NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

EARLY VALUE ASSESSMENT PROGRAMME

Early value assessment guidance consultation document

Virtual reality technologies for treating agoraphobia and agoraphobic avoidance: early value assessment

Guidance development process

Early value assessment (EVA) guidance rapidly provides recommendations on promising health technologies that have the potential to address national unmet need. NICE has assessed early evidence on these technologies to determine if earlier patient and system access in the NHS is appropriate while further evidence is generated.

The medical technologies advisory committee has considered the evidence and the views of clinical and patient experts.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered and sets out the recommendations made by the committee. NICE invites comments from registered stakeholders, healthcare professionals and the public. This document should be read along with the evidence (an EVA report and addendum).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Has all of the evidence on any population subgroups, such as more severe agoraphobia, been taken into account and reasonably interpreted?

- Are the recommendations sound, and a suitable basis for guidance to the NHS?
- Has the unmet need been appropriately considered, including any additional needs for specific subgroups?

Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the recommendations may need changing to meet these aims. In particular, please tell us if the recommendations:

- could have a different effect on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology
- could have any adverse effect on people with a particular disability or disabilities.

Please provide any relevant information or data you have about such effects and how they could be avoided or reduced.

Note that this document is not NICE's final guidance on virtual reality technologies for treating agoraphobia and agoraphobic avoidance. The recommendations in section 1 may change after consultation.

After consultation, NICE will consider the comments received. The final recommendations will be the basis for NICE's early value guidance.

Key dates:

Closing date for comments: 19 July 2023

1 Recommendations

1.1 There is not enough evidence to recommend virtual reality (VR) technologies for early routine use in the NHS. The following technologies should only be used in research for people aged 16 and over, once they have appropriate regulatory approval:

- Amelia Virtual Care for agoraphobia and agoraphobic avoidance
- gameChangeVR for agoraphobic avoidance in psychosis
- XR Therapeutics for agoraphobia and agoraphobic avoidance.

1.2 Further research is recommended on:

- clinical effectiveness including what the long-term benefits are, and how well and long they last
- rates of relapse, including use and effectiveness of top-up sessions and repeat VR therapy
- patient selection, including who may benefit most from using VR technologies
- health-related quality of life
- adverse effects
- resource use during and after treatment, including maintenance and lifespan of the hardware, and healthcare professional grade and time needed to deliver treatment or support.

Key gaps in the evidence:

- VR technologies show promise in improving access to care for people who would not otherwise access treatment. But the evidence on VR technologies is limited. There are 2 clinical trials comparing Amelia Virtual Care and gameChangeVR, both with standard care, with standard care alone. These suggest some benefit with virtual reality to treat agoraphobia and agoraphobic avoidance. But it is not clear whether these benefits are because of the VR technology or the standard care used. Additional analysis of the gameChangeVR trial suggests that it only has potential benefits for people with psychosis and more severe agoraphobia. But this needs confirming.

- There is some evidence that people like VR technologies and may be less likely to stop treatment with them than medications or face-to-face therapy alone. But it is unclear whether this is because of better treatment adherence or more initial interest in using VR technologies.

- The cost effectiveness of VR technologies is inconclusive because the clinical evidence is limited and uncertain compared with current pricing of the technologies. Cost modelling suggests that VR technologies are unlikely to be cost effective for treating agoraphobia and agoraphobic avoidance, but gameChangeVR may be cost effective in people with psychosis and more severe agoraphobia.

Overall, more evidence is needed on:

- the benefits of VR technologies, including benefits in more severe agoraphobia and agoraphobic avoidance
- whether people are more likely to continue treatment with virtual reality
- how using VR technologies may affect clinical and system outcomes.

2 The technologies

2.1 Virtual reality is a simulated environment with scenes and objects that people can explore while wearing a headset or viewing a screen. This creates an immersive experience that can trigger emotional responses like those in real-world situations. Virtual reality may be used as a tool in therapy sessions or as a standalone intervention with the support of a mental health professional. It can help deliver techniques such as exposure therapy by allowing people to immerse themselves in real-world situations while being in the safety of their home or clinic. Virtual environments can be adjusted based on a person's needs and individual treatment plan. This could allow more gradual exposure to stressful situations and increased comfort in completing interventions.

2.2 NICE has assessed 3 virtual reality (VR) technologies for treating agoraphobia and agoraphobic avoidance. The criteria for including technologies in this assessment are in the topic scope on the NICE website. The technologies are:

- Amelia Virtual Care (Amelia Virtual Care) for treating mental health conditions including agoraphobia. It is a software-only VR platform delivered using a VR headset. It is designed to be used by therapists as a tool to support treatment in clinics or at home.
- gameChangeVR (Oxford VR) for treating agoraphobic avoidance in people with schizophrenia spectrum disorders or affective disorders with psychotic symptoms. It is a software-only VR therapy delivered using a VR headset. The intervention is delivered by an automated virtual therapist and is supported by a mental health professional.
- XR Therapeutics (XR Therapeutics) for treating anxiety disorders including agoraphobia. It uses a fully immersive screen-based VR studio and is delivered in person by a therapist in combination with therapy.

During scoping, NICE also identified Invirto (Invirto) for treating anxiety disorders including agoraphobia. The company did not respond to requests for information and no evidence was identified. So, this technology was not assessed and was excluded from recommendations.

Care pathway

2.3 NICE's guideline on common mental health problems recommends a stepped-care approach for treating agoraphobia with any underlying panic disorder. The first step involves recognition and diagnosis, including identifying any comorbidities. This is used to develop a treatment plan that may involve lifestyle changes and unguided or guided self-help. If needed or preferred, more intensive treatments should be offered. NICE's guideline on generalised anxiety disorder and panic disorder in adults recommends that people with moderate to severe panic disorder with or without agoraphobia should be offered cognitive behavioural therapy (CBT) or an antidepressant. Antidepressants may be offered if the disorder is long-standing or if the person has not benefited from or has declined psychological intervention.

2.4 People with psychosis who have agoraphobia or agoraphobic avoidance should also be offered treatment in line with their treatment plan. NICE's guideline on psychosis and schizophrenia in adults recommends that people with psychosis are offered oral antipsychotic medication and psychological interventions including family intervention and individual CBT. Clinical experts advised that access to CBT is limited, so people are more likely to be offered antipsychotic medication with simple contact and monitoring from their mental health service.

2.5 Agoraphobia may further impact a person's ability to access mental health services and support. Clinical and patient experts advised that agoraphobia is often untreated or undertreated especially when it occurs

with other mental health conditions. Some people with agoraphobia or agoraphobic avoidance may also stop treatment because of difficulty tolerating techniques such as exposure therapy. VR technologies may increase access to care by offering another treatment option for agoraphobia and agoraphobic avoidance. It would be used as an alternative or addition to standard care. It is not intended to replace treatment for comorbid mental health conditions.

The comparator

2.6 The comparator is standard care for agoraphobia or agoraphobic avoidance. This may vary depending on a person's individual needs and preferences and may include guided self-help, CBT with exposure therapy, applied relaxation, antidepressants or simple contact and monitoring with mental health services.

3 Committee discussion

NICE's medical technologies advisory committee considered evidence on virtual reality (VR) technologies for treating agoraphobia and agoraphobic avoidance in people aged 16 and over from several sources, including an early value assessment (EVA) report by the external assessment group (EAG), and an overview of that report. Full details are in the project documents for this guidance on the NICE website.

Unmet need and patient considerations

3.1 Mental health services are in high demand and access varies widely across the NHS. Because of this high demand, many people are not getting the treatment and support they need. Clinical and patient experts advised that people with agoraphobia and agoraphobic avoidance may have even greater difficulty accessing treatment. Some people may have had negative previous experiences of healthcare services, which may affect their willingness and ability to seek treatment when needed. Some VR technologies can be delivered remotely, which would allow some

people to get help in their homes. People may be more comfortable and willing to engage with VR therapy rather than attending face-to-face treatment in a clinic. The clinical experts considered this could be a first step to getting further help and accessing other healthcare services in the future if needed.

3.2 One clinical expert recalled the challenges of treating agoraphobia in Improving Access to Psychological Therapies services (now named NHS Talking Therapies for anxiety and depression) because some people did not come to sessions. They considered it may be more helpful to offer VR therapy in both primary and secondary care to increase access to treatment both in clinics and people's homes.

Potential benefits of the technologies

New treatment option for agoraphobia

3.3 VR technologies may offer a new treatment option that allows people with agoraphobia or agoraphobic avoidance to safely encounter threatening situations and challenge their fear response. Clinical experts believed this offers a different way of delivering treatment and support, which has the potential for quick impact. The clinical and patient experts considered that VR technologies may help some people reduce their symptoms of agoraphobia. This could have wider benefits on their social engagement, daily living and overall wellbeing. Benefits in reducing anxiety and paranoia could help people leave their homes to go to work, or access education and other healthcare services. This could have a positive knock-on effect on people's lives. For example, it could improve their quality of life. But the clinical and patient experts advised that this benefit may not be fully captured using standard health-related quality-of-life measures.

Acceptability and reduced rates of stopping treatment

3.4 Clinical and patient experts said that there is high interest and acceptability of VR technologies for treating agoraphobia and agoraphobic avoidance. A patient expert advised that people seemed to prefer virtual reality to medication because medicines often have side effects. Virtual reality was particularly acceptable to people with more severe agoraphobia. It may offer another treatment option for people on waiting lists or who cannot have or do not want treatment with medicines.

Clinical effectiveness

Limited evidence

3.5 The committee considered that there was limited evidence supporting the clinical effectiveness of VR technologies for treating agoraphobia and agoraphobic avoidance. The relevant evidence consisted of 5 studies reported in 10 publications, specifically 2 randomised controlled trials (for Amelia Virtual Care and gameChangeVR), 2 non-comparative studies (for Amelia Virtual Care and XR Therapeutics) and 1 design process study (for gameChangeVR). The EAG reported that there was some evidence of potential benefits for agoraphobia symptoms for Amelia Virtual Care and gameChangeVR. But there were considerable uncertainties about the interpretation and reliability of these findings.

Uncertainty of clinical effects

3.6 The committee considered that it was unclear whether the effects reported in the clinical trials were because of VR technologies or standard care. The clinical trials compared the use of virtual reality plus standard care with standard care alone. Castro et al. (2014) showed that Amelia Virtual Care with cognitive behavioural therapy (CBT) plus antidepressants and CBT plus antidepressants were both more effective than antidepressants alone. There was no statistically significant difference between CBT plus antidepressants with or without Amelia Virtual Care. So, the EAG advised

that it was uncertain whether the benefits were driven primarily or exclusively by CBT. For gameChangeVR, the randomised controlled trial (Freeman et al. 2022) showed that gameChangeVR plus usual care was more effective than usual care alone in reducing agoraphobic avoidance and distress at 6 weeks. But there were no statistically significant differences in the primary outcomes between groups at the 6-month follow-up. There was also no statistically significant difference in quality of life or other psychological symptoms except perceived recovery at 6 weeks. Post-hoc analysis showed that treatment benefits were only seen in people with high and severe agoraphobia at baseline with these benefits maintained at 6 months. Details of these findings can be found in the assessment report and assessment report overview on the NICE website. The committee considered that gameChangeVR had potential benefit in people with high and severe agoraphobia, but more research is needed to confirm this. More evidence is also needed on the long-term effects of VR therapies because the durability of their effects is unknown.

3.7 The evidence on XR Therapeutics was limited to autistic people with fears and phobias but there was no evidence in agoraphobia. The relevant evidence (Maskey et al. 2019) showed equivocal improvement in target behaviour in people with fears and phobias that may be relevant to agoraphobia. The committee concluded that evidence is needed in people aged 16 and over with agoraphobia or agoraphobic avoidance.

Adherence and stopping treatment

3.8 The evidence showed high satisfaction and completion of VR therapy for all technologies. Castro et al. (2014) reported that statistically fewer people stop treatment when using Amelia Virtual Care with CBT plus antidepressants than with CBT plus antidepressants or antidepressants alone. The EAG noted that these differences were seen before exposure sessions had begun. So, it was unclear whether Amelia Virtual Care had better treatment adherence than standard care alone or whether people

were just more interested in using virtual reality. The committee concluded that more evidence is needed on the benefit of VR technologies in improving treatment adherence and completion and the effect of this on clinical outcomes. See the assessment report on the NICE website for further details on the clinical effectiveness of the VR technologies.

Costs and resource use

3.9 Base-case results from the exploratory decision analytical model showed that on average Amelia Virtual Care and gameChangeVR were not cost effective from an NHS and Personal Social Services (PSS) perspective. This was using the conventional range of willingness to pay (£20,000 to £30,000 per quality-adjusted life year [QALY] gained). The EAG advised that there was substantial decision uncertainty in the modelling. It suggested gameChangeVR had around 26% (at £20,000 per QALY gained) and 31% (at £30,000 per QALY gained) probability of being cost effective from an NHS and PSS perspective. Modelling suggested Amelia Virtual Care had around 41% probability of being cost effective at both ends of the range from an NHS and PSS perspective. The incremental cost-effectiveness ratios could not be reported here because the prices of Amelia Virtual Care and gameChangeVR are considered commercial in confidence. It was not possible to model the cost effectiveness of XR Therapeutics because it did not have evidence in agoraphobia. See the assessment report on the NICE website for a detailed description of the model.

3.10 The EAG's model included incremental utility, relapse rates and costs to deliver virtual reality plus standard care compared with standard care alone. Costs included licence fees, costs of the VR headset, healthcare professional costs based on staff grade and time, and other health service use costs. The assumptions used in the model are outlined in section 10.3.4 of the assessment report on the NICE website. The EAG noted that the main drivers of the model were incremental utility, licence fees,

relapse rates and effectiveness of subsequent VR therapy. Sensitivity and scenario analyses suggested that Amelia Virtual Care plus standard care was unlikely to be cost effective compared with standard care alone. This was because of the lower utility of Amelia Virtual Care (indirectly estimated from data reported in the clinical trial). There were scenarios where gameChangeVR may be cost effective, particularly in scenarios with lower licence costs or in people with high and severe agoraphobia. The EAG advised that more evidence is needed to confirm these findings. The committee concluded that limitations and uncertainties in the clinical evidence created limitations and uncertainties in the economic model. Further research on clinical and cost effectiveness is needed.

Implementation

Healthcare professional resources

3.11 The committee considered that healthcare professional resources including staff grade and time would likely impact the cost effectiveness of VR technologies. Mental health professional grade and time needed to deliver or support the delivery of virtual reality varies across the technologies. Amelia Virtual Care and XR Therapeutics are designed to be used by therapists to support the delivery of CBT. gameChangeVR is delivered by an automated virtual therapist with the support of a mental health professional. One clinical expert advised that they had trained a range of staff from band 3 to band 5 to implement gameChangeVR with supervision provided within the clinical teams. Training was half a day and staff were said to have quickly acquired the skills needed for implementation.

Technical considerations

3.12 Clinical and patient experts advised on technical issues that should be considered when implementing VR technologies in the NHS. Some VR technologies need Wi-Fi to deliver the intervention or to upload

content. Two of the 3 VR technologies were software-only platforms that could be delivered using a range of commercially available VR headsets. The committee discussed that NHS services should consider how to maintain, recycle and responsibly dispose of broken headsets in order to minimise electronic waste and maximise potential cost effectiveness.

Use in the NHS

3.13 One clinical expert advised that while healthcare professionals were interested in using VR therapies, they were unsure how this would be rolled out in the NHS. There were uncertainties around how many sessions would be needed in clinical practice and whether people would need repeat sessions or top-up sessions. The clinical experts advised that clinical effectiveness would likely vary depending on how VR technologies were used. The committee considered that more evidence was needed on the use of VR technologies for treating agoraphobia and agoraphobic avoidance in different clinical settings.

3.14 The committee considered that it is important to identify who may benefit most from using VR technologies to treat agoraphobia or agoraphobic avoidance. The trial for gameChangeVR used a standardised measure for agoraphobic avoidance (Oxford Agoraphobic Avoidance Scale, O-AS) to measure symptoms and severity of agoraphobia. The clinical experts said that this could be used in clinical practice. But standard care in the NHS varies and specific measures for agoraphobia are not widely used. Healthcare professionals may instead develop treatment plans based on a person's presenting problem during clinical assessment rather than scores on a specific scale.

Managing risks

3.15 The committee carefully considered the safety of VR technologies for treating agoraphobia and agoraphobic avoidance. Evidence on adverse events was limited and included only 1 study on gameChangeVR

(Freeman et al. 2022). This showed no serious adverse effects related to the use of VR technologies for treating agoraphobia and agoraphobic avoidance. One clinical expert advised that their NHS trust used the safety data from the clinical trial to inform their use of gameChangeVR for psychosis with agoraphobic avoidance. There is interest in using gameChangeVR in agoraphobia without psychosis, but there is currently no evidence to support this use.

3.16 Clinical experts said that adverse effects were generally mild and transient. These included reports of dizziness, motion sickness and mild headaches. One clinical expert noted that VR technologies were used for a relatively short time of about 20 minutes. If someone felt unwell while using VR technologies, they could remove the headset or leave the immersive studio. A patient expert advised that some people may have difficulty transitioning from VR environments to the real-world. A clinical expert said that they had protocols for delivering VR therapy, which included grounding exercises to help people reorient after using VR technologies. VR technologies for treating agoraphobia and agoraphobic avoidance may not be suitable for everyone. Treatment options should be discussed by healthcare professionals, people with agoraphobia and agoraphobic avoidance and (when appropriate) carers. The discussion should consider clinical assessment, individual risk, personal preferences and needs, and the level of support needed.

Equality considerations

3.17 VR technologies may increase access to care for people who otherwise would not access treatment. Patient experts advised that there are limited treatment options for people with agoraphobia, particularly when presenting with co-occurring serious mental health problems like psychosis. They suggested that options for self-referral would further increase access to treatment for people who are less likely to engage with mental health services. The patient experts shared that some people from

some ethnic backgrounds may feel shame in accessing mental health services and may be more comfortable using VR technologies.

3.18 Additional support and resources may be needed for people who are unfamiliar with digital technologies or who do not have access to the internet. Additional support and resources may also be needed for people with visual or hearing impairments, cognitive impairment, problems with manual dexterity, a learning disability or who are unable to read or understand English. Some people would benefit from VR technologies in languages other than English. XR Therapeutics has adapted its intervention for autistic people and people with a learning disability. The company said its VR studio is also accessible for disabled people, including people using wheelchairs. The committee considered that other treatment options may be more appropriate for some people with agoraphobia.

Evidence gap overview

3.19 Evidence gaps were identified for all of the VR technologies. These are:

- Population: the relevant clinical evidence for XR Therapeutics included 2 people with phobias that the EAG considered to be relevant to agoraphobia. But there was no evidence in people aged 16 and over with agoraphobia. There was no UK evidence for Amelia Virtual Care which may limit generalisability of findings to the NHS. Post-hoc analysis on gameChangeVR suggested benefits in people with high and severe agoraphobia but primary evidence is needed to confirm this finding. More evidence on all technologies is needed to guide patient selection on who may benefit most from using VR technology for agoraphobia.
- Intervention: there is limited evidence for all of the technologies. There was no evidence on Invirto and no comparative evidence on

XR Therapeutics. There were no ongoing or unpublished studies that would address the evidence gaps.

- Comparators: there was uncertainty about how closely comparators matched routine practice in the NHS. Amelia Virtual Care and gameChangeVR were delivered in addition to standard care and compared with standard care alone, but standard care differed across trials. So, the committee was unsure whether virtual reality was the driver of the effect or whether the effect was primarily or exclusively because of standard care.
- Outcomes: published evidence was not available for some outcomes. There was also heterogeneity in how clinical measures were reported. It was unclear whether some statistically significant differences were clinically meaningful. There was no evidence on the durability of the effect or relapse rates for any of the VR technologies. Evidence on adverse events was limited and reported in only 1 study on gameChangeVR.
- Decision modelling: evidence gaps for the economic modelling mostly related to the limited clinical evidence, quality-of-life outcomes, utilities and relapse rates. The uncertainties would be reduced with further research addressing the outlined evidence gaps including longer-term data on durability of effect and the repeat use of VR technology.

Committee conclusions

3.20 The committee considered that VR technologies showed some potential to address an unmet need for treating agoraphobia and agoraphobic avoidance. But there were considerable uncertainties about its clinical and cost effectiveness because of the limited evidence. The committee concluded that further research was needed on all VR technologies before they could be recommended for routine use in the NHS. Research should include well-designed and adequately powered studies with appropriate comparators in the NHS. The main outcomes prioritised by the committee

are outlined in section 1.2. Studies should address the evidence gaps outlined in this guidance and show the benefit of using these technologies for people aged 16 and over with agoraphobia and agoraphobic avoidance.

4 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the test to be evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technologies advisory committee meetings, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Additional specialist committee members took part in the discussions for this topic:

Specialist committee members

Professor Robert Dudley
Consultant clinical psychologist, Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust

Dr Elizabeth Murphy
Research clinical psychologist, Greater Manchester Mental Health NHS Foundation Trust

Dr Immanuel Rhema
Specialist psychiatry registrar, East London NHS Foundation Trust

Dr Thomas Kabir

Lay member

Ms Eva Roberts

Lay member

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more health technology assessment analysts (who act as technical leads for the topic), a health technology assessment adviser and a project manager.

Dionne Bowie and Oyewumi Afolabi

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