NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health technology evaluation

Assessment report overview

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

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the external assessment group (EAG) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the committee may wish to discuss. It should be read along with the external assessment report. The overview forms part of the information received by the medical technologies advisory committee when it develops its recommendations on the technologies.

Key issues for consideration by the committee are described in section 9, following the brief summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is underlined and highlighted in either [redacted] (for academic in confidence information) or in [redacted] (for commercial in confidence information). Any depersonalised data in the submission document is underlined and highlighted in [redacted].

This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Additional analyses carried out by EAG

1 The technology

This early value assessment (EVA) focuses on the use of virtual reality (VR) for treating agoraphobia and agoraphobic avoidance. VR is a simulated 3-dimensional environment with scenes and objects that people can explore, most typically using a VR headset. This creates an immersive experience that can trigger emotional responses like those in real-world situations. VR may be used as a tool in therapy sessions or as a digital intervention with the support of a mental health worker. It can help deliver techniques such as exposure therapy, which gradually increases a person's exposure to situations they fear and avoid. It allows 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 and confidence in completing interventions.

In total, 4 VR technologies are included in this assessment. Details on these technologies are provided in the topic scope and assessment report:

- Amelia Virtual Care (Amelia Virtual Care) for mental health disorders including agoraphobia. It is a software-only VR platform designed to be used by therapists as a tool to support treatment in clinics or at home.
- gameChangeVR (Oxford VR) for agoraphobic avoidance in people with schizophrenia spectrum disorders or affective disorders with psychotic symptoms. It is a software-only VR therapy delivered by an automated virtual therapist and supported by a mental health worker in clinic or at home. It is designed to be used as part of a treatment plan for psychosis.
- Invirto (Invirto) for anxiety disorders including agoraphobia. The company did not respond to requests for information and no evidence was identified. This technology was therefore noted but not assessed.
- XR Therapeutics (XR Therapeutics) for anxiety disorders including agoraphobia. It uses a fully immersive screen-based VR studio and is delivered in-person by a therapist in combination with CBT.

2 Proposed use of the technology

2.1 Disease or condition

Agoraphobia is an anxiety disorder characterised by marked and excessive fear of being in situations where escape may be difficult or help may not be available (World Health Organization (WHO) 2022). Some people may describe this experience as feeling threatened or worried about going out. It involves fear and avoidance of places or situations that might cause panic and feelings of being trapped, helpless or embarrassed. This anxious avoidance of everyday situations may occur with other mental health disorders including panic disorder, depression, social anxiety and psychosis. More information on agoraphobia is provided in the topic scope.

2.2 Patient group

The patient group for this assessment is people aged 16 years and over with agoraphobia or agoraphobic avoidance. This includes agoraphobia and agoraphobic avoidance that occurs with other common mental health problems or severe mental illness. This EVA includes a subpopulation of people with psychosis who have agoraphobia or agoraphobic avoidance but does not exclude any other co-occurring mental health conditions.

2.3 Unmet need and current management

The NHS recommends a stepped care approach for treating agoraphobia and any underlying panic disorder (NHS 2022). The first step involves recognition and diagnosis, including identifying any comorbidities. This is used to develop a treatment plan. This may involve lifestyle changes and self-help techniques to help relieve symptoms. People may also be offered guided self-help with therapist support. 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 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.

People with psychosis who have agoraphobia or agoraphobic avoidance should also be treated in line with their treatment plan. NICE's guideline on psychosis and schizophrenia in adults states that people with psychosis should be offered oral antipsychotic medication and psychological interventions including family intervention and CBT. But experts advised that access to CBT is limited with people more likely to be offered antipsychotic medication and simple contact and monitoring with services.

The most recent Adult Psychiatric Morbidity Survey reports that only 1 in 3 people with a common mental health disorder accesses treatment (McManus et al. 2016). There may be considerable barriers to accessing treatment, including a shortage of trained mental health professionals and limited clinical resources. Agoraphobia may further impact a person's ability to access mental health services and support. Clinical experts advised that agoraphobia is often untreated or undertreated when it occurs with other mental health conditions because treatment tends to focus on the more severe or prominent disorder. Some people with agoraphobia or agoraphobic avoidance may also discontinue treatment because of difficulty tolerating techniques such as exposure therapy. VR may increase access to care by offering another treatment option for agoraphobia and agoraphobic avoidance.

2.4 Proposed management with new technology

VR for treating agoraphobia and agoraphobic avoidance would be offered after clinical assessment and diagnosis. It would be an alternative or addition to standard care. VR may be delivered by a therapist as part of face-to-face therapy or teletherapy. Some technologies may also be used as a standalone intervention with the support of a mental health worker such as an assistant psychologist, peer support worker or therapist. VR could support the remote delivery of treatment which would allow some people to receive treatment at home. This could increase access to care for those who are unable or prefer not to attend face-to-face treatment.

The place in the care pathway may differ for agoraphobia and agoraphobic avoidance with or without other mental health disorders such as psychosis.

VR for treating agoraphobia and agoraphobic avoidance is not intended to replace treatments for other mental health disorders, such as antipsychotic medication. Treatment options should be discussed by healthcare professionals and patients and should consider clinical assessment and judgement, patient preferences and risk, and the level of support needed.

3 The decision problem

Details of the decision problem are described in the scope. No changes were made to the decision problem during the assessment.

4 The evidence

4.1 Summary of evidence of clinical benefit

The EAG found 5 studies with a total of 10 publications that were relevant to the decision problem (Table 1). The rationale for selecting these studies is outlined in section 7 of the assessment report.

Table 1. Studies included in the assessment

Technology	Publication and study design
Amelia Virtual Care	2 publications: • 1 RCT (Castro et al. 2014) • 1 single-arm study (poster) (Gelabert and Giner 2018)
gameChangeVR	7 publications: • 1 RCT (Freeman et al. 2022a) with embedded qualitative study (Bond et al. 2023, Freeman et al. 2022b) and economic evaluation (Altunkaya et al. 2022) • Secondary analysis of RCT (Freeman et al. 2022c) • Design process study (Knight et al. 2021, Lambe et al. 2020)
Invirto	No evidence found
XR Therapeutics	1 publication: • 1 single-arm feasibility study (Maskey et al. 2019)
Abbreviation: RCT: randomised controlled trial	

A summary of the clinical evidence is presented for each technology. More details can be found in Table 2 of this overview and section 8 of the assessment report.

Amelia Virtual Care. The relevant evidence included 1 RCT in adults with long-term agoraphobia (Castro et al. 2014) and 1 single-arm study in adults with agoraphobia with or without panic disorder (Gelabert and Giner 2018). The RCT showed that Amelia Virtual Care with CBT plus antidepressants and CBT plus antidepressants were more effective than antidepressants alone. There were no significant differences in CBT plus antidepressants with or without Amelia Virtual Care. There was a statistically significant difference between groups in dropout rates during treatment, with fewer dropouts in the Amelia Virtual Care arm. This could suggest increased interest in or adherence to Amelia Virtual Care compared with standard care alone. The authors reported that people with long-term agoraphobia tend to have high dropout rates and may be reluctant to new exposure treatment. They suggested that using Amelia Virtual Care could increase compliance and reduce dropouts. The single-arm study showed that 82% of people completed treatment, with an average satisfaction rating of 68%.

gameChangeVR. Relevant clinical evidence included 1 RCT (Freeman et al. 2022a) with embedded qualitative studies (Bond et al. 2023, Freeman et al. 2022b) and secondary analysis (Freeman et al. 2022c). The RCT showed that gameChangeVR plus usual care was more effective than usual care alone in reducing agoraphobic avoidance and distress at 6 weeks, but benefits were not maintained at follow-up. There was no significant difference between groups 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 based on the Oxford Agoraphobic Avoidance Scale (O-AS), with these benefits maintained at 26 weeks. The O-AS was developed by researchers at Oxford University who were also involved in the development of gameChangeVR. Experts advised that the O-AS is not routinely used in the NHS.

Secondary analysis (Freeman et al. 2022c) showed significant post-treatment improvements from gameChangeVR with usual care compared with usual care alone in people with severe agoraphobia, specifically in agoraphobic avoidance ($p<0.001$) and distress ($p=0.002$), symptoms of psychosis,

recovering quality of life (p=0.004), and perceived recovery (p=0.038). Most people were mostly (31%) or very (69%) satisfied with gameChangeVR.

XR Therapeutics. Relevant evidence was only available from 1 single-arm feasibility study in autistic adults with fears and phobias (Maskey et al. 2019). This study had a small sample size of 8 people, of whom only 2 reported fears or phobias relevant to agoraphobia. Findings for these 2 people showed equivocal improvement in target behaviours and no benefit in general symptoms of anxiety, depression or quality of life.

Table 2. Details of studies included in the assessment report, grouped by technology

Study design	Participants & setting	Intervention & comparator	Key outcomes measures and results
Amelia Virtual Care (number of studies=2)			
Castro et al. (2014) RCT Location: Spain	80 adults with long-term agoraphobia (5 years or more) **Setting**: Mental health units	**Intervention**: Amelia Virtual Care with CBT plus antidepressants (n=30), delivered in 11 sessions of 30 to 45 minutes each (AMELIA). **Comparator**: • CBT plus antidepressants (n=30), delivered in 11 sessions of 30 to 45 minutes each (CBT) • Waitlist plus antidepressants (n=20) (DRUGS) Follow-up: 6 months	**Agoraphobia symptoms** Both the AMELIA and CBT groups had better treatment effects than DRUGS for agoraphobic cognitions (ACQ) and cognitive and overt behaviours related to agoraphobia when alone (AI-alone) or when in company (AI-accompanied). There were no statistically significant differences between AMELIA and CBT. **General anxiety symptoms** Both the AMELIA and CBT groups had better treatment effects than DRUGS for physical sensations associated with anxiety (BSQ) and general anxiety (BAI). There were no significant differences between AMELIA and CBT. **Clinical improvement** Neither AMELIA nor CBT showed a clinical improvement in ACQ and BSQ pre-post treatment or pre-post follow-up. Only AMELIA showed clinical improvement at follow-up for AI-alone, AI-accompanied, LSAS-fear and LSAS-avoidance. **Social functioning** People in the AMELIA arm spent more time in scenarios in the Behavioral Avoidance Test and had lower self-perceived anxiety (SUA) (p=0.02) **Dropout rate** during treatment across all groups was 37.5%. There was a significant difference in dropout rates between groups (p=0.05), with more dropouts in the CBT (53.3%) and DRUGS (35.3%) groups than AMELIA (23.3%).
Gelabert and Giner (2018) Single-arm study Location: Spain	51 adults with agoraphobia with or without panic disorder **Setting**: 7 adult mental health centres	**Intervention**: Amelia Virtual Care **Comparator**: None Follow-up: 6 months	**Therapeutic adherence** 42 people (82.4%) completed the treatment protocol. The main reason for non-completion was a lack of presence in the virtual environment, that is how much a person feels they are in the scenario or situation.

			Number of sessions needed 98% of people who completed the course did so within the prescribed 8 sessions, with 2 people needing an extra 2 sessions beyond the protocol. **Client Satisfaction Questionnaire-8** Average satisfaction rating was 68%. 57% of people reported high or very high presence, while 12% reported null or low presence.
gameChangeVR (number of studies=2)			
Freeman et al. (2022a) RCT Location: UK Related papers: • Altunkaya et al. (2022) • Bond et al. (2023) • Freeman et al. (2022b) • Freeman et al. (2022c)	346 people aged 16 years or older with schizophrenia spectrum psychosis or an affective diagnosis with psychotic symptoms who have difficulties going outside because of anxiety **Setting**: 9 NHS mental health trusts in England	**Intervention**: gameChangeVR with usual care, delivered in about 6 weekly sessions of 30 minutes each (n=174) **Comparator**: Usual care alone (n=172) Freeman et al. (2022a) stated "usual care was recorded using the Client Service Receipt Inventory, and usually comprised prescription of antipsychotic medications, regular visits from a community mental health worker and occasional outpatient appointments with a psychiatrist". Follow-up: 6 months	131 people in the gameChangeVR arm had the least minimum dose of VR therapy (at least 3 sessions). Provision of VR therapy was affected by COVID-19 pandemic restrictions for 27 people. The effect of the pandemic on usual care was not reported. Most common components of usual care from baseline to 6 weeks [n (%)]: • antipsychotic: 155 (89%) in gameChangeVR group, 155 (90%) in comparator • antidepressant: 94 (54%) gameChangeVR, 94 (55%) comparator • anxiolytic: 12 (7%) gameChangeVR, 14 (8%) comparator • care coordinator meetings: 126 (72%) gameChangeVR, 124 (72%) comparator • psychiatrist meetings: 44 (25%) gameChangeVR, 52 (30%) comparator • counselling or therapy: 9 (5.2%) gameChangeVR, 14 (8.1%) comparator • GP meetings: 41 (24%) gameChangeVR, 49 (29%) comparator **Agoraphobic avoidance** Compared with usual care, gameChangeVR had a statistically significant reduction in agoraphobic avoidance (p=0.026) and distress (p=0.014) at 6 weeks. Differences between groups were not significant at follow-up. Post-hoc analysis showed people with severe and high agoraphobia at baseline were the only groups to benefit from gameChangeVR with benefits maintained at follow-up: • O-AS avoidance adjusted mean difference at 6 weeks: moderate 0.08, high -0.34, and severe -1.63 (p=0.014) • O-AS avoidance adjusted mean difference at 26 weeks: moderate 0.10, high 0.33, and severe -2.06 (p<0.001)

			Secondary analysis showed significant post-treatment improvements from gameChangeVR in people with severe agoraphobia compared with usual care alone: • O-AS avoidance adjusted mean difference: post-treatment -1.63 (p<0.001), follow-up -2.06 (p<0.001) • O-AS distress adjusted mean difference: post-treatment -10.5 (p=0.002), follow-up -12.97 (p=0.001) **Other psychological symptoms** People in the gameChangeVR group reported better recovery (Questionnaire about the Process of Recovery) at 6 weeks than usual care alone (p=0.004). There were no other statistically significant differences in secondary outcomes on psychological symptoms such as paranoia, depression (PHQ-9) and activity levels. **Quality of life** There was no statistically significant difference in quality of life between arms. Secondary analysis showed significant benefits from gameChangeVR compared with usual care alone on ReQoL-20 in people with severe agoraphobia (adjusted mean difference 6.90, 95% confidence interval 2.20 to 11.60; p=0.004). There was no significant difference on the EQ-5D between groups. **Participant experiences** People reported that using gameChangeVR created an anxiety response that was useful for learning and practicing a different response in a safe environment. It was important to be motivated to engage with the intervention and the anxiety response, with people who completed activities to reinforce learning having a better treatment response. People who had the most difficulty managing their agoraphobic avoidance were said to be more motivated and to benefit most from gameChangeVR. **Patient satisfaction** 68.5% of people were very satisfied with gameChangeVR, 30.8% were mostly satisfied and the remaining were mildly dissatisfied or quite dissatisfied. **Safety** There were 25 adverse events (12 serious) in the gameChangeVR group and 29 (8 serious) in usual care alone. 10 serious adverse events for gameChangeVR were rated as definitely not related to the intervention and 2 were probably not related.

Lambe et al. (2020) Design process study Location: UK Related paper: • Knight et al. (2021)	Stakeholders including mental health workers, designers and people with lived experience	**Intervention**: Development of gameChangeVR using a person-centred design process **Comparator**: None	**User acceptability ratings** All users (n=6) rated gameChangeVR as immersive, easy to use and engaging
XR Therapeutics (number of studies=1)			
Maskey et al. (2019) Single-arm feasibility study Location: UK	8 autistic adults with fears and phobias recruited from NHS adult autism diagnosis team and a local autism support network. Of these, 2 had phobias relevant to scope (open space and crowded buses) **Setting**: VR facility	**Intervention**: XR Therapeutics delivered in 2 visits, each comprising of 2 20-to-30-minute sessions **Comparator**: None Follow-up: 6 months	**Retention and participation** Achieved for all sessions. The role of the supporter was important and needed further exploration. Supporters reported needing more guidance about their role and how best to support the person to tackle their real-life anxiety target. **Target Situation Rating (professional rating scores ranging 0 to 9)** 5 out of 8 people were rated as showing an improvement in symptoms related to their phobia. This did not include the 2 people with phobias relevant to agoraphobia who were rated as 'equivocally improved' at post-treatment and follow-up. **Confidence in managing target anxiety situation** Confidence ratings increased pre-post treatment **Other symptoms** There was no pattern of reliable or observable changes on the GAD-7, BAI or PHQ-9. **Quality of life** There was an increase in the WHOQOL-BREF social subscales post-treatment (mean 41.7 pre- to 47.0 post) and follow-up (mean 51.0) but no other subscales.
Abbreviations: ACQ: Agoraphobic Cognition Questionnaire, AI: Agoraphobia Inventory, BAI: Beck Anxiety Inventory, BSQ: Body Sensations Questionnaire, EQ-5D: EuroQoL-5 dimensions, GAD-7: Generalised Anxiety Disorder-7, LSAS: Liebowitz Social Anxiety Scale, O-AS: Oxford Agoraphobic Avoidance Scale, O-BAT: Oxford Behavioural Avoidance Test, PHQ-9: Patient Health Questionnaire-9, RCT: randomised controlled trial, ReQoL: Recovering Quality of Life questionnaire, SUA: Subjective Units of Anxiety, WHOQOL-BREF: World Health Organization Quality of Life scale			

The EAG made the following comments on the limitations and generalisability of the evidence base:

Population. Studies for gameChangeVR and XR Therapeutics were conducted in the UK, while the evidence for Amelia Virtual Care was from Spanish settings. This is likely to be comparable to the UK but there may be some differences in the delivery of care. All 3 technologies had study populations broadly relevant to the decision problem. Amelia Virtual Care had evidence in people with agoraphobia including long-term agoraphobia. gameChangeVR and XR Therapeutics focused on subgroups, specifically psychosis with agoraphobic avoidance and autism with fears and phobias, respectively. There was no evidence on XR Therapeutics in a population with agoraphobia. This limits the generalisability of the evidence to the broader scoped population.

Intervention. There was no evidence on Invirto and there was limited relevant evidence on the clinical effectiveness of the other technologies. This consisted of 2 RCTs (Amelia Virtual Care and gameChangeVR) and 2 single-arm studies (Amelia Virtual Care and XR Therapeutics).

Comparator. There are limitations with comparators for all technologies:

- Amelia Virtual Care: Only 1 study included a comparator arm. Amelia Virtual Care with CBT plus antidepressants was compared with CBT plus antidepressants and antidepressants alone. The EAG noted that it was unclear whether the treatment effects were driven by CBT.
- gameChangeVR: There was only 1 comparative study which compared gameChangeVR plus usual care with usual care alone, but usual care varied across patients. The EAG considered that there are limitations to using treatment as usual as a comparator because of the variation in routine practice across centres.
- XR Therapeutics: There was no relevant comparative evidence.

Outcomes. All studies reported some outcomes of interest, but evidence was not available on all scoped outcomes for all technologies. gameChangeVR was the only technology with evidence on adverse events. Some studies

reported statistically significant differences in pre-post treatment outcomes, but the clinical significance of these changes was not always reported. There was variation in outcomes across studies and the instruments used.

In summary, the EAG considered the clinical effectiveness to be uncertain for all technologies. While there was some evidence of potential benefits on agoraphobia symptoms for Amelia Virtual Care and gameChangeVR, the EAG concluded that there were considerable uncertainties about the interpretation and reliability of these findings. More evidence is needed including evidence on the longer-term effects of all interventions.

4.2 Summary of economic evidence

The EAG identified 1 economic study (Altunkaya et al. 2022) that was relevant to the decision problem. This was a within-trial cost-effectiveness analysis of gameChangeVR conducted alongside the RCT (Freeman et al. 2022a). There was no economic evidence on any of the other technologies.

Altunkaya et al. (2022) aimed to estimate the maximum cost-effective price for gameChangeVR using the conventional willingness-to-pay thresholds. It reported incremental gain in utilities for gameChangeVR plus usual care of +0.008 (-0.010 to 0.026) QALYs (E5-5D) and +0.003 (-0.011 to 0.017) QALYs (ReQoL) compared with usual care alone. Using an NHS and personal social services (PSS) perspective and EQ-5D-based QALYs, the maximum cost-effective price for gameChangeVR was £262 or £341 per person based on a £20,000 or £30,000 threshold respectively. This increased to £682 (£20,000 per QALY) and £844 (£30,000 per QALY) for the subgroup of people with high or severe agoraphobic avoidance and distress.

The EAG noted that the base case results were disproportionately driven by 4 people in psychiatric inpatient settings. When these were removed, there was no positive price at which gameChangeVR was cost-effective in the general population of psychosis with agoraphobia from an NHS and PSS perspective. However, gameChangeVR had the potential to be cost-effective in subgroups with high or severe avoidance and/or distress. The most optimistic of these scenarios showed a max price of £125 at a £20,000 threshold or £324 at

£30,000. The maximum cost-effective price of gameChangeVR was greater when considering the intervention's impact on wider societal costs but this is beyond the scope of this assessment.

4.2.1 Conceptual modelling

The EAG used Altunkaya et al. (2022) as a starting point to develop a decision model to explore uncertainties in the cost-effectiveness of the VR technologies, specifically the duration of the treatment effect and the effect of subsequent rounds of treatment. The primary purpose of the analysis was to assess the plausibility of the technologies being cost-effective and to identify evidence gaps for future evidence generation. The EAG advised that this modelling is exploratory and does not provide conclusive findings on the cost-effectiveness of the technologies compared with standard care.

The EAG developed 2 identical decision analytical models that differed in populations and comparators in line with the evidence for each technology:

- gameChangeVR plus usual care compared with usual care alone in people with psychosis who have agoraphobic avoidance (DP1)
- Amelia Virtual Care with CBT compared with CBT alone in people with agoraphobia (DP2).

The EAG excluded XR Therapeutics and Invirto from the analysis because of the limited or lack of relevant clinical evidence.

The model was a 2-state Markov model transitioning between psychosis with agoraphobia and psychosis alone (DP1) or agoraphobia and no agoraphobia (DP2). The choice of a state-transition model was driven by the need to explore uncertainties in longer-term costs and effects of the different technologies. The model structure is outlined in section 10.2.2 and Figure 1 of the assessment report. The transition period was 6 months with a time horizon of 5 years. This reflected the follow-up periods in the evidence and aimed to provide a reasonable time horizon to explore uncertainties in relapse or recurrence (referred to as 'relapse rate') and effectiveness of subsequent courses of treatment. The EAG also conducted an additional analysis using a

shorter time horizon of 2 years. This is outlined in Appendix B of this overview and supplementary Appendix F of the assessment report.

Markov models require discrete health states to be defined, such as 'responder' and 'non-responder'. The EAG noted that this is not reported in the evidence. It therefore assumed that everyone having VR therapy responded to treatment at 6 months with the mean per person utility changing in line with the adjusted mean difference reported in the evidence. The model assumed that everyone transitioned from the 'agoraphobia' health state to the 'non-agoraphobia' health state in cycle 1. Subsequent cycles allowed the EAG to explore uncertainties around relapse rate and effectiveness of further courses of VR therapy. Key assumptions in the model are outlined in section 10.3.4 of the assessment report.

4.2.2 Model inputs

Clinical parameters

Clinical parameters were sourced from the evidence and expert advice. Interventions and comparators were based on the clinical trials. In Freeman et al. (2022a), gameChangeVR was delivered with usual care and compared with usual care alone. Amelia Virtual Care was also delivered alongside standard care (CBT plus antidepressants) and compared with CBT plus antidepressants and antidepressants alone (Castro et al. 2014). This reflects the intended use of Amelia Virtual Care as a tool to help therapists deliver treatment. Castro et al. (2014) did not collect 6-month follow-up data for the antidepressants only arm. The EAG therefore excluded this from the model.

Response to treatment was driven by the health state utility derived from the findings of the clinical trials (Castro et al. 2014, Freeman et al. 2022a). The model used the utility difference between VR therapy and standard care as the driver of effect rather than a probability of response. The EAG assumed a base case relapse rate of 25% which was varied according to a uniform distribution between 0% and 50%. There was no evidence on the effectiveness of subsequent courses of VR therapy for any of the

technologies. The EAG included the relative risk of response for subsequent courses of treatment to explore scenarios. This was set at 1 in the base case.

Health state utilities

For DP1, baseline health state utility was set to the weighted mean baseline utility across both arms in the gameChangeVR trial (Altunkaya et al. 2022, Freeman et al. 2022a). The change in utility associated with VR therapy was equal to the adjusted mean difference between gameChangeVR plus usual care and usual care alone at 6 months (+0.007, 95% confidence interval -0.043 to 0.057).

For DP2, health state utilities were based on a crude conversion of BAI scores. The rationale and method of calculating these utilities are provided in section 10.3.3 of the assessment report. Baseline health state utility was calculated from the weighted mean baseline BAI scores across all 3 arms in the trial (Castro et al. 2014). The change in utility associated with VR therapy was converted using the difference in change in BAI scores pre-post follow-up between Amelia Virtual Care with CBT and CBT alone (-0.005, standard error (SE) 0.027). Further detail is provided in Table 9 of the assessment report.

Costs and resource use

The base case calculated costs and resource use from an NHS and PSS perspective. Costs and resource use in the model are presented in Table 3 and Table 4. These are the incremental costs and resources needed for delivering VR therapy in addition to standard care as outlined in DP1 and DP2. Costs of standard care are not presented because these were assumed to be the same in both arms. Intervention costs included licence costs, therapist time and apportionment of capital cost of the VR headset. The model for gameChangeVR (DP1) also considered a point estimate difference in other health service costs between gameChangeVR plus usual care and usual care alone. This was -£112.15 (SE £280.50) per person based on findings in Altunkaya et al. (2022) adjusted to 2021 prices. No data was available on other health service costs for Amelia Virtual Care (DP2). This was therefore not included in the model which the EAG noted may have underestimated

uncertainty in the cost-effectiveness of Amelia Virtual Care. More information on intervention costs is provided in section 10.3.2.1 of the assessment report.

In line with Altunkaya et al. (2022), the EAG also considered costs from a broader societal perspective as additional analyses for gameChangeVR (DP1). These included criminal justice costs and costs of informal caregiving (see sections 10.3.2.3 and 10.3.2.4 of the assessment). Cost modelling using a societal perspective is not detailed in this overview because it is outside the scope of this assessment.

Table 3. Unit costs

Item (unit)	Unit Cost	Source
Mental health worker (per hour)	£33.00	Band 4, equivalent to clinical psychology assistant practitioner (ch 17, and hourly cost from ch 10.1 PSSRU 2021)
Clinical psychologist (per hour)	£105.00	Consultant clinical psychologist (Band 8c, Ch 9, PSSRU 2021)
VR headset	£300	Notional cost
gameChangeVR licence (per person per course)	[redacted]	Company
Amelia Virtual Care licence (per centre per month)	[redacted]	Company

Table 4. Intervention resource use

Item	Quantity	Total Cost
gameChangeVR (per session)		
Mental health worker intervention delivery	1 hour	£33.00
Mental health worker weekly supervision	1 hour with clinical psychologist, assuming mental health worker conducts 15 sessions per week	£9.20
Training	4.5 hours with clinical psychologist with 6 mental health workers in attendance, assuming training lasts 2 years before refresher required	£0.17
VR Headset	One per mental health worker conducting 15 sessions per week for 44 weeks/year, lasting 2 years	£0.64
Total per session		£43.01
gameChangeVR (per course)		
Per session costs	Six sessions per course	£258.05
Licence cost		[redacted]
Total per course		[redacted]

Amelia Virtual Care (per session)		
Licence cost	Assuming used for 60 sessions per month	[redacted]
VR Headset	One per mental health worker conducting 15 sessions per week for 44 weeks/year, lasting 2 years	£0.64
Training	4.5 hours per clinical psychologist, assuming training lasts 2 years before refresher required	£0.36
Total per session		[redacted]
Total per course	Assuming six sessions per course	[redacted]

4.2.3 Approach to analysis

The EAG conducted a cost utility analysis estimating the incremental cost per incremental QALY gained from:

- gameChangeVR plus usual care compared with usual care alone in people with psychosis who have agoraphobic avoidance (DP1)
- Amelia Virtual Care with CBT compared with CBT alone in people with agoraphobia (DP2).

Analyses were conducted from an NHS and PSS perspective. Only costs that differed between arms were measured and valued. The EAG reported mean costs and QALYs gained per person in each arm, incremental cost-effectiveness ratios and probability of cost-effectiveness at £20,000 and £30,000 per QALY thresholds. Means and uncertainty distributions were generated from probabilistic sensitivity analysis of 10,000 simulations sampled from the distributions of input parameters. The EAG also conducted several probabilistic sensitivity analyses and scenarios which are outlined in sections 10.4.1 to 10.4.8 of the assessment report.

4.2.4 Results

The exploratory base case results are presented separately for gameChangeVR (Table 5) and Amelia Virtual Care (Table 6). Point estimate ICERs suggest that on average gameChangeVR and Amelia Virtual Care are not cost-effective from an NHS and PSS perspective. But the EAG base case suggests there is substantial decision uncertainty with around 25% to 30% probability of gameChangeVR being cost-effective and 42% probability of

Amelia Virtual Care being cost-effective from an NHS and PSS perspective at conventional thresholds of willingness to pay. gameChangeVR may be cost-effective from a wider societal perspective, but this falls outside the scope of this assessment.

Table 5. gameChangeVR (DP1) base case results

Costs			QALYs				P(CE)	
gC+TAU	TAU	Inc.	gC+TAU	TAU	Inc.	ICER	£20k	£30k
[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	26.3%	31.2%
Abbreviations: gC: gameChangeVR, P(CE): probability of cost-effectiveness, QALYs: quality adjusted life years, TAU: treatment as usual								

Table 6. Amelia Virtual Care (DP2) base case results

Costs			QALYs				P(CE)	
A+CBT	CBT	Inc.	A+CBT	CBT	Inc.	ICER	£20k	£30k
[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	41.0%	41.6%
Abbreviations: A: Amelia Virtual Care, CBT: cognitive behavioural therapy, ICER: incremental cost-effectiveness ratio, P(CE): probability of cost-effectiveness, QALYs: quality adjusted life years, TAU: treatment as usual								

Scenario and sensitivity analyses

The EAG considered that while the point estimates from the decision modelling were only indicative, the modelling provided a useful platform to explore several uncertainties:

Incremental utility gain. The minimum utility gain for gameChangeVR (DP1) to achieve an ICER below the £30,000 threshold is [redacted] ([redacted] for an ICER below £20,000 per QALY). In DP2, the minimum utility gain needed for Amelia Virtual Care (DP2) to be cost-effective is less than [redacted]. Additional analysis for gameChangeVR using utilities from high and severe agoraphobia subgroups found point estimate ICERs within the range considered to be cost-effective from an NHS and PSS perspective. More information is provided in Appendix B of this overview and Appendix F of the assessment report.

Licence fees. Results for gameChangeVR (DP1) were highly sensitive to licence fees. The licence fee associated with a 50% probability of cost-

effectiveness was about [redacted] at a £20,000 per QALY threshold or [redacted] at a £30,000 threshold. There was no licence fee associated with a 50% probability of cost-effectiveness for Amelia Virtual Care because the point estimate incremental utility was negative.

Incremental utility versus licence fees. The maximum cost-effective licence fee for gameChangeVR increased as incremental utility increased. Two-way sensitivity analysis of gameChangeVR licence costs versus incremental utility can be found in section 10.5.2.8 and Table SA8 of the assessment report.

Cost of VR headset. ICERs of gameChangeVR (DP1) and Amelia Virtual Care (DP2) were not sensitive to changes in the cost of the VR headset.

Relapse rate. One-way sensitivity analysis suggested the ICERs of both gameChangeVR (DP1) and Amelia Virtual Care (DP2) deteriorate as the relapse rate increases. Under the base case, gameChange was only cost-effective if relapse rates were less than [redacted] at a £30,000 per QALY threshold and less than [redacted] at the £20,000 threshold.

Relapse rate versus licence fees. The maximum cost-effective licence fees for gameChangeVR decreased as the probability of relapse increased. Two-way sensitivity analysis of gameChangeVR licence costs versus relapse rate can be found in section 10.5.2.7 and Table SA7 of the assessment report.

Effectiveness of subsequent therapy. ICERs in both decision problems deteriorate with a decline in the relative effectiveness of subsequent VR therapy. This is because the same cost is incurred with less relative benefit.

In summary, the EAG noted that gameChangeVR is priced above what would normally be considered cost-effective from an NHS and PSS perspective. But there is great uncertainty in the base case which was highly sensitive to the assumptions in the model. The EAG concluded that there are scenarios where gameChangeVR may be cost effective particularly in people with high and severe agoraphobia, but more evidence is needed.

The point estimate treatment effect of Amelia Virtual Care with CBT was approximately zero when compared with CBT alone, but with very wide confidence intervals. The EAG advised that more evidence is needed to establish a reliable estimate of cost-effectiveness.

The EAG did not model the possible cost-effectiveness of XR Therapeutics because of its limited clinical evidence. But it noted that the licence cost of this technology is [redacted] suggesting it would [redacted] to be cost-effective.

5 Ongoing research

The companies for gameChangeVR and XR Therapeutics said there were no ongoing trials, but XR Therapeutics are monitoring real-world outcomes. Amelia Virtual Care provided information marked as academic in confidence on 5 ongoing studies, but the populations are not in scope. The EAG also found 2 ongoing studies for Invirto which may be relevant when completed:

- Evaluation of "Invirto aftercare" for anxiety disorders: a pilot study (DRKS00027001)
- Evaluation of "Invirto Therapy" for people with panic disorder: a randomized-controlled trial (DRKS00027585)

6 Evidence gap analysis

The EAG presented a summary of the evidence gaps pertaining to outcomes from the scope (Table 7) and the decision modelling (Table 8). There was no published evidence on Invirto which is a noted evidence gap.

Table 7. Evidence gaps in outcomes from the scope

Outcomes	Amelia Virtual Care	gameChangeVR	XR Therapeutics
Intermediate outcomes			
Patient choice and preferences	No studies **RED**	No studies **RED**	No studies **RED**
Acceptability and satisfaction	One study **AMBER**	One study **AMBER**	One study **AMBER**

Outcomes	Amelia Virtual Care	gameChangeVR	XR Therapeutics
Accessibility and digital access	No studies **RED**	No studies **RED**	No studies **RED**
Intervention adherence and completion	Two studies **GREEN**	One study **AMBER**	One study **AMBER**
Intervention-related adverse events	No studies **RED**	One study **AMBER**	No studies **RED**
Device-related adverse events	No studies **RED**	One study **AMBER**	No studies **RED**
Clinical outcome			
Change in agoraphobia symptoms	One study **AMBER**	One study **AMBER**	One study, mixed results **AMBER**
Change in other psychological symptoms	One study **AMBER**	One study, negative results **RED**	One study, negative results **RED**
Global functioning and work and social adjustment	One study, negative results **RED**	No studies **RED**	No studies **RED**
Rates of recovery, time to recovery	No studies **RED**	No studies **RED**	No studies **RED**
Rates of relapse or deterioration, time to relapse or deterioration	No studies **RED**	No studies **RED**	No studies **RED**
Patient reported outcomes			
Health-related quality of life	No studies **RED**	One study, negative results **RED**	One study, negative results **RED**
Recovering quality of life	No studies **RED**	One study, negative results **RED**	No studies **RED**
Patient experience	No studies **RED**	One study **AMBER**	No studies **RED**
Social contact	No studies **RED**	One study, negative result **RED**	No studies **RED**

Table 8. Evidence gaps in modelling and economic outcomes

Effectiveness evidence	
Populations and comparative data	Each intervention has been trialled in very different populations. It is unknown whether any of the interventions are interchangeable between different populations and thus require head-to-head comparison **RED**
Comparative data	There is no randomised evidence on the effectiveness of XR Therapeutics. **RED**
Comparative data	There is no evidence on durability of treatment effect and/or relapse rates. **RED**
Comparative data	There is no evidence on effect of second or subsequent courses of therapy. **RED**
Comparative data	Is there an impact on other health service use from VR-based therapies? **AMBER**
Generalisability	Is there any difference in effect between who delivers the interventions? **AMBER**
Costs	
Criminal justice costs	Is the impact of gameChangeVR on criminal justice costs in people with psychosis of meaningful? **AMBER**
Lost productivity	Is there a case for including time off work within economic evaluations of agoraphobia (outside NICE reference case)? The evidence base contains no data on lost productivity. **RED**
Health related quality of life	
Health state utilities	Evidence on health state utilities is currently very weak **RED**

6.1 Summary and conclusions of evidence gap analysis

The EAG identified several evidence gaps in the clinical evidence base. These in part drive key uncertainties in the economic analysis:

Population gaps. The populations studied for each intervention differed. The 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 adults with agoraphobia. There was no UK evidence for Amelia Virtual Care which may limit the generalisability of findings to the NHS.

Intervention gaps. There is limited evidence for all interventions. There was no evidence on Invirto and no comparative evidence on XR Therapeutics.

Comparator gaps. There is uncertainty about how closely comparators match routine practice in the NHS, especially for treatment as usual (usual care). Both Amelia Virtual Care and gameChangeVR were delivered in addition to standard care and compared with standard care alone, but standard care differed across trials and interventions.

Outcome gaps. 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 in outcomes were clinically meaningful. There was no evidence on the durability of the effect (relapse rates) of VR therapies for any of the technologies. Clinical evidence on safety outcomes (adverse effects) were only available for gameChangeVR.

Decision modelling. Evidence gaps for the economic modelling are mostly related to the limited clinical evidence, quality of life outcomes, utilities and relapse rates. Whilst outside the reference case, employment status and lost time at work may be an important factor to consider in economic analysis of treatments for agoraphobia. This was not measured in any of the studies.

7 Equalities considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Several potential equality issues and considerations in using VR for treating agoraphobia have been identified:

- Some VR technologies need Wi-Fi to use the intervention or to upload content. Additional support and resources may be needed for people who are unfamiliar with digital technologies or do not have access to the internet.
- People with visual or cognitive impairment, problems with manual dexterity, a learning disability or who are unable to read or understand health-related information (including people who cannot read English) may need additional support to use VR. Some people would benefit from VR in languages other than English. XR Therapeutics has

adapted its intervention for autistic people and people with learning disabilities. The company said its VR studio is also accessible for people with physical disabilities, including people using wheelchairs.

- VR may not be suitable for use by people with photosensitive epilepsy; significant visual, auditory, or balance impairment; organic mental disorder; primary diagnosis of alcohol or substance disorder or personality disorder; significant learning disability; or active suicidal plans. Some VR interventions may involve moving around the room or standing. This may be difficult for some people with physical disabilities or additional accessibility needs.
- People's ethnicity, religious or cultural background may affect their views of mental health problems and interventions. Healthcare professionals should discuss the language and cultural content of VR with patients before use.
- People facing social inequality and disadvantage, discrimination and exclusion are at higher risk of mental health problems. Agoraphobia and agoraphobic avoidance can significantly affect people's daily living. Under the Equality Act 2010, a person has a disability if they have a physical or mental impairment that has a substantial and long-term effect on their ability to do typical day-to-day activities.

Age, disability, race and religion or belief are protected characteristics under the Equality Act (2010).

8 Implementation

Some of the scoped technologies are already used in the NHS. The EAG reported that wider use would involve upscaling across more trusts. Potential challenges with integration into the NHS included having enough staff resources and training to deliver the interventions. There may also be challenges with access to the technologies and equipment particularly for people who work during the day or are unable to leave home. NHS trusts would also have to purchase and maintain VR headsets when used for the delivery of VR therapy as these are not usually provided by the companies.

NICE's adoption and implementation team spoke with clinical experts who had experience of VR for treating agoraphobia and agoraphobic avoidance. Some implementation considerations may not apply to all technologies. Key considerations raised in the adoption of these technologies include:

Safety and comfort. Potential safety considerations based on the clinical evidence on VR therapy delivered via headsets includes concerns with possible side effects such as dizziness and motion sickness. This may be less of a concern with more recent versions of devices. There were also concerns with the space needed to use VR and issues with bumping into things in the room. Experts advised that a couple of metres is enough to use these technologies. Other considerations are whether the headset is comfortable to wear over glasses or use if the person's eyes are sensitive to glare. If people have any discomfort or concerns with using VR, they can remove the headset or leave the immersive setting.

Patient selection. Some VR therapies may be used as a standalone intervention if there is appropriate and careful patient selection. gameChangeVR includes a virtual coach that guides the person through treatment. Interventions have been found to work best with a mental health worker who helps with patient engagement. VR may not be suitable for everyone. Healthcare professionals and patients should discuss treatment options before use.

Acceptability. Preliminary implementation work and input from people with lived experience showed good acceptability of using VR for agoraphobia and agoraphobic avoidance. People reported good immersive quality of the technologies and were motivated to try the interventions because they wanted a solution to their difficulties. Anecdotal reports suggested some people have quick progress and symptom improvement including increase in real-world activities. Experts suggested that people with more severe symptoms may have greater response to treatment. Healthcare professionals may initially be a little hesitant to using VR but demonstrations, training and support can help.

9 Issues for consideration by the committee

9.1 Unmet need

Only 1 in 3 people with a common mental health disorder accesses treatment. This may be even lower for people with agoraphobia who may have increased challenges getting the treatment and support they need. These may include:

- underdiagnosis or undertreatment of agoraphobia or agoraphobic avoidance when presenting with more severe or prominent mental health disorders such as psychosis
- difficulty leaving home to access treatment
- difficulty completing treatments such as in vivo exposure
- limited clinical resources which means people may not be offered NICE recommended treatments such as CBT but may instead receive drug treatments and simple contact with services and monitoring.

VR therapy may increase access to care by offering another treatment option. It could support the remote delivery of treatment which would allow some people to receive treatment at home. This could increase access to care for those who are unable or prefer not to attend face-to-face treatment.

9.2 Population

Evidence on the effectiveness of each technology was in a specific agoraphobia subgroup. Amelia Virtual Care and XR Therapeutics are both indicated for use in a broader population of agoraphobia. The committee may wish to consider the generalisability of the evidence for these technologies to this population.

The evidence for gameChangeVR showed benefits in reducing agoraphobic avoidance in people with severe agoraphobia at baseline. This aligns with anecdotal reports from clinical experts that people with the greatest difficulty in managing their agoraphobia or agoraphobic avoidance may be more motivated to use VR therapy and may see the greatest benefits.

9.3 Care pathway

There was limited comparative evidence comparing Amelia Virtual Care and gameChangeVR with standard care, specifically:

- Amelia Virtual Care with CBT plus antidepressants compared with CBT plus antidepressants and antidepressants alone
- gameChangeVR plus usual care compared with usual care alone.

This reflects the use of VR therapy as an addition to traditional standard care. But there was no evidence on other possible uses of these technologies, such as the remote use of Amelia Virtual Care as part of teletherapy for people who may be unable to attend face-to-face sessions. There was also no evidence on the use of gameChangeVR as a standalone therapy with asynchronous remote support. The committee may wish to consider the generalisability of the evidence across treatment settings and how variation in treatment delivery may affect outcomes.

9.4 Clinical evidence

There is limited evidence on all technologies. The clinical evidence consists of 5 studies including 1 RCT each for Amelia Virtual Care and gameChangeVR. The evidence for Amelia Virtual Care and gameChangeVR suggests benefits in improving symptoms of agoraphobia. But the EAG advised that there were substantial uncertainties.

For gameChangeVR, key uncertainties were:

- the lack of a treatment effect in the broader population of psychosis with agoraphobic avoidance, suggesting benefits may be limited to people with more severe symptoms at baseline
- the long-term benefits of gameChangeVR compared with usual care
- the lack of benefit on EQ-5D-based quality of life outcomes.

For Amelia Virtual Care, key uncertainties were:

- no significant difference in effectiveness between Amelia Virtual Care with CBT and CBT alone, with the EAG questioning if the benefits were primarily or exclusively from CBT
- the reasons for differences in dropout rates and the impact of this on treatment outcomes
- the long-term benefits of Amelia Virtual Care compared with standard care including benefits associated with reduced dropouts.

For XR Therapeutics, key uncertainties were the lack of evidence in adults with agoraphobia and the limited evidence on clinical effectiveness in adults.

9.5 Economic evidence

The economic modelling is exploratory and should not be used as a definitive result of cost-effectiveness. Findings were highly sensitive to the assumptions in the model, including incremental utility from the limited clinical evidence.

The exploratory base case suggested that based on the clinical evidence, licence costs and assumed relapse rates, none of the technologies would be cost-effective from an NHS and PSS perspective. The cost-effectiveness of gameChangeVR was driven by the licence fees, utility and relapse rates. The EAG noted that gameChangeVR was priced above the maximum cost-effective price [redacted]. The cost-effectiveness of Amelia Virtual Care was largely driven by the incremental utility compared with CBT. Modelling did not consider dropout rates and the impact this may have on cost-effectiveness. The committee may wish to consider if it is possible to mitigate the degree of uncertainty in the cost modelling to increase probability of cost-effectiveness for the technologies.

9.6 Key gap analysis conclusions

There is no evidence on Invirto and limited evidence on the effectiveness and long-term benefits of the other 3 technologies. The EAG did not identify any ongoing studies that would address these evidence gaps in line with the decision problem but noted that some technologies may be collecting real-world outcomes.

10 Authors

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NICE Medical Technologies Evaluation Programme

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11 Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report

- Barnish MS, Lovell A, Robinson S, et al. Virtual reality for treating agoraphobia and agoraphobic avoidance [GID-HTE10016]: external assessment group report. May 2023.

A list of registered stakeholders and expert adviser Specialist Committee Members can be found in the published project documents.

B Companies of technologies included in the final scope:

- Amelia Virtual Care
- Invirto
- Oxford VR
- XR Therapeutics

C Related NICE guidance

- Mental health problems in people with learning disabilities: prevention, assessment and management (2016) NICE guideline 54
- Psychosis and schizophrenia in adults: prevention and management (2014) NICE clinical guideline 178. Last updated 1 March 2014.
- Common mental health problems: identification and pathways to care (2011) NICE clinical guideline 123
- Generalised anxiety disorder and panic disorder in adults: management (2011) NICE clinical guideline 113. Last updated 15 June 2020

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McManus S, Bebbington P, Jenkins R et al. editors (2016) Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014. Leeds: NHS Digital.

National Health Service (NHS) Treatment – Agoraphobia [online; accessed 29 May 2023]

World Health Organisation (WHO) (2023) International Classification of Diseases, Eleventh Revision (ICD-11)

12 Appendix B: Additional analyses carried out by the EAG

The EAG conducted additional analyses after submitting the assessment report exploring (1) a reduced time horizon of 2 years and (2) scenario analysis with more severe subgroups for gameChangeVR. This is reported in supplementary Appendix F of the assessment report.

12.1 Time horizon scenario analysis

The EAG conducted a scenario analysis using a 2-year time horizon for gameChangeVR (DP1) and Amelia Virtual Care (DP2). At a 2-year time horizon, gameChangeVR was found to be less cost-effective than the base case. But there was very little difference from the base case for Amelia Virtual Care. Results for gameChangeVR from an NHS and PSS perspective are presented in Table 9.

Table 9. Time horizon scenario analysis (gameChangeVR)

Time horizon	Costs			QALYs				P(CE)	
	gC+TAU	TAU	Inc.	gC+TAU	TAU	Inc.	ICER	£20k	£30k
5 years	[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	26.3%	31.2%
2 years	[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	9.8%	13.4%

12.2 Severe subgroup scenario analysis (gameChangeVR)

The EAG conducted a scenario analysis using utility differences for high and severe agoraphobia subgroups from Freeman et al. (2022c). The change in utility associated with VR therapy at 6 months was +0.04 (SE 0.05) for high agoraphobic avoidance and +0.05 (SE 0.053) for severe avoidance. Results of this analysis are presented in Table 10. It shows that point estimate ICERs for the high and severe avoidance subgroups from an NHS and PSS perspective are within the range normally considered cost-effective by NICE. But the EAG advised that there is substantial uncertainty associated with this. For the severe agoraphobia subgroup, Freeman et al. (2022c) reported the point estimate incremental utility at 6-months follow-up was higher than

6-weeks post-treatment. The EAG considered that a tailing off of treatment effect over time would typically be expected and concluded that further exploration is needed.

Table 10. Severity subgroup scenario analysis (gameChangeVR)

Group	Costs			QALYs				P(CE)	
	gC+TAU	TAU	Inc.	gC+TAU	TAU	Inc.	ICER	£20k	£30k
All	[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	26.3%	31.2%
High	[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	57.1%	65.2%
Severe	[redacted]	£0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	63.1%	70.4%