

Single-arm feasibility and preliminary efficacy national pilot study of Empowered Relief in patients with chronic pain taking methadone or buprenorphine

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Abstract

Background: Approximately 45% of individuals taking methadone or buprenorphine have chronic pain. These medications are commonly prescribed for chronic pain or Opioid Use Disorder (OUD). To optimize pain management as well as reduce opioid-related symptoms (e.g., craving) and risks (misuse, overdose), there is a critical need for a brief, effective, and accessible pain skills intervention for this population.

Objective: The objective of this single-arm study is to examine the feasibility, and preliminary efficacy of online Empowered Relief (ER), a 1-session pain relief skills class, for individuals with chronic pain taking methadone or buprenorphine for chronic pain or OUD.

Methods: A priori feasibility criteria were defined as at least 75% of enrolled participants attending ER class and the mean satisfaction rating of at least 8 on a 0-10 scale. Participants were recruited nationally across the U.S. Out of the 69 enrolled participants, 55 attended the ER class. Self-report measures were collected at baseline, immediately post-class, and at follow-up points of 2 weeks, and months 1-3. Additionally, qualitative interviews were conducted in a small sample (n = 14) to obtain in-depth participant feedback. Among the class attendees, 51 participants (52.9% Female; mean age = 48.6, range: 28 – 71) completed at least one follow-up survey, and their treatment outcomes were analyzed using repeated measures ANOVA, with missing data imputed using linear regression. This analytic sample consisted of 24 taking methadone and 27 taking buprenorphine, and 43.1% endorsed at least 2 OUD symptoms within the past 12 months, meeting the DSM-5 diagnostic criteria for current OUD.

Results: Feasibility was achieved with 79.7% attendance and M= 8.6 treatment appraisal and satisfaction ratings. Qualitative feedback demonstrated high acceptability of the class content and delivery, with suggestions for refinements. Repeated-measures ANOVAs and Bonferroni post-hoc tests revealed significant reductions at 1-month post-ER class (primary endpoint) in pain intensity (d = 0.41), pain bothersomeness (d = 0.54), and pain interference (d = 0.61). At 3-month post-ER class, efficacy was maintained for pain bothersomeness (d = 0.44) and pain interference (d = 0.), but not for pain intensity. No significant time effects were observed for pain catastrophizing, sleep disturbance, physical function, fatigue, depression, anxiety, social isolation, and opioid craving.

Conclusions: This study is the first to test ER in patients taking methadone or buprenorphine for pain or OUD. Findings showed feasibility, acceptability, and preliminary evidence of treatment efficacy. Participant feedback will inform future study designs. Findings support a randomized trial to fully evaluate the efficacy and scalability of ER in this population. Clinical Trial:

NCT05057988; <https://clinicaltrials.gov/study/NCT05057988>

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Original Manuscript

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Keywords: pain management, treatment, behavioral, online, group

ABSTRACT

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Results: Feasibility was achieved with 79.7% attendance and $M = 8.6$ treatment appraisal and satisfaction ratings. Qualitative feedback demonstrated high acceptability of the class content and delivery, with suggestions for refinements. Repeated-measures ANOVAs and Bonferroni post-hoc tests revealed significant reductions at 1-month post-ER class (primary endpoint) in pain intensity ($d = 0.41$), pain bothersomeness ($d = 0.54$), and pain interference ($d = 0.61$). At 3-month post-ER class, efficacy was maintained for pain bothersomeness ($d = 0.44$) and pain interference ($d = 0.$), but not for pain intensity. No significant time effects were observed for pain catastrophizing, sleep disturbance, physical function, fatigue, depression, anxiety, social isolation, and opioid craving.

Conclusion: This study is the first to test ER in patients taking methadone or buprenorphine for pain or OUD. Findings showed feasibility, acceptability, and preliminary evidence of treatment efficacy. Participant feedback will inform future study designs. Findings support a randomized trial to fully evaluate the efficacy and scalability of ER in this population.

ClinicalTrials.gov NCT05057988; <https://clinicaltrials.gov/study/NCT05057988>

INTRODUCTION

Chronic pain affects roughly 20% of U.S. adults.¹ Among individuals with chronic pain, nearly one-third report using prescription opioids.² However, long-term opioid therapy provides only modest pain relief³⁻⁵ and is often accompanied by adverse side effects.^{6,7} Consequently, those taking long-term opioids frequently report insufficient pain relief,⁷⁻⁹ and their overall pain management remains suboptimal. Behavioral pain interventions have emerged as a safe and potentially effective strategy to improve pain-related outcomes, which in turn may help reduce prescription opioid use.¹⁰⁻¹² To date, few studies have examined the effect of behavioral interventions in individuals with chronic pain taking long-term prescription opioids.^{10,12-14} While meta-analytic evidence suggests that behavioral pain interventions may lead to moderate reductions in pain intensity and small reductions in opioid use, the overall quality of evidence remains limited.^{13,14}

Methadone (full mu agonist)¹⁵ and buprenorphine (partial mu agonist)¹⁶ are FDA-approved opioid medications for the indications of opioid use disorder (OUD) and chronic pain.^{17,18} Estimates suggest that 45% of patients taking these medications have chronic pain, regardless of the primary indication for prescription.^{19,20} Given that patients taking either of these medications have chronic pain, OUD, or both, targeted behavioral interventions may improve pain outcomes and/or reduce opioid use or misuse. To date, 12-session cognitive behavioral therapy (CBT; 6-9 hours total) and 8-session Mindfulness-Oriented Recovery Enhancement (MORE; 16 hours total) are among the few interventions tested in this population. The 12-session CBT for chronic pain has shown no significant effects on pain intensity and pain interference,²¹ though reductions in opioid misuse have been reported.²² The 8-session MORE has shown consistent reductions in opioid use and craving across two in-person Phase I trials and one online Phase III trial.²³⁻²⁵ However, findings regarding its effects on pain have varied.²³⁻²⁵

Evidence is promising for behavioral pain treatment in individuals taking medications for OUD, yet significant barriers impede broad patient access.²⁶⁻²⁸ A 1-session pain relief skills intervention (Empowered Relief; ER) overcomes many existing barriers to care owing to its brief format, and online delivery provides even greater access while keeping treatment burden low.²⁹ ER has demonstrated efficacy for reducing pain intensity, pain interference, pain bothersomeness, sleep disturbance, depression and anxiety in heterogeneous pain conditions.³⁰⁻³⁵ In-person ER has shown non-inferior efficacy compared to traditional, 8-session CBT for chronic low back pain and has produced sustained improvements in pain catastrophizing, pain intensity, pain bothersomeness, and pain interference as well as associated symptoms (e.g., fatigue, sleep, depression, and anxiety) up to 3-6 months.^{29,36} When delivered online, ER remains effective in improving pain-related outcomes,³⁷ and has shown preliminary efficacy among individuals with long-term use of short- or long-acting opioids.³⁸ To date, ER has not been tested in patients with OUD or history of OUD. The current single-arm study sought to test the feasibility and preliminary efficacy of online ER in individuals with chronic pain taking methadone or buprenorphine. We hypothesized that ER would (a) be feasible (as indexed by 75% attendance rate and an average treatment satisfaction rating of ≥ 8 on a 0-10 scale); (b) significantly reduce primary outcomes of interest (pain catastrophizing, pain intensity, pain bothersomeness, and sleep disturbance), and improve other outcomes (i.e., physical function, fatigue, depression, anxiety, and anger), and opioid craving at one month post-treatment (primary endpoint). Additionally, we hypothesized that (c) these effects would be maintained at 3-month post-treatment (durability endpoint). Finally, we aimed to collect qualitative interview data from a subset of participants to inform potential treatment refinements.

METHODS

The Stanford Institutional Review Board approved the study procedures. This study was pre-registered (NCT05057988), and the study protocol is published open access.³⁹ Informed consent was obtained from all participants.

Recruitment

Participants were recruited nationally through pain and addiction clinics via physician

referrals and self-referral through research posting on a Stanford Pain Division website and the clinicaltrials.gov website. Email invitations were also sent to the Pain Division's research registry. Study advertisements invited individuals with chronic pain who were taking methadone or buprenorphine to attend a single online pain relief skills class and complete a series of surveys. The study was opened for enrollment in September 2021, and 71 participants were recruited between May 2022 and October 2023 (18 months). Among the 69 consented participants, 55 attended an ER class (Figure 1).

Inclusion criteria: ≥ 18 years of age, ongoing body pain for more than half of the day for ≥ 3 months, currently taking methadone or buprenorphine, and verbal English fluency. To make ER more accessible, internet or computer access was not required. Participants could use any device with video call capability, as long as the referring clinics could accommodate Zoom sessions. Written English fluency was not required as participants had an option of completing their surveys either online, via mailed paper-based format, or with research coordinator-assisted methods. None used the assisted method, and only one participant completed the survey on paper and used pre-paid postal mail to return the survey to the study team. Exclusion criteria: pregnancy or having previously received the ER intervention.

Procedures

The inclusion and exclusion criteria were posted on the study website and communicated with referring physicians. Individuals, who were either self-referred or received the study flyer or study contact information from referring physicians, contacted the research coordinator via a phone call, text message, or email. Following initial contact, the research coordinator scheduled a phone call to confirm eligibility (Figure 2) and explain the study goals, procedures, risks and the compensation schedule. Those expressing interest were sent an electronic consent form and were encouraged to take as much time as needed to review the consent form and contact a research coordinator with any questions.

Following electronic consent, participants received the baseline survey link, zoom instructions, and ER class handouts. During the ER group session, participants were asked to display only their first name and keep their cameras off for privacy. They were encouraged to ask questions either directly to the class instructor or through the online chat function. Upon completion of the ER class, participants received a document of the class slides and binaural app instructions as well as a treatment appraisal and satisfaction survey. Participants received follow-up surveys at 2 weeks, 1 month (primary endpoint), 2 months, and 3 months post-treatment (durability endpoint). For the interview portion, we sent an email invitation to the first 20 participants who completed the study, and 14 provided the feedback. Compensation was provided in the form of Amazon gift cards (Figure 2) with amounts ranging from US \$10 to US \$30, depending on how many surveys a participant completed, and up to \$145 possible. Notably, the compensation at 1-month was slightly higher to improve the data collection at the primary endpoint. Those who participated in a 30-minute qualitative interview ($n = 14$) received an additional US \$20 Amazon gift card.

Figure 1. Consort Diagram

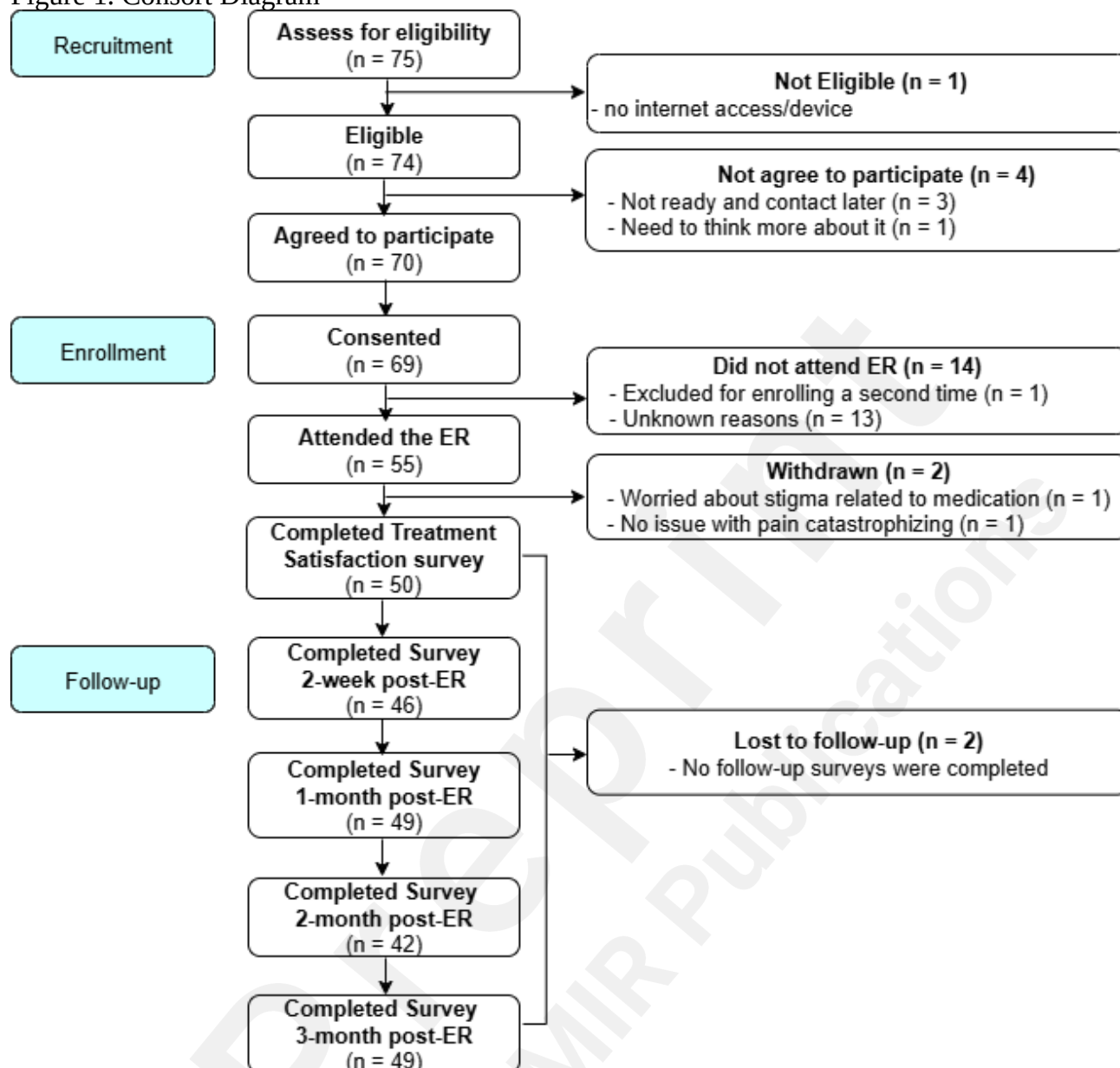
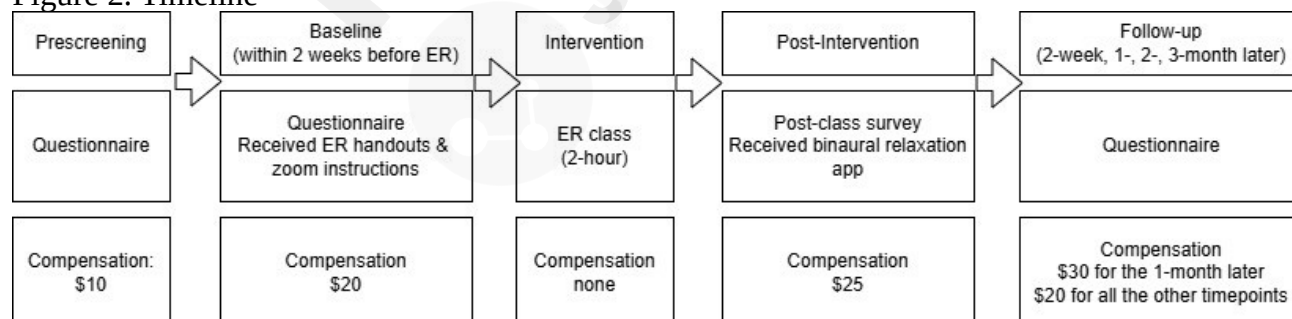


Figure 2. Timeline



Empowered Relief (ER)

ER is a 2-hour didactic class consisting of pain neuroscience education, experiential and interactive exercises, and three core pain management skills such as cognitive reappraisal of pain catastrophizing, self-soothing, and relaxation techniques. During the class, participants self-tailor the content to create a personalized plan for empowered relief, and they receive a binaural calming audio application for downloading onto their smartphone or other devices and with unlimited use. Participants were encouraged to use the calming app daily.

Data Collection

All study data were obtained via self-report measures and through qualitative interviews (for a subset of participants). The study was designed to be untethered from medical care and as such medical records were not accessed, nor was there any communication with participants' clinicians.

Self-Report Measures

Demographic and clinical characteristics were assessed at baseline. The demographics questionnaire included sex, age, race/ethnicity, marital status, education, employment status, household annual income, and housing situation. Clinical questionnaires included pain duration, pain location, pain diagnosis, and mental health diagnoses. Pain duration was assessed using preselected categories, such as (a) < 3 months, (b) between 3 and <6 months, (c) between 6 and 12 months, and (d) > 1 year. Pain diagnoses, opioid medication, and mental health diagnoses were assessed in a free text format. Additionally, prior experience with a pain self-management class was asked in a yes or no question. Lastly, the DSM-5 OUD symptom checklist was administered to evaluate the participants' current OUD severity (past 12 months).^{40,41}

To assess the primary study outcome of feasibility and acceptability, 11 questions³⁹ were asked to evaluate 1) overall satisfaction, 2) ease of understanding the class content, 3) relevancy, 4) usefulness, 5) likelihood of using the skills, 6) likelihood of recommending the class to others, 7) ease of operating Zoom, 8) concerns about privacy while attending the Zoom class, 9) feeling comfortable engaging with the Zoom instructor and class participants, 10) feeling of connection with the instructor, and 11) preference for a single, 2-hour class or two 1-hour classes. All questions were rated on a 0-10 scale except for the last question with 3 response options (1. Prefer single, 2-hour class; 2. Prefer 1-hour two classes; and 3. Other). When selecting "Other" as a response, a free text box was generated to elicit detailed information. To ensure consistency in directionality of scale items, 8) the concern about privacy was reverse coded. To gain deeper insight into acceptability and future refinements, structured qualitative interviews were conducted with 14 volunteers after attending the class.

Preliminary treatment efficacy was assessed with the following patient-reported outcome measures. First, the 13-item Pain Catastrophizing Scale (PCS) was administered to assess the levels of pain catastrophizing ($\alpha = .87$) on a 5-point scale from 0 (not at all) to 4 (all the time).⁴² Pain catastrophizing is a maladaptive cognitive-emotional response to pain, characterized by magnification, rumination, and helplessness about pain.⁴² The PCS total score ranges from 0 to 52, with higher scores indicating higher levels of pain catastrophizing. The levels of average pain intensity⁴³ and pain bothersomeness⁴⁴ in the past 7 days were assessed with a single-item measure. Pain intensity was rated on a 0 (no pain) to 10 (worst pain imaginable) scale and pain bothersomeness was rated on a 0 (not at all bothersome) to 10 (extremely bothersome) scale. The Patient Reported Outcomes Measurement Information System (PROMIS) sleep disturbance v1.0 (6a) short-form was administered to assess level of sleep difficulties in the past 7 days (M = 50, SD = 10), with higher T-scores indicating greater difficulty.⁴⁵ Sleep disturbance was assessed because poor sleep is associated with worse pain⁴⁶ and opioid misuse,^{47,48} and because ER has shown to improve sleep disturbance.^{29,37}

Additional efficacy measures. The PROMIS measure short-forms were administered to assess pain-related symptoms in the past 7 days.⁴⁹ Specifically, PROMIS-pain interference v1.1 (6a),⁵⁰ physical function v2.0 (6b),⁵¹ fatigue v1.0 (4a),⁵² depression v1.0 (6a),⁵³ anxiety v1.0 (6a),⁵³ and

social isolation v2.0 (4a) were used.⁴⁹ Each measure was rated on a 1-5 scale. Responses on each measure were uploaded in the publicly available, web-based scoring system (www.assessmentcenter.net/) to calculate T-scores ($M = 50$, $SD = 10$), with higher scores indicating worse symptom or higher function. Additionally, current craving intensity was assessed on a 0 (not at all)-10 (extremely) scale.⁵⁴ Finally, the 6-item Global Impression of Change (GIC) measure was administered at all post-ER class timepoints to assess the perceived improvement after the intervention. The 6 GIC items were about improvement on overall health, physical activity, social activity, work-related activity, mood, and pain, which were rated on a 7-Point scale, ranging from 1 (very much worse) to 4 (no change) to 7 (very much improved) scale.⁵⁵ Adverse events were assessed at all follow-up time points.

Preliminary Efficacy Endpoint at 1 month

A prior online ER study (chronic pain and no medication inclusion criterion) showed significant reductions in PCS scores at 2-week post-treatment, with significant reductions in pain intensity and pain bothersomeness emerging at 1-month post-treatment.³⁷ These treatment effects were maintained at 3 months after ER class, which informed the durability timepoint for the current study.

Analysis Plan

Feasibility Thresholds: The following criteria were evaluated to determine feasibility. First, $\geq 75\%$ of enrolled participants would attend ER. Second, the mean scores of the primary feasibility outcome measures would meet or exceed an 80% threshold for treatment appraisal and satisfaction (8 or higher on a 0-10 scale).^{38,56} Content analysis was conducted by two authors (KE, MZ) for qualitative interview data to evaluate perceived feasibility and to identify areas for improvement.

Preliminary efficacy: Repeated-measures ANOVAs were performed to assess whether pain and related outcomes significantly improved one month after ER (efficacy endpoint) and whether these improvements were maintained at three months (durability). The Greenhouse-Geisser correction was used to adjust the degrees of freedom when sphericity assumption was violated. When a significant main effect of time was found, Bonferroni correction was applied to address multiplicity and risk of false positives. Cohen's d was calculated to estimate the effect size of reduction at each time point compared to baseline, using the sample standard deviation of mean difference adjusted by the correlation between measures.

Power Analysis

The G*Power 3.1.9.7. software was used to calculate sample sizes needed to detect a moderate ($f = 0.25$) effect in a repeated measures ANOVA, with alpha level of .05 and 0.30 autocorrelation between time points. The analysis indicated that the sample sizes of 36, 43, and 59 would yield the power of 90%, 95%, and 99%, respectively. The final sample of 51 corresponded to an estimated power of 98%.

Missing Data

Of the 55 participants who attended ER, two participants withdrew consent after the ER class (3.6%) because one expressed concern about stigma related to the use of methadone or buprenorphine, and the other stated having no problem with pain catastrophizing. Two participants did not complete any follow-up surveys. Therefore, data from 51 participants who attended the class and completed at least one follow-up survey were analyzed. Missing rates ranged from 1.9% (pain intensity and pain bothersomeness at 1-month post-treatment) to 17.6% (PROMIS-measure at 2-month post-treatment). Missing values were estimated and replaced using linear regression.

Appendix 1.1 shows the results of repeated measures ANOVA with pairwise deleted data collected at baseline, 2 weeks post-treatment, and 1-month post-treatment (efficacy endpoint). Paired t-tests were conducted as a post-hoc test to identify time points of significant symptom reduction and its maintenance up to 3 months post-treatment. These results were consistent with analyses using missing data replacement.

RESULTS

Participants

Table 1.1 summarizes the demographic characteristics of the study sample. Notably, only one participant identified a methadone or buprenorphine prescribing clinic as the study referral source. Eleven participants (20%) did not provide their referral source. Briefly, participants reported an average age of 48.6 years ($SD = 12.2$) and were predominantly female (52.9%), non-Hispanic (82.4%), White/Caucasian (70.6%). Most participants were married or were living with a partner (60.8%). Just over half (51.0%) held a bachelor's degree or higher. While these demographic characteristics were consistent with our previous studies of participants without prescription opioids,^{29,36,37} a notable distinction was that 51.0% were not working due to medical reasons, suggesting a higher burden of illness and greater disease severity than observed in prior research. The median income was between \$45,000 and \$64,999. To note, U.S. individual annual income was \$47,960 in 2022.⁵⁷ Finally, most people were not homeless (90.2%) and two were residing in a homeless shelter.

The baseline clinical characteristics are summarized in Table 1.2. Most participants (82.4%) reported experiencing pain for at least one year. While 88.2% ($n = 45$) reported having a pain-related diagnosis, only 37 provided specific diagnoses, with an average of 2.0 diagnoses per participant ($SD = 1.6$). The five most common diagnoses were back or spine pain, arthritis, fibromyalgia, neuralgia, and migraine. Nearly half of the participants were taking methadone (47.1%), while the remainder were on buprenorphine (52.9%); 43.1% met the diagnostic criteria for current OUD. The mean DSM-5 OUD symptom severity score was 2.7 ($SD = 3.3$), indicating overall mild OUD severity. Among the 28 participants who reported a history of mental health conditions, 26 provided specific diagnoses, with an average of 1.9 diagnoses per person ($SD = 0.8$). Depression (69.2%) and anxiety (50.0%) were the most frequently reported diagnoses. Regarding current mental health treatment, 23.5% were engaged in psychotherapy with a counselor, psychologist, or social worker. Additionally, 53.1% reported prior participation in a pain management class, excluding ER.

Table 1.1 Demographic characteristics (n = 51)

		<i>M</i>	<i>SD</i>	Range
Age (years)		48.6	12.2	28 - 71
		<i>n</i>	%	
Gender	Female	27	52.9	
	Male	21	41.2	
	Non-binary	1	2.0	
Ethnicity	Non-Hispanic	42	82.4	
	Hispanic	7	13.7	
Race	White/Caucasian	36	70.6	
	Black/African American	9	15.7	
	More than one race	4	7.8	
	Decline to answer	1	2.0	
Marital Status	Married/Living together	31	60.8	
	Divorced/separate/widowed	11	21.6	
	Never married	5	9.8	
	Partnered/not living together	2	3.9	
Education	High school	3	5.9	
	Some colleges, no degree	12	23.5	
	Associate's or Vocational Certificate	8	15.7	
	Bachelor's or higher	26	51.0	
Employment	Full-time	11	21.6	
	Part-time	4	7.8	
	Not employed	1	2.0	
	Retired	7	13.7	
	Not working due to medical reasons	26	51.0	
Annual Income (\$)	< 10,000	6	11.8	
	10,000 – 24,999	7	13.7	
	25,000 - 44,999	10	19.6	
	45,000 – 64,999 (Median)	4	7.8	
	65,000 – 104,999	10	19.6	
	> 105,000	9	17.6	
	Decline to answer	3	5.9	
Housing Status	Not homeless	46	90.2	
	Homeless sheltered	2	3.9	
	Decline to answer	1	2.0	

Note: Missing n = 1 for race and n = 2 for all the other demographic data

Table 1.2 Clinical characteristics (n = 51)

		<i>n</i>	%	
Pain Duration †	< 6 months	2	3.9	
	6 and < 12 months	5	9.8	
	1 or more years (median)	42	82.4	
Received pain diagnosis? †	Yes	45	88.2	
	No	4	7.8	
Pain Diagnosis (n = 37)	Back and spinal pain condition	9	24.3	
	Arthritis	5	13.5	
	Fibromyalgia	5	13.5	
	Neuralgia	5	13.5	
	Migraine	4	10.8	
	Connective Tissue Disorder	3	8.1	
	Complex Regional Pain Syndrome	3	8.1	
	Stenosis	2	5.4	
	Pelvic pain conditions	2	5.4	
	Orthopedic conditions	2	5.4	
	Other*	9	24.3	
Opioid Medication	Methadone	24	47.1	
	Buprenorphine	27	52.9	
Current OUD	No	25	49.0	
	Yes	22	43.1	
	- mild (2-3)	10	19.6	
	- moderate (4-5)	3	5.9	
	- severe (6-11)	9	17.6	
	Missing	4	7.8	
Ever received mental health diagnosis? †	Yes	28	54.9	
	No	21	41.2	
Mental Health History (n = 26)	Depression	18	69.2	
	Anxiety	13	50.0	
	PTSD	8	30.7	
	Bipolar disorder	3	11.5	
	Other**	5	19.2	
Currently seeing a therapist?	Yes	12	23.5	
	No	15	29.4	
	Decline to answer/missing	24	47.1	
Previous pain management class? †	Yes	22	43.1	
	No	27	52.9	
		<i>M</i>	<i>SD</i>	Range
Number of pain diagnosis (n = 37)		2.0	1.6	1 - 9
Number of mental health diagnosis (n = 26)		1.9	0.8	1 - 4

†: missing n = 2

Other*: tendonitis, pancreatitis, interstitial cystitis, restless leg syndrome, esophageal dysmotility, CSF leak, viremia, stomach ulcer, frozen shoulder, sum is > 100% for multiple diagnoses per person
 Other**: ADHD, Insomnia, OCD, Personality Disorder, Substance Abuse, sum is > 100% for multiple diagnoses per person

Primary Outcome: Feasibility

The ER attendance rate of 79.7% (n=55) exceeded the pre-registered attendance threshold of 75.0%. Fifty participants completed the post-class treatment appraisal and satisfaction survey. As summarized in Table 2, all item ratings exceeded the feasibility threshold of 8.0, except for concerns about privacy during the Zoom class (M=7.3); because this single item is interpreted in the reverse direction (i.e., higher scores reflect greater concerns), the mean score for the privacy concern item was notably high. The mode for feasibility and acceptability ratings was 10 across all items, indicating strong endorsement. Participants gave high ratings for ER intervention (overall satisfaction, easy to understand, relevant, useful, likelihood to use the skills learned and to recommend to others, and easy to use a zoom platform: M = 8.2–9.5). Lowest rating was feeling connected with the instructor (M = 8.1).

Table 2. Primary outcome: ER treatment appraisal, satisfaction and acceptability ratings (n = 50)

Item response scale (0-10)	M	SD	Mode
1) Please rate your overall satisfaction with the class.	8.6	2.0	10
2) Was the content easy to understand?	9.5	1.0	10
3) How relevant was the class to you?	8.6	2.0	10
4) How useful was the information presented in the class?	8.2	2.4	10
5) How likely are you to use the skills and information you learned?	8.4	2.1	10
6) Rate your likelihood to recommend this class to another person who has chronic pain.	8.3	2.4	10
Please indicate how much you agree with the following statements:			
7) It was easy for me to operate Zoom as a platform for attending the class.	8.8	3.4	10
8) While attending the Zoom class, I worried about privacy.	7.3	2.2	10
9) I felt comfortable engaging with the Zoom instructor and class participants.	8.4	2.5	10
10) I felt connected to the instructor.	8.1	2.1	10
Item responses (see below note for the three response options)	R.1	R.2	R.3
	n (%)	n (%)	n (%)
11) Would you prefer to have a single class (2 hours) or two classes (1 hour each)?	43 (84.3)	5 (9.8)	2 (3.9)

Note: Three responses were R.1: Prefer single, 2-hour class; R.2. Prefer 1-hour two classes; R.3. Other.

Content Analysis of Qualitative Data

At the end of the study, participants provided feedback about the study processes by responding to a set of questions related to class content, discomfort experienced during the class, suggestions for future participants, technical issues operating zoom, concerns about the recruitment methods, and suggestions for better advertising methods.

In analyzing feedback on class content, all participants reported the class content easy to understand and did not report any discomfort with the class material. Six participants reported that no changes were needed for future participants, while others suggested more advanced material (n=2), more time to process the class content (n = 1), a more interactive component (n=1), greater sharing

of personal experiences by the moderators ($n=1$), more breaks ($n=1$), and more reminder calls ($n=1$). Only two participants experienced technical issues with zoom and required additional support in downloading the relaxation audio file. Regarding the recruitment process, 13 out of 14 participants did not express concerns, and one participant requested a specified timeframe for receiving a follow-up call after initial contact. Finally, for feedback regarding advertising, participants suggested expanding outreach through social media and video advertising (e.g., Facebook, TikTok), printed materials and advertisements on college campuses, direct referrals from physicians (including those in palliative care, pain management, and primary care), flyers in clinic waiting rooms, curated patient lists with targeted email invitations, and referrals from past participants.

Preliminary Efficacy

Repeated Measures ANOVAs were conducted to examine if our primary variables of interest (pain catastrophizing, average pain intensity, pain bothersomeness, and sleep disturbance) would be significantly improved after ER intervention (Table 3). The results revealed a significant main effect of time only in PCS total scores, average pain intensity, and pain bothersomeness. However, with post-hoc Bonferroni correction applied (summarized in Table 4) the PCS effect over time was lost ($p > .358$) while average pain intensity and pain bothersomeness retained significance (Figure 3). Compared to the baseline ($M = 6.49$, $SD = 1.70$), pain intensity was significantly reduced at 2-week ($M_{DIFF} = 0.55$, $p = .0495$, $d = 0.41$) and 1-month post-treatment ($M_{DIFF} = 0.86$, $p = .0001$, $d = 0.41$), but no significant reduction was found at 2-month ($p = .2167$) and 3-month posttreatment ($p = .5018$). For pain bothersomeness, however, compared to the baseline ($M = 6.92$, $SD = 2.05$), it was significantly reduced at 2-week ($M_{DIFF} = 0.81$, $p = .0339$, $d = 0.43$) and 1-month post-treatment ($M_{DIFF} = 0.956$, $p = .0033$, $d = 0.54$) and this reduction maintained at 2-month ($M_{DIFF} = 1.05$, $p = .0102$, $d = 0.49$) and 3-month posttreatment ($M_{DIFF} = 0.94$, $p = .0299$, $d = 0.44$).

Taken together, our hypotheses were partially supported. Different from our hypotheses, pain catastrophizing and sleep disturbance were not significantly reduced after ER intervention, but pain intensity and pain bothersomeness were significantly reduced to a moderate degree at 1-month post-treatment. Only pain bothersomeness reduction remained significant at the 3 month time point (durability time point).

Table 3. Repeated measures ANOVA for outcome measures (n = 51)

Measures		Type III Sum of Squares	<i>df</i> *	<i>F</i>	<i>p</i>	η^2		
PCS		Time	590.92	3.2	3.01	.029	.057	
		Error	9820.59	159.5				
Average pain intensity		Time	19.53	3.0	3.90	.010	.072	
		Error	250.68	151.49				
Pain bothersomeness		Time	37.36	3.6	4.73	.002	.086	
		Error	394.79	180.5				
PROMIS	Sleep disturbance	Time	185.38	3.2	1.74	.156	.034	
		Error	5315.61	160.4				
	Pain interference	Time	476.74	3.1	8.53	< .001	.146	
		Error	2796.21	153.0				
	Physical function	Time	53.15	3.7	1.98	.105	.038	
		Error	1345.59	186.23				
	Fatigue	Time	193.14	3.5	1.37	.250	.027	
		Error	7058.26	177.2				
	Depression	Time	211.51	3.5	1.89	.123	.036	
		Error	5586.66	174.3				
	Anxiety	Time	77.91	3.1	0.60	.623	.012	
		Error	6483.81	157.1				
	Social Isolation	Time	217.05	3.1	1.67	.173	.032	
		Error	6488.51	155.4				
	Opioid craving scale (0 – 10)		Time	22.46	2.9	2.94	.037	.056
			Error	381.73	145.1			

Note: *adjusted *df* using the Greenhouse-Geisser correction. Eta-squared (η^2) of 0.01, 0.06, and 0.14 would indicate small, medium, and large, respectively.

Table 4 Post-hoc Bonferroni-corrected time-effect comparisons between the baseline and follow-ups (n = 51)

	Time points	<i>M</i>	<i>SD</i>	<i>M</i> _{DIFF}	<i>SE</i> _{DIFF}	<i>p</i>	<i>d</i> *
PCS total scores	Baseline	20.18	13.53	Ref.	Ref.	Ref.	Ref.
	2-week	17.49	9.72	2.69	1.40	.610	0.27
	1-month	19.40	10.65	0.78	1.31	>.999	0.08
	2-month	16.26	9.96	3.91	1.81	.358	0.30
	3-month	16.73	11.82	3.45	1.60	.361	0.30
Average pain intensity	Baseline	6.49	1.70	Ref.	Ref.	Ref.	Ref.
	2-week	5.94	1.73	0.55	0.19	<.050	0.41
	1-month	5.63	1.65	0.86	0.17	<.001	0.41
	2-month	5.96	1.60	0.53	0.22	.217	0.71
	3-month	5.94	1.73	0.55	0.28	.502	0.70
Pain bothersomeness	Baseline	6.92	2.05	Ref.	Ref.	Ref.	Ref.
	2-week	6.11	1.78	0.81	0.26	.034	0.43
	1-month	5.97	1.92	0.96	0.25	.003	0.54
	2-month	5.88	1.86	1.05	0.30	.010	0.49
	3-month	5.98	1.99	0.94	0.30	.030	0.44
PROMIS-pain interference	Baseline	67.78	5.40	Ref.	Ref.	Ref.	Ref.
	2-week	64.08	5.44	3.70	0.88	.001	0.59
	1-month	64.73	4.68	3.05	0.70	<.001	0.61
	2-month	64.33	5.62	3.45	0.88	.003	0.55
	3-month	64.47	6.46	3.32	0.96	.011	0.49
Craving	Baseline	2.69	3.48	Ref.	Ref.	Ref.	Ref.
	2-week	2.41	2.90	0.28	0.28	>.999	0.14
	1-month	2.51	2.81	0.18	0.33	>.999	0.08
	2-month	1.83	2.34	0.86	0.36	.227	0.33
	3-month	2.17	2.64	0.52	0.33	>.999	0.23

Ref. refers to a reference time point. *d** was calculated from paired-sample t-tests.

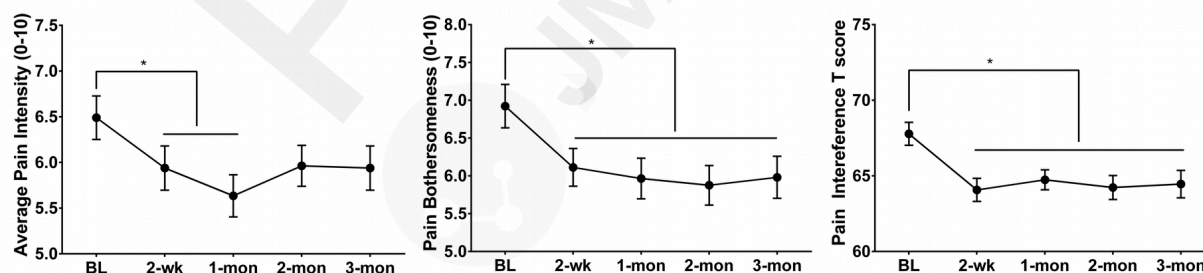


Figure 3. Results with Bonferroni correction revealed significant changes in average pain intensity (Left), pain bothersomeness (Middle), and PROMIS-Pain Interference T scores (Right). * $p < .05$, error bars = SEM

Preliminary Efficacy – additional measures

Repeated Measures ANOVAs were performed to examine if pain interference, physical function, fatigue, depression, anxiety, social isolation, and opioid craving symptoms would be significantly improved after ER intervention (Table 3). The results revealed a significant main effect of time in PROMIS-pain interference T-scores and opioid craving. Application of Bonferroni correction for multiplicity revealed significant changes in PROMIS-pain interference T-scores were retained (Figure 3), but not for craving ($p > .227$, Table 4). Compared to the baseline ($M = 67.78$, $SD = 5.40$), pain interference T-scores were significantly reduced at 2-week ($M_{DIFF} = 3.70$, $p = .0011$, $d = 0.59$) and 1-month post-treatment ($M_{DIFF} = 3.05$, $p = .0007$, $d = 0.61$) and this reduction maintained at 2-month ($M_{DIFF} = 3.45$, $p = .0026$, $d = .55$) and 3-month post-treatment ($M_{DIFF} = 3.32$, $p = .0111$, $d = .49$, Figure 3). Taken together, our hypotheses were partially supported. Among our additional measures, a moderate reduction was observed only in pain interference at 1-month post-treatment (efficacy endpoint) and this reduction maintained at 3 months post-treatment (durability time point).

Finally, ratings on the 6-item GIC measures were analyzed to examine perceived improvement at 1-month and 3-month post-treatment compared to baseline (Table 5). The overall improvement rating was minimum at 1- ($M = 4.5$, $SD = 1.1$) and 3-month post-treatment ($M = 4.5$, $SD = 1.2$). Regarding pain improvement, 17 participants (37.0%) at 1-month post-treatment and 21 participants (42.9%) at 3-month post-treatment rated 5 or higher on the GIC pain item.

Table 5. The GIC ratings on the six domains

	1-month post-treatment (n = 46)					3-month post-treatment (n = 49)				
Improvement in:	<i>M</i>	<i>SD</i>	Min	Max	> 4 (%)	<i>M</i>	<i>SD</i>	Min	Max	> 4 (%)
Overall	4.5	1.1	2	6	52.2	4.5	1.2	2	7	51.0
Physical activity	4.5	0.9	2	6	41.3	4.4	1.1	2	6	46.9
Social activity	4.3	0.9	2	7	37.0	4.5	1.2	1	7	38.8
Work-related activity	4.3	0.9	2	7	32.6	4.3	1.2	2	7	38.8
Mood	4.2	1.1	2	6	43.5	4.5	1.2	2	7	51.0
Pain	4.4	0.8	2	6	37.0	4.2	1.1	2	6	42.9

Ratings of > 4 would indicate perceived improvement after ER

Adverse Events related to ER intervention

There were no serious adverse (SAEs) and adverse events (AEs) related to the ER intervention. Regarding SAE, one participant reported ER visit for chest and abdominal pain at 2-month post-treatment. The reported AEs included: a) injury (n = 9, fall, sprained ankle, neck and back injury, 2nd degree burn, cat bite), b) infection (n = 7, COVID, flu, infection from cat bite), c) new medical diagnosis (n = 6, rheumatoid arthritis, cancer, aneurysm, R/O brain cyst, and cannabis hyperemesis syndrome), d) medical treatment (n = 6, surgery, injection, ablation, removal of 15 teeth, low dose naltrexone), e) gastrointestinal issue (n=3, bowel obstruction, stomach pain), and f) unhealed wound (n=1).

DISCUSSION

This single-arm pilot study investigated online ER in individuals with chronic pain taking methadone or buprenorphine. The primary goal was to evaluate the feasibility and acceptability of the ER intervention in this population. We also examined the preliminary efficacy of ER for reducing pain catastrophizing, pain intensity, pain bothersomeness and sleep disturbance at 1-month post-treatment, as well as additional outcomes (pain interference, physical function, fatigue, depression, anxiety, social isolation, and opioid craving). Further, we tested the durability of treatment effects at 3-month post-treatment.

Feasibility and Acceptability (Primary outcomes)

The current study demonstrated acceptable feasibility of ER intervention, as indexed by a class attendance rate of 79.7% among consented participants, which exceeded the predefined threshold of 75%. Of the 55 class attenders, only two withdrew their consent and two were lost to follow-up. Additionally, the treatment engagement rate among all eligible participants was 74.3%, calculated as the proportion who attended the ER class. This rate fell within the range reported in other single-arm studies of single-session intervention for chronic pain (56% to 96%).⁵⁸⁻⁶¹ Furthermore, additional evidence of acceptable feasibility might be the recruitment of 74 eligible participants over the course of 18 months, with 69 consenting to participate. However, the initial recruitment challenge should be noted. The original plan was to recruit participants exclusively through physician referrals only from methadone or buprenorphine clinics in the US, aiming to create a homogenous group with automatically verified the use of these medications. However, relying entirely on external physician referrals resulted in zero participants recruitment for eight months. Subsequently, we expanded recruitment by using multiple methods, including physician referrals from pain and addiction clinics, self-referral via research posting on the Stanford Pain Lab website and ClinicalTrials.gov, and email invitations to patients with chronic pain through Stanford Pain Division's research registry.

Participants reported high overall satisfaction with the class ($M = 8.6$ on a 0-10 scale), and high ratings of relevance, usefulness and ease of understanding the material, in addition to high likelihood of using the skills and recommending the class to others ($M_s = 8.3 - 9.5$). Participants also reported high ratings related to feeling connected with the instructor ($M = 8.1$). These ratings indicate strong endorsement of web-based ER intervention. Concerns about privacy during the zoom class were notably high, with higher scores reflecting greater privacy concerns ($M = 7.3$). To minimize privacy concerns during the class, participants were instructed to turn off their cameras and use first name only, and this method was previously used to deliver a group online program for individuals with OUD.⁶² It is worth noting that one participant withdrew from the study after attending the ER class due to discomfort with the fact that this study focused on individuals taking methadone or buprenorphine and concerns about associated stigma. This highlights a potential impact of opioid-related stigma on participant engagement and the need for sensitive approaches when recruiting individuals receiving opioid treatment. Although qualitative interview was conducted to identify areas for improvement, no participants raised privacy concern during the interview, limiting the opportunity to explore this issue. Future study should examine privacy concerns in online group interventions and identify strategies to address them.

Qualitative Data

The current study collected qualitative feedback regarding class content and process, any technical issues, and future recommendations. All participants found the class content easy to understand and did not report any discomfort with the class material. Most participants did not report technical issues with the online surveys, the zoom, and binaural relaxation app. A few participants offered suggestions to improve the content and delivery of ER. For example, two participants requested more advanced content, but one expressed a need for additional time to process the content. This opposite request is expected for group-based intervention. One solution is to provide individualized options after ER session. For example, offering supplemental materials for those

seeking more advanced content and a brief follow-up check-in for participants who need additional process time. Delivery-related suggestions included adding interactive components and time to share personal experiences. These are expected because ER is designed as a didactic format for efficient, scalable delivery. Minor suggestions for improvement will be considered in future study designs.

Preliminary Efficacy

Among our primary preliminary efficacy outcomes, pain intensity and pain bothersomeness evidenced small effects ($d = 0.41$ and 0.43 , respectively) at one month, and the effect was maintained for pain bothersomeness only at the durability time point of 3-month posttreatment ($d = 0.44$). Bonferroni correction lends confidence in these findings as true effects vs. spurious findings. For other efficacy outcomes, pain interference evidenced a moderate effect at 1-month posttreatment ($d = 0.61$) and this effect was maintained 3 months post-treatment ($d = 0.49$). In summary, for the current pilot study, best effects for ER were found for pain bothersomeness up to 3 months, with pain intensity showing initial effects and regression to the mean after one month. As this was the first test in this population, our hypotheses were based on prior studies conducted in other chronic pain populations. However, the current study did not replicate an effect for pain catastrophizing, a finding that is surprising and unique to this patient population taking partial or full-agonist prescription opioids, and with 43% of the sample having OUD.

In multiple other studies, ER was found to significantly and clinically meaningfully reduce pain catastrophizing, with this variable often showing the largest treatment effects and multidimensional benefits. Indeed, randomized controlled trials (RCTs) of ER in general chronic pain have revealed that ER was superior to control and significantly improved multiple variables, including pain catastrophizing, pain intensity, pain bothersomeness, and sleep disturbance, pain interference, physical function, fatigue, depression, anxiety, and social isolation. Specifically, results from one 3-arm RCT in 263 patients with chronic low back pain showed that compared to health education control, in-person ER was significantly reduced all secondary (Glass $ds = 0.54 - 0.93^{36}$) and tertiary outcome measures (Glass $ds = 0.31 - 0.45^{36}$) at 3 months. Another general chronic pain RCT ($N=104$) showed that compared to a waitlist control, online ER was significantly better in improving all secondary outcome measures (Cohen's $ds = 0.60 - 0.67$) at 3 months post-treatment and sleep disturbance was not measured.³⁷ This RCT also showed that compared to the control, online ER was significantly better in improving some of the tertiary outcome measures at 3 months post-treatment such as anxiety and anger (Cohen's $ds = 0.68$ and 0.59 , respectively), but no significant between group differences were found for pain interference, physical function, and social isolation at 3 months.³⁷ These two controlled chronic pain trials suggest that regardless of delivery method (in-person or online), ER significantly improved pain catastrophizing, pain intensity, and pain bothersomeness to a moderate to large degree, but pain interference was moderately improved only after in-person ER (Glass $d = 0.64$).^{29,36}

The surprising lack of effects for pain catastrophizing and other variables in the current trial may relate to OUD, to prescription opioids, or both. To the latter, some efficacy evidence exists for ER in patients taking daily prescription opioids. A single arm study examined the feasibility and preliminary efficacy of online ER in 41 individuals who were prescribed daily opioids (≥ 10 morphine-equivalent daily dose) including both short and long-acting medications.³⁸ This study found a significant small improvement in pain catastrophizing, pain intensity, and pain interference at 3-months posttreatment (Cohen's $ds = 0.27 - 0.39$). The current study suggests that improvements in pain-related outcomes after ER intervention may not always be accompanied by reduction in pain catastrophizing, which was initially considered a primary mechanism of change. Two ER randomized controlled trials conducted in surgical patients similarly found no effect for pain catastrophizing but significant effects for reducing opioid use and pain after surgery,^{34,63} though in these studies a floor effect for pain catastrophizing at baseline is likely.

Finally, it is unclear whether additional treatment "dosing" might yield effects on pain catastrophizing and other variables where no effects were observed (e.g., opioid craving). For

instance, booster sessions, intensive or multi-session interventions, or a different type of treatment may be needed to reduce pain catastrophizing and further optimize outcomes in this population. Multi-session, behavioral interventions for chronic pain have shown slightly different patterns, demonstrating consistent efficacy in opioid-related outcomes, but limited effect on pain-related outcomes for this population. Specifically, multi-session CBT and MORE consistently demonstrated reductions in opioid misuse, opioid craving, and other substance use,^{21,23-25} but their effects on pain-related outcomes were predominantly non-significant.²¹⁻²⁵ This contrasting pattern may be attributable to differences in sample characteristics related to OUD and pain status. The CBT and MORE studies recruited participants taking methadone for OUD^{21,24} whereas the current study recruited participants taking methadone or buprenorphine for either chronic pain or OUD. As a result, 52.9% of our participants were taking buprenorphine, and 43.1% had a current OUD diagnosis. Craving levels in our sample were low at baseline ($M = 2.7$ on a 0-10 scale) and remained low throughout the 3-month follow-up period ($M_s = 1.8 \sim 2.5$), in contrast to its levels in the MORE study sample at baseline ($M = 4.5$ on a 0-10 scale). Conversely, baseline pain levels were higher in our sample ($M = 6.5$, $SD = 1.7$) compared to those in the CBT ($M = 5.9$, $SD = 1.5$)²¹ and MORE ($M = 4.7$, $SD = 3.1$)²⁴ studies. These differences in OUD and pain characteristics should be considered when comparing treatment outcomes. Additionally, treatment hours should be taken into account: the current outcomes are based on a single-session intervention (2 hours) whereas other outcomes are based on 12-session CBT (6-9 hours) and 8-session MORE (16 hours).

Limitations

Our findings should be interpreted considering study limitations. First, this single-arm pilot trial was primarily designed to examine the feasibility and acceptability of ER in individuals with chronic pain who were taking methadone or buprenorphine. Therefore, inferences about the ER intervention effect cannot be assumed. Additional study is needed, and particularly a randomized controlled trial of ER in this population. Our sample size was sufficient to detect moderate changes over time, but likely underpowered to detect significant small effects. Despite this limitation, several outcomes remained significant even after a Bonferroni correction was applied to minimize type 1 errors. Furthermore, we reported results using both linear trend replacement and pair-wise deletion (see supplement). Consistent results across these two methods indicate that our results were reliable regardless of the methods used to address missing data. The study sample consisted of predominantly white, non-Hispanic/Latino, educated individuals, with high rates of unemployment, which limits study generalizability. Future trials should examine ER efficacy in diverse and underserved patient populations who often experience greater barriers to treatment.⁶⁴ Lastly, our initial recruitment strategy focused only on methadone or buprenorphine clinics, but this strategy was unsuccessful for the first 8 months. Subsequently, we expanded recruitment to include pain clinics and self-referrals and then, we recruited only one participant from a methadone or buprenorphine clinic. Future research may consider using additional engagement strategies to better reach individuals receiving care at methadone or buprenorphine clinics, who often lack access to effective behavioral pain interventions.

Conclusions

Our findings suggest that online ER appears feasible and is a promising intervention that may improve pain-related outcomes in individuals with chronic pain taking methadone and buprenorphine. Disseminating brief, accessible, and scalable pain psychology interventions, such as ER, may enhance more equal access to effective behavioral pain treatments and reduce pain burden. A fully powered randomized controlled trial in diverse patient participants is needed to determine ER efficacy in patients chronic pain who are receiving methadone or buprenorphine for chronic pain or OUD.

Appendix 1.1 Repeated measures ANOVA for outcome measures up to the primary study endpoint (1-month)

Measures		n		Type III Sum of Squares	df^*	F	p	η^2
PCS		43	Time	126.62	1.5	2.30	.121	.052
			Error	2312.71	64.5			
Average pain intensity		46	Time	14.97	2.0	9.14	< .001	.169
			Error	73.70	89.3			
Pain bothersomeness		46	Time	18.36	1.9	6.06	.004	.119
			Error	136.30	87.0			
PROMIS	Sleep disturbance	43	Time	37.04	1.8	1.21	.301	.028
			Error	1283.73	76.6			
	Pain interference	43	Time	262.58	1.7	10.24	< .001	.196
			Error	1077.40	70.7			
	Physical function	43	Time	14.40	1.9	1.32	.271	.031
			Error	456.75	81.1			
	Fatigue	43	Time	32.18	1.7	0.73	.468	.017
			Error	1854.19	73.1			
	Depression	43	Time	79.50	1.6	1.94	.159	.044
			Error	1719.82	68.3			
	Anxiety	43	Time	32.34	1.8	0.68	.493	.016
			Error	1997.04	74.7			
	Social Isolation	43	Time	27.21	1.9	0.59	.545	.014
			Error	1926.00	79.0			
	Opioid craving scale	43	Time	2.67	1.5	0.86	.396	.020
			Error	130.00	61.3			

Note: *adjusted df using the Greenhouse-Geisser correction

Appendix 1.2 Pairwise T-test to compare outcomes at the baseline and follow-up points

		Baseline		Post-Treatment							
		M	SD		n	M	SD	M _{DIFF}	SE _{DIFF}	<i>p</i>	<i>d</i>
Average intensity	pain	6.4	1.7	2-week	46	5.9	1.8	0.46	0.19	.023	0.26
		6.5	1.7	1-month	49	5.6	1.4	0.86	0.17	< .001	0.51
		6.4	1.7	2-month	42	6.0	1.8	0.48	0.24	.058	0.28
		6.5	1.7	3-month	49	5.9	1.7	0.57	0.28	.050	0.33
Pain bothersomeness		6.8	2.1	2-week	46	6.1	1.9	0.74	0.28	.011	0.37
		7.0	2.1	1-month	49	6.0	2.0	1.00	0.26	< .001	0.50
		6.9	2.1	2-month	42	5.9	2.1	1.00	0.34	.006	0.48
		6.9	2.1	3-month	49	6.0	2.0	0.96	0.31	.003	0.47
PROMIS-pain interference		67.9	5.7	2-week	46	64.1	5.7	3.84	0.97	< .001	0.68
		67.5	5.4	1-month	46	64.7	4.9	2.82	0.72	< .001	0.55
		67.5	5.7	2-month	42	64.3	6.2	3.17	1.03	.004	0.53
		67.8	5.5	3-month	49	64.5	6.6	3.29	0.99	.002	0.54

REFERENCE

1. Yong RJ, Mullins PM, Bhattacharyya N. Prevalence of chronic pain among adults in the United States. *Pain*. 2022;163(2):e328–e332.
2. Zajacova A, Grol-Prokopczyk H, Limani M, Schwarz C, Gilron I. Prevalence and correlates of prescription opioid use among US adults, 2019–2020. *PLoS One*. 2023;18(3):e0282536.
3. Lazaridou A, Paschali M, Edwards RR, Gilligan C. Is buprenorphine effective for chronic pain? A systematic review and meta-analysis. *Pain Med*. 2020;21(12):3691–3699.
4. Papa A, Salzano AM, Di Dato MT, et al. Long-term efficacy and reduced side-effects of buprenorphine in patients with moderate and severe chronic pain. *Front Pharmacol*. 2024;15:1454601.
5. Neumann AM, Blondell RD, Jaanimägi U, et al. A preliminary study comparing methadone and buprenorphine in patients with chronic pain and coexistent opioid addiction. *J Addict Dis*. 2013;32(1):68–78.
6. Jamison RN, Kauffman J, Katz NP. Characteristics of methadone maintenance patients with chronic pain. *J Pain Symptom Manage*. 2000;19(1):53–62.
7. Delorme J, Pennel L, Brousse G, et al. Prevalence and characteristics of chronic pain in buprenorphine- and methadone-maintained patients. *Front Psychiatry*. 2021;12:641430.
8. Latif ZEH, Skjærvø I, Solli KK, Tanum L. Chronic pain among patients with an opioid use disorder. *Am J Addict*. 2021;30(4):366–375.
9. Macey TA, Weimer MB, Grimaldi EM, Dobscha SK, Morasco BJ. Patterns of care and side effects for patients prescribed methadone for treatment of chronic pain. *J Opioid Manag*. 2013;9(5):325–333.
10. Van Denburg AN, Vilaradaga JP, Shelby RA, Keefe FJ. Opioid therapy and persistent pain: can cognitive behavioral therapy help? *Pain*. 2018;159(3):411–415.
11. Majeed MH, Sudak DM. Cognitive behavioral therapy for chronic pain—One therapeutic approach for the opioid epidemic. *J Psychiatr Pract*. 2017;23(6):409–414.
12. Wilson M, Dolor RJ, Lewis D, Regan SL, Vonder Meulen MB, Winhusen TJ. 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. *Pain*. 2023;164(4):877–885.
13. Avery N, McNeillage AG, Stanaway F, et al. Efficacy of interventions to reduce long-term opioid treatment for chronic non-cancer pain: systematic review and meta-analysis. *BMJ*. 2022;377:e070520.
14. Garland EL, Brintz CE, Hanley AW, et al. Mind-body therapies for opioid-treated pain: a systematic review and meta-analysis. *JAMA Intern Med*. 2020;180(1):91–105.
15. Rhodin A, Grönbladh L, Nilsson LH, Gordh T. Methadone treatment of chronic non-malignant pain and opioid dependence—a long-term follow-up. *Eur J Pain*. 2006;10(3):271–278.
16. Webster L, Gudín J, Raffa RB, et al. Understanding buprenorphine for use in chronic pain: expert opinion. *Pain Med*. 2020;21(4):714–723.
17. Dematteis M, Auriacombe M, D’Agnone O, et al. Recommendations for buprenorphine and methadone therapy in opioid use disorder: a European consensus. *Expert Opin Pharmacother*. 2017;18(18):1987–1999.
18. Fipps DC, Oesterle TS, Kolla BP. Opioid maintenance therapy: A review of methadone, buprenorphine, and naltrexone treatments for opioid use disorder. *Semin Neurol*. 2024; 44 (04):441-451.
19. Yang J, Jung M, Picco L, et al. Pain in people seeking and receiving opioid agonist treatment: a systematic review and meta-analysis of prevalence and correlates. *Addiction*. 2024;119(11):1879–1901.
20. Delorme J, Kerckhove N, Authier N, Pereira B, Bertin C, Chenaf C. Systematic review and meta-analysis of the prevalence of chronic pain among patients with opioid use disorder and

- receiving opioid substitution therapy. *J Pain*. 2023;24(2):192–203.
21. Barry DT, Beitel M, Cutter CJ, et al. An evaluation of the feasibility, acceptability, and preliminary efficacy of cognitive-behavioral therapy for opioid use disorder and chronic pain. *Drug Alcohol Depend*. 2019;194:460–467.
 22. Barry DT, Savant JD, Beitel M, et al. The feasibility and acceptability of groups for pain management in methadone maintenance treatment. *J Addict Med*. 2014;8(5):338–344.
 23. Cooperman NA, Hanley AW, Kline A, Garland EL. A pilot randomized clinical trial of mindfulness-oriented recovery enhancement as an adjunct to methadone treatment for people with opioid use disorder and chronic pain: impact on illicit drug use, health, and well-being. *J Subst Abuse Treat*. 2021;127:108468.
 24. Garland EL, Hanley AW, Kline A, Cooperman NA. Mindfulness-oriented recovery enhancement reduces opioid craving among individuals with opioid use disorder and chronic pain in medication-assisted treatment: ecological momentary assessments from a stage 1 randomized controlled trial. *Drug Alcohol Depend*. 2019;203:61–65.
 25. Cooperman NA, Lu S-E, Hanley AW, et al. Telehealth mindfulness-oriented recovery enhancement vs usual care in individuals with opioid use disorder and pain: a randomized clinical trial. *JAMA Psychiatry*. 2024;81(4):338–346.
 26. Darnall BD, Scheman J, Davin S, et al. Pain psychology: a global needs assessment and national call to action. *Pain Med*. 2016;17(2):250–263.
 27. Baker MB, Liu EC, Bully MA, et al. Overcoming barriers: a comprehensive review of chronic pain management and accessibility challenges in rural America. *Healthcare*. 2024;12(10):1765.
 28. Langenbahn D, Matsuzawa Y, Lee YSC, et al. Underuse of behavioral treatments for headache: a narrative review examining societal and cultural factors. *J Gen Intern Med*. 2021;36(10):3103–3112.
 29. Darnall BD, Roy A, Chen AL, et al. Comparison of a single-session pain management skills intervention with a single-session health education intervention and 8 sessions of cognitive behavioral therapy in adults with chronic low back pain: a randomized clinical trial. *JAMA Netw Open*. 2021;4(8):e2113401.
 30. Darnall BD, Roy A, Chen AL, et al. Comparison of a single-session pain management skills intervention with a single-session health education intervention and 8 sessions of cognitive behavioral therapy in adults with chronic low back pain: a randomized clinical trial. *JAMA Netw Open*. 2021;4(8):e2113401.
 31. Ziadni MS, Gonzalez-Castro L, Anderson S, Krishnamurthy P, Darnall BD. Efficacy of a single-session “Empowered Relief” Zoom-delivered group intervention for chronic pain: randomized controlled trial conducted during the COVID-19 pandemic. *J Med Internet Res*. 2021;23(9):e29672.
 32. Perez L, Palenski P, Adair E, et al. Online 1-session Empowered Relief in Marfan syndrome and related diseases: a single-arm feasibility and pilot efficacy study. In review.
 33. Watson H, Bindler R, Perez L, Darnall BD, Wilson M. Randomized controlled trial of nurse-delivered online Empowered Relief for chronic pain. In review.
 34. Ziadni M, You DS, Keanne RT, et al. “My Surgical Success”: feasibility and impact of a single-session digital behavioral pain medicine intervention on pain intensity, pain catastrophizing, and time to opioid cessation after orthopedic trauma surgery—a randomized trial. *Anesth Analg*. 2022;135(3):614–625.
 35. Darnall BD, Burns JW, Hong J, et al. Empowered Relief, cognitive behavioral therapy, and health education for people with chronic pain: a comparison of outcomes at 6-month follow-up for a randomized controlled trial. *Pain Rep*. 2024;9(1):e1116.
 36. Darnall BD, Burns JW, Hong J, et al. Empowered Relief, cognitive behavioral therapy, and health education for people with chronic pain: a comparison of outcomes at 6-month follow-up

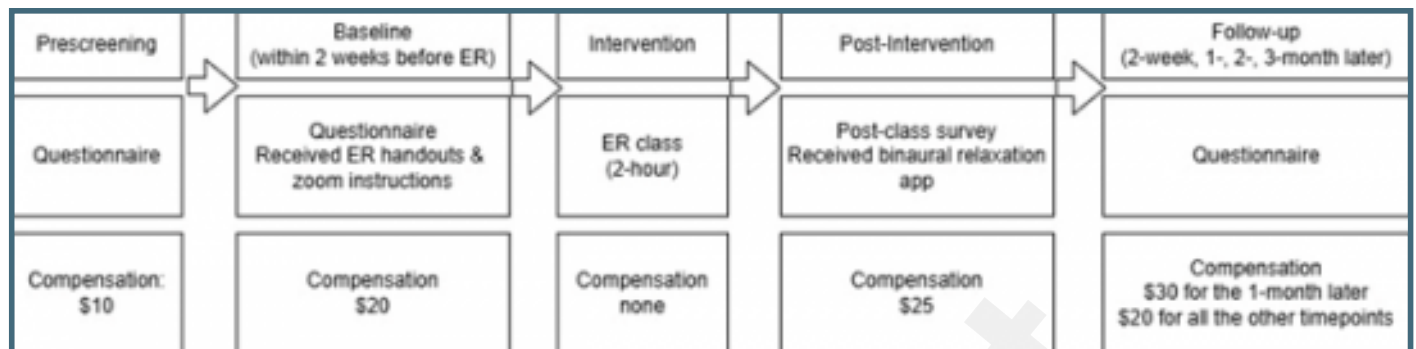
- for a randomized controlled trial. *Pain Rep.* 2024;9(1):e1116.
37. Ziadni MS, Gonzalez-Castro L, Anderson S, Krishnamurthy P, Darnall BD. Efficacy of a single-session “Empowered Relief” Zoom-delivered group intervention for chronic pain: randomized controlled trial conducted during the COVID-19 pandemic. *J Med Internet Res.* 2021;23(9):e29672.
 38. Edwards KA, Dildine TC, You DS, et al. Zoom-delivered Empowered Relief for chronic pain: observational longitudinal pilot study exploring feasibility and pain-related outcomes in patients on long-term opioids. *JMIR Form Res.* 2025;9(1):e68292.
 39. Klein MR, Darnall BD, You DS. Feasibility of web-based single-session Empowered Relief in patients with chronic pain taking methadone or buprenorphine: protocol for a single-arm trial. *JMIR Res Protoc.* 2024;13(1):e53784.
 40. You DS, Mardian AS, Darnall BD, et al. A brief screening tool for opioid use disorder: EMPOWER study expert consensus protocol. *Front Med.* 2021;8:591201.
 41. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.) 2013.
 42. Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. *Psychol Assess.* 1995;7(4):524.
 43. Stone AA, Broderick JE, Junghaenel DU, Schneider S, Schwartz JE. PROMIS fatigue, pain intensity, pain interference, pain behavior, physical function, depression, anxiety, and anger scales demonstrate ecological validity. *J Clin Epidemiol.* 2016;74:194–206.
 44. Edwards KA, You DS, Lannon EW, Dildine TC, Darnall BD, Mackey SC. Beyond pain intensity: Validating single-item pain bothersomeness measures. *J Pain.* 2025;31:105395.
 45. Yu L, Buysse DJ, Germain A, et al. Development of short forms from the PROMIS™ sleep disturbance and sleep-related impairment item banks. *Behav Sleep Med.* 2012;10(1):6–24.
 46. Koffel E, Kroenke K, Bair MJ, Leverty D, Polusny MA, Krebs EE. The bidirectional relationship between sleep complaints and pain: Analysis of data from a randomized trial. *Health Psychol.* 2016;35(1):41.
 47. Hah JM, Sturgeon JA, Zocca J, Sharifzadeh Y, Mackey SC. Factors associated with prescription opioid misuse in a cross-sectional cohort of patients with chronic noncancer pain. *J Pain Res.* 2017;10:979–987.
 48. Lintzeris N, Moodley R, Campbell G, et al. Sleep quality among people living with chronic noncancer pain: Findings from the Pain and Opioids IN Treatment (POINT) cohort. *Clin J Pain.* 2016;32(5):380–387.
 49. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *J Clin Epidemiol.* 2010;63(11):1179–1194.
 50. Amtmann D, Cook KF, Jensen MP, et al. Development of a PROMIS item bank to measure pain interference. *Pain.* 2010;150(1):173–182.
 51. Schalet BD, Hays RD, Jensen SE, Beaumont JL, Fries JF, Cella D. Validity of PROMIS physical function measured in diverse clinical samples. *J Clin Epidemiol.* 2016;73:112–118.
 52. Cella D, Lai JS, Jensen SE, et al. PROMIS fatigue item bank had clinical validity across diverse chronic conditions. *J Clin Epidemiol.* 2016;73:128–134.
 53. Schalet BD, Pilkonis PA, Yu L, et al. Clinical validity of PROMIS depression, anxiety, and anger across diverse clinical samples. *J Clin Epidemiol.* 2016;73:119–127.
 54. McHugh RK, Fitzmaurice GM, Carroll KM, et al. Assessing craving and its relationship to subsequent prescription opioid use among treatment-seeking prescription opioid-dependent patients. *Drug Alcohol Depend.* 2014;145:121–126.
 55. Scott W, McCracken LM. Patients’ impression of change following treatment for chronic pain: Global, specific, a single dimension, or many? *J Pain.* 2015;16(6):518–526.

56. Darnall BD, Sturgeon JA, Kao MC, Hah JM, Mackey SC. From catastrophizing to recovery: A pilot study of a single-session treatment for pain catastrophizing. *J Pain Res.* 2014;7:219–226.
57. Guzman G, Kollar M. Income in the United States: 2022. United States Census Bureau; 2023. Accessed October 17, 2025. <https://www.census.gov/content/dam/Census/library/publications/2023/demo/p60-279.pdf>
58. Costa F, Janela D, Molinos M, et al. Digital rehabilitation for hand and wrist pain: A single-arm prospective longitudinal cohort study. *Pain Rep.* 2022;7(5):e1026.
59. Azizoddin DR, Zhao J, DeForge SM, et al. Initial feasibility and acceptability of Cancer Pain 101: An interdisciplinary, single-session, telehealth intervention for patients with cancer-related pain. *Cancer Med.* 2025;14(9):e70898.
60. Payne LA, Seidman LC, Romero T, Sim MS. An open trial of a mind-body intervention for young women with moderate to severe primary dysmenorrhea. *Pain Med.* 2020;21(7):1385–1392.
61. Yamin JB, Wilson JM, Pester BD, et al. Feasibility and acceptability of a single-session perioperative acceptance and commitment therapy workshop for preventing chronic postsurgical pain: A single-arm, nonrandomized pilot trial. *Front Pain Res.* 2025;6:1558753.
62. Moore DJ, Goyal D, Rodriguez L. Experiences of opioid use disorder patients receiving buprenorphine through a telehealth program. *J Addict Nurs.* 2021;32(3):205–210.
63. Darnall BD, Ziadni MS, Krishnamurthy P, et al. My surgical success: Effect of a digital behavioral pain medicine intervention on time to opioid cessation after breast cancer surgery—a pilot randomized controlled clinical trial. *Pain Med.* 2019;20(11):2228–2237.
64. Janevic MR, McLaughlin SJ, Heapy AA, Thacker C, Piette JD. Racial and socioeconomic disparities in disabling chronic pain: Findings from the Health and Retirement Study. *J Pain.* 2017;18(12):1459–1467.

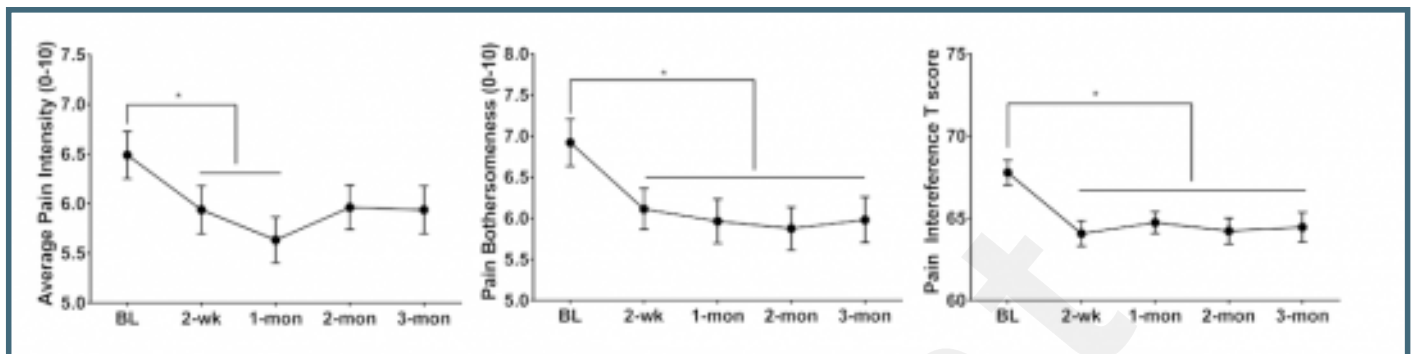
Supplementary Files

Figures

Timeline.



Results with Bonferroni correction revealed significant changes in average pain intensity (left), pain bothersomeness (middle), and PROMIS-Pain Interference T scores (right). Asterisks indicate significant differences ($p < .05$); error bars = SEM.



CONSORT (or other) checklists

Figure 1. Consort Diagram.

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