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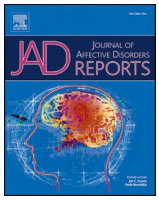

Virtual Reality in the treatment of depression; what therapeutic strategies does VR target?

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ABSTRACT

Background: Major Depressive Disorder (MDD) is one of the most prevalent mental health conditions and has a tremendous impact on those affected. Immersive Virtual Reality (VR) technology has high potential to improve psychotherapy for MDD, as VR can personalize the treatment process and directly influence affect. Research on VR interventions for MDD is emerging, but current applications for treatment are heterogeneous and lack strong theoretical support. This scoping review aims to identify the therapeutic strategies that should and can be targeted in VR interventions for depression.

Methods: A systematic search of the literature was conducted in PubMed, PsycINFO, Ovid Medline, Embase, Web of Science, Google Scholar, Clinical Trials Register, and the 'Dutch Trial Register' from inception through November 2023 to identify the most relevant research.

Results: Findings from 43 studies included in this review resulted in the following potential therapeutic strategies: 1) psychoeducation (n=5), 2) behavioral activation (n=16), 3) cognitive restructuring (n=4), 4) enhancing positive affect (n=5), 5) mental imagery (n=4), 6) skills training (n=3), 7) enhancing cognitive functioning (n=3), and 8) other (n=3).

Limitations: We did not conduct a systematic assessment of the methodological quality of the studies nor perform a statistical analysis of the results.

Conclusions: VR shows potential to facilitate the treatment process for patients with depression in different ways, providing excellent prospects for personalizing and potentially improving the treatment of MDD. Future studies should focus on evaluating presumed mechanisms of change to fully understand the added value of VR in the treatment of depression.

1. INTRODUCTION

Major Depressive Disorder (MDD) is one of the most prevalent mental health conditions and has a tremendous impact both on those affected and on society. MDD significantly worsens quality of life, leads to disruption in interpersonal relationships, and is associated with considerable morbidity and mortality (Mental Disorders Collaborators, 2022). Although various treatment options are available for depression, a recent evaluation of meta-analyses shows that across all forms of psychotherapy, only 43% of depressive patients fully recover from MDD. Effect sizes for treatment with pharmacotherapy for depressive disorder are small as well (SMD = 0.30) (Leichsenring et al., 2022). Moreover, relapse rates are high, and there is no indication that current treatments for MDD have improved over the past years (Bockting et al., 2015a). Thus, there is a strong need for innovative interventions with better treatment outcomes.

An alternative, promising innovative tool with the potential to improve psychotherapy for MDD is virtual reality (VR) therapy. In VR, a

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person uses electronic equipment, such as a head-mounted display (HMD), to enter a computer-generated simulation of real-life situations, in which they can explore and interact with the virtual surroundings (Gorini et al., 2011). VR is often used to simulate the real world, but one of its strengths is that it can also create entirely new worlds that are inaccessible or impossible in real life, such as embodying a child avatar, travelling around the world, diving with dolphins, flying. VR simulations can trigger the same emotional, psychological, and physical reactions as real-life experiences (Martens et al., 2019). The "mediated sense of presence" – an illusion of being present in a simulated place when one is actually in another physical place – offers great potential for using VR in psychotherapy. This immersive experience forms the foundation for various approaches or modalities in VR therapy, each designed to address distinct therapeutic needs and objectives. For example, VR-based CBT applies traditional CBT techniques in a controlled virtual environment, such as practicing cognitive restructuring (Prudenzi et al., 2019). Virtual exposure therapy is mostly used to treat anxiety disorders and PTSD by gradually exposing patients to virtual representations of feared objects or scenarios in a controlled setting (Botella et al., 2017; Carl et al., 2019). Other examples include immersive mindfulness and relaxation experiences (Anderson et al., 2017) as well as the use of VR for cognitive rehabilitation (Dehn et al., 2018).

Overall, VR has been increasingly used in psychotherapy over the past few years, and recent meta-analyses of VR interventions for anxiety and depression have shown that VR-based therapies are as effective as other active control conditions for anxiety and depression, such as face-to-face Cognitive Behavioral Therapy (CBT) (Baghaei et al., 2021a; Fodor et al., 2018; Wu et al., 2021). Since VR technology has advanced rapidly and the possibilities of VR in psychotherapy have greatly expanded, the time has come to aim for an even more targeted and efficient use of VR interventions to improve treatment outcomes.

In all recent systematic or scoping reviews of studies on VR in the treatment of psychiatric disorders, studies focusing on depression were far outnumbered by those focusing on other psychiatric disorders, such as anxiety disorders or psychosis. This is also exemplified in the most recent systematic review in this field: Wiebe et al. (2022) described 18 studies concerning the assessment and treatment of depression, in contrast to 159 studies on anxiety disorders and 91 studies on schizophrenia spectrum disorders. The paucity of information on VR and depression in current reviews makes it difficult to draw conclusions about the efficacy of VR in the treatment of MDD, especially given the large variety of methods used to implement VR, as well as the target areas ranging from VR-based compassion training to VR-based stress management programs (Wiebe et al., 2022).

The current state of research on VR therapy for depression raises questions that are of both scientific and practical value, such as the best way to implement VR in the treatment of depression and which therapeutic strategies should be targeted. Lindner and colleagues took a first step in answering these questions with their theoretical overview of how specific CBT techniques for depression can be incorporated into VR experiences, including psychoeducation, behavioral activation, cognitive restructuring, and social skills training. Moreover, they considered VR to be a powerful tool for enhancing positive affect (Lindner et al., 2019). Positive affect refers to the ability to experience and express positive feelings and emotions, including cheerfulness, pride, and enthusiasm, in contrast to negative affect, which involves the experience of negative emotions such as sadness and distress. In conclusion, to improve psychotherapy for depression with VR, it is crucial to understand when and how VR provides additional value in the treatment of MDD.

1.1. Objective

The main aim of this scoping review is to examine which therapeutic strategies should and can be targeted in VR interventions for depression to improve treatment outcomes. More specifically, we analyze how evidence-based psychological treatment strategies for depression can be transferred in a way that allows them to be utilized through virtual reality techniques. To answer this question, we will provide an overview of the VR technology and types of interventions that have been studied in the treatment of depression and describe their theoretical background.

This is the first scoping review to focus exclusively on VR in the treatment of depression. In contrast to earlier reviews, there will be a greater emphasis on the theoretical background of the included studies. We will critically discuss the results and provide implications for the next steps in VR depression research.

2. METHODS

2.1. Search strategy

This review aimed to identify the most relevant published articles that have studied VR in the treatment of depression. We searched the databases for study titles (all search terms had to be present in the title of the article, not only in the article body) using the following search terms for the core symptoms of depression: *Depression, major depressive disorder, mood disorder, depressive symptoms, depressive mood, positive affect, and anhedonia*, which were combined with *VR* or *Virtual Reality* (see Appendix A for the full search string). We conducted electronic searches using PubMed, PsycINFO, Ovid Medline, Embase, Web of Science, Google Scholar, Clinical Trials Register, and the Dutch Trial Register from inception up to November 1st, 2023, to identify the most relevant research. We also searched the references of these studies and related citations to identify eligible articles not found through the initial search of the electronic databases. Both the search and screening of titles for relevance were performed independently by two researchers. Studies from trial registers were included in the search to provide a comprehensive overview of current and near-future VR interventions for depression. Since the extent to which the interventions on trial registers are described varies between studies, we present relevant information from these studies in Table 2, rather than describing them in the text.

2.2. Eligibility Criteria

The present study aimed to include a wide selection of studies and used broad eligibility criteria to provide a comprehensive overview of the research conducted in the field of VR and depression. Studies were included if: 1. The research concerned a VR environment specifically designed for the treatment of depression or depressive symptoms; 2. The research involved a VR intervention not specifically designed for depression but studied in a sample of patients with MDD (e.g., a VR relaxation intervention tested in participants with MDD). Exclusion criteria were as follows: 1. Written in a language other than English or Dutch; 2. Systematic reviews, theoretical papers, book chapters, and theses; 3. Subclinical depressive symptoms (unless the VR intervention was specifically designed for the treatment of depression); 4. VR used for diagnostic/assessment purposes for depression.

3. RESULTS

3.1. Study selection

The search strategy yielded a total of 319 articles. The first step was to remove all duplicates.

Subsequently, the titles and abstracts of 192 articles were screened for relevance. If a decision could not be made based on the title and abstract, the full article was reviewed and, if necessary, discussed with the research team. In total, 46% (89/192) of the articles were excluded during screening. Non-relevant articles included studies that did not target depression or did not involve an intervention for depression.

Subsequently, 99 studies were reviewed in full text to assess their eligibility according to the defined eligibility criteria. A total of 33

articles and 10 studies from trial registers met the eligibility criteria and were included in the review. The study selection process is described in accordance with PRISMA guidelines in Fig. 1.

3.2. Organization of results

To organize our results, the treatment strategies mentioned by Lindner and colleagues (2019) were considered a starting point. However, since we encountered other therapeutic strategies in addition to CBT techniques, our current paper does not focus exclusively on CBT techniques. A detailed analysis of the therapeutic strategies explored in the included studies led to the following categories: psychoeducation, behavioral activation (i.e., operant conditioning), cognitive restructuring, enhancing positive affect, mental imagery, skills training, enhancing cognitive functioning and other types of VR therapy for depression. In describing the studies, the primary focus is on therapeutic strategies for the VR intervention. We used the authors' own theoretical explanation of the intervention as a guiding principle. When the theoretical background was not clearly described in the study, or VR interventions appeared to be founded on multiple therapeutic strategies; the primary and secondary therapeutic strategies that best fit were selected through agreement between researchers.

An overview of the published studies included in this review, including their main study characteristics, treatment details, and results, is provided in Table 1. Studies retrieved from trial registers are presented in Table 2. An overview of the studies with their primary and, if applicable, secondary therapeutic strategies is illustrated in Fig. 2.

3.3. VR and psychoeducation

To date, five studies have investigated -or are currently investigating- the use of VR in a psychoeducation intervention, to increase symptom awareness and understanding, enhance empathy or change attitudes towards depression.

Migoya-Borja et al. (2020) designed a VR psychoeducational tool to increase symptom awareness in depressive patients. In this VR intervention, the participant must engage in a conversation with a digital character about the symptoms of depression. According to the authors, self-stigma — the loss of self-esteem and efficacy and the internalization of public prejudices — is an important barrier to seeking treatment among patients with depression. The authors claim that the advantage of VR in their intervention is that patients may feel more comfortable discussing their symptoms with a digital avatar than face-to-face with a therapist. Findings from their pilot study showed that participants rated the VRight intervention as useful and user-friendly. Interestingly, participants with lower baseline depressive symptoms showed a decrease in depressive symptoms, while participants with higher baseline depressive symptoms showed an increase in depressive symptoms after the VR intervention.

Hussain et al. (2018) also focused on the importance of stigmatization as a barrier to help-seeking for patients with depression. The intervention consists of 360-degree VR videos in which a virtual person shares stories about their experiences of living with depression. After the video, participants were asked to share their personal experiences of living with depression. According to the authors, patients with depression can benefit from both hearing others' stories about depression, which helps them realize they are not alone, and from expressing their deepest feelings and thoughts. The authors argue that VR can offer a more immersive and engaging experience, enhancing positivity and promoting help-seeking behavior. Results from their pilot study showed that participants expressed more positive emotions and a significantly more positive attitude toward help-seeking behavior. However, they did not report greater intentions to seek help.

Hadjipanayi & Michael-Grigoriou (2021) explored the effect of an educational VR intervention that focused on depressive disorder, using a gamified VR simulation. Their intervention consists of two VR scenarios, with only one featuring a positive outcome. In the VR environment, the participant embodies the perspective of a woman struggling with

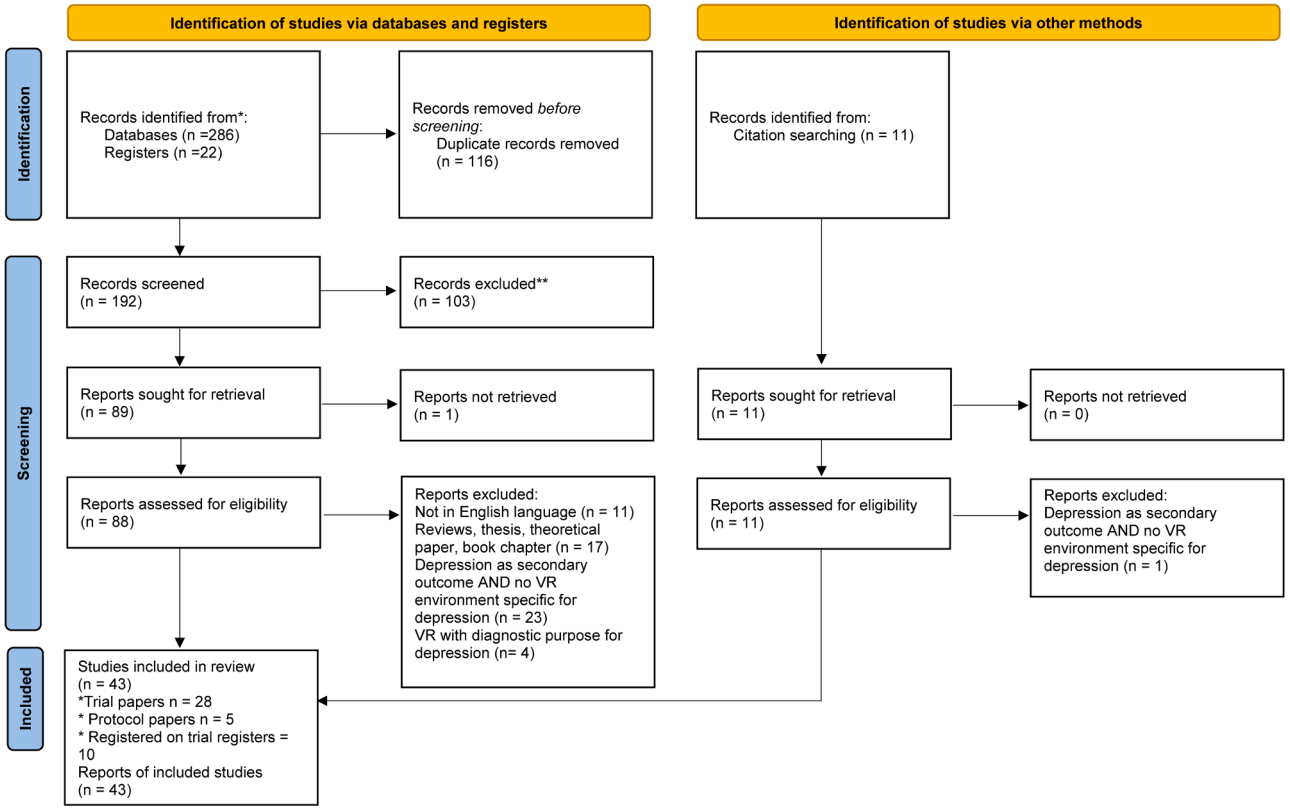

Fig. 1. Literature screening and selection flowchart following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines.

Table 1
Study and treatment characteristics and main results of clinical trials and design papers.

Target	Author	Clinical condition	N	#VR	VR treatment	Study type / design	Control	Main findings
*Psycho-education	Migoya-Borja et al. (2020)	Diagnosis of depressive disorder	28	1	VRight: Conversation about depression with a virtual character	Pilot study – pretest posttest design	None	Participants with lower depression baseline scores showed a decrease in depressive symptoms after intervention, participants with higher depression baseline scores showed an increase in depressive symptoms after the intervention ($r = 0.39$, $p = 0.02$).
*Psycho-education	Hussain et al. (2018)	Participants with mild and moderate depressive symptoms	12	1	Watch 360 ° VR videos +speak-out - share their narratives of living with depression	Pilot study – single group posttest design	None	Participants expressed more positive emotions ($M = 4.89$, $SD = .81$), compared with negative emotions ($M = 2.34$, $SD = .66$). Participants expressed a considerably high positive attitude toward help seeking behavior ($M = 4.34$, $SD = .96$).
*Psycho-education	Hadjipanayi and Michael-Grigoriou (2021)	Healthy participants	30	1	Gamified VR simulation	Pre-test/post-test design and between-subjects approach	Same VR experience, although without positive ending	Significant positive correlation between emotional impact and post-knowledge test on MDD symptoms in experimental group (ρ=0.60, p=0.01).
*Psycho-education	Schleider et al. (2019)	Adolescents with elevated depressive symptoms / recent history of depression	159	1	VR-based GM SSI—the VR Personality Project - VR classrooms where participants can choose to speak to various scientists	3-arm RCT	*Web-based mindset intervention *Active, Web-based control program	None, Design paper
*Psycho-education	Kramer Freher et al., 2022a	Diagnosis of MDD	160	1	VR experience video from perspective of depressive patient and partner	Randomized Controlled Trial	Standard psycho-education	None, Design paper
*Behavioral activation	Suwanjatuporn and Chintakovid (2019)	Elderly participants with mild to moderate depressive symptoms	5	3	360 ° video of a garden scene	Feasibility study	None	Results showed that almost all of the participants could learn and walk a loop through the VR system and gave positive feedback about using this new system. Participants were satisfied with the use of VR towards learning how to use it (4.2/ 5.0).
*Behavioral activation	Paul et al. (2020)	Diagnosis of MDD	1	4	VR-BA: 360 ° videos with pleasant activities	Case report	None	The participant's depressive symptoms decreased by five-points on the PHQ-9 over a month, with a beginning score of 10 (moderate depression) and a final score of 5 (mild depression).
*Behavioral activation	Paul et al. (2022a)	Diagnosis of MDD	13 (VR=5 BA=4 TAU=4)	4	VR-BA: 360 ° videos with pleasant activities	3-armed, unblinded, randomized controlled pilot design; VR BA, BA and TAU	BA and TAU BA: homework with in person activity list	VR BA group experienced a greater decrease (< 5.67 points) in PHQ-9 scores than BA or TAU - sample size was not large enough to analyze this effect by significance.
*Behavioral activation	Szczepańska-Gieracha et al. (2021a)	Elderly women with MDD	25 (VR=13 control =12)	8	VRTierOne: Virtual Therapeutic Garden	Randomized pilot study	Standard treatment (fitness training, health-promoting education, and psychoeducation)	In the VR group was a significant decrease in GDS score ($F(2,20) = 17.36$, $p < 0.001$), by approximately 36% (12.27 vs. 8.27, $p = 0.001$) in the post-intervention tests. The GDS score did not change significantly in the control group ($p = 0.61$).
*Behavioral activation	Szczepanska-Gieracha et al. (2021b)	CAD + elevated anxiety/depression	34 (V =17 control =17)	8	VRTierOne: Virtual Therapeutic Garden	Randomized Controlled Trial	Schultz autogenic training sessions	Significant decrease in the HADS scores in the intervention group ($p = 0.003$). Control group: No difference in general

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Table 1 (*continued*)

Target	Author	Clinical condition	N	#VR	VR treatment	Study type / design	Control	Main findings
								HADS score - increase in the HADS-Depression score ($p = 0.003$).
*Behavioral activation	Cieslik et al. (2023)	Elderly women with depressive symptoms	60 (VR=30 control=30)	8	VRTierOne: Virtual Therapeutic Garden	Randomized Controlled Trial	Relaxation and psychoeducation without VR	IVR was more effective than group relaxation for reducing anxiety and depressive symptoms: adjusted mean difference for depression (GDS) was 4.10 points, with a large effect size (ηp^2) of 0.26.
*Behavioral activation	Rutkowski et al. (2021)	COPD + elevated anxiety/depression	50 (VR=25 control =25)	10	VRTierOne: Virtual Therapeutic Garden	Randomized Controlled Trial	Schultz autogenic training sessions	Significant improvement in the HADS-Anxiety ($p < 0.0009$), HADS-Depression ($p < 0.0001$) and general HADS ($p < 0.0001$) scores in the experimental group; Control group: No significant changes.
*Behavioral activation	Lin et al. (2020)	Healthy participants	20	1	VR game: Various activities and optional social communication (multiplayer)	Feasibility study	None	Results of this pilot study showed that the VR game resulted in mood improvement in 20 young healthy volunteers, no quantitative data.
*Cognitive restructuring	Falconer et al. (2016)	Diagnosis of MDD	15	3	Immersive VR scenario: Task includes practicing delivering compassionate words to oneself	Case studies with varying baseline length prior to intervention	None	Significant reductions in depression severity ($F(1, 12)=14.04$, $P=0.003$) and self-criticism ($F(1, 12)=23.41$, $P<0.001$), and an increase in self-compassion ($F(1, 12)=6.65$, $P=0.02$).
*Cognitive restructuring	Baghaei et al. (2021b)	Students with and without elevated symptoms of depression	23	1	iVR in Unreal Game: Participants can practice with delivering and receiving compassionate words	Feasibility study	None	Results show that participants with lower PHQ-9 scores found iVR easier to use compared with others. The difference between the two groups (High vs Low) on ease of use is statistically significant ($p = 0.021$).
*Cognitive restructuring	Ito et al. (2023)	Diagnosis of MDD	12	16	VR-CBT: Manual of standard CBT, but content is provided through VR	Interventional, exploratory, single-arm, nonrandomized, open, pre-post–comparative feasibility study	None	None, Design paper
*Enhancing positive affect	Chen et al. (2021)	Diagnosis of MDD	6	13	VR-BA with imaginal recounting and homework	Pilot study – repeated measures design	None	Significant reduced symptoms of anhedonia, depression (MASQ-AD; $t(17) = -4.875$, $p < 0.001$; CAT-DI; $t(17) = -3.892$, $p = 0.001$), anxiety (CAT-ANX; $t(17) = -3.843$, $p = 0.001$), and impairments in functioning (SDS^1; $t(17) = -6.347$, $p < 0.001$).
* Enhancing Positive affect	Li et al. (2021)	Mild to moderate anxiety and depression symptoms	189 (urban = 39 rest.= 35 rest. int.= 37 fishing = 40 water=38)	1	Experience diverse interactive VR restorative scenarios	Randomized experimental design with 5 experimental groups	*VR urban *VR restorative *VR restorative - interactive *VR fishing *VR watering	Increase in positive emotions = $F(1141) = 6.984$ and $p = 0.009$; decrease in negative emotions = $F(1141) = 63.215$ and $p < 0.001$), increase in self-efficacy ($F(1141) = 23.593$ and $p < 0.001$) and cognitive function. EEG indicators; activation of prefrontal lobe.
* Enhancing Positive affect	Wang et al. (2022)	Mild to moderate anxiety and depression symptoms	20 Study 1: Elevated symp.=12 others = 8) Study 2: urban = 39 park = 35 free-roam =36 fishing = 38 water = 38)	4	Experience diverse interactive VR restorative scenarios	Study 1: 2 (anxiety + depression state) x 4 (VR scenario) experimental design. Study 2: One-way randomized experimental design	Study 1: 1) mild to moderate anxiety and depression 2) the other participants Study 2: 1) VR urban. 2) VR park 3) VR free-roaming	Study 1: In group 1: sign. lower rate of depression post VR ($SDS\ t(11) = 2.799$, $p = 0.017$). Study 2: Presence was different among groups $F(4,174) = 4.093$, $p = 0.003$ Only for Group 5, sign. diff. between SDS^2 scores, $t(31) = 2.639$, $p = 0.013$.

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Table 1 (*continued*)

Target	Author	Clinical condition	N	#VR	VR treatment	Study type / design	Control	Main findings
							4) VR fishing 5) VR watering	
* Enhancing Positive affect	Hernandez et al. (2023)	*On hemo-dialysis for at least 3 months + *Mild to severe depressive symptoms	84	5	VR software; Joviality; strengths-based positive psychological intervention, consists of a skill-based curricula to boost positive emotion	Randomized Controlled Trial	Sham VR: consists of 2D wildlife and nature-based videos with background music	None, Design paper
*Mental imagery	Habak et al. (2020)	Self-report mental health diagnosis, previous experience with suicidality or depression	79	1	Edge of the Present; mixed reality environment, in which participants get rewarded by positive experiences	Pre-post design	None	Significant decrease in levels of hopelessness (t (78) = 5.18, p < 0.001) from pre to post; increase in positive mood (t (78) = −8.26, p < 0.001), decrease in negative mood (M = 14.13, SD = 4.44).
*Mental imagery	Fernández-Álvarez et al. (2021)	Moderate to moderately severe depressive symptoms	18	2	VR-based autobiographical memory task: Google Earth VR	Single-case, multiple baseline experimental design	None	Almost all participants showed moderate-to-large improvements at least at one of the outcomes on the short term (0-3 days); 72% for PA, however these gains were not mantained in the mid-term (4-10 days after intervention).
*Mental imagery	Colombo et al. (2022)	Diagnosis of MDD	7	4	VR-BA: Google Earth VR application for Oculus Rift	Single-case experimental design with multiple baselines	None	Moderate-to-large improvements in the level of daily activity (as assessed with the BADS-BA) and six out of seven patients reported a moderate-to-large reduction in daily depressive symptoms and improved mood.
*Mental imagery	Montesano et al. (2021)	Participants with a diagnosis mild to moderate MDD	225	10-13	VR + Personal Construct Therapy (PCT): VR app EYME to visualize personal relationships	Multicenter Randomized Clinical Trial	CBT or PCT without VR	None, Design paper
*Skills training	Shah et al. (2015)	Diagnosis of MDD or bipolar disorder (with depressive episode)	22	3	VR DE-STRESS program: 3 relaxation videos in VR	Single-group, pretest–posttest, quasi-experimental research design	None	Significant lower subjective stress (X difference = 7.62, SD = 5.17, t =6.91, p < 0.001), depression (X difference = 8.09, SD = 6.75, t =5.62, p < 0.001), and anxiety (X difference = 5.64, SD = 4.77, t = 5.54, p < 0.001).
*Skills training	Stamou et al. (2019)	Diagnosis of (postnatal) depression	6	1	CGT+VR: VR house environment in which stressors can be manipulated	Feasibility pilot study	None	There was a consistent reduction of final scores for EPDS for five participants (no statistical data).
*Skills training	Stamou et al. (2021)	Diagnosis of PND	15	1	CGT+VR: VR house environment in which stressors can be manipulated	Single-case study trial	None	Reduction in posttreatment and follow-up periods for Kessler-10 (Cohen's d 0.67 baseline-post) and EPDS (Cohen's d=1.17 baseline-post).
*Enhancing cognitive functioning	Dehn et al. (2018)	Diagnosis of MDD + at least 14 days of hospital stay	38 (VR = 21 control =17)	8	Cognitive training program with VR: 360° VR supermarket environment	Pre-post design	Cognitive training on a 26" LCD-touch-screen instead of VR	There was a significant decrease of depressive symptoms (BDI-II) across the study procedure ($F(1,36) = 27.32$, $p < 0.001$, $\eta^2 = 0.431$), but no difference between groups ($F(1,36) = 2.76$, $p = 0.106$, $\eta^2 = 0.071$) or an interaction effect (F(1, 36) = 0.225, p = 0.638, $\eta^2 = 0.006$).
*Enhancing cognitive functioning	Huang et al. (2022)	Patients with MDD	87 (46 patients with MDD + 41 healthy controls; (VR =23 control =23)	20	Virtual reality (VR)-based WMT	Pre-test/post-test design and between-subjects approach	Waiting list	Participants in VR group showed an increase in EBPM accuracy (Cohen's d = 1.20 [95% CI: 0.53, 1.86], $p = 0.001$).

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Table 1 (*continued*)

Target	Author	Clinical condition	N	#VR	VR treatment	Study type / design	Control	Main findings
*Enhancing cognitive functioning	Wu et al. (2022)	Patients with PSD	44 (VR = 22 control = 22)	20	VR rehabilitation training: VR environment of living room	Between group design	2D VR Rehabilitation training	VR group showed a significant reduction in HAMD compared to the baseline levels ($p < 0.001$).
*Residual category	Cai et al.(2017)	Healthy participants	12	1	VR-based neurofeedback game for depression rehabilitation	Pilot study – posttest design	None	No quantitative data available.
*Residual category	Dilgul (2021)	Participants with a diagnosis of MDD in the last 12 months	10	8	vTime app: Virtual Reality Group Therapy (VRGT)	*Feasibility study	None	Overall, the response of patients and therapists in this study was largely positive (qualitative research).
*Residual category	Kaup et al. (2023)	Participants with mild to moderate depressive symptoms	12	2	Psyrreal: mimics the phenomeno-logical components of psychedelic and mystical experiences	Feasibility study	None	75% of the participants showed a decrease of depressive symptoms two days after the intervention (EST-Q2 scores; $t(10) = 3.75$, $p = 0.004$, Cohen's $d = 1.13$).

Note: BA = Behavioral Activation; BADS = Behavioral Activation for Depression Scale; CAT-DI = Computerized Adaptive Testing tool depression inventory; CAT-ANX = Computerized Adaptive Testing tool anxiety inventory; CBT = Cognitive Behavioral Therapy; CAD = Coronary artery disease, COPD = Chronic obstructive pulmonary disease; EBPM = Event-based prospective memory; EPDS = Edinburgh Postnatal Depression Scale; EST-Q2 = Emotional State Questionnaire; GDS= Geriatric Depression Scale; HAMD = Hamilton Rating Scale for Depression;, HADS = Hospital Anxiety and Depression Scale; Kessler10 = Kessler Psychological Distress Scale; MASQ-AD = Anhedonic Depression subscale of Mood and Anxiety Symptoms Questionnaire; MDD = Major Depressive Disorder; PA = Positive affect; PHQ-9 = Patient Health Questionnaire; PND = Postnatal depression; PCT = Personal Construct Therapy; PSD = Post Stroke Depression; SDS[1] = Sheehan Disability Scale; SDS[2] = Self-rating Depression Scale; TAU = Treatment As Usual; WMT = Working Memory Training.

depression as she shares her personal experience. The participant is encouraged to explore the virtual environment while learning about the pathology of MDD. At a certain point, one of the scenarios transitions to a positive ending, highlighting the moment at which the patient with MDD is effectively treated after seeking help. The authors claim that experiencing a positive resolution may have a more emotionally powerful effect, offering a more rewarding experience that could enhance information retention. The current pilot study showed little difference in the overall emotional impact and knowledge about the symptoms of MDD between groups.

Schleider et al. (2019) are currently investigating the acceptability and efficacy of a novel, single-session VR depression intervention for adolescents. This VR intervention is based on teaching the growth mindset, which encourages youth to view traits and attributes as adaptable or changeable, rather than fixed. In the VR environment, the participant receives information about the growth mindset and can share feelings or experiences with same-aged peer characters or talk to scientists within the VR world. According to the authors, VR can offer a more immersive, fun, engaging, and user-directed experience for adolescents to promote the growth mindset. Since this is an ongoing trial, no results are available yet.

Kramer Freher et al. (2022a) are currently investigating the added value of VR in psychoeducation for MDD, involving both patients and their significant others. For this study, two immersive 360° videos were developed, summarizing multiple fragments of a day in the life of a female depressive patient, from both her perspective and that of her male partner. According to the authors, an effective form of psychoeducation for both the patient and their relative can increase mutual understanding and reduce self-stigma. VR might be able to improve the effectiveness of psychoeducation for depression due to the strength of embodiment. Since this is an ongoing trial, no results are available yet.

To sum up, VR can potentially be useful in psychoeducation interventions for depression, offering advantages over verbal or written information. One benefit is that patients may feel more comfortable learning about depression by being represented by an avatar or sharing their story with an anonymous one, which shows similarities with VR group therapy (Dilgul, 2021). Moreover, the strength of embodiment — the illusion of being within another body from a first-person perspective — can be effectively used in psychoeducational interventions. This immersive experience may help relatives of patients with depression by increasing their understanding, which can also benefit the patient. The power of embodiment is also used in the studies on cognitive restructuring (Falconer et al., 2016; Baghaei et al., 2021b). Several researchers argue that the VR scenario might offer a more enjoyable and pleasant experience to learn theoretical information about depression, which can strengthen motivation to seek help or engage in therapy. Intrinsic motivation is an important element in facilitating meaningful behavioral changes (Cheek et al., 2015).

3.4. VR and behavioral activation (operant conditioning)

Currently, sixteen studies have investigated or are currently investigating the use of VR to stimulate behavioral activation or enhance positive feelings, using the principle of operant conditioning or reward learning.

Suwantjatuporn & Chintakovid (2019) developed a virtual reality system to promote the quality of life in the treatment of depression in the elderly. The VR intervention consists of a 360° virtual garden scene, with the purpose of encouraging the elderly to move and participate in virtual activities. According to the authors, performing activities in the VR environment can stimulate brain function in elderly individuals with depression, thereby speeding up the recovery process. For the current feasibility study, 60 elderly participants with mild to moderate levels of depression were recruited. The results showed that almost all of the participants were able to learn and walk through a loop in the VR system and provided positive feedback about using this new system.

Paul et al. (2020, 2022a) developed a four-session online VR Behavioral Activation (BA) therapy for depression. Participants in the VR BA group used VR for their homework; they could choose from 37 immersive 360° VR videos featuring pleasant activities to watch, using their VR headset at home. The authors argued that VR BA would eliminate many obstacles to receiving care or engaging in pleasant activities, such as cost-related impediments or access-related difficulties, including COVID-19 restrictions. Their randomized controlled pilot study showed that VR BA had high levels of acceptability and tolerability. Moreover, in this sample, the VR BA participants experienced a greater decrease in depression scores than those who completed traditional BA or treatment as usual (TAU). However, the sample size was not large enough to statistically analyze this effect.

Szczepańska-Gieracha et al. (2021a) assessed the effectiveness of VR in elderly women with depression, using the Virtual Therapeutic Garden (VTG), which is based on the Ericksonian psychotherapy approach (Matthews, 2000). The virtual garden is initially weak and grey, becoming more colorful and lively with each session. The participants color a mandala in VR and are rewarded with beautiful flowers in the garden. According to the authors, the VR environment has a calming and mood-improving effect, which can help motivate the patients in their rehabilitation process. Results from their randomized pilot study showed that the VR intervention was effective in reducing the intensity of depressive symptoms, as well as stress and anxiety levels, compared to the standard treatment. The same research group also examined the beneficial effects of the VTG in patients with cardiovascular disease and elevated depression and anxiety, compared to Schultz's Autogenic Training (Schwickert et al., 2006). Results showed a statistically significant decrease in anxiety and depression scores in the intervention group, in contrast to no difference in the control group (Szczepańska-Gieracha et al., 2021b).

The effect of the VTG was also studied by Rutkowski et al. (2021) in patients with COPD and elevated symptoms of depression and anxiety during a pulmonary rehabilitation program. According to the authors, there is a scarcity of research evaluating how VR therapy affects depressive and anxiety symptoms in COPD patients undergoing pulmonary rehabilitation in a hospital, and they aimed to gain more insight into this with their research. They did not provide a clear theoretical foundation for their intervention. Results showed a statistically significant improvement in anxiety and depression scores in the VR group, with no statistically significant changes in the control group, which used Schultz's Autogenic Training.

Cieslik et al. (2023) also conducted research on the effect of the VTG in older women with depression. According to the authors, nature-based interventions can have positive psychological effects on older adults with depressive symptoms; however, a natural environment is not always available. In this context, VR may offer a solution. Results from their randomized controlled trial showed a significantly greater reduction in depression scores in the VR group, compared to the control group, which received standard psychoeducation and relaxation exercises.

Lin et al. (2020) investigated another form of reward learning with VR, by designing a VR video game to improve mood for people with depression. Their VR game can be played multiplayer and features nature scenes and activities such as bicycling, canoeing, swimming, and skiing. When participants complete a level successfully, they are rewarded. According to the authors, video games are effective in improving mood, and their positive impact can be amplified by using VR due to its immersive experience. Results from their pilot study showed that the VR game resulted in mood improvement in twenty young, healthy volunteers.

We found eight pre-registered studies in trial registers with a focus on behavioural activation, which are described in Table 2.

In conclusion, VR can be a compelling tool to stimulate behavioral activation as part of behavior therapy, and enhance positive affect in patients with depression by applying the principle of operant conditioning in various ways. Patients with depression often find it difficult to become more active in daily life, and VR may serve as a useful intermediate step toward activation. VR can directly impact behavioral activation by allowing patients to move and perform activities in VR, for instance by walking around in a virtual garden. Moreover, VR can be an effective tool for stimulating social activation through engagement in virtual social gatherings, thereby reducing loneliness, as demonstrated in the VR video game by Lin et al. (2020). Finally, VR allows for the easy incorporation of rewarding elements, such as rewards for performance in the virtual world or virtual incentives for completing behavioral activation homework. Receiving rewards may also enhance positive affect. In fact, VR interventions designed to stimulate behavioral activation as part of behavior therapy often incorporate overlapping elements with those aimed at enhancing positive affect and mental imagery, which will be discussed later.

3.5. VR and cognitive restructuring

Currently, four studies have investigated a VR intervention for depression with the focus on cognitive restructuring or – reappraisal.

Falconer et al. (2016) examined the effect of embodiment in VR to increase self-compassion in patients with depression. They developed an immersive VR scenario in which participants with depression practiced delivering compassion through one avatar and subsequently receiving it from themselves in another avatar. According to the authors, self-criticism is an important factor in the vulnerability and maintenance of depression, and people with depression are not accustomed to hearing self-directed compassionate words in their own voice. The added value of VR, according to the authors, is that individuals can experience both giving and receiving compassion with their own voice, which can be a positive experience for the self. Results from various case studies showed that three repetitions of this VR scenario led to significant reductions in depression severity and self-criticism, as well as an increase in self-compassion.

Inspired by the study of Falconer et al. (2016), Baghaei and colleagues (2021b) developed a novel individualized VR application aimed at enhancing self-compassion in individuals with depressive symptoms. In this application, participants deliver compassionate words to an avatar, to which the avatar responds positively. A key feature of their intervention is that participants have more opportunities to make their own choices in the VR environment, such as selecting the therapy setting. The authors emphasize the importance of individualized care in mental health, and argue that VR offers a solution to this need. Their feasibility study showed that most participants found the individualization options engaging, and most mental health professionals felt it would enhance their understanding of clients.

Ito et al. (2023) developed a VR-based CBT (CBT-VR), in which VR is used to deliver CBT content to patients with treatment-resistant depression. Their 16-session treatment protocol includes the same content as standard CBT; however, in CBT-VR, most of the content is provided through VR, such as skill training for cognitive reappraisal. According to the authors, CBT-VR can replace part of the face-to-face sessions in standard CBT, potentially reducing both the long-term time burden on patients and the intervention time required from medical personnel. Since this is an ongoing trial, no results are available yet.

We found one pre-registered study in trial registers with a focus on cognitive restructuring, which is described in Table 2.

In a nutshell, VR offers the potential to enhance the effectiveness of cognitive restructuring techniques, which are commonly used in CBT for depression. The strength of embodiment plays a crucial role here; unique to VR is the ability for patients to receive positive feedback from (the virtual body of) themselves, which can be a positive experience for their self-image. Moreover, unlike face-to-face roleplays with a therapist, VR provides flexibility and personalization by immersing participants in a different world, tailoring the therapist's avatar characteristics to suit the patient's scenario, and altering perspectives—features that would be

impossible in real life (Holsteg et al., 2024).

3.6. VR and enhancing positive affect

Currently, six studies have investigated or are currently investigating a VR intervention for depression with the focus on increasing positive affect, using positive elements in the VR environment.

Chen et al. (2021) developed a VR treatment protocol based on the Positive Affect Treatment (PAT) (Craske et al., 2016, 2019). Each session of their VR treatment protocol comprised three stages: VR viewing, imaginal recounting of the VR scene, recounting of an autobiographical memory focusing on positive emotions, and homework. Regarding the theoretical underpinnings of their intervention, PAT has proven effective in improving both positive and negative affect (Craske et al., 2019). However, for some patients, lack of motivation is an obstacle to engaging in behaviorally rewarding activities. According to the authors, VR may offer a solution for these patients. Their VR protocol targets finding and engaging in rewarding activities by performing pleasant activities in VR and savoring pleasurable moments to enhance their positive impact. The results of their pilot study suggest that the VR protocol significantly reduces symptoms of anhedonia, depression, anxiety, and impairments in functioning.

Li et al. (2021) investigated a VR restorative environment intervention for individuals with mild to moderate depressive symptoms. Their intervention consists of several different VR environments, such as exposure to a garden or an interactive fishing task. According to the authors, since research has shown that increased levels of pressure and stress have a major impact on mental health, restorative environments can restore attention, reduce stress, and improve both physical and mental health. This positive effect can be amplified by using VR, as VR can facilitate immersive, high-presence experiences from a first-person perspective. Overall, their randomized experimental study showed that the experience of a VR-based restorative environment had a restorative effect, which was reflected in improved positive and negative emotions, self-efficacy, and cognitive function.

Elaborating on the combination of restorative environments and VR, Wang et al. (2022) examined the restorative effects of different environment types and interactive activities, such as watering vegetables and fishing in a water area. The authors argue that natural environmental settings and interactive spaces in VR might promote parasympathetic activity and induce feelings of safety and relaxation in individuals, thereby relieving physical and mental stress. Results from their experimental study showed that the restorative environment and presence were significantly and positively related to a reduction in anxiety and depression symptoms.

Hernandez et al. (2023) are investigating the effects of a positive psychological intervention for individuals on hemodialysis with comorbid depression, using an immersive VR program that teaches various skills to boost positive emotions, such as noticing positive events. According to the authors, VR offers the technology to deliver strength-based interventions and positive experiences, with the added advantage of allowing individuals on hemodialysis to virtually travel outside the clinical walls. Since this is an ongoing trial, there are no results yet.

We found one pre-registered studies in trial registers with a focus on enhancing positive affect, which are described in Table 2.

In conclusion, VR environments offer a wide range of possibilities to directly target positive affect by exposing participants to positive stimuli or by allowing them to perform pleasurable activities in VR. Patients can engage in enjoyable experiences that are inaccessible or impossible in real life, such as traveling around the world or flying like a bird. VR offers numerous possibilities to combine the direct experience of positive affect with methods that encourage patients to focus on positive emotions, for instance noticing positive things, along with virtual rewards to stimulate both positive affect and motivation. Furthermore, positive experiences in VR may boost motivation and engagement in therapy, as well as promote daily activity levels and encourage behavioral activation.

3.7. VR and mental imagery

To date, five studies have investigated or are currently investigating a VR intervention for depression using the strength of mental imagery to stimulate positive affect or increase behavioral activation.

Habak et al. (2020) demonstrated VR as a potential tool for enhancing positive affect and fostering positive thoughts about the future in individuals with depressive symptoms. The authors examined the intervention *Edge of the Present* (EOTP), a mixed-reality environment in which participants are invited to explore a virtual room. Exploration is rewarded by positive imagery, such as immersive landscapes, and environmental effects like a warm breeze. The intervention is based on the power of mental imagery-based processing, or sensory processing, using VR to amplify the emotional impact of both negative and positive stimuli. According to the authors, the mixed-reality environment can generate positive affect, thereby facilitating positive future thinking and episodic imagining in individuals. Results of their interventional study showed a significant decrease in levels of hopelessness, an increase in positive mood, and a decrease in negative mood following the VR intervention.

Fernandez-Alvarez et al. (2021) developed a VR intervention based on mental imagery, using Google Earth VR to enhance autobiographical memory (AM) recall. In each session, participants were asked to recall a positive memory, which was then visually recreated using Google Earth VR. The intervention targeted AM impairments commonly seen in depression, such as negative bias (more negative than positive memories) and overgeneral memory (lack of specific details). According to the authors, VR can improve memory recall by presenting realistic, personally relevant scenarios that elicit positive emotions. Results from their single-case, multiple baseline experimental design study showed that most participants experienced moderate-to-large short-term improvements in outcomes like positive affect. However, these clinical gains were not maintained in the mid-term.

Colombo et al. (2022) explored the same VR application as Fernandez-Alvarez et al. (2021) in their four-session VR-based behavioral activation (BA) study. In each session, participants chose a place in Google Earth VR to virtually engage in a planned activity and focus on the positive outcomes. They were asked to recall pleasant memories related to the activity and then schedule it in their daily life. The authors based their intervention on several ideas: VR may be more effective than imagery in visualizing pleasurable past activities, VR has been shown to stimulate positive emotions, and VR enhances mental simulations through the immersive "being there" experience, which can induce positive emotions. Results from their single-case, multiple baseline experimental design study showed moderate-to-large improvements in daily activity levels, with most participants also reporting a reduction in depressive symptoms and improved mood.

Montesano et al. (2021) are investigating the efficacy of VR-enhanced personal construct therapy (PCT-VR), based on PCT (Kelly, 1955; Winter & Viney, 2008). In PCT-VR, participants can visualize and eventually change their interpersonal world in VR, instead of using 2D displays in the standard PCT condition. According to the authors, PCT-VR will enhance the attractiveness of the treatment for young adults, increasing their engagement in the therapy process. Since this is an ongoing trial, there are no results yet.

Overall, VR interventions for depression might amplify the powerful effect of imagery-based processing over traditional verbal processing by enhancing the vividness of mental simulations to target both negative and positive affect. Given the significant variation in individuals' mental imagery vividness (Kosslyn et al., 2006), VR can enhance or even replace mental imagery, potentially having an equal or greater impact on emotions. VR imagery can be used to directly stimulate positive affect, to highlight positive memories and facility positive (future) thinking.

Table 2
Study and treatment characteristics of studies derived from trial registers.

Target	Author / registration	Clinical Condition	N	#VR	VR treatment	Study type / design	Control	Status
*Behavioral activation	Paul (2022b) / NCT05525390	Diagnosis of MDD	26	4	Behavioral activation activities in extended reality	Randomized Controlled Trial	BA activities in real life	Study completed, not published (yet)
*Behavioral activation	De Connor (2018)/ NCT03621488	Diagnosis of depression	80	10	Brief Behavioral Self Activation (BATD) program with VR	Randomized blinded study	BATD without VR	Study ongoing
*Behavioral activation	Lake (2019) / NCT04165681	Depressive symptoms	30	N.a.	CBT-based mobile app + VR program, designed to implement BA	Single group study	None	Study completed, not published (yet)
*Behavioral activation	Jacob (2022) / NCT05529797	Moderate to severe depressive symptoms	128	1	VR intervention (Veovita-VR): expose people with depressive symptoms to positive emotional stimuli and positive BA	Randomized Controlled Trial	Care as usual	Study completed, not published (yet)
*Behavioral activation	Cullen (2022) NCT05342077	Symptoms of anhedonia / depression	80	9	Virtual Reality-Reward Training (VR-RT)	Randomized Controlled Trial	Virtual Reality-Memory Training (VR-MT)	Study ongoing
*Behavioral activation	Wilson (2022) / NCT05973461	Participants with and without symptoms of depression	100	1	Exposing to VR surroundings while riding a cycle ergometer	Randomized Controlled Trial	Cycle ergometer without VR	Study ongoing
*Behavioral activation	Kramer Freher (2022b) / NCT05486676	Diagnosis of MDD	10	12	VR-Moodboost; performing pleasurable activities in VR, getting virtual rewards, other interventions that target positive affect	Non-concurrent multiple baseline single case design	None	Study ongoing
*Behavioral activation	Yilmaz (2023) / NCT05985096	Healthy participants	60	12	Physical activity in VR (Racket, Climb, Acron, Skiing and Cycling games)	Randomized Controlled Trial	Individual exercises without virtual reality	Not yet recuiting
Cognitive restructuring	Louer- van Eck et al. (2020) / NL8949	Diagnosis of MDD	18	5	VR in CBT: role-playing in VR and challenging automatic negative thoughts	non-concurrent randomized multiple baseline single case design	None	Study completed, not published (yet)
*Enhancing positive affect	Richieri (2017) / NCT03336788	Diagnosis of MDD and resistant depression	66	/	VR in Transcranial Magnetic Stimulation (TMS): participants experience positive images and sounds in VR, during TMS	Randomized Controlled Trial	TMS alone	Study completed, not published (yet)

Note: BA = Behavioral Activation; CBT = Cognitive Behavior Therapy; MDD = Major depressive disorder

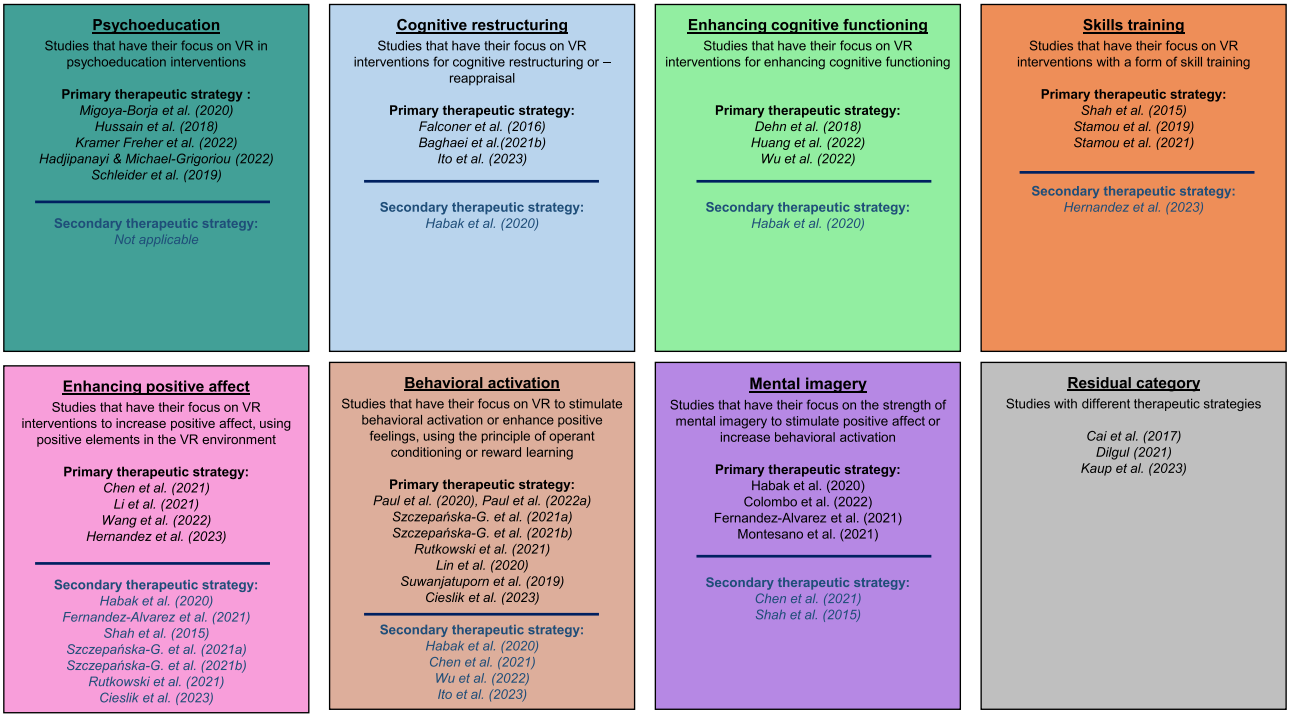

Fig. 2. Overview of studies with primary and secondary therapeutic strategies of clinical trials and design papers.

Moreover, VR imagery may lower the threshold for being active in daily life, as studied by Colombo et al. (2022).

3.8. VR and skills training

Currently, three studies have investigated -or are investigating- VR interventions for depression with the focus on a form of skill training, namely: relaxation skills and emotion regulation skills.

Shah and colleagues (2015) developed a three-session VR-based stress management (VR DE-STRESS) program for people with mood disorders to learn skills for coping with stress. Participants practice relaxation techniques in VR, including abdominal breathing, muscle relaxation, and guided imagery. The authors argue that a VR environment can serve as a powerful visual imagery tool to elicit positive affect and relaxation. Their theoretical underpinnings are based on the Neuman System Model (Neuman & Fawcett, 2002); the VR DE-STRESS program serves as a nursing tertiary prevention intervention to maintain well-being and restore balance. Results of their quasi-experimental study show that after the intervention, participants had significantly lower levels of subjective stress, depression, and anxiety.

Stamou et al. (2019, 2021) examined the effect of traditional Cognitive Behavioral Therapy (CBT) supplemented with one VR session in patients with postnatal depression (PND). In VR, participants were tasked with completing activities surrounding a virtual house while being confronted with several stressors, such as a toddler attempting to climb a high chair. According to the authors, VR can be an effective tool for patients with PND to learn how to manage stressful situations; the nature of the VR tasks can help participants raise awareness of their difficulties in coping and stress management. This intervention was initially studied in a small pilot study, followed by a multiple baseline single-case study trial. Results indicate that VR is a promising addition to CBT for PND, as the intervention resulted in improvements in awareness, decision-making, and self-appreciation in participants diagnosed with PND.

To conclude, several interventions for depression focus directly on the training, learning, or practicing of specific skills in a realistic VR setting. The advantage of practicing these skills in VR lies in the fact that the VR environment can be tailored and personalized to meet the optimal learning environment for a specific patient, allowing for the creation of environments that would otherwise be difficult to replicate in the physical world. This customization can stimulate the transfer of what has been learned to daily life. VR-based skill training for depression, such as the studies by Stamou (2019, 2021) that teach prioritization and attention transfer, shares similarities with Virtual Reality Exposure Therapy (VRET), where individuals are gradually exposed to stimuli they fear within a contextually relevant setting and learn to cope with them (Krijn et al., 2004). Moreover, learning relaxation skills in VR can be effectively done independently at home, without the need for a therapist, reducing costs. It may also be easier to engage in a relaxation exercise in VR, as complete immersion allows individuals to escape from reality, which not only aids in learning the relaxation technique but also directly stimulates positive emotions.

3.9. VR and enhancing cognitive functioning

Currently, three studies have investigated -or are investigating- VR interventions for depression with the focus on enhancing cognitive functioning.

Dehn et al. (2018) investigated the added value of VR in cognitive rehabilitation for Major Depressive Disorder (MDD), comparing a 360° VR supermarket environment to a desktop PC application. Participants were tasked with memorizing and then verbally recalling several items before purchasing them in the virtual supermarket. According to the authors, VR has the potential to enhance the ecological validity of cognitive rehabilitation by creating naturalistic settings and incorporating challenges that require "real-world" functional behaviors. However, the results showed that patients with depression did not experience greater benefits from the cognitive training program in the virtual supermarket environment compared to the standard PC desktop training.

Huang et al. (2022) examined whether VR-based working memory training (WMT) improves event-based prospective memory (EBPM) in patients with MDD. Tasks in their VR-based WMT intervention included a working memory span task in the VR supermarket and a visual-spatial working memory task in a flower shop. The authors argue that VR-based memory training has not yet been used in treating EBPM in MDD patients. They argue that VR offers opportunities for self-training at home, is well accepted by participants, has high ecological validity, which makes it an accessible tool in the training of memory. The results showed that participants in the VR intervention demonstrated a significant increase in EBPM accuracy compared to the waiting list control group.

Wu et al. (2022) investigated the use of VR in the rehabilitation of stroke survivors with post-stroke depression (PSD), comparing it to conventional 2D rehabilitation activities. In the VR task, participants were asked to select fruit prompted by sound or text within the virtual scene, while 3D upper limb movements were tracked. Successful task completion resulted in encouraging feedback. The authors argue that little research has been conducted on the functional brain alterations induced by immersive VR rehabilitation in PSD and emphasize the need for further investigation. They also suggest that VR rehabilitation may increase patient motivation, as it allows patients to practice in a more ecologically effective environment, and propose that changes in causal connectivity within emotional networks could be the neural mechanism driving VR rehabilitation for PSD. Results showed that only the VR group experienced a significant reduction in depression scores, with several causal connectivity's—such as those involving the amygdala, insula, and middle temporal gyrus—strengthened after VR training. In contrast, these causal connectivity's were weakened in the control group after treatment.

All in all, VR has the potential to enhance cognitive functioning in patients with MDD, either directly, such as through a working memory task in VR, or indirectly, by providing physical tasks in VR aimed at improving cognitive abilities. Since VR offers highly immersive and interactive experiences that engage multiple senses and brain regions simultaneously, it may have a powerful effect on learning, memory, and cognitive functioning. Another benefit is that individuals can practice in VR at home without the need for a therapist, which can save costs—similar to using VR in skills training (Shah et al., 2015).

3.10. Other types of VR therapy for depression

Three studies had different therapeutic strategies, than the aforementioned categories.

Cai and colleagues (2017) examined a virtual-reality-based neurofeedback game for depression rehabilitation, combining EEG sensor technology, VR gaming, and biofeedback therapy. In their intervention, the EEG sensor monitors the brain's physiological activity of the participant, which is then connected to the gaming environment in the patient's VR headset. However, neither the therapeutic strategy of the VR aspect nor the added value of VR is described in this study, other than the fact that participants showed interest in VR games. Since the prototype is still in the early development stage, no quantitative data is available regarding its effectiveness.

Dilgul (2021) studied the added value and acceptability of VR in group therapy for depression (VRGT). Their intervention involves networked VR, in which both therapists and patients participate remotely, represented by avatars. The authors argue that the anonymity provided by avatars could encourage patients to speak more freely and honestly. Moreover, the ability to attend group therapy sessions from home may reduce barriers for patients with depression. Overall, the responses from the first ten patients and therapists who tested the application were largely positive. Factors such as the lack of travel time, being in the safe

environment of home, and the reduction of stigma may be crucial for encouraging patients with depression to actively engage in and commit to their treatment process.

A different approach to VR therapy for depression was studied by Kaup et al. (2023). They examined the effect of a VR intervention that mimics the phenomenological components of psychedelic and mystical experiences. Participants begin in a virtual "real-world" environment and encounter different virtual settings that combine various psychedelic effects, mainly consisting of abstract shapes and geometric patterns, allowing participants to interpret the experience for themselves. The authors suggest that the therapeutic benefits of psychedelics might stem from the subjective experiences elicited by these substances and propose that similar benefits could be achieved by eliciting comparable experiences in VR. In their study, 75% of participants showed a decrease in depressive symptoms after the intervention.

Several other studies employed different therapeutic strategies than those discussed above, or their theoretical underpinnings could not be clearly derived from the articles. However, these studies highlight interesting developments in VR interventions for depression, such as using VR to mimic psychedelic experiences. This approach might help participants connect with their emotions and let go of control, without the harmful side effects associated with actual psychedelic drugs. Additionally, using VR as a tool for group therapy at home for depression appears promising and warrants further investigation, as it could offer a solution for individuals unable to leave their homes due to depression. Furthermore, patients may feel more comfortable being represented by an avatar, which might decrease being confronted with dysfunctional thoughts and feelings associated with self-stigma and shame.

4. DISCUSSION

The purpose of this study was to examine the therapeutic strategies that are presumed to be targeted in VR treatment for depression. We analyzed how evidence-based psychological treatment strategies for depression can be transferred in a way that allows them to be utilized through virtual reality techniques. Findings from the 43 studies included in this review indicate a great variety in the presumed therapeutic strategies associated with VR treatment for MDD.

In order to answer the research question, this scoping review provided a comprehensive overview of VR interventions currently applied in depression treatment, along with their corresponding theoretical underpinnings. The results were categorized as accurately as possible by therapeutic strategy, resulting in the following categories: VR and 1) psychoeducation, 2) behavioral activation (operant conditioning), 3) cognitive restructuring, 4) enhancing positive affect, 5) mental imagery, 6) skills training, 7) enhancing cognitive functioning, and 8) other types of VR therapy for depression. When the description of the theoretical background was unclear or when VR interventions appeared to be based on multiple therapeutic strategies, the most appropriate category was selected by inter-researcher agreement.

A remarkable finding was the significant variation between studies in the extent to which the authors described the studied VR intervention or its theoretical background. In some studies, it remained unclear what the VR intervention entailed or why VR would provide added value, making it impossible to draw conclusions about the therapeutic strategy. In certain studies, the main argument put forward was that the research had not been done before. Additionally, it appeared that researchers often made broad conclusions about the added value of VR based on relatively small (pilot) studies, even though these conclusions are not yet supported by scientific evidence. This indicates that the research field of VR in depression treatment is still in its early stages, with theoretical frameworks and experimental designs not yet fully developed. Regarding the interventions themselves, it became clear that the number of VR sessions varied widely between studies, ranging from 1 to 30 sessions. Furthermore, there was considerable variability in approaches and VR environments, as almost every researcher developed or studied their own VR environment. This variability further justifies the notion that the research field of VR in depression remains a relatively new area of study. In future studies, it is essential to clearly define the specific objectives of the research and the underlying rationale, so that VR designs are likely to become more refined and the most successful approaches will emerge.

Several key therapeutic strategies were frequently highlighted in VR interventions, with those based on behavioral activation (BA) or operant conditioning, mental imagery, and positive affect being the most researched and supported by scientific insights. These techniques were often combined to enhance the effectiveness of VR interventions. According to learning theories by Ferster (1973) and Skinner (1957), a reduction in positive reinforcement can lead to negative affect and passivity, typical of depression (Lewinsohn., 1974). BA models suggest that decreased positive reinforcement for healthy behavior contributes to reduced activity levels, which in turn can cause depression (Manos et al., 2010). By targeting behavior activation, patients can increase rewarding experiences mood-independently, potentially breaking the negative cycle of depression (Martell et al., 2021). Years of research has shown BA to be an effective treatment for depression (Arjadi et al., 2018; Cuijpers et al., 2007; Dimidjian et al., 2011), though engaging individuals with depression can be quite challenging due to the nature of their symptoms and external barriers (Paul et al., 2020).

VR-BA interventions might help overcome this challenge; VR has the potential to elicit excitement and motivation for engaging in a virtual activity without the obstacles of the real world, which could lower the threshold for becoming more active in daily life. VR can have a direct effect on behavioral activation by encouraging the performance of activities in VR, such as walking around in a virtual garden or engaging in pleasant activities. Since VR offers a wide range of possibilities for physical activities, for instance with programs like VR/Wii Fit and VR fitness games, it would be interesting to conduct more research on the direct effect of exercise while being exposed to VR. Encouraging physical activities in VR may not only improve physical health, but also enhance motivation and engagement—key factors in driving behavioral change in daily life (Paul et al., 2020). Moreover, VR interventions can have a direct effect on social BA by stimulating engagement in virtual social gatherings, such as with multiplayer VR video games, thereby reducing loneliness and promoting social connectedness. Furthermore, patients with depression can engage in enjoyable activities in VR, feel happy, enthusiastic or relaxed for a moment again, and then translate those experiences into real-life tasks that evoke similar positive feelings as the virtual activity. Since imagining oneself completing a future event has been shown to significantly increase the likelihood of that event being completed in real life (Libby et al., 2007), this effect might be amplified by actually performing—and seeing oneself perform—the activity in VR. Finally, rewards, such as earning points or unlocking a trophy, can be easily incorporated into VR. One can be rewarded for activities in VR or for completing behavioral activation homework. This is an illustration of combining behavioral activation, reward learning, and imagery as therapeutic strategies for VR interventions.

Elaborating on mental imagery as therapeutic strategy in VR interventions: imagery can be a tool to stimulate BA, but it can also be a powerful tool to elicit positive emotions (Clark et al., 2006; Ehlers & Clark, 2000; Holmes et al., 2006, 2008). Various studies show that imagination has a much stronger effect on emotions than verbal reasoning (Holmes & Mathews, 2005; Holmes et al., 2006; Holmes et al., 2008; Ehlers and Clark, 2000). Moreover, experimental studies suggest that positive imagination (as opposed to verbally processing positive material) results in a stronger positive interpretation bias and an enhancement of positive mood (Holmes et al., 2009). Research has shown that many patients suffering from depression experience negative intrusive images (Holmes et al., 2007; Kuyken & Brewin, 1994; Patel et al., 2007) and a lack of positive imagery (Birrer et al., 2007; Holmes et al., 2009). Preventive Cognitive Therapy (PCT), a psychotherapy

model for relapse prevention in depression, focuses on enhancing positive affect through positive imagery and has demonstrated positive and enduring effects in multiple randomized controlled trials (Biesheuvel-Leliefeld et al., 2015; Bockting et al., 2005, 2009, 2015b; Breedvelt et al., 2018, 2020, 2021; de Jonge et al., 2019; Legemaat et al., 2022). VR can be considered an advanced form of the imaginal system, with more vivid and realistic images than those created by a patient's own imagination (Vincelli & Riva, 2000). Moreover, since individuals vary greatly in the vividness of mental imagery (Kosslyn et al., 2006), VR can enhance or even replace it, potentially having the same, if not a stronger, impact on boosting positive emotions.

Rather than relying on mental imagery to boost positive affect, VR interventions can also have more direct impact on enhancing positive affect. In general, there has been increasing attention for the focus on positive affect in the treatment of depression (Craske et al., 2016, 2019; de Jonge et al., 2017; Dunn, 2012; Holmes et al., 2009; Holmes et al., 2006, 2008). Neurobiological research shows that a lack of positive affect is related to reduced activation of the brain's reward system (Der-Avakian & Markou, 2012), and psychotherapy for depression can focus on reactivating the reward system. Furthermore, in recent decades, there has been an expanding body of literature on emotion regulation (ER) in the treatment of depression, which involves employing strategies to modulate emotional responses and achieve desirable outcomes. In this context, Positive ER refers to efforts aimed at creating, sustaining, and enhancing positive emotions, an area in which virtual reality presents numerous opportunities (Colombo et al., 2021). VR can enhance positive affect in several ways. VR can enhance positive affect by exposing individuals to positive environments or enabling pleasurable activities, such as experiencing mood-boosting nature scenes that are difficult to achieve in daily life (Bratman et al., 2021). Research has shown that even exposure to the sound of birds has a positive effect on mood (Stobbe et al., 2022), which can be easily manipulated in VR. Moreover, VR offers the possibility to create enjoyable experiences that are not possible or achievable in real life, such as traveling around the world, going on a husky sled tour, or flying like a bird. In addition, VR provides numerous opportunities to combine the immediate experience of positive affect with techniques that help patients focus on positive experiences, for instance with affect labeling of positive emotions (Kircanski et al., 2012), where positive words are reflected in the VR environment, as well as incorporating virtual rewards to stimulate the reward system, as previously described. This again illustrates a great combination of therapeutic strategies in VR treatment for depression.

Another way of implementing VR in depression treatment that shows potential is using VR for psychoeducational purposes. Although psychoeducation for depression has generally proven to be effective (Tursi et al., 2013), VR can be potentially useful to enhance psychoeducation for MDD. VR allows both patients and relatives to actually *experience*, rather than simply *perceive*, what it is like to think, feel, or act like someone with depression, which can facilitate understanding and feelings of empathy (Shin, 2018). Previous research has confirmed the strength of VR in stimulating empathy (Louie et al., 2018; Schutte & Stilinovic, 2017). Moreover, due to the increased emotional engagement in VR, it has the potential to foster positive attitudinal changes (Bujic et al., 2020), which could enhance self-esteem, reduce self-stigma, or promote more positive attitudes toward seeking help.

The principal strength of this study is that it is the first scoping review to focus exclusively on VR in the treatment of depression and critically review its theoretical underpinnings. Moreover, we have provided an essential foundation for identifying points of reference for effective VR interventions, which could eventually improve treatment for MDD. However, it is important to consider potential limitations of the current research. To provide as complete an overview as possible, we used broad eligibility criteria with no restrictions regarding the methodology of the studies. This allowed us to review substantially more studies investigating VR for depression treatment than earlier systematic reviews (Baghaei et al., 2021a; Fodor et al., 2018; Wiebe et al., 2022). However, we did not conduct a systematic evaluation of the methodological quality of the studies or perform a statistical analysis of the results. It is worth noting that most of the studies had small sample sizes or used a pre-posttest design without a control group. Moreover, several (n=8) feasibility studies focused on exploring the acceptability and usability of VR interventions rather than their effectiveness. Therefore, the results from the trial papers we mentioned may be less generalizable and reliable. However, our primary focus was on the content of the VR interventions and the proposed therapeutic strategy, rather than on providing a clear picture of the outcomes of the VR interventions.

Despite its limitations, the study certainly contributes to our understanding of the application of VR in the treatment of depression. At this point, there is no standard for using VR in therapy for depression. VR can be a valuable addition to the treatment process in many ways, and it can be customized to meet the individual needs of the patient. After all, there is considerable variability among individuals with depression, due to differences in patient characteristics or triggers that may have elicited the depression. Therefore, the same mechanism in psychotherapy might not be suitable for every person with depression (Slofstra et al., 2019). Research shows that personalizing treatments, a key strength of virtual reality (VR), can lead to greater effectiveness and increased motivation for treatment (Kaptein et al., 2015; Kip et al., 2019; Lentferink et al., 2017). Moreover, VR has the potential to develop new treatment techniques and innovative options for information processing that are hard to achieve with traditional face-to-face methods (Holmes et al., 2018), offering opportunities to complement and enhance conventional treatment approaches. Overall, the field of VR technology is expanding rapidly, as is the field of clinical VR, which will remain closely linked (Lindner, 2021). However, the pace at which this technology is advancing is now so rapid that clinical researchers are struggling to keep up and fully utilize the new capabilities it offers.

There are many other innovative technologies with the potential to improve depression treatment that are worthy of further investigation. For instance, significant developments have been made in the field of serious games—games designed for purposes other than pure entertainment (Göbel et al., 2016; Djaouti et al., 2011). Serious games have been utilized as alternative therapeutic interventions for mental health disorders (Zayeni et al., 2020), specifically for the treatment of depressive disorders (Merry et al., 2012; Li et al., 2014, 2016). Games have the ability to captivate users through gameplay that can be rewarding, such as earning points or progressing through storylines (Flemming et al., 2016), which can directly induce self-efficacy and positive affect. The effect of a serious game could be enhanced by using VR to create an even more immersive experience (Lin et al., 2020). Another potentially interesting medium is augmented-reality games, such as the once-popular AR game Pokémon Go, which encourages participants to go outside and earn rewards. Such augmented reality interventions are accessible and easy to use, offering opportunities for people struggling with depression.

However, technological progress must align with psychological theory and our understanding of the mechanisms of change (Holmes et al., 2018). The most essential focus in future studies on VR in depression treatment should be on how VR can target specific mechanisms of therapeutic change. It is striking that after decades of psychotherapy research, we are still unable to offer an evidence-based explanation for how or why even our most thoroughly studied interventions lead to change (Kazdin, 2007). Similarly, research on mechanisms of change in digital interventions, including VR, for depression is still in its infancy (Angerer et al., 2025). Similarly, research on mechanisms of change in digital interventions for depression is still in its infancy (Angerer et al., 2025). It would be valuable to examine trajectories of change at an individual level to gain more insight into which targets (e.g., positive affect, negative affect, daily activity) change during each treatment phase in therapy (Hayes et al., 2015). This research approach could also increase our understanding of who benefits most

from VR treatment.

In conclusion, the past few years have witnessed impressive growth in the field of VR for depression treatment, driven by major developments in new technologies. VR shows potential to facilitate the treatment process and motivate patients with depression in various ways, which may improve treatment outcomes. However, the next crucial step in investigating VR for depression treatment is to evaluate the presumed mechanisms of change using a study design that is appropriate for this purpose. Overall, the possibilities of VR are numerous, and new VR techniques are developing rapidly, offering excellent prospects for personalizing and potentially improving the treatment of patients with depression.

Authors contributions

NKF drafted this paper, which was added to and revised by all other authors. All authors read and approved the final manuscript.

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During the preparation of this work the author(s) used Chat GPT in order to improve grammar. After using this tool, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

CRediT authorship contribution statement

Nancy Kramer Freher: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Martine van Bennekom:** Writing – review & editing, Validation, Supervision, Methodology, Data curation, Conceptualization. **Anika Bexkens:** Writing – review & editing, Validation, Supervision, Methodology, Data curation, Conceptualization. **Wim Veling:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Claudi L.H. Bockting:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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