Examining the Efficacy of Virtual Reality-Enhanced Behavioral Activation for Adults with Major Depressive Disorder: A Randomized Controlled Trial

Margot Paul, Kim Bullock, Jeremy Bailenson, David Burns

Submitted to: JMIR Mental Health
on: August 30, 2023

Table of Contents

Examining the Efficacy of Virtual Reality-Enhanced Behavioral Activation for Adults with Major Depressive Disorder: A Randomized Controlled Trial

Margot Paul[1] PsyD; Kim Bullock[1] MD; Jeremy Bailenson[2] PhD; David Burns[1] MD

[1]Department of Psychiatry and Behavioral Sciences Stanford University School of Medicine Stanford US
[2]Department of Communication Stanford University Stanford US

Corresponding Author:
Margot Paul PsyD
Department of Psychiatry and Behavioral Sciences
Stanford University School of Medicine
401 Quarry Rd
Stanford
US

Abstract

Background: Major depressive disorder (MDD) is a global concern with increasing prevalence. While many evidence-based psychotherapies (EBPs) have been identified to treat MDD, there are many barriers to successfully doing so. Virtual reality (VR) has been used as an effective treatment tool for a variety of mental health disorders, but few have examined its effectiveness for the treatment of MDD as a primary outcome measure. While our prior study illustrated that VR is a feasible, acceptable, and tolerable method of delivering VR-enhanced behavioral activation (BA) therapy, no study to date has examined its efficacy in treating MDD.

Objective: To examine the clinical efficacy of using VR to engage in BA compared to a traditional BA treatment for adults diagnosed with MDD. To corroborate our previous study's findings that VR is a feasible, acceptable, and tolerable method of delivering BA for adults diagnosed with MDD.

Methods: We conducted a nonblinded between-subjects randomized controlled trial. This study took place remotely via Zoom telehealth between December 19, 2022 and July 24, 2023. This study utilized the same brief three week, four-session BA protocol documented in our previous study, with the main difference being this study's VR-enhanced BA participants used the more immersive and interactive Meta Quest 2 VR headset to complete their BA homework. The primary outcome was measured by the Patient Health Questionnaire-9 (PHQ-9). The secondary outcome was measured by dropout rates, serious adverse events, completion of homework, an adapted telepresence scale, a simulator sickness questionnaire, and an adapted technology acceptance model.

Results: Of 71 participants assessed for eligibility, 26 were recruited and randomized to receive either VR-enhanced BA (n=13) or traditional BA (n=13). The mean age of the 26 participants (6 male, 19 female, 1 non-binary/third gender) was 50.3 (SD = 17.3). This study demonstrated that VR-enhanced BA is as efficacious as traditional BA in treating symptoms of depression, as both groups experienced a statistically significant decrease in symptoms as measured by the PHQ-9, with both groups experiencing about a 4-point decrease in symptoms between sessions 1 and 4. This study also corroborated our previous study's findings that VR is a feasible, acceptable, and tolerable method of experiencing pleasurable activities in conjunction with a brief BA protocol for individuals diagnosed with MDD. No serious adverse events were reported.

Conclusions: The findings of this study demonstrate that VR-enhanced BA is efficacious in treating adults with symptoms of MDD, akin to a traditional BA protocol. The findings also corroborate that VR-enhanced BA is a feasible treatment for MDD. Clinicians can consider incorporating VR into their BA treatment protocol, as indicated by patient presentation, in order to decrease barriers to care. Clinical Trial: ClinicalTrials.gov Identifier: NCT05525390

(JMIR Preprints 30/08/2023:52326)
DOI: https://doi.org/10.2196/preprints.52326

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Original Paper

Margot Paul, Psy.D.[1]; Kim Bullock, M.D.[1], Jeremy Bailenson, Ph.D.[2], David D. Burns, M.D.[1]

[1]Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA, USA
[2]Department of Communication, Stanford University, Stanford, CA, USA

Examining the Efficacy of Virtual Reality-Enhanced Behavioral Activation for Adults with Major Depressive Disorder: A Randomized Controlled Trial

Address correspondence to:

Margot Paul, Psy.D.
Virtual Reality & Immersive Technology (VR-IT) Program
Room 1324
Stanford University, Department of Psychiatry and Behavioral Sciences
401 Quarry Rd.
Stanford, CA 94305-5546, USA

Phone: +1 (781) 572-4136
Email: mdpaul@stanford.edu

Disclosures: No conflicts of interest exist to declare

Abstract

Background: Major depressive disorder (MDD) is a global concern with increasing prevalence. While many evidence-based psychotherapies (EBPs) have been identified to treat MDD, there are many barriers to successfully doing so. Virtual reality (VR) has been used as an effective treatment tool for a variety of mental health disorders, but few have examined its effectiveness for the treatment of MDD as a primary outcome measure. While our prior study illustrated that VR is a feasible, acceptable, and tolerable method of delivering VR-enhanced behavioral activation (BA) therapy, no study to date has examined its efficacy in treating MDD.

Objectives: To examine the clinical efficacy of using VR to engage in BA compared to a traditional BA treatment for adults diagnosed with MDD. To corroborate our previous study's findings that VR is a feasible, acceptable, and tolerable method of delivering BA for adults diagnosed with MDD.

Methods: We conducted a nonblinded between-subjects randomized controlled trial. This study took place remotely via Zoom telehealth between December 19, 2022 and July 24, 2023. This study utilized the same brief three week, four-session BA protocol documented in our previous study, with the main difference being this study's VR-enhanced BA participants used the more immersive and interactive Meta Quest 2 VR headset to complete their BA homework. The primary outcome was measured by the Patient Health Questionnaire-9 (PHQ-9). The secondary outcome was measured by dropout rates, serious adverse events, completion of homework, an adapted telepresence scale, a simulator sickness questionnaire, and an adapted technology acceptance model.

Results: Of 71 participants assessed for eligibility, 26 were recruited and randomized to receive either VR-enhanced BA (n=13) or traditional BA (n=13). The mean age of the 26 participants (6 male, 19 female, 1 non-binary/third gender) was 50.3 (SD = 17.3). This study demonstrated that VR-enhanced BA is as efficacious as traditional BA in treating symptoms of depression, as both groups experienced a statistically significant decrease in symptoms as measured by the PHQ-9, with both groups experiencing about a 4-point decrease in symptoms between sessions 1 and 4. This study also corroborated our previous study's findings that VR is a feasible, acceptable, and tolerable method of experiencing pleasurable activities in conjunction with a brief BA protocol for individuals diagnosed with MDD. No serious adverse events were reported.

Conclusions: The findings of this study demonstrate that VR-enhanced BA is efficacious in treating adults with symptoms of MDD, akin to a traditional BA protocol. The findings also corroborate that VR-enhanced BA is a feasible treatment for MDD. Clinicians can consider incorporating VR into their BA treatment protocol, as indicated by patient presentation, in order to decrease barriers to care.

Keywords: Virtual Reality; Major Depressive Disorder; Behavioral Activation; Depression; Meta quest 2

Trial Registration: ClinicalTrials.gov Identifier: NCT05525390

Original Paper
Introduction
Background
Major depressive disorder (MDD) is a global concern with increasing cases worldwide [1]. Depressive disorders are the most significant contributor to non-fatal health loss worldwide, with a 37.9% increase in its economic burden from 2010 to 2020 [1, 2].

Numerous evidence-based treatments exist for MDD, with behavioral activation (BA) widely viewed as one of its first-line treatments [3]. The behavioral theory of depression states that individuals experience symptoms of depression due to a less frequent engagement in activities that are pleasurable or lead to a feeling of accomplishment [4, 3]. BA provides the tools for individuals to become more behaviorally activated or less avoidant through scheduling and engaging in these positive activities, thus enhancing mood.

Despite the many evidence-based treatments for depression, less than one out of four people in low- to middle-income countries receive the proper treatment [5]. Furthermore, there may be external obstacles that prevent those who experience MDD from engaging in BA, such as physical or psychological limitations, financial constraints, or mental health stigma.

The use of technology can effectively solve barriers to care by allowing individuals access to content that may not have been readily accessible in real life. Virtual reality (VR) is one technology medium that is becoming increasingly popular, with about one in five consumers in the United States using it in 2020 and an estimated 70.8 million people in the United States using it at least once per month in 2023 [6]. While there is a preponderance of support illustrating that virtual reality (VR) is efficacious in treating various mental health conditions, no clinical studies have examined its use directly in MDD populations [7]. Only one study has illustrated that VR-enhanced therapy is a feasible method of treating MDD as a primary outcome measure [8]. While our previous feasibility study observed a possible clinical improvement in using VR to simulate activities in a BA protocol, similar to results from traditional BA, no studies to date have shown statistically efficacious results for the use of VR in treating MDD. If simulating pleasant activities in VR is similarly statistically effective in reducing symptoms of depression as engaging in real-life activities, VR-enhanced BA could provide increased access for patients to engage in BA by minimizing barriers to access, such as mobility restraints and socioeconomic costs. If VR-enhanced BA is not inferior to traditional BA, individuals and clinicians may have a larger diversity of options and modalities for treating MDD.

Objectives
The primary aim of this study was to examine whether using VR to partake in simulated pleasurable and/or mastery activities in conjunction with a brief BA protocol was as efficacious in reducing symptoms of depression as engaging in these activities in real life. In addition, the present study examined the feasibility, tolerability, and acceptability of using an immersive and interactive VR-headset to engage in a brief BA protocol.

Methods
Study Design
This study was a 2-arm, nonblinded, between-participant randomized controlled trial (RCT) created to test the efficacy of decreasing symptoms of depression by using VR to engage in simulated

pleasurable and/or mastery activities compared to engaging in these activities in real life. This study also examined the feasibility, acceptability, and tolerability of using freely chosen, room scale, immersive, embodied, and interactive experiences using the Meta Quest 2 VR headset to engage in these simulated activities. The study aimed to recruit and enroll 40 participants and recruitment took place remotely via Zoom delivered telehealth sessions between December 19, 2022, and July 24, 2023. The study ended recruitment in July, given the clinical psychology fellow's postdoctoral end date.

Participants

After gaining human-participant consideration and clearance from the Stanford Institutional Review Board (IRB- 66488), participants were recruited nationwide from study flyers posted in the Stanford School of Medicine's Department of Psychiatry and Behavioral Sciences located in Palo Alto, California. The description of the study was also electronically listed on the department's currently recruiting studies website, on ClinicalTrials.gov, and on Craigslist. In addition, and without solicitation, a private web-based company called *Power* included our study on their website and connected participants to this study without any formal agreement, consent, or payment from our research group. The inclusion criteria were as follows: aged ≥18 years; speaks English; and meeting the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, criteria for MDD. The exclusion criteria were as follows; a substance use disorder in the past year, diagnosis of any psychotic or bipolar I disorder, seizure in the last 6 months or untreated epilepsy, current suicidal urges or intent, current nonsuicidal self-injury or parasuicidal behavior, changing psychotherapy treatment within the last four months of study entry, or changing psychotropic medication(s) within two months of study entry. This study offered no compensation for participation.

Procedures

The study was conducted by a clinical psychology postdoctoral fellow at Stanford School of Medicine in the Department of Psychiatry and Behavioral Sciences and took place over Zoom. The initial screening procedure consisted of two steps: an initial phone screen and a face-to-face Zoom intake session. During the initial phone screen, callers were assessed for preliminary eligibility and given the opportunity to ask questions about the study [Multimedia Appendix 1]. If initial eligibility criteria were met, potential participants were securely sent a consent form [Multimedia Appendix 2] by email to read, review, and sign at their leisure. Potential participants were informed that they could reach out to the postdoctoral fellow with any questions prior to signing the consent form. After potential participants securely returned their signed consent form to the postdoctoral fellow, the Zoom intake session was held to determine complete study eligibility and acquire demographic information [Multimedia Appendix 3]. See the previously published case report and feasibility study for further details [9, 8].

Enrollment/Randomization

When a participant met full study eligibility and expressed a continued desire to participate in the study, the postdoctoral fellow randomly assigned them to one of the two study arms in a single-blind fashion by using permuted blocks of 4 in sealed envelopes. Participants were notified of their randomization outcome via secure email prior to session 1.

Intervention

The postdoctoral fellow met with each participant for 30-50 minutes once per week for 4 sessions

over Zoom to administer a brief BA therapy protocol. At the beginning of each session, all participants were verbally administered the Patient Health Questionnaire–9 (PHQ-9). If item 9 was endorsed, a risk assessment was conducted in real time, and proper measures were taken in accordance with risk. Both arms followed the protocol for brief BA based on the guidance of published literature [10, 11]. No participants were provided with a stipend for activities.

VR-Enhanced BA: The VR participants were shipped a VR headset prior to the first session, with a prepaid return label. The Meta Quest 2 headset was used for this study. This headset has a resolution of 1832 x 1920 pixels, a 60, 72, 90 Hz refresh rate supported, and room scale [12]. This headset was chosen based on the previous study's participant feedback that they would have preferred a more immersive and interactive headset as well as the Meta Quest 2 being responsible for 75% of the VR market share [13].

All sessions followed the previously established protocol detailed in the case report and feasibility study [9, 8], with two key changes. First, this study's goal was to more closely mimic traditional BA by refraining from confining participants to pre-selected VR choices. Consequently, the Meta Quest 2 headsets did not have any software preloaded or pre-chosen on the device, as it was important to be software agnostic. While VR participants were provided an activity list akin to the Pleasant Events Schedule (PES), containing different category options and ideas within VR, it was made clear that participants could choose any activity offered within the headset [See Multimedia Appendix 4; 14]. In between each session, participants were asked to complete ≥4 VR activities per week and one post-VR questionnaire, pertaining to all completed VR activities from the week, to assess spatial presence, simulator sickness, and acceptability [See Multimedia Appendix 5].

Traditional BA: The traditional BA participants followed the same protocol as the VR-Enhanced BA participants, except that they were not provided with a VR headset, were sent the PES, and were asked to choose and complete ≥4 activities in the physical world.

For further details about the intervention and control arms, see the previously published case report and feasibility study [9, 8].

Measures

See the previously published case report [9] for information on the following outcome measures: demographics, the Mini-International Neuropsychiatric Interview, PHQ-8, PHQ-9, presence scale, acceptability, feasibility, and tolerability. Of note, agitation (i.e., the brief agitation measure) was not used as a measure of tolerability in the present study. Additionally, unlike the prior study, the number of times the headset was used was not determined from the device itself; rather, it was attained via participant self-report.

Statistical Methods

To assess the clinical efficacy of the VR-enhanced BA treatment compared with the traditional BA treatment group, the participants' depression scores were measured using the PHQ-8 from the initial phone screen and the PHQ-9 from the subsequent 4 session timepoints. Structural Equation Modeling (SEM) with the Analysis of Moment Structures [AMOS; 15], Version 28.0, was used because of its ability to compare competing models using nested tests, compare parameter estimates across groups, and estimate missing data models using Full-Information Maximum Likelihood [15, 16, 17]. SEM is widely used in the social sciences and was chosen for this study given

its ability to adeptly manage missing data and exhibit greater statistical power compared to conventional multiple regression analyses [18], which was important given this study's relatively low sample size. Only the X^2 statistic was used to evaluate model fit [19]. Changes in X^2 values relative to changes in degrees of freedom (X^2 difference tests) were used to compare nested models. These results were also confirmed by using traditional linear growth models [20]. SEM with AMOS was also used to assess whether there were any significant differences between age and gender in the two groups, and whether these variables had any causal effects on mood, as measured by the PHQ.

Please see the previously published feasibility study for information on how presence, feasibility, acceptability, and physical tolerability were calculated [8]. Emotional tolerability was not assessed in the present study.

Ethics Approval

This study was approved by Stanford University's IRB (protocol #66488) and registered on ClinicalTrials.gov (ID #NCT05525390). A CONSORT (Consolidated Standards of Reporting Trials) checklist is also included in Multimedia Appendix 6.

Results

Participant Demographics

The sample consisted of 26 adults (mean age 50.3, SD 17.3 years; 6/26, 23% male; 19/26, 73% female; and 1/26, 4% nonbinary or third gender), with 21 (81%) adults (mean age 47.9, SD 17.7 years; 5/21, 24% male; 15/21, 71% female; and 1/21, 5% nonbinary or third gender) completing the full protocol. SEM AMOS was used in a test to determine whether there was a significant difference in age or gender between the two arms. When their means were set to be equal, the X^2 (12 df, n=13) = 12.65, *P*=.40. These results indicate that there were no significant differences in age or gender between groups.

See Figure 1 for the CONSORT diagram and Table 1 for more participant demographic information.

Figure 1. CONSORT diagram.

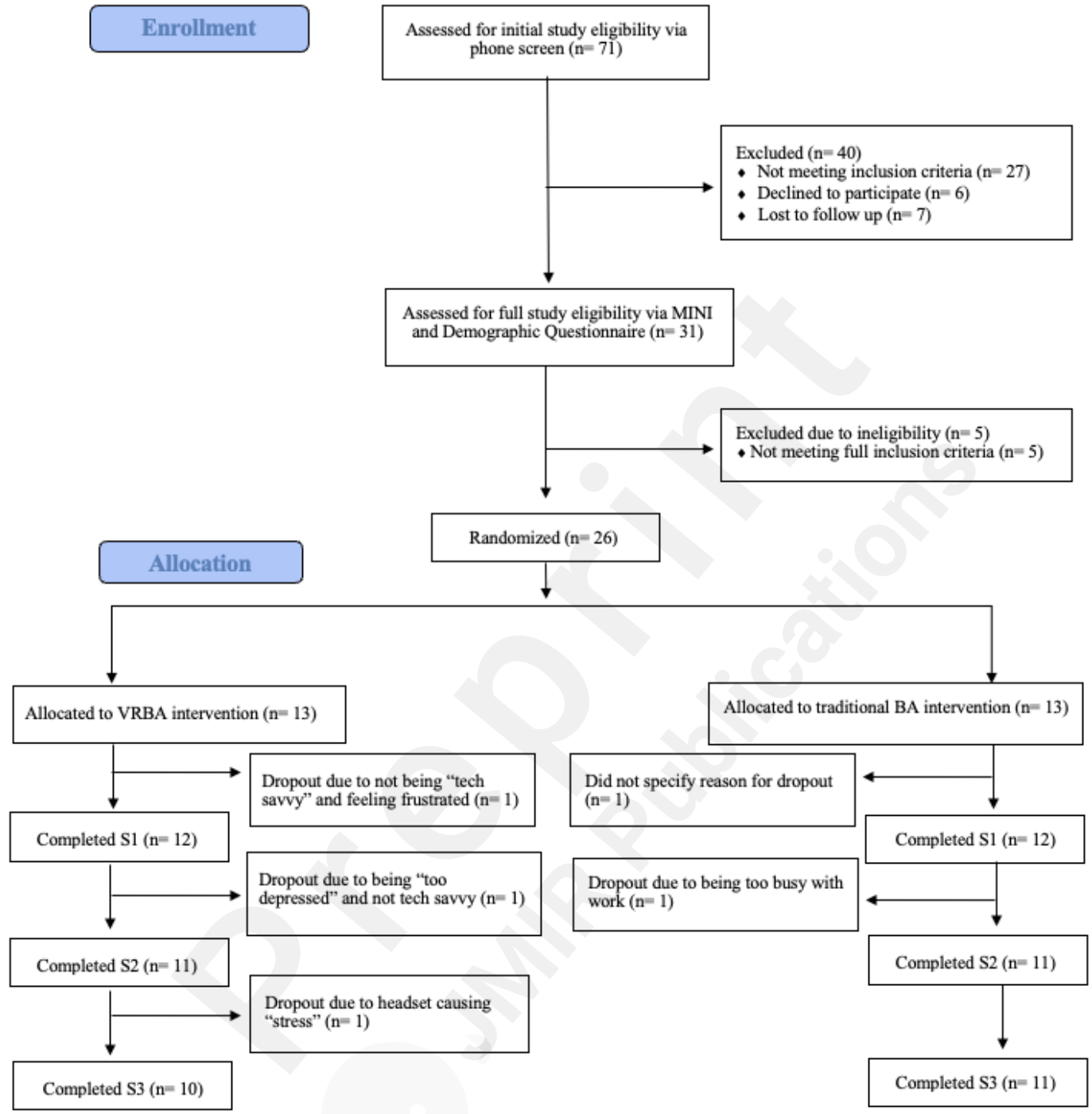


Table 1. Participant demographics (N=26).

Characteristic	VR[a] BA[b] (n=13), n (%)	Traditional BA (n=13), n (%)	Total, n (%)
Gender			
Male	1 (8)	5 (39)	6 (23)
Female	11 (85)	8 (62)	19 (73)
Nonbinary or third gender	1 (8)	0 (0)	1 (4)
Age (years)			
20 to 29	3 (23)	2 (15)	5 (19)
30 to 39	3 (23)	0 (0)	3 (12)

	40 to 49	1 (8)	2 (15)	3 (12)
	50 to 59	3 (23)	3 (23)	6 (23)
	60 to 69	1 (8)	5 (39)	6 (23)
	70 to 79	2 (15)	1 (8)	3 (12)
Race or ethnicity				
	Non-Hispanic White	10 (77)	8 (62)	18 (69)
	Hispanic/Latino	0 (0)	1 (8)	1 (4)
	Indian	1 (8)	2 (15)	3 (12)
	Black	0 (0)	1 (8)	1 (4)
	Mexican	1 (8)	0 (0)	1 (4)
	Asian	1 (8)	1 (8)	2 (8)
Past mental health treatment				
	Yes	12 (92)	12 (92)	24 (92)
	No	1 (8)	1 (8)	2 (8)
Current mental health treatment				
	Yes	11 (85)	6 (46)	17 (65)
		Psychotherapy only	1 (9)	1 (17)	2 (12)
		Psychotropic medications only	3 (27)	3 (50)	6 (35)
		Psychotherapy and medications	7 (64)	2 (33)	9 (53)
	No	2 (15)	7 (54)	9 (35)
Previous experience using VR				
	0 times	9 (69)	9 (69)	18 (69)
	1 to 4 times	3 (23)	3 (23)	6 (23)
	5 to 9 times	1 (8)	1 (8)	2 (8)
	≥10 times	0 (0)	0 (0)	0 (0)
Purpose of past VR use				
	Gaming	3 (75)	2 (50)	5 (63)
	Treatment	0 (0)	0 (0)	0 (0)
	Research	1 (25)	2 (50)	3 (38)

[a]VR: virtual reality.

[b]BA: behavioral activation.

Clinical Efficacy

Protocol completers in the VR-enhanced BA arm went from an average of moderately severe (15.8, phone intake) to moderate (12.8, session 1) to mild (8.4, session 4) symptoms of depression (Figure 2). The average decrease of 7.4 points on the PHQ between the initial phone screen and session 4 was not only statistically significant but also represents a clinically significant and meaningful decrease in symptoms [>5; 21]. Participants in the traditional BA arm remained at an average of moderately severe (16.0) between the phone intake to the beginning of session 1 (14.5) and reduced to moderate (10.7) symptoms of depression by session 4 (Figure 2). This average decrease of 5.3 points on the PHQ between the initial phone screen and session 4 was also both statistically and clinically significant. Participants in both study arms experienced around a 4-point decrease in symptoms of depression between sessions 1 and 4, with participants in the VR-enhanced BA arm experiencing a 4.4 point decrease and participants in the traditional BA arm experiencing a 3.7 point

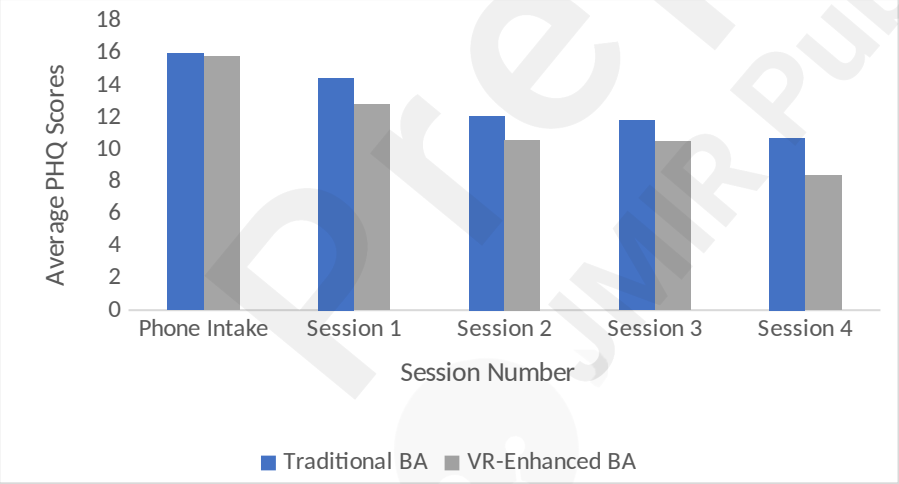
decrease.

In the SEM models, the ITT participant mean of the initial PHQ was 15.3 with a variance of 8.7 in the VR arm and 16.1 with a variance of 8.8 in the traditional arm. In a test to determine whether there was a significant difference in depression symptoms between the initial phone screening and the start of session 1, their means were set to be equal. The X^2 (1 df, n=13) = 1.9, *P*=.17 in the traditional BA arm and X^2 (1 df, n=13) = 4.7, *P*=.03 in the VR-enhanced BA arm. These results indicate that the participants in the VR-enhanced BA arm already saw a significant decrease in PHQ symptoms before the treatment began.

In order to determine whether the participants experienced a further statistically significant decrease in PHQ-9 symptoms between the beginning of session 1 and session 4, these means were set to be equal. The X^2 (1 df, n=13) = 5.3, *P*=.02 in the traditional BA arm and X^2 (1 df, n=13) = 4.4, *P*=.04 in the VR-enhanced BA arm. These results indicate that the participants in both study arms saw a significant decrease in PHQ-9 symptoms between the start and end of the study.

In a nested test, the causal effects of the Arm at each time point were set to zero, in order to determine whether there were statistically significant changes in the PHQ scores in the VR-enhanced BA compared to the traditional BA group. The increase in chi-square was not significant: X^2 (5 df, N = 26) = 3.4, *P*=.64. These encouraging results indicate that both traditional BA and VR-enhanced BA interventions were similarly effective in reducing symptoms of depression.

Figure 2. Protocol completer average PHQ scores with standard deviation bars per group across time.



VR-Enhanced BA Feasibility

The completion rate was 77% (10/13) in the VR-enhanced BA arm and 85% (11/13) in the traditional BA arm. No participants reported any serious adverse events. The participants in the VR-enhanced BA arm used the headset, on average, slightly less than required (Table 2). Only one participant did not submit a post-VR questionnaire during one week of treatment. This participant reported that she did not use the headset during that week due to being more busy than usual with work deadlines and feeling physically ill.

The average total presence rating of the ITT VR BA participants was 68% (8.1/12), whereas the average rating of all the VR BA protocol completers was 71% (8.5/12; Table 2). The participant with the lowest presence rating (3.7/12) shared that “tactile” sensations, such as feeling the sun on her

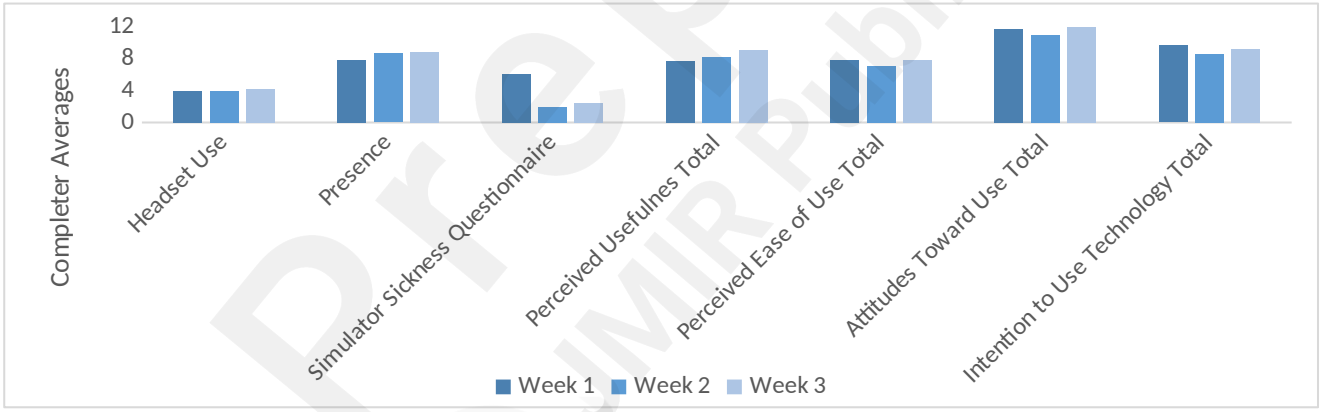
skin, are important to her; and consequently, the VR did not feel immersive. Participants who completed the protocol indicated a higher level of presence, on average, after each subsequent week of VR use (Figure 3).

Table 2. Virtual reality behavioral activation feasibility.

	Adverse events, N	Times headset was used between session 1 and session 4[a], N	Completed homework worksheets[b], N	Level of presence experienced in headset[c] (0-12; 3 items), mean (SD)
Completer average	0	12	2.9	8.5 (2.2)
ITT[e] average	0	11.2	2.3	8.1 (2.5)

[a]Minimum required headset use was 12.
[b]Minimum required completed homework worksheets was 3.
[c]Level of presence contained 3 items with a range of 0 (not at all) to 4 (very strongly) for each item. Higher numbers indicate greater presence.
[d]N/A: not applicable.
[e]ITT: intention-to-treat.

Figure 3. Headset use and post-VR questionnaire results by week among protocol completers.



VR-Enhanced BA Acceptability

Overall, the participants who completed the protocol were “neutral” to “agreed,” with an average rating of 2.8 (where 2=neutral and 3=agree) on the Likert scale and 71% (37/52) acceptability (Table 3), that the VR treatment was acceptable. The participant who had the lowest level of acceptability (26.7/52) informed that the learning curve of the headset and the discomfort from the weight of the headset made it less enjoyable and acceptable. Participants who completed the protocol indicated a higher level of perceived usefulness of the VR, on average, after each subsequent week of use (Figure 3). Between the conclusion of weeks 1 and 3, participants who completed the protocol reported a lower level of desire to continue to use the headset after treatment, on average (Figure 3).

Table 3. Virtual reality behavioral activation acceptability.

	Perceived usefulness[a] (0-12;	Perceived ease of use[a] (0-12; 3	Attitudes toward use[b] (0-16; 4	Intention to use technology[a] (0-12; 3

	3 items), mean (SD)	items), mean (SD)	items), mean (SD)	items), mean (SD)
Completer average	8.4 (2.2)	7.7 (2.6)	11.7 (2.6)	9.2 (1.9)
ITT[c] average	8.1 (2.3)	7.5 (2.5)	11.1 (3.0)	8.4 (3.3)

[a]Domains comprising the technology acceptance model (higher numbers indicate greater acceptability). Perceived usefulness, perceived ease of use, and intention to use technology contained 3 items with a range of 0 (strongly disagree) to 4 (strongly agree) for each item.
[b]Attitudes toward use contained 4 items with a range of 0 (strongly disagree) to 4 (strongly agree) for each item.
[c]ITT: intention-to-treat.

VR-Enhanced BA Tolerability

The average overall physical tolerability of those who completed the full protocol and the ITT participants was 92% (44/48) and 93% (44.4/48), respectively (Table 4). *Eyestrain* was the most endorsed symptom of physical intolerability. *Burping* and *increased salivation* were the least endorsed symptoms of physical intolerability, with one participant endorsing burping after week 1 headset use and one participant endorsing increased salivation after week 1 headset use. The participant who endorsed a relatively higher overall average simulator sickness symptoms (17/48) compared to other participants, experienced the majority of these symptoms after the first week (30/48) of using the headset. This participant shared that the headset felt uncomfortable and heavy on her head and she experienced symptoms of nausea when she was immersed in any activity that had a quick-moving image. Upon trying other activities within the headset, such as the slower moving *Liminal* and YouTube 360 videos, this participant's symptoms reduced to 4/48. Overall, participants who completed the protocol experienced a decrease in simulator sickness symptoms between the conclusion of weeks 1 and 3, on average (Figure 3).

Table 4. Physical tolerability.

	Physical tolerability[a] (0-48; 16 items), total mean[b] (SD)
Completer average	4.0 (5.0)
ITT[c] average	3.6 (4.9)

[a]Physical tolerability determined using the Simulator Sickness Questionnaire. Possible responses for the 16 items ranged from 0 (no more than usual) to 3 (severely more than usual). Lower numbers indicate greater tolerability.
[b]The mean scores for physical tolerability were summed for each participant.
[c]ITT: intention-to-treat.

Discussion

Principal Findings

The results of this study illustrate that using a VR-enhanced BA protocol was as efficacious in decreasing symptoms of depression as administering a traditional BA protocol. Both participants in the traditional and VR-enhanced BA arms experienced a statistically significant reduction in depression symptoms between the initial phone screen and session 4 and between sessions 1 and

4.

While both arms saw a decrease in PHQ symptoms between the initial phone screen and the beginning of session 1, which were prior to treatment, only the VR arm illustrated a statistically significant decrease in symptoms between the phone screen and session 1. These results may indicate that participants in the VR arm had an enhanced expectancy effect and were excited to be receiving the "novel" VR treatment and anticipated that the treatment would be helpful, leading to increased levels of hope and decreases in depressive symptoms [22, 23]. This aligns with qualitative data from participants who learned they were randomized into the VR arm and expressed more excitement than participants who were randomized into the traditional BA arm.

While our prior study suggested the possibility of a greater reduction in symptoms of depression among participants in the VR-enhanced BA arm compared to the traditional BA arm, this study did not demonstrate any such superiority, as the symptom reduction was not statistically or clinically different between groups. The noninferiority of VR-enhanced BA may be attributed to both the positives and negatives of using VR as noted by participants.
Similar to the prior study, participants shared that they found the VR to be "novel," using the VR showed them they could again enjoy activities, and the VR inspired them to engage in real-life activities. This latter fact was true both among participants who found the VR to be a positive experience (i.e., watching a Youtube 360 of a beach inspired them to visit the beach in person) and also for a participant who did not enjoy the VR because of preferences for tactile experiences, and consequently made an increased effort to go outside to feel the sun on their skin. Many participants also noted that the VR-enhanced BA helped improved their mood by taking them to a new place in an immersive way, thereby increasing their attention and decreasing distraction, allowing for a fully mindful experience in the present moment.

Participants also noted several negatives and VR-related struggles that impacted their ability to gain mood improvements. Mainly, the learning curve of the headset device was burdensome. While our previous study purposely chose a simple headset preloaded with activity choices, the present study chose to employ a more immersive and interactive headset with more choices that came with a greater learning curve. Despite research indicating that it is important to learn *how* to use VR before learning *in* VR [24], participants did not need prior VR experience to meet study eligibility, and no part of the study was dedicated to teaching participants how to use the headset, as this was determined to be too divergent from traditional BA.

Consequently, many participants in the VR arm stated that they became "frustrated" while trying to learn how to use the headset. One participant also noted that the ability to choose any activity on the headset led to "decision paralysis," an interesting juxtaposition from the prior study that only had a limited selection of 37 pre-selected videos, of which the feedback was a desire to have more activity options. While activity ideas were provided, when using VR for activity engagement, it may be more helpful to provide a more detailed database of activity options [25].

The conclusion that VR-enhanced BA is as efficacious in reducing symptoms of depression as traditional BA is a critical finding, as patients can use VR to improve their mood if they encounter barriers to engaging in activities in real-life. Participants comments stating, "VR is easier and more convenient than having to go places," "I have been able to visit a few places I have always wanted to travel, so I noticed being so absorbed [by the places]," "VR has a larger realm of possibilities. In the

real world I need to check hours [that events are occurring/open] and the weather," and "I would recommend [using VR] to a friend if they didn't want to do therapy," qualitatively support the notion that VR can help decrease barriers to in-person activity engagement. These statements further corroborate the previous study's suggestion that clinicians can use VR as a first step in behavioral activation for patients that may not have the motivation or desire to engage in activities in real life.

This study also confirmed that using VR-enhanced BA with a more interactive and immersive headset is a feasible, acceptable, and tolerable treatment for individuals diagnosed with MDD. The attrition rate of 23% (3/13) of the participants in the VR-enhanced BA arm of the study is comparable with other VR studies [26, 27], lower than that of many RCTs of internet-based interventions for depression [28], and lower than that of a small-sample pilot RCT exploring exercise as a treatment for depression [29]. Importantly, no participant in the VR-enhanced BA treatment arm dropped out of the study because of serious adverse events, and no serious adverse events were reported throughout the duration of the study.

While participants in the prior study completed, on average, more VR activities than required, the participants in the present study did not meet their total required headset use of ≥4 activities each week. This was due to many participants reporting that the headset was difficult to use and felt like an overwhelming task to learn. Participants remarked that they would have used the headset more often if they had increased familiarity. In this vein, participants reported that the headset became more enjoyable and useful over time, which aligns with the research that states the easier to use the device, the more acceptable it is to users [30]. When working with people unfamiliar with VR, future prototypes of VR-enhanced BA may want to opt for designs that allow simplicity, pre-loaded experiences, and decreased choices.

Considering participant feedback from the prior study that the requirement to complete a post-VR questionnaire after each use was a hindrance and burden, this study only asked participants to complete one post-VR questionnaire a week. While only 20% (1/5) of the participants in the prior study completed a post-VR questionnaire for each completed VR activity, all participants in the present study completed a post-VR questionnaire during the weeks they used the device. Participants in the current study subsequently did not comment on the administrative burden of completing the post-VR questionnaire; however, they did acknowledge that having all the tracking and scheduling accessible online or through an app would make it more convenient for them to remember and complete all the required tasks.

Participants in the present study rated their presence higher, on average, than participants in the prior study, a finding that is consistent with research suggesting that achieving a strong sense of presence is more influenced by interactivity than by realism [31]. Participants noted feeling so present while using the headset that they made comments such as, "[it was] good to be able to go elsewhere [in VR] since I don't have a car," "it is nice to be able to take a break from my kids and be present at home, but not be," and "I was so immersed in the VR that I lost track of time." Additionally, presence ratings increased week-to-week, on average, consistent with participant report that the more familiar they became with the device the more immersed they felt.

The acceptability ratings in the current study were comparatively lower than those recorded for the device utilized in the previous study. Nevertheless, a noteworthy observation from the current study

is that acceptance levels in the domains of *Perceived Usefulness* and *Attitudes Towards Use* exhibited an average increase between the conclusion of weeks 1 and 3. It would be intriguing to extend the study timeline and ascertain if this trend of escalating acceptance continues, potentially surpassing the ratings for the simpler headset. Equally fascinating would be to explore whether the gradual rise in acceptance over time corresponds with more substantial improvements in mood over the same period. This is particularly relevant considering that some participants mentioned that they would have used the device more frequently if they hadn't perceived the learning curve as a hindrance. Further, participants qualitatively indicated that the *Intention to Use Technology* rating was lower given the cost, and lack of affordability, of the Meta Quest 2 headset.

The participants rated the protocol as largely physically tolerable, and no participants dropped out because of adverse effects. While the ratings of physical tolerability were the same (92-93%) between the two studies, the participants in this study qualitatively endorsed more simulator sickness. Participants particularly noted that they found the Meta Quest 2 headset itself to be “heavy” and “uncomfortable” on their faces. Additionally, consistent with the research on simulator sickness, participants noted that they experienced more symptoms of simulator sickness while partaking in activities with a faster-moving image compared to a slower-moving image [32]. However, also aligned with research, participants quantitatively and qualitatively reported a habituation effect, where their simulator sickness symptoms largely decreased over time [33]. All participants reported that their symptoms were quickly resolved upon removal of the headset and did not persist.

While this study expanded upon the prior study by increasing the sample size and employing a more immersive, interactive headset that offered a wider range of activity options, it would be interesting to conduct a similar study that also uses a mobile app to decrease administrative burden for providers and patients and streamline the homework process. It is postulated that the focus on homework in BA is essential to treatment outcome success. Research has demonstrated that homework completion is significantly related to a decrease in symptoms [34]. Specifically, the behavioral tasks of completing pleasant activities contributed the most strongly to decreasing symptoms of depression [34]. Hence, addressing barriers to completing homework tasks becomes pivotal for optimizing treatment results.

Given that previous participants noted decreased headset usage due to administrative constraints and current study participants independently expressed the value of a tracking and reminder app for homework compliance, the next crucial phase involves evaluating whether implementing a mobile app that consolidates scheduling and activity tracking can enhance homework completion rates. This, in turn, could potentially lead to more accurate and consistent homework adherence, thereby further reducing depressive symptoms and enhancing mood, ultimately maximizing the effectiveness of treatment outcomes.

Limitations

While many of the enumerated findings are promising, this study had several limitations. First, the quantitative and qualitative measures were subjective and completed by the participants. Both participants in the VR-enhanced BA and traditional BA arms self-reported their completed activity and mood scores, which allows for inaccurate reporting. Similarly, although the PHQ is a self-report measure, due to the study being conducted remotely, the postdoctoral fellow read the questions aloud for participants to answer. This method may have resulted in less accurate reporting if the

participants felt inclined to respond in a certain way. Additionally, as there were no official follow-ups, it is unknown whether the mood gains that the participants reported were lasting.

In a similar vein, a second limitation is the relatively short study duration, particularly for the participants in the VR-enhanced BA arm. As aforementioned, participants remarked on the learning curve of the headset and both qualitative and quantitative data illustrated that the headset became more acceptable and tolerable each week. Thus, given a longer trial, participants may experience greater mood gains as they become more familiar with the headset. Additionally, one participant in the VR-enhanced BA arm of the study was unable to use the headset between sessions 2 and 3, given both a heavy work week and being physically ill. This participant expressed sadness about this outcome and a desire to expand the study timeline, in order to have more time with the headset. Further, the study's short duration may have led to mood changes due to factors external to the study, such as a relatively heavy or light work week or an illness. Lastly, many participants expressed that there were few free trials or free options within the Meta Quest 2 headset. Some participants informed that they would be more willing to purchase activities if they were able to keep the headset or if the study were longer, so that they had more time with their purchase. Overall, participants in both study arms expressed a desire to lengthen the study timeline and noted that the 3-week, 4-session protocol felt too short.

Lastly, as in our prior study, recruitment was a large obstacle. Although the goal was to randomize 40 MDD participants into one of each study arm, only 26 participants were randomized because other potential participants were excluded based on ineligibility, declining to participate, or being lost to follow-up. Nevertheless, it's important to recognize that this could underscore an inherent challenge in depression studies, where health state and conditional altruism are large contributing factors in participation interest [35]. Moreover, given the diverse nature of the disorder, the findings might not universally apply to all those dealing with symptoms of depression.

Conclusions

The current study findings support our previous report that using VR as a method of administering pleasant activities in a brief BA protocol for individuals diagnosed with MDD is feasible, acceptable, and tolerable. This remained true even when utilizing a more difficult and interactive headset that posed technical and physical challenges.

This study also expanded upon our feasibility trial to perform the first known efficacy trial of VR-enhanced BA. This study demonstrated that VR-enhanced BA was not inferior to traditional BA, as it was equally and statistically efficacious in improving symptoms of depression in a MDD sample, as measured by the PHQ-9.

The results of this study demonstrate it may not be unreasonable for clinicians to suggest the use of VR simulated pleasant activities to patients when delivering behavioral activation, as VR simulated pleasant activities may offer solutions for some of the common problems and barriers encountered when using BA. In deciding on a clinical approach, professionals may need to weigh the advantages and disadvantages of using simpler versus complex headsets. Regardless of the hardware or software specifics, this study supports the notion that utilization of VR may enhance mood in those suffering from major depressive disorder when used in conjunction with individual therapy delivering behavioral activation principles and protocols. More research on the implementation of such an approach is needed to understand how most effectively to leverage this technology in

depressive disorders.

Conflicts of Interest

None declared.

Funding

Wu Tsai Neurosciences Institute.

Abbreviations

BA: behavioral activation
CONSORT: Consolidated Standards of Reporting Trials
EBP: evidence-based psychotherapy
HMD: head-mounted display
ITT: intention-to-treat
MDD: major depressive disorder
PHQ-9: Patient Health Questionnaire–9
RCT: randomized controlled trial
TAU: treatment as usual
VR: virtual reality

References

1. World Health Organization. (2017). *Depression and other common mental disorders: Global health estimates*. https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf
2. Greenberg, P. E., Fournier, A. A., Sisitsky, T., Simes, M., Berman, R., Koenigsberg, S. H., & Kessler, R. C. (2021). The Economic Burden of Adults with Major Depressive Disorder in the United States (2010 and 2018). *PharmacoEconomics*, *39*(6), 653–665. https://doi.org/10.1007/s40273-021-01019-4
3. Halverson, J., Beevers, C., & Kamholz, B. (2016, February 2). *Clinical practice review for major depressive disorder*. Anxiety & Depression Association of America. https://adaa.org/resources-professionals/practice-guidelines-mdd
4. Dimidjian, S., Barrera, M., Martell, C., Muñoz, R. F., & Lewinsohn, P. M. (2011). The origins and current status of behavioral activation treatments for depression. *Annual Review of Clinical Psychology*, *7*(1), 1–38. https://doi.org/10.1146/annurev-clinpsy-032210-104535
5. World Health Organization. (2023). *Depressive disorder (depression)*. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/depression
6. Lin, Y. (2023, April 17). *10 virtual reality statistics you should know in 2023 [infographic]*. Oberlo. https://www.oberlo.com/blog/virtual-reality-statistics
7. Park, M. J., Kim, D. J., Lee, U., Na, E. J., & Jeon, H. J. (2019). A literature overview of virtual reality (VR) in treatment of psychiatric disorders: Recent advances and limitations. *Frontiers in Psychiatry*, *10*. https://doi.org/10.3389/fpsyt.2019.00505
8. Paul, M.D., Bullock, K., & Bailenson, J. (2022). Behavioral Activation for Adults With Major Depressive Disorder: Feasibility Randomized Controlled Trial. *JMIR Ment Health*, 9(5):e35526. https://doi.org/10.2196/35526
9. Paul, M.D., Bullock, K., & Bailenson, J. (2020). Virtual Reality Behavioral Activation as an Intervention for Major Depressive Disorder: Case Report. JMIR Ment Health, 7(11):e24331. https://doi.org/10.2196/24331
10. Jacobson, N. S., Martell, C. R., & Dimidjian, S. (2006). Behavioral activation treatment for depression: Returning to contextual roots. *Clinical Psychology: Science and Practice*, *8*(3), 255–270. https://doi.org/10.1093/clipsy.8.3.255
11. Funderburk, J. S., Pigeon, W. R., Shepardson, R. L., & Maisto, S. A. (2020). Brief behavioral activation intervention for depressive symptoms: Patient satisfaction, acceptability, engagement, and treatment response. *Psychological Services*, *17*(4), 443-451. http://dx.doi.org.stanford.idm.oclc.org/10.1037/ser0000328
12. *Meta quest 2: Our most advanced new all-in-one VR headset: Oculus*. Meta. (2023). https://www.meta.com/quest/products/quest-2/tech-specs/#tech-specs
13. Armstrong, M., & Richter, F. (2023, February 28). *Infographic: Meta leads the way in VR headsets*. Statista Daily Data. https://www.statista.com/chart/29398/vr-headset-kpis/
14. MacPhillamy, D. J., & Lewinsohn, P. M. (1982). The pleasant events schedule: Studies on reliability, validity, and scale intercorrelation. *Journal of Consulting and Clinical Psychology*, *50*(3), 363–380. https://doi-org.stanford.idm.oclc.org/10.1037/0022- 006X.50.3.363
15. Arbuckle, J.L. (1996). Full information estimation in the presence of incomplete data. In G.A. Marcoulides & R.E. Schumacker [Eds.] *Advanced structural equation modeling*. Mahwah,

New Jersey: Lawrence Erlbaum Associates.
16. Wothke, W. (2000). Longitudinal and multigroup modeling with missing data. In T. D. Little, K. U. Schnabel, & J. Baumert (Eds.), *Modeling longitudinal and multilevel data: Practical issues, applied approaches, and specific examples* (pp. 219–240, 269–281). Lawrence Erlbaum Associates Publishers.
17. Burns, D. D., & Spangler, D. L. (2001). Do changes in dysfunctional attitudes mediate changes in depression and anxiety in cognitive behavioral therapy? *Behavior Therapy*, *32*(2), 337–369. https://doi.org/10.1016/S0005-7894(01)80008-3
18. Beran, T.N., Violato, C. (2010). Structural equation modeling in medical research: a primer. *BMC Res Notes* 3, 267. https://doi.org/10.1186/1756-0500-3-267
19. Barrett, P. (2007). Structural equation modelling: Adjudging model fit. *Personality and Individual Differences*, *42*(5), 815–824. https://doi.org/10.1016/j.paid.2006.09.018
20. Grimm, K. J., Ram, N., & Estabrook, R. (2016). *Growth modeling: Structural equation and multilevel modeling approaches*. Guilford Publications.
21. Kroenke, K. & Spitzer, R. L. (2002). The PHQ-9: A new depression diagnostic and severity measure. *Psychiatric Annals*, *32*(9), 509–515. https://doi.org/10.3928/0048-5713-20020901-06
22. Rutherford BR, Wager TD, Roose SP. Expectancy and the Treatment of Depression: A Review of Experimental Methodology and Effects on Patient Outcome. Curr Psychiatry Rev. 2010 Feb 1;6(1):1-10. doi: 10.2174/157340010790596571. PMID: 24812548; PMCID: PMC4011659.
23. Ritschel, L. A., & Cassiello-Robbins, C. (2023). Hope and depression and personality disorders. Current Opinion in Psychology, 49, 101507. https://doi.org/10.1016/j.copsyc.2022.101507
24. Han, E., Nowak, K. L., & Bailenson, J. N. (2022). Prerequisites for Learning in Networked Immersive Virtual Reality. *Technology, Mind, and Behavior*, *3*(4: Winter). https://doi.org/10.1037/tmb0000094
25. Mado, M., Fauville, G., Jun, H., Most, E., Strang, C., & Bailenson, J. N. (2022). Accessibility of Educational Virtual Reality for Children During the COVID-19 Pandemic. *Technology, Mind, and Behavior*, *3*(1: Spring 2022). https://doi.org/10.1037/tmb0000066
26. Bouchard, S., Dumoulin, S., Robillard, G., Guitard, T., Klinger, É., Forget, H., Loranger, C., & Roucaut, F. X. (2017). Virtual reality compared with in vivo exposure in the treatment of social anxiety disorder: A three-arm randomised controlled trial. *The British Journal of Psychiatry*, *210*(4), 276–283. https://doi.org/10.1192/bjp.bp.116.184234
27. du Sert, O. P., Potvin, S., Lipp, O., Dellazizzo, L., Laurelli, M., Breton, R., Lalonde, P., Phraxayavong, K., O'Connor, K., Pelletier, J.-F., Boukhalfi, T., Renaud, P., & Dumais, A. (2018). Virtual reality therapy for refractory auditory verbal hallucinations in schizophrenia: A pilot clinical trial. *Schizophrenia Research*, *197*, 176–181. https://doi.org/10.1016/j.schres.2018.02.031
28. Christensen, H., Griffiths, K. M., & Farrer, L. (2009). Adherence in internet interventions for anxiety and depression: Systematic review. *Journal of Medical Internet Research*, *11*(2), e1194. https://doi.org/10.2196/jmir.1194
29. Foley, L. S., Prapavessis, H., Osuch, E. A., De Pace, J. A., Murphy, B. A., & Podolinsky, N. J. (2008). An examination of potential mechanisms for exercise as a treatment for depression: A pilot study. *Mental Health and Physical Activity*, *1*(2), 69–73. https://doi.org/10.1016/j.mhpa.2008.07.001
30. Manis, K. T., & Choi, D. (2019). The virtual reality hardware acceptance model (VR-HAM): Extending and individuating the technology acceptance model (TAM) for virtual reality

hardware. *Journal of Business Research*, *100*, 503–513. https://doi.org/10.1016/j.jbusres.2018.10.021

31. IJsselsteijn, W.A. (2002). Elements of a multi-level theory of presence: phenomenology, mental processing and neural correlates. Presented at Presence 2002: International Workshop on Presence, Porto, Portugal.
32. Wilson, J.R. (1996). Effects of participating in Virtual Environments: a review of current knowledge. *Safety Science*, *23*, 39-51
33. Davis, S., Nesbitt, K., Nalivaiko, E. (2014, December 2-3). *A systematic review of cybersickness*. Proceedings of the 2014 Conference on Interactive Entertainment, Newcastle, N.S.W. http://dx.doi.org/10.1145/2677758.2677780
34. Rees, C. S., McEvoy, P., & Nathan, P. R. (2005). Relationship between homework completion and outcome in cognitive behaviour therapy. Cognitive Behaviour Therapy, 34(4), 242–247. https://doi.org/10.1080/16506070510011548
35. Hughes-Morley, A., Young, B., Waheed, W., Small, N., & Bower, P. (2015). Factors affecting recruitment into depression trials: Systematic review, meta-synthesis and conceptual framework. *Journal of Affective Disorders*, *172*, 274–290. https://doi.org/10.1016/j.jad.2014.10.005

Multimedia Appendix 1

Telephone Screen Questions

1. What is your name?
2. When is your birthday?
3. What is the language you feel most comfortable speaking?
4. Have you ever been diagnosed with psychosis or bipolar disorder?
5. Have you experienced any seizures in the past 6 months?
6. If yes, are your seizures currently being treated?
7. Are you currently seeing a psychotherapist?
    a. If yes, how long have you been seeing them?
8. Have you changed (or are you planning to change) psychotropic medications within two months?

Ask PHQ-8

Multimedia Appendix 2

Consent Form

Multimedia Appendix 3

Demographic Questionnaire

1. Name: _____
2. What is your date of birth? _____
3. What gender do you identify as?
    a. Female
    b. Male
    c. Transgender
    d. Non-binary/third gender
    e. Prefer not to say
    f. Other
2. What is your racial background?
    a. African American
    b. Black
    c. Chinese
    d. Other Pacific Islander
    e. Indian
    f. Japanese
    g. Korean
    h. Southeast Asian
    i. White – Non-Hispanic
    j. Hispanic or Latino
    k. Mexican
    l. American Indian
    m. Alaskan Native
    n. Hawaiian Native
    o. Middle Eastern
    p. More than one race
    q. Unknown or not reported
    r. Decline to answer
3. Have you received mental health treatment(s) in the past?
    a. Yes: _____
    b. No
4. Which, if any, of the following mental health treatment(s) are you receiving? How often?
    a. Counseling: _____
    b. Psychotropic medication: _____
    c. None
    d. Other: please write _____
5. How many times have you used VR before?
    a. This is my first-time using VR
    b. 1 – 4
    c. 5 – 9
    d. 10+
6. In what capacity have you used VR in the past?
    a. Gaming: _____

b. Treatment: _____
c. Research: _____
d. Other: _____
e. N/A

7. Have you been diagnosed with epilepsy?
    a. Yes
        1. If yes, are you currently receiving treatment for it? Y N (please circle)
    b. No

8. Have you experienced any seizure(s) in the past 6 months?
    a. Yes
    b. No

Multimedia Appendix 4

XR Activity List

Check the ones you are willing to do, and then add any other activities you can think of:

Gaming

- A Fisherman's Tale
  - Puzzle and adventure game
- Demeo
  - Play a magical VR board game
- Echo VR
  - Battle robots in zero gravity
- Eleven: Table Tennis
  - Play table tennis
- Space Pirate Trainer DX
  - Enter the arcade game
- The Climb
  - Rock climb in VR
- The Room VR: A Dark Matter
  - Use clues to solve puzzles
- Ultrawings 2
  - Fly aircrafts and win missions
- Unplugged
  - Play some air guitar
- Walkabout Mini Golf
  - Play mini golf alone or with friends
- Others
  - Choose hundreds of others from the app store

Fitness and Wellness

- Beat Saber
  - Slice blocks to the beat
- Liminal
  - Experience calm, energy, and awe on this platform
- Tripp
  - Explore amazing visuals while you meditate
- Dance Central
  - Dance and groove to the music
- Fit XR
  - Join on demand workout classes
- Holofit
  - Workout in VR
- OhShape VR
  - Move your body with rhythm
- Smash Drums
  - Drum in VR

- Supernatural
    - Workout in VR
- Thrill of the Fight
    - Try your hand at VR boxing
- VZ Fit
    - Workout in VR while exploring the world (can use a stationary bike)
- Others
    - Choose hundreds of others from the app store

Social (Note: Due to the fact that other users are able to interact with you in these environments, there are inherent risks such as being exposed to profanity or other inappropriate language/remarks.)

- Altspace
    - Create and/or attend live events (i.e., concerts, conferences, comedy shows, festivals, etc).
    - EvolVR: partake in daily meditation groups
- Bigscreen
    - Watch movies with other people in VR
- Couch
    - Watch YouTube with other people in VR
- Engage VR
    - Attend or host conferences, meetings, or classes
    - Build your own content or explore what is already out there
- Horizon Venues
    - Attend a concert or game
- Horizon Worlds
    - Join block parties and events around the world
- Rec Room
    - Build, play games, and chat with people from around the world
- vTime XR
    - Meet chat, share photos, and watch content with other people around the world
- VRChat
    - Embody an avatar to play games (i.e., mini golf, escape rooms, karaoke, etc.) and chat with people from around the world
- Others
    - Choose hundreds of others from the app store

Productivity and Education

- Anne Frank House
    - Learn about Anne Frank
- Google Tilt Brush
    - Paint in VR
- Mission: ISS
    - Simulate being in space and learn how to navigate zero gravity
- Mondly
    - Practice languages in VR

- National Geographic Explore VR
    - Visit some of the world's most iconic sites
- Noda
    - Build and share 3D mental models
- Ocean Rift
    - Explore and learn about the ocean
- Painting VR
    - Paint in VR
- Traveling While Black
    - Learn about the history of the restriction of movement for Black individuals
- Tribe XR
    - Become a DJ in VR
- Others
    - Choose hundreds of others from the app store

VR 360

- Check the Views at Whistler, Just Scroll Around
    - Ski and observe the beautiful winter sights of Whistler
- Hamilton: An American Musical 360
    - Practice "Wait for It" with the cast of Hamilton
- National Geographic: "As it is"
    - Explore the Grand Canyon
- National Geographic: Expedition Everest: The Science
    - Learn about climate change in Everest
- National Geographic: Free Solo 360
    - Climb Yosemite's famous El Capitan with Alex Honnold
- National Geographic: Journey into the Deep Sea
    - Explore the oceans of Palau
- National Geographic: Lions 360
    - Learn about African lions
- Others (Tip: When in YouTube, click the "360 Videos" button and search for a complete immersive experience)

Multimedia Appendix 5

Post-XR Questionnaire

Please complete this questionnaire once per week.

Date**:**

Presence

1. **To what extent did you feel like you were actually inside the virtual experience?**

   Not at all Slightly Moderately Strongly Very Strongly

2. **To what extent did you feel surrounded by the virtual world you saw?**

   Not at all Slightly Moderately Strongly Very Strongly

3. **How much did it feel as if you visited another place?**

   Not at all Slightly Moderately Strongly Very Strongly

Please fill in the below questionnaire. Circle the description that best describes the severity of the specified symptom compared to **your baseline.** For example, if you are normally slightly fatigued, and this experience made you no more fatigued than usual, you would answer *no more than usual*. If this experience made you moderately more fatigued that normal, than you would answer *moderately more than usual.*

Nausea	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
General discomfort	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Stomach awareness	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Sweating	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Increased salivation	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Vertigo	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Burping	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual

Difficulty concentrating	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Difficulty focusing	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Eyestrain	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Fatigue	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Headache	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Blurred vision	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Dizzy (eyes open)	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Dizzy (eyes closed)	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual
Fullness of head	No more than usual	Slightly more than usual	Moderately more than usual	Severely more than usual

Technology Acceptance Model (TAM) of XR Headset:

Perceived Usefulness

1. **Using the VR system would encourage me to do things I wouldn't normally do**

Strongly Disagree Disagree Neutral Agree Strongly Agree

2. **Using the VR system would give me something to look forward to during the day**

Strongly Disagree Disagree Neutral Agree Strongly Agree

3. **I feel the VR system is useful**

Strongly Disagree Disagree Neutral Agree Strongly Agree

Perceived Ease of Use

4. **I feel the VR system is easy to use**

Strongly Disagree Disagree Neutral Agree Strongly Agree

5. Learning to use the VR system would be easy for me

Strongly Disagree Disagree Neutral Agree Strongly Agree

6. My interaction with the VR system would be clear and understandable

Strongly Disagree Disagree Neutral Agree Strongly Agree

Attitudes Toward Use

7. I like the idea of using this VR system to engage in enjoyable activities

Strongly Disagree Disagree Neutral Agree Strongly Agree

8. I have a generally favorable attitude toward using this VR system

Strongly Disagree Disagree Neutral Agree Strongly Agree

9. I believe it is a good idea to use this system as part of my treatment process

Strongly Disagree Disagree Neutral Agree Strongly Agree

10. I am satisfied with the VR system

Strongly Disagree Disagree Neutral Agree Strongly Agree

Intention to Use Technology

11. If it were made available to me, I intend to use the VR system

Strongly Disagree Disagree Neutral Agree Strongly Agree

12. If it were made available to me, I would continue to use the VR system after completion of this study

Strongly Disagree Disagree Neutral Agree Strongly Agree

13. I would adopt the VR system in the future

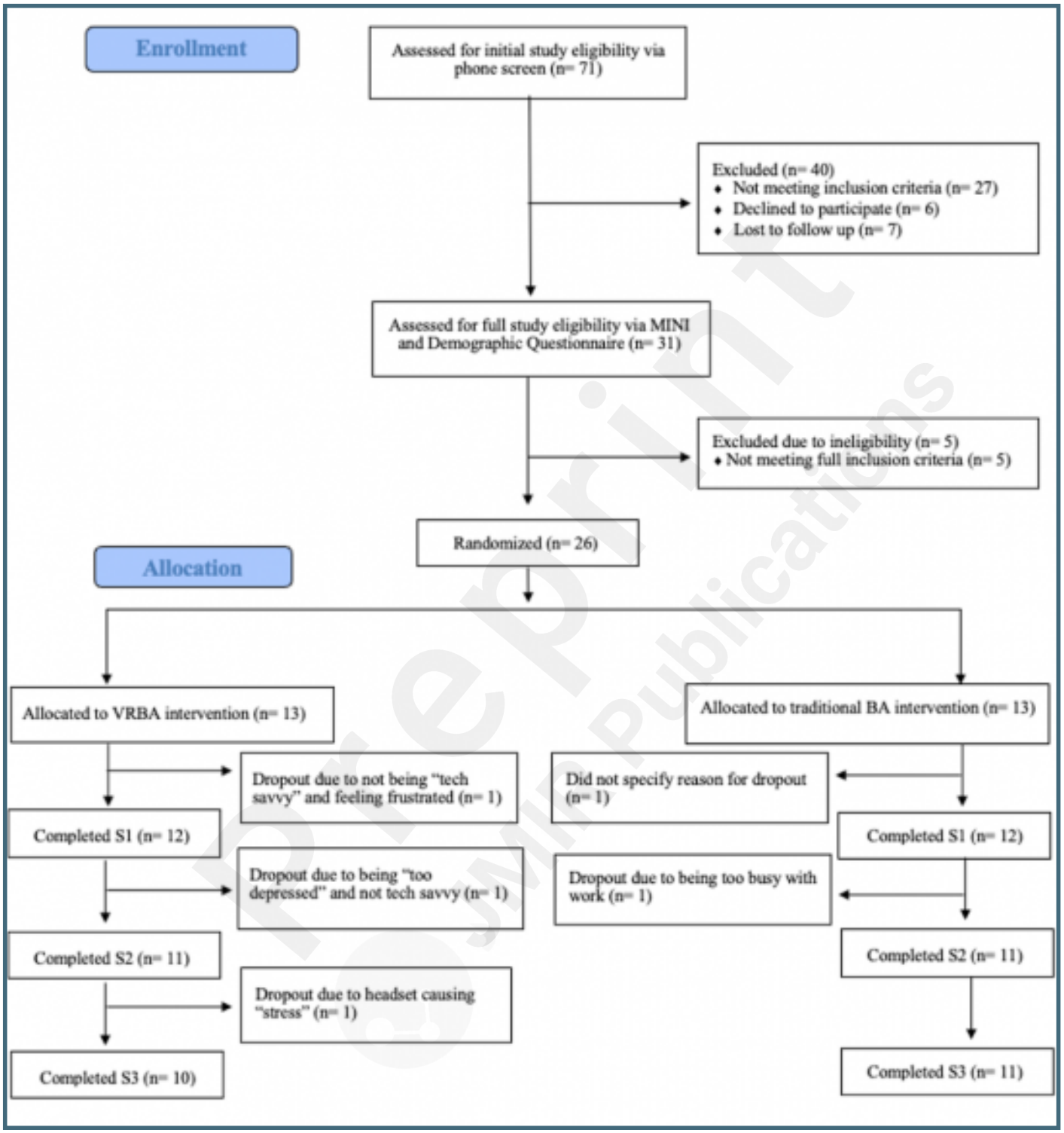
Strongly Disagree Disagree Neutral Agree Strongly Agree

Multimedia Appendix 6
CONSORT-EHEALTH (V 1.6.1)

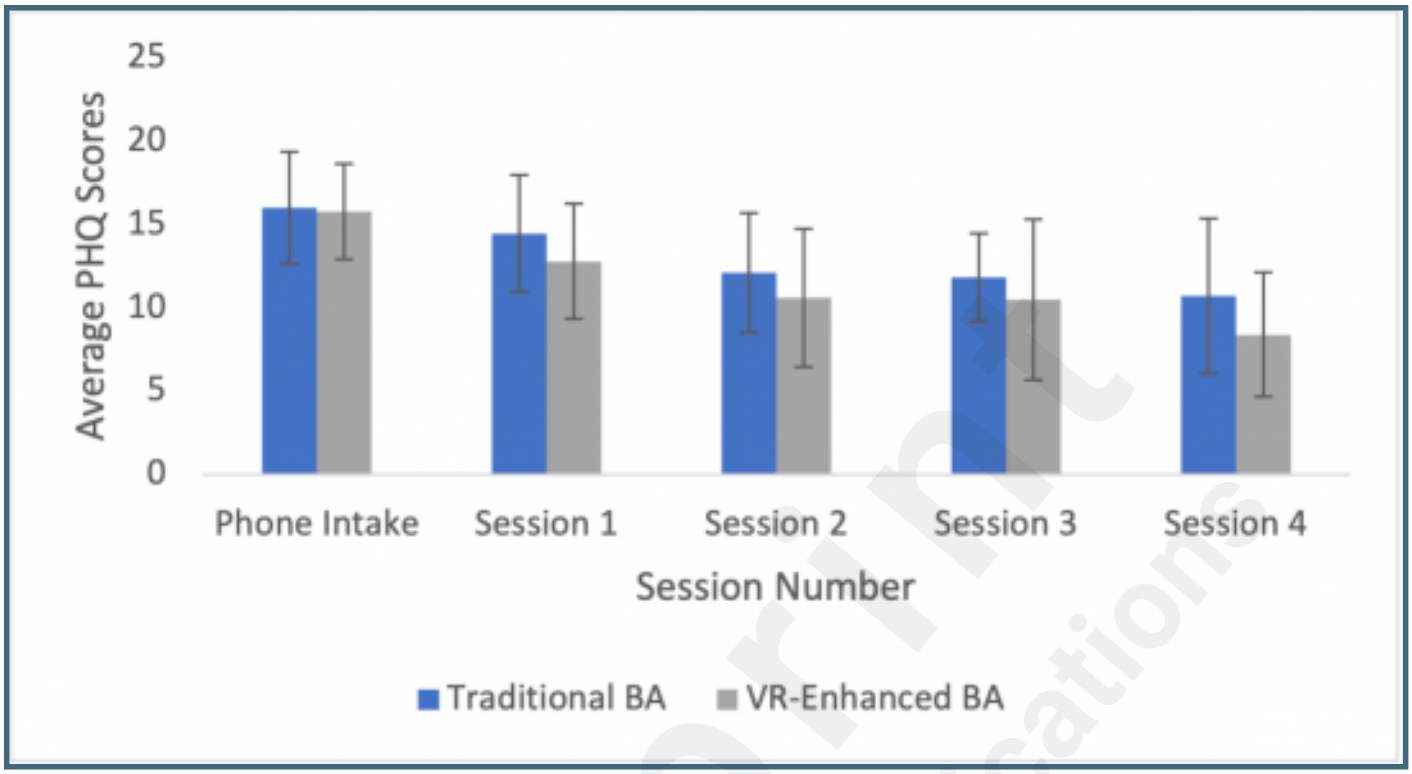
Supplementary Files

Figures

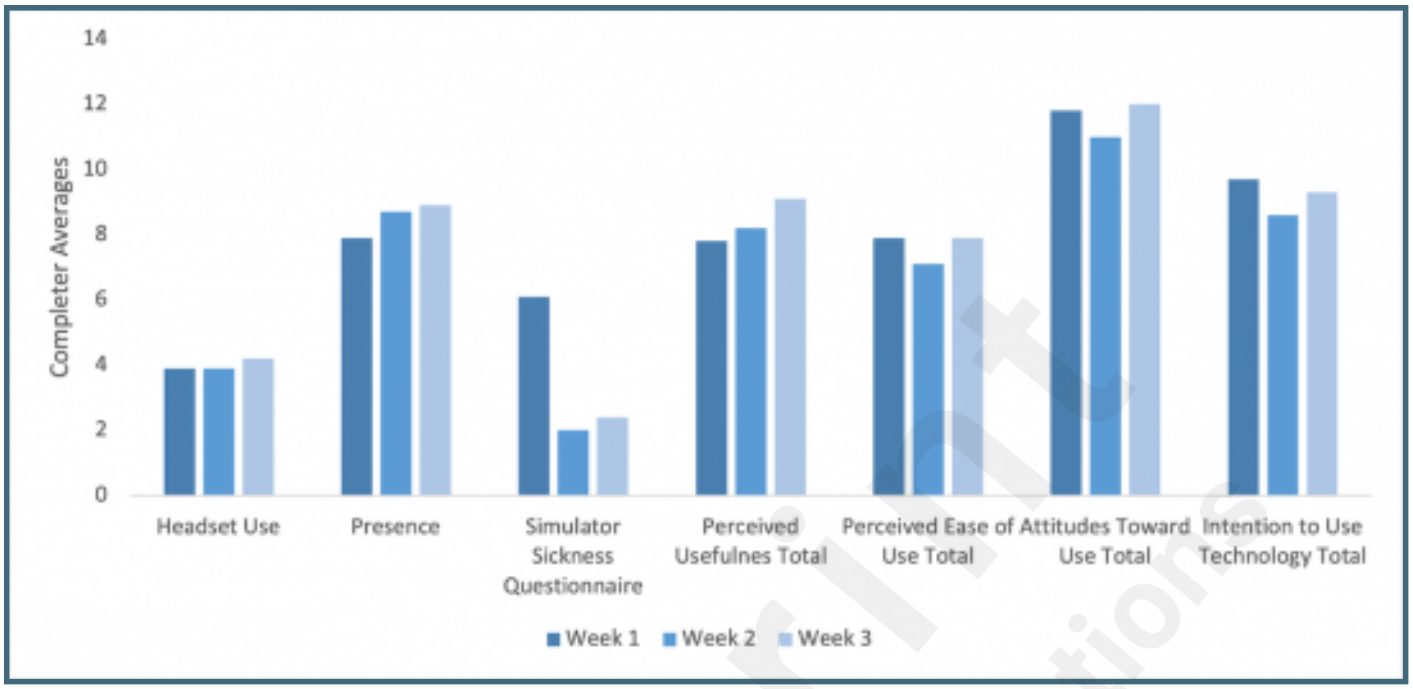
CONSORT diagram.



Protocol completer average PHQ scores with standard deviation bars per group across time.



Headset use and post-VR questionnaire results by week among protocol completers.



Multimedia Appendixes

Telephone Screen Questions.
URL: http://asset.jmir.pub/assets/6db89ceb8dfde471c0bd4243de1c3285.docx

Consent Form.
URL: http://asset.jmir.pub/assets/d16898c817e8d0f2a3f0008294fcd105.docx

Demographic Questionnaire.
URL: http://asset.jmir.pub/assets/d6ce9af4765045cf7e54ce3cfe4e0c34.docx

XR Activity List.
URL: http://asset.jmir.pub/assets/faa8d81a6de82aec3d8ededd4fd26290.docx

Post-XR Questionnaire.
URL: http://asset.jmir.pub/assets/5a81e7ddfb4948f616687ebcf4998faf.docx

CONSORT (or other) checklists

CONSORT Checklist.
URL: http://asset.jmir.pub/assets/36257b23a0403447a9321ed3502175b1.pdf