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ORIGINAL ARTICLE

In-Home Virtual Reality Program for Chronic Lower Back Pain: A Randomized Sham-Controlled Effectiveness Trial in a Clinically Severe and Diverse Sample

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Abstract

Objective: To determine whether an 8-week, self-administered in-home, behavioral skills virtual reality program for chronic low back pain (RelieVRx) that trains diaphragmatic breathing, biofeedback, cognition and emotion regulation, mindfulness, and pain education skills, is superior to a strong active Sham at day 56 for improving pain intensity and pain interference, in a large real-world sample.

Patients and Methods: Participants included a national sample of demographically diverse individuals with self-reported nonmalignant chronic low back pain ≥3 months duration with an average pain intensity and pain interference of ≥4/10. Participants were randomized 1:1 to RelieVRx or active Sham, and data were collected from January 31, 2022, to October 31, 2022. We evaluated group differences in brief pain inventory, pain intensity, and pain interference to day 56 (end of treatment).

Results: Of the 1067 participants (772 women, 293 men, and 2 others; mean ± SD age, 50.8±13.2 years) randomized (1:1) into 2 groups: RelieVRx (n=536) and Sham (n=531) comprised the modified intention-to-treat analytic dataset. RelieVRx was superior to Sham for pain intensity and pain interference reductions from pretreatment to day 56 (difference from Sham, pain intensity: 0.406 [0.170-0.642] and pain interference: 0.523 [0.285-0.760]). Pain intensity and interference reductions for RelieVRx at day 56 were clinically meaningful (pain intensity: 2.0 [out of 10] points [1.73-2.06], pain interference: 2.3 points [1.99-2.33]).

Conclusion: An 8-week self-administered behavioral skills virtual reality program was found to impart clinically meaningful improvements above a strong active control comparison on pain intensity and pain interference in clinically severe and diverse adults with chronic low back pain.

Trial Registration: clinicaltrials.gov Identifier: NCT05263037

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Chronic low back pain (cLBP) is the most prevalent pain condition globally.[1] As clinicians decrease opioid prescribing, effective and accessible low-risk cLBP treatments are needed. Pain education and cognitive behavior therapy (CBT) are recommended as first-line treatments,[2–5] but access is poor due to multisession and therapist-led formats.[6] By combining pain education and evidence-based skills such as diaphragmatic breathing, biofeedback, and mindfulness with easy-to-use in-home immersive technologies like virtual reality (VR),[7] one can target brain regions[8] that are implicated in cLBP[9,10] and are responsive to CBT treatment.[11–14] Thus, VR

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might provide an effective, low-risk, and accessible cLBP treatment.

We previously conducted a double-blind, randomized, placebo-controlled trial (ClinicalTrials.gov NCT04415177) comparing an 8-week RelieVRx program with ShamVR in 188 community-based adults with cLBP.[7,15] Both 56-day treatments were self-administered in-home through VR headsets. Clinically meaningful pain reductions (2 points or ≥30%) [16,17] observed for ReliveVRx were statistically superior to ShamVR and durable up to 24 months posttreatment.[18,19] Two recent reviews found that RelieVRx performed favorably relative to other VR-based cLBP therapies. [20,21]

Limitations of this study included a modest size sample, homogeneity (mainly women, White, and college-educated), and low depressive symptoms.[18] The current study extends previous work by including a large sample of diverse participants with a range of clinical severity and depressive symptoms to better represent real-world patients. Consent for medical records and claims was obtained to facilitate a health care utilization analysis that is forthcoming.

PATIENTS AND METHODS

Study Design and Participants

This double-blind, randomized, placebo-controlled, decentralized clinical trial was conducted in a large (N=1093 adults), diverse national sample of community-based cLBP individuals. The trial compared the effectiveness of RelieVRx with Sham and laid the groundwork for health and economic analysis. The protocol was approved by the WCG Institutional Review Board in December 2021 and followed Consolidated Standards of Reporting Trials reporting guidelines. Informed consent was obtained, and data were collected from January 31, 2022, to October 31, 2022.

Individuals with cLBP were recruited nationally through online advertisements, chronic pain organizations, and clinics. Inclusion criteria included self-reported cLBP of 3+ months, average pain intensity and interference score of ≥4 on the BPI,[22] English fluency, age 18-85 years, internet access and smartphone or computer availability, physical mailing address for device shipping, photo identity document (ID) verification, and completion of the baseline survey, and 2+ of 5 sets of participant surveys administered during the 5-day pretreatment phase. Study participants received $210 for the completion of all study surveys up to day 56 and an additional $635 for completing 1, 2, 3, 6, 12, 18, and 24-months posttreatment follow-up surveys.

Randomization Procedures and Participant Blinding

This is part of a 4-arm study that examines the effectiveness of a program extension introduced after day 56 primary treatment is complete (see appendix). Up until day 56, treatment for pairs of arms was identical. This report focuses on treatment effectiveness to end-of-treatment only and we summarize the 2 primary arms in Figure 1. E-randomization was applied 1:1 with allocation to: (1) a 56-day behavioral skills pain relief VR program (RelieVRx) or (2) a 56-day Sham VR program. Participants were blinded to treatment and remained blinded to 24-months posttreatment.

Data Protection and Investigator Blinding

Participant identification was protected with a unique study identification number. Data were received electronically through Curebase, locked in the database, and stored with double-password protection. The VR device operations team was unblinded to individual group assignments at trial initiation, with the research team remaining blinded until 3 months posttreatment. Once randomized, study devices were mailed to their homes with remote technical support available by phone, email, or text.

Assessment Times and Measures

After eConsent, identification was confirmed through photo ID, and demographic characteristic data were collected, including height and weight (used to compute body mass index [BMI] [calculated as the weight in kilograms divided by the height in meters squared]). The baseline survey was administered after ID verification. This was followed by 5 consecutive days of BPI administration. Completion of at least 2 was required to continue in the trial. Once randomized, twice-weekly intratreatment surveys were administered through day 56, marking the end of the study. All

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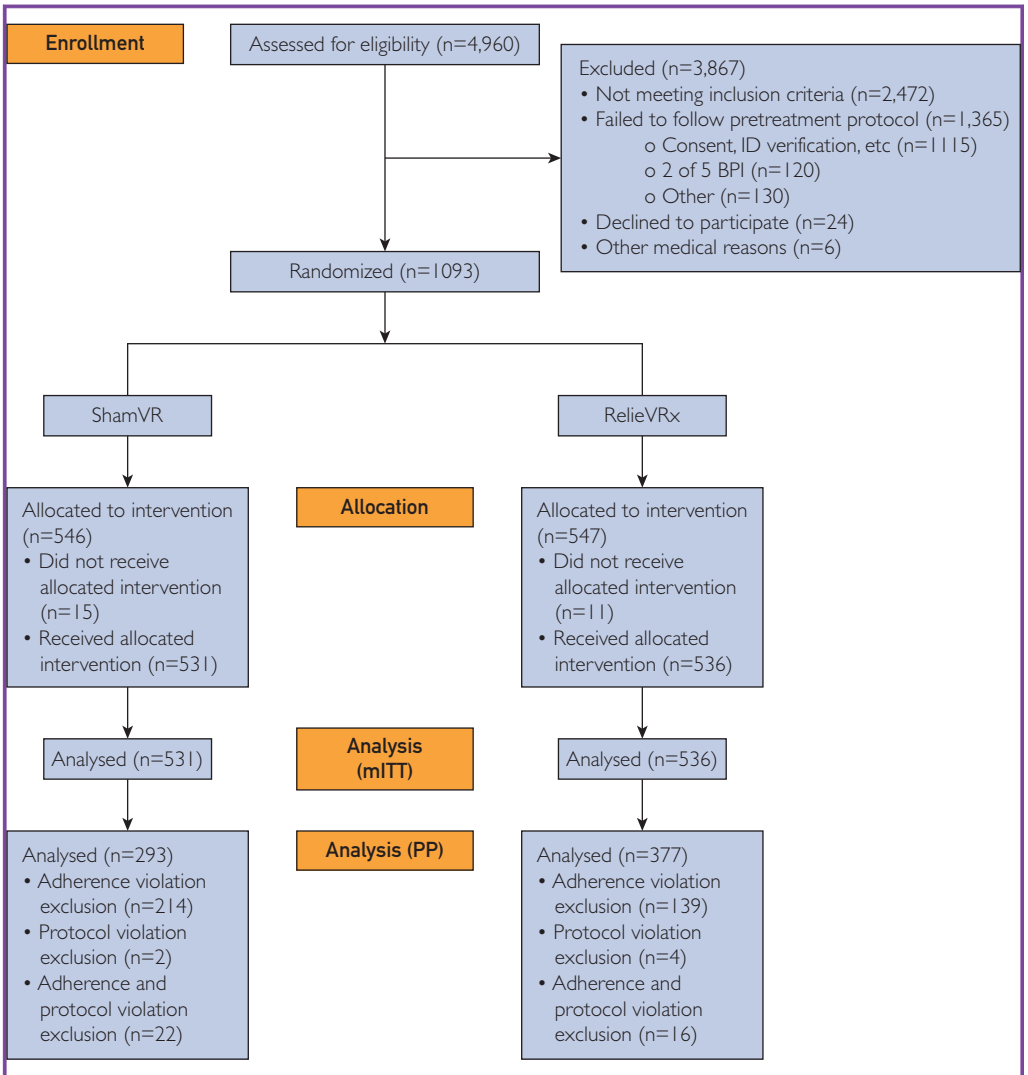

FIGURE 1. CONSORT flow diagram.

data were self-reported, except VR device usage data that were quantified from a VR device upload on device return.

The primary effectiveness outcome for group superiority was the change in the BPI[22] from pretreatment (average of BPI ratings from baseline and pretreatment) to day 56. The BPI measures average pain intensity over the past 24 hours using a 0-10 numeric pain rating scale. Pain interference is assessed across 7 domains of daily life (enjoyment of life, general activity, mood, normal work, relations with other people, sleep, and walking ability), averaged to generate a global pain interference score.[23] Secondary outcomes included the PROMIS short-form for anxiety (version 7a) (T-score range: 36.3-82.7; mild-moderate threshold: 60), depression (version 8b) (T-score range: 37.1-81.1; mild-moderate threshold: 60), sleep disturbance (version 8b) (T-score range: 28.9-76.5; mild-moderate threshold: 60),[24,25] and the Oswestry disability index (ODI). The ODI measures how low back pain affects one's ability to manage in everyday life (version 2.1b);[26] (range: 0-50; mild-moderate threshold: 25). Each measure was evaluated at baseline and day 56. Other self-report measures included

the system usability scale[27] and treatment satisfaction evaluated on day 56, and the VR Comfort Survey to assess dizziness, vertigo, and nausea that was administered once each week during the treatment.

Study Group Interventions

All participants received a Pico G2 4K all-in-one head-mounted VR device at no cost. The Pico G2 4K device has a 3,840 x 2,160 screen resolution, 72 FPS frame rate, and minimal visual latency. The Pico G2 4K allows for displaying 3D images (RelieVRx) and 2D images (ShamVR). At the end-of-treatment, staff managed the postage-paid return of the devices.

Therapeutic VR (RelieVRx)

RelieVRx (AppliedVR) is a Food and Drug Association de novo authorized immersive, multi-modal VR treatment program for cLBP. The 56-day program integrates evidence-based skills such as diaphragmatic breathing, biofeedback, cognition and emotion regulation, mindfulness, and pain education into an 8-week therapeutic journey. Daily immersive experiences are organized into 8 weekly themes. Interactive biodata-enabled therapeutics that capture user exhalation through an embedded microphone provide synchronized 3D visual and auditory biofeedback. The duration of daily VR treatment sessions ranges from 2-16 minutes.

ShamVR

In adherence with VR-CORE clinical trial guidelines, the Sham was active and composed of nonimmersive, 2D visual content.[28] ShamVR content was delivered through the Pico G2 4K, and the participants were told the device was delivering VR treatment. Sham offers a form of focused attention on nature scenes and restricted vision on a display that is similar to a large-screen television. Content included 20 rotating nature videos overlaid with music that were devoid of pain management skills, experiences, or practices. The session duration ranged from 2-16 minutes. All packaging and directions were identical across Sham and RelieVRx. Participants in both groups were instructed to complete 1 treatment session daily for 56 days.

Statistical Analyses

The multi-primary outcome was the between-group pretreatment to end-of-treatment change in BPI pain intensity or pain interference. Study success is declared with a statistically significant result in 1 of the 2 primary end point measures after Hochberg step-up multiplicity correction and alpha splitting. The mixed model for repeated measures (MMRM) using PROC MIXED in SAS Version 9.4 analyzes change scores for both end points. The MMRM model uses an indicator variable for treatment group (RelieVRx or Sham), categorical time factor (pretreatment or end-of-treatment), and treatment group—time factor interaction. Baseline pain intensity or interference, age, sex, and BMI are included as covariates. The MMRM model uses an unstructured covariance matrix for random effects, with alternative formulations (eg, Toeplitz) for nonconverging cases. The contrast evaluating pain score differences between the randomized arms at end-of-treatment is derived from the MMRM. The MMRM imputes missing data on the basis of outcomes observed at earlier time points, and multiple imputation is used for participants with missing baseline and follow-up data.

Primary end point success leads to a responder analysis. Two definitions are used: a $\geq$30% reduction in pain score from pretreatment to end-of-treatment (responder definition #1) or a reduction in pain score of at least 2 points (responder definition #2).[16,17] To be consistent with the MMRM approach for the primary end point, binary responder analyses are performed using PROC GLIMMIX in SAS Version 9.4. Model parameters and a random residual statement are the same as defined for the primary end point. The covariance matrix used in the analysis assumes the same covariance estimate for all measurements an equal number of visits apart.

Prespecified secondary end points are as follows: (a) ODI; (b) PROMIS anxiety; (c) PROMIS sleep disturbance; and (d) PROMIS depression. Secondary end point analyses focus on between-group and within-group differences, with linear regression models used to compare changes between the groups. Models are adjusted for baseline

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values of the end point, age, sex, and BMI. Statistical significance is determined on the basis of a Hochberg step-up procedure to maintain an overall 2-sided type I error rate of 0.05.

All participants randomized were included in the intent-to-treat (ITT) analysis set. The modified ITT (mITT) analysis set includes all ITT participants who received the device and was the primary analysis set. The per protocol (PP) analysis set includes all mITT participants except those who have clinically meaningful violations of inclusion or exclusion criteria or who have posttreatment protocol violations that may reasonably be predicted to impact on effectiveness of the end points (eg, lack of treatment adherence). On the basis of treatment engagement rates in our previous efficacy trial,[7] for the current trial we a priori defined treatment completion as 24 sessions over the 8-week program.

RESULTS

Participants and Sample Characteristics

Figure 1 presents the Consolidated Standards of Reporting Trials diagram. Of the 4960 assessed individuals, 3867 were excluded (detailed in Figure 1). N=1093 participants were enrolled, randomized, and allocated to the treatment groups (ITT). After randomization, 26 did not receive a VR device, leaving 1067 (RelieVRx [n=536] and Sham [n=531]) in the mITT analysis set. The PP analysis set excluded mITT participants with clinically meaningful protocol violations impacting effectiveness of the end points, such as noncompliance. The PP analysis set comprised 670 participants (detailed in Figure 1).

Table 1 summarizes the mITT sample characteristics: 72% women, 50.8 years average age, with broad racial and ethnic diversity. Baseline clinical measures suggest a diverse sample with baseline pain intensity, interference, sleep disturbance, and disability in the moderate to severe range. Only baseline anxiety and depression were mild. No significant group differences were observed except the proportion of women, which serves as a covariate.

VR Device Usage, Device Safety, and Adverse Events

RelieVRx participants completed a total of 37.5 (SD=17.1) daily treatment sessions (4.7 per week) and Sham participants completed 31.0 (SD=19.1) sham treatment sessions (3.9 per week) ($P<.001$). During the treatment, 26 of the 536 participants (4.9%) in RelieVRx and 8 of the 531 participants (1.5%) in Sham reported dizziness, vertigo or nausea, with 5 of the 536 (.9%) of these in RelieVRx and 3 of the 531 (.6%) in Sham being deemed moderate or severe (1 in each group was severe). Treatment withdrawal because of dizziness, vertigo, or nausea occurred for 2 of the 536 participants (.4%) in RelieVRx and 3 of the 531 participants (.6%) in Sham.

Treatment Group Pain Reductions

Figures 2A and Figures 2B display the time course of average pain intensity (Figure 2A) and interference (Figure 2B) for the RelieVRx and Sham mITT groups (standard error bars included), and the RelieVRx vs Sham difference scores. The RelieVRx group reported an average pain intensity drop of 2.0 points from 6.63 to 4.67, yielding an effect size of 1.02, and an average pain interference drop of 2.3 points from 6.21 to 3.95, yielding an effect size of 1.04.

The statistical analysis plan outlined above governed all analyses including the 2 primary outcomes. Primary end point success was observed for both pain intensity and pain interference. On the basis of the MRMM results and after correcting for multiple comparisons, RelieVRx showed a 0.406 (0.170-0.642) point larger improvement in pain intensity ($P<.001$; effect size=0.24) and a 0.523 (0.285-0.760) point larger improvement in pain interference ($P<.001$; effect size=0.26) relative to Sham. Because VR device usage was statistically larger in the RelieVRx group, we replicated the primary end point analysis with VR device usage as a covariate and found RelieVRx superiority for pain intensity and

TABLE 1. Participant Demographic Characteristics and Select Pretreatment Conditions Among the mITT Analysis Set[a]

Characteristic	RelieVRx (n=536)	Sham (n=531)	*P*
Sex			
Woman	411 (76.7)	361 (68)	.006
Man	124 (23.1)	169 (31.8)	
Non-binary	1(0.2)	1 (0.2)	
Race and Ethnicity			.46
American Indian/Alaska Native	4 (0.7)	5 (1.0)	
Asian/Pacific Islander	12 (2.2)	16 (3.0)	
Black/African American	81 (15.1)	95 (27.1)	
Caucasian	370 (69.0)	351 (66.1)	
Hispanic/Latin	18 (3.4)	10 (2.8)	
Multiracial	51 (9.5)	54 (15.4)	
Age (y)	50.4 (13.5)	51.1 (128)	.35
Household annual income			.26
<$10,000	40 (7.5)	44 (8.3)	
$10,000-$19,999	75 (14)	57 (10.7)	
$20,000-$29,999	52 (9.7)	60 (11.3)	
$30,000-$39,999	56 (10.4)	58 (10.9)	
$40,000-$49,999	51 (9.5)	46 (8.7)	
$50,000-$59,999	40 (7.5)	44 (8.3)	
$60,000-$69,999	31 (5.8)	40 (7.5)	
$70,000-$79,999	46 (8.6)	63 (11.9)	
≥$80,000	145 (27.1)	119 (22.4)	
Body mass index	31.3 (7.9)	31.7 (8.4)	.34
BPI pain intensity	6.6 (1.5)	6.7 (1.5)	.35
BPI pain interference	6.2 (1.8)	6.2 (1.8)	.87
PROMIS anxiety	56.1 (9.1)	55.6 (9.5)	.39
PROMIS sleep disturbance	60.7 (7.1)	60.8 (7.3)	.78
PROMIS depression	54.9 (9.3)	54.6 (8.9)	.50
Oswestry disability index (ODI)	41.5 (15.6)	41.0 (16.9)	.61

[a]BPI, brief pain inventory. Data are presented as n (%) or mean ± SD. *P*-value from χ^2 (or Fisher's exact) test comparing RelieVRx with Sham.

pain interference relative to Sham ($P<.001$). Results were also consistent in both the ITT and PP analysis sets.

Pain Score Responder Analysis

Because the primary outcomes were achieved, supportive analyses examining clinically significant pain responses were conducted (30% improvement or 2-point improvement). In the mITT analysis set, RelieVRx had ∼40% higher odds of pain intensity response and ∼50% higher odds of pain interference response, achieving success for both responder end points after Hochberg correction.

Specifically, RelieVRx showed increased prevalence and odds of being a pain intensity responder (30% definition: OR [95% CI]= 1.39 [1.08-1.80], $P=.006$; 2-point definition: OR [95% CI]=1.41 [1.09-1.82], $P<.001$). Similarly, the RelieVRx group reported greater odds of meeting pain interference responder

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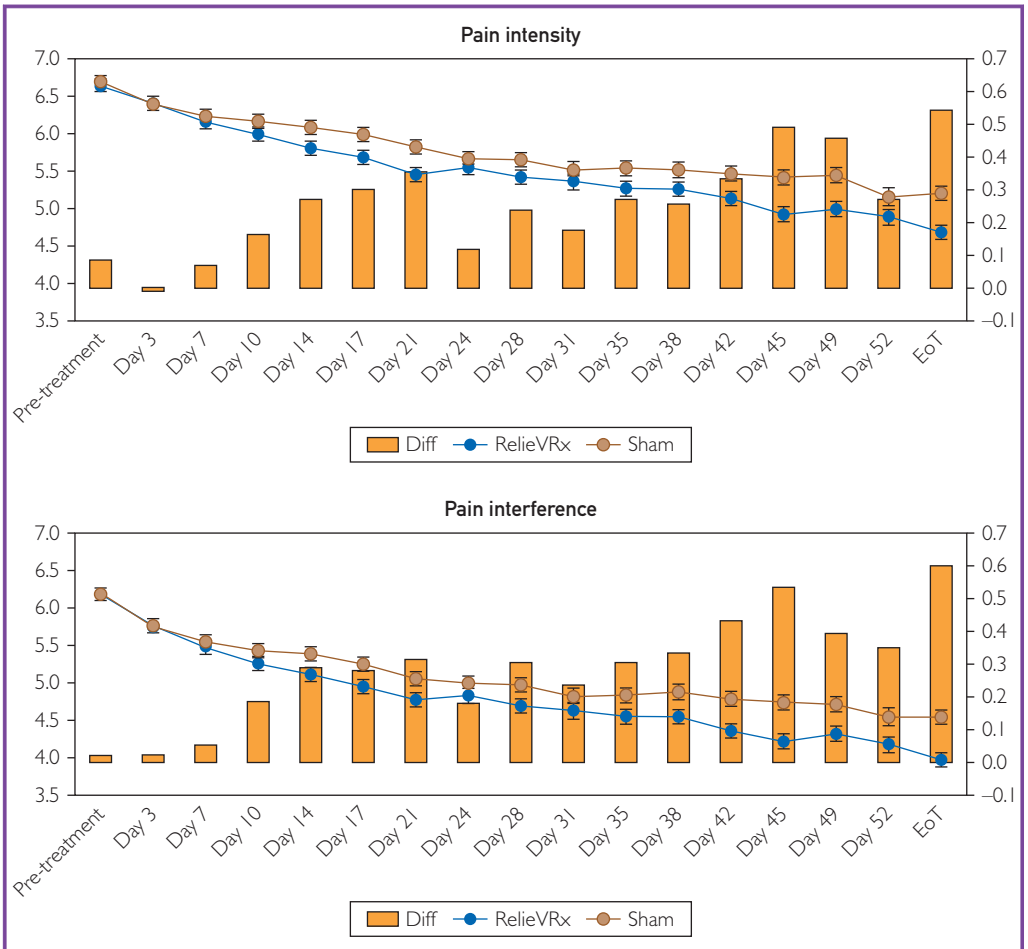

FIGURE 2. Average (A) BPI pain intensity and (B) BPI pain interference from pretreatment to end-of-treatment for the RelieVRx and Sham groups. Standard error bars included. Sham minus RelieVRx difference also displayed. BPI, brief pain inventory.

criteria (30% definition: OR [95% CI]=1.52 [1.18-1.97], $P<.001$; 2-point definition: OR [95% CI]=1.51 [1.17, 1.95], $P<.001$). In the RelieVRx group, 47% achieved a 30% reduction in pain intensity, 58% achieved a 30% reduction in pain interference, and 43% achieved a 30% reduction in both. 61% achieved a 30% reduction in pain intensity, pain interference, or both. In addition, 46% achieved a 2-point reduction in pain intensity, 51% achieved a 2-point reduction in pain interference, and 44% achieved a 2-point reduction in both. 58% achieved a 2-point reduction in pain intensity, pain interference, or both. In the Sham group, 37% achieved a 30% reduction in pain intensity, 46% achieved a 30% reduction in pain interference, and 33% achieved a 30% reduction in both. 50% achieved a 30% reduction in pain intensity, pain interference, or both. Additionally, 38% achieved a 2-point reduction in pain intensity, 40% achieved a 2-point reduction in pain interference, and 36% achieved a 2-point reduction in both. Fifty percent achieved a 2-point reduction in pain intensity, pain interference, or both. The ITT and PP analysis set results were similar.

Secondary Outcome Analysis

The study observed significant differences between RelieVRx and Sham for multiple secondary end points after correction for

TABLE 2. Average PROMIS and ODI Scores at Pretreatment and End-of-Treatment for RelieVRx and Sham (SD in Parentheses)

Treatment	PROMIS Anxiety	PROMIS Sleep Disturbance	PROMIS Depression	Oswestry Disability Index
RelieVRx				
Pretreatment	56.10±9.14	60.73±7.13	54.95±9.28	41.46±15.55
End-of-treatment	55.39±9.29	56.28±8.18	53.79±9.56	33.16±16.58
Within-group difference	0.71	4.45	1.16	8.30
Within-group *P*	.15	<.001	.005	<.001
Within-group effect size	0.078	0.575	0.123	0.515
Sham				
Pretreatment	55.61±9.48	60.85±7.34	54.57±8.92	40.95±16.93
End-of-treatment	55.55±9.48	58.12±7.89	55.11±9.28	35.12±17.62
Within-group difference	0.06	2.73	−0.54	5.83
Within-group *P*	.71	<.001	.14	<.001
Within-group effect size	0.007	0.36	0.06	0.34
Between-group difference	0.65	1.72	1.70	2.47
Between-group *P*	.79	<.001	.003	.004
Between-group effect size	0.02	0.23	0.14	0.115

multiplicity, with larger reductions from pretreatment to end-of-treatment within the RelieVRx group (largest $P=.004$; Table 2). The RelieVRx group reported improvements in PROMIS sleep disturbance (4.45 points), PROMIS depression (1.16 points), and ODI (8.30 points). No statistically reliable within-group improvements or differences between groups were observed for PROMIS anxiety. Results were consistent in the ITT analysis set. Within the PP analysis set, statistical significance was observed only for the PROMIS sleep disturbance measure ($P=.004$) after correction for multiplicity.

Additional Analysis

The RelieVRx group reported greater treatment satisfaction (on a 5-point scale) than the Sham group (4.61 vs 4.01, respectively; $P<.001$), greater likelihood to recommend VR to someone else (on a 10-point scale; 9.12 vs 7.32, respectively; $P<.001$), and greater likelihood to continue using VR (on a 10-point scale) if they could keep their headset (8.83 vs 6.98, respectively; $P<.001$). Both groups reported high usability with statistically greater perceived usability for the RelieVRx group (RelieVRx usability rating=91.64; Sham usability rating=86.01; $P<.001$).

DISCUSSION

We conducted a randomized effectiveness trial of RelieVRx, an FDA authorized skills-based, pain self-management VR program in a demographically diverse and clinically severe national sample of 1093 individuals with cLBP. Statistically larger decreases in pain intensity and pain interference from pretreatment to end-of-treatment were observed for RelieVRx relative to Sham, with small between-group differences in effect size. Average pain reductions for RelieVRx were clinically meaningful and similar to our previous efficacy trial (pain intensity reduction: current=2.0; previous=2.2; pain interference reduction: current=2.3; previous=2.5). It was reported that 58% of RelieVRx participants achieved at least a 2-point reduction in pain intensity, pain interference, or both. Although direct

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treatment comparisons are unavailable, RelieVRx performs well in cLBP compared with pharmacological and nonpharmacological interventions,[5,29] and other VR interventions,[20,21] while also being low-risk, easy to use, and accessible. Sleep disturbance decreased from moderate to mild and disability decreased from completely disabled to severe disability in the RelieVRx group, indicating a qualitative improvement in sleep quality and physical function. Depression decreased, but not enough to cross a clinically meaningful threshold. The reductions in depression, sleep disturbance, and disability were statistically larger in the RelieVRx group compared with Sham. No significant within-group improvements or differences between groups were observed for PROMIS anxiety. This result is surprising given the direction of all other effects. Future work will investigate this anomalous result further. The system usability scale reported high usability (SUS=92), suggesting that RelieVRx is easier to use than an ATM. Patient satisfaction was significantly higher for the RelieVRx group (4.61 out of 5) than Sham (4.01).

Treatment outcomes were clinically meaningful for RelieVRx, and the strong Sham outcomes resulted in modest between-group effect sizes (pain intensity=.24, pain interference=.26). Strong placebo effects for active controls are well established[29,30] and our Sham adhered to elements recommended by expert consensus[30] for rigor in clinical research. In particular, our active VR Sham involved device novelty and strong motivational pull of VR. In addition, although not designed to be therapeutic, the active VR Sham content has therapeutic value in the form of pain distraction and relaxation,[31] and thus cannot be considered a pure therapeutic-free control. Despite this strong control, RelieVRx evidenced statistically larger reductions in pain intensity and pain interference (with modest between-group effect sizes). In terms of realistic expectation of treatment efficacy when applied in clinical settings, the RelieVRx group evidenced clinically meaningful reductions in pain intensity and pain interference.

RelieVRx has few adverse effects, and any health risks are mild compared with pharmacology that always includes severe or major risks for some people. RelieVRx is easier to use than an ATM (on the basis of the SUS), is engaging (4.7 experiences per week on average) and leads to high satisfaction (4.6 on a 5-point scale). RelieVRx is highly effective with 60% of participants yielding a clinically meaningful reduction in pain intensity, interference, or both.

Limitations

Limitations to consider when evaluating the study results includes the following: (a) self-reported cLBP that was not confirmed by health care professionals; (b) treatment adherence (4.7/week; 67% of treatment) that was below the 7/week requested but greater than the 62% treatment adherence threshold applied in CBT for cLBP studies[32] (c) lack of other arms (eg, a wait-list); and (d) a focus on cLBP without examining other chronic pain conditions.

CONCLUSION

Historically, community-based clinicians have few options to offer their patients outside of pharmacology. The promising results of this study suggest that in-home VR treatment could reduce pain intensity and pain interference at scale for people with cLBP and provide clinicians a new way to offer their patients standardized and effective nonpharmacologic treatment.

POTENTIAL COMPETING INTERESTS

Dr Maddox, Dr Oldstone, Alexis Oyao, Roselani Maddox, Kelsey Ffrench, and Takisha Adair are employees of AppliedVR, Inc. Joshua Sackman is president of AppliedVR, Inc. Dr Sparks, Dr Garcia, Heidy Garcia, and Ann Irvin are former employees of AppliedVR, Inc, who were employed during execution of the study. Dr Maislin, Dr Bonakdar, and Brendan Keenan are consultants or contractors for AppliedVR, Inc. Dr Darnall is chief science advisor for AppliedVR, Inc and receives consulting fees for this role. Dr Darnall has authored or coauthored 5 pain treatment books for patients and clinicians and receives royalties for 4. Dr Darnall is the principal investigator for pain research grants and awards from the National Institutes of Health (NIH) and the Patient-Centered Research Outcomes Research Institute (none specific to the

current work). Dr Darnall is a co-investigator on 2 NIH research grants investigating virtual reality analgesia; neither of these grants is specific to the current work. Dr Darnall serves on the Board of Directors for the American Academy of Pain Medicine, the Medical Advisory Board for the Facial Pain Association, and is on the Board of Directors for the Institute for Brain Potential. Dr Darnall is a scientific member of the NIH Interagency Pain Research Coordinating Committee, the Centers for Disease Control and Prevention Opioid Workgroup (2020-2021), and the Pain Advisory Group of the American Psychological Association.

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AUTHOR CONTRIBUTORS

TM, LO, CS and JS were involved in all aspects of the study. AO and LG were involved in study implementation. RM was involved in data analysis, data presentation, and project and participant management. KF, HG, TA, and AI were involved in project and participant management. DM and BK conducted the primary and secondary end point biostatistical analysis. RB served as medical monitor. BD was involved in study design, data interpretation, and manuscript preparation. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

DATA SHARING

A data dictionary and de-identified participant data will be made available after publication and upon approved request of a detailed meta-analytic study proposal. Requests should be made to the corresponding author along with a study proposal and a signed data access agreement.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at https://www.mcpdigitalhealth.org/. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **cLBP,** chronic low back pain; **CBT,** cognitive behavior therapy; **ITT,** intent-to-treat; **mITT,** modified intent-to-treat; **PP,** per protocol; **VR,** virtual reality

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