Heliyon 9 (2023) e17870

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Virtual reality in the management of stress and anxiety disorders: A retrospective analysis of 61 people treated in the metaverse

Eran Orr [a], Tal Arbel [b], Miki Levy [b], Yaron Sela [c], Omer Weissberger [c], Omer Liran [d,e], Jeremy Lewis [f,g,*]

[a] XR Health Inc, Brookline, USA
[b] XR Health Ltd, Tel Aviv, Israel
[c] School of Psychology, Reichman University, Herzliya, Israel
[d] Division of Health Services Research, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, USA
[e] Department of Psychiatry and Behavioral Sciences, Cedars-Sinai Medical Center, Los Angeles, USA
[f] Therapy Department, Central London Community Healthcare National Health Service Trust, London, United Kingdom
[g] Musculoskeletal Research, Clinical Therapies, University of Limerick, Limerick, Ireland

ARTICLE INFO

Keywords:
Virtual reality
Metaverse
Stress
Anxiety

ABSTRACT

Mental health is the second largest group of health disorders associated with prolonged disability. Treating conditions such as stress and anxiety are a global health challenge due to inadequate funding and resources. Therefore, providing virtual treatment in the metaverse may provide a novel method of treatment for these conditions. We conducted a retrospective analysis of health records of people experiencing stress and anxiety who were treated principally in the metaverse using virtual reality. The main objective was to determine if virtual mental health treatment was achievable and safe, with measurable outcomes repeated at multiple time points. Here, 61 participants health records were evaluated (50% were female, 19% male, 31% identified as other). The cohort was 45.7 ± 15.7 years of age and reported no adverse effects with outcomes measured. Specifically, anxiety (via Generalized Anxiety Disorder Scale) decreased by 34% ($p = 0.002$) and stress (via Perceived Stress Scale) decreased by 32% ($p < 0.001$) after virtual intervention. The data suggests that this method of treatment was feasible, safe, and outcomes were obtainable over a range of time points. This early data suggest that management in the metaverse for these conditions may be beneficial, however, further prospective studies are necessary to better understand these clinical findings.

1. Introduction

After musculoskeletal disorders, mental health conditions rank globally as the second largest group of health conditions associated with years lived with disability [1]. The impact of the SARS-CoV-2 appears to have exacerbated this with higher reported levels of

Abbreviations: AMAR, Ministry of Health, Medical devices Department, Israel; Apps, applications; ARTG, Australian Register of Therapeutic Goods; BRANY, Biomedical Research Alliance of New York; CBT, cognitive behavioral therapy; FDA, Food and Drug Administration; GAD-7, Generalized Anxiety Disorder Scale-7; HMD, head mount display; M, mean; N, count; PHQ-9, Patient Health Questionnaire – 9; PSS, Perceived Stress Scale; SD, standard deviation; VAS, visual analog scale; VR, virtual reality; VRET, virtual reality exposure therapy; WL, waiting list.

* Corresponding author. Therapy Department, Central London Community Healthcare National Health Service Trust, London, United Kingdom.
E-mail address: prof.jeremylewis@gmail.com (J. Lewis).

https://doi.org/10.1016/j.heliyon.2023.e17870
Received 23 January 2023; Received in revised form 12 June 2023; Accepted 29 June 2023
Available online 7 July 2023

anxiety, stress, poor sleep, and depression globally, and more so in younger people [2]. Pre-pandemic, studies suggest up to 58% of college students suffer from unhealthy levels of stress and up to 74% from unhealthy levels of anxiety [3–5]. Again, the Covid-19 pandemic appears to have increased student stress and anxiety, and of concern, the majority of students with moderate or severe mental health symptoms have not sought help from mental health services [6]. Acute stress disorders may occur in up to 45% of injury survivors [7]. In Australia, over half (54%) of 201 participants (age range 18–94 years) reported above average scores for persistent depression, anxiety and/or stress after an intensive care admission for trauma [8]. Although certain groups in society appear to be more prone to anxiety and stress related disorders [2–4], these conditions are endemic and affect people of all ages, social groups, and genders.

Virtual reality (VR) applications may reduce stress and anxiety by presenting relaxing environments, encouraging relaxed breathing, by improving physical fitness, providing a fun, challenging virtual experience, and mindfulness. Stress, assessed by heart rate and an online survey, was measured in 11 participants, aged 18–34 years, who experienced augmented reality in the form of a virtual island, with a waterfall and campfire, and with an option of listening to music, via an iPad (www.apple.com). Stress was reported to reduce in 73% of participants, more so in female participants and younger participants, aged 18–24 years [9]. In another study, 18 participants (9 men and 9 women, average 32 (standard deviation [SD] = 12) years of age) were shown three, 15-min 360° high-definition VR scenes in a randomized order. One scene, designated as the control, consisted of an empty classroom, with no people, plants, or animals. The other two scenes were outdoor vistas, one of rural Ireland, and the other of beach locations in Australia. The outdoor scenes were accompanied by soothing music and ocean sounds. Prior to watching each scene participants were mentally stressed arithmetically for 2 min. Extra dermal activity and heart-rate variability of the participants were measured continuously before and during the 15-min VR sessions. The Positive and Negative Affect Schedule questionnaire was given at the beginning of the experiment, between the stress test and VR, and after VR. The 15-question Modified Reality Judgment and Presence Questionnaire was given after VR. The results indicated a better response to the outdoor scenes with the suggestion that *"VR could improve life* (for people living in isolated and confined environments) *by providing a sense of being away and an escape from daily operational pressures and stressors. For people in these kinds of environments (such as astronauts, submariners, and others), VR may be a way to improve mental health outcomes."* [10]. In a randomized controlled investigation, nurses and teachers received a package of care that included VR (n = 40), or cognitive behavioral therapy (CBT, n = 42) or waiting list for treatment (WL, n = 39). Both the VR group and the CBT group demonstrated better outcomes than the WL group, with the VR group participants reporting significant reduction in chronic anxiety and significant improvement in coping skills [10]. Early results of a mindfulness based stress reduction provided in an immersive VR environment suggested higher levels of life satisfaction, and improvement in the Mindful Attention Awareness Scale and Satisfaction with Life Scale [11].

Worldwide there has been a marked increase in stress and anxiety, including people who have experienced a traumatic brain injury. Moreover, anxiety disorders affect approximately 18% of adults [12] with a worldwide prevalence of 7.3% [13], detrimentally impacting the quality of life, increased stress, and increasing the incidence of persistent pain [14]. The statistics are concerning and suggest a global health system that is in crisis with limited access to care in traditional brick and mortar environments, points to a need for novel adjunct or standalone therapies to improve care. Reports suggest more than 50% of people who require care do not access services due to inconvenience, embarrassment, or stigmatization concerns around mental health [11], which also suggests a new approach is needed. Health service providers in response to research, as well as patient and society values, are increasingly introducing drug-free therapies that include mindfulness programs, alongside or instead of traditional treatments.

The primary aim of this study was to determine if people seeking care for stress and anxiety would be willing to participate in virtual reality treatment. The secondary aims were to [1]: Determine if there were any side effects, adverse events, or serious adverse events [2]; Learn if outcome measures could be applied and completed remotely in a VR environment and via telehealth. Pain, fatigue, functional ability, sleep, and memory has a bidirectional relationship with stress and anxiety [15–19]. As such, our final secondary aim was to Ref. [3] gain formative information if virtual reality treatment delivered in the metaverse and supported by telehealth had a potential positive benefit and whether there was any early evidence of effectiveness. To assess this, we included outcomes that measured stress, anxiety, pain, fatigue, functional ability, sleep, memory, and a series of physical parameters.

To achieve these aims, data were analyzed retrospectively from multiple sets of health records (also known as a medical records review) across three countries for participants experiencing low back pain.

2. Methods

A retrospective health and medical records review was conducted with a waiver of consent on participants who had remote VR rehabilitation services between July 2020 and May 2022 at XRHealth clinics (https://www.xr.health/), an international hybrid technology and healthcare company specializing in the provision of healthcare through the metaverse. In this unique healthcare delivery model, licensed clinicians augment remote healthcare interventions with VR applications, after screening for contraindications for use of the technology.

2.1. Participants

Participants in this retrospective analysis of health records were from the United States of America, Israel, and Australia.

2.2. Ethical approval

This protocol received an exempt status with a waiver of consent from the Biomedical Research Alliance of New York (BRANY) IRB Protocol #22-12-618-947.

2.3. Outcome measures

Outcome measures were assessed at baseline, and every 30 days until discharged from care/follow-up. Thirty days was considered the minimum level to receive treatment for these conditions. The outcome measures applied across the participants are detailed in Table 1.

To address the primary aim (*Would people seeking care for stress and anxiety be willing to participate in virtual reality treatment?)*, we assessed the number of participants who consented to and commenced treatment using home based virtual reality treatment and compared that to the number of people who completed treatment. We also assessed the level of satisfaction with the treatment each participant received. Satisfaction was assessed using the Customer Effort Score (CES), and Customer Satisfaction Score (CSAT) and a series of questions using Likert measurements to assess response. CES is a metric used to measure a product or service's ease of use to customers, and CSAT measures happiness with a service, product, and/or customer support.

2.4. Customer Effort Score

Participants were asked, "How easy was it for you to setup and use your VR headset?" To assess this a Likert Scale ranging from 1 (worse response) to 7 (best response).

2.5. Customer Satisfaction Score

Participants were asked, "How satisfied are you with your treatment outcome?" To assess this a Likert Scale ranging from 1 (worse response) to 5 (best response).

A secondary aim was to determine if there were any side effects, adverse events, or serious adverse events. Side effects were defined as events that were known to occur when using VR. Adverse events were defined as undesired and unpredicted response to VR treatment that may occur to some people when using VR. Examples include any event that was unwanted, and the risk of that event is not currently known and did not result in hospitalization, permanent disability, or death. Serious adverse events were defined as an event that resulted in hospitalization, permanent disability, or death.

Another secondary aim was to learn if outcome measures could be applied and completed remotely in a VR environment and via telehealth. To assess this, the rates of completion of the outcome measures that were scheduled to be collected, before the start of treatment, every 30 days of treatment, and at the end of treatment, were analyzed.

Our final aim was to gain formative information if virtual reality treatment delivered in the metaverse and supported by telehealth had a potential positive benefit and whether there was any early evidence of effectiveness. To assess this, we included outcomes that measured stress, anxiety, pain, fatigue, functional ability, sleep, memory, and a series of physical parameters.

2.6. Virtual reality hardware and therapeutic software

Participants were provided with the Pico Neo 2 (ByteDance, Beijing, China) head mount display (HMD) and hand controllers.

Table 1
Outcome Measures Used in this Retrospective Analysis.

Outcome Measure	Description
Activities-Specific Balance Confidence (ABC) Scale [20]	A questionnaire developed to assess older individual's balance confidence in performing daily activities.
Adult Executive Functioning Index [21]	Executive functioning rating instrument (14 items) focusing specifically on working memory and inhibitory control.
Adult Executive Functioning Index – Working Memory [21]	
Adult Executive Functioning Index – Inhibition [21]	
Lower Extremity Functional Scale (LEFS) [22]	Used to assess the functional impairment in individuals with musculoskeletal lower limb dysfunction.
NIH PROMIS – Pain Intensity [23]	PROMIS® is a publicly available system for assessment of patient-reported health status for physical, mental, and social well-being.
PROMIS CAT v1.0 - Sleep Disturbance [23]	
Brief Pain Inventory – Pain Interference [23]	
NIH PROMIS CAT – Fatigue [23]	
PROMIS v1.0 Sleep disturbance-SF [4a,23]	
Generalized Anxiety Disorder Scale (GAD-7)	This self-administered patient questionnaire is used as a screening tool and severity measure for generalized anxiety disorder.
Perceived Stress Scale (PSS)	10 items used to assess the level of subjective stress over the past month.
Depression, Anxiety and Stress Scale - 21 (DASS-21)	A set of 3 self-report scales designed to measure the emotional states of depression, anxiety, and stress.

Treatment software was uploaded to the HMD. Table 2 provides a description of the XRHealth therapeutic software provided for the participants. The software is registered with the FDA (U.S. Food and Drug Administration), AMAR (Ministry of Health, Medical devices Department, Israel), and has an ARTG (Australian Register of Therapeutic Goods) Certificate. The software generates motion tracking and movement kinematics data. These data were collected but not analyzed in this retrospective analysis and will be used to inform the design of future case control, cohort, and randomized clinical trials.

2.7. Application of treatment

Based on the assessment process, the clinician (licensed physical therapists, physiotherapists, and occupational therapists) determined which software package(s) to prescribe the participants. Clinicians utilized training applications (apps) that were relevant for the required rehabilitation (Table 2), which may have included one or more apps per patient. For example, an individual diagnosed with stress and anxiety may be prescribed relaxation software, such as Mindset, while an individual presenting with symptoms in the cervical region that includes pain may be prescribed Rotate in combination with Luna. Moreover, each application allows the clinician

Table 2
XR health therapeutic software applications used by the participants.

Therapeutic Software Company Code and Name	Intended Use
CT-610* (ReAct)	The VRCogni CT-610 ("Re-Act") is a prescription only medical device software applications that provide various VR environments to aid mitigate or assess conditions related to cognitive function by providing cognitive exercises and cognitive ability measurements. The cognitive exercises and cognitive ability measurements rely on inputs from visual and auditory stimuli, and functional use of the hands and enable: • Guiding patients in the performance of various cognitive exercises. • Track and analyze motion and movement kinematics. The VRCogni CT-610 can be used as an assessment aid to determine the level of cognitive function for which there exists other valid methods of cognitive assessment.
CB-510 (Luna)	The CB-510 ("Luna") is intended to assist in the mitigation of pain, hot flashes and physical discomfort through distraction and supporting exercises, performed in a virtual reality (VR) environment using commercially available VR headsets. The CB-510 is a prescription only device that can be used in clinical setting or at home, with or without the assistance of licensed health care provider. The CB-510 provides VR exercises and takes measurements that enables the patient and/or clinician to monitor changes over time.
MC-320* (Color Match)	The MC-320 ("Color Match") is a physical medicine and motor-cognitive rehabilitation software, as a medical device, intended for use in upper extremity, full body and motor-cognitive conventional rehabilitation. The software enables: • Tracking motion and movement kinematics. • Guiding patients in the performance of motor-cognitive exercises according to the treating medical practitioner's guidelines. • The MC-320 provides VR exercises and takes measurements that enables the patient and/or clinician to monitor changes over time.
CT-620 (Memorize)	The VRCogni CT-620 ("Memorize") is a prescription only medical device software applications that provide various VR environments to aid mitigate or assess conditions related to cognitive function by providing cognitive exercises and cognitive ability measurements. The cognitive exercises and cognitive ability measurements rely on inputs from visual and auditory stimuli, and functional use of the hands and enable: • Guiding patients in the performance of various cognitive exercises. • Track and analyze motion and movement kinematics. • Monitoring changes in patient's measurements over time. • The VRCogni CT-620 can be used as an assessment aid to determine the level of cognitive function for which there exists other valid methods of cognitive assessment.
PD-810 (Mindset)	The PD-810 ("Mindset") is intended to assist in relaxation and management of pain and physical discomfort through distraction and supporting meditation and relaxation exercises, performed in a virtual reality (VR) environment using commercially available VR headsets. The PD-810 is a prescription only device that can be used in clinical setting or at home, with or without the assistance of licensed health care provider. The PD-810 provides VR exercises and takes measurements which enables the patient and/or clinician to monitor changes over time.
MT-220* (Balloon Blast)	The MT-220 ("Balloon Blast") is a physical medicine and rehabilitation software, as a medical device, intended for use in upper extremity and full body conventional rehabilitation and active shoulder ROM assessment. The software enables: • Tracking motion and movement kinematics. • Guiding patients in the performance of physical exercises according to the treating clinician's guidelines. • Monitoring changes in patient's measurements over time.
N-140* (Rotate)	The N-140 ("Rotate") is a physical medicine and rehabilitation software, as a medical device, intended for use in cervical region conventional rehabilitation and active cervical spine ROM assessment. The software enables: • Tracking motion and movement kinematics. • Guiding patients in the performance of physical exercises according to the treating clinician's guidelines. • Monitoring changes in patient's measurements over time.
MD-710 (Relax8)	The MD-710 ("Relax8®) is intended to assist in relaxation and management of pain and physical discomfort through distraction and supporting meditation and relaxation exercises, performed in a virtual reality (VR) environment using commercially available VR headsets. The MD-710 is a prescription only device that can be used in clinical setting or at home, with or without the assistance of licensed health care provider. The MD-710 provides VR exercises and takes measurements which enables the patient and/or clinician to monitor changes over time.

All the motion software (*) generates motion tracking and movement kinematics data. These data were not analyzed in this retrospective analysis but will be used to inform the design of future case control, cohort, and randomized clinical trials.

to adjust specific training parameters, such as training area, speed, and cognitive challenge according to specific patient's medical needs.

Further information on the description and use of the applications used is available; https://www.xr.health/products/.

2.8. Statistical analysis

Data were analyzed using R software (V. 4.1.0) and R studio software (V. 2022.02.3). Descriptive statistics were reported using means (m) and SDs for continuous variables and absolute and relative frequencies for categorical variables. Bivariate comparisons were conducted using paired t-tests to examine pre-post change. Outliers that exceeded 3 standard deviations were examined using box plots and excluded. For each participant, the pre-treatment data was calculated based on the average of the first three scores of the test. The post-treatment data were calculated as the average of the last three scores on the test.

To examine effectiveness of the VR intervention, we conducted a series of paired t-tests between the baseline (pre) and the final (post) measurements. *P*-values <0.05 were considered significant. We also report p-values <0.10 as a trending toward significance. It was determined a priori that analyses of results would be conducted for participants who were treated for a minimum of 30 days and had a minimum of two full data sets. These time points were baseline (prior to initiation of treatment) and at the conclusion of treatment.

3. Results

3.1. Participants

The sample consisted of 61 participants seeking treatment for stress and anxiety, with a mean age of 45.7 (15.7) years. The cohort consisted of 50% females, 19% males and 31% self-identified as other. Overall, the participants in this sample had an average of 125.2 (51.4) days in treatment, with 18.7 (14.3) appointments on average and a mean of 128.3 sessions. Descriptive statistics and data from the cohort's virtual sessions in the metaverse with and without a clinician are provided in Table 3.

3.2. Primary aim: would people seeking care for stress and anxiety would be willing to participate in virtual reality treatment?

One month of treatment (30 days) was considered a priori to be a minimum time to receive treatment (Table 4). We also assessed the participants level of satisfaction with the treatment that they received (Table 5).

3.3. Secondary aim: side effects, adverse events, and serious adverse events

As part of the data collection, clinicians asked participants if they had experienced any side effects or adverse events and participants were encouraged to report them. Any serious adverse events would also be reported. A review of the health records suggest that this patient population did not report any side effects, adverse events, or serious adverse events.

3.4. Secondary aim

To learn if outcome measures could be applied and completed remotely in a VR environment and via telehealth. These data are presented in Table 6.

3.5. Secondary aim

To gain formative information if virtual reality treatment delivered in the metaverse and supported by telehealth had a potential

Table 3
Demographic and therapeutic intervention characteristics of the patients.

	M (SD)	With a clinician	Without a clinician
Days in treatment	125.2 (51.4)		
Total appointments	18.7 (14.3)		
Total treatments in the metaverse	128.3 (142.8)		
Virtual sessions			
Light Punch		1.3 (3.7)	2.4 (3.7)
Luna		1.1 (2.0)	4.3 (6.2)
MC320		21.5 (34.5)	25.0 (50.3)
Memorize		7.6 (12.3)	15.4 (28.8)
Mindset		0.0	13.0 (16.0)
MT220		8.1 (16.0)	12.9 (17.7)
N140		1.7 (4.0)	3.0 (6.3)
Reducept		0.0	2.4 (7.5)

Abbreviations: M, mean; SD, standard deviation.

Table 4
Participant flow through treatment.

Participants	Baseline (n)	Cohort at minimum 30 days study cohort (% of baseline)	Drop out before 30 days n (% of baseline)	Drop out between 31 and 59 days n (% of baseline)	Completed 60 or more days in treatment n (% of baseline)
Men	20	12 (60%)	8 (40%)	4 (20%)	8 (40%)
Women	45	31 (68%)	14 (31%)	9 (20%)	22 (48%)
Other	22	18 (81%)	4 (18%)	3 (13%)	15 (68%)
<29 years	28	18 (64.3%)	10 (36%)	4 (14%)	5 (18%)
30–59 years	49	38 (77.6%)	11 (22%)	10 (20%)	12 (24%)
>60 years	10	5 (50.0%)	5 (50%)	3 (30%)	4 (40%)

Table 5
Participant satisfaction.

	N	Mean (SD)	Median (Range)
CES***	25	5.12 (1.28)	6 [3–7]
CSAT*	34	4.12 (1.31)	5 [2–5]
My condition and plan of care were clearly explained by my therapist.*	18	4.68 (0.51)	5 [3–5]
How would you rate your overall experience with XRHealth?**	18	9.04 (1.15)	10 [5–10]
I am satisfied with my treatment, and I have made progress since starting VR treatment.*	18	4.71 (0.45)	5 [3–5]
The VR headset was easy to set up and use during treatment.*	18	4.37 (0.71)	4.5 [2–5]
My therapist was sensitive to my needs and adjusted my treatment based on my progress.*	18	4.83 (0.23)	5 [4,5]
I prefer XRHealth to other therapy/rehabilitation options (e.g., going to a clinic to see a therapist in person)*	18	4.39 (0.81)	4.5 [3–5]

***Scale 1-7.
*Scale 1-5.
**Scale 1-10.
CES, Customer Effort Score; CSAT, Customer Satisfaction Score; N, number; SD, standard deviation.

positive benefit and whether there was any early evidence of effectiveness.

3.5.1. Post intervention change for pain, fatigue, function, and sleep outcomes

Due to the bidirectional relationship between stress and anxiety, and, pain, fatigue, function, and sleep [15–19] outcome measures that could assess these variables were included. Table 7 presents pre-post intervention change for all participants with recorded pre-post data points for each of the outcomes measured. The findings of this analysis of the medical records suggest that overall, participants did not report any deterioration over the course of treatment using VR in the metaverse. Moreover, several significant results indicated improvement in health over the course of time. The remaining outcome measures indicate a trend of improving health and function, with no evidence for deterioration. Examples of the findings include anxiety, as measured by the Generalized Anxiety Disorder Scale (GAD-7), decreased by 34.4% ($p = 0.002$); pain severity, measured by the Brief Pain Inventory, decreased by 40.1% ($p = 0.01$); and finally, pain interference, also measured by the Brief Pain Inventory, decreased by 46.4% ($p = 0.07$).

3.5.2. Post intervention change for impairment outcomes and memory

Due to the bidirectional relationship between stress and anxiety, and, pain, fatigue, function, and sleep [15–17,19] outcome measures that could assess these variables were included. Table 8 presents pre- and post-intervention change in VR applications.

4. Discussion

Mental health conditions including stress and anxiety are associated with substantial morbidity. These conditions may detrimentally impact on an individual's ability to participate in valued activities. Once diagnosed and following a shared decision-making process between clinician and patient, an appropriate and agreed upon management strategy is put in place. Current interventions for the management of stress and anxiety include pharmacological management, CBT, talking therapies, clinical meditation, relaxation, participation in physical activity, and more recently VR exposure therapy (VRET) and other VR applications that aim to promote relaxation [9–11,16,24]. VRET gradually and repeatedly exposes people to an anxiety provoking situation, such as seeing spiders, experiencing flying, heights, participating in job interviews, and public speaking [25].

For many people living with persistent stress and anxiety the requirement to frequently travel for ongoing assessment, investigations, medication evaluation, and rehabilitation presents challenges in terms of time, convenience, and cost. The results of this retrospective analysis of health records strongly suggest that people seeking care for stress and anxiety disorders are willing to consent for treatment and participate for a prescribed course of treatment in the metaverse. The data indicate that a minimum of 50.0% (people over the age of 60 years) to a maximum of 77.6% (people aged between 30 and 59 years) were willing to participate for a minimum of one month in treatment. Comparable levels of men (71.4) and women (68.9%) across the spectrum of ages were willing to participate in one months of training. Between 22% and 50% of participants in all categories dropped out in the first month. The reasons for this are not available from the health records. This may indicate participants had achieved acceptable levels of improvement, had deteriorated, had not changed in status, were experiencing side-effects, or were dissatisfied with the treatment they were receiving. To

Table 6
Complete and incomplete data sets.

Outcome	N baseline	Complete outcome data at end of treatment		Incomplete outcome data for any reason at any time point	
		N	% of baseline	N	% of baseline
Generalized Anxiety Disorder Scale (GAD-7)	29	14	48.3%	15	51.7%
Perceived Stress Scale (PSS)	53	14	26.4%	39	73.6%
DASS21	52	11	21.2%	41	78.8%
DASS21 – Anxiety	52	8	15.4%	44	84.6%
Patient Health Questionnaire – 9 (PHQ-9)	27	7	25.9%	20	74.1%
NIH PROMIS CAT – Pain Interference	16	6	37.5%	10	62.5%
NIH PROMIS CAT – Fatigue	18	5	27.8%	13	72.2%
NIH PROMIS – Pain Intensity	14	4	28.6%	10	71.4%
Brief Pain Inventory – Pain Severity	12	4	33.3%	8	66.7%
PROMIS CAT v1.0 – Anxiety	18	4	22.2%	14	77.8%
Adult Executive Functioning Index	10	4	40.0%	6	60.0%
PROMIS CAT v1.0 - Sleep Disturbance	12	3	25.0%	9	75.0%
Brief Pain Inventory – Pain Interference	9	3	33.3%	6	66.7%
Adult Executive Functioning Index – Working Memory	8	3	37.5%	5	62.5%
Adult Executive Functioning Index – Inhibition	6	3	50.0%	3	50.0%
Pain					
VAS-pain (at start of VR session)	59	43	72.9%	16	27.1%
VAS-pain (at start of VR session)	54	40	74.1%	14	25.9%
Change in VAS-pain (within session)	54	39	72.2%	15	27.8%
Range of Movement					
Flexion left	9	5	55.6%	4	44.4%
Flexion right	8	5	62.5%	3	37.5%
Abduction left	11	5	45.5%	6	54.5%
Abduction right	7	5	71.4%	2	28.6%
Horizontal abduction left	6	5	83.3%	1	16.7%
Horizontal abduction right	9	4	44.4%	5	55.6%
Quality of movement					
Left hand	59	40	67.8%	19	32.2%
Right hand	59	41	69.5%	18	30.5%
Average	59	44	74.6%	15	25.4%
Peak velocity left hand	60	40	66.7%	20	33.3%
Peak velocity right hand	60	41	68.3%	19	31.7%
Peak velocity average	60	41	68.3%	19	31.7%
Response time left hand	60	40	66.7%	20	33.3%
Response time right hand	60	41	68.3%	19	31.7%
Response time average	60	44	73.3%	16	26.7%
Efficiency left hand	57	32	56.1%	25	43.9%
Efficiency right hand	57	33	57.9%	24	42.1%
Efficiency average	57	33	57.9%	24	42.1%
Action time left hand	58	34	58.6%	24	41.4%
Action time right hand	58	33	56.9%	25	43.1%
Action time average	58	38	65.5%	20	34.5%
Speed	58	36	62.1%	22	37.9%
Neck rotation					
ROM rotation right	8	2	25.0%	6	75.0%
ROM rotation left	8	2	25.0%	6	75.0%
ROM extension	8	2	25.0%	6	75.0%
Session accuracy	21	12	57.1%	9	42.9%
Session constant error	21	12	57.1%	9	42.9%
Final speed level	41	36	87.8%	5	12.2%
Memory					
Final number of items	39	27	69.2%	12	30.8%

understand this more fully, these variables need to be the focus of prospective investigations and concomitant qualitative research.

With many health systems facing considerable challenges in terms of available space and the ability to provide care remotely when pragmatic, safe, effective, and possible, this approach may help to improve care by offering in-house care when an alternative does not exist. The finding that people would be willing to participate in virtual and remote treatment for stress and anxiety may support many of the challenges faced by health systems globally. Arguably this may contribute to reducing the environmental impact of healthcare by decreasing the number of road journeys required to attend traditional 'brick and mortar' institutions. This hypothesis requires testing in future research, as well as identifying those that would be willing and would benefit from remote treatment.

Although not a direct measure of willingness to participate, patient satisfaction or lack of it, might be a reason for continuation or cessation of treatment. The mean CES was 5.12 (SD = 1.28) and mean CSAT was 4.12 (SD = 1.31), both scores supported substantial participant satisfaction. This is further supported by the responses to the six questions, notably question three (I am satisfied with my treatment, and I have made progress since starting VR treatment) with a mean response 4.71 (SD = 0.71) where 5 represents best score.

Table 7
Pre-post intervention change for impairment outcomes and memory.

Test	N	Pre		Post		Pre-Post Delta (%)	Mean Difference	95% CI		t	p
		M	SD	M	SD			L	U		
Pain											
VAS-pain (at start of VR session)	43	5.0	2.1	3.7	1.9	27.3%	1.4	0.8	1.9	5.1	<0.001
VAS-pain (at start of VR session)	40	3.8	1.6	3.0	1.5	20.4%	0.8	0.2	1.4	2.8	0.009
Change in VAS-pain (within session)	39	1.0	0.9	0.5	0.7	49.5%	0.5	0.2	0.8	3.4	0.001
Range of Movement											
Flexion left	5	178.0	26.5	162.0	25.2	8.9%	15.4	−17.5	48.3	1.3	0.26
Flexion right	5	170.0	15.3	163.0	26.0	4.1%	6.9	−20.6	34.3	0.7	0.53
Abduction left	5	189.0	31.7	168.0	36.5	11.1%	21.6	−61.9	105.2	0.7	0.51
Abduction right	5	192.0	18.4	160.0	20.5	16.7%	31.5	−15.7	78.6	1.9	0.14
Horizontal abduction left	5	82.6	25.6	89.0	32.0	7.8%	−6.4	−67.9	55.1	−0.3	0.79
Horizontal abduction right	4	73.8	9.5	77.9	21.5	5.6%	−4.0	−52.2	44.1	−0.3	0.81
Quality of movement											
Left hand	40	71.7	8.5	72.1	9.8	0.6%	−0.4	−3.1	2.3	−0.3	0.78
Right hand	41	71.5	8.6	74.0	10.0	3.5%	−2.4	−5.3	0.4	−1.7	0.09
Average	44	71.0	8.9	73.3	10.2	3.2%	−2.3	−5.2	0.6	−1.6	0.11
Peak velocity left hand	40	1.9	0.7	1.9	0.7	1.1%	−0.02	−0.2	0.2	−0.2	0.84
Peak velocity right hand	41	1.9	0.6	1.9	0.9	0%	0.01	−0.1	0.2	0.1	0.93
Peak velocity average	41	1.9	0.6	1.9	0.6	2.1%	−0.04	−0.2	0.1	−0.1	0.58
Response time left hand	40	646.0	233.0	508.0	164.0	21.4%	137.5	67.5	207.4	3.9	<0.001
Response time right hand	41	643.0	223.0	539.0	210.0	16.2%	103.6	28.5	178.8	2.8	0.008
Response time average	44	570.0	235.0	469.0	213.0	17.7%	101.0	21.3	180.8	2.6	0.01
Efficiency left hand	32	78.1	9.1	79.4	8.9	1.7%	−1.3	−3.9	1.3	−1.0	0.32
Efficiency right hand	33	77.2	10.5	80.6	8.2	4.4%	−3.3	−6.6	−0.04	−2.1	0.05
Efficiency average	33	76.8	10.1	79.6	8.7	3.7%	−2.8	−5.8	0.2	−1.9	0.07
Action time left hand	34	1073.0	309.0	977.0	246.0	8.9%	95.3	8.4	182.2	2.2	0.03
Action time right hand	33	1085.0	291.0	973.0	265.0	10.3%	111.6	24.8	198.3	2.6	0.01
Action time average	38	865.0	534.0	813.0	346.0	6.0%	52.3	−90.9	195.5	0.7	0.46
Speed	36	11.8	4.3	12.9	3.9	9.3%	−1.1	−2.6	0.5	−1.4	0.16
Neck rotation											
ROM rotation right	2	67.4	0.4	75.3	1.5	11.7%	−7.88	−24.8	9.10	−5.9	0.11
ROM rotation left	2	64.0	14.6	71.4	0.9	11.6%	−7.48	−146.4	131.5	−0.7	0.62
ROM extension	2	61.6	6.2	66.5	2.8	7.9%	−4.88	−35.5	25.7	−2.0	0.29
Session accuracy	12	85.3	12.5	88.8	12.1	4.1%	−3.55	−15.4	8.30	−0.7	0.52
Session constant error	12	2.5	1.5	2.3	1.7	9.5%	.24	−1.35	1.83	0.3	0.74
Final speed level	36	5.5	3.8	4.3	2.7	21.8%	1.2	.14	2.24	2.3	0.03
Memory											
Final number of items	27	3.3	1.4	7.4	3.7	125.5%	−4.1	−5.5	−2.7	−6.1	<0.001

Abbreviations: L, lower confidence interval; M, mean; ROM, range of motion; SD, standard deviation; U, upper confidence interval; VAS, visual analog scale.

Table 8
Pre- and post-intervention change in anxiety, stress, pain, fatigue, disability, and sleep outcomes.

Outcome	N	Pre		Post		Pre-Post Delta (%)	Mean Difference	95% CI		t	*P*-Value
		M	SD	M	SD			L	U		
Generalized Anxiety Disorder Scale (GAD-7)	14	12.3	5.4	8.1	5.5	34.39%	4.2	1.9	6.5	3.9	0.002
Perceived Stress Scale (PSS)	14	22.0	4.1	14.9	7.3	32.27%	7.1	3.6	10.5	4.4	<0.001
DASS21	11	8.8	4.8	6.4	2.0	27.89%	2.5	−0.8	5.7	1.7	0.12
DASS21 – Anxiety	8	5.9	3.0	3.1	2.4	46.94%	2.8	−0.8	6.3	1.8	0.11
Patient Health Questionnaire – 9 (PHQ-9)	7	9.1	4.2	5.3	2.2	42.12%	3.9	0.1	7.6	2.5	0.04
NIH PROMIS CAT – Pain Interference	6	0.9	0.9	0.6	0.3	39.18%	0.4	−0.4	1.1	1.3	0.26
NIH PROMIS CAT – Fatigue	5	1.0	0.5	0.9	0.6	10.00%	0.1	−0.8	1.0	0.3	0.77
NIH PROMIS – Pain Intensity	4	0.7	0.6	0.7	0.4	0.00%	0	−0.4	0.4	0.1	0.95
Brief Pain Inventory – Pain Severity	4	4.7	1.8	2.8	1.5	40.09%	1.9	0.8	2.9	5.7	0.01
PROMIS CAT v1.0 – Anxiety	4	1.4	0.8	1.1	0.6	20.44%	0.3	−0.4	0.9	1.3	0.27
Adult Executive Functioning Index	4	47.2	9.9	37.2	9.4	21.19%	10.0	−3.9	23.9	2.3	0.11
PROMIS CAT v1.0 - Sleep Disturbance	3	0.8	0.01	0.7	0.3	13.58%	0.1	−0.5	0.8	0.8	0.52
Brief Pain Inventory – Pain Interference	3	5.2	2.3	2.8	3.4	46.37%	2.4	−0.6	5.5	3.5	0.07
Adult Executive Functioning Index – Working Memory	3	28.7	2.5	23.0	5.3	19.86%	5.7	−13.0	24.3	1.3	0.32
Adult Executive Functioning Index – Inhibition	3	13.7	3.1	12.3	6.4	10.22%	1.3	−9.9	12.5	0.4	0.66

Abbreviations: L, lower confidence interval; M, mean; SD, standard deviation; U, upper confidence interval.

VR applications generally are not useable by individuals with cognitive or visual deficiencies, and prolonged exposure to a digital screen a few centimeters from the eyes may lead to strain, headaches, and symptoms of cybersickness (Brady et al., 2021, 2022). This is an encouraging finding as it suggests that not only were participants willing to be treated in a virtual environment, but they were able to complete a course of treatment with no reported harm.

Findings suggest that data collection in a virtual environment although variable was highly viable. Sixty per cent of all outcome measures were collected on at least two occasions. The data suggest that patient reported outcome measures were less likely to be collected on two occasions in comparison to the data collected primarily via the software while using the headset and hand controllers. Future consideration need focus on methods that would increase the response rate for such outcome measures. Thus, prospective feasibility and pilot trials will be needed to more robustly analyze the viability and veracity of outcome data collected virtually in the metaverse.

Data suggest that no individual reported deterioration during the treatment and data collection periods. The reported findings suggest there is a statistically significant reduction in anxiety and stress by using a VR treatment approach, as measured by the GAD-7 and the Perceived Stress Scale (PSS). There were also statistically significant improvements in health and pain as measured by the Patient Health Questionnaire – 9 (PHQ-9), Brief Pain Inventory – Pain Severity, and Brief Pain Inventory – Pain Interference. Improvements in visual analog scale (VAS) (pain) at the end of a single VR session and statistically significantly improvements for movement quality as demonstrated by movement response times and action times for both hands, neck movement speed and the number of items remembered was also observed.

Another important finding was that more than half (52.6%) of treatments were conducted without any clinical input. This strongly suggests that this model of treatment supports self-management. It allows people requiring care to access treatment at a time and place convenient for them and reduces the need for both clinical input and attendance at physical 'brick and mortar' health establishments. This finding will be of interest to patients, clinicians, educators, policy makers, funders, and all stake holders in the provision of healthcare for people seeking care with stress and anxiety disorders.

This study has limitations that need be acknowledged. The retrospective analysis of data was not blinded, is subject to selection bias, respondent bias, recall bias, and response bias. The study design did not include a non-treatment control group and, therefore, the outcomes may be due to natural improvement over time or contextual effects such as placebo. There were potential confounding variables that were unmeasured and uncontrolled in the analysis which includes unequal populations in the three countries where participates received treatments. Other examples include age of participants, duration of symptoms, concurrent comorbidities, and potential lack of standardization of condition education within and between clinicians for the various conditions being treated. Finally, although the findings suggest that statistical significance was achieved in several patient-reported outcomes, it is uncertain if clinically important change occurred during the VR intervention. While not the focus of this study, it must be addressed in future more robust prospective clinical trials.

5. Conclusions

After musculoskeletal disorders, mental health conditions rank globally as the second largest group of health conditions, associated with years lived with disability. More than 50% of people who live with stress and anxiety do not access services due to inconvenience, embarrassment, or concerns relating to stigmatization around mental health. This suggests that additional approaches are needed. Virtual reality can offer several interventions recommended for reducing stress and anxiety, such as embodying people in relaxing environments, encouraging relaxed breathing, and increasing physical activity. The results of this retrospective review of health records for people being treated with virtual reality in the metaverse suggest that this method is safe, can be performed by patients independent of clinicians, and away from traditional 'brick and mortar' institutions. The data also suggest that some outcomes used to assess change in people being treated for stress and anxiety significantly improved. The value of this approach needs to be more robustly tested in prospective randomized clinical trials.

Author disclosures

Eran Orr, Miki Levy, Omer Weissberger, and Tal Arbel are directly employed by XRHealth in a full-time capacity. Jeremy Lewis works in a part-time consultancy basis for XRHealth contributing to Research and Clinical Development.

Funding source

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author contribution statement

Eran Orr; Miki Levy: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Tal Arbel: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Yaron Sela: Analyzed and interpreted the data.

Omer Weissberger: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis

tools or data; Wrote the paper.

Omer Liran; Jeremy Lewis: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Additional information

No additional information is available for this paper.

Declaration of competing interest

Data will be made available on request.

References

[1] T. Vos, R.M. Barber, B. Bell, A. Bertozzi-Villa, S. Biryukov, I. Bolliger, et al., Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013, Lancet 386 (9995) (2015) 743–800.

[2] P. Varma, M. Junge, H. Meaklim, M.L. Jackson, Younger people are more vulnerable to stress, anxiety and depression during COVID-19 pandemic: a global cross-sectional survey, Prog. Neuro Psychopharmacol. Biol. Psychiatr. 109 (2021), 110236.

[3] J.M. Bogardus, M. Blackinton, B. Litwin, T.M. Nelson, K. Mitchell, Depression, anxiety, and stress in doctor of physical therapy students: analysis of incidence and lived experiences, J. Phys. Ther. Educ. 35 (3) (2021) 251–257.

[4] M.H. Browning, L.R. Larson, I. Sharaievska, A. Rigolon, O. McAnirlin, L. Mullenbach, et al., Psychological impacts from COVID-19 among university students: risk factors across seven states in the United States, PLoS One 16 (1) (2021), e0245327.

[5] B. Kumar, M.A.A. Shah, R. Kumari, A. Kumar, J. Kumar, A. Tahir, Depression, anxiety, and stress among final-year medical students, Cureus 11 (3) (2019).

[6] J. Lee, H.J. Jeong, S. Kim, Stress, anxiety, and depression among undergraduate students during the COVID-19 pandemic and their use of mental health services, Innovat. High. Educ. 46 (5) (2021) 519–538.

[7] D.F. Zatzick, J.E. Russo, W. Katon, Somatic, posttraumatic stress, and depressive symptoms among injured patients treated in trauma surgery, Psychosomatics 44 (6) (2003) 479–484.

[8] T.A. Wiseman, K. Curtis, M. Lam, K. Foster, Incidence of depression, anxiety and stress following traumatic injury: a longitudinal study, Scand. J. Trauma Resuscitation Emerg. Med. 23 (1) (2015) 29.

[9] K. Gao, C. Boyd, M.D. Wiederhold, B.K. Wiederhold, VR mobile solutions for chronic stress reduction in young adults, Annu. Rev. 88 (2014).

[10] A.P. Anderson, M.D. Mayer, A.M. Fellows, D.R. Cowan, M.T. Hegel, J.C. Buckey, Relaxation with immersive natural scenes presented using virtual reality, Aerosp. Med. Hum. Perform. 88 (6) (2017) 520–526.

[11] I. Cikajlo, U. Cizman Staba, S. Vrhovac, F. Larkin, M. Roddy, A cloud-based virtual reality app for a novel telemindfulness service: rationale, design and feasibility evaluation, JMIR Res. Protoc. 6 (6) (2017) e108.

[12] R.C. Kessler, A. Sonnega, E. Bromet, M. Hughes, C.B. Nelson, Posttraumatic stress disorder in the national comorbidity survey, Arch. Gen. Psychiatr. 52 (12) (1995) 1048–1060.

[13] A.J. Baxter, K.M. Scott, T. Vos, H.A. Whiteford, Global prevalence of anxiety disorders: a systematic review and meta-regression, Psychol. Med. 43 (5) (2013) 897–910.

[14] A. Scott, J.L. Cook, D.A. Hart, D.C. Walker, V. Duronio, K.M. Khan, Tenocyte responses to mechanical loading in vivo: a role for local insulin-like growth factor 1 signaling in early tendinosis in rats, Arthritis Rheum. 56 (3) (2007) 871–881.

[15] S.R. Chekroud, R. Gueorguieva, A.B. Zheutlin, M. Paulus, H.M. Krumholz, J.H. Krystal, et al., Association between physical exercise and mental health in 1·2 million individuals in the USA between 2011 and 2015: a cross-sectional study, Lancet Psychiatr. 5 (9) (2018) 739–746.

[16] A. Kandola, D. Vancampfort, M. Herring, A. Rebar, M. Hallgren, J. Firth, et al., Moving to beat anxiety: epidemiology and therapeutic issues with physical activity for anxiety, Curr. Psychiatr. Rep. 20 (8) (2018) 1–9.

[17] K.M. Lukasik, O. Waris, A. Soveri, M. Lehtonen, M. Laine, The relationship of anxiety and stress with working memory performance in a large non-depressed sample, Front. Psychol. 10 (2019) 4.

[18] A. Michaelides, P. Zis, Depression, anxiety and acute pain: links and management challenges, PGM (Postgrad. Med.) 131 (7) (2019) 438–444.

[19] A. Prikhidko, H. Long, M.G. Wheaton, The effect of concerns about COVID-19 on anxiety, stress, parental burnout, and emotion regulation: the role of susceptibility to digital emotion contagion, Front. Public Health 8 (2020), 567250.

[20] L.E. Powell, A.M. Myers, The activities-specific balance confidence (ABC) scale, J. Gerontol. A Biol. Sci. Med. Sci. 50a (1) (1995) M28–M34.

[21] Y. Holst, L.B. Thorell, Adult executive functioning inventory (ADEXI): validity, reliability, and relations to ADHD, Int. J. Methods Psychiatr. Res. 27 (1) (2018).

[22] J.M. Binkley, P.W. Stratford, S.A. Lott, D.L. Riddle, N.A.O.R.R. Network, The Lower Extremity Functional Scale (LEFS): scale development, measurement properties, and clinical application, Phys. Ther. 79 (4) (1999) 371–383.

[23] D. Cella, W. Riley, A. Stone, N. Rothrock, B. Reeve, S. Yount, 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. 63 (11) (2010) 1179–1194.

[24] A. Gaggioli, F. Pallavicini, L. Morganti, S. Serino, C. Scaratti, M. Briguglio, et al., Experiential virtual scenarios with real-time monitoring (Interreality) for the management of psychological stress: a block randomized controlled trial, J. Med. Internet Res. 16 (7) (2014) e167.

[25] M.R. Donnelly, R. Reinberg, K.L. Ito, D. Saldana, M. Neureither, A. Schmiesing, et al., Virtual reality for the treatment of anxiety disorders: a scoping review, Am. J. Occup. Ther. 75 (6) (2021).