarra M, Whelan J, Thorn BE, Martin RL, Schatman ME, Gregory MD, Kirz J, Robinson P, Marx JG, Stewart JR, Keck PS, Hadland SE, Murphy JL, Lumley MA, Brown KS, Leong MS, Fillman M, Broatch JW, Perez A, Watford K, Kruska K, Sophia You D, Ogbeide S, Kukucka A, Lawson S, Ray JB, Wade Martin T, Lakehomer JB, Burke A, Cohen RI, Grinspoon P, Rubenstein MS, Sutherland S, Walters K, Lovejoy T. International stakeholder community of pain experts and leaders call for an urgent action on forced opioid tapering. Pain Med 2019;20:429–33.
[10] DasMahapatra P, Chiauzzi E, Pujol LM, Los C, Trudeau KJ. Mediators and moderators of chronic pain outcomes in an online self-management program. Clin J Pain 2015;31:404–13.
[11] Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. JAMA 2016;315:1624–45.
[12] Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. MMWR Recomm Rep 2016;65:1–49.
[13] Du S, Hu L, Dong J, Xu G, Chen X, Jin S, Zhang H, Yin H. Self-management program for chronic low back pain: a systematic review and meta-analysis. Patient Educ Couns 2017;100:37–49.
[14] Farmer R, Mathur R, Bhaskaran K, Eastwood SV, Chaturvedi N, Smeeth L. Promises and pitfalls of electronic health record analysis. Diabetologia 2018;61:1241–8.
[15] Farrar JT, Young JP Jr, LaMoreaux L, Werth JL, Poole MR. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. PAIN 2001;94:149–58.
[16] Gewandter JS, Smith SM, Dworkin RH, Turk DC, Gan TJ, Gilron I, Hertz S, Katz NP, Markman JD, Raja SN, Rowbotham MC, Stacey BR, Strain EC, Ward DS, Farrar JT, Kroenke K, Rathmell JP, Rauck R, Brown C, Cowan P, Edwards RR, Eisenach JC, Ferguson M, Freeman R, Gray R, Giblin K, Grol-Prokopczyk H, Haythornthwaite J, Jamison RN, Martel M, McNicol E, L Oshinsky M, Sandbrink F, Scholz J, Scranton R, Simon LS, Steiner D, Verburg K, Wasan AD, Wentworth K. Research approaches for evaluating opioid sparing in clinical trials of acute and chronic pain treatments: initiative on methods, measurement, and pain assessment in clinical trials recommendations. PAIN 2021;162:2669–81.
[17] Glasgow RE, Estabrooks PE. Pragmatic applications of RE-AIM for health care initiatives in community and clinical settings. Prev Chronic Dis 2018;15:E02.
[18] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
[19] Hastie BA, Riley JL III, Fillingim RB. Ethnic differences in pain coping: factor structure of the coping strategies questionnaire and coping strategies questionnaire-revised. J Pain 2004;5:304–16.
[20] Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. Qual Life Res 2009;18:873–80.
[21] Institute of Medicine 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.
[22] Interagency Pain Research Coordinating Committee. National pain strategy, 2018. Available at: https://www.iprcc.nih.gov/sites/default/files/documents/NationalPainStrategy_508C.pdf. Accessed April 2, 2022.
[23] Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials—a practical guide with flowcharts. BMC Med Res Methodol 2017;17:162.
[24] Kaelber DC, Foster W, Gilder J, Love TE, Jain AK. Patient characteristics associated with venous thromboembolic events: a cohort study using pooled electronic health record data. J Am Med Inform Assoc 2012;19:965–72.
[25] Mun C, Karoly P, Okun M, Ruehlman L. Does fear of pain mediate the effect of an online chronic pain management program on medication use? 123rd Annual Convention of the American Psychological Association; August 2015; Toronto, Ontario, Canada.
[26] Nicholl BI, Sandal LF, Stochkendahl MJ, McCallum M, Suresh N, Vasseljen O, Hartvigsen J, Mork PJ, Kjaer P, Søgaard K, Mair FS. Digital support interventions for the self-management of low back pain: a systematic review. J Med Internet Res 2017;19:e179.
[27] Pollack SW, Skillman SM, Frogner BK. The health workforce delivering evidence-based non-pharmacological pain management. Health workforce policy brief. Center for Health Workforce Studies, University of Washington, 2020. Available at: https://depts.washington.edu/fammed/chws/wp-content/uploads/sites/5/2020/02/Non-Pharmacological-Pain-Management-PB-2020.pdf. Accessed June 25, 2022.
[28] Rothrock NE, Amtmann D, Cook KF. Development and validation of an interpretive guide for PROMIS scores. J Patient Rep Outcomes 2020;4:16.
[29] Ruehlman LS, Karoly P, Enders C. A randomized controlled evaluation of an online chronic pain self management program. PAIN 2012;153:319–30.
[30] Ruehlman L, Wilson M. Enhancing pain self-management via Internet-based technology. In: Karoly P, Crombez G, editors. Motivational perspectives on chronic pain. New York, NY: Oxford UP, 2018. p. 537–91.
[31] Saver JL, Lewis RJ. Number needed to treat: conveying the likelihood of a therapeutic effect. JAMA 2019;321:798–9.
[32] Tonkin L. The pain self-efficacy questionnaire. Aust J Physiother 2008;54:77.
[33] Utne I, Miaskowski C, Bjordal K, Cooper BA, Valeberg BT, Rustoen T. Confirmatory factor analysis of the coping strategies questionnaire-revised in samples of oncology outpatients and inpatients with pain. Clin J Pain 2009;25:391–400.
[34] Wasan AD, Butler SF, Budman SH, Benoit C, Fernandez K, Jamison RN. Psychiatric history and psychologic adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. Clin J Pain 2007;23:307–15.
[35] Wilson M, Finlay M, Orr M, Barbosa-Leiker C, Sherazi N, Roberts MLA, Layton M, Roll JM. Engagement in online pain self-management improves pain in adults on medication-assisted behavioral treatment for opioid use disorders. Addict Behav 2018;86:130–7.
[36] Wilson M, Roll JM, Corbett C, Barbosa-Leiker C. Empowering patients with persistent pain using an internet-based self-management program. Pain Manag Nurs 2015;16:503–14.
[37] Winhusen T, Wilson M, Dolor RJ, Theobald J, Lewis D, Regan SL, Vonder Meulen MB. Design considerations for a remote randomized multi-site clinical trial evaluating an E-health self-management program for chronic pain patients receiving opioid therapy. Contemp Clin Trials 2021;101:106245.
[38] World Health Organization. Guidelines on the management of chronic pain in children. Geneva: World Health Organization, 2020. License: CC BY-NC-SA 3.0 IGO.