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Advances in the field of virtual reality for mental health disorders

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- Keywords: virtual reality, treatment, assessment, mental disorders

Abstract

Virtual reality (VR) has emerged as a promising tool in the field of mental health. Key affordances of this novel technology centre on the ability to immerse individuals in highly controlled virtual environments that feel real. This offers a powerful methodology for research, as well as significant opportunities to enhance the accessibility, engagement and effectiveness of psychological treatments. In this review, we provide an overview of novel developments in the use of VR as a tool for treatment of mental health conditions, highlighting the core mechanisms which drive these benefits. We aim to provide readers with an understanding of how VR treatments work and review key research studies using VR treatments across major mental health conditions. We discuss novel emerging areas of development and address ethical and implementation considerations and highlight key priorities for future research. As the use of VR in mental health continues to evolve, conducting rigorous studies, and remaining up to date with the latest technological advances, are critical for ensuring the ongoing improvement of mental health treatments.

Introduction

The past 25 years have seen a rapid expansion in digital technologies designed to support assessment and treatment of mental health conditions. This has arisen through recognition that technologies such as online therapies, smartphone apps and wearables, provide innovative avenues for improving the quality and reach of available treatments^{1,2}. Research evidence is mounting in favour of the potential clinical utility of these digital tools, particularly when combined with human support³. Within this body of literature, virtual reality (VR) has emerged as one highly promising technology that offers new opportunities for clinical research, assessment, and intervention^{1,4-7} (see Box 1 for historical overview).

Through a head mounted display which projects three-dimensional images onto a screen, VR users are immersed in a computer-generated virtual environment which can closely simulate the real world (see Figure 1 and Figure 2). Audio and hand tracking sensors offer the ability to interact with objects and virtual avatars, which may be computer-generated or other VR users. At its core, VR offers possibilities to simulate reality that simply did not exist with the traditional methods that were available in the past⁸. These capabilities represent transformative opportunities for human interaction and experience, including for mental health assessment and treatment⁹.

Psychological treatment has long suffered limitations in bridging the gap between the therapeutic context and the real world where mental health challenges play out. Accurate assessment is critical for characterising and diagnosing mental health conditions; however, it is heavily reliant on individuals to recall detailed experiences that are often forgotten or misremembered¹⁰. Psychological interventions seek to help individuals manage symptoms and improve functioning in everyday life, however they are typically delivered in clinical settings in the absence of relevant triggers and contexts. This 'therapy-real world gap' can limit the accuracy of assessments and hamper the effectiveness of treatments. The ability to recreate real world environments with a high degree of precision and control within VR offers opportunities to overcome these challenges¹¹. Virtual environments can provide an ecologically valid context in which to conduct assessments and treatments, whilst also offering individuals the opportunity to learn and adapt to relevant situations and scenarios in real time, progressively, and safely under supervision of a therapist¹². Further, as technologies like VR grow increasingly accessible in modern society, harnessing these tools as a vehicle for remote treatment provides an avenue for enhancing the accessibility and scalability of mental health solutions. Improving access to mental health treatment is a critical and urgent unmet need in the face of rising rates of mental ill-health globally¹³. Through persuasive systems design and gamification, VR and other digital mental health technologies also have capacity to address

barriers to help seeking and poor engagement¹, particularly amongst youth populations who lead increasingly digital lives and are interested in using technologies to support their mental health¹¹.

Cutting-edge innovations in VR treatments are rapidly developing across sectors, driven by promising research findings and associated industry attention to the potential commercial viability of these platforms. Indeed, there has been significant growth in VR research over the past decade¹⁴. Whilst similar immersive reality technologies including augmented reality, referred to broadly as 'extended reality' or 'XR', have some emerging potential in mental health¹⁵, these are distinguished from VR by their level of immersion and are at a relatively early phase of development. Therefore, the current review will focus on fully immersive VR only. Incorporating evidence from several comprehensive and recent systematic reviews and meta-analyses ^{6,16-19}, this narrative review aims to provide up to date evidence on the application of VR across mental health conditions, highlight advances and challenges in the field, and set forth key priorities for future research. Commencing with a summary of the core elements and mechanisms of immersive VR treatments, followed by a summary of key evidence for VR treatments across mental health conditions, and ending with discussion of major emerging areas of innovation and development, including considerations for ethics and implementation, and priorities for future research.



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Figure 1: Typical setup of therapist-delivered VR treatment. The individual is immersed in a virtual environment by wearing a VR headset. The therapist launches and controls a VR program on a computer which then sends the virtual environment to the headset via Wi-Fi or cable. The therapist can view and change what the individual sees and communicate with them via headphones and microphone.

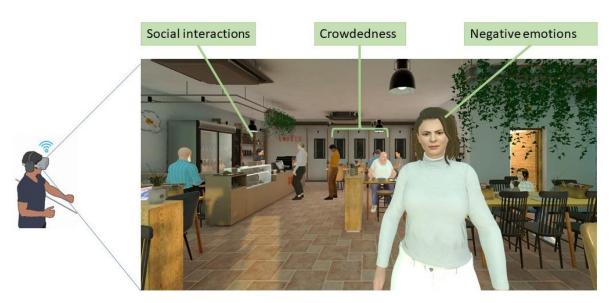


Figure 2: Illustration of a VR social environment and relevant elements used in treatment of paranoid and social anxiety. Source: Orygen Digital - Revive study.

Active characteristics of immersive VR

Immersion is achieved when our sensory system is triggered to respond to the virtual world in a similar way to the response that would be triggered by a real environment. An immersive system, sense of presence and ecological validity are central to how immersive a virtual reality experience feels⁸. By immersive system we mean the technical aspects of the VR equipment and software, for example: the field of view, how you can move in the VR environment, how you can interact with objects, how your movements are tracked. Sense of presence is the individual's perception of being in a VR environment and that what is happening in the environment is plausible⁸. Together, immersion and sense of presence correlate highly with how realistic an environment looks and feels (ecological validity)²⁰ and with the emotional, behavioural and physiological response experienced in the VR environment. Finally, the setting in which VR is experienced (e.g. safe space, full privacy) alongside user characteristics, such as motivation and willingness to do the experience also influence presence and immersion (Figure 3). Before moving on to describing how VR is used in the

treatment of mental health, we want to expand on motivation as presence as they are both key elements of an effective VR treatment.

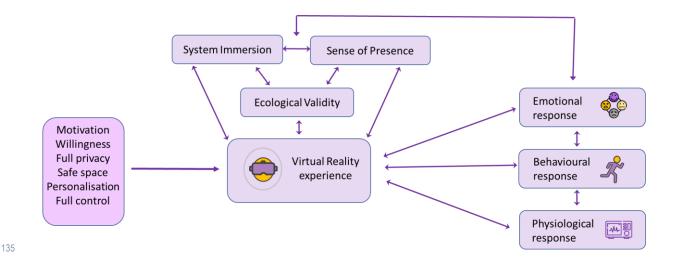


Figure 3: Active characteristics of immersive simulation

VR and motivation

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While Motivation is not specific for VR, it does play a central role in how individuals engage with this medium. Difficulties with motivation are common across different mental health conditions and are closely linked to poor functioning. Consequently, adequate assessment and targeting of motivation is seen as a key part of the recovery process^{21,22}. A common claim of VR based methods is that this technology is engaging and may help to overcome individuals' motivational difficulties. This is claimed to be achieved via gamification but also immersion and the structure and control that VR environments can provide. This rationale has prompted the use of VR in mental health conditions where motivational difficulties are part of the presenting problems²³. However, the application of VR specifically to address motivational difficulties has only been partially fulfilled and interventions had a broader span targeting both difficulties in pleasure experience²⁴ but also motivational difficulties²⁵. Paul and colleagues (2022), for example, tested a VR-based version of behavioural activation in a group of individuals with major depression and found that this paradigm was equivalent to traditional behavioural activation but superior to standard care²⁶. This suggests that VR can effectively harness motivational elements from both activation and exposure to everyday life events without the need for participants to experience it from daily life. This is relevant both in terms of offering people choice and it may have implications for cost effectiveness and resource use. A recent VR supported therapy, called V-NeST, had a specific focus on the negative symptoms of psychosis and distinctly targeted motivational and pleasure experience difficulties²³. This therapy used environments with different motivational needs and provides opportunities for experiential learning on the use of positive feedback to promote goal directed behaviour. Motivational difficulties also play a central role in theories of recovery from addiction. In this area VR assessments have predominantly focussed on attentional bias and physiological reaction to addictions cues²⁷. Some VR assessment procedures have focussed on craving and motivation, and showed how both que exposure and scenario realism are associated with higher craving for alcohol and cigarettes²⁸. Most of the intervention studies using VR in addiction focussed on cue exposure therapy where craving is targeted via exposure to visual cues of the desired substance. This paradigm target motivation indirectly similarly to serious games programmes which tend to calibrate rewards and use pleasure experience to maintain therapy engagement²⁹.

In summary, while motivational issues are relevant to many mental health conditions these, so far, tend to be addressed only indirectly by VR paradigms. This may be through having more engaging procedures, more enjoyment and gamification embedded. Addressing motivational issues in VR procedures will require considering more systematically effort for task completion and the value reward and feedback can have to drive behaviour.

Sense of presence and therapeutic change

Within the framework of embodied cognition, which holds that cognitive processes are rooted in the body's interactions with the world³⁰; a sense of presence refers to the individual's psychological sensation of "being there" in the environment with the ability "to act there" 31. Previous studies have shown that people report feeling some level of presence in almost all computerised mediated environments³². This psychological phenomenon has been linked to stronger user effects (e.g., the extent to which user responses to virtual stimuli and virtual interactions resemble responses to real-world equivalents) and, in consequence, to an increase of effectiveness of VR applications (e.g., the practical use of such environments as tools for entertainment, learning, training, or therapy)33-35. The most applied method for assessing sense of presence is by self-reporting questionnaire (Hein et al., 2018). recently, there is an increased desire to measure physiological correlates of sense of presence such as EEG and fMRI³⁶. Certain immersive technology components have been found to be more important to enhance presence, particularly tracking level (the degree of accuracy and precision with which a VR system can track the movements and positions of a user's head and hands), stereoscopy (creating a three-dimensional perception), and field of view (the extent of the visible environment or scene that a user can see while wearing a VR headset)³⁷.

From a clinical perspective, sense of presence transforms VR into an "empowering environment", a safe setting where people can start exploring and acting without feeling threatened³⁸. Nothing the individual fears can "really" happen to them in VR. With such safety assurance, they can freely explore, experiment, feel, live, and experience feelings and/or thoughts³⁹. In this regard, sense of presence has also been linked to clinical improvement when using mediated environments designed for the treatment of anxiety disorders. In particular, some studies have shown the bidirectional relationship between presence and emotions: on one hand, that the higher the presence, the higher the intensity of emotions experienced during the therapy and, on the other hand, the higher the intensity of the emotions, the higher the sense of presence and reality judgment⁴⁰. When the therapy uses relevant environments with emotionally significant content for the individual, with the goal of targeting specific emotions and related cognitions, this can potentially result in a more significant clinical change⁴¹. Therefore, sense of presence alone has not been supported as contributing to treatment outcome: feeling present during exposure may be necessary but not sufficient to achieve benefit from VR therapy. The interaction between sense of presence and relevant therapeutic processes need to be taken into consideration to understand clinical and meaningful change.

Now that we have seen how technical, perceptual, cognitive, and emotional aspects contribute to how immersive a VR experience is, we move on to describe how it can be used in the treatment of mental health.

Treatment through VR

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VR has been used for the treatment of various mental disorders, including anxiety, depression, psychosis, eating disorders, and trauma-related conditions. In particular, the immersive and controlled nature of VR environments has led to a growing body of research on VR-based exposure therapies, as well as broader treatments involving skill building and symptom management in real world environments. Findings from recent randomised controlled trials (RCTs) have demonstrated that these treatments can be effective¹⁷. The mechanisms driving these effects are still being studied, however existing findings suggest that it may be due to engagement and presence with the virtual environments, enabling repeat and safe exposure and adaptation to relevant feared stimuli.

Treatment of anxiety

One of the largest and most developed areas of research has been in the use of VR in the treatment of anxiety disorders (see Schröder et al., 2023 for latest meta-analysis⁴²). Anxiety

disorders, characterized by pathological fear and anxiety, account for 14.6% of disabilityadjusted life years globally, indicating that these disorders have a significant disease burden 43. A robust findings is that VR exposure-based treatments can reduce anxiety disorders for adults⁹ and treatment effects generalise to real life⁴⁴. Exposure treatment involves repeated confrontation with feared stimuli either external (objects, people, situations) or internal (bodily sensations, memories, hallucinations) in the absence of the feared outcome. This is equivalent to fear extinction, in which the feared stimulus (conditional stimulus) that was previously paired with an aversive outcome (unconditional stimulus) is presented without being followed by the aversive outcome. Experiencing the stimuli without that aversive outcome creates a corrective learning experience, where believability of the feared outcome and anxiety decrease (see figure 4). VR therapy for anxiety disorders has been shown to be more effective than treatment as usual or waiting list control 42,45. When virtual reality exposure is compared with in vivo exposure, no significant difference can be found, illustrating the non-inferiority of VR therapy compared with conventional treatment for anxiety disorders⁴². However, findings suggest that for some specific phobias standard in vivo procedures might be more effective than VR (i.e. Arachnophobia; Panic Disorder and Agoraphobia), especially where VR might not reach the level of *in vivo* exposure immersion and presence⁴⁶. Dropout rates do not differ between VR and in vivo treatment for anxiety disorders⁴², highlighting that VR treatments may be equally as acceptable for individuals with these conditions. While overall evidence supports the effectiveness of VR therapy for anxiety disorders, evidence gaps remain, especially with Panic Disorder and Agoraphobia & Social Anxiety Disorders⁶. Additionally, despite the potential of VR therapies for treating children and adolescents with anxiety disorders, there is a considerable lack of controlled trials in these age groups⁴⁷. Health economic evaluations on the cost effectiveness of VR for the treatment of anxiety are also lacking⁴². Another underdeveloped area is the use of VR to overcome limitations of assessments for anxiety disorders by generate highly controlled real-world experiences⁴. Virtual environments are known to produce physiological changes that are consistent with emotional responses to realworld experiences⁴⁸. VR therefore can elicit real world ecological valid anxiety responses⁴⁹. Currently, most applications for the assessment of anxiety disorders are not yet mature enough for clinical application⁶.

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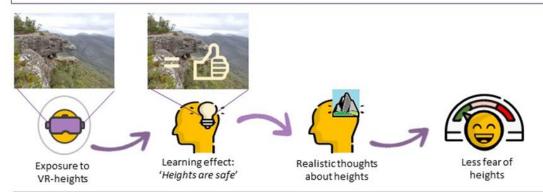
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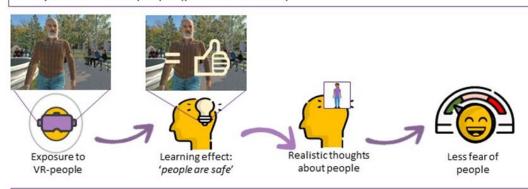
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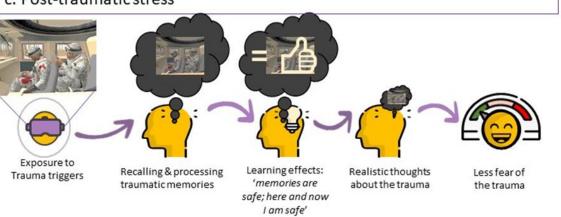
a. Anxiety - fear of heights



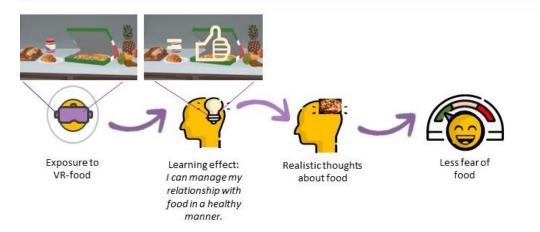
b. Psychosis - fear of people (paranoid ideation)



c. Post-traumatic stress



d. Eating disorders



e. Stress reduction



Figure 4: examples of VR-based treatments

Treatment of psychosis

Most of the evidence for the use of VR for treating of psychosis focusses on paranoia and auditory hallucinations^{7,49,50}. Overall, findings suggest that VR treatment for psychosis is effective, safe and cost effective⁵⁰, and clients' attitudes towards VR are positive⁷.

Virtual reality treatment of paranoia is based on the same model as anxiety disorders. VR treatments for psychosis involve exposure to environments and scenarios which offer corrective experiences that challenge underlying assumptions which maintain paranoid beliefs⁷. A personalised case formulation informs the selection of relevant feared social situations. During the VR exposure individuals are guided to drop safety behaviours, such as avoiding eye contact or acting hostile, and reshape their beliefs about safety and harm through positive learning experiences. Unfounded dysfunctional beliefs lose credibility across sessions as the individual learns that they are safe, resulting in reduced anxiety and improved

confidence in social situations. Several Randomised Controlled Trials (RCT) have shown that paranoid thoughts and anxiety are reduced^{51,52}, and that effects generalise to real life⁵². In summary, there is good evidence supporting the efficacy of VR treatments for paranoia⁵³, but direct comparison to exposure in vivo, and long-term effects post three months are lacking.

Virtual reality is also being used in the treatment of auditory hallucinations. The application of VR and associated technology offer the opportunity to connect interventions with the lived experience of voice-hearing in a novel and potentially powerful way. One of the most established approaches is AVATAR therapy, in which voice-hearers create a digital avatar to embody their main distressing voice, which is personalised with respect to visual and sound characteristics⁵⁴. Voice-transformation software allows the therapist to facilitate "face to face" dialogues between the person and the avatar in which the aim is to reduce anxiety and increase power, control, and confidence in dealing with voice. This approach was pioneered by Professor Julian Leff 55 and further developed by a London-based team, who conducted the first fully powered trial (AVATAR1), which demonstrated significant reductions in voice frequency and distress (with large effect sizes), against an active control at the primary (end of therapy) timepoint ^{54,56} using 2D virtual environment. The interaction of reduced anxiety and strong sense of voice presence has been associated with positive therapy outcomes⁵⁷. The first test of this approach in fully immersive 3D VR environments suggested large effects on auditory verbal hallucinations and significant effects on persecutory beliefs and quality of life, albeit involving comparatively small-scale studies ^{58,59}. Danish researchers have independently developed their own VR software and are conducting the CHALLENGE trial 60 as a fully powered replication of the original AVATAR1 randomised trial ⁵⁶ using a fully immersive approach. While implementation of the standard non-immersive AVATAR therapy is continuing apace 61, including remote delivery through video conferring platforms, the broader question as to whether use of full VR immersion confers specific benefits remains open.

Treatment of post-traumatic stress

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The use of VR for Post-traumatic Stress Disorder (PTSD) is supported by a growing evidence base. In VR Exposure Therapy (VRET) the individual engages in the narrative recounting of the traumatic event while being activated in a VR simulation that represents it. This approach, informed from evidence-based imaginal prolonged exposure strategies⁶², is believed to provide a low-threat context where the Individual can begin to confront and therapeutically process the emotions that are relevant to a traumatic event as well as de-condition the learning cycle of the disorder via an extinction learning process⁶³.

A variety of clinical trials have tested the efficacy of VRET in the treatment of combat-related posttraumatic stress disorder⁶⁴⁻⁷⁹. The consensus from this research suggests that VRET can produce outcomes that at a minimum, are equivalent to the strongest evidence-based treatments and produce better outcomes when compared to placebo controls^{44,70,72,76,80-83}. Two of the largest and most recent RCTs (Reger et al., 2016; Difede et al, 2022) have produced findings of note. In both trials, VRET and prolonged exposure demonstrated equivalent positive outcomes on the "gold standard" Clinician Administered PTSD Scale (CAPS) at posttreatment. However, in Reger et al. (2016), prolonged exposure produced more durable symptom reductions at 3-month follow-up. This may be in part due to the limited variety of VR scenario content available at the time of that trial (4 virtual Iraq contexts) that may have limited the customization of content needed to address diverse client needs, particularly for individuals who had deployments only in Afghanistan. In the later Difede et al. (2022) trial, that limitation was remedied with the system content offering 14 Iraq/Afghanistan virtual contexts, and positive post-treatment outcomes were equivalent at all follow-up time points. Moreover, in this trial, in pre-planned predictions, VRET was hypothesized to outperform prolonged exposure in persons with PTSD and co-morbid major depression, and that was confirmed across all outcome time points. Also relevant from this study⁷⁰ is the finding that when research participants were asked at the start of the trial (right after informed consent) that if they were to have a choice of treatment (all participants knew they would be randomly assigned to treatment condition): 76.7% would have chosen VRET. These findings are instructive on three points: 1) Customization of VR scenarios that are more relevant to the Individuals' trauma experience may lead to better outcomes; 2) PTSD clients with co-morbid major depression, who may have a more difficult time engaging imaginably in their trauma memory, may achieve more benefit from the emotionally evocative experience that a VR simulation offers; 3) VRET may have elements that appeal to clients compared to traditional treatment formats and serve a role in breaking down barriers to care. These findings provide insights that are relevant both in the design of future outcome studies and for informing treatment recommendations based on VR content availability and the client's current clinical characteristics/treatment preferences.

Finally, multiple studies have reported positive outcomes using VRET with non-combat related PTSD clients (i.e., World Trade Center and Sexual Trauma survivors) who in many cases were unresponsive to a previous course of imaginal-only prolonged exposure treatment^{67,68,71,84}. Together, the overall trend of the published findings is encouraging for the view that VRET can be safely applied clinically and is an efficacious approach for delivering an evidence-based treatment for PTSD.

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<u>Treatment of eating disorders</u>

Eating disorders are psychiatric illnesses characterized by high ambivalence towards change and disappointingly low recovery rates (i.e., between 40 to 60%)⁸⁵. New learning and repeated practice are needed to develop healthier attitudes and behaviors. Digital technology, such as mobile apps and VR are particularly well suited for this purpose. VR is one of the earliest forms of digital technology that has been tested in the field of eating disorders ⁸⁶⁻⁸⁸. Most studies have employed this technology to measure (i.e., assessment studies) or change (i.e., treatment studies) people's unhelpful behaviors and attitudes towards illness-related cues, such as food and body shape. Ecological validity studies have established that virtual food elicits similar emotional reactions as real food (and higher emotional reaction compared to food pictures) and higher levels of negative emotions and eating disorder attitudes and behaviors (e.g., anxiety, body dissatisfaction, craving) in clients, compared to healthy controls. Virtual reality has also been employed to measure clients' perception and dissatisfaction of own and others' (typically avatars') body sizes. While these studies provide inconclusive findings with regards to the accuracy of body size estimation, they are more concordant in highlighting negative attitudes towards own's bodies in individuals.

RCTs have conducted on the use of VR to deliver, supplement, or enhance standard psychological treatments for eating disorders^{6,86-88}. Repeated exposure to illness-related cues (food and bodies) is associated with a reduction of core eating disorder symptoms, such as episodes of loss of control overeating and body dissatisfaction, compared to control conditions, in people with binge type eating disorders (e.g., standard cognitive behavioral therapy). Although fewer VR studies have been conducted in anorexia nervosa, preliminary findings are promising in this client group too, in that exposure to virtual foods is associated with lower eating-related anxiety and greater approach to food^{89,90}. Finally, a fast-growing field of application is the use of VR to correct perceptual body distortions and body representations through the embodiment of avatars of different sizes and shapes and the induction of "body size illusions"⁸⁷.

<u>Treatment of stress symptoms</u>

VR relaxation is an innovative and accessible low intensity psychological intervention to support wellbeing and reduce stress (see Figure 4e). The virtual environments used in VR relaxation studies are typically pleasant, picturesque, calming environments, often depicting graphics or video of features of the natural world, for example, beaches, oceans, forests, meadows, mountains, lakes, and waterfalls. Some environments include interactive, gamified components, such as mindfulness or guided meditations, or games and activities that enable individuals to playfully interact with features of the environment. Intervention time in VR is

typically brief and, in the existing research, often offered as a single session; while interventions can be facilitated in-person by a therapist or administered by the user as a self-help intervention.

A recent systematic review of applications of VR relaxation for people with mental health disorders concluded that it is a feasible, acceptable, and effective intervention in the short term to promote relaxation and reduce stress⁹¹. The largest studies have been with outpatients, where VR relaxation has been coupled with other interventions, such as meditation⁹² or physical activity⁹³. Small studies have also been carried out on individuals with conditions such as eating disorders, depression, bipolar disorder, and psychosis, including with inpatients on psychiatric wards⁹⁴⁻⁹⁷, where there appears to be some initial evidence that VR relaxation may reduce levels of violence and aggression from clients and the number of restrictive practices administered by ward staff⁹⁸. One pilot study has tested adolescent outpatients at a specialist secondary school with psychiatric and behavioural problems, including autism and attention deficit hyperactivity disorder. It found that the calm or relaxed state of participants after playing DEEP lasted for about 2 hours on average. ⁹⁹.

VR relaxation, with its common focus on simulated natural environments, has sought to harness research findings that indicate that exposure to real-world nature has many physical and mental health benefits¹⁰⁰. Delivery of VR relaxation to psychiatric clients can be particularly powerful and useful because many of these picturesque natural environments can be inaccessible to many psychiatric clients due to a range of factors, such as financial restrictions, experience of severe anxiety or paranoia in open or social environments, physical disabilities or chronic conditions, living in busy, inner city environments where there is a lack of green natural spaces, or because they are staying in restrictive environments, such as psychiatric hospitals.

Another systematic review highlighted the benefits of VR relaxation in the general population as a means of increasing psychological wellbeing, managing stress, and protecting mental health¹⁰¹. These interventions appear to have self-help applications for the home or in the workplace¹⁹, where staff support and wellbeing applications of VR relaxation have focused on people in high pressured jobs or keyworkers, such as healthcare professionals, including mental health staff, who can experience burn out and compassion fatigue^{102,103}.

Key strengths of VR relaxation are its accessible self-help and transdiagnostic applications for stress and anxiety management, and its potential on psychiatric wards as a novel approach to crisis management and de-escalation. Limitations of the current research include limited standardisation of interventions, VR environments, duration of time in VR, number of sessions, and outcome measures. There is also a lack of large RCTs, studies on the longer-term impact

of VR relaxation, and studies on real-world behaviour change in clients, i.e., whether individuals change their relaxation and stress management practices because of their experience of VR relaxation. Nevertheless, there appears to be huge potential for VR relaxation as a low-intensity stress-management intervention in mental health clinics or psychiatric wards, or as a self-help intervention in clients' homes.

In summary, there is growing evidence for the use of VR treatment in anxiety disorders, post traumatic stress, and psychosis. Some evidence is emerging for the use of VR treatment in eating disorders and stress reduction, but larger and controlled trials are much needed. Research on VR treatment for other symptoms is still in its infancy.

Emerging areas in VR

Owning to the potential benefit of enhanced ecological validity, VR research has historically focused on the delivery of exposure-based treatments within real-world virtual environments, delivered under supervision of a therapist. More recently technological advances have brought new opportunities to extend and enhance the capabilities of VR to deliver more tailored, targeted and engaging treatments, including integration with artificial intelligence (AI), real time data capture, biofeedback and therapeutic VR games. Whilst these opportunities bring hope for new and improved mental health treatments, they also raise important ethical implications and considerations for implementation beyond the research setting. This section provides an overview of key emerging areas of development and discusses key issues facing the field.

Artificial intelligence

Al is a broad term that captures a range of techniques including machine learning and natural language processing (NLP) which harness algorithms and computer systems to analyse large amounts of data to detect patterns and make predictions. An area of particular potential is the use of Al to automate the delivery of VR treatments, which has important implications for increasing the availability of effective treatments for those in need, many of whom struggle to access often overburdened mental healthcare systems. Basic forms of Al have already been integrated into VR treatments for fear of heights^{104,105}, public speaking anxiety¹⁰⁶, spider phobia¹⁰⁷, and psychosis^{108,109}. Within automated VR treatments, individuals are typically guided by an avatar, which has some capability to personalise and direct the treatment based on the individual's response to different scenarios. However, the level of personalisation is currently limited to basic decision trees which are restricted in the degree to which they can adapt the treatment over time. Recent developments in Al have the potential to overcome this by harnessing real-time data within the headset to track and adapt the therapy automatically,

much like a clinician would in everyday practice. As the level of personalisation is a known driver of treatment effects¹¹⁰, this affordance offered by AI will be an important future direction in VR therapies, whether it be fully automated or supplement the work of a clinician. However, clinicians' attitudes around trust, confidence and system transparency may form a potential barrier¹¹¹. Beyond personalisation, automated VR therapy offers the potential for self-guided treatment that can be accessed independently from a clinician. Whilst this affords great potential in terms of the scalability of mental health solutions, more research is needed to establish the safety and efficacy of these approaches, including for which populations it may be suited. Nonetheless, basic forms of AI have already been integrated into VR treatments for fear of heights^{104,105}, public speaking anxiety¹⁰⁶, spider phobia¹⁰⁷, and psychosis^{108,109}, with good research evidence. For example, Freeman et al¹⁰⁸ conducted an RCT in which 174 people diagnostic with a psychotic condition and experiencing agoraphobia were randomised to treatment-as-usual or an automated VR therapy targeting fear in social situations ('gameChange VR'). Individuals were guided by an automated avatar, or 'virtual coach', to progress through increasingly challenging situations, providing encouragement to drop safety behaviours and feedback to tailor progress. Findings indicated a greater reduction in avoidance behaviours in the VR compared to the control group with a moderate effect size, mediated by improved safety beliefs and reduced defence behaviours. Although there was a mental health care worker present during intervention delivery, they did not have training in cognitive therapy and had minimal therapeutic involvement. When deliverable at scale, automated VR treatments such as gameChange VR have important opportunities to improve access to effective treatment, potentially at a reduced cost.

Real-time analysis of multiple sources

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Within the VR headset, a comprehensive network of sensors, including heart rate monitors, eye-tracking cameras, head movement sensors (accelerometers, gyroscopes, magnetometers), hand tracking technology, and facial expression recognition cameras, continually collect a wealth of physiological and emotional data from the individual. These diverse data streams are then analysed to interpret the client's responses. Eye tracking in VR is a relatively new development but has already shown promise in research concerning human perception and behaviour. Using only eye-tracking, studies have been shown to classify user emotions with an accuracy between 60% to 90%¹¹². Heart rate monitoring is another area of opportunity. Whilst there are no studies on the clinical implications of heart rate monitoring in VR therapy, the use of heart rate monitors such as smart bracelets can be used to characterise clinically relevant mood states 113. While research is still in its infancy, the integration of facial recognition software 114 into psychological treatments also holds promise as an innovative avenue for improving outcomes. Through integrated systems that provide real-time analysis

of data in the VR headset, patterns indicative of stress, anxiety, or discomfort can be rapidly detected, informing real-time decisions to provide a dynamic and highly personalized therapeutic journey. For example, if a user is experiencing a VR simulation, and the psychologist's intent is to increase the level of anxiety, the system could detect the current state of the user and update the environment (e.g., by adding more people and noise) or make the avatar react to the user's current actions (see Figure 5). For instance, if the user is avoiding eye contact to limit interaction, the avatar inside the VR simulation could highlight that behaviour, thereby causing an increase in anxiety.

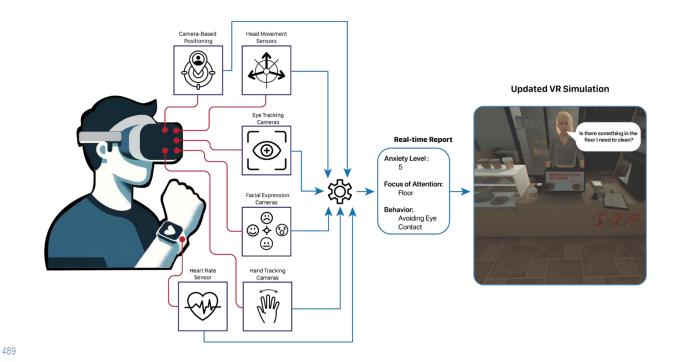


Figure 5: An example VR Sensors and Cameras used for real-time updates of the VR simulation. A multitude of sensors are used to identify users state and can be used to update the VR simulation.

Biofeedback within VR environments

A small number of studies have explored how biofeedback could be used within VR¹¹⁵. Biofeedback involves real-time feedback of physiological signals to help individuals learn to regulate their responses to stressors. For example, individuals can learn to identify and alleviate anxiety by receiving immediate feedback from biosensors that monitor muscle tightness or heart rate. Traditional biofeedback can be effective, however difficulties with engagement and maintained attention are common challenges. By feeding back physiological signals into the VR environment using novel stimuli, individuals may experience more enjoyment and focus during sessions whilst learning to regulate their responses to triggers in personally relevant contexts. For example, combining the use of biofeedback and gamification

in VR, the DEEP application immerses users in an ocean environment where they can control their movement by regulating their breathing, which is measured continuously using a chest band. An RCT in university students with elevated anxiety showed improvements in anxiety symptoms following four sessions using the application, and greater levels of engagement and self-efficacy relative to a control condition¹¹⁶. In the context of psychosis, a new approach is being developed which combines CBT and neurofeedback within VR to treat anxiety related to hallucinations¹¹⁷. A systematic review including four RCTs of VR biofeedback for anxiety found some evidence for improving outcomes¹¹⁵, however this emerging area requires more development and rigorous trials in different clinical populations to confirm effectiveness.

Therapeutic VR games

Using gamification in VR to boost engagement and enjoyment of therapy is also a unique affordance that is relatively unexplored. In the broader digital mental health literature, gamification elements such as rewards, feedback or challenges have been used within smartphone apps, online therapy programs and wearables to motivate and engage users^{118,119}. For example, a non-immersive computerised VR game called SPARX uses storytelling to support young users to develop and practice therapeutic skills in an enjoyable, playful matter, incorporating exploration, puzzles, games and quizzes¹²⁰. A non-inferiority trial found SPARX was equally effective for reducing depressive symptoms as usual treatment amongst adolescents, with good retention rates and users reporting the games helped with their engagement¹²¹. Outside of research, therapeutic VR games are more progressed, with a review conducted in 2020 of the STEAM store (a large VR app store) finding 182 games which had some link to mental health¹²². The majority of these were for mindfulness and meditation, however none had clear links to research studies, and some contained concerning content such as aiming to induce digital hallucinogenic experiences, highlighting the need for more rigorous research and oversight (see Box 2).

Summary and future directions

Although research into VR was first established several decades ago, the field is still developing as technological advances continue to evolve rapidly. Research to date has established good evidence for the feasibility and acceptability of VR across several clinical populations, though clear gaps still exist particularly in youth populations^{18,47}. VR can provide an immersive and engaging environment that captivates adolescents, making therapy sessions more appealing and potentially increasing their participation and motivation in treatment. However, there is limited understanding of the long-term psychological impact of prolonged VR exposure on developing brains and research exploring how VR affects social

skills, empathy, and emotional development in children and adolescents is still relatively sparse. Understanding the influence of VR on cognitive functions like attention, memory, and learning in youth is also an area that needs more attention. Finally, limited research exists on the potential physical health implications, such as eye strain, motion sickness, and the effects of prolonged exposure to VR on the developing visual system.

As discussed in this review, good evidence exists for the efficacy of CBT-based VR treatments for anxiety disorders, psychosis, and trauma-related conditions, and emerging evidence for eating disorders and stress reduction. However more high quality RCTs are required to fully establish the efficacy of VR treatments across different populations.

In order to avoid a risk of failure in uptake and utilisation of VR technologies in the real world, as we have often seen in the first generation of digital mental health technologies 130, we need to work alongside the end users of these technologies to confirm they are fit for purpose, and ensure that the system is adequately trained and supported to translate the great potential this technology has for improving outcomes for people suffering from mental ill-health. Research priorities in the field of virtual reality for mental health focus on expanding our understanding, improving interventions, and ensuring ethical and effective use (see Box 3). Some key priorities include: a) exploring how VR experiences can be inclusive and representative of diverse cultural, social, and economic backgrounds; b) embedding those with lived experience in the conception, development and testing of new VR interventions to create treatments that are more engaging, resonant, and relatable for users, potentially increasing their efficacy; c) investigating the long-term impact of VR interventions on mental health outcomes and examining their sustainability over time; d) understanding how to tailor VR interventions to individual needs and specific mental health conditions, ensuring personalized treatment integrating AI, biofeedback, and gamification; e) formulating regulatory standards and ethical guidelines for the development, deployment, and evaluation of VR-based mental health interventions, particularly concerning adolescent populations; f) investigating strategies for integrating VR interventions into existing mental health care systems, addressing issues related to training, infrastructure, and reimbursement.

Box 1: Origins and development of VR treatments for mental health conditions.

This box provides a brief historical overview of VR and of the use of VR in mental health.

VR Creation Methods: Two primary methods for immersive Virtual Reality (VR) exist. The first employs VR headsets, also known as Head Mounted Displays (HMDs). These wearables, fitted with displays for each eye, generate depth perception through slight projection variations. Many HMDs incorporate movement sensors, allowing the virtual environment to respond to user actions, cultivating a sense of "Presence." The origins of VR headsets date back to the 1960s, with Ivan Sutherland's 'The Sword of Damocles' in 1968¹²³, which was so heavy it required ceiling suspension for use. Until 2013, VR headsets remained scarce and costly, primarily found in university settings. A transformative moment occurred in 2013 with the release of the affordable Oculus Developer Kit 1 (DK1). Over the past decade, high-quality, user-friendly consumer VR headsets have proliferated. The second method involves a "cave automatic virtual environment" (CAVE), pioneered by the University of Illinois in 1992¹²⁴. In a CAVE, virtual environments are projected onto at least three walls. Modern variations include flat panel displays. Real-time motion capture sensors track user movements, and like HMDs, the displays respond to user actions, creating a sense of presence.

Psychology and VR: the field of Psychology began exploring VR's clinical applications in the early 1990s. A pivotal moment occurred in 1995 when Barbara Rothbaum et al 125, published a groundbreaking study using VR to treat acrophobia (fear of heights). Therapists mostly employed VR headsets for exposure-based interventions. Impressively, positive treatment outcomes were observed despite the limited visual and software quality. In the past decade, more complex and tailored VR interventions have emerged. However, despite three decades of psychological research, clients have yet to fully benefit from VR in clinical settings. The next decade holds promise for overcoming this challenge, as affordable VR hardware, advanced software, and comprehensive clinical training all become mainstream.

Box 2: Challenges to emerging VR technologies.

This box explores two main challenges of the use of VR in mental health: ethics and regulation, and implementation and engagement.

Ethics and regulation: With the proliferation of digital health products available directly to consumers, many of which make strong claims without sufficient scientific evidence 126, there is a need to address growing concerns about ethics and regulation in the digital mental health field. Issues pertaining to privacy, data security and safety are well documented in the broader

digital mental health literature ¹²⁷⁻¹³⁰ and are of equal relevance to VR, where the collection and storage of potentially sensitivity digital information raises important security questions. There are several specific aspects of VR which call for unique ethical considerations. Critically, little is known about adverse effects of VR therapies ¹³¹, although results from RCTs suggest that major adverse effects are no more likely than routine treatment. Nonetheless, the harms or discomfort that may come about from using VR may be more nuanced than traditional safety monitoring protocols allow for. For example, qualitative studies suggest that VR experiences can be disorienting for some people, and cybersickness is a known side effect. For populations where dissociative experiences are common, it is not currently unknow whether VR has any adverse immediate or long terms effects, although these side effects have been detected ¹³². Finally, whilst the ability to control exposure to feared stimuli in VR is key to its therapeutic potential, this level of control also offers the potential for harms if not carefully considered. There is a clear need for further research to more thoroughly understand the potential negative effects of VR, and establishing appropriate clinical protocols with sufficient training and supervision will be important for protecting against any potential harms.

Implementation and engagement: The integration of technology within existing service structures as well as use of digital interventions by end users 'in the real world' are an area of complexity facing the field. Indeed, digital interventions which perform well in clinical trials do not necessarily translate to strong uptake and engagement beyond the research context 133. A lack of consideration for the implementation context, whether it be within clinical settings or people's everyday lives, is a key reason for this gap. Employing methodologies such as user centred design in the development of new interventions is critical to ensure the real-world needs and perspectives are accounted for in this process¹³⁴. Implementation models such as the NASSS framework 135 can be used as a tool to guide development and determine the likelihood that a digital solution will be successful in the real world. In terms of implementing VR within clinical settings, success hinges on the degree to which it fits within existing systems and workflows^{135,136}. Whilst VR equipment is becoming more affordable, most setups require a headset, computer and headphones, which is expensive. It can also be time consuming to setup the equipment and require some level of experience, though VR apps are becoming more user friendly. Whilst it is possible to create a mobile setup of this equipment on a trolley or use relatively low-fidelity programs contained within the headset that do not require connection to a computer, in future clinics may contain a dedicated room where VR treatments are delivered for optimum efficiency. Adequate training and resources are also needed to up skill clinicians to deliver VR treatments¹³⁷, as well as ongoing education and awareness building of evidence-based VR treatments for consumers. Finally, currently the biggest implementation barrier may be the limited availability of evidence-based VR therapy programs.

Whilst the number of available programs is growing¹²², few have been scientifically validated, and the software is costly to build and maintain, with many companies yet to establish sustainable sources of funding.

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Box 3: Research priorities for the field of virtual reality for mental health disorders.

Ensure representation of lived experience perspectives:

- Embed perspectives of individuals with lived experience throughout all research phases, from conception to implementation, ensuring their voices guide the research process.
- Prioritise lived experience leadership within research teams to ensure research decision making is responsive the needs of individuals with lived experience across all phases.

Embed Culture, Equality, Diversity & Inclusion:

- Involve a diverse range of individuals, including those from different cultural backgrounds, in all phases of the design, development and testing process to ensure cultural sensitivity and authenticity.
- Design VR experiences that can be customized to reflect diverse cultural backgrounds, allowing users to feel represented and comfortable within the virtual environment.
- Include diverse characters and settings in VR environments that accurately represent various cultural backgrounds, identities, and lived experiences.

Standardise VR Study Reporting:

- Develop and promote guidelines for standardised reporting in VR research, ensuring consistency, transparency, and replicability (e.g., the RATE-VR guidelines under development by Vlake et al., 2023¹³⁸).
- Transparently report and acknowledge lived experience involvement in research within publications, including relevant limitations.

Establish effectiveness and unpack mechanisms:

- Undertake randomised controlled trials (RCTs) to establish the evidence base for VR treatments in various demographic groups and clinical contexts, particularly youth populations
- Utilise innovative methods to deconstruct VR treatment mechanisms, including active control comparisons, mediation analyses, dismantling studies, and real-time data capture techniques like ecological momentary assessment, eye tracking, and biosensors.
- Conduct trials to establish the cost-effectiveness of VR treatments compared to traditional methods.

Determine optimum personalisation and tailoring:

- Identify suitable candidates for VR treatments through subgroup analysis and individual response predictors, including qualitative insights from patients and clinicians.
- Investigate the impact of VR treatment personalization and the extent of tailoring required for optimal outcomes.
- Explore Al-driven personalization and tailoring in VR interventions.

Develop novel VR treatments and assessments:

- Incorporate culturally relevant coping strategies, therapies, or mindfulness practices into VR interventions to resonate with specific cultural groups.
- Research new intervention targets within VR, such as representation and interaction with cognitive and emotional states.
- Explore the use of VR for novel therapeutic paradigms, such as acceptance and commitment therapy and mindfulness.
- Develop and validate VR assessment tools.

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- Integrate VR with cutting-edge technologies like AI, gamification, biosensors, and real-time data capture.
- Assess the feasibility and efficacy of self-administered VR treatments and the required level of clinician involvement.
- Conduct pilot tests within diverse communities to assess the cultural appropriateness and acceptance of VR mental health interventions.

Facilitate Clinical Implementation and Training:

- Conduct implementation trials to facilitate clinician adoption of VR in mental health.
- Identify and address barriers to widespread clinical adoption, including technological, financial, and training barriers.
- Explore strategies to increase patient engagement and retention in VR treatment.
- Develop resources and guidelines to support individuals to make informed decisions about VR treatment based on clear and transparent expectations.
- Develop comprehensive training programs and resources for clinicians to effectively implement VR.
- Engage policy advisors to produce guidelines on the implementation of VR.
- Engage with communities to gather feedback and insights on the relevance and effectiveness of VR interventions within different cultural contexts.

Prioritise user experience and accessibility:

- Employing appropriate participatory design methods such as user centred design and codesign with end users (typically people with lived experience and clinicians) to ensure VR treatments are fit-for-purpose and engaging with excellent user experience.
- Ensure the design of VR treatments are appropriate for diverse and representative lived experiences.
- Actively address equity and accessibility in VR treatment design, especially for diverse groups with specific accessibility requirements or from varied cultural and linguistic backgrounds.
- Ensure that VR technology is accessible and affordable across diverse socioeconomic backgrounds to minimize disparities in access to mental health care.

Address ethical and safety considerations:

- Investigate and address ethical concerns, particularly in the context of AI integration in VR.
- Study the safety profile of VR usage, focusing on adverse events and developing protocols for reporting these in research publications.

Establish industry and clinical partnerships:

- Strengthen collaboration between researchers and industry to ensure the scalability and sustainability of VR solutions.
- Collaborate with clinical service providers to develop models for integrating VR treatments within routine clinical settings.

 Develop funding models and engage with policy advisors to support long-term VR treatment implementation.

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Author contributions

- 729 IHB, RPK and LV conceived of the article and drafted, edited and revised the manuscript.
- Authors IHB, RPC, LV, AR, MRC, VC, MC, TW, SR, and MR write sections of the article, and
- MAJ and AT contributed feedback. All authors reviewed and approved the final manuscript.
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Competing interests

The authors declare no competing interests.

References

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- Torous, J. *et al.* The growing field of digital psychiatry: current evidence and the future of apps, social media, chatbots, and virtual reality. *World Psychiatry* **20**, 318-335, doi:10.1002/wps.20883 (2021).
- Jameel, L., Valmaggia, L., Barnes, G. & Cella, M. mHealth technology to assess, monitor and treat daily functioning difficulties in people with severe mental illness: A systematic review. *J Psychiatr Res* **145**, 35-49, doi:10.1016/j.jpsychires.2021.11.033 (2021).
 - Philippe, T. J. *et al.* Digital Health Interventions for Delivery of Mental Health Care: Systematic and Comprehensive Meta-Review. *JMIR Ment Health* **9**, e35159, doi:10.2196/35159 (2022).
- Bell, I. H., Nicholas, J., Alvarez-Jimenez, M., Thompson, A. & Valmaggia, L. Virtual reality as a clinical tool in mental health research and practice. *Dialogues Clin Neurosci* **22**, 169-177, doi:10.31887/DCNS.2020.22.2/Ivalmaggia (2020).
- Rizzo, A., Koenig, S. & Lange, B. in *APA handbook of neuropsychology, Volume 2:*Neuroscience and neuromethods, Vol. 2 APA handbooks in psychology®. 473-491

 (American Psychological Association, 2023).
- Wiebe, A. *et al.* Virtual reality in the diagnostic and therapy for mental disorders: A systematic review. *Clin Psychol Rev* **98**, 102213, doi:10.1016/j.cpr.2022.102213 (2022).
- Rus-Calafell, M., Garety, P., Sason, E., Craig, T. J. K. & Valmaggia, L. R. Virtual reality in the assessment and treatment of psychosis: a systematic review of its utility, acceptability and effectiveness. *Psychol Med* **48**, 362-391, doi:10.1017/S0033291717001945 (2018).
- Slater, M. & Sanchez-Vives, M. V. Enhancing Our Lives with Immersive Virtual Reality. *Frontiers in Robotics and AI* **3**, doi:10.3389/frobt.2016.00074 (2016).
- Freeman, D. *et al.* Virtual reality in the assessment, understanding, and treatment of mental health disorders. *Psychol Med* **47**, 2393-2400, doi:10.1017/S003329171700040X (2017).
- Solhan, M. B., Trull, T. J., Jahng, S. & Wood, P. K. Clinical assessment of affective instability: comparing EMA indices, questionnaire reports, and retrospective recall. *Psychol Assess* **21**, 425-436, doi:10.1037/a0016869 (2009).
- Bell, I. *et al.* Digital technology for addressing cognitive impairment in recent-onset psychosis: A perspective. *Schizophr Res Cogn* **28**, 100247, doi:10.1016/j.scog.2022.100247 (2022).
- Valmaggia, L. The use of virtual reality in psychosis research and treatment. *World Psychiatry* **16**, 246-247, doi:10.1002/wps.20443 (2017).
- Organisation, W. H. The WHO special innitiative for mental health (2019-2023): universal health coverage for mental health (World Health Organisation 2019).
- Cipresso, P., Giglioli, I. A. C., Raya, M. A. & Riva, G. The Past, Present, and Future of Virtual and Augmented Reality Research: A Network and Cluster Analysis of the Literature. *Front Psychol* **9**, 2086, doi:10.3389/fpsyg.2018.02086 (2018).
- Eckert, M., Volmerg, J. S. & Friedrich, C. M. Augmented Reality in Medicine: Systematic and Bibliographic Review. *JMIR Mhealth Uhealth* **7**, e10967, doi:10.2196/10967 (2019).
- Cieślik, B. *et al.* Virtual reality in psychiatric disorders: A systematic review of reviews. *Complement Ther Med* **52**, 102480, doi:10.1016/j.ctim.2020.102480 (2020).
- Dellazizzo, L., Potvin, S., Luigi, M. & Dumais, A. Evidence on Virtual Reality—Based Therapies for Psychiatric Disorders: Meta-Review of Meta-Analyses. *Journal of Medical Internet Research* **22**, e20889, doi:10.2196/20889 (2020).
- Halldorsson, B. *et al.* Annual Research Review: Immersive virtual reality and digital applied gaming interventions for the treatment of mental health problems in children and young people: the need for rigorous treatment development and clinical evaluation. *J Child Psychol Psychiatry* **62**, 584-605, doi:10.1111/jcpp.13400 (2021).

Riches, S. *et al.* Virtual reality relaxation for people with mental health conditions: a systematic review. *Social Psychiatry and Psychiatric Epidemiology*, 1-19 (2023).

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- Loomis, J. M., Blascovich, J. J. & Beall, A. C. Immersive virtual environment technology as a basic research tool in psychology. *Behavior Research Methods, Instruments & Computers* **31**, 557-564, doi:10.3758/BF03200735 (1999).
 - Cella, M. *et al.* Psychosocial and behavioural interventions for the negative symptoms of schizophrenia: a systematic review of efficacy meta-analyses. *Br J Psychiatry* **223**, 321-331, doi:10.1192/bjp.2023.21 (2023).
- Edwards, C. J., Garety, P. & Hardy, A. The relationship between depressive symptoms and negative symptoms in people with non-affective psychosis: a meta-analysis. *Psychol Med* **49**, 2486-2498, doi:10.1017/s0033291719002381 (2019).
- Cella, M. *et al.* Virtual Reality Therapy for the Negative Symptoms of Schizophrenia (V-NeST):
 A pilot randomised feasibility trial. *Schizophrenia Research* **248**, 50-57,
 doi:https://doi.org/10.1016/j.schres.2022.07.013 (2022).
 - Szczepańska-Gieracha, J., Cieślik, B., Serweta, A. & Klajs, K. Virtual Therapeutic Garden: A Promising Method Supporting the Treatment of Depressive Symptoms in Late-Life: A Randomized Pilot Study. J Clin Med 10, doi:10.3390/jcm10091942 (2021).
- Ventura, J. *et al.* Virtual reality assessment of functional capacity in the early course of schizophrenia: Associations with cognitive performance and daily functioning. *Early Intervention in Psychiatry* **14**, 106-114, doi:https://doi.org/10.1111/eip.12831 (2020).
- Paul, M., Bullock, K. & Bailenson, J. Virtual Reality Behavioral Activation for Adults With Major Depressive Disorder: Feasibility Randomized Controlled Trial. *JMIR Ment Health* **9**, e35526, doi:10.2196/35526 (2022).
 - Schroder, B. & Muhlberger, A. Assessing the attentional bias of smokers in a virtual reality anti-saccade task using eye tracking. *Biol Psychol* **172**, 108381, doi:10.1016/j.biopsycho.2022.108381 (2022).
 - Simon, J., Etienne, A. M., Bouchard, S. & Quertemont, E. Alcohol Craving in Heavy and Occasional Alcohol Drinkers After Cue Exposure in a Virtual Environment: The Role of the Sense of Presence. *Front Hum Neurosci* **14**, 124, doi:10.3389/fnhum.2020.00124 (2020).
- Caballeria, E. *et al.* Rehabilitation Gaming System for Alcohol-Related Cognitive Impairment:
 A Pilot Usability Study. *Alcohol and Alcoholism* **57**, 595-601 (2022).
- Wilson, M. Six views of embodied cognition. *Psychonomic Bulletin & Review* **9**, 625-636, doi:10.3758/BF03196322 (2002).
- Slater, M. How Colorful Was Your Day? Why Questionnaires Cannot Assess Presence in Virtual Environments. *Presence* **13**, 484-493, doi:10.1162/1054746041944849 (2004).
- Nowak, K. L. & Biocca, F. The Effect of the Agency and Anthropomorphism on Users' Sense of Telepresence, Copresence, and Social Presence in Virtual Environments. *Presence: Teleoperators and Virtual Environments* **12**, 481-494, doi:10.1162/105474603322761289 (2003).
- Slater, M. & Wilbur, S. A Framework for Immersive Virtual Environments (FIVE): Speculations on the Role of Presence in Virtual Environments. *Presence: Teleoperators and Virtual Environments* **6**, 603-616, doi:10.1162/pres.1997.6.6.603 (1997).
- 92 34 Nunez, D. & Blake, E. in *Proceedings of the 1st international conference on Computer* 93 *graphics, virtual reality and visualisation* 115–118 (Association for Computing Machinery, 94 Camps Bay, Cape Town, South Africa, 2001).
- Tamborini, R. & Skalski, P. The role of presence in the experience of electronic games. Playing video games: Motives, responses, and consequences 1, 225-240 (2006).
- 97 36 Grassini, S. & Laumann, K. Questionnaire Measures and Physiological Correlates of Presence: 98 A Systematic Review. *Front Psychol* **11**, 349, doi:10.3389/fpsyg.2020.00349 (2020).

- Cummings, J. J. & Bailenson, J. N. How Immersive Is Enough? A Meta-Analysis of the Effect of Immersive Technology on User Presence. *Media Psychology* **19**, 272-309, doi:10.1080/15213269.2015.1015740 (2016).
- Botella, C. *et al.* Virtual reality and psychotherapy. *Stud Health Technol Inform* **99**, 37-54 (2004).
- Riva, G. & Mantovani, F. Being there: understanding the feeling of presence in a synthetic environment and its potential for clinical change. *Virtual reality in psychological, medical and pedagogical applications*, 3-34 (2012).
- Riva, G. *et al.* Affective interactions using virtual reality: the link between presence and emotions. *Cyberpsychol Behav* **10**, 45-56, doi:10.1089/cpb.2006.9993 (2007).
- Ling, Y., Nefs, H. T., Morina, N., Heynderickx, I. & Brinkman, W. P. A meta-analysis on the relationship between self-reported presence and anxiety in virtual reality exposure therapy for anxiety disorders. *PLoS One* **9**, e96144, doi:10.1371/journal.pone.0096144 (2014).
- Schroder, D. *et al.* Impact of virtual reality applications in the treatment of anxiety disorders:
 A systematic review and meta-analysis of randomized-controlled trials. *J Behav Ther Exp*Psychiatry **81**, 101893, doi:10.1016/j.jbtep.2023.101893 (2023).
- Whiteford, H. A. *et al.* Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *Lancet* **382**, 1575-1586, doi:10.1016/s0140-6736(13)61611-6 (2013).
- Morina, N., Ijntema, H., Meyerbröker, K. & Emmelkamp, P. M. G. Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments. *Behaviour Research and Therapy* **74**, 18-24, doi:10.1016/j.brat.2015.08.010 (2015).
- Valmaggia, L. R., Latif, L., Kempton, M. J. & Rus-Calafell, M. Virtual reality in the psychological treatment for mental health problems: An systematic review of recent evidence. *Psychiatry Res* **236**, 189-195, doi:10.1016/j.psychres.2016.01.015 (2016).
- Freitas, J. R. S. *et al.* Virtual Reality Exposure Treatment in Phobias: a Systematic Review. *Psychiatr Q* **92**, 1685-1710, doi:10.1007/s11126-021-09935-6 (2021).
- Kothgassner, O. D. & Felnhofer, A. Lack of research on efficacy of virtual reality exposure therapy (VRET) for anxiety disorders in children and adolescents: A systematic review.

 Neuropsychiatr 35, 68-75, doi:10.1007/s40211-020-00349-7 (2021).
- van Bennekom, M. J., de Koning, P. P. & Denys, D. Virtual Reality Objectifies the Diagnosis of Psychiatric Disorders: A Literature Review. *Frontiers in Psychiatry* **8**, doi:10.3389/fpsyt.2017.00163 (2017).
- Geraets, C. N. W., van der Stouwe, E. C. D., Pot-Kolder, R. & Veling, W. Advances in immersive virtual reality interventions for mental disorders a new reality? *Current Opinion in Psychology*, doi:10.1016/j.copsyc.2021.02.004 (2021).
- Pot-Kolder, R. M. C. A. *et al.* Cost-Effectiveness of Virtual Reality Cognitive Behavioral Therapy for Psychosis: Health-Economic Evaluation Within a Randomized Controlled Trial. *J Med Internet Res* **22**, e17098, doi:10.2196/17098 (2020).
- Freeman, D. *et al.* Virtual reality in the treatment of persecutory delusions: randomised controlled experimental study testing how to reduce delusional conviction. *Br J Psychiatry* **209**, 62-67, doi:10.1192/bjp.bp.115.176438 (2016).
- Pot-Kolder, R. *et al.* Virtual-reality-based cognitive behavioural therapy versus waiting list control for paranoid ideation and social avoidance in patients with psychotic disorders: a single-blind randomised controlled trial. *Lancet Psychiatry* **5**, 217-226, doi:10.1016/S2215-0366(18)30053-1 (2018).
- Rus-Calafell, M. & Schneider, S. Are we there yet?!-a literature review of recent digital technology advances for the treatment of early psychosis. *Mhealth* **6**, 3, doi:10.21037/mhealth.2019.09.14 (2020).

- Ward, T. *et al.* AVATAR therapy for distressing voices: A comprehensive account of therapeutic targets. *Schizophrenia Bulletin* **46**, 1038-1044, doi:https://doi.org/10.1093/schbul/sbaa061 (2020).
- Leff, J., Williams, G., Huckvale, M. A., Arbuthnot, M. & Leff, A. P. Computer-assisted therapy for medication-resistant auditory hallucinations: proof-of-concept study. *Br J Psychiatry* **202**, 428-433, doi:10.1192/bjp.bp.112.124883 (2013).
- Craig, T. K. *et al.* AVATAR therapy for auditory verbal hallucinations in people with psychosis: a single-blind, randomised controlled trial. *The Lancet Psychiatry* **5**, 31-40, doi:https://doi.org/10.1016/S2215-0366(17)30427-3 (2018).
- Rus-Calafell, M. *et al.* The Role of Sense of Voice Presence and Anxiety Reduction in AVATAR Therapy. *Journal of Clinical Medicine* **9**, 2748 (2020).
- Dellazizzo, L., Potvin, S., Phraxayavong, K. & Dumais, A. One-year randomized trial comparing virtual reality-assisted therapy to cognitive—behavioral therapy for patients with treatment-resistant schizophrenia. *npj Schizophrenia* **7**, 1-11 (2021).
- Du Sert, O. P. *et al.* Virtual reality therapy for refractory auditory verbal hallucinations in schizophrenia: a pilot clinical trial. *Schizophrenia research* **197**, 176-181 (2018).

- Smith, L. *et al.* The CHALLENGE-trial: the effects of a virtual reality-assisted exposure therapy for persistent auditory hallucinations versus supportive counselling in people with psychosis: study protocol for a randomised clinical trial. (2022).
 - Garety, P. A. *et al.* Optimising AVATAR therapy for distressing voices: Study protocol for the AVATAR2 multi-centre randomised controlled trial. *Trials* (2021).
- Foa, E. B. Prolonged exposure therapy: Past, present, and future. *Depression and Anxiety* **28**, 1043-1047, doi:10.1002/da.20907 (2011).
- Rizzo, A. S. & Shilling, R. Clinical Virtual Reality tools to advance the prevention, assessment, and treatment of PTSD. *European Journal of Psychotraumatology* **8**, 1414560, doi:10.1080/20008198.2017.1414560 (2017).
- Beidel, D. C. *et al.* Trauma management therapy with virtual-reality augmented exposure therapy for combat-related PTSD: A randomized controlled trial. *J Anxiety Disord* **61**, 64-74, doi:10.1016/j.janxdis.2017.08.005 (2019).
- Beidel, D. C., Frueh, B. C., Neer, S. M. & Lejuez, C. W. The efficacy of Trauma Management
 Therapy: A controlled pilot investigation of a three-week intensive outpatient program for
 combat-related PTSD. *Journal of Anxiety Disorders* **50**, 23-32,
 doi:https://doi.org/10.1016/j.janxdis.2017.05.001 (2017).
- Botella, C., Serrano, B., Baños, R. M. & Garcia-Palacios, A. Virtual reality exposure-based therapy for the treatment of post-traumatic stress disorder: a review of its efficacy, the adequacy of the treatment protocol, and its acceptability. *Neuropsychiatric Disease and Treatment* 11, 2533-2545, doi:10.2147/NDT.S89542 (2015).
- Difede, J. *et al.* A randomized controlled clinical treatment trial for World Trade Center attack-related PTSD in disaster workers. *J Nerv Ment Dis* **195**, 861-865, doi:10.1097/NMD.0b013e3181568612 (2007).
- Difede, J. *et al.* D-Cycloserine Augmentation of Exposure Therapy for Post-Traumatic Stress
 Disorder: A Pilot Randomized Clinical Trial. *Neuropsychopharmacology* **39**, 1052-1058,
 doi:10.1038/npp.2013.317 (2014).
- Peskin, M. *et al.* The relationship between posttraumatic and depressive symptoms during virtual reality exposure therapy with a cognitive enhancer. *J Anxiety Disord* **61**, 82-88, doi:10.1016/j.janxdis.2018.03.001 (2019).
- Difede, J. et al. Enhancing exposure therapy for posttraumatic stress disorder (PTSD): a randomized clinical trial of virtual reality and imaginal exposure with a cognitive enhancer.

 Translational Psychiatry 12, 299, doi:10.1038/s41398-022-02066-x (2022).

- Loucks, L. *et al.* You can do that?!: Feasibility of virtual reality exposure therapy in the treatment of PTSD due to military sexual trauma. *J Anxiety Disord* **61**, 55-63, doi:10.1016/j.janxdis.2018.06.004 (2019).
- Maples-Keller, J. L., Yasinski, C., Manjin, N. & Rothbaum, B. O. Virtual Reality-Enhanced Extinction of Phobias and Post-Traumatic Stress. *Neurotherapeutics* **14**, 554-563, doi:10.1007/s13311-017-0534-y (2017).
- 204 73 Reger, G. M. *et al.* Does virtual reality increase emotional engagement during exposure for 205 PTSD? Subjective distress during prolonged and virtual reality exposure therapy. *J Anxiety Disord* **61**, 75-81, doi:10.1016/j.janxdis.2018.06.001 (2019).
- Rizzo, A. S. *et al.* Development and early evaluation of the Virtual Iraq/Afghanistan exposure therapy system for combat-related PTSD. *Annals of the New York Academy of Sciences* **1208**, 114-125, doi:https://doi.org/10.1111/j.1749-6632.2010.05755.x (2010).
- Rizzo, A. *et al.* Virtual Reality as a Tool for Delivering PTSD Exposure Therapy and Stress
 Resilience Training. *Military Behavioral Health* **1**, 52-58, doi:10.1080/21635781.2012.721064
 (2013).
- Norr, A. M. *et al.* Virtual reality exposure versus prolonged exposure for PTSD: Which treatment for whom? *Depression and Anxiety* **35**, 523-529, doi:https://doi.org/10.1002/da.22751 (2018).
- Rothbaum, B. O. *et al.* Virtual reality exposure therapy for PTSD Vietnam veterans: A case study. *Journal of Traumatic Stress* **12**, 263-271, doi:https://doi.org/10.1023/A:1024772308758 (1999).
- Rothbaum, B. O., Hodges, L. F., Ready, D., Graap, K. & Alarcon, R. D. Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. *Journal of Clinical psychiatry* **62**, 617-622 (2001).
- Rothbaum, B. *et al.* Early Intervention Following Trauma May Mitigate Genetic Risk for PTSD in Civilians. *The Journal of clinical psychiatry* **75**, doi:10.4088/JCP.13m08715 (2014).
- 224 80 Carl, E. *et al.* Virtual reality exposure therapy for anxiety and related disorders: A meta-225 analysis of randomized controlled trials. *J Anxiety Disord* **61**, 27-36, 226 doi:10.1016/j.janxdis.2018.08.003 (2019).
- Roy, M. J., Costanzo, M. E., Blair, J. R. & Rizzo, A. A. Compelling evidence that exposure therapy for PTSD normalizes brain function. *Studies in Health Technology and Informatics* **199**, 61-65 (2014).
- McLay, R. N. *et al.* A randomized, controlled trial of virtual reality-graded exposure therapy for post-traumatic stress disorder in active duty service members with combat-related post-traumatic stress disorder. *Cyberpsychology, behavior, and social networking* **14**, 223-229 (2011).
- Reger, G. M. *et al.* Randomized controlled trial of prolonged exposure using imaginal exposure vs. virtual reality exposure in active duty soldiers with deployment-related posttraumatic stress disorder (PTSD). *Journal of Consulting and Clinical Psychology* **84**, 946-959, doi:10.1037/ccp0000134 (2016).
- Difede, J. & Hoffman, H. G. Virtual reality exposure therapy for World Trade Center posttraumatic stress disorder: A case report. *Cyberpsychology & behavior* **5**, 529-535 (2002).
- Monteleone, A. M. *et al.* Treatment of eating disorders: A systematic meta-review of metaanalyses and network meta-analyses. *Neurosci Biobehav Rev* **142**, 104857, doi:10.1016/j.neubiorev.2022.104857 (2022).
- Butler, R. M. & Heimberg, R. G. Exposure therapy for eating disorders: A systematic review.
 Clin Psychol Rev 78, 101851, doi:10.1016/j.cpr.2020.101851 (2020).
- 245 87 Riva, G., Malighetti, C. & Serino, S. Virtual reality in the treatment of eating disorders. *Clin Psychol Psychother* **28**, 477-488, doi:10.1002/cpp.2622 (2021).

- Low, T. L., Ho, R., Ho, C. & Tam, W. The efficacy of virtual reality in the treatment of bingepurging eating disorders: A meta-analysis. *Eur Eat Disord Rev* **29**, 52-59, doi:10.1002/erv.2804 (2021).
- 250 89 Cardi, V. *et al.* The use of a nonimmersive virtual reality programme in anorexia nervosa: a single case-report. *Eur Eat Disord Rev* **20**, 240-245, doi:10.1002/erv.1155 (2012).
- 252 90 Cardi, V. *et al.* Transition Care in Anorexia Nervosa Through Guidance Online from Peer and
 253 Carer Expertise (TRIANGLE): Study Protocol for a Randomised Controlled Trial. *Eur Eat Disord*254 *Rev* **25**, 512-523, doi:10.1002/erv.2542 (2017).
- 255 91 Riches, S. *et al.* Virtual reality relaxation for people with mental health conditions: a 256 systematic review. *Social Psychiatry and Psychiatric Epidemiology* **58**, 989-1007, 257 doi:10.1007/s00127-022-02417-5 (2023).
- Mistry, D. *et al.* Meditating in virtual reality: Proof-of-concept intervention for posttraumatic stress. *Psychological Trauma: Theory, Research, Practice, and Policy* **12**, 847 (2020).
- Wang, T. C., Tsai, C. L., Tang, T. W., Wang, W. L. & Lee, K. T. The Effect of Cycling Through a Projection-Based Virtual Environment System on Generalized Anxiety Disorder. *J Clin Med* 8, doi:10.3390/jcm8070973 (2019).
- Manzoni, G. M. *et al.* New technologies and relaxation: an explorative study on obese patients with emotional eating. *Journal of CyberTherapy and Rehabilitation* **1**, 182-192, doi:10.26481/dis.20100922ag (2008).
- Mark, I., Bell, D., Kirsh, L. & O'Brien, A. The use of virtual reality in a psychiatric intensive care unit: a pilot study. *Journal of Psychiatric Intensive Care* **17**, 123-128, doi:10.20299/jpi.2021.008 (2021).
- Tan, H. L. E., Chng, C. M. L., Lau, Y. & Klainin-Yobas, P. Investigating the effects of a virtual reality-based stress management programme on inpatients with mental disorders: A pilot randomised controlled trial. *International Journal of Psychology* **56**, 444-453 (2021).
- Veling, W., Lestestuiver, B., Jongma, M., Hoenders, H. J. R. & van Driel, C. Virtual Reality
 Relaxation for Patients With a Psychiatric Disorder: Crossover Randomized Controlled Trial. J
 Med Internet Res 23, e17233, doi:10.2196/17233 (2021).
- 275 98 Riches, S. *et al.* Integrating a virtual reality relaxation clinic within acute psychiatric services: A pilot study. *Psychiatry Res* **329**, 115477, doi:10.1016/j.psychres.2023.115477 (2023).
- Bossenbroek, R. *et al.* Efficacy of a Virtual Reality Biofeedback Game (DEEP) to Reduce
 Anxiety and Disruptive Classroom Behavior: Single-Case Study. *JMIR Ment Health* **7**, e16066, doi:10.2196/16066 (2020).
- 280 100 Li, H. *et al.* Access to Nature via Virtual Reality: A Mini-Review. *Front Psychol* **12**, 725288, doi:10.3389/fpsyg.2021.725288 (2021).
- Riches, S., Azevedo, L., Bird, L., Pisani, S. & Valmaggia, L. Virtual reality relaxation for the general population: a systematic review. *Social Psychiatry and Psychiatric Epidemiology*, doi:10.1007/s00127-021-02110-z (2021).
- Nijland, J., Veling, W., Lestestuiver, B. P. & Van Driel, C. M. G. Virtual Reality Relaxation for Reducing Perceived Stress of Intensive Care Nurses During the COVID-19 Pandemic. *Front* Psychol 12, 706527, doi:10.3389/fpsyg.2021.706527 (2021).
- 288 103 Williams, G. & Riches, S. Virtual Reality Relaxation for Staff Wellbeing on a Psychiatric
 289 Rehabilitation Ward: A Feasibility and Acceptability Study. *Journal of Psychiatric Intensive*290 *Care* 19, 51-58, doi:10.20299/jpi.2023.006 (2023).
- Donker, T. *et al.* Effectiveness of Self-guided App-Based Virtual Reality Cognitive Behavior Therapy for Acrophobia: A Randomized Clinical Trial. *JAMA Psychiatry* **76**, 682-690, doi:10.1001/jamapsychiatry.2019.0219 (2019).
- Freeman, D. *et al.* Automated psychological therapy using immersive virtual reality for treatment of fear of heights: a single-blind, parallel-group, randomised controlled trial. *The Lancet Psychiatry* **5**, 625-632, doi:10.1016/s2215-0366(18)30226-8 (2018).

- Lindner, P. *et al.* Therapist-led and self-led one-session virtual reality exposure therapy for public speaking anxiety with consumer hardware and software: A randomized controlled trial. *J Anxiety Disord* **61**, 45-54, doi:10.1016/j.janxdis.2018.07.003 (2019).
- Lindner, P. *et al.* Gamified, Automated Virtual Reality Exposure Therapy for Fear of Spiders:
 A Single-Subject Trial Under Simulated Real-World Conditions. *Front Psychiatry* **11**, 116,
 doi:10.3389/fpsyt.2020.00116 (2020).
- Treeman, D. et al. Automated virtual reality therapy to treat agoraphobic avoidance and distress in patients with psychosis (gameChange): a multicentre, parallel-group, single-blind, randomised, controlled trial in England with mediation and moderation analyses. Lancet Psychiatry 9, 375-388, doi:10.1016/S2215-0366(22)00060-8 (2022).
- Freeman, D. *et al.* Automated virtual reality cognitive therapy versus virtual reality mental relaxation therapy for the treatment of persistent persecutory delusions in patients with psychosis (THRIVE): a parallel-group, single-blind, randomised controlled trial in England with mediation analyses. *Lancet Psychiatry*, doi:10.1016/S2215-0366(23)00257-2 (2023).
- van der Gaag, M., Valmaggia, L. R. & Smit, F. The effects of individually tailored formulationbased cognitive behavioural therapy in auditory hallucinations and delusions: a metaanalysis. *Schizophr Res* **156**, 30-37, doi:10.1016/j.schres.2014.03.016 (2014).
- Higgins, O., Short, B. L., Chalup, S. K. & Wilson, R. L. Artificial intelligence (AI) and machine learning (ML) based decision support systems in mental health: An integrative review. *Int J Ment Health Nurs*, doi:10.1111/inm.13114 (2023).
- Lim, J. Z., Mountstephens, J. & Teo, J. Emotion recognition using eye-tracking: taxonomy, review and current challenges. *Sensors* **20**, 2384 (2020).
- Shu, L. *et al.* Wearable emotion recognition using heart rate data from a smart bracelet. *Sensors* **20**, 718 (2020).
- Fei, Z. *et al.* Deep convolution network based emotion analysis towards mental health care.

 Neurocomputing **388**, 212-227 (2020).
- Kothgassner, O. D. *et al.* Virtual reality biofeedback interventions for treating anxiety: A systematic review, meta-analysis and future perspective. *Wiener klinische Wochenschrift*, 1-11 (2022).
- Weerdmeester, J., van Rooij, M. M., Maciejewski, D. F., Engels, R. C. & Granic, I. A randomized controlled trial assessing the efficacy of a virtual reality biofeedback video game: anxiety outcomes and appraisal processes. (2021).
- 117 Dzafic, I. et al. in IEPA 2023 Conference (Lausanne, Switserland 2023).
- Fleming, T. M. *et al.* Serious games and gamification for mental health: current status and promising directions. *Frontiers in psychiatry* **7**, 215 (2017).
- Fleming, T., Poppelaars, M. & Thabrew, H. The role of gamification in digital mental health.

 World Psychiatry 22, 46 (2023).
- Fleming, T., Lucassen, M., Stasiak, K., Sutcliffe, K. & Merry, S. Technology Matters: SPARX—computerised cognitive behavioural therapy for adolescent depression in a game format.

 Child and Adolescent Mental Health 26, 92-94 (2021).
- Merry, S. N. *et al.* The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *Bmj* **344** (2012).
- Thunström, A. O., Sarajlic Vukovic, I., Ali, L., Larson, T. & Steingrimsson, S. Prevalence of virtual reality (VR) games found through mental health categories on STEAM: a first look at VR on commercial platforms as tools for therapy. *Nordic Journal of Psychiatry* **76**, 474-485 (2022).
- Sutherland, I. E. A head-mounted three dimensional display. *Proceedings of AFIPS* **68**, 757–764 (1968).
- Manjrekar, S. et al. in 2014 UKSim-AMSS 16th International Conference on Computer Modelling and Simulation 131-136 (2014).

- Rothbaum, B. O. *et al.* Effectiveness of computer-generated (virtual reality) graded exposure in the treatment of acrophobia. *Am J Psychiatry* **152**, 626-628, doi:10.1176/ajp.152.4.626 (1995).
- Larsen, M. E. *et al.* Using science to sell apps: Evaluation of mental health app store quality claims. *NPJ Digit Med* **2**, 18, doi:10.1038/s41746-019-0093-1 (2019).
- Gooding, P. Mapping the rise of digital mental health technologies: Emerging issues for law and society. *International journal of law and psychiatry* **67**, 101498 (2019).
- Torous, J. & Roberts, L. W. The ethical use of mobile health technology in clinical psychiatry.

 The Journal of nervous and mental disease 205, 4-8 (2017).
- Wies, B., Landers, C. & Ienca, M. Digital mental health for young people: a scoping review of ethical promises and challenges. *Frontiers in digital health* **3**, 697072 (2021).
- Wykes, T., Lipshitz, J. & Schueller, S. M. Towards the design of ethical standards related to digital mental health and all its applications. *Current Treatment Options in Psychiatry* **6**, 232-242 (2019).
- Lundin, R. M., Yeap, Y. & Menkes, D. B. Adverse Effects of Virtual and Augmented Reality Interventions in Psychiatry: Systematic Review. *JMIR Mental Health* **10**, e43240 (2023).
- van Heugten-van der Kloet, D., Cosgrave, J., van Rheede, J. & Hicks, S. Out-of-body experience in virtual reality induces acute dissociation. *Psychology of Consciousness: Theory, Research, and Practice* **5**, 346 (2018).
- Mohr, D. C., Lyon, A. R., Lattie, E. G., Reddy, M. & Schueller, S. M. Accelerating Digital Mental Health Research From Early Design and Creation to Successful Implementation and Sustainment. *J Med Internet Res* **19**, e153, doi:10.2196/jmir.7725 (2017).
- Mohr, D. C., Riper, H. & Schueller, S. M. A Solution-Focused Research Approach to Achieve an Implementable Revolution in Digital Mental Health. *JAMA Psychiatry* **75**, 113-114, doi:10.1001/jamapsychiatry.2017.3838 (2018).
- Greenhalgh, T. *et al.* Beyond adoption: a new framework for theorizing and evaluating nonadoption, abandonment, and challenges to the scale-up, spread, and sustainability of health and care technologies. *Journal of medical Internet research* **19**, e8775 (2017).
- Graham, A. K. *et al.* Implementation strategies for digital mental health interventions in health care settings. *Am Psychol* **75**, 1080-1092, doi:10.1037/amp0000686 (2020).
- Lindner, P. *et al.* Attitudes toward and familiarity with virtual reality therapy among practicing cognitive behavior therapists: a cross-sectional survey study in the era of consumer VR platforms. *Frontiers in psychology* **10**, 176 (2019).

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Vlake, J. H. *et al.* Reporting the early stage clinical evaluation of virtual-reality-based intervention trials: RATE-VR. *Nat Med* **29**, 12-13, doi:10.1038/s41591-022-02085-7 (2023).