NICE National Institute for Health and Care Excellence

Medical technologies advisory committee (MTAC)

Friday 8 December 2023

Information pack for draft guidance considerations on

GID-HTE10020 Digital health technologies to help manage symptoms of psychosis and prevent relapse: early value assessment

This topic was selected for early value assessment in 2023. Clinical and economic evidence has been submitted to NICE by the company, and an external assessment centre report has been completed.

This pack presents the information required for the MTAC to make draft recommendations on this topic. The consultation period on these draft recommendations is scheduled to take place between 18 January 2024 and 1 February 2024.

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Papers included in pack:

1. Front sheet
2. Final scope
3. External Assessment Group Report (EAR)
4. Assessment Report Overview (ARO)
5. Patient survey summary report
6. Equality impact assessment (EIA)
7. Register of interest

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Digital health technologies to help manage symptoms of psychosis and prevent relapse

Final Scope

September 2023

1 Introduction

The topic has been identified by NICE for consideration for early value assessment (EVA). The objective of EVA is to identify promising technologies in health and social care where there is greatest need and where the evidence base is still emerging. It will provide an early indication to the system that they could be used while evidence is generated. The process will enable the technologies to be recommended for use only if further data is collected before NICE makes a final evaluation. NICE's topic selection oversight panel ratified this topic as potentially suitable for an EVA by the HealthTech programme.

The technologies identified for this assessment are those used to help manage symptoms of psychosis and prevent relapse.

The purpose of this EVA evaluation is to map the evidence that is available on the technologies; assess their potential clinical and cost-effectiveness and to identify evidence gaps to help direct data collection and further research. This evaluation will inform Committee recommendations on the conditional use of these technologies in the NHS while further evidence is generated.

2 Description of the technologies

This section describes the digital health technologies used to help manage symptoms of psychosis and prevent relapse. The information is based on information provided to NICE by technology developers and experts, and information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technology

The demand for psychological therapy for people with psychosis in the NHS outstrips the available capacity to provide this in a timely manner (Mind report on access to talking therapies). In addition, the use of antipsychotic medication is a contributor to poor physical health in people living with psychosis and so there is a need to provide non-drug intervention alternatives. The prolonged use of antipsychotic medication causes obesity, diabetes, hypertension and hypercholesterolaemia. An area of priority is enabling access to approved interventions quickly after diagnosis, as early intervention has been shown to improve outcomes. Digital health technologies are available that could help clinical teams in the effective management of psychosis by providing specialist support to manage symptoms of psychosis or by providing remote monitoring to help prevent relapses by alerting healthcare professionals to deterioration.

2.2 Product properties

This scope focuses on digital health technologies for symptom management and relapse prevention of psychosis. For this EVA, NICE will consider technologies that:

- are digital health interventions designed to provide specialist support for managing symptoms of psychosis or to prevent relapse in people with psychosis who are receiving care from healthcare professionals.

- meet the standards within the digital technology assessment criteria (DTAC), including the criteria to have a CE or UKCA mark where required. Products may also be considered if they are actively working towards required CE or UKCA mark and meet all other standards within the DTAC.

- are available for use in the NHS.

In total, 4 digital health technologies were identified which met the selection criteria above. One of the technologies, gameChange, is currently being evaluated as an EVA topic in virtual reality for treating agoraphobia and agoraphobic avoidance and so will not be included in the decision problem of this EVA. The final list of included technologies may be subject to change.

AVATAR Therapy

AVATAR Therapy [Avatar Therapy] is treatment for distressing auditory verbal hallucinations ('voices') for people with psychosis. This therapy aims to reduce the distress that can be experienced when hearing voices by facilitating a three-way conversation between the patient, their distressing voice and the therapist. This technology uses digital avatars which are a digital representation, both visual and auditory, of the distressing voice created by the patient supported by the therapist. Whilst supported by the therapist in a different room or remotely, using video conferencing, the patient engages in dialogue with the avatar (voiced by the therapist) to take power and control within the conversation. The treatment is provided over 6 to 12 sessions and may be provided as a stand-alone treatment or as one component of CBT for psychosis therapy, where persecutory voices are part of the overall condition.

CareLoop

CareLoop [CareLoop Health] is a remote monitoring system for people with psychosis that facilitates early identification and intervention when symptoms escalate. It includes a patient-facing app where users record symptoms daily,

using proprietary questionnaires, and can add journal entries of their thoughts and feelings. The daily symptom data based in the questionnaire responses are transferred to the cloud-based CareLoop system for storage and processing. The CareLoop system includes an algorithm that is designed to recognise changes in a person's mental health, identifying deterioration and predicting acute events before they occur. The daily symptom data is also used to generate information on the app for patients which shows how their symptoms have changed over time. It is also shared with the patient's clinical team. Output from the algorithm is expected to provide early warning signs for clinical teams to flag a patient's deterioration and to generate insights at an individual level to optimise treatment and care- for example in medication management. A web-based dashboard is used for symptom monitoring by the clinical team.

SlowMo

SlowMo [King's College London] is a blended digital therapy which aims to reduce distressing worries or paranoia by supporting people with psychosis to notice and slow down their unhelpful fast thinking habits. The blended approach combines face-to-face therapy sessions with interactive digital content on a webapp and mobile app. The SlowMo webapp has modules for each session with interactive stories and games. Users can also record personalised messages. From each module, personalised session content is synchronised with a SlowMo mobile app that supports people with paranoia to use strategies to combat fast thinking in daily life.

SlowMo can be used as an alternative to conventional CBT for psychosis where paranoia is the main presenting problem. However, it has the flexibility to be integrated into a longer course of conventional CBT for psychosis, which is also targeting other psychosis symptoms such as auditory hallucinations.

3 Target conditions

3.1 Psychosis

Psychosis is a state of mind where a person's abilities to understand and test reality are impaired. Conditions with psychosis as a main feature are called psychotic disorders and these are characterised by "positive" and "negative" symptoms, not caused by a substance or medication, and not secondary to another medical condition or mood disorder. Psychosis caused by medications or medical conditions is called "secondary psychosis". Positive symptoms of psychosis include delusions or hallucinations where an individual believes implausible ideas usually with strong paranoia or hearing voices. Negative symptoms include impaired ability to perform everyday tasks, language impairment, abnormal motor behaviour and negative symptoms such as avolition (decreased ability to initiate tasks), alogia (inability to speak) and anhedonia (decreased ability to experience pleasure).

In England, the prevalence and incidence of psychosis are 0.7% and 24.2 per 100,000 population per year respectively (Psychosis Data Report). The prevalence and incidence of psychosis in England varies by geographical location and are associated with inequalities. Geographical variation in prevalence and incidence of psychosis is likely to be linked to the nature of the development of psychosis and its association with poverty and access to life chance opportunities.

There is evidence linking the onset of psychotic disorders with the social environment, such as: inner city living, deprivation, population density, social fragmentation and ethnic density; and individual life experiences such as childhood adversity and abuse, early experience of alcohol or substance use and abuse, discrimination and adult social disadvantage (Psychosis Data Report).

3.2 Care pathway

NICE clinical guideline for psychosis and schizophrenia treatment and management provides recommendations on the management of the condition

at different stages. Management of psychosis usually requires early intervention in psychosis (EIP) specialist teams for the first episode, or a specialist community mental health team (CMHT) for longer-term psychosis. EIP services should be accessible to all people with a first episode or first presentation of psychosis, irrespective of the person's age or the duration of untreated psychosis. In both EIP and CMHT, people living with psychosis should be offered a full range of pharmacological, psychological, social, occupational, and educational interventions.

Current practice for treatment of psychosis is with an antipsychotic medication alongside psychological and social support. NICE clinical guideline for psychosis and schizophrenia treatment and management states that standard psychological support should include provision of cognitive based therapy (CBT) to all people with psychosis delivered on a one-to-one basis over at least 16 planned sessions. It should follow a treatment manual and be led by a healthcare professional with an appropriate level of competence in delivering the intervention to people with psychosis and schizophrenia who is regularly supervised by a competent supervisor.

A person with psychosis can be discharged back to their GP if they have responded effectively to treatment and remain stable. Acute episodes of psychosis may require psychiatric hospitalisation or crisis management services.

Potential place of technologies in the care pathway

The proposed technologies for symptom management would usually be used as part of the psychological support provided by the EIP team or the CMHT. If these technologies are used as a component of the CBT for psychosis programme, they could reduce the number of CBT for psychosis sessions required. The trained therapist who would deliver the digital technologies could be less specialised than the therapists providing CBT for psychosis. Expert advice is that there is significant unmet demand for CBT for psychosis within the NHS. These technologies could also be used for people waiting to receive CBT for psychosis.

CareLoop would be used for remote monitoring of symptoms by both the EIP teams and those working in the CMHT treating people with long-term psychosis.

3.3 Patient issues and preferences

Digital health technologies to help manage symptoms of psychosis such as Avatar and SlowMo could be an option for some patients who do not have access or have limited access to specialist psychological therapy because of a lack of resources. These interventions have been designed to be used by a range of trained healthcare professionals and to be used as a component of broader psychological therapy.

CareLoop could be an option for patients who are willing to engage in remote monitoring. It may help them better understand their condition and provide their clinical teams with useful insights and the ability to intervene if there are signs of relapse or deterioration.

People may have some of the following concerns when considering whether they want to use a digital technology as part of their psychosis symptom management or relapse prevention:

- ability to use the technology
- unpredictable nature of their co-morbidities
- possible costs incurred from using digital technologies, for example mobile data charges
- level of human support provided during digitally supported management of psychosis symptoms or relapse prevention
- data security and quality control

People should be supported by healthcare professionals to make informed decisions about their care, including the use of digital technologies. Shared

decision making should be supported so that people are fully involved throughout their care (see the NICE guideline for shared decision making)

4 Comparator

The comparator for this assessment is standard care relevant to the prevailing symptoms and relapse prevention. Current standard care for psychosis is based on NICE clinical guideline for psychosis and schizophrenia treatment and management (see summary in section 3.2 above). Access to CBT for psychosis varies depending on location, and some people are on waiting lists to access services. Other forms of psychological therapy such as group therapy, supportive counselling could be available to people on the waiting list. In some areas people on waiting lists may not be offered any form of psychological support.

Monitoring of patients for relapse prevention varies across NHS services. It usually involves regular follow-ups with a care co-ordinator alongside periodic reviews by a psychiatrist. Clinical experts advised there is no formal relapse prevention process. People are often considered at high risk of relapse when there are changes to their medication or other aspects of their treatment and support.

Table 1 Scope of the assessment

Population	• People aged 14 and over living with primary psychosis Where data permits, subgroups will be considered based on: • Severity of psychosis • High risk of relapse • Age
Interventions (proposed technologies)	Digital health technologies which help manage the symptoms of psychosis including: • AVATAR Therapy for auditory hallucinations • SlowMo for paranoia

	or which provide remote monitoring of symptoms to help prevent a relapse including: • CareLoop
Comparator	<u>For AVATAR and SlowMo</u> Standard psychological care for managing symptoms of psychosis. This may include: • CBT for psychosis. The intervention could be used to replace symptom-specific components of a CBT for psychosis programme. • Psychological support whilst waiting for CBT for psychosis • No access to psychological support <u>For CareLoop</u> Standard care for monitoring people at risk of a relapse of psychosis.
Healthcare setting	• Outpatient clinic • Inpatient care • Home based care
Outcomes.	Outcomes for consideration include: <u>Symptom management</u> <u>High priority outcomes</u> • Change in targeted psychotic symptoms such as paranoia, agoraphobia, hearing distressing voice etc • Intervention adherence and completion • Health related quality of life • Patient experiences and well being • Intervention-related adverse events Other outcomes • Healthcare professional acceptance • Changes in other psychological symptoms

	• Changes in medications or appointments • Impact on carers and family <u>Relapse prevention</u> <u>High priority outcomes</u> • Rates of relapse or deterioration • Time to relapse or deterioration • Severity of relapse • Intervention adherence and completion • Patient experiences and well being • Health related quality of life • Intervention-related adverse events Other outcomes • Healthcare professional acceptance • Changes in other psychological symptoms • Impact on carers and family
Costs	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Cost of the technology including licence fees and training • Cost of healthcare professional time (various grades) to deliver therapy (both intervention and comparator) • Health service use • Cost of relapse treatment (including costs of any adverse events and hospitalisation, GP visits and mental health appointments)
Time horizon	The time horizon for estimating the clinical and economic value should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

5 Other issues for consideration

Eligible digital health technology excluded from the scope

- gameChange is a virtual reality device designed for the treatments of agoraphobia associated with paranoia. This technology is within scope but has already been assessed under virtual reality for treating agoraphobia and agoraphobic avoidance.

Characteristics of digital technologies

- The digital technologies are likely to have periodic updates and upgraded versions as new functionality becomes available. These updates may have an impact on the effectiveness of the technology. This means that evidence based on the earlier versions of the technology may not accurately reflect the effectiveness of the current versions. Evidence in older technology versions should be examined to see if it is relevant to the decision question.

Evidence

- This assessment will look across a range of evidence types including RCTs and real-world evidence. Evidence considered will include evidence of clinical effectiveness, comparative outcomes to standard care interventions, adverse effects and clinician and patient perspectives.

6 Potential 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.

Prevalence of psychosis differs between socio-economic groups. The incidence and prevalence of psychosis are higher in deprived communities. A significantly higher percentage of black men are diagnosed with psychotic disorder than white men. CORE20PLUS5, a national NHS England approach to inform action to reduce healthcare inequalities at both national and system level, lists severe mental illness (SMI) as one of the five priority areas.

Digital health technologies to help manage symptoms of psychosis and prevent relapse are accessed via a mobile phone, tablet, or computer. People may need regular access to a device with internet access to use the technologies. Additional support and resources may therefore be needed for people who are unfamiliar with digital technologies or people who do not have access to smart devices or the internet. People with visual, hearing, 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) or neurodivergent people may need additional support to use digital health interventions. Some people would benefit from digital health technologies in languages other than English. People's ethnic, religious, and cultural background may affect their views of digital health interventions. Healthcare professionals should discuss the language and cultural content of digital health interventions with patients before use.

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

7 Potential implementation issues

Training

Training is needed for healthcare professionals to work through and fully understand the intervention modules and content. Knowledge of the technologies will vary across healthcare professionals, within services, and across regions. This will impact the delivery and effectiveness of the interventions.

Cost

Costs may differ between technologies. Smaller service areas may have higher costs per user because fewer licences are needed. Digital health interventions may be chosen based on the balance between costs and expected outcomes.

Risk of harm

Digital health technologies must be able to identify potential risks for patients. Initial assessment is important to ensure people get access to the right care at the right level. Some digital health interventions have inbuilt processes to flag the need for more intervention. This is important to consider when choosing digital health technologies.

8 Authors

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Date 4 September 2023

Appendix C Abbreviations

CBT: Cognitive Behavioural Therapy

CE: Conformité Européene (European Conformity)

CMHT: Community Mental Health Team

DTAC: digital technology assessment criteria

EIP: Early Intervention in Psychosis

EVA: Early Value Assessment

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

SMI: Severe Mental Illness

UKCA: United Kingdom Conformity Assessed

Document cover sheet

Assessment report: Psychosis EVA

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EAG sign off: Rhys Morris

Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
0.1	First version	SB	11/09/2023	
0.2	Decision problem, overview of technology, clinical context	SB	26/09/2023	
0.3	Clinical evidence selection, added in search details, clinical evidence review, and evidence gap analysis Review and addition of Adverse events section.	SB LK	27/09/2023 02/10/2023	
0.4	Economic and clinical sections merged	SB	02/10/2023	
0.5	RM review	SB	02/10/2023	
0.6	Final additions	SB, MD, HYC, SW	03/10/2023	
1.0	Final additions and review	LK	03/10/2023	
1.1	Addressed NICE's comments	SB	13/10/2023	
1.2	Interpretation of clinical evidence section	SB	17/10/2023	

1.3	Review and updates to various sections	MG, HYC, SB, LK	23/10/2023	
1.4	Executive summary	MG, HYC, SB, LK	27/10/2023	
1.5	Review	LK, RM	30/10/23	
1.6	Amendments after final review	MD, SB, HYC	31/10/23	
2.0	Final version	LK	31/10/23	
2.1	Addressing fact check comments	SB, MD, HYC, LK	13/11/23	
3.0	Final version following fact check	LK	14/11/23	
4.0	Final version following additions requested from NICE	LK, SB, HYC, MD	23/11/23	

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Early Value Assessment

GID-HTE10020 Digital health technologies to help manage symptoms of psychosis and prevent relapse

External Assessment Group report

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Date completed: 31/10/2023

Contains confidential information: Yes

Number of attached appendices: 8

Purpose of the assessment report

The purpose of this External assessment group (EAG) report is to review the evidence currently available for included technologies and advise what further evidence should be collected to help inform decisions on whether the technologies should be widely adopted in the NHS. The report may also include additional analysis of the submitted evidence or new clinical and/or economic evidence. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about the early value assessment.

Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

None

Acknowledgements

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Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Any [redacted] information in the submission document should be underlined and highlighted in turquoise.

Any [redacted] information in the submission document should be underlined and highlighted in yellow.

Contents

List of Tables

List of Figures

Abbreviations

Term	Definition
CBTp	Cognitive behaviour therapy for psychosis
CEA	Cost effectiveness analysis
CI	Confidence interval
CMHT	Community mental health team
DHSC	Department of Health and Social Care
DSA	Deterministic sensitivity analysis
EAG	External assessment group
EIP	Early intervention in psychosis
EMR	Electronic medical records
HCP	Health care professional
HRG	Healthcare resource groups
IQR	Interquartile range
ITT	Intention to treat
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
MTEP	Medical Technologies Evaluation Programme
NCC	National cost collection
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
NICE MTG	NICE medical technology guidance
NICE QS	NICE quality standard
NMB	Net monetary benefit
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta - Analyses
PSA	Probabilistic sensitivity analysis
PSSRU	Personal Social Services Research Unit
PSYRATS-AH	Psychotic Symptom Rating Scales, auditory and hallucination
PSYRATS-DEL	Psychotic Symptom Rating Scales, delusions
QALY	Quality adjusted life year
QUORUM	Quality of Reporting of Meta -analyses
RCT	Randomised controlled trial
R-GPTS	Revised Green et al., Paranoid Thoughts Scale
SD	Standard deviation
SMR	standardised mortality ratio
TAU	Treatment as usual
VAS	Visual analogue scale
VAT	Value added tax
Vs	Versus

Glossary

Term	Definition
Primary psychosis	A group of mental disorders where the symptoms of psychosis are the primary features of the disorder, and not secondary to an affective disorder (such as bipolar disorder or unipolar psychotic depression), or caused by medications or other medical conditions.
Affective psychosis	A group of mental disorders where the symptoms of psychosis come secondary to a mood disorder (such as bipolar disorder or unipolar psychotic depression).

Executive summary

Background

1.1 *The technology and clinical context*

The purpose of this early value assessment is to review 3 digital health technologies, that will be available through the NHS, that are designed to provide support for the treatment of psychosis. All technologies have regulatory approval, or are actively working towards regulatory approval. These technologies are AVATAR therapy, SlowMo, and CareLoop.

AVATAR therapy

AVATAR therapy is CE-marked class I medical device, intended for the treatment of distressing auditory verbal hallucinations. It allows a conversation between the person hearing voices, the distressing voice, and the therapist, using a digital avatar as a representation of the distressing voice. Over 6 to 12 sessions, people are encouraged to engage in dialogue with this avatar to take control within the conversation with the distressing voice.

SlowMo

SlowMo is a UKCA/CE-marked class I medical device intended to reduce distressing worries and paranoia in those with psychosis. SlowMo works by supporting users to recognise their unhelpful fast thinking habits and slow down their thinking to find ways of feeling safer and living well. SlowMo involves 8 sessions with a therapist (face-to-face or remote) which are supported by a webapp (displayed via the therapist's desktop, laptop, or tablet device), with content synchronised to a mobile app on the patient's smartphone for use outside of sessions.

CareLoop

CareLoop is a remote monitoring system for people with psychosis that facilitates relapse prevention through identification of symptoms allowing appropriate intervention. It uses an app where people record symptoms, and their thoughts and feelings, through questionnaires and journal entries. It relies on an algorithm to recognise deterioration in a person's mental health, and to identify potential relapse. This information is then fed to health care professionals who then provide early intervention to prevent relapse.

Further details about these technologies in found in Table 2.

1.2 *Decision problem*

The 3 technologies have been divided into 2 categories – symptom management for AVATAR therapy and SlowMo, and relapse prevention for CareLoop. They have been assessed for use with people over the age of 14

who are living with primary psychosis. These people will primarily be receiving care in secondary mental health services, EIP and CMHT services. This includes outpatient clinics and home-based care. Those receiving inpatient care will also be considered. The high priority outcomes for symptom management includes changes in targeted psychotic symptoms, and for relapse prevention includes; rates of relapse or deterioration, time to relapse or deterioration, and severity of relapse. For all technologies it includes; health related quality of life, patient experiences and wellbeing, intervention adherence and completion, and intervention related adverse events. Other outcomes for all technologies include; healthcare professional acceptance, changes in other psychological symptoms, and impact on family and carers. For cost analysis, costs have been considered from an NHS and Personal Social Services perspective. Considerations have been made for the cost of the technology, the cost of healthcare professional time, health service use, and the cost of relapse treatment.

Further details about the decision problem can be found in Table 1.

Summary of clinical evidence

1.1 Key studies and results

The EAG included 12 studies in total across 13 publications. The EAG also presents unpublished data from the AVATAR2 study. Five studies for AVATAR therapy, 4 for SlowMo, and 3 for CareLoop were included. For all technologies, the studies are reported in peer-reviewed full text publications. For AVATAR therapy, these include 2 RCTs (Leff 2013, and Craig 2018), an observational study (Rus-Calafell 2020), 1 published protocol (Garety, 2021a) and a qualitative study (Rus-Calafell 2022). For SlowMo, these include an RCT (Garety 2021b), a qualitative study (Greenwood 2021), and 2 observational studies (Hardy 2022 and Ward 2022). There is an additional HTA report (Garety et al, 2021c) which reports the findings from Garety et al (2021b) in more detail. However, as there were no additional findings that would be included from the HTA report, we will only refer to Garety et al (2021b) for the purpose of this EVA. For CareLoop, these include 2 RCTs (Lewis 2020 and Gumley 2022a and b (Journal article and HTA report)), and 1 qualitative study (Allan 2023). Further details about the study selection procedure can be found in Section 4.

Leff (2013) compares AVATAR therapy to treatment as usual, and Craig (2018) compares it to supportive counselling. Results from both indicate that it is effective at improving symptoms of auditory verbal hallucinations in people with psychosis over the medium term. This includes a decrease in voice frequency and the distress caused from voices, an increased acceptance of voices, and less negative and more positive associations of voices. The

results do not indicate that it is effective at reducing more general symptoms of psychosis or mental health symptoms. Results from 1 study indicate that it is effective at decreasing anxiety and paranoia. Results from the 1 qualitative study indicate that it is acceptable to those that completed the therapy, and that no negative long-term effects were reported.

[redacted]

The 1 RCT for SlowMo compared its use to usual care. The results from this indicate that it is effective at reducing delusions and paranoia in people with psychosis over the medium term. It is also effective at improving the quality of life of people with psychosis. Results from the 1 qualitative study indicate that SlowMo was helpful for some users, and can provide users with new skills to help manage their symptoms. A subjective reduction in other mental health symptoms, as well as feeling more confident and sociable, were also reported. One study for SlowMo reports on a digital divide that exists between subgroups of the population. There are significant differences in smartphone ownership, and the ability and confidence using smartphones. There were also significant differences in the self-reported use of the app. There also exists evidence showing that SlowMo therapy is acceptable for use by people with psychosis, and therapy fidelity is high for those using it.

Results from CareLoop are mixed. Both RCTs compared CareLoop to standard care. The first RCT assessed the use of CareLoop over 12 weeks. It indicates that CareLoop had no impact on any outcome measures, which includes symptoms of psychosis. Its accuracy at detecting relapses in psychosis are also suboptimal compared to standard care. The relapse prediction algorithm of CareLoop was improved because of this study, and then assessed in its second RCT. The second RCT indicates that CareLoop was effective at preventing and delaying relapses, and was also effective at reducing positive and negative symptoms of psychosis. The qualitative study for CareLoop indicates that CareLoop is acceptable to users, and that usage of the app was high and users were engaged in its use.

Further details about the studies selected as evidence can be found in Table 3.

1.2 Quality appraisal summary

The EAG considers the larger RCT (Craig 2018) for AVATAR therapy to be of high quality. It is powered to detect an effect with a large sample size, and includes a large number of relevant outcome measures within scope. It is compared against supportive counselling which is not necessarily standard care for psychosis. The smaller proof of concept RCT (Leff 2013) is of moderate quality. It has a small sample size, and the diagnoses of participants is not reported. It is a partial crossover study, and those that began in the treatment arm did not crossover to the control arm afterwards. Neither studies reported adverse events. The qualitative studies for AVATAR therapy are good quality studies that provide useful subjective experience data of using AVATAR therapy.

The EAG considers the RCT for SlowMo (Garety 2021b) to be of high quality. It is powered to detect an effect with a large sample size. It includes a large number of relevant outcomes measures within scope. It is compared against standard care alone, defined as typically involving antipsychotic medication, contact with a mental health worker, and outpatient appointments. The effects of time spent with mental health workers were not controlled for however. The qualitative data is good quality and provides useful subjective experience data of using SlowMo.

The EAG considers there to be some good quality evidence for the efficacy of CareLoop. Lewis (2020) has a relatively moderate-sized sample but no power calculations are reported. The study did not find any data to show effectiveness. Gumley (2022a and b), is a good quality feasibility study that shows clinical efficacy of CareLoop's relapse prevention, however it was not fully powered. It shows the feasibility of a larger powered RCT. Additionally, it did show the acceptability and usability of the CareLoop app for users. The qualitative study for CareLoop provides good qualitative data regarding how well CareLoop was implemented by people and staff using it.

Further details about the quality appraisal can be found in Section 5.1.

Summary of economic evidence

1.3 Economic evidence

Two technologies (AVATAR and CareLoop) had available within trial economic analyses, while none were identified for SlowMo (Section 10.1 and Table 12)

For AVATAR, an unpublished economic analysis (Morris, unpublished) based on the Craig (2018) RCT found that the trial arm using AVATAR [redacted]

[redacted] compared to supportive counselling. Quality of life was collected using EQ-5D-5L and was not mapped to EQ-5D-3L for utility calculation. Over the 24-week period, [redacted] after controlling for baseline utility than the comparator. The authors reported a [redacted].

For CareLoop, Gumley (2022b) included a within trial economic analysis as part of the HTA report. The authors found that CareLoop incurred slightly lower costs (£251 cost saving over 1 year, non-significant) compared to treatment as usual. Over a one-year period, there was a mean QALY gain of 0.056 in CareLoop participants compared to treatment as usual. Costs and utilities were adjusted for baseline values, country, age and gender. Quality of life was collected using EQ-5D-5L and was mapped to EQ-5D-3L for utility calculation, as recommended by NICE. Key limitations are that the study is a small feasibility study and some costs are mixed for Australian and UK participants.

1.4 Economic model, including EAG changes

For the two technologies that address symptom management, the EAG have used a cost consequences approach. These find that both technologies are likely to cost more to deliver than waiting list, psychological group support, or as an adjunct to treatment as usual, but are likely to be less costly to deliver than individual CBTp. The available evidence found them more effective than the comparators used. Additional detail is presented in Section 10.2 with results and limited comparison to CBTp in Section 10.3, Table 18 and Table 19 The EAG calculated that delivering the interventions over a 3-year period (allowing for equipment purchase, training 10 clinicians and treatment of 100 patients per year, based on company estimate per trust per year) would cost £548 per patient for AVATAR, and £826 per patient for SlowMo. The largest cost for each of these is clinician time for face to face sessions.

	Adjusted mean difference between groups (95%CI)			
	AVATAR vs supportive counselling	**Source**	**SlowMo+TAU vs TAU**	**Source**
Costs per patient				
Intervention delivery only	£218 (unadjusted)	EAG calculation	£826 (Unadjusted)	EAG calculation
Health care resource use (including intervention)	24 weeks[redacted]	(within trial analysis, unpublished)	Not available	
Outcomes:				

Symptom scores	12 weeks: -3.82 24 weeks: -1.55	PSYRATS-AH-Total (Craig 2018)	12 weeks: -1.53 24 weeks: -1.55	PSYRATS-DEL-Total (Garety 2021b)
QALYs	24 weeks: [redacted]	based on EQ-5D-5L, (within trial analysis, unpublished))	0.014 (unadjusted) 0.013 (Unadjusted)	EAG calculation using R-GPDS social reference & R-GPTS persecution

For symptom monitoring and relapse prevention, the EAG calculated that delivering CareLoop over a 3-year period (allowing for equipment purchase, training 100 Care Coordinators and monitoring 1000 patients per year, based on company estimate per trust per year) would cost [redacted] per patient per year.

For CareLoop, the EAG were able to complete economic modelling using a healthcare perspective and a 3-year time horizon. A Markov model with 1-year cycle length and stable or relapse states was used, as reflected in many existing models. Over the 3-year time horizon, the model finds that CareLoop strategy is less costly and more effective. The cost of delivering CareLoop is less than the savings because of fewer people experiencing relapses and a lower proportion requiring hospital stays. The key limitation for this finding is that the clinical evidence is from a small pilot study (Section 10.3 and Table 20).

	Standard care without CareLoop monitoring	Standard care with CareLoop monitoring	Incremental (CareLoop-Std Care only)
Total costs	£56,802	[redacted]	[redacted]
Total QALYs	2.24	2.27	0.03

Key evidence gaps

Key point	Description
Limited peer-reviewed data	The evidence for AVATAR therapy and SlowMo is limited to 1 large powered RCT each. For CareLoop, there are no fully powered studies demonstrating efficacy.
Lack of evidence for relapse prevention	Additional evidence for CareLoop to further support the claim of relapse prevention is needed through a fully powered RCT.
Symptom use	For AVATAR and SlowMo there is no evidence available to link the change in symptoms to changes in health care

	resource use that might be used to model intermediate time horizons.
Lack of longer term follow up and evidence to inform modelling	For AVATAR and SlowMo there is no evidence available on the longer-term impacts such as relapses.

1 Decision problem

Full details of the decision problem can be found in the topic Scope Document and key elements are outlined in Table 1.

Table 1: Decision Problem

Decision problem	Scope	EAG Comment
Population	People aged 14 years and older living with primary psychosis. Where data permits, subgroups were considered for: • Severity of psychosis • High risk of relapse • Age	High risk of relapse as a subgroup is only relevant to the use of CareLoop. In some of the studies used for evidence, diagnoses of affective psychosis are included within the study sample. The EAG will consider these on a case by case basis, and include a summary highlighting any potential limitations.
Intervention	Digital health technologies which help manage the symptoms of psychosis including: • AVATAR Therapy for auditory hallucinations • SlowMo for paranoia Or which provide remote monitoring of symptoms to help prevent a relapse including: • CareLoop	
Comparator(s)	For AVATAR and SlowMo Standard psychological care for managing symptoms of psychosis. This may include: • CBTp. The intervention could be used to replace symptom-specific components of a CBTp programme • Psychological support whilst waiting for CBTp • No access to psychological support For CareLoop Standard care for monitoring people at risk of a relapse of psychosis.	There is currently no formal relapse prevention process. Monitoring of patients for relapse varies across NHS services.
Healthcare setting	• Outpatient clinic • Inpatient care • Home based care	The use of AVATAR and SlowMo for the management of symptoms would apply to people who are receiving care at all these locations. The use of CareLoop for monitoring people at risk of relapse applies primarily to people who are receiving care in early intervention services; community mental health teams; crisis intervention services; rehabilitation services; home-based treatment teams.
Outcomes	High priority outcomes for symptom management include: • Change in targeted psychotic symptoms such as paranoia, agoraphobia, hearing distressing voice etc • Health related quality of life	

	• Patient experiences and well being • Intervention adherence and completion • Intervention related adverse events High priority outcomes for relapse prevention include: • Rates of relapse or deterioration • Time to relapse or deterioration • Severity of relapse • Intervention adherence and completion • Patient experience and wellbeing • Health related quality of life • Intervention-related adverse events Additional outcomes relevant to both include; healthcare professional acceptance, changes in other psychological symptoms, and impact on family and carers.	
Cost analysis	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Cost of the technology including licence fees and training • Cost of healthcare professional time (various grades) to deliver therapy (both intervention and comparator) • Health service use • Cost of relapse treatment (including costs of any adverse events and hospitalisation, GP visits and mental health appointments)	
Study Design		All study designs will be considered and the decision to include or exclude a study based on design will be made on a technology by technology basis.

2 Overview of the technology

Included in this early value assessment (EVA) are digital health technologies, available in the NHS, that are designed to provide specialist support for managing symptoms of psychosis or to prevent relapse in people with psychosis who are receiving care from healthcare professionals. All technologies included have regulatory approval or are actively working towards regulatory approval, specifically DTAC and CE or UKCA mark where needed, and are available for use in the NHS.

The purpose of this EVA is to summarise and critically appraise the existing evidence of these technologies. The aim is to evaluate clinical-effectiveness and cost-effectiveness, identify evidence gaps, and highlight any risks

associated with the potential use of these technologies in the NHS whilst further evidence is generated.

2.1 *Included technologies*

Three digital health technologies for people with primary psychosis were identified as relevant to the assessment. These are summarised in Table 2.

Table 2: Summary of Technologies

Technology (Company)	Regulatory Status	Delivery	Key Features	EAG Comments
AVATAR Therapy	Class I Medical Device under CE Partially completed DTAC, with plans to complete it in the coming months	Software based download on laptop or desktop PC	• For the treatment of distressing auditory verbal hallucinations • It allows a three-way conversation between the person hearing voices, their distressing voice, and the therapist • Uses a digital avatar as a digital representation, both visually and audibly, of the distressing voice created by the person hearing voices • Using video conferencing, the person hearing voices engages in dialogue with the avatar to take power and control within the conversation • Treatment is provided over 6 to 12 sessions either alone, or as a component of CBTp	Literature searching revealed the existence of other more generic avatar therapies, where the term 'avatar' is used to describe a digital representation of a person. This assessment focuses on the assessment of the named 'AVATAR therapy' as developed by researchers at University College London. Some evidence found was a combination of AVATAR Therapy and immersive virtual reality. This iteration of AVATAR Therapy was considered out of scope for this assessment.
CareLoop (CareLoop Health)	[redacted]	Mobile app delivered via smart phone users Web-based for the clinical team	• A remote monitoring system for people with psychosis that facilities early identification and intervention when symptoms escalate • Users record symptoms daily, using proprietary questionnaires, and can add journal entries of their thoughts and feelings • Users' data is stored on a cloud-based system • It uses an algorithm that is designed to recognise changes in mental health to identify deterioration, and predict relapses • It can generate insights at an individual level to optimise treatment and care	'CareLoop for Psychosis' is the full name of the intervention being considered for this assessment. ClinTouch is the original name for the smartphone app, and one of the studies refers to it as such. After improvements were made following this study, the app was renamed to EMPOWER. The app was then renamed to CareLoop for Psychosis. CareLoop also exists for perinatal health to screen and treat postnatal depression.

				This assessment does not consider CareLoop in this context.
SlowMo	Class I Medical Device under CE In the process of completing DTAC application. Aiming for Dec 2023.	Desktop PC, laptop and/or smart device. Non-digital options are available	• Aims to reduce distressing worries and paranoia by supporting users to notice their unhelpful fast thinking habits • Combines face-to-face therapy with interactive digital content such as stories and games • Personalised therapy session content is synchronised with the app to provide strategies to combat fast thinking in daily life • Proposed as an alternative to CBTp where paranoia is the main presenting problem	Does generally need to be used with other forms of CBTp depending on the symptoms present.

3 Clinical context

Guidance on the management of psychosis at different stages is provided by NICE clinical guidance for psychosis and schizophrenia in adults. This covers adults over the age of 18. Guidance on the management of psychosis for people under the age of 18 is provided by NICE clinical guidance for psychosis and schizophrenia in children and young people. The scope of this assessment covers people over the age of 14 living with psychosis, making both NICE CG relevant. Guidelines for the management of adults with complex psychosis is provided by NICE clinical guidance for rehabilitation for adults with complex psychosis.

Management of psychosis usually requires early intervention in psychosis (EIP) specialist teams for the first episode, and a specialist community mental health team (CMHT) for longer-term psychosis. EIP services should be accessible to all people with a first episode or first presentation of psychosis, irrespective of the person's age or the duration of untreated psychosis. In both EIP and CMHT, people living with psychosis should be offered a full range of pharmacological, psychological, social, occupational, and educational interventions.

Current practice for treatment of psychosis is with an antipsychotic medication alongside psychological and social support. The NICE clinical guideline for psychosis and schizophrenia treatment and management states that psychological support should include provision of cognitive based therapy for psychosis (CBTp) to all people with psychosis delivered on a one-to-one basis over at least 16 planned sessions. It should follow a treatment manual and be led by a healthcare professional with an appropriate level of experience in delivering the intervention to people with psychosis and schizophrenia who is regularly supervised by a competent supervisor.

Management of psychosis through EIP services should be available for 3 years at a minimum, with the possibility of extending this if the person has not made a stable recovery from psychosis. If a person’s symptoms respond effectively to treatment and remain stable, the option to be transferred back to primary care should be offered. If a person then presents with a suspected relapse, then consideration of re-referral to secondary care services should be made.

Monitoring of patients for relapse prevention varies across NHS services. It usually involves regular follow ups with their care co-ordinator every 6-12 weeks, and with a psychiatrist every 6-12 months. There is no formal relapse prevention process in the NHS.

Potential place of digitally enabled therapies in the care pathway

The proposed technologies for symptom management (AVATAR, SlowMo) would usually be used as part of the psychological support provided by the EIP team or the CMHT. If these technologies are used as a component of the CBTp programme, they could reduce the number of CBTp sessions needed. The trained therapist who would deliver the digital technologies could be less specialised than the therapists providing CBTp. Expert advice suggests there is significant unmet demand for CBTp within the NHS. These technologies could also be used for people waiting to receive CBTp.

CareLoop focuses on relapse prevention as well as symptom monitoring. It would be used for remote monitoring of symptoms by both the EIP teams and those working in the CMHT treating people with long-term psychosis. Usually, a care co-ordinator from community nursing will take on the role of co-ordinating health and social care for people under mental health services for psychosis. This will be the person that will receive alerts from CareLoop, and be responsible for ensuring the patient is appropriately followed up.

Special considerations, including issues related to equality

Digital inequity needs to be considered as 1 of the 3 technologies would need people to have regular access to a smartphone capable of running the CareLoop app. SlowMo requires patient access to a mobile app. However, this only requires a data connection for initial install or for optional data synching during therapy sessions. Paper based alternatives are available..

4 Clinical evidence selection

4.1 *Evidence search strategy and study selection*

The EAG did literature searches to ensure that all relevant evidence had been identified. The EAG literature searches identified a total of 601 records. Details of the EAG searches are provided in Appendix A.

Our criteria for inclusion were an appropriate diagnosis of a primary psychotic disorder and use of one of the 3 included technologies. Exclusion criteria included any results that were deemed as out of scope for outcomes, indication and technologies, and any studies where the technologies were used in conjunction with other technologies (for example virtual reality in conjunction with AVATAR).

A total of 12 published studies, reported in 13 publications, are included in the clinical review and are summarised in Table 3 below. There were 3 studies for CareLoop, 4 for SlowMo, and 5 for AVATAR. Appendix B shows those studies excluded at full text review. Appendix C shows the study selection process in

the form of a PRISMA diagram. Unpublished results from the AVATAR2 trial is also presented in the results section.

With AVATAR, there was some confusion regarding the specifics of the technology. A few studies were found in literature searching that had taken AVATAR therapy as described here, and added additional elements to it. Most notably was the inclusion of immersive VR that was used to view the avatar. After discussing with the NICE technical team, it was decided that only AVATAR in its original form would be considered within scope of this EVA. Therefore, these studies were not considered within scope and were excluded.

With CareLoop, there was initially some confusion regarding the specifics of the technology. A previous iteration of the technology known as ClinTouch was found during literature searching. After discussing with the NICE technical team, it was decided that ClinTouch would be considered within scope for this EVA.

A rating of **GREEN** indicates an element that meets the scope fully, **AMBER** meets the scope partially, and **RED** does not meet the scope.

Table 3: Studies selected by the EAG as the evidence base

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
AVATAR Therapy				
Study: Garety 2021a(AVATAR2) **Location:** UK	**Design:** Multi-site parallel group randomised controlled trial **Aim:** To determine treatment efficacy and cost-effectiveness of brief and extended version of AVATAR therapy in the NHS **Intervention:** AVATAR Therapy. Two arms: 1 of 6 sessions, 1 of 12 sessions. Referred to as AVATAR-Brief and AVATAR-Extended respectively **Comparator:** Treatment as usual **GREEN**	**Participants:** N=345 people receiving care for psychosis from NHS psychiatric services, who have current frequent and distressing voices **Setting:** NHS psychiatric services **AMBER**	Follow up at 16 and 28 weeks from the start of treatment **Primary outcome:** • Score of distress dimension of Psychotic Symptom Rating Scales, auditory hallucinations subscale (PSYRATS-AH) at 16 and 28 weeks **Secondary outcomes:** • Total score of PSYRATS-AH • Score of frequency dimension of PSYRATS-AH • Hallucinations Remission Score • Revised Beliefs about Voices Question (BAVQ-R) • Voice Acceptance and Action Scale (VAAS) • First item (power) from the Voice Power Differential Scale (VPDS) • Psychotic Symptoms Rating Scale – Delusions (PSYRATS-DEL) • Beck Depression Inventory-II (BDI) • Depression Anxiety and Stress Scales (DASS-21) • EQ-5D-5L • Warwick-Edinburgh Mental Well-being Scale • Choice of Outcome in CBTp (CHOICE) • International Trauma Questionnaire (ITQ) **GREEN**	This study is not published, but the study team have provided the EAG with access to the early results. The information provided here was obtained from the study's published protocol. Potentially a good quality study. Large sample size. Outcomes all within scope. Inclusion criteria includes those diagnosed with affective psychosis, which is out of scope.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Study: AVATAR 1 Craig (2018) **Location:** UK	**Design:** Single centre, assess-blinded RCT **Aim:** To determine clinical efficacy of AVATAR Therapy in reducing the frequency and severity of auditory verbal hallucinations **Intervention:** AVATAR Therapy. One introduction session followed by 6 weekly 50-minute sessions **Comparator:** Supportive counselling. One introduction session followed by 6 weekly 50-minute sessions. **GREEN**	**Participants:** N=150 people receiving care for psychosis from NHS psychiatric services, that have experienced distressing auditory verbal hallucinations for at least 12 months • 77% diagnosed with schizophrenia • 11% diagnosed with schizoaffective disorder • 5% diagnosed with bipolar disorder • 5% diagnosed with unspecified psychosis • 3% diagnosed with depression with psychotic symptoms **Setting:** NHS psychiatric services **AMBER**	Follow up at 12 and 24 weeks from the start of treatment **Primary outcome:** • Total score of Psychotic Symptom Rating Scales, auditory hallucinations subscale (PSYRATS-AH) at 12 weeks **Secondary outcomes:** • Dimensional subscales of PSYRATS–AH; voice frequency, and voice distress • BAVQ-R • VAAS • VPDS • Scale for Assessment of Positive and Negative Symptoms (SAPS and SANS) • PSYRATS-DEL • DASS-21 • Calgary Depression Scale (CDS) • Rosenberg self-esteem • Manchester Short Assessment of Quality of Life (MANSA) • Maudsley Addiction Profile (MAP) **GREEN**	Good quality study. Powered with a large sample size. Outcomes are all within scope. Diagnosis included those with affective psychosis, which is out of scope. Comparison is not standard care, but supportive counselling that can be effective at treating symptoms. Information regarding any adverse events is not reported. The sum of the percentages of participant diagnoses equals 101%. This is how it was reported in the publication.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Study: Leff (2013) **Location:** UK	**Design:** Single centre, assess-blinded, partial crossover RCT **Aim:** Proof-of-concept study for AVATAR Therapy **Intervention:** AVATAR Therapy. Six 30-min sessions over 7 weeks (immediate therapy group) **Comparator:** Treatment as usual for 7 weeks (delayed therapy group) **GREEN**	**Participants:** N=26 people aged 14-75 from a single CMHT hearing persecutory voices for at least 6 months, and who had not responded adequately to antipsychotic medication **Setting:** NHS CMHT **AMBER**	Follow up at 1 week and 3 months from the end of treatment **Outcomes (no primary outcome):** • PSYRATS • BAVQ-R • CDS **GREEN**	Moderate quality study. Small sample size. Immediate therapy group did not crossover to TAU following intervention. Outcomes are all within scope. Diagnosis is not reported, possibly includes non-primary psychosis diagnoses. Information regarding any adverse events is not reported.
Study: Rus-Calafell (2020) **Location:** UK	**Design:** Observational sub-study of RCT (Craig 2018) **Aim:** To assess the impact that the contribution of sense of voice presence, together with a reduction in anxiety and paranoid attributions about the avatar, has on primary therapy outcomes following AVATAR therapy **GREEN**	**Participants:** N=39 people that participated in Craig (2018) **Setting:** NHS CMHT **GREEN**	Follow up at 12 weeks from the start of treatment **Outcomes:** • PSYRATS-AH • BAVQ-R • State Social Paranoia Scale • Sense of Presence Scale • Anxiety VAS **GREEN**	Observational sub-study to Craig (2018). Small sample size. Provides insight into how AVATAR therapy works. Reports on outcomes impacted by AVATAR therapy not covered by Craig (2018), but still in scope.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Study: Rus-Calafell (2022) **Location:** UK	**Design:** Semi-structure interviews sub-study of RCT (Craig 2018) **Aim:** To explore participant experience of receiving AVATAR Therapy as part of the Craig (2018) study **GREEN**	**Participants:** N=14 people that completed AVATAR Therapy as part of the Craig (2018) study. One person did not complete **Setting:** NHS psychiatric services **AMBER**	**Outcomes (no primary outcome):** Semi-structured interviews were done. These explored: • Reason to participate in the study • Experience of creating the 'avatar' • Experience of dialoguing with the avatar • Reflections on therapy sessions • Use of the MP3 player • Impact of the therapy on voices and everyday life • The therapist • Post therapy experience • Overall experience • Software improvement **GREEN**	Good quality study providing useful insight into the subjective experience of AVATAR Therapy. People that did not complete AVATAR Therapy from having a negative experience are unrepresented (only 1 interviewed). Small sample size.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
SlowMo				
Study: Garety (2021b) **Location:** UK	**Design:** Parallel-arm, assessor-blinded, RCT **Aim:** To investigate the effects on paranoia and mechanisms of action of SlowMo, a digitally supported reasoning intervention, plus usual care compared with usual care only **Intervention:** SlowMo - 8 digitally supported face to face sessions with mobile app, plus usual care **Comparator:** Usual care alone **GREEN**	**Participants:** N=363 people diagnosed with schizophrenia spectrum psychosis with distressing, persistent paranoia **Setting:** Community health setting **GREEN**	Follow up at 12 and 24 weeks from the start of treatment **Primary outcome:** • Green et al Paranoid Thoughts Scale (GPTS) score at 24 weeks **Secondary outcomes:** • GPTS score at 12 weeks • GPTS part A and B scores • PSYRATS • Adherence • MANSA quality of life score **GREEN**	Good quality study. Large sample size. Outcomes are all within scope. Primary outcome was self-reported, and not observer rated. However, 2 standard observer rated assessments of the same outcome were included. Includes only people diagnosed with primary psychosis. Adverse events are reported. The effects of time with a therapist was not controlled for in the TAU group.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Study: Greenwood (2021) **Location:** UK	**Design:** Qualitative co-produce sub-study of an RCT (Garety 2021b) **Aim:** To explore the subjective service-user experience of the SlowMo therapy content and design; the experience of the blended therapy approach, including the triangle of the therapeutic alliance; and the experience of the digital aspects of the intervention **GREEN**	**Participants:** N=22 people that took part in Garety (2021b) who had completed 1 session of SlowMo, and the 24 week follow up **Setting:** Community health setting **GREEN**	**Outcome:** Develop and validate theme structure from qualitative interviews to address the aims of the study **GREEN**	Good qualitative study providing insight into the subjective experience of using SlowMo, and the impact it can have on quality of life. Unclear if those that volunteered to be interviewed were more positive about therapy.
Study: Hardy (2022) **Location:** UK	**Design:** Observational sub-study of the SlowMo RCT (Garety 2021b) **Aim:** To explore the "digital divide" and mobile app engagement in the SlowMo randomized controlled trial **GREEN**	**Participants:** Those that took part in Garety (2021b) **Setting:** Community health setting **GREEN**	Follow up 12 weeks from the start of treatment **Outcome:** • Digital literacy • Adherence • Engagement using a User Experience Survey (UES) **GREEN**	Qualitative study providing insight into the usability of the SlowMo app. Quantitative data regarding digital literacy and user experience is reported.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Study: Ward (2022) **Location:** UK	**Design:** Narrative account of SlowMo as delivered through Garety (2021b) **Aim:** To provide a comprehensive account of SlowMo therapy, and to provide data on session adherence and behavioural work adherence **GREEN**	**Participants:** N=181 that received SlowMo as part of Garety (2021b) **Setting:** Community health setting **GREEN**	**Outcome:** • Therapy engagement and withdrawals • Session adherence • Behavioural work adherence **GREEN**	While this study is not a clinical study, it reports on patient adherence to SlowMo, and so contains data within the scope.
CareLoop				
Study: Lewis (2020) **Location:** UK	**Design:** Open RCT **Aim:** To assess the acceptability of continuous monitoring to SMI patients and health professionals over 3 months, the impact of active self-monitoring on positive psychotic symptoms assessed at 6 and 12 weeks and the feasibility of detecting early warning signs of relapse **Intervention:** ClinTouch symptom monitoring for 12 weeks **Comparator:** Treatment-as-usual **GREEN**	**Participants**: N=81 people diagnosed with schizophrenia or related disorders aged 16-65 **Setting:** NHS CMHT and EIP team **GREEN**	Follow up 6 and 12 weeks from randomisation **Outcomes (no primary outcome):** • Positive and Negative Syndrome Scale (PANSS) • Global Assessment of Functioning (GAF) • Empowerment rating scale (ERS) • Efficacy of early warning signs algorithm **GREEN**	ClinTouch is an earlier iteration of CareLoop, the results of this study lead to improvements being made. This study did not show any impact of ClinTouch to predict relapse in psychosis. Moderate sample size. Short follow up of only 12 weeks.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Study: Gumley (2022a and b) **Location:** UK	**Design:** Multicentre, feasibility, cluster randomised controlled trial **Aim:** To establish the feasibility of undertaking a definitive randomised controlled trial to determine the effectiveness of a blended digital intervention for relapse prevention in schizophrenia **Intervention:** EMPOWER relapse prevention over 12 months **Comparator:** Treatment-as-usual **GREEN**	**Participants**: N=74 people diagnosed with schizophrenia or related disorders aged 16+ **Setting:** NHS CMHT **GREEN**	Follow up 12 months from the start of treatment. **Outcomes:** • Feasibility, acceptability, usability, and safety were the main outcomes • Relapse • Fear of relapse • PANSS **GREEN**	Good quality feasibility study with moderate sample size. Long follow up period. Feasibility study and so not fully powered. Shows feasibility of a larger study and acceptability and usability of the CareLoop app. This study is reported in two separate publications, this and the HTA report Both were used for data extraction.

Study: Allan (2023) **Location:** UK	**Design:** Qualitative Semi-structured one-on-one interviews **Aim:** Understand implementation of EMPOWER, including barriers and facilitator **GREEN**	**Participants**: N=16 people that participated in Gumley (2022a and b), N=6 mental health staff, and N=1 carer **Setting:** NHS CMHT **GREEN**	Themes derived from the interview data in relation to the implementation of EMPOWER (CareLoop). **GREEN**	Provides qualitative data regarding how well CareLoop was implemented, the thoughts and opinions of people and staff using CareLoop.

5 Clinical evidence review

5.1 *Quality assessment of included studies*

The approach the EAG has taken for quality assessment and evidence synthesis is outlined in the final protocol. This section outlines key information on factors such as study methodologies, potential risk of bias, and key strengths and limitations of each of the included studies (Table 4). A summary comment is provided on EAG conclusions on the quality of the evidence for each technology.

For AVATAR therapy, there are 5 publications available as evidence. Two of these are RCTs (Craig 2018 and Leff 2013), 1 is a qualitative sub-study (Rus-Calafell 2022) of one of the interventional studies (Craig 2018), and, 1 is a published protocol (Garety, 2021a) and 1 is an observational sub-study (Rus-Calafell 2022) of Craig (2018). We have also included unpublished results from the AVATAR2 study. Craig (2018) compares AVATAR therapy against supportive counselling. While supportive counselling would not be the first choice of standard care according to NICE guidelines (this would be CBTp), it is still offered as standard care to some people when CBTp is unavailable because of waiting lists. It was noted by the authors that supportive counselling would be effective in its own right at treating symptoms of psychosis. Leff (2013) and the unpublished AVATAR2 study compare AVATAR against treatment-as-usual. Craig (2018) and the unpublished AVATAR2 have large sample sizes, are powered to detect an effect, and have broad outcomes all within the scope of the assessment. Leff (2013) has a much smaller sample size, but the outcomes are all within scope. There is no mention of the study being powered. In the partial crossover section of the trial, those that received the intervention first were not crossed over to the treatment as usual arm of the trial. All of these RCTs only partly meet the scope for participants included in them. In Craig (2018) and the unpublished AVATAR2, the diagnoses of participants included affective psychoses. In Leff (2013), participant diagnoses were not reported, leading to the possibility of some participants having a diagnoses of affective or drug/medication induced psychosis. The qualitative sub-study consisted of semi-structured interviews of participants that took part in Craig (2018). This provides rich qualitative data on the subjective experience of receiving AVATAR therapy. However, the data is limited to mostly those that completed the therapy and whose opinions were therefore positive enough to not discontinue early. Rus-Calafell (2022) is a small observational study that looked at outcomes not related to the participant's experiences of auditory hallucinations, but paranoia and anxiety. These outcomes are within scope, although come secondary to symptoms of psychosis.

For SlowMo, there are 4 studies available as evidence. One RCT (Garety 2021b), and 3 sub-studies of that interventional study (Greenwood 2021, Hardy 2022, and Ward 2022). There is an additional HTA report (Garety et al, 2021c) which reports the findings from Garety et al (2021b). However, as there were no additional findings that would be included from the HTA report, we will only refer to Garety et al (2021b) for the purpose of this EVA. Garety (2021b) is an RCT with a large sample size, and has broad outcomes all within scope. The primary outcome was a self-reported score rather than being observer rated, however, the RCT also included two observer-rated assessments of the same outcome. The participants are only those diagnosed with primary psychosis, and so are within scope. SlowMo is compared against standard care alone which is defined in the study as 'delivered according to UK national and local service guidelines and typically involved antipsychotic therapy, contact with a mental health worker, and outpatient psychiatric appointments.' However, the effects of time with a therapist that participants had with the treatment as usual group was not controlled for, although they are reported in the supplementary material of Garety (2021b). Greenwood (2021) provides rich qualitative data on the subjective experience of using SlowMo, and the impact it has on symptoms of psychosis. Hardy (2022) provides rich qualitative data on the usability of the SlowMo app, and of digital literacy of those using the app.

For CareLoop, there are 3 studies available as evidence. Two RCTs (Lewis 2020 and Gumley 2022a and b), and 1 qualitative sub-study of an RCT (Allan 2023). In Lewis 2020, CareLoop is compared to an undefined standard care, and the treatment participants received in this is not controlled for. Gumley (2022a and b) is a feasibility RCT, CareLoop is compared to treatment as usual that is defined as 'secondary care and relapse prevention delivered by adult community services, which largely involved regular follow-up with a care coordinator and periodic review by a psychiatrist.'

Table 4: Methodologies and Quality Assessment

Technology	Evidence Quality Comments	Quality conclusion
AVATAR Therapy	There is RCT evidence available; • This is limited to 3 studies • Neither study uses participants that are fully within scope • Outcome measures are broad and within scope • The comparator is within scope, although not the ideal standard care for psychosis	There is good quality evidence that is positive for indicating a benefit of AVATAR therapy, that could be generalisable to a UK setting. This evidence is limited to 2 powered RCTs. There is good qualitative evidence indicating a positive response to AVATAR therapy among those that have received it.

Technology	Evidence Quality Comments	Quality conclusion
	The qualitative evidence provides rich data on the subjective experience of having AVATAR therapy. The observational study is small, but provides outcome data for anxiety and paranoia.	
SlowMo	There is RCT evidence available; • This is limited to 1 study • It has a large sample size • Outcome measures are broad and within scope • The primary outcome is not observer rated. However, 2 observer-rated assessments of the same outcome were included • Not all aspects of the standard care treatment are controlled for The qualitative evidence provides rich data on the subjective experience of using SlowMo and its impact on symptoms, as well as including its usability. There is data showing a high level of acceptability from patients for SlowMo.	There is good quality evidence, but it does not indicate a strong positive benefit from the use of SlowMo for symptoms of psychosis. There is good qualitative evidence indicating a positive response among users of SlowMo, and providing useful insight into the applicability of SlowMo to the wider population.
CareLoop	There is RCT evidence available; • This is limited to 2 studies, one of these is a feasibility study and is not fully powered. In the conclusion of this feasibility study, it is reported that a sample size of 500 would be needed.,	There is some good quality evidence for CareLoop. The first RCT did not find any positive results for CareLoop. The second RCT, while it showed clinical efficacy, was a feasibility study and not fully powered.

5.2 *Results from the evidence base*

Results for each technology included in the scope are presented in this section. Table 5 shows each of the measures used in studies with a brief description. The results from the evidence base have been grouped by technology. Because each technology aims to address a different facet of psychosis, there is little homogeneity between the outcomes used by studies for the 3 different technologies. AVATAR therapy primarily addresses the

impact on auditory hallucinations through voices, SlowMo primarily addresses the impact on paranoia and delusions, and CareLoop primarily address the impact on psychosis relapse rates.

Table 5: Included measures and description

Measure	Description
PSYRATS–AH	Assessment of auditory hallucination symptoms. Range of 0-44. Higher score indicates more symptomatic
BAVQ-Q	Assessment of participant belief about vocal hallucinations. Range of 0-18. Higher score indicates more symptomatic
VAAS-Acceptance, and -Action	Assessment of participant acceptance and action of vocal hallucinations. Acceptance: range of 16-80. Action: range of 15-75. Higher score indicates a greater acceptance of voices.
VPDS	Assessment of perceived power differential between voice and voice hearer. Range of 0-5. High score indicates a greater perceived power of voices
PANSS	Assessment of psychosis symptoms. Range of 30-112. Higher score indicates more symptomatic
PSYRATS-DEL	Assessment of delusion symptoms. Range of 0-24. Higher score indicates more symptomatic
MANSA	Assessment of quality of life. Range of 16-112. Higher score indicates a greater quality of life
EQ-5D	Assessment of quality of life. Lower score equals greater quality of life
GAF	Assessment of functioning. Range of 1-100. Higher score indicates greater functioning
GPTS Part A and Part B	Assessment of paranoid thoughts. Part A: social reference. Part B: persecution. Range of 32-160. Higher score indicates more paranoia.
R-GPTS	Assessment of paranoid thoughts. Revised version of GPTS
DASS-12	Assessment of anxiety and depression. Range of 0-36. Higher score indicates more symptomatic.
BDI-II	Assessment of depression. Range of 0-63. Higher score indicates more symptomatic.
SAPS	Assessment of positive symptoms of psychosis. Range from 0-40. Higher score indicates more symptomatic.

Abbreviations: BAVQ-Q: Beliefs about Voices Questionnaire; BDI-II: Beck Depression Inventory-II; DASS-12: Depression, Anxiety, and Stress Scale; GPTS: Green et al. Paranoid Thought Scales; R-GPTS: Revised Green et al. Paranoid Thought Scales; MANSA: Manchester Short Assessment of Quality of Life; PANSS: Positive and Negative Syndrome Scale; PSYRATS–AH: Psychotic Symptom Rating Scales, auditory and hallucinations; PSYRATS–DEL: Psychotic Symptom Rating Scales, delusions; VAAS: Voice Acceptance and Action Scale; VPDS: Voice Power Differential Scale

AVATAR Therapy

The results from the evidence for AVATAR therapy from the RCTs are presented in Table 6 below.

Craig (2018) showed a significant decrease in PSYRATS–AH for the AVATAR group compared to the control group at 12 weeks. At 24 weeks, the decreased score was maintained for AVATAR, while the score of the control group continued to decrease, resulting in no significant difference between the groups at 24 weeks. This pattern was observed for BAVQ-R, VPDS, and VAAS scores as well.

In Leff (2013), there was a significant decrease in PSYRATS–AH for the AVATAR group compared to the control group post-treatment. There was also a significant decrease in PSYRATS–AH within the control group before and after they received AVATAR therapy. This pattern was observed with BAVQ-R score as well. At 3 months post-treatment, these improvements were found to have been maintained.

[redacted]

In both Craig (2018) and Leff (2013), there was no effect of AVATAR on more general symptoms of psychosis (i.e. those besides auditory hallucinations), depression and anxiety, or quality of life scores.

[redacted]

In Rus-Calafell (2020), there was a significant decrease in anxiety symptoms and paranoid thoughts between the first and last sessions of AVATAR therapy.

The qualitative evidence suggested that AVATAR therapy is found to be acceptable for use by the people that completed therapy. They were positive towards the therapist providing the therapy, and reported engaging well with the therapist and feeling supported. There were no reported negative long-term effects related to participation in AVATAR therapy. Half of participants

reported a positive impact of AVATAR therapy on how they engage with other people following therapy.

The results indicate that AVATAR therapy is effective at improving symptoms of hearing voices in people with psychosis. Based on the scores of dimensional subscales of the various outcome measures used, this improvement translates into; a decrease in voice frequency, a decrease in distress caused from hearing voices, a decrease in the malevolence associated with voices, an increase in the benevolence of voices, a decrease in the perceived omnipotence of voices, an increase in acceptance of voices, an increase in accept taken against voices, a decrease in voice power, and a decrease in voice assertiveness.

Table 6: Results for AVATAR therapy RCTs

Study	PSYRATS–AH score (mean)	BAVQ-R score (mean)	VPDS score (mean)	VAAS-Acceptance score (mean)	VAAS-Action score (mean)
Craig (2018)	**Baseline** Control: 30.46 AVATAR: 29.63 **12 weeks** Control: Decrease of 2.93 AVATAR: Decrease of 6.84 p=0.0093 **24 weeks** Control: Decrease of 2.35 AVATAR: Decrease of 0.61 p=0.39	**Baseline** Control: 50.99 AVATAR: 46.94 **12 weeks** Control: Decrease of 3.32 AVATAR: Decrease of 7.66 p=0.0018 **24 weeks** Control: Decrease of 6.26 AVATAR: Decrease of 2.52 p=0.43	**Baseline** Control: 22.37 AVATAR: 22.13 **12 weeks** Control: Decrease of 1.16 AVATAR: Decrease of 3.83 p=0.0018 **24 weeks** Control: Decrease of 0.97 AVATAR: Decrease of 0.35 p=0.09	**Baseline** Control: 48.12 AVATAR: 50.19 **12 weeks** Control: Increase of 3.01 AVATAR: Increase of 5.7 p=0.033 **24 weeks** Control: Increase of 1.54 AVATAR: Increase of 0.42 p=0.23	**Baseline** Control: 47.78 AVATAR: 49.48 **12 weeks** Control: Increase of 1.78 AVATAR: Increase of 4.8 p=0.019 **24 weeks** Control: Increase of 2.2 AVATAR: Increase of 0.77 p=0.25

Study	PSYRATS–AH score (mean)	BAVQ-R score (mean)	VPDS score (mean)	VAAS-Acceptance score (mean)	VAAS-Action score (mean)
Leff (2013)	**Baseline** Control: 31.75 AVATAR: 29.25 **Post-treatment** Control: Increase of 0.13 AVATAR: Decrease of 5.62 p=0.003 **Control post-AVATAR** Decrease of 11 (p=0.006)	**Baseline** Control: 21.38 AVATAR: 22.63 **Post-treatment** Control: Decrease of 0.38 AVATAR: Decrease of 3.75 p=0.004 **Control post-AVATAR** Decrease of 8.63 (p=0.014)	N/A	N/A	N/A
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

SlowMo

Greenwood (2022) addressed 6 core themes; starting the SlowMo journey, central role of supportive therapist relationship, slowing things down, value and learning from social connections, approaches and challenges of technology, and Improvements in paranoia and wellbeing. The findings for each theme are summarised in Table 7 below.

Table 7: Qualitative results from Greenwood (2022)

Theme	Summary of findings
Starting the SlowMo journey	Participants felt this was an opportunity to try something new and potentially helpful., especially if they had been experiencing symptoms for a long time. However, some people felt anxious and nervous to try SlowMo, especially those who were experiencing voices at the time of starting.
Central role of supportive therapist relationship	People emphasised the importance of human interaction, of talking and being listened to by someone supportive as opposed to only interactive with a technology. The therapist was seen as crucial in enabling access to both the therapeutic process and the technology
Slowing things down	The central concept of slow and fast thinking was helpful and valued as a new learnt skill. However, those more cognitively able found the intervention to be too slow and suggested that delivery speed be adapted.
Value and learning from social connections	Some people felt a connection with the vignette video characters who were viewed as peers by some and helped them feel not alone and less isolated. Some people described trying to emulate the video characters responding to their own experiences, to validate their distress and motivate behaviour change even when challenging
Approaches and challenges of technology	Some people found the combined cognitive and sensory demands of SlowMo stimulating whilst others found it overwhelming at times. The relationship with the app would change over time, paranoia and self-consciousness were barriers to use in public for some whilst others described it as a best friend. Some felt the app was insufficient support on its own once the therapy ended and wanted more face-to-face sessions or to take part again. Several issues with the app itself were noted such as limitations of the interface, needing a second phone for use, larger fonts, a 'check-in' feature and written instructions for how to use it.
Improvements in paranoia and wellbeing	Some people described a reduction in paranoia and worry, others described how they were now going out more and being more sociable, feeling more confident, seeing a reduction in other mental health symptoms and finally several people said they had a more positive outlook as a result of using SlowMo.

The results from the evidence for SlowMo from the RCT is presented in Table 8 below. Garety (2021b) showed a significant decrease in GPTS score (part A and B of GPTS) for the SlowMo group compared to control group at 12

weeks. This was not maintained at 24 weeks. However, this was maintained on a psychometrically improved version of this primary outcome measure, the R-GPTS for the total score and part B, persecution, but not part A, social reference. There was a significant decrease in PSYRATS-DEL and SAPS score for the SlowMo group when compared to control at 12 weeks, and this significant decrease was maintained at 24 weeks. There were no significant differences between groups for MANSA, WEMWBS and BCSS positive self-scores at 12 weeks, however, there were significant increases in MANSA, WEMWBS and BCSS positive self-concept scores for SlowMo when compared to control at 24 weeks. There were consistent significant differences between the groups in PSWQ and BCSS negative self-concept scores with improvements in the SlowMo arm compared to the control at 12 and 24 weeks. Improvement in slower thinking (acknowledging the possibility of being mistaken) was found to mediate change in paranoia at 12- and 24-week follow-ups.

Table 8: Results from SlowMo RCT

Study	GPTS total score (mean)	PSYRATS-DEL score (mean)	MANSA score (mean)
Garety (2021b)	**12 weeks** Control: Decrease of 13.4 SlowMo: Decrease of 19.9 p=0.005 **24 weeks** Control: Decrease of 19.6 SlowMo: Decrease of 23 p=0.06	**12 weeks** Control: Decrease of 1.7 SlowMo: Decrease of 3.3 p=0.002 **24 weeks** Control: Decrease of 2.2 SlowMo: Decrease of 4 p=0.001	**12 weeks** Control: Increase of 0.8 SlowMo: Increase of 1.3 p=0.40 **24 weeks** Control: Increase of 1 SlowMo: Increase of 3.7 p=0.003

Hardy (2022) showed that there exists a ‘digital divide’ between subgroups of the population. Computer access was significantly lower (p=0.02) in black people compared to white people. Smartphone ownership and confidence was significantly lower (p<0.001) in people aged 50+ compared to those aged <49. Smartphone confidence was also lower in black people (p=0.03). Computer confidence was lower in females (p=0.02), older people (p<0.001) and black people (p=0.01). These differences related to age and ethnicity did not impact engagement or experience of using SlowMo.

With regards to adherence of using SlowMo; females had significantly higher rates of self-reported current frequency of app use (p>0.001) and significantly

higher rates of self-reported future frequency of app use (p<0.001). Most people provided positive ratings for enjoyability, usefulness and usability (mean score 75%). However, these varied greatly between participants. Females reported higher levels of enjoyment (p<0.001) and usefulness (p=0.02).

Ward (2022) showed that SlowMo is acceptable to patients (85% of those that attended the first session went on to complete therapy). Fidelity in the delivery of SlowMo was achieved for 95% of people, with fidelity ratings of 90% for each of the 8 modules.

CareLoop

The results from the evidence for CareLoop from the RCTs are presented in Table 9 below.

In Lewis (2020), there were no significant differences between control and CareLoop for any of the outcome measures between baseline and 12 weeks. However, when results were analysed by individual sites (EIP and CMHT), a significant decrease from CareLoop when compared to control for the PANSS positive score was observed for the EIP site, but not the CMHT site.

The frequency of early warning signs documented in patient records was less in the ClinTouch (CareLoop) group (33%) than it was in the control group (46%). ClinTouch was suboptimal in terms of ClinTouch alerts vs documented early warning signs. Sensitivity was 75%, specificity 8%, giving a predictive value of 29%.

In Gumley (2022b), there was a lower proportion of people that relapsed in the CareLoop arm compared to the control arm. Time to relapse was also longer in the CareLoop arm compared to the control arm. Participants on the CareLoop arm were also less fearful of having a relapse than those in the control arm. There was a larger decrease in PANSS positive score for those in the control arm at 12 months compared to the CareLoop arm. However, there was a larger decrease in total PANSS score in the CareLoop arm compared to the control arm. Usage of the app was high, 91% of participants met the a priori criterion of acceptable engagement with the app (>33%). The median time of discontinuation for that >33% was 32 weeks.

Table 9: Results from CareLoop RCTs

Study	PANSS total score (mean)	EQ-5D score (mean)	GAF score (mean)	ERS score (mean)
Lewis (2020)	**Baseline** Control: 76.8 CareLoop: 72.9	**Baseline** Control: 9.6 CareLoop: 8.8	**Baseline** Control: 49.3 CareLoop: 49.7	**Baseline** Control: 81.4 CareLoop: 86.3

	Week 12 Control: 69.3 CareLoop: 64.5 p=0.492	**Week 12** Control: 8.4 CareLoop: 8.0 p=0.812	**Week 12** Control: 52.2 CareLoop: 51.8 p=0.850	**Week 12** Control: 83.6 CareLoop: 86.5 p=0.983

6 Adverse events and Technical Failures

Four studies reported adverse events; 1 for AVATAR, 2 for CareLoop and 1 for SlowMo. We have also included unpublished results from the AVATAR2 study all of which are summarised in Table 10 below.

Table 10: Adverse events

Study	Technology	Details
Craig (2018)	**AVATAR**	22 adverse events were reported in the study as a whole. The seriousness of each event was not reported. 5 participants in the AVATAR therapy group and 7 in the supportive counselling were admitted to hospital. 1 additional participant in each group required acute home treatment. 1 participant in the AVATAR group and 2 in the supportive counselling group suffered severe mental or physical health deterioration. 3 participants in the AVATAR group and 2 in the supportive counselling group had reported violent incidents. There were no recorded incidents of self-harm or suicide attempts. The independent data monitoring and ethics committee found none of the adverse events to be attributable to AVATAR therapy or supportive counselling.
[redacted]	[redacted]	[redacted]
Gumley (2022a and b)	CareLoop	29 adverse events were reported for CareLoop, 11 of which were classed as serious. 25 were reported for TAU, 15 of which were classed as serious. For CareLoop, 9/11 SAEs were classed as severe. 1 classed as related to the app and 1 to study procedure.

		Of the 18 remaining adverse events that were not classed as serious, 3 were related to study procedure and 12 to the app. For TAU, 15/15 were classed as severe, none of which were related to the app or study procedure. Of the 10 remaining adverse events that were not classed as serious, 2 were related to the study procedure.
Lewis (2020)	CareLoop	3 adverse events were related to CareLoop. 1 reported increased anxiety because of the amount of questions being asked, 1 reported increase in irritation because of beeps from app and 1 participants charger exploded. No details on TAU group given.
Garety (2021b)	SlowMo	28 adverse events reported for SlowMo versus 26 for TAU. 25 of these were serious for SlowMo and 26 for TAU. Of the 25 SlowMo SAEs, 8 related to physical harm, 8 were readmissions to a psychiatric hospital, 5 were crisis care referral, 1 was self-harm, 1 was serious violent incident (accused) and 5 were classed as other. One was classed as 'possibly related' to SlowMo, 1 'unlikely related' and 23 'definitely unrelated' to the treatment given. For the TAU group, most (14) SAEs were for readmission to a psychiatric hospital, 2 were for physical events, 1 for serious violent incident (victim), 2 for serious violent incident (accused), 2 for referral to crisis care and 5 were classed as 'other'. One of these was classed as 'definitely related' and 25 'definitely unrelated' to the treatment given.

The number of adverse events, both serious and not serious, was comparable when compared with TAU. However, one finding that should be highlighted is the difference in number of readmissions to a psychiatric hospital in the Garety et al (2021b) study which are nearly double the number in the TAU group compared to the SlowMo group. From the details reported on the adverse events themselves, the technologies appear to be safe to use within this patient population.

7 Evidence synthesis

It was not feasible to undertake meta-analysis for evidence within any of the technologies in this EVA because of the lack of available evidence and data

available. Evidence synthesis within technologies is limited because of a lack of completed studies with available data. Additionally, because of differences in populations, it was also not feasible to synthesise findings across the three technologies.

8 Ongoing Studies

A list of the current ongoing studies that the EAG are aware of are presented in Table 11 below.

During searches, the EAG were not able to find any references to McCrone et al, [redacted] Hardy et al, and the CONNECT trial.

Table 11: Ongoing studies

Identifier	Country	Primary Outcomes	Intervention	Comparator	Design	Enrolment	Start Date	End Date	Status
NCT04054778	Canada	PSYRATS-AH 1 week after treatment GREEN	AVATAR therapy low-intensity, and high-intensity GREEN	CBTp GREEN	Assessor-blinded RCT GREEN	136	01/04/2019	01/04/2025	Recruiting
ISRCTN55682735 AVATAR2 Trial	UK	PSYRATS-AH at 16 and 28 weeks GREEN	AVATAR-Brief and AVATAR-Extended GREEN	Treatment as usual GREEN	Three arm single-blinded RCT GREEN	345	01/12/2019	31/10/2023	No longer recruiting. Some data has been reported here. A full publication will be published soon.
NCT05982158 AMETHYST trial	Australia	PSYRATS-AH 3 months after treatment GREEN	AVATAR therapy GREEN	Cognitive Behavioural Therapy GREEN	Assess-blinded parallel group RCT GREEN	212	09/2023	12/2025	Recruiting
IRCT20220226054121N1	Iran	PSYRATS-AH 1 month after treatment GREEN	AVATAR therapy GREEN	Treatment as usual GREEN	Parallel group RCT GREEN	40	28/05/2023	Unknown	Unknown

Identifier	Country	Primary Outcomes	Intervention	Comparator	Design	Enrolment	Start Date	End Date	Status
McCrone et al (in prep)	UK	Wellbeing Adjusted Life Year (WALY) **GREEN**	SlowMo **GREEN**	TAU **GREEN**	Cost-effectiveness evaluation **GREEN**	381	05/2017	05/2019	No longer recruiting
[redacted]	[redacted]	[redacted] *****	[redacted] *****	[redacted]	[redacted] *****	[redacted]	[redacted]	[redacted]	[redacted]
Hardy et al (in prep)	UK	Implementation outcomes, effectiveness (R-GPTS, part B and WEMWBS), Wellbeing Adjusted Life Year (WALY) **GREEN**	SlowMo **GREEN**	N/A	Process evaluation, effectiveness, and cost-effectiveness **GREEN**	150	07/2023	06/2026	Not yet recruiting
CONNECT trial	UK		CareLoop	Unknown	Unknown	1000	Unknown	Unknown	Unknown

9 Interpretation of the clinical evidence

9.1 *AVATAR therapy*

The efficacy of AVATAR therapy is supported by 3 unique studies of good quality, utilising appropriate comparators to assess its efficacy. This evidence indicates that AVATAR therapy effectively reduces auditory hallucination symptoms in people with psychosis. [redacted] However, the evidence does not indicate efficacy compared to other psychological therapies, and there is a lack of evidence regarding its longer-term effectiveness (beyond 12 months). The effectiveness of AVATAR therapy versus established NHS treatments like CBTp remains unknown. However, since AVATAR targets specific symptoms of psychosis, this comparison might not be fully appropriate.

Craig (2018) utilised supportive counselling as a comparator rather than the standard of care, while Leff (2013) used treatment as usual for comparison, though the study was not adequately powered to detect an effect. AVATAR2 used treatment as usual for comparison.

AVATAR therapy shows efficacy specifically in reducing auditory hallucination symptoms in psychosis. There is no evidence to suggest it is more effective than supportive counselling in treating other general symptoms of psychosis or concurrent mental disorders like depression and anxiety. [redacted]

Qualitative evidence suggests that AVATAR therapy would be acceptable for use by those that are willing to engage with the therapy. More qualitative evidence is needed from those that either turned down AVATAR therapy, or did not complete a whole course of therapy.

AVATAR therapy is very generalisable for use within the NHS as it could be used in addition to other psychological therapies currently available. It is most effective at reducing auditory hallucinations, and so it is suggested that it is used in conjunction with other psychological therapies. So despite the evidence suggesting little difference in efficacy compared to other psychological therapies, it would still have a use for treating people that are particularly troubled by auditory hallucination symptoms.

9.2 *SlowMo*

The efficacy of SlowMo is supported by 1 unique study of good quality, utilising an appropriate comparator to assess its efficacy. The evidence indicates that SlowMo effectively reduces symptoms of delusion and paranoia in people with psychosis over the medium term (up to 24 weeks). It is also effective at improving the quality of life of people with psychosis. However, there is a lack of evidence regarding its longer-term effectiveness (beyond 12 months).

SlowMo has only been compared to standard of care, and no other psychological treatments. Standard care consisted of treatment as usual, where people continued to receive their antipsychotic medication, and psychological therapies.

The qualitative evidence suggests that SlowMo was found to be helpful by some users, and that the therapy provided by the app can provide people with psychosis new skills to help manage their symptoms. While some flaws for SlowMo were identified by users, none of these are insurmountable to improve upon in future versions of SlowMo. There is also data showing that SlowMo is acceptable for use by people with psychosis, and that fidelity is high for those receiving SlowMo therapy.

SlowMo would be very generalisable for use within the NHS. It could be used in additional to psychological therapies currently available. Therefore, its lack of comparison to psychological therapies already on the NHS does not impact its usefulness in treating symptoms. It is suggested that it is used alongside currently available psychological therapies for those particularly troubled by symptoms of paranoia and delusion. SlowMo does not require a data package for use, and so supports generalisability. While a digital divide exists, with black people and older people having poorer digital literacy, this did not translate to the user experience of the SlowMo app. There were no differences observed due to age or ethnicity. Additionally, a paper option is available for those that are unable or unwilling to use the app.

9.3 *CareLoop*

The efficacy of CareLoop is supported through 1 unique study. The evidence indicates that CareLoop effectively reduces the number of people experiencing relapse, and for those that do experience a relapse, it increases the time until a relapse. However, this study was a feasibility study and not fully powered to detect an effect. Nonetheless, the findings reported by Gumley (2022a and b) do indicate the feasibility, safety, and acceptability of conducting a fully powered RCT. There is a lack of evidence for the efficacy of CareLoop in the longer-term (over 12 months). These insights support the idea that more extensive research is warranted to fully explore the potential

efficacy of CareLoop in relapse prevention. In addition, there is some evidence showing that CareLoop can reduce symptoms of psychosis compared to treatment as usual.

Gumley (2022a and b) utilised treatment-as-usual as a comparator. This is considered the most appropriate comparator for CareLoop.

Acceptability and feasibility of patient use of the CareLoop app has also been shown. The EAG therefore considers it generalisable for use in the NHS. Since there is no formal relapse prevention process in the NHS, it would fit well into current standard care. However, the required access to a smartphone with internet needs to be considered.

9.4 *Evidence gaps*

AVATAR and SlowMo require further evidence on the longer-term impact they have on psychosis symptoms, and there is value in comparing them both against and with current NHS standard psychological treatments. CareLoop requires further evidence of its clinical and long-term efficacy in a fully powered RCT. Further evidence gap analysis for each technology has been conducted, and can be found in Section 11.

10 Economic evidence

10.1 *Published economic evidence*

Economic evidence on included technologies

The EAG combined clinical and economic searches identified one study that included economic analysis (Gumley 2022b). An additional unpublished economic analysis was supplied by AVATAR (Morris unpublished), as academic in confidence. Both were assessed using Drummond (1996) and appraisal results are in Appendix D.

Both papers report cost–effectiveness analyses carried out alongside RCTs that were done at least partially in the UK.

Gumley (2022b) find that CareLoop cost less than treatment as usual over a one-year period, from a health services payer perspective, and resulted in improved utilities (measured by EQ-5D-5L mapped to EQ-5D-3L). The analysis is based on a well conducted RCT using an appropriate comparator, with resource use and unit costs reported in detail. The key limitations for Gumley (2022b) were that it was based on a feasibility study that was not powered to show effectiveness, and that patient data and costs were included from both the UK and Australia.

Morris (unpublished) is a cost effectiveness analysis based on an RCT reported by Craig (2018). The analysis is for a 24-week period, comparing AVATAR to supportive counselling of the same duration, in one NHS site in London, UK. The analysis found that [redacted]. Utilities were measured and valued [redacted]. The analysis is based on a well-conducted RCT using an active comparator that may control for improvements that are not specific to AVATAR, although it would not necessarily represent normal practice in the UK. [redacted]

Table 12: Intervention specific economic study results

Study	Intervention, Comparator, Setting	Population	Setting, time horizon, perspective, analysis	Included Costs and Outcomes	Results	Notes:
Gumley 2022b	CareLoop n=42 (delivered as EMPOWER) plus TAU Treatment as usual (TAU) n=31 UK NHS Australia Carer resource use n=17	• Adults (≥16 years) • In contact with CMHS • Admitted to psychiatric inpatient service, or received crisis intervention in last 2 years for relapse of psychosis • Diagnosis of schizophrenia related disorder • Able to provide informed consent	12 months Primary perspective • Health-care payer Secondary perspectives • Health-care sector • Societal Analysis by ITT, with complete case analysis in sensitivity Missing data: imputation by MICE. RUQ completed by service users: 97% at baseline 81% at 3 months 77% at 6 months 75% at 1 year	**Intervention costs** Initial R&D & maintenance costs including server Delivering intervention, including Smartphone if needed (mean £109.52), data (mean £69.20), staff training and delivery time **Health service use costs:** Including HCP visits, emergency care, admissions, accommodation and medication. **Societal costs** included Criminal justice, absenteeism, presenteeism, carer productivity loss and informal care. **Outcomes** For participants EQ-5D-5L, AQoL-8D For carers EQ-5D-5L, CarerQoL-7D	**Total intervention costs:** EMPOWER: £2202 TAU: £0 **Total health care payer costs:** EMPOWER: £10,899.30 (SD £2,609.83) TAU: £11,140.40 (SD £2,802.01) Incremental -£251 (95% CI –8073.34 to +7571.15) **Total societal costs:** EMPOWER: £12,990.60 (SD £2,622.58) TAU: £12,820.30 (SD £2,891.64) **Utilities(EQ-5D-5L) EMPOWER vs TAU** Baseline: 0.644(0.258) vs 0.620(0.268) 3 months: 0.666 (0.234) vs 0.593(0.285) 6 months: 0.694 (0.197) vs 0.657(0.209) 12 months: 0.732 (0.231) vs 0.607(0.254) **QALYs** (Adjusted 12 month mean): EMPOWER: 0.684 (SD 0.041) TAU: 0.628 (SD 0.049) Incremental 0.056 (95% CI -0.031 to 0.143) **ICER EMPOWER vs TAU** Health care payer: EMPOWER dominant Societal: £3,089.2 per QALY	**Conclusions:** In the feasibility study, EMPOWER cost less to deliver from a health service perspective and was more effective than TAU alone. **Limitations:** Small feasibility study Mixed costs and resource use for UK and Australian participants Carer costs not included in analysis because of small numbers available. Costs per avoided relapse reported, but unclear how avoided relapses are calculated

Study	Intervention, Comparator, Setting	Population	Setting, time horizon, perspective, analysis	Included Costs and Outcomes	Results	Notes:
[redacted]	AVATAR therapy with 7 x 50 minute sessions (n=66,) Supportive counselling with assistant or graduate psychologist, 7 x 50 minutes, including emotion focussed therapy (n=65)	• Adults 18 or over • Diagnosis of a schizophrenia spectrum disorder OR affective disorder with psychotic symptoms who experienced auditory hallucinations for at least 12 months despite treatment. • Able to provide informed consent	Single site NHS, London, UK Single blind RCT 6 month follow up Health and social services perspective	[redacted]	[redacted]	[redacted]

HCP health care professional; ICER incremental cost effectiveness ratio; ITT Intention to treat; MICE Multiple imputation using chained equations; QALY quality adjusted life year; R&D research and development; RUQ resource use questionnaire; TAU treatment as usual;

Economic evidence and modelling for psychosis

The EAG carried out a rapid literature search to identify economic modelling on psychosis or UK-based economic analyses. The purpose of the search was to identify the key modelling strategies used in literature, and relevant UK cost information to inform model inputs. It was a pragmatic search that was not intended to be exhaustive. The search strategy is shown in Appendix E. Papers were sifted by a single reviewer by title and abstract, resulting in 12 systematic reviews. From full texts, a second reviewer identified 6 relevant systematic reviews. An additional paper was identified through reference searching. A total of 7 systematic reviews were included and summarised in Appendix G.

From the 7 included systematic reviews (Zhou 2018, Németh 2018, Jin 2020b, Aceituno 2019, Shields 2019, Shields 2020, Buck 2017), the most common models are decision tree and Markov models. Discrete event simulation was developed and reported in Jin 2020a. The health states included in Markov models are highly variable, with stable and relapse states the most commonly used alongside many other states. The models had variable time horizon, ranging from <1 year to lifetime. In some economic models, utility values were derived using a mapping algorithm from PANSS scores.

There are a number of learnings related to evidence base, model structure and key issues impacting the cost-effectiveness findings of digital technologies in psychosis. First, although there are economic evaluations of EIP and CBTp in schizophrenia, the outcomes considered are highly variable and measured by different evaluation methods, although PANSS was the most common. Clinical experts explained that scoring systems are not used clinically, as outcomes are normally very individual and patient-centred. EIP and CBTp costs are not explicitly reported, and utility values vary with the different health states considered in the models. Second, the time horizon is important to capture all important long-term consequences because of the chronic nature of psychosis (Németh 2018, Jin 2020b). Where a longer time horizon is considered, treatment switching and adherence are important and need to be incorporated to better capture costs and outcomes as psychosis progresses over time.

10.1 *Identification of key economic and purchasing factors*

The costs considered below are from an NHS and Personal Social Services perspective, however impacts on patients such as travel time or requirements for digital literacy, or a smart phone are also noted. The technologies have different aims, and are appropriate for different patient groups and so any costs or health economic analysis are not comparative across the technologies.

AVATAR and SlowMo are both designed to be used together with the person with psychosis to improve symptoms in particular areas, combining clinician time and technology. The technology is provided, but is implemented by NHS staff who have been suitably trained, and interact with the patient while using the technology.

CareLoop is intended to monitor symptoms and alert NHS staff to a deterioration that needs intervention. It is offered as a package that includes the technology and also staff who will help patients to set it up on devices, provide technological support and monitor alerts, ensuring that the correct NHS staff receive these.

The costs and other resource use requirements are broken down for each technology in Table 13.

Table 13: Summary of costs and resource use for each included technology

	AVATAR	SlowMo	CareLoop
Description	Therapy sessions enhanced by AVATAR	8 face to face sessions, website and mobile app for use by patient	Remote monitoring with algorithm to escalate to HCP if needed
System costs			
System set up costs	None	Not yet determined	[redacted]
Training costs	Not included, cost currently unknown. May be offered as additional package, including supervision of 2 cases.	Training materials are supplied as part of site set up. Automated training is planned and would be part of technology cost.	Training session included eLearning being developed
Training time	7.5 hours plus supervision of 2 cases, over duration of 12 weeks	1 day if experienced (2-3 days otherwise) plus 1 case supervised	2 hours
Supporting hardware (not included)	Laptop for therapist Laptop for patient including webcam (if not using own device) Speakers for patient[#] Microphone for patient[#] Headset for therapist	Laptop for therapy sessions Patient mobile phone (if not using own device)	Standard office equipment including PC or laptop Patient mobile phone (if not using own device)
Other infrastructure	Face to face: Room with partition and internet connection	Data connection required for initial install and synching at each	Internet to access platform and alerts

	between clinician and patient (>10Mbps) Virtual: Internet (>2Mbps in both directions)	session (where patient using app)	
Per patient costs			
Licensing costs	£100+VAT Expected to be for 15 sessions over 12 months	£50 - £100+VAT Expected 2-3 year duration	[redacted]
Set up time per patient	Included in 1st session time	Time to install on device if support needed	Included in cost
Administrative time	Time to book appointments	Time to book appointments	none
HCP time per session	50 minutes per session	60 – 90 minutes	n/a
HCP band	Trained therapist, broad range of possible bands, Morris (unpublished) costed at psychologist, £97 from PSSRU 2018	Doctoral level psychologists, delivery by other bands being investigated	Care coordinator, band 6
Number of sessions	7 (over 12-week duration)	8	n/a
Total HCP time	5.8 hours	10 hours (assuming mean of 75 min per session)	Only needed when alert triggered. Will depend on alert frequency and response needed
	Can be face to face or video call		
Patient requirements (hardware)	Face to face: None Virtual: Own device	Smart phone or similar Data for synchronisation at therapy session only	Smart phone with data
Patient requirements (time)	Face to face: Travel to appointment plus appointment time Virtual: Appointment time only	Face to face: Travel to appointment plus appointment time Use of app between appointments## Virtual: Appointment time only Use of app between appointments##	70 seconds per day to input data in app
# optional depending on quality of webcam or inbuilt audio-visual equipment in laptop ## paper- based versions are available if patient does not want to use the app			

AVATAR

AVATAR Therapy is a computer-based programme that is used during therapy sessions. There is a requirement for a standard laptop for both therapist and patient together with audio-visual capacity. The devices need internet connectivity during the therapy session.

Training for staff consists of 7.5 hours of online learning plus two supervised sessions. This is likely to be costed as an additional package. The software is purchased with a one-off licence fee of £100 per patient excluding VAT, and with an expected maximum duration of 15 sessions over 12 months.

The programme is used during 7 therapy sessions of 50 minutes, with an experienced psychologist. The company noted that it may also be provided by psychologists, but might be suitably trained nurse therapists, psychologists or psychiatrists.

Neither staff nor patient are needed to interact with the programme outside of therapy sessions and the patient does not need any hardware or software to participate, unless the consultations are virtual.

There are no set up fees listed, however there may be an initial cost to cover training. The cost of reversing the decision would primarily be staff training, any additional IT equipment that was purchased plus per patient licence fees during the trial period.

The cost of a patient who tried the intervention but subsequently withdrew would be the cost of the licence fee, as well as clinician time for any completed therapy sessions.

SlowMo

SlowMo provides a mobile phone-based app to patients, which prompts alternative responses to hearing voices, alongside 8 therapy sessions, where the therapist is also able to synchronise with the app and view interactions via a webapp on their own device.

There is a requirement for a standard laptop, tablet or PC and internet connectivity for initial set up and synchronisation at the start of each session. The patient device does not need internet connectivity for use of the app.

Training for staff consists of 1 day if they are an experienced therapist, or 2 to 3 days for less experienced staff, with a requirement for completion of 1 supervised case. Training can be provided face to face or online, and is included in licencing costs. The software is purchased with a one-off licence fee which is expected to be between £50 and £100 per patient excluding VAT, and last 2 to 3 years.

The programme is used during 8 therapy sessions of 60 to 90 minutes, with a clinician who is qualified in cognitive-behaviour therapy for psychosis. Currently it has been provided by qualified clinical and counselling psychologists, however training is planned for psychological therapists with relatively less training, including Mental Health and Wellbeing Practitioners and Clinical Associate Psychologists.

The patient is required to use either their own android smartphone, or one provided by the service, and interact with it on a regular basis as needed, as well as attending therapy sessions. The app can remain on the patient's phone for the duration of the licence period. The company stated that the app has been designed to support inclusion, including digital literacy, and that a paper based version can also be made available.

There are no set up fees required, and the cost of reversing the decision would primarily be staff training and any mobile handsets or additional IT equipment that was purchased. The cost of a patient who tried the intervention but subsequently withdrew would be the cost of the licence fee, any completed therapy sessions and potentially the cost of a mobile device if it had been purchased and not returned.

CareLoop

CareLoop is a symptom monitoring programme that interacts with patients who enter their symptoms in response to a daily questionnaire. An algorithm is used to monitor symptoms and alert a nominated HCP if there is a risk of relapse.

There is a requirement for each patient to have a smartphone with the app installed, this may be their own smartphone or one provided by the service. The nominated HCP will need a laptop, PC or tablet to view the dashboard and receive any alerts. They are able to use this to inform patient follow up and any therapy sessions or medication reviews, but are not required to do so to enable CareLoop basic functions.

The system is set up and monitored by CareLoop and this requires an initial set up fee of between [redacted] depending on the scope of the system. There may also be an additional [redacted]

Minimal training is needed for the HCP (2 hours), as the patient interaction is through CareLoop and the HCP would react to any alert according to their normal clinical procedures. This would normally be expected to be the care coordinator.

In addition to the set-up fee there is a licencing fee per patient which is [redacted]

The patient is required to use either their own android smartphone, or one provided by the service, and interact with it on a daily basis. If provided by CareLoop the phone would be [redacted].

The cost of reversing the decision would be the initial set up fee of [redacted] plus any mobile handsets or additional IT equipment that was purchased as well as licences for individual patients. The cost of a patient who tried the intervention but subsequently withdrew would be the cost of the licence fee for either 6 months or one year, according to the option chosen, and potentially the cost of a mobile device and associated data contract if it had been purchased and not returned.

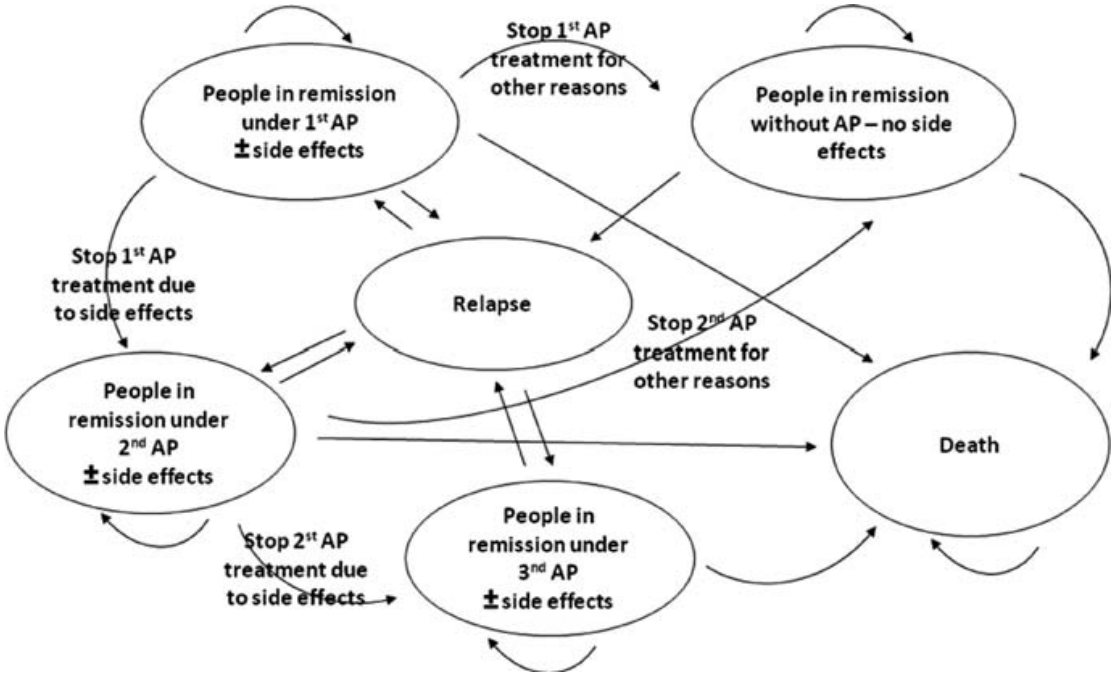
10.2 *Conceptual modelling*

Model structure

A Markov model over a lifetime time horizon would be needed to fully evaluate the long-term economic impact of the digital technology in managing psychosis. The CG178 model was developed to evaluate the cost-effective of antipsychotic drugs in schizophrenia. The model consists of 3 health states: remission, relapse and death (Figure 1). In addition, it considers treatment switching because of side effects or other reasons. This is consistent with findings in two systematic reviews of model-based economic evaluations (Zhou 2018, Németh 2018).

Both AVATAR and SlowMo are intended to improve a specific area of symptoms for people with psychosis, and it is likely that they would be delivered in addition to other medication and psychological interventions. A full lifetime model would need to understand more about the likely additional therapies and the impact that improving current symptoms may have on subsequent long-term outcomes.

Figure 1: Model structure used in CG178 guideline



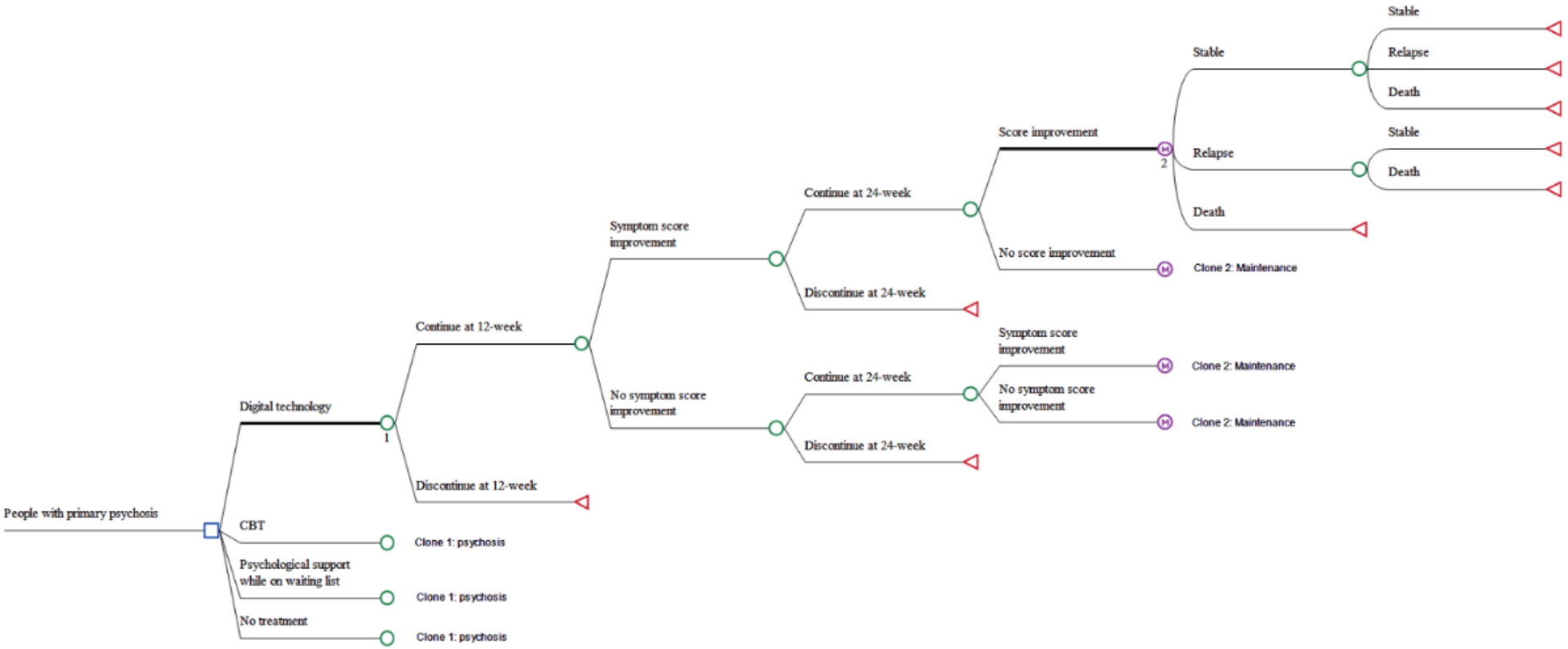
EAG conceptual model structure

Given the lack of existing clinical and economic evidence of the digital technologies and time limitation, the development of a new full Markov or microsimulation model was not feasible. The primary purpose of this analysis is to assess whether there is a plausible case for the cost-effectiveness of the digital technologies for managing psychosis.

An EAG decision analytic model was developed in TreeAge (Figure 2) that would be suitable to assess the included digital technologies and better fit the available clinical evidence on symptom score for AVATAR and SlowMo, however it is not possible to fully populate it at this point in time.

In this EAG conceptual model, patients receive either a digital technology, CBTp, psychological support while on a waiting list, or no treatment. They enter an initial acute phase which is modelled by a decision tree, with the response level to treatment used as an outcome at different timepoints (12-week and 24-week). A response is indicated by a fall in the evaluation score. Treatment discontinuation or dropout is considered at 12 and 24 weeks. After 24 weeks, patients move to a Markov model with 3 health states is included to simulate the maintenance phase, including stable, relapse and death. Because the positioning in the care pathway for each digital technology is different, the AVATAR and SlowMo model would include both initial acute and maintenance phase, whereas CareLoop model would begin with the maintenance phase.

Figure 2: EAG conceptual model structure



For symptom management (AVATAR and SlowMo), the EAG have explored the possibility of populating the model. Given the lack of evidence to link short-term symptom improvement to long-term relapse outcome and any downstream changes in healthcare resource use, it is not feasible to populate the whole EAG conceptual model. Although the impacts on patients' symptoms are clearly described in terms of psychological scoring tools as well as qualitative studies, these are not mapped through to utility values or healthcare resource use. This does not allow robust modelling. Therefore the EAG adopted a cost-consequences approach that transparently presents the incremental costs of delivering the intervention, together with the patient outcomes and utilities. For AVATAR the utility change is supplemented by existing trial-based analysis of cost effectiveness. For SlowMo, the EAG attempted the utility calculation using a secondary patient outcome (R-GPTS) in Garety (2021b). Because of the inherent problems associated with GPTS (the primary outcome in Garety (2021b)), Freeman (2019) recommends stand-alone R-GPTS assessments on social reference and persecution. Therefore, the EAG applied the cut-off for symptom severity categories using R-GPTS social reference and persecution subscales separately, and mapped these categories to the corresponding utility values.

For CareLoop, the EAG model consists of the Markov model with 1-year cycle length comparing standard care without monitoring and standard care with CareLoop remote monitoring. Patients enter the Markov model through the stable state, and transition between health states over time. A time horizon of 3 years was used in the base case, to reflect the length of an EIS, based on expert opinion. The costs, QALYs, mean net monetary benefit (NMB) and number of relapses were reported. Mean NMB was calculated as (incremental QALYs x WTP at £20,0000 per QALY) - incremental costs. A discount rate of 3.5% was applied to costs and outcomes beyond 12 months. In addition, a series of deterministic sensitivity analyses were carried out to explore the key uncertainties. Table 14 summarises the economic approaches undertaken by the EAG.

Table 14: Summary of modelling approaches and other available evidence

Economic analysis	AVATAR	SlowMo	CareLoop
Cost consequences	✓	✓	×
Cost effectiveness (CEA), model used	×	×	✓ Markov model
Time horizon	24 weeks	24 weeks	3 years

Comparators	CBTp & Family Intervention, Psychological support groups, waiting list		Treatment as usual
Additional available economic evidence	RCT-based CEA	none	RCT-based CEA

Modelling Assumptions:
Full commercialisation packages are not available for any of the technologies at present. The companies' current pricing estimates have been used in modelling, but there are some elements, that may change by the time the technologies come fully to market.

In particular set up and training packages are not yet determined for AVATAR and SlowMo. These have been included at no cost in the model, and are unlikely to be a substantial per patient increase, but would have more of an impact on the initial budget to set up the service, or the cost of reversing the decision.

For CareLoop there is an optional integration of electronic medical records, and the cost for this has not yet been developed

For estimating the per patient cost of training and system set up, both AVATAR and SlowMo advised that they recommended training at least 10 clinicians in one site, and therefore this has been costed in the model, with an assumption of 100 patients per year being treated. This is based on the company statements, together with the median number of referrals to EIP services of 85 referrals per CCG (Mental Health DataSet, 2021, NHS Digital).

For CareLoop, assuming that 1000 patients are followed up for a year, based on an assumed 50% take up from an organisation with 2,000 eligible patients. The EAG assumed 100 care coordinators would to be trained per purchasing organisation. Both figures are based on expert opinion and company statements.

It is assumed that IT hardware would need to be provided for AVATAR and SlowMo, because it is a new service, however the normal office equipment would be sufficient for CareLoop as minimal IT interaction is needed for staff.

For model simplicity, it is assumed that patients could only have one relapse per year, and at the end of that year they reverted to a stable state. In reality, some patients might have recurrent relapses leading to treatment switching.

Clinical parameters

Effectiveness

Effectiveness is indicated by the change in psychological rating scales and utility values in the EAG analyses for AVATAR and SlowMo, whereas, for CareLoop, it is indicated by the change in relapse risk and hospitalisation following a relapse.

Effect on psychological rating scales: A rapid literature search using the terms 'psychosis', 'schizophrenia', 'cognitive behavioural therapy', 'psychological intervention' and 'systematic review' on PubMed was done to identify review-level effectiveness evidence for other comparators in the scope. Three relevant systematic reviews were identified from the search (van der Gaag 2014, Jones 2018, Guaiana 2022). The systematic review and meta-analysis by van der Gaag (2014) was selected and used in the EAG costs-consequences analyses, because the findings were pooled predominantly from UK-based papers. However, Cochrane reviews on CBTp by Jones (2018) and Guaiana (2022) were excluded because the pooled results were derived from very small number of non-UK based papers.

PSYRATS-AH and PSYRATS-DEL were selected as one of the main outcomes in the EAG cost-consequences analyses as these were the common outcome measures across studies, thus allowing comparability between interventions. A brief description of the systematic review included in EAG analyses is shown in Table 15.

Table 15: Summary of systematic review identified and used in EAG analyses

Review	Population, intervention and comparators	Outcome measures	Included papers for meta-analysis (UK-based?)	EAG comments
van der Gaag (2014)	Population: Delusions and auditory hallucinations Intervention: Individually tailored case-formulation group or individual CBTp Comparator: TAU/waiting list, supportive counselling, psychoeducation, attention placebo control, social activity treatment	PSYRATS MADS BAVQ PDI CPRS Del	Auditory hallucinations: 11 (9 UK-based: 7 reported PSYRATS, 8 individual CBTp) Delusions: 9 (5 UK-based: 4 reported PSYRATS, 5 individual CBTp)	Effect size was predominantly derived using PSYRATS score change reported in UK-based papers. However, PSYRATS was not the primary outcome measure in some individual papers. The authors rated 9 studies as poor quality based on the Clinical Trials Assessment Measure criteria, but meta regression analysis on study quality show no evidence of lower effect size in high quality papers.

BAVQ Beliefs about Voices Questionnaire; CBTp Cognitive behavioural therapy for psychosis; CPRS Comprehensive Psychiatric Rating Scale Delusion and Hallucination Scales; MADS MacArthur-Maudsley Delusions Assessment Schedule; PDI Peters Delusion Inventory; PSYRATS Psychotic symptom rating scale; TAU treatment as usual.

Effect on utility: For AVATAR, the EAG have obtained mean utility at each timepoint and mean QALYs over 24 weeks derived from EQ5D-5L from Morris (unpublished) comparing AVATAR and supportive counselling.

For SlowMo, the EAG requested additional data from the company on the breakdown of patients with different R-GPTS persecution and references score ranges at each timepoint (Garety 2021b). The mean utility value at each timepoint was calculated using utility values of PANSS-generated health states derived from the US general population (Lenert 2004), because of a lack of UK-based utility values for different psychosis severities. Despite the utility values in Lenert (2004) being generated in US population, these values have previously been used in UK-based cost-effectiveness analyses including CG178 and Jin (2020a). Total QALYs were estimated using an area under the curve approach, assuming linear extrapolation between timepoints (Manca 2005).

For CareLoop, the utility values of relapse and stable health state in the Markov model were sourced from Lenert (2004). From this, the EAG estimated the total QALYs gained over the 3-year time horizon.

Effect on relapse and hospitalisation following relapse: A 3-year relapse rate in standard care was sourced from a systematic review and meta-analysis of longitudinal studies (Alvarez-Jimenez 2012). The relapse rate for CareLoop was estimated by applying the relative risk reported in Gumley (2022b) to the relapse rate in standard care. Subsequently, the proportion of hospitalisation following a relapse for both standard care and CareLoop arms was used to give the number of relapses requiring hospitalisations for each strategy (Gumley 2022b). Because patients with psychosis have significant excess mortality than those in the general population, an age-specific standardised mortality ratio (SMR) of psychosis was applied to age- and sex-specific UK national life table.

Table 16 presents the clinical parameters used in EAG economic analyses.

Table 16: Main clinical parameters

Variable	Value	Source	EAG commentary on availability, quality and reliability of the source/s
AVATAR and SlowMo			
Standardised mean difference of CBTp vs control:			
Hallucination Delusion	-0.44 -0.36	van der Gaag 2014	The authors reported positive effect sizes, in favour of CBTp. However, for comparability and consistency with other papers, the EAG report the effect sizes as negative values.
Proportion of severity categories based on R-GPTS at each timepoint (%):			
R-GPTS Social Reference subscale	SlowMo (%) vs TAU (%)		
0-9 (Average)	Baseline: 23.9 vs 20.6 12 weeks: 41.0 vs 27.6 24 weeks: 46.3 vs 34.9	Company data	
10-15 (Elevated)	Baseline: 22.8 vs 22.2 12 weeks: 27.1 vs 31.9 24 weeks: 24.4 vs 28.5	As above	

16-20 (Moderately severe)	Baseline: 21.1 vs 23.3 12 weeks: 17.5 vs 17.2 24 weeks: 16.3 vs 18.6	As above	
21-24 (Severe)	Baseline: 14.4 vs 11.7 12 weeks: 8.4 vs 9.2 24 weeks: 6.9 vs 8.1	As above	
>24 (Very severe)	Baseline: 17.8 vs 22.2 12 weeks: 6.0 vs 14.1 24 weeks: 6.3 vs 9.9	As above	
R-GPTS Persecution subscale	SlowMo (%) vs TAU (%)		
0-9 (Average)	Baseline: 0 vs 0 12 weeks: 15.7 vs 14.7 24 weeks: 23.6 vs 17.8	Company data	
10-15 (Elevated)	Baseline: 6.1 vs 3.3 12 weeks: 16.3 vs 8.0 24 weeks: 12.4 vs 14.2	As above	
16-20 (Moderately severe)	Baseline: 23.9 vs 21.7 12 weeks: 20.5 vs 19.0 24 weeks: 20.5 vs 18.3	As above	
21-24 (Severe)	Baseline: 28.9 vs 36.1 12 weeks: 23.5 vs 27.0 24 weeks: 24.2 vs 26.0	As above	
>24 (Very severe)	Baseline: 41.1 vs 38.9 12 weeks: 24.1 vs 31.3 24 weeks: 19.3 vs 23.7	As above	
Utility:			
Average	0.89	Jin 2020a, Fusar-Poli 2013	Interpreted as normal level of paranoia (Freeman 2019) EAG applied weighted average of general population utility values (Fusar-Poli 2013) based on mean age and % male in Garety 2021b.
Elevated	0.88	Lenert 2004	Assumed to be mild

Moderately severe	0.75	As above	Average of different moderate severity categories
Severe	0.61	As above	Average of different severe severity categories
Very severe	0.42	As above	
CareLoop			
Relapse:			
Relapse rate of standard care per year (%) *1-year follow up* *2-year follow up* *3-year follow up*	 28 43 54	 Alvarez-Jimenez 2012 As above As above	
Relative risk of relapse of CareLoop vs standard care	0.5	Gumley 2022b	
Proportion of patients requiring hospital admission following a relapse (%):			
CareLoop	25	Gumley 2022b	
Standard care	69	As above	
SMR for people with psychosis:			
30-44 years	5.80	Jin 2020a, Reininghaus 2015	
45-49 year	2.50	As above	
Starting age (year)	43	Gumley 2022b	
Utility:			
Relapse	0.67	Lenert 2004	
Stable	0.80	As above	
Death	0	As above	
CBTp cognitive behavioural therapy for psychosis; R-GPTS Revised Green et al., Paranoid Thoughts Scale; SMR standardised mortality ratio.			

Resource identification, measurement, and valuation of expected key cost drivers

Technology costs: these have been explained in Section 10.1 above, and are summarised in Table 17. Training, hardware and set up fees are split over a 3-year period. For AVATAR and SlowMo there is an assumption that 100 patients would be treated annually and that 1 set of hardware would be

sufficient for this. The EAG investigated the impact of 200 patients a year requiring additional hardware, however the impact is small compared to the staff cost of delivering the intervention. The assumption of patient numbers is guided by information from the companies as well as Mental Health Bulletin data (2021-22) reporting a mean of 116 (median of 85) referrals per year to EIS per Clinical Commissioning Group (CCG).

Both AVATAR and SlowMo have previously been delivered by highly trained psychologist staff members, and are therefore costed at a band 8a of the NHS Agenda for Change payscale, because this reflects available evidence on both costs and outcomes. The companies indicate that they are considering delivery by less specialised staff, and the EAG has considered delivery by a band 6 mental health nurse in sensitivity analysis.

For CareLoop, all NHS interactions are led by Care Coordinators in the model, and they are assumed to spend 30 minutes per alert triggered by CareLoop. Expert advice was that many alerts would be resolved by a phone call, however some may need a visit to the patient, or escalation to more specialised staff. The number of triggers generated was 15 per patient, over the course of one year, based on Gumley 2022b.

Comparator costs: several alternative comparators are specified in the scope; the available comparator will vary locally.

CBTp is based on 16 sessions, as recommended in NICE CG178 as a minimum provision, with a cost of £109.55 per session. This is taken from PSSRU 2016 and inflated, because it has not been published more recently. Staffing is based on a mixture of a speciality doctor, clinical psychologist and mental health nurse. CBTp may be delivered with or without family intervention.

Experts advised that if CBTp was not available, patients may be offered group support sessions. These are not included in the NICE guidance, and experts reported that the format was very variable. The EAG based the costing of these sessions on NICE HTE9 Digitally enabled therapies for adults with anxiety disorders: early value assessment, which used the IAPT pathway and PSSRU costs for staff.

Additional healthcare costs: For both AVATAR and SlowMo, no evidence was found that enabled the EAG to model changes in healthcare resource based on the improvement on symptoms. Therefore cost data is limited to the cost of delivering each intervention, and does not consider additional healthcare or social care. For AVATAR there is a within trial economic analysis that reports total healthcare resource use and costs for the

intervention arm and the comparator of supported counselling, over a 24-week period.

For CareLoop, there are multiple models that include health care resource use information for relapse and remission states. The EAG considered information in (CG178), Jin (2020a) and Dymond (2022) to update costs to 2022 where required, and split relapse cost into those treated in hospital, and those treated at home. This enables us to consider changes in the proportion of patients admitted to hospital for treatment of relapse.

Remission: Costs for remission include outpatients, primary and community care, including a small proportion of people who live in residential care and long-term hospital care. Costs have been inflated to 2022 costs using PSSRU to £16,456 per year.

Relapse: Costs in CG178, Jin(2020a) and Dymond (2022) all include a proportion of patients who are treated for relapse by admittance into hospital, and a proportion who are treated at home by the crisis resolution and home treatment teams. The EAG used the method described in CG178, updating the source information. The number of bed days for a relapse episode was adjusted from 111 (HES 2006-7) to 82 (HES 2022-3), based on bed days for patients with hospitalisation for people with schizophrenia or psychosis (F20-F29, according to ICD-10). Jin (2020a) used an alternative length of stay (139 days) based on Munro (2011), however because most of the patients in the study had long term or severe psychosis, the EAG used HES data as the source.

For treatment at home by the CRHT team, the EAG updated the CG178 costs, keeping the assumption of 8 weeks duration, and inflating the cost of £264 per case per week to £341, using PSSRU indices. Jin (2020a) used an alternative source with 16.3 contacts and a cost of £197 per contact (NHS Reference Costs 2012 inflated to 2017), with a similar total cost per case.

For both treatment methods CG178 included Olanzapine as a modelling assumption for the duration of the inpatient stay or equivalent. Expert advice was that people would be likely to receive medication during a relapse, and may not have been using it previously. The medication, and associated cost, vary considerably. The EAG found that Olanzapine was less costly than when the CG178 was modelled, however there were a range of other options that would be more expensive. Therefore, the EAG inflated the cost from CG178 to approximate this range of medication. When applied this to the lower number of bed days, this resulted in a change from £473 to £450 per relapse. The impact on the model is very small compared to other costs associated with relapse treatment.

Table 17: Key cost parameters

Parameter	Value	Source
Intervention Costs		
Set up costs for AVATAR, per system		
System set up	£0	
2 x laptops	£798	14” HP laptop, 128GB SSD, 8GB RAM
Speakers	£99	M Audio AV-42
Microphone	£62	Soundtech CM-1000 USB desk top microphone
Headset	£75	Sennheiser HD 350BT
Total	**£1,034**	**Per system set up**
Training costs for AVATAR, per trained clinician		
7.5 hours	£548	For each clinician, assuming band 8a psychologist, PSSRU 2022 £73 per hour
Training package	-	Currently no cost, however there may be a future cost for training.
Supervision cost	-	2 cases must be supervised. This would be provided by company, however cost is not yet known and may be included in training package.
Total	**£548**	**Per trained clinician**
Delivery costs for AVATAR, per patient		
Set up and staff training	£21.73	Assuming 10 clinicians trained, 1 set of hardware purchased for a 3-year period, with 100 patients treated annually
Licence fee	£100	Company, for max 15 sessions over 12 months
Sessions	£426	Assume 7 sessions of 50 minutes delivered by band 8a psychologist (£73 per hour)
Total	**£548**	**Per patient treated**
Set up costs for SlowMo, per system		
System set up	£0	
Laptops	£399	14” HP laptop, 128GB SSD, 8GB RAM
Total	**£399**	**Per system set up**
Training costs for SlowMo, per trained clinician		
7.5 hours	£548	For each clinician, assuming band 8a psychologist, PSSRU 2022 £73 per hour. This may be longer for less experienced clinician
Training package	-	Currently no cost, however there may be a future cost for training.
Supervision cost	-	1 case must be supervised. This would be provided by the company, however cost is not yet known and may be included in training package.
Total	**£548**	**Per trained clinician**
Delivery costs for SlowMo, per patient		

Set up and staff training	£19.61	Assuming 10 clinicians trained, 1 set of hardware purchased for a 3-year period, with 100 patients treated annually
Licence fee	£75	Company estimated £50 -£100 with 2-3 year duration
Sessions	£730	Assume 8 sessions of 75 minutes delivered by band 8a psychologist (£73 per hour), based on company estimate of 60 – 90 minutes
Total	**£826**	**Per patient treated**
Optional additional costs:		Mobile phone for patients as needed.
Set up costs for CareLoop, per system		
System set up	[redacted]	Mid point taken for calculations
EMR	[redacted]	Costs not defined currently, depending on purchaser requirements
Total	[redacted]	**Per system set up**
Training costs for CareLoop, per trained care coordinator		
2 hours	£106	For each care coordinator, assuming band 6, PSSRU 2022 £53 per hour. Likely to need training of several staff
Training package	-	Currently no cost, however there may be a future cost for training.
Total	**£106**	**Per trained clinician**
Delivery costs for CareLoop, per patient, per year		
Set up and staff training	[redacted]	Assuming 100 clinicians trained, set up implemented for a 3-year period, with 1000 patients accessing it annually
Licence fee	[redacted]	[redacted]
Number of CareLoop alerts	15.08	Per patient per year (Gumley 2022b)
Care Coordinator time	£400.52	Assuming 30 minutes time for band 6 staff per alert.
Total	[redacted]	**Per patient per year**
Optional additional costs:		Mobile phone and data for patients as needed.
Comparator costs		
CBTp	£1,752.83	16 sessions (NICE CG178), with a cost of £109.55 per session (PSSRU 2016 £97 per session inflated to 2022 values)
Family intervention	£1,264.93	10 sessions (NICE CG178), with a cost of £126.49 per session (PSSRU 2016 £97 per session based on multi-systemic therapy, inflated to 2022 values)
Psychological support	£38	6 sessions, 2 hours each (IAPT guidance), staff cost a mean of band 4 (£34) and band 5 (£41) PSSRU 2022

Waiting list	£0	This is an assumption, patients may need to access additional healthcare during this time
Supportive Counselling	[redacted]	This is included as a comparator for AVATAR, as this is used in the available RCT (Craig 2018). The cost is based on Morris (Unpublished).
Relapse and Remission costs		
Remission:	£16,456	Inflated from CG178, using PSSRU 2022
Relapse:	Total cost comprised of outpatient, primary and community care, residential and long-term hospital care plus either acute admission or care at home for psychosis	
outpatient, primary and community care	£5,590	Inflated from CG178, using PSSRU 2022
Residential and long-term hospital care	£7,010	Inflated from CG178, using PSSRU 2022
Acute hospital admission	£28,300	81 days hospital admission (HES 2022-23 ICD F20-F29), £341 per bed day, PSSRU 2022 Mental health clusters.
Care at home for psychosis	£3,181	8 weeks support from CRHTT at £341 per week (CG178 (£264) inflated using PSSRU).
CG Clinical guideline; CRHTT Crisis Resolution and Home Treatment Team; EMR electronic medical records; HES Hospital Episode Statistics; PSSRU personal and social services research unit		

10.3 *Results from the economic modelling*

Base case

Base case results are reported in Table 18, 19, and 20. For AVATAR and SlowMo, a summary of costs and consequences is presented (Table 18 and Table 19), while the cost-effectiveness findings for CareLoop are summarised in Table 20.

Full costings of health care resource use changes following AVATAR or SlowMo were not modelled, therefore the EAG results are for the delivery of the intervention only.

The EAG found that delivery of AVATAR was £548 per patient, incurring an additional cost of £218 per patient compared to supportive counselling (comparator in Craig, 2018). It would be an additional cost of £510 compared to group counselling, or a cost saving of £1,205 compared to CBTp. The delivery of SlowMo was £826 per patient, which is assumed to be an adjunct to treatment as usual (Garety 2021b), or would be an additional cost of £788 compared to group therapy, or a cost saving of £927 compared to CBTp. In terms of outcomes, the available evidence suggests AVATAR and SlowMo more effective than the comparators, where both technologies were associated with reduced PSYRATS score and QALYs gained over study

period. For the comparison between CBTp and comparators, the existing literature reports that CBTp is associated with symptom improvement.

Table 18: Costs and consequences between AVATAR and comparators

	AVATAR	Supporting counselling	CBTp	Adjusted mean difference between groups (95%CI)	
				AVATAR vs supportive counselling	Group or individual CBTp vs TAU/Std Care (van der Gaag 2014)
Costs:					
Intervention per patient	£548	[redacted]	£1753	£218 (unadjusted)	NA
Outcomes:					
PSYRATS-AH-Total (Craig 2018)	Baseline: 29.63 12 weeks: 22.79 24 weeks: 22.18	Baseline: 30.46 12 weeks: 27.53 24 weeks: 25.18	NA	12 weeks: -3.82 (-6.70 to -0.94) 24 weeks: -1.55 (-5.09 to 1.98)	-0.44 (-0.26 to -0.61)
Utility (EQ5D-5L) Morris (unpublished)	Baseline: [redacted] 12 weeks: [redacted] 24 weeks: [redacted] Total QALYs over 24 weeks: [redacted]	Baseline: [redacted] 12 weeks: [redacted] 24 weeks: [redacted] Total QALYs over 24 weeks: [redacted]	NA	Total QALYs over 24 weeks: [redacted]	NA

Table 19: Costs and consequences comparing SlowMo and comparators

	SlowMo + TAU	TAU	CBTp	Adjusted mean difference between groups (95%CI)	
				SlowMo vs TAU	Group or individual CBTp vs TAU/Std Care(van der Gaag 2014)
Costs:					
Intervention per patient	£826	£0	£1753	£826 (Unadjusted)	NA
Outcomes:					
PSYRATS-DEL-Total	Baseline: 16.5 12-week: 13.2 24-week: 12.5	Baseline: 16.2 12-week: 14.5 24-week: 14.0	NA	12 weeks: -1.53 (-2.50 to -0.56) 24 weeks: -1.62 (-2.59 to -0.65)	-0.36 (-0.09 to -0.63)
Utility (derived from R-GPTS scores)					
R-GPTS social reference	Baseline: 0.734 12-week: 0.812 24-week: 0.817 Total QALYs over 24 weeks: 0.366	Baseline: 0.717 12-week: 0.771 24-week: 0.792 Total QALYs over 24 weeks: 0.352	NA	0.014 (Unadjusted)	NA
R-GPTS persecution	Baseline: 0.580 12-week: 0.680 24-week: 0.701 Total QALYs over 24 weeks: 0.305	Baseline: 0.573 12-week 0.639 24-week: 0.678 Total QALYs over 24 weeks: 0.292	NA	0.013 (Unadjusted)	NA

For AVATAR and SlowMo the costs of providing the intervention have been described and compared to typical alternatives. In both cases these may not avoid the need for CBTp or other therapy to address additional symptoms, but may improve the specific symptoms they are designed to address.

Because the lack of evidence in dividing patients to 'clinically improved' and 'not clinically improved' through cut-off points with PSYRATS and GPTS rating scales, it is unclear if the reduced scores reported for AVATAR and SlowMo would be considered as a clinically significant response, hence translated to any utility changes.

[redacted] The key driver of cost for both AVATAR and SlowMo is the staff time needed to deliver it, and this remains the case when less specialised staff deliver the intervention.

CareLoop

The base case results show that the digital monitoring technology (CareLoop) is more effective and less costly than standard care without monitoring, therefore a cost-saving strategy.

The total costs for both strategies are dominated by remission costs given the short time horizon. CareLoop costs are driven primarily by the licence fee per patient, with significant additional costs for the care coordinator responding to the alerts. Because of the reduction in relapses and avoiding hospitalisation in some relapse cases with CareLoop, relapse costs in CareLoop arm are lower thus the total CareLoop costs become lower, leading to overall cost savings.

Table 20: EAG base case cost-effectiveness results comparing CareLoop and standard care

	Standard care	Standard care with CareLoop monitoring	Differences
Total costs	£56,802	[redacted]	[redacted]
Remission costs	£38,308	£42,433	£4,125
Relapse costs	£18,494	£6,770	-£11,724
Intervention costs	£0	[redacted]	[redacted]
Total QALYs	2.24	2.27	0.03
Mean NMB @ £20,000	-	-	[redacted]

Number of relapses	0.369	0.218	-0.151

10.4 *Sensitivity analysis*

For AVATAR and SlowMo the costs were considered if delivery was by a band 6 or band 7 member of staff. For SlowMo the provision of 50% of patients with a mobile phone was used for an additional scenario in Table 21. Hardy (2022) reported that 77% of patients recruited to a study of SlowMo owned a smartphone (102 patients in 3 UK sites).

Table 21: Cost of delivering symptom management interventions in different scenarios

Analyses	AVATAR	SlowMo
Delivered by band 6 staff (£53 per hour, PSSRU 2022)	£426.57	£620.77
Delivered by band 7 staff (£64 per hour PSSRU 2022	£492.09	£731.16
50% of patients receive mobile phones (EAG assumption £70 per phone, no data)		£861

For CareLoop, results from deterministic sensitivity analysis scenarios suggest that the cost saving results are robust to the variations in the model inputs (Table 22). The threshold analysis shows that CareLoop base case results would change from being cost-saving (less costly and more effective) to not cost-effective based on the willingness-to-pay threshold of £20,000 per QALY gained, when CareLoop costs increase from [redacted] per year (with all other inputs remaining the same).

Table 22: Results of sensitivity analysis for symptom monitoring, CareLoop

Analyses	Standard care		Standard care with CareLoop monitoring		Incremental costs (£)	Incremental QALYs
	Total costs (£)	Total QALYs	Total costs (£)	Total QALYs		
Base case	**56,802**	**2.24**	[redacted]	**2.27**	[redacted]	**0.03**
CareLoop cost, including 50% provision of pre-installed mobile handset with CareLoop app [redacted]	56,802	2.24	[redacted]	2.27	[redacted]	0.03
RR relapse of CareLoop, using lower 95%CI (0.26)	56,802	2.24	[redacted]	2.29	[redacted]	0.05
RR relapse of CareLoop, using upper 95% CI (0.98)	56,802	2.24	[redacted]	2.24	[redacted]	0.00
Probability of hospitalisation following relapse with CareLoop, +50% (0.375)	56,802	2.24	[redacted]	2.27	[redacted]	0.03
Relapse rate per year with standard care, using lower 95%CI (first year 12%, second year 35%, third year 40%)	54,200	2.26	[redacted]	2.28	[redacted]	0.02
Relapse rate per year with standard care, using upper 95%CI (first year 47%, second year 54%, third year 63%)	59,497	2.21	[redacted]	2.25	[redacted]	0.04
Threshold analysis: CareLoop costs per year [redacted]	56,802	2.24	[redacted]	2.27	[redacted]	0.03

10.5 *Interpretation of the economic evidence*

AVATAR and SlowMo are both symptom management interventions that could be used at any stage of psychosis intervention. They are directed at very specific symptoms so may be used to improve these symptoms instead of a broader based intervention such as CBTp, in addition to interventions such as CBTp, or while waiting for these additional interventions.

The key implementation costs are for staff training and in the case of AVATAR for laptops and audio hardware. These are not large, and subsequently the key drivers of the intervention costs are staff time. In the research setting in which clinical evidence was produced, both interventions were delivered by staff at a similar or higher level of qualification to those who would typically deliver CBTp, but over fewer sessions than are recommended by NICE for CBTp. Both companies state that they are developing training to allow a wider mix of staff to deliver the interventions in the future.

The clinical evidence shows an improvement in symptoms for both interventions compared to prior to the intervention, and compared to the comparator. The EAG identified no evidence that would allow modelling of a link between the reported symptom improvement to changes in health care resource use and long-term relapse outcome. The within-trial analysis for AVATAR showed [redacted]. The AVATAR trial also reported [redacted]. The EAG used SlowMo symptom reporting to calculate total utilities for SlowMo compared to treatment as usual, based on Garety (2021b). Neither had sufficient information to allow utilities to be included in a more detailed model.

Therefore, the EAG adopted a cost consequence approach, considering available information from systematic reviews comparing CBTp or psychological support to treatment as usual. The key limitations of this approach is that the populations and settings may not be equivalent to the intervention studies, and there are no direct comparisons with the interventions under consideration. It is therefore difficult to make any firm conclusions on the outcomes comparing AVATAR or SlowMo to CBTp.

CareLoop is designed to monitor symptoms and trigger alerts when needed in order to prevent or reduce severity of relapses. The intervention is introduced across a care provider, with relatively high initial set up costs. This is likely to be only a small per patient cost, but will be an unrecoverable cost in case of decision reversal. Because CareLoop is intended to have a direct impact on the number and severity of relapses, it is possible to create an economic

model based on existing literature. The key model drivers are the cost of the license fee, the number of avoided relapses and the number of relapses that can be treated in the community, avoiding hospitalisation. CareLoop economic modelling is based on a pilot RCT that is not fully powered, however within this limitation, the economic modelling shows CareLoop to be dominant compared to standard care. The CareLoop arm of the model is cheaper and more effective than standard care. This is in agreement with the within trial economic analysis for the pilot RCT (Gumley 2022b). Both the model and the analysis reflect the scope comparator.

Additional limitations are to understand how CareLoop will be adopted into routine use in the NHS, the ability of CareLoop to support new patients to use the app if needed, and the capacity of care coordinators to respond to alerts, with available resources to escalate patient needs if required.

11 Evidence Gap Analysis

The primary evidence gap relates to a lack of evidence for all of the technologies. While evidence of efficacy exists for all of the technologies, this is limited to only 1 fully powered RCT for AVATAR and SlowMo, and none for CareLoop.

The EAG has identified a number of ongoing studies that may contribute to identified evidence gaps. Table 23 and Table 24 summarises what the evidence gaps are for the 3 technologies.

A **GREEN** indicates that there is evidence available, **AMBER** indicates that limited evidence is available, and **RED** that no evidence is available.

Table 23: Symptom management evidence gaps

Outcomes	AVATAR	SlowMo
Clinical trials		
Comparator *CBTp and/or family intervention*	No studies **RED**	No studies **RED**
Comparator *Psychological support*	Yes – one RCT **GREEN**	Partial – one RCT, not controlled for **AMBER**
Comparator *No psychological support*	Yes – Two RCTs, control is TAU, psychological support not reported or controlled for **GREEN**	No studies **RED**
High priority outcome *Change in targeted psychotic symptoms*	Yes – Three RCTs, 2 powered, 1 observational study **GREEN**	Yes – one RCT **GREEN**
High priority outcome *Intervention adherence and completion*	Partial – Two RCTs providing limited data on adherence **AMBER**	Yes – 1 qualitative study, 1 RCT, 1 observational study **GREEN**
High priority outcome *Health related quality of life*	Yes – 2 RCTs **GREEN**	Yes – one RCT **GREEN**
High priority outcome *Patient experiences and well being*	Yes – one qualitative study **GREEN**	Yes – one qualitative study **GREEN**
High priority outcome *Intervention-related adverse events*	Yes – two RCTs, both powered **GREEN**	Yes – one RCT **GREEN**
Other outcome *Healthcare professional acceptance*	No studies **RED**	No studies **RED**
Other outcome *Changes in other psychological symptoms*	Yes – two RCTs, both powered, 1 observational study **GREEN**	Yes – one RCT **GREEN**

Outcomes	AVATAR	SlowMo
Models and economic outcomes		
Cost of the technology including licence fees and training	Partial – provided by company, some details not yet finalised **AMBER**	Partial – provided by company, some details not yet finalised **AMBER**
Cost of healthcare professional time (various grades) to deliver therapies	Partial – reported in 1 RCT, however real world implementation may differ **AMBER**	Partial – reported in 1 RCT, however real world implementation may differ **AMBER**
Health care resources associated with changes in symptom severity	Yes – one RCT, aggregated mean values **AMBER**	No studies **RED**
Utilities associated with changes in symptom severity	Yes – one RCT, aggregated mean utility **AMBER**	No studies **RED**
Longer term impact	No studies **RED**	No studies **RED**

Table 24: Relapse prevention evidence gaps

Outcomes	CareLoop
Clinical trials	
Comparator *Standard care*	Yes – two RCTs, not powered **AMBER**
High priority outcome *Rates of relapse or deterioration*	Yes – two RCTs, not powered **AMBER**
High priority outcome *Time to relapse or deterioration*	Yes – one RCT, not powered **AMBER**
High priority outcome *Intervention adherence and completion*	Yes – one RCT, not powered **AMBER**
High priority outcome *Patient experiences and well being*	Yes – one qualitative study **GREEN**
High priority outcome *Health related quality of life*	Yes – two RCTs, not powered **AMBER**
High priority outcome *Intervention-related adverse events*	Yes – two RCTs, not powered **AMBER**
Other outcome *Healthcare professional acceptance*	Yes – one qualitative study **GREEN**
Other outcome *Changes in other psychological symptoms*	Yes – two RCTs, not powered **AMBER**
Other outcome *Impact on carers and family*	No – a carer was interviewed in Allan (2023), but did not consent to their data being used for the study **RED**

Models and economic outcomes	
Cost of the technology including licence fees and training	Partial – provided by company, some details not yet finalised **AMBER**
Cost of healthcare professional time (various grades) to deliver therapies	Partial – reported in 1 RCT, however real world implementation may differ **AMBER**
Avoidance and severity of relapse	Yes – two RCTs, not powered **AMBER**
Health care resources associated with relapse and remission	Yes – one RCT, not powered **AMBER**
Utilities associated with relapse and remission	Yes – one RCT, aggregated mean utility **AMBER**
Longer term impact	No studies **RED**

11.1 *Summary and conclusions of evidence gap analysis*

The largest amount of clinical evidence was available for AVATAR therapy, followed by SlowMo, and finally CareLoop with the least amount of evidence available. The 3 technologies have been split into 2 categories of outcomes, AVATAR and SlowMo are designed to manage the symptoms of psychosis and so share outcomes, whereas CareLoop is designed to prevent relapse and so has different outcomes.

For AVATAR and SlowMo, the key outcomes involve reducing symptoms, and improving the health and wellbeing of people using them. A key evidence gap also relates to the comparator used. According to NICE clinical guidance for psychosis and schizophrenia in adults, CBTp and/or family intervention are the first line psychological treatments that are suggested for psychosis. Based on the NICE CG and scope of this EVA, these are therefore ideally what AVATAR and SlowMo should be compared against. Neither of the RCTs for these technologies compare against CBTp and/or family intervention, and so there is no evidence of increased clinical efficacy over the current most effective treatment. However, it is recognised that AVATAR and SlowMo are targeted treatments for specific symptoms of psychosis, and so a comparison against these might not be fully appropriate. Craig (2018) for AVATAR does compare against supportive counselling, however it is not clear how this itself would compare against CBTp. However, because both of these technologies can also be used alongside CBTp, another area to explore is their clinical efficacy when combined with CBTp. It may be that these technologies are always combined with CBTp or other psychological therapies. Therefore, evidence of their combination with these may be more important than evidence of their comparison with them.

Another area neglected by the current evidence is people with newly diagnosed psychosis. In Craig (2018) for AVATAR, and Garety (2021b) for SlowMo, most participants had been experiencing psychosis for 6+ years. The impact these technologies can have on people with a diagnosis of less than 1 year is worth exploration.

AVATAR has evidence (Morris, unpublished) on the impact of the intervention on [redacted]. This direct evidence is helpful to understand the wider health economic implications of AVATAR, due to the lack of alternative information that would enable modelling. Similar evidence for SlowMo is not currently available, however the company state that health economic analysis for the existing RCT (Garety 2021b) is currently underway.

For CareLoop, the main evidence gap is a lack of a powered RCT to show clinical efficacy. The feasibility RCT (Gumley 2022b) covered most of the outcomes in the scope for CareLoop, and included within trial health economic analysis. Therefore, a fully powered RCT would go far to fill these evidence gaps. It was concluded by the authors of this study that a sample size of 500 would be needed.

All three interventions are not yet in routine use in the NHS, and the model of implementation may change as this happens. Therefore future evidence of real-life implementation, including adherence, clinical outcomes and costs will be useful.

12 Integration into the NHS

Most of the evidence included was done solely in the UK, with some of the studies also including Australian and Canadian groups. These studies and the use of the technologies are therefore very relevant to the NHS. The adoption of AVATAR and SlowMo technologies would not involve a significant change in the current care pathway as they would be used in conjunction with the current recommended psychological treatment, CBTp. The adoption of CareLoop into the NHS would need a change to follow up care. Currently, the care coordinator would follow up with people every 6-8 weeks, and a psychiatrist every 6-12 months. With CareLoop, care coordinators would be following up with patients over the phone every time an alert of new symptoms is flagged through CareLoop. Depending on the specifics of the flag, the care coordinator would either resolve the alert by phone or also refer to either inpatient services, the psychiatrist, or the at-home treatment team.

For AVATAR and SlowMo, the training needed would be one day for those that are already trained to deliver CBTp, plus supervision of initial cases. For

CareLoop, the training is minimal and would mostly involve how to use the IT interface of CareLoop when receiving alerts.

Currently AVATAR and SlowMo have been used by psychologists trained in CBTp, however both are hoping to implement training and delivery by a broader range of staff in the future.

The additional factor of access to a smartphone with internet capability also needs to be considered CareLoop. However, it is possible that a smartphone can be provided to patients by psychiatric services. While SlowMo is augmented by access to a smartphone, it is not required and patients can access non-digital versions if needed. For AVATAR, access to two computers connected by a network, audio connections, and somewhere to set them up would only be needed by the healthcare team.

13 Conclusions

13.1 *Conclusions from the clinical evidence*

Symptom management: There is good quality evidence from large studies using appropriate comparators and relevant outcome measures, that suggests that AVATAR and SlowMo are effective at reducing symptoms of psychosis for the specific symptoms they target. For AVATAR, this is auditory voice hallucinations, and for SlowMo this is paranoia and delusions. The evidence suggests these reductions can persist up to 24 weeks post treatment.

For AVATAR, there is some evidence that it has an impact on other symptoms of psychosis, and quality of life. There is evidence that it can reduce anxiety and depression. For SlowMo, there is evidence suggesting that it is effective at improving quality of life scores, wellbeing, self-concept and worry scores. Qualitative evidence for both AVATAR and SlowMo suggests that it is acceptable and feasible for use by people with psychosis. There are no identified safety issues with AVATAR or SlowMo.

AVATAR and SlowMo would both integrate well into current NHS practice, and can be used alongside current psychological therapies for psychosis. There are no issues regarding generalisability. AVATAR does not require patients have access to a smartphone with internet. While SlowMo is augmented by access to a smartphone, there are non-digital options available.

The EAG concludes that both AVATAR and SlowMo show promise, but additional evidence is needed comparing their use against and alongside currently used psychological therapies in the NHS. Longer term evidence regarding recovery and relapse rates should also be explored.

Relapse prevention: There is some good quality evidence that suggests CareLoop is effective at recognising and reducing relapses of psychosis, and mixed evidence that CareLoop is effective at reducing symptoms of psychosis. However, this evidence comes from a feasibility RCT that is not fully powered to detect an effect. This same RCT suggests that CareLoop is acceptable and safe for use by those with psychosis, and it suggests that a larger RCT would be feasible to conduct.

CareLoop can be integrated into NHS care. However, it would need a change to the current care pathway. Access to a smartphone with internet needs to be considered. There is evidence suggesting that some people with psychosis would find it difficult or be unable to access CareLoop.

The EAG concludes that CareLoop shows promise, but more evidence is needed to shows its efficacy compared to standard care, in a powered RCT.

13.2 *Conclusions from the economic evidence*

Symptom management: AVATAR and SlowMo are relatively straightforward to implement and do not have large unrecoverable costs. If used as an adjunct, or during waiting list time, they will add an additional cost to the delivery of the service, unless other interventions are avoided. If they are used instead of CBTp there would be a reduction in delivery costs, but no direct evidence to compare clinical outcomes.

For AVATAR there is [redacted], but there is no similar evidence available for SlowMo.

If they are used instead of CBTp there would be a reduction in delivery costs, but no direct evidence to compare clinical outcomes. They have evidence for clinical improvement of symptoms compared to treatment as usual or supportive counselling. AVATAR also, if used as an adjunct or during waiting list time, will add an additional cost to the service. For AVATAR there is some evidence of a [redacted] this is not available for SlowMo. If they are used instead of CBTp there would be a reduction in delivery costs, but no direct evidence to compare clinical outcomes.

Symptom monitoring and relapse prevention: CareLoop would be introduced across a care provider, which the EAG has assumed to be 200 patients, with a 50% uptake. There is a relatively high initial set up costs, however over a three-year time horizon, this is a small cost per patient modelled. However, the set-up cost would be an unrecoverable cost if the adoption of CareLoop was reversed.

The EAG created a cost effectiveness model for CareLoop, using a three-year time horizon, and modelled states of remission, relapse and death. The EAG model showed CareLoop to be cost saving when compared to standard care. The key model drivers were the cost of the licence fee, the number of avoided relapses and the number of relapses that can be treated in the community, avoiding hospitalisation. care. This is in agreement with the within trial economic analysis for the pilot RCT (Gumley 2022b).

Key limitations are that CareLoop economic modelling is based on a pilot RCT that is not fully powered, and that routine integration into the NHS may have some differences compared to the reported research study. Both the model and the analysis reflect the scope comparator.

14 Summary of the combined clinical and economic sections

While there is evidence of efficacy for AVATAR and SlowMo, there is no evidence of them being more effective at reducing symptoms than CBTp. There is also no long-term evidence for the impact of these two technologies. AVATAR has within trial economic [redacted], but neither AVATAR or SlowMo have evidence to build an economic model. Future outcomes linking changes in symptom severity to changes in utility and healthcare resource use would allow modelling of short to intermediate time frames. Longer follow up with information on relapse rates would allow a more complete model.

The evidence of the efficacy of CareLoop is based on a feasibility RCT with insufficient power. This feasibility RCT did demonstrate the acceptability and feasibility of CareLoop. If a larger powered RCT could replicate the findings of the feasibility RCT, then both the EAG modelling and within trial analysis find it to be cost saving at 3 years and 1 year respectively. A larger study would add confidence to this finding, as would information on routine real-world implementation using Care Co-ordinators to respond to alerts.

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16 Appendices

Appendix A: Clinical data search strategy

Appendix B: Studies excluded at full text

Appendix C: Clinical searches PRISMA Diagram

Appendix D: Economic studies quality appraisal

Appendix E: Economic searches

Appendix F: Economic searches PRISMA diagram

Appendix G: Systematic reviews for economic evidence in psychosis

Appendix A: Clinical data search strategy

The EAG did a search for both clinical and economic evidence as directed by the scope. Eight bibliographic databases were searched from inception to 6th September 2023, using a range of free text terms and, where appropriate, indexed terms. The searches were not restricted by language of publication. Two clinical trial registries were also searched for ongoing and unpublished trials; the companies' websites were also searched for additional literature. The MHRA's medical device alerts and field safety notices and the FDA MAUDE database were searched for adverse events.

Clinical searches

Date	Database Name	Total Number of records retrieved	Total number of records after de-duplication
07/09/23	Medline ALL	176	
07/09/23	Embase	286	
07/09/23	PsycInfo	204	
07/09/23	The Cochrane Library CDSR CENTRAL	 3 99	
07/09/23	INAHTA	2	
08/09/23	Company website: Avatar Therapy Ltd SlowMo Therapy CareLoop Health	 35 6 15	
07/09/23	Guidelines NICE SIGN	 4 1	
07/09/23	MHRA– search MDA & FSN in following:	0	
07/09/23	FDA MAUDE	0	
07/09/23	Clinical Trials.gov	Avatar therapy: 11 CareLoop: 0 SlowMo: 0	
07/09/23	ICTRP	Avatar therapy: 23 CareLoop: 2 SlowMo: 1	
			462 records after manual deduplication

EAG search strategies

Ovid MEDLINE(R) ALL <1946 to September 06, 2023>

1 slowmo.tw. 12

2 "slow mo".tw. 9

3 (fast adj3 (think* or thought*)).tw. 178

4 (reasoning adj3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1406

5 or/1-4 1597

6 careloop.tw. 0

7 "care loop".tw. 16

8 careloop.in. 0

9 (("early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 291

10 or/6-9 307

11 avatar*.tw. 2031

12 avatar therapy.in. 0

13 (digital adj (representation or simulation)).tw. 424

14 or/11-13 2446

15 5 or 10 or 14 4350

16 Psychotic Disorders/ 52530

17 exp Schizophrenia/ 115452

18 Affective Disorders, Psychotic/ 2317

19 Paranoid Disorders/ 4279

20 Delusions/ 8159

21 Hallucinations/ 11934

22 psychos#s.tw. 51128

23 psychotic.tw. 38981

24 schizophreni*.tw. 138804

25 paranoi*.tw. 8987

26 delusion*.tw. 12329

27 hallucin*.tw. 20263

28 (hear* adj2 voice*).tw. 1513

29 (see* adj thing*).tw. 180

30 or/16-29 247365

31 15 and 30 176

32 exp animals/ not humans.sh. 5152453

33 31 not 32 176

Embase <1974 to 2023 September 06>

1 slowmo.tw. 13

2 "slow mo".tw. 8

3 (fast adj3 (think* or thought*)).tw. 229

4 (reasoning adj3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1672

5 or/1-4 1914

6 careloop.tw. 1

7 "care loop".tw. 18

8 careloop.in. 0

9 (("early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 426

10 or/6-9 445

11 avatar*.tw. 2655

12 avatar therapy.in. 0

13 (digital adj (representation or simulation)).tw. 507

14 or/11-13 3147

15 5 or 10 or 14 5506

16 psychosis/ 106552

17 acute psychosis/ 2194

18 affective psychosis/ 1970

19 brief psychotic disorder/ 661

20 childhood psychosis/ 64

21 exp schizophrenia spectrum disorder/ 211464

22 exp paranoid psychosis/ 18210

23 delusion/ 18071

24 exp hallucination/ 44251

25 psychos#s.tw. 72769

26 psychotic.tw. 59980

27 schizophreni*.tw. 184083

28 paranoi*.tw. 12963

29 delusion*.tw. 18798

30 hallucin*.tw. 31006

31 (hear* adj2 voice*).tw. 2014

32 (see* adj thing*).tw. 255

33 or/16-32 367077

34 15 and 33 286

APA PsycInfo <1806 to August Week 4 2023>

1 slowmo.tw. 5

2 "slow mo".tw. 1

3 (fast adj3 (think* or thought*)).tw. 166

4 (reasoning adj3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1914

5 or/1-4 2084

6 careloop.tw. 0

7 "care loop".tw. 1

8 careloop.in. 0

9 (("early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 163

10 or/6-9 164

11 avatar*.tw. 2185

12 avatar therapy.in. 0

13 (digital adj (representation or simulation)).tw. 76

14 or/11-13 2246

15 5 or 10 or 14 4493

16 psychosis/ 32920

17 brief psychotic disorder/ 1342

18 exp childhood onset psychosis/ 1807

19 chronic psychosis/ 250

20 exp schizophrenia/ 99476

21 affective psychosis/ 591

22 exp paranoid psychosis/ 1502

23 reactive psychosis/ 286

24 delusions/ 6054

25 delusional disorder/ 4

26 hallucinations/ 3890

27 hallucinosis/ 158

28 auditory hallucinations/ 2429

29 visual hallucinations/ 1117

30 psychos#s.tw. 61159

31 psychotic.tw. 47561

32 schizophreni*.tw. 135741

33 paranoi*.tw. 15226

34 delusion*.tw. 16120

35 hallucin*.tw. 19674

36 (hear* adj2 voice*).tw. 2376

37 (see* adj thing*).tw. 430

38 or/16-37 212874

39 15 and 38 204

INAHTA

((see* AND thing*) OR (hear* AND voice*) OR (hallucin*) OR (delusion*) OR (paranoi*) OR (schizophreni*) OR (psychotic) OR (psychoses) OR (psychosis) OR ("Hallucinations"[mh]) OR ("Delusions"[mh]) OR ("Paranoid Disorders"[mh]) OR ("Affective Disorders, Psychotic"[mh]) OR ("Schizophrenia"[mhe]) OR ("Psychotic Disorders"[mh])) AND (((digital AND (representation or simulation)) OR ("avatar therapy") OR (avatar*)) OR ((reasoning AND (digital* or app* or web* or internet or comput* or online or

mhealth or smartphone*)) OR (fast AND (think* or thought*)) OR ("slow mo") OR (slowmo)))

*Careloop terms searched returned 0 results and created an error when included in the search strate*gy: ((early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)) OR ("care loop") OR (careloop)

Cochrane Library

Date Run: 07/09/2023 10:44:56

ID Search Hits

#1 (slowmo):ti,ab,kw (Word variations have been searched) 10

#2 ("slow mo"):ti,ab,kw (Word variations have been searched) 10

#3 (fast NEAR/3 (think* or thought*)):ti,ab,kw 15

#4 (reasoning NEAR/3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)):ti,ab,kw 78

#5 #1 OR #2 OR #3 OR #4 97

#6 (careloop):ti,ab,kw 2

#7 ("care loop"):ti,ab,kw 3

#8 (("early warning signs" or "early signs monitoring") AND (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)):ti,ab,kw 69

#9 #6 OR #7 OR #8 71

#10 (avatar*):ti,ab,kw 428

#11 (digital NEAR/1 (representation or simulation)):ti,ab,kw 23

#12 #10 OR #11 443

#13 #5 OR #9 OR #12 611

#14 MeSH descriptor: [Psychotic Disorders] explode all trees 3766

#15 MeSH descriptor: [Schizophrenia] explode all trees 10059

#16 MeSH descriptor: [Affective Disorders, Psychotic] explode all trees 105

#17 MeSH descriptor: [Paranoid Disorders] explode all trees 113

#18 MeSH descriptor: [Delusions] this term only 203

#19 MeSH descriptor: [Hallucinations] this term only 433

#20 (psychos?s):ti,ab,kw 7806

#21 (psychotic):ti,ab,kw 8212

#22 (schizophreni*):ti,ab,kw 19965

#23 (paranoi*):ti,ab,kw 995

#24 (delusion*):ti,ab,kw 1479

#25 (hallucin*):ti,ab,kw 3199

#26 (hear* NEAR/2 voice*):ti,ab,kw 223

#27 (see* NEAR/1 thing*):ti,ab,kw 71

#28 #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 28730

#29 #13 AND #28 102

NICE guidelines

Searched for “psychosis”

Published: 4 results, 3 relevant (1 on psychosis and substance misuse)

NG181 Rehabilitation for adults with complex psychosis

CG155 Psychosis and schizophrenia in children and young people: recognition and management

CG178 Psychosis and schizophrenia in adults: prevention and management

In consultation, In development, Awaiting development, Topic selection: 0

Searched for “schizophrenia”

Published: 2 duplicates (CG155, CG178)

In consultation, In development, Awaiting development, Topic selection: 0

From scope

NG197 Shared decision making

SIGN guidelines

131 Management of schizophrenia

MAUDE

AVATAR Therapy: 0 results

AVATAR: 9 results, 0 relevant

CareLoop: 0 results

Care Loop: 500 results, 0 relevant (all for diabetes care technology)

SlowMo: 0 results

Slow Mo: 500 results, 0 relevant

MHRA

AVATAR: 0 results

CareLoop: 0 results

SlowMo: 0 results

ClinicalTrials.gov

Avatar therapy

35 ongoing 5 relevant

39 completed 6 relevant

CareLoop: 0 results

SlowMo: 0 results

ICTRP

Avatar therapy: 23 results

CareLoop: 2 results

SlowMo: 1 result

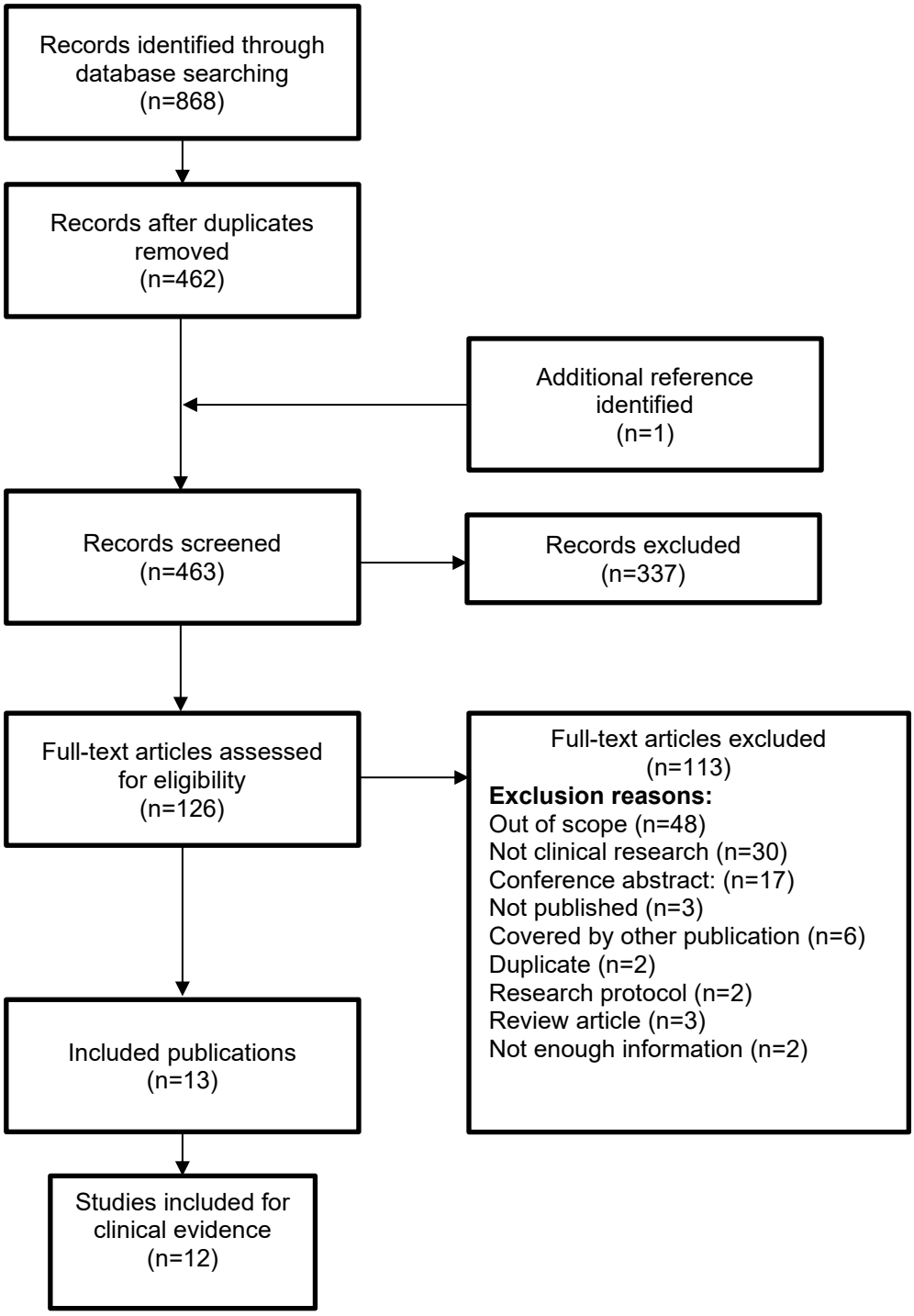
Appendix B: Studies excluded at full text

Study author and year Study title	Reason for exclusion at full-text
Aali et al, 2020	Review article
Abu Sabra et al, 2022	Out of scope
Adler et al, 2020	Out of scope
Alderson-Day and Jones 2018	Not clinical research
Allan et al, 2019	Out of scope
Allan et al, 2020	Out of scope
Allan et al, 2021	Out of scope
Beaudoin et al, 2021	Not clinical research
Beaudoin et al, 2023	Out of scope
Beaudoin et al, 2023	Out of scope
Berry et al, 2020	Out of scope
Brander et al, 2021	Out of scope
Brunet-Gouet et al, 2016	Conference abstract
Bucci et al, 2018	Conference abstract
Bucci et al, 2018	Out of scope
Burr et al, 2022	Not clinical research
ChiCTR1900027254	Not enough information
ChiCTR2100053045	Not enough information
ChiCTR2200063483	Out of scope
Clarke et al, 2019	Review article
Craig 2019	Not clinical research
Craig 2020	Conference abstract
Craig et al, 2014	Conference abstract
Craig et al, 2015	Research protocol
Craig et al, 2016	Not clinical research
Craig et al, 2018	Not clinical research
Craig et al, 2021	Not clinical research
Craig et al, 2022	Conference abstract
Deamer and Hayward 2018	Not clinical research
Deamer and Wilkinson 2015	Not clinical research
Dellazizzo et al, 2018	Not clinical research
Dellazizzo et al, 2018	Out of scope
Dellazizzo et al, 2018	Out of scope
Dellazizzo et al, 2018	Out of scope
Dellazizzo et al, 2020	Out of scope
Dellazizzo et al, 2021	Out of scope
Dellazizzo et al, 2021	Out of scope
Dellazizzo et al, 2022	Out of scope
Donath 2007	Out of scope
Edwards et al, 2023	Out of scope
Eisner et al, 2019	Out of scope
Firth and Torous 2015	Review article
Garety 2019	Conference abstract
Garety et al, 2011	Out of scope
Garety et al, 2015	Out of scope
Garety et al, 2017	Research protocol
Garety et al, 2019	Conference abstract
Garety et al, 2020	Not clinical research
Garety et al, 2021	Duplicate
Garety et al, 2022	Conference abstract
Gerner 2015	Conference abstract
Glantz et al, 2003	Not clinical research
Greenwood et al, 2022	Out of scope

Study author and year Study title	Reason for exclusion at full-text
Gumley et al, 2018	Out of scope
Hall et al, 2018	Out of scope
Han et al, 2012	Out of scope
Hardy et al, 2018	Out of scope
Huckvale et al, 2013	Not clinical research
Hudon et al, 2022	Not clinical research
Hudon et al, 2023	Not clinical research
Hudon et al, 2023	Not clinical research
Hudon et al, 2023	Not clinical research
ISRCTN10781027	Out of scope
ISRCTN32448671	Included in another publication
ISRCTN65314790	Included in another publication
ISRCTN88145142	Included in another publication
ISRCTN99559262	Included in another publication
Kapadia 2022	Out of scope
Ku et al, 2005	Out of scope
Ku et al, 2006	Out of scope
Leff 2013	Not clinical research
Leff et al, 2014	Not clinical research
Lewis et al, 2018	Conference abstract
Lewis et al, 2018	Conference abstract
Liang et al, 2021	Out of scope
Marcos-Pablos et al, 2016	Out of scope
Marcos-Pablos et al, 2016	Out of scope
Moazzen and Shokraneh 2015	Out of scope
NCT03148639	Unpublished
NCT03585127	Out of scope
NCT04054778	Unpublished
NCT04054778	Out of scope
NCT04099940	Included in another publication
NCT04661163	Out of scope
NCT05982158	Unpublished
Ngo-Minh et al, 2018	Conference abstract
NIHR, HSC 2016	Included in another publication
Nordentoft 2022	Conference abstract
O'Brien et al, 2021	Out of scope
Ozerol and Andic 2023	Not clinical research
Palmier-Claus et al, 2012	Out of scope
Palmier-Claus et al, 2013	Out of scope
Palmier-Claus et al, 2013	Out of scope
Palmier-Claus et al, 2014	Out of scope
Peters & Wykes, 2014	Conference abstract
Rehm et al, 2016	Not clinical research
Rus-Calafell et al, 2015	Duplicate
Rus-Calafell et al, 2015	Not clinical research
Rus-Calafell et al, 2016	Conference abstract
Sagalakova et al, 2021	Not clinical research
Skoneczny et al, 2019	Conference abstract
Stark 2017	Not clinical research
Stefaniak et al, 2017	Out of scope
Stefaniak et al, 2019	Out of scope
Surmann et al, 2017	Not clinical research
The Psychologist. Vol.26,(7), 2013, pp. 478	Not clinical research
Thomas et al, 2019	Not clinical research

Study author and year Study title	Reason for exclusion at full-text
Ward et al, 2014	Conference abstract
Ward et al, 2019	Not clinical research
Ward et al, 2020	Not clinical research
Ward et al, 2022	Not clinical research
Whelan et al, 2015	Out of scope
Xenitidis et al, 2013	Out of scope

Appendix C: Clinical searches PRISMA Diagram



Appendix D: Economic studies quality appraisal

Item Morris (unpublished)	Yes	No	Not clear	Not appropriate
Study design				
1. The research question is stated.				
2. The economic importance of the research question is stated.				
3. The viewpoint(s) of the analysis are clearly stated and justified.				
4. The rationale for choosing alternative programmes or interventions compared is stated.				
5. The alternatives being compared are clearly described.				
6. The form of economic evaluation used is stated.				
7. The choice of form of economic evaluation is justified in relation to the questions addressed.				
Data collection				
8. The source(s) of effectiveness estimates used are stated.				
9. Details of the design and results of effectiveness study are given (if based on a single study).				

10.	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies).				
11.	The primary outcome measure(s) for the economic evaluation are clearly stated.				
12.	Methods to value benefits are stated.				
13.	Details of the subjects from whom valuations were obtained were given.				
14.	Productivity changes (if included) are reported separately.				
15.	The relevance of productivity changes to the study question is discussed.				
16.	Quantities of resource use are reported separately from their unit costs.				
17.	Methods for the estimation of quantities and unit costs are described.				
18.	Currency and price data are recorded.				
19.	Details of currency of price adjustments for inflation or currency conversion are given.				
20.	Details of any model used are given.				
21.	The choice of model used and the key parameters on which it is				

	based are justified.				
Analysis and interpretation of results					
22.	Time horizon of costs and benefits is stated.				
23.	The discount rate(s) is stated.				
24.	The choice of discount rate(s) is justified.				
25.	An explanation is given if costs and benefits are not discounted.				
26.	Details of statistical tests and confidence intervals are given for stochastic data.				
27.	The approach to sensitivity analysis is given.				
28.	The choice of variables for sensitivity analysis is justified.				
29.	The ranges over which the variables are varied are justified.				
30.	Relevant alternatives are compared.				
31.	Incremental analysis is reported.				
32.	Major outcomes are presented in a disaggregated as well as aggregated form.				
33.	The answer to the study question is given.				
34.	Conclusions follow from				

	the data reported.				
35.	Conclusions are accompanied by the appropriate caveats.	[redacted]			

Item Gumley 2022b		Yes	No	Not clear	Not appropriate
Study design					
1.	The research question is stated.	✓			To test feasibility of collecting economic measures and inform design of full trial
2.	The economic importance of the research question is stated.			✓	
3.	The viewpoint(s) of the analysis are clearly stated and justified.	✓			Yes, 3 clearly explained
4.	The rationale for choosing alternative programmes or interventions compared is stated.	✓			
5.	The alternatives being compared are clearly described.	✓			TAU described as largely involving regular (fortnightly or monthly) follow up with a care-coordinator and regular review by a psychiatrist.
6.	The form of economic evaluation used is stated.	✓			CEA
7.	The choice of form of economic evaluation is justified in relation to the questions addressed.	✓			
Data collection					
8.	The source(s) of effectiveness estimates used are stated.	✓			EMPOWER RCT
9.	Details of the design and results of effectiveness study are given (if based on a single study).	✓			In published paper and RCT
10.	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies).				n/a
11.	The primary outcome measure(s) for the economic evaluation are clearly stated.	✓			EQ-5D-5L
12.	Methods to value benefits are stated.	✓			Mapping to EQ-5D-3L and use of UK value set
13.	Details of the subjects from whom valuations were obtained were given.	✓			
14.	Productivity changes (if included) are reported separately.	✓			Carer productivity reported
15.	The relevance of productivity changes to the study question is discussed.				
16.	Quantities of resource use are reported separately from their unit costs.			✓	Unit costs are provided and total costs
17.	Methods for the estimation of quantities and unit costs are described.	✓			

18.	Currency and price data are recorded.			✓	Local costs applied to patients from each country. These are summed together for total results due to size of sample
19.	Details of currency of price adjustments for inflation or currency conversion are given.				n/a
20.	Details of any model used are given.				n/a
21.	The choice of model used and the key parameters on which it is based are justified.				n/a
Analysis and interpretation of results					
22.	Time horizon of costs and benefits is stated.	✓			12 months
23.	The discount rate(s) is stated.				n/a
24.	The choice of discount rate(s) is justified.				n/a
25.	An explanation is given if costs and benefits are not discounted.	✓			Short time horizon
26.	Details of statistical tests and confidence intervals are given for stochastic data.	✓			
27.	The approach to sensitivity analysis is given.	✓			Complete case analysis and use of AQoL-8D
28.	The choice of variables for sensitivity analysis is justified.		✓		
29.	The ranges over which the variables are varied are justified.		✓		
30.	Relevant alternatives are compared.	✓			In the sensitivity analysis
31.	Incremental analysis is reported.	✓			
32.	Major outcomes are presented in a disaggregated as well as aggregated form.	✓			
33.	The answer to the study question is given.	✓			
34.	Conclusions follow from the data reported.	✓			
35.	Conclusions are accompanied by the appropriate caveats.	✓			

Appendix E: Economic searches

In addition to the technology specific searches described in Appendix A, the EAG also completed a broader search to inform modelling structures and inputs. The initial search found 730 results after automatic EndNote deduplication on import, and it was therefore restricted to identify existing models, or economic analysis that was based in the UK. One additional review was identified through references, and a total of 6 systematic reviews of economic models were included and summarised in Appendix F.

Economic search summary

Date	Database Name	Total Number of records retrieved	Total number of records from

			database after automatic de-duplication
21/09/23	Medline	181	181
21/09/23	Embase	179	96
21/09/23	PsycInfo	83	30
21/09/23	Cochrane CDSR	8	6
21/09/23	INAHTA	34	31
	Total	485	344
	Total after manual deduplication: 313		

Ovid MEDLINE(R) ALL <1946 to September 20, 2023>

1 (slowmo or "slow mo").tw. 21

2 (fast adj3 (think* or thought*)).tw. 178

3 (reasoning adj3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1411

4 (careloop or "care loop").tw. 16

5 careloop.in. 0

6 (("early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 292

7 ((prevent* adj relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1357

8 ((predict* adj2 relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1508

9 avatar*.tw. 2046

10 avatar therapy.in. 0

11 (digital adj (representation or simulation)).tw. 426

12 computer-assisted therap*.tw. 66

13 ((digital or smartphone) adj3 "monitoring system").tw. 76

14 (relapse* adj1 prevent*).tw. 7850

15 (early warning signs or EWS).tw. 3160

16 early signs monitoring.tw. 10

17 blended digital intervention.tw. 1

18 personali?ed smartphone-based app*.tw. 1

19 intervention*.tw. 1338291

20 or/1-19 1352154

21 Psychotic Disorders/ 52627

22 exp Schizophrenia/ 115571

23 Affective Disorders, Psychotic/ 2317

24 Paranoid Disorders/ 4284

25 Delusions/ 8165

26 Hallucinations/ 11945

27 psychos#s.tw. 51228

28 psychotic.tw. 39056

29 schizophreni*.tw. 139001

30 paranoi*.tw. 8999

31 delusion*.tw. 12344

32 hallucin*.tw. 20301

33 (hear* adj2 voice*).tw. 1517

34 (see* adj thing*).tw. 180

35 or/21-34 247710

36 20 and 35 18939

37 Cost-Benefit Analysis/ 93061

38 (cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. 17601

39 ((incremental* adj2 cost*) or ICER).tw. 18092

40 (cost adj2 utilit*).tw. 6945

41 (cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. 2344

42 ((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. 23956

43 (cost and (effect* or utilit*)).ti. 39033

44 or/37-43 114805

45 36 and 44 393

46 exp animals/ not humans.sh. 5156723

47 45 not 46 393

48 (uk or "united kingdom" or england or wales or scotland or "northern ireland" or britain or english or welsh or scottish or "northern irish" or british).tw. 455160

49 model*.tw. 3788354

50 48 or 49 4182228

51 47 and 50 181

Embase <1974 to 2023 September 20>

1 (slowmo or "slow mo").tw. 20

2 (fast adj3 (think* or thought*)).tw. 232

3 (reasoning adj3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1676

4 (careloop or "care loop").tw. 19

5 careloop.in. 0

6 (("early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 427

7 ((prevent* adj relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 2202

8 ((predict* adj2 relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 2947

9 avatar*.tw. 2669

10 avatar therapy.in. 0

11 (digital adj (representation or simulation)).tw. 507

12 computer-assisted therap*.tw. 88

13 ((digital or smartphone) adj3 "monitoring system").tw. 129

14 (relapse* adj1 prevent*).tw. 12049

15 (early warning signs or EWS).tw. 4715

16 early signs monitoring.tw. 10

17 blended digital intervention.tw. 1

18 personali?ed smartphone-based app*.tw. 1

19 intervention*.tw. 1850317

20 or/1-19 1871117

21 psychosis/ 106782

22 acute psychosis/ 2196

23 affective psychosis/ 1974

24 brief psychotic disorder/ 661

25 childhood psychosis/ 64

26 exp schizophrenia spectrum disorder/ 211810

27 exp paranoid psychosis/ 18244

28 delusion/ 18130

29 exp hallucination/ 44382

30 psychos#s.tw. 72893

31 psychotic.tw. 60125

32 schizophreni*.tw. 184368

33 paranoi*.tw. 12984

34 delusion*.tw. 18860

35 hallucin*.tw. 31102

36 (hear* adj2 voice*).tw. 2028

37 (see* adj thing*).tw. 255

38 or/21-37 367774

39 20 and 38 34003

40 cost utility analysis/ 12347

41 (cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. 29947

42 ((incremental* adj2 cost*) or ICER).tw. 30638

43 (cost adj2 utilit*).tw. 10980

44 (cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. 3259

45 ((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. 36470

46 (cost and (effect* or utilit*)).ti. 57156

47 or/40-46 90360

48 39 and 47 398

49 (uk or "united kingdom" or england or wales or scotland or "northern ireland" or britain or english or welsh or scottish or "northern irish" or british).tw. 759299

50 model*.tw. 4766197

51 49 or 50 5418113

52 48 and 51 179

APA PsycInfo <1806 to September Week 2 2023>

1 (slowmo or "slow mo").tw. 6

2 (fast adj3 (think* or thought*)).tw. 166

3 (reasoning adj3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 1916

4 (careloop or "care loop").tw. 1

5 careloop.in. 0

6 (("early warning signs" or "early signs monitoring") and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 166

7 ((prevent* adj relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 680

8 ((predict* adj2 relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. 436

9 avatar*.tw. 2190

10 avatar therapy.in. 0

11 (digital adj (representation or simulation)).tw. 76

12 computer-assisted therap*.tw. 115

13 ((digital or smartphone) adj3 "monitoring system").tw. 6

14 (relapse* adj1 prevent*).tw. 6538

15 (early warning signs or EWS).tw. 442

16 early signs monitoring.tw. 12

17 blended digital intervention.tw. 1

18 personali?ed smartphone-based app*.tw. 0

19 intervention*.tw. 487003

20 or/1-19 495980

21 psychosis/ 32954

22 brief psychotic disorder/ 1286

23 exp childhood onset psychosis/ 1797

24 chronic psychosis/ 251

25 exp schizophrenia/ 99525

26 affective psychosis/ 591

27 exp paranoid psychosis/ 1492

28 reactive psychosis/ 287

29 delusions/ 6058

30 delusional disorder/ 4

31 hallucinations/ 3890

32 hallucinosis/ 158

33 auditory hallucinations/ 2430

34 visual hallucinations/ 1118

35 psychos#s.tw. 61206

36 psychotic.tw. 47598

37 schizophreni*.tw. 135818

38 paranoi*.tw. 15233

39 delusion*.tw. 16133

40 hallucin*.tw. 19684

41 (hear* adj2 voice*).tw. 2382

42 (see* adj thing*).tw. 431

43 or/21-42 213004

44 20 and 43 19718

45 "costs and cost analysis"/ 19280

46 (cost* and ((qualit* adj2 adjust* adj2 life*) or qaly*)).tw. 1572

47 ((incremental* adj2 cost*) or ICER).tw. 1436

48 (cost adj2 utilit*).tw. 975

49 (cost* and ((net adj benefit*) or (net adj monetary adj benefit*) or (net adj health adj benefit*))).tw. 408

50 ((cost adj2 (effect* or utilit*)) and (quality adj of adj life)).tw. 2722

51 (cost and (effect* or utilit*)).ti. 3540

52 or/45-51 22688

53 44 and 52 217

54 (uk or "united kingdom" or england or wales or scotland or "northern ireland" or britain or english or welsh or scottish or "northern irish" or british).tw. 265730

55 model*.tw. 892014

56 54 or 55 1122874

57 53 and 56 83

Cochrane CDSR

Date Run: 21/09/2023 12:58:26

ID	Search	Hits
#1	(slowmo):ti,ab,kw (Word variations have been searched)	10
#2	("slow mo"):ti,ab,kw (Word variations have been searched)	10
#3	(fast NEAR/3 (think* or thought*)):ti,ab,kw	15
#4	(reasoning NEAR/3 (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)):ti,ab,kw	78
#5	(careloop):ti,ab,kw	2
#6	("care loop"):ti,ab,kw	3
#7	(("early warning signs" or "early signs monitoring") AND (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)):ti,ab,kw	69
#8	((prevent* NEAR/1 relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)):ti,ab,kw	1494
#9	((predict* NEAR/2 relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)):ti,ab,kw	237
#10	(avatar*):ti,ab,kw	428
#11	(digital NEAR/1 (representation or simulation)):ti,ab,kw	23
#12	(computer-assisted therap*):ti,ab,kw	9368
#13	((digital or smartphone) NEAR/3 "monitoring system"):ti,ab,kw	28
#14	(relapse* NEAR/1 prevent*):ti,ab,kw	3780
#15	(early warning signs or EWS):ti,ab,kw	307
#16	(early signs monitoring):ti,ab,kw	709

#17 (blended digital intervention):ti,ab,kw 50

#18 (personali?ed smartphone-based app*):ti,ab,kw 59

#19 (intervention*):ti,ab,kw 563945

#20 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 573785

#21 MeSH descriptor: [Psychotic Disorders] explode all trees 3766

#22 MeSH descriptor: [Schizophrenia] explode all trees 10059

#23 MeSH descriptor: [Affective Disorders, Psychotic] explode all trees 105

#24 MeSH descriptor: [Paranoid Disorders] explode all trees 113

#25 MeSH descriptor: [Delusions] this term only 203

#26 MeSH descriptor: [Hallucinations] this term only 433

#27 (psychos?s):ti,ab,kw 7806

#28 (psychotic):ti,ab,kw 8212

#29 (schizophreni*):ti,ab,kw 19965

#30 (paranoi*):ti,ab,kw 995

#31 (delusion*):ti,ab,kw 1479

#32 (hallucin*):ti,ab,kw 3199

#33 (hear* NEAR/2 voice*):ti,ab,kw 223

#34 (see* NEAR/1 thing*):ti,ab,kw 71

#35 #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 28730

#36 #20 AND #35 9984

#37 MeSH descriptor: [Cost-Benefit Analysis] explode all trees 9846

#38 (cost* AND ((qualit* NEAR/2 adjust* NEAR/2 life*) OR qaly*)):ti,ab,kw 6529

#39 ((incremental* NEAR/2 cost*) or ICER):ti,ab,kw 5989

#40 (cost NEAR/2 utilit*):ti,ab,kw 2631

#41 (cost* AND ((net NEAR/1 benefit*) OR (net NEAR/1 monetary NEAR/1 benefit*) OR (net NEAR/1 health NEAR/1 benefit*))):ti,ab,kw 571

#42 ((cost NEAR/2 (effect* OR utilit*)) AND (quality NEAR/1 of NEAR/1life)):ti,ab,kw 10953

#43 (cost AND (effect* OR utilit*)):ti 9664

#44 #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 24103

#45 #36 AND #44 332

#46 (uk OR "united kingdom" OR england OR wales OR scotland OR "northern ireland" OR britain OR english OR welsh OR scottish OR "northern irish" OR british):ti,ab,kw 50242

#47 (model*):ti,ab,kw 171205

#48 #46 OR #47 214228

#49 #45 AND 48 24

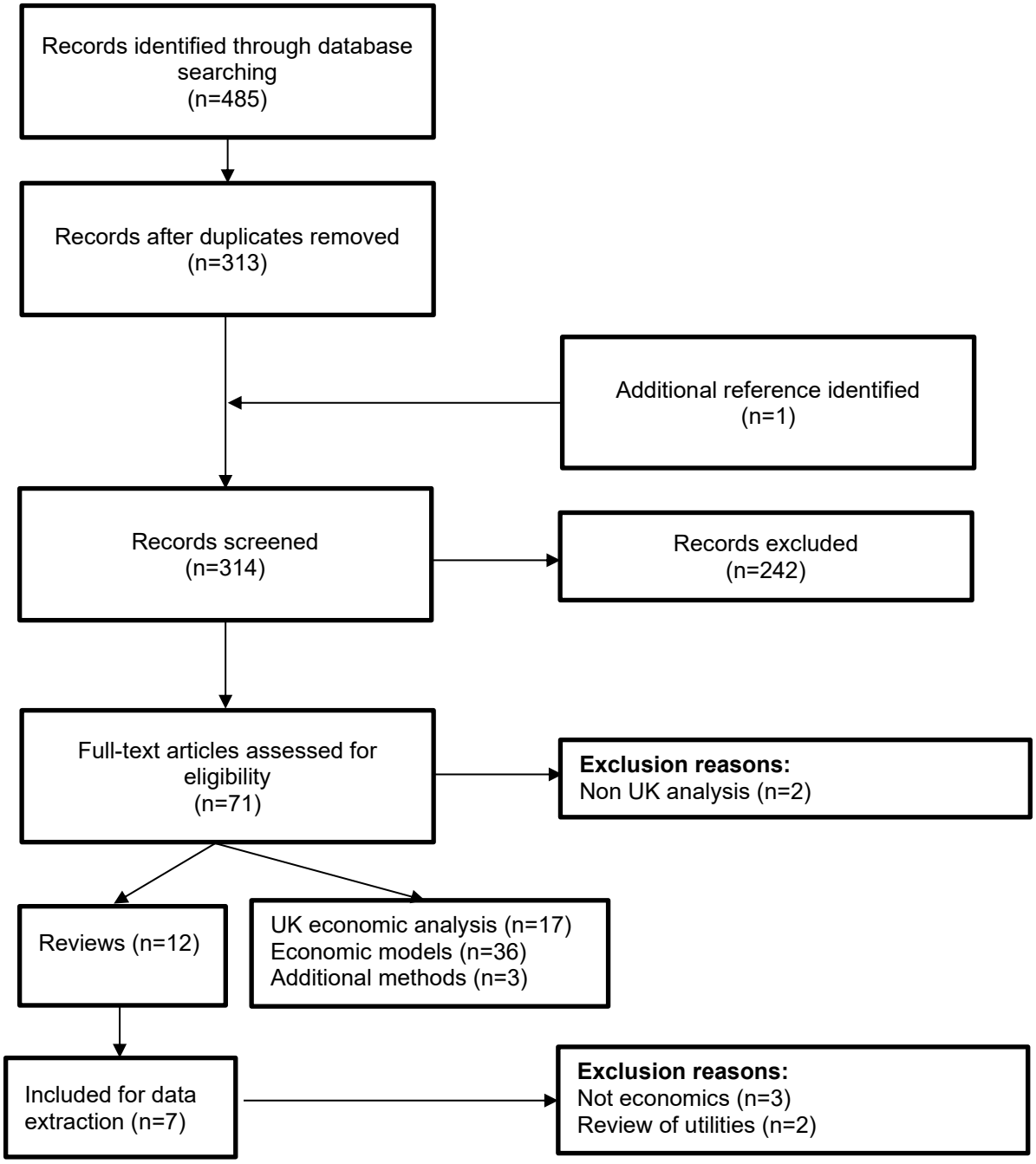
CDSR: 8 results

INAHTA

((((see* AND thing*) OR (hear* AND voice*) OR (hallucin*) OR (delusion*) OR (paranoi*) OR (schizophreni*) OR (psychotic) OR (psychoses) OR (psychosis) OR ("Hallucinations"[mh]) OR ("Delusions"[mh]) OR ("Paranoid Disorders"[mh]) OR ("Affective Disorders, Psychotic"[mh]) OR ("Schizophrenia"[mhe]) OR ("Psychotic Disorders"[mh])) AND (((digital OR representation OR simulation OR avatar* OR app* OR web* OR internet OR comput* OR online OR mhealth OR smartphone* OR intervention*) OR (fast AND (think* or thought*)) OR ("slow mo") OR (slowmo))) AND ((cost* OR (net benefit*) OR (net monetary benefit*) OR (net health benefit*) OR (cost effect*) OR (cost utilit*) or (quality of life)))) AND ((uk or "united kingdom" or england or wales or scotland or "northern ireland" or britain or english or welsh or scottish or "northern irish" or british or model*))

34 results

Appendix F: Economic searches PRISMA diagram



Appendix G: Systematic reviews for economic evidence in psychosis

Study details	Review aim	Search strategy	Included papers	Model specific findings	UK-based CBTp cost-effectiveness results
Zhou 2018	To summarise model structures used in decision tree, cohort- and patient-level Markov model and discrete-event simulation	Medline, Embase From 2000 to April 2016 Evidence of reference checking and previous reviews Eligibility: model-based economic evaluations of pharmacotherapy for schizophrenia	79 papers CUA (n=48) UK-based (n=9) Models: decision tree (n=29) and cohort-level Markov models (n=32) Time horizon: 1-year (n=32), 5-year (n=26) Outcomes: QALY, DALY, life years, duration of relapse, extrapyramidal symptoms, and duration of first-line treatment	Decision tree: branching at relapse level (72%), response level (41%), discontinuation option (62%), or adherence level (38%). Response was defined as an outcome for acute phase treatment and relapse as an outcome for maintenance treatment. Discontinuation (switch or dropout) and adherence level were incorporated to adjust outcome probability in some models. Cohort-level Markov model: 2 to 33 health states were considered. The most common states used were stable and relapse (n=22). Some models replaced stable state with response level (PANSS improvement: > 30%, 30%–20%, < 20%), symptoms state (mix/positive/ negative/no symptom). The other elements of states were care setting, treatment (lines of treatments and no treatment), adherence level, presence of side effect, and death. The methods of evaluation (PANSS scale or Brief Psychiatric Rating Scale) and the thresholds to determine response or relapse (20% or 30% changes) differed across models. A 1-year cycle was most commonly used. Patient-level Markov models: health states with or without side effects. DES: remission, relapse, psychiatric visit and death.	NA
Németh 2018	To review economic models and utility mapping algorithm in schizophrenia	Medline From inception to Jul 2017 No evidence of hand or reference searching	59 papers – model-based Markov model (n=26), decision tree (n=16) CUA (n=33), CEA (n=24)	Therapeutic adherence, compliance or persistence was considered. Treatment switching was included due to AEs, non-compliance or lack of efficacy. PANSS scores were used to elicit utility values in 17 models. Four mapping algorithm were identified –	NA

		Eligibility: model-based economic evaluation of interventions in schizophrenia	Intervention: atypical antipsychotics Outcomes: QALY, DALY, number of relapses Time horizon: <1 year (n=24), 5 years (n=19), 10 years and lifetime (n=11)	Mohr-Lenert method (n=11) was the most commonly used, where 8 health states were based on the defined threshold of PANNS score, and an utility value was assigned to each health state.	
Buck 2017 (poster)	To summarise the cost-effectiveness of psychological interventions compared to usual care/alternative interventions, in schizophrenia or bipolar disease	PsycINFO, Medline, EMBASE From 2000 to Jan 2017 No evidence of hand searching or reference searching Eligibility: cost-effectiveness of psychological therapy in adults with schizophrenia or bipolar disease	11 papers – 11 trial-based economic analysis CEA and/or CUA NR Intervention: CBTp (n=6) Outcomes: QALY, GAF, PANSS Follow up: 6 months to 5 years	NR	Not limited to UK-based studies: Interventions were found to be cost-effective (n=9) where ICERs ranged from cost-saving to £18844 per QALY. The probability of being cost-effective was between 50% to 99.5% at pre-defined thresholds.
Aceituno 2019	To review the cost-effectiveness of EIP services	Cochrane library, Medline, PsycINFO, EMBASE, EconLit and NHS EED of University of York Evidence of reference checking and hand searching Eligibility: trial-based and model-based economic evaluation comparing EIP and alternative approach	16 papers – 14 trial-based, 2 model-based economic evaluations Model: decision tree (n=2) CUA (n=4) UK-based (n=4) Intervention: EIP Time horizon (model-based EE): 2, 4, 10 years Outcomes: quality of life, QALY, GAF	Park's model assessed EIP in relation to employment, education, homicide and suicide, with variable time horizon for each outcome dependent on the available effectiveness data – 2 years in the employment and education model, 10 years in the homicide model and 4 years in the suicide model. Perez's model assessed the cost-effectiveness per true positive patient detected, by considering 4 screening outcomes – true positive, false positive, true negative and false negative.	4 papers – 2 trial-based, 2 model-based EIP showed to be a cost-saving intervention (McCrone 2010, Tsiachristas 2016, Perez 2015, Park 2016).
Shields 2019	To review the cost-effectiveness of psychological	PsycINFO, Medline, Embase From 2000 to Nov 2018	12 papers – 11 trial-based, 1 trial and model-based economic evaluation	Camacho's model includes a decision tree branching at the number of group sessions attended, and a Markov model consists of health states - relapse, no relapse, alive, recover and dead. It considers the	4 papers – trial-based CBTp was found to be dominant or cost-

	interventions, determine the robustness of available evidence base and identify evidence gaps	No evidence of hand or reference searching Eligibility: economic evaluation comparing psychological intervention and routine practice/no intervention/alternative psychological therapy	Model: decision tree and Markov model (n=1) CEA (n=10), CUA (n=6) UK-based (n=8) Intervention: CBTp (n=6) Time horizon: 96 weeks Outcomes: QALY, GAF	probability and time to first relapse following treatment. Three cycles of 32 weeks were applied. Utilities were derived – 0.689 (no relapse) and 0.590 (relapse). A published mapping algorithm to estimate utility weights from PANSS scores using standard gamble and visual analogue scales in In Rosenheck et al.	effective (ICER £18844 per QALY) in UK papers (Haddock 2003, Lam 2005, Barton 2009, Patel 2010).
Jin 2020b	To evaluate the availability, quality and consistency of cost-effectiveness findings reported by economic models evaluating interventions for schizophrenia	Medline, Embase and PsycINFO From inception to Jan 2020 Evidence of reference searching Eligibility: model-based economic evaluations of interventions targeted at the prevention, detection, diagnosis, treatment or follow-up of schizophrenia, published from 2005 onwards.	77 papers – model-based Model: Markov model (n=34), decision tree (n=24) CUA (n=58), CEA (n=15) UK-based (n=11) Intervention: antipsychotic medication (n=57), CBTp (n=1) Time horizon: 1-5 years (n=52)	Common problems identified – potential conflict of interest (n=58), time horizon not sufficient long to reflect all important outcomes (n=54), source used to derive baseline outcome data.	None
Shields 2022	To evaluate the evidence base of the cost-effectiveness of interventions for people at risk of psychosis and for first-episode psychosis	PsycINFO, Medline, Embase From inception to Aug 2020 No evidence of reference or hand searching Eligibility: economic evaluation of intervention targeted at preventing or	14 papers – 8 trial-based, 5 model-based Model: Markov model (n=2), DES (n=1), decision tree (n=1), statistical simulation (n=1) CEA (n=11), CUA (n=7) UK-based (n=3)	A state-transition Markov model begins with an acute phase of FEP and subsequent states included stable (subdivided to with and without complications), relapse, treatment resistant, unstable and death (Health Quality Ontario 2018). Wijnen 2020 developed a state-transition Markov model (“PsyMod”) consists of 6 health states: ultra-high risk of psychosis, no ultra-high risk of psychosis, first-episode psychosis, post first-episode psychosis, recovery/remission or death.	3 papers – 1 trial-based, 2 model-based At risk patients: CBTp was found to be dominant over comparator (Jin 2020, Perez 2015) First-episode psychosis: EIP was

		reducing psychosis symptoms	Intervention: CBTp (at-risk), EIP (first episode psychosis) Outcome: symptom scores, relapse, averted cases of psychosis, QALY Time horizon: 1 year to lifetime		dominant compared with comparator in McCrone 2010. Jin 2020 reported that antipsychotic and family intervention was dominant vs comparators (family intervention alone and antipsychotic alone).

GID-HTE10020 Digital health technologies to help manage symptoms of psychosis and prevent relapse

Medical technologies advisory committee 08 Dec 2023

Committee introducers: Isabel Ellory, Teik Goh

Lay SCMs: Karen Persaud, Tony Middleton

External assessment group: Megan Dale, Samuel Bird (CEDAR)

Technical team: Oyewumi Afolabi, Alice Pritchard and Bernice Dillon

NICE National Institute for Health and Care Excellence

Digital health technologies to help manage symptoms of psychosis and prevent relapse

The following slides provide an overview of the external assessment group (EAG) report for this topic. Not all these slides will be presented at the committee meeting but the main information in this set of slides will be summarised. We have tried not to repeat information found in the other documents and references can be found in the slide notes.

Key documents in this assessment include:

- The final scope - contains the decision problem for the assessment
- The external assessment report (EAR)* - assessment of the included technologies by the EAG.
- The EVA psychosis patient survey report*

The slides contain information that has been supplied in confidence. Academic in confidence information is underlined and highlighted in yellow and commercial in confidence information in blue

* These documents are in the Committee pack and will be published at consultation

Technology purpose and unmet need

- Psychosis is a state of mind where a person's abilities to understand and test reality are impaired. The prevalence of psychosis across all ages and population in the UK is 0.7%
- Conditions with psychosis as a main feature are called psychotic disorders and can have "positive" and "negative" symptoms.
    - "Positive" symptoms include delusions / hallucinations which involve believing implausible ideas usually with paranoia or hearing voices
    - "Negative" symptoms can be language impairment, inability to perform everyday tasks, inability to speak and decreased ability to experience pleasure
- The NHS is committed to improving and widening mental health services however, the demand for psychological therapy for people with psychosis outweighs available capacity. There is significant unmet need for CBT for psychosis within the NHS.
- Prolonged use of antipsychotic medication contributes to poor physical health
- Digital health technologies can potentially:
    - Allow more people to access an effective intervention
    - Reduce the number of CBT for psychosis (CBTp) sessions required
    - Be used whilst people wait to receive CBTp
    - Be delivered online through apps with varying levels of practitioner support

NICE

The technologies

3 digital health technologies were included in the assessment and classified as follows:

Managing symptoms
• AVATAR Therapy – a treatment for distressing auditory verbal hallucinations for peole with psychosis
• SlowMo – a blended digital therapy which aims to reduce distressing worries or paranoia by supporting people with psychosis to notice and slow down their unhelpful fast thinking habits
Monitoring to prevent relapse
• CareLoop – a remote monitoring system for people with psychosis that facilitates early identification and intervention when symptoms escalate [Other names associated with this technology are “EMPOWER” and “ClinTouch”]

Summary of the technologies (1)

Technology [Company]	AVATAR Therapy [AVATAR Therapy]	SlowMo [King's College London]	CareLoop [CareLoop Health]
Delivery	Software based download on laptop or desktop PC	Desktop PC, laptop and/or smart device. Non-digital options are available	Delivered through an app on a smartphone Web-based for the clinical team
Target conditions	Treatment for distressing auditory verbal hallucinations	Aims to reduce distressing worries and paranoia in those with psychosis	Remote monitoring system for people with psychosis that facilitates early identification and intervention when symptoms escalate
NHS staff involvement	Used during therapy sessions with therapist support	Used during therapy sessions with therapist support Patients can access app content to support therapy sessions (face-to-face or remote)	Clinical team review a web-based dashboard to monitor symptoms
Pathway placement	Whilst waiting for CBTp or alongside CBTp	Whilst waiting for CBTp or alongside CBTp	Preventing relapse

For further details see EAR pages 20-21

Summary of the technologies (2)

Technology [Company]	AVATAR Therapy [AVATAR Therapy]	SlowMo [King's College London]	CareLoop [CareLoop Health]
Key features	Allows a three-way conversation between the person hearing voices, their distressing voice and a therapist Uses a digital avatar to represent the visual/auditory voice Treatment is provided over 6 to 12 sessions either alone or as a component of CBTp	Combines face-to-face therapy with interactive digital content such as stories and games Personalised therapy session content is synchronised with the app to provide strategies to combat fast thinking in daily life Proposed as an alternative to CBTp where paranoia is the main presenting problem	Users record symptoms daily using questionnaires, and can add journal entries of their thoughts and feelings CareLoop uses an algorithm to recognise changes in mental health to identify deterioration and predict relapse Users' data is stored on a cloud-based system It can generate insights at an individual level to optimise treatment and care

For further details see EAR pages 20-21

Treatment care pathway

Preventing psychosis

- Individual CBT with/without family intervention
- Assess and treat anxiety disorders, depression, emerging personality disorders or substance abuse (if present)

First episode psychosis

- Early intervention in psychosis services
- Antipsychotic medication with psychological intervention (family intervention & individual CBT)
- Assess symptoms and behaviour for affective psychosis or disorder

Subsequent acute episodes

- Crisis resolution and home treatment teams
- Antipsychotic medication with psychological intervention (family intervention & individual CBT)
- Other considerations: acute community treatment, inpatient units

AVATAR & SlowMo - can be used for managing symptoms while waiting for CBTp or with CBTp

CareLoop – can be used for monitoring to prevent relapse

Current management overview

- Current treatment of psychosis is with antipsychotic medication alongside psychological and social support. Guidelines on the management of psychosis and schizophrenia at different stages is provided by NICE clinical guidance CG178 for adults over the age of 18 and NICE clinical guidance CG155 for children and young people.
- The guideline recommends that psychological support should include provision of CBT to all people with psychosis delivered on a one-to-one basis over at least 16 sessions
- Management of psychosis uses an early intervention in psychosis (EIP) specialist teams for the first episode, and specialist community mental health teams (CMHT) for longer term psychosis. EIP services should be accessible to all people irrespective of age or duration of untreated psychosis
- In both EIP and CMHT services, people living with psychosis should be offered a full range of pharmacological, psychological, social, occupational, and educational interventions.
- Individuals should be monitored and regularly supervised by a competent supervisor
- Crisis resolution should be offered for subsequent episodes and inpatient hospital care considered
- There is no formal relapse prevention process in the NHS. Monitoring of patients for relapse prevention varies across NHS services. It usually involves regular follow ups with their care co-ordinator every 6-12 weeks, and with a psychiatrist every 6-12 months

NICE

CBTp: cognitive behavioural therapy for psychosis

Decision problem

PICO	
Population	People aged 14 years and older living with primary psychosis.
Subgroups	Where data permits, subgroups were considered for: Severity of psychosis, high risk of relapse and age
Interventions	Digital health technologies which help manage the symptoms of psychosis including: • AVATAR Therapy for auditory hallucinations • SlowMo for paranoia Or which provide remote monitoring of symptoms to help prevent a relapse including • CareLoop
Comparator	For AVATAR and SlowMo: • Standard psychological care for managing symptoms of psychosis. For CareLoop: • Standard care for monitoring people at risk of a relapse of psychosis
Key Outcomes	Outcomes for symptom management: • Change in targeted psychotic symptoms such as paranoia, agoraphobia, hearing distressing voice etc, HRQoL, patient experiences and wellbeing, intervention related adverse events, intervention adherence and completion Outcomes for relapse prevention: • Rates of relapse or deterioration, time to relapse or deterioration, severity of relapse, intervention adherence and completion, patient experience and wellbeing, HRQoL, intervention related adverse events

HRQoL: health related quality of life

For further details see EAR pages 17 - 18

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

- The incidence and prevalence of psychosis are higher in deprived communities
- A significantly higher percentage of black men are diagnosed with psychotic disorder than white men
- Digital health technologies to help manage symptoms of psychosis and prevent relapse are accessed via a mobile phone, tablet, or computer. People may need regular access to a device with internet access to use the technologies.
    - SlowMo only requires data connection for initial install and occasional data syncing during therapy session. The technology has paper-based alternatives
- Additional support and resources may be needed for people:

  who are unfamiliar with digital technologies or do not have access to the internet

  with visual, hearing or cognitive impairments or a learning disability

  with problems with manual dexterity or learning disability

  who are unable to read or understand English or health-related information

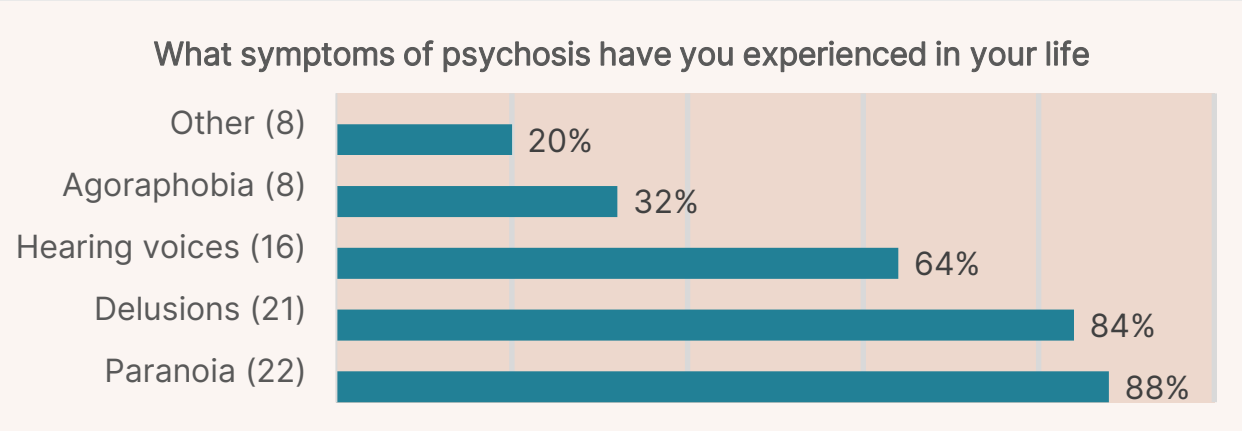
Equality considerations

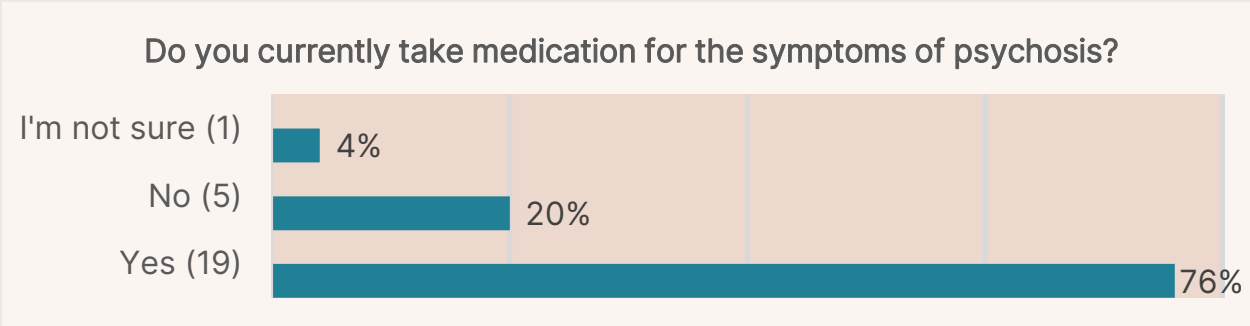
NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

- Some people would benefit from digital health technologies in languages other than English. Technologies should be flexible enough to address diverse language and provide additional support as needed
- People's ethnic, religious, and cultural background may affect their views of digital health interventions. Healthcare professionals should discuss the language and cultural content of digital health interventions with patients before use
    - Age, disability, race and religion or belief are protected characteristics under the Equality Act (2010)

Patient survey

- NICE's patient survey received a total of 25 responses
- 56% was from people with psychosis and 44% from a parent, carer or guardian of someone with psychosis





- Respondent's first experience of psychosis ranged from less than 1 year (16%) to more than 3 years (68%) ago
- Other reported symptoms include hallucinating and hearing music, seeing figures and disordered and conflicting thoughts
- 68% (13) reported being on medication for over 6 years
- In the last 3 years, 5 respondent reported no relapse episode of psychosis; 10 had 1-3 episodes; 3 had 3-9 episodes and 5 reported more than 10 episodes

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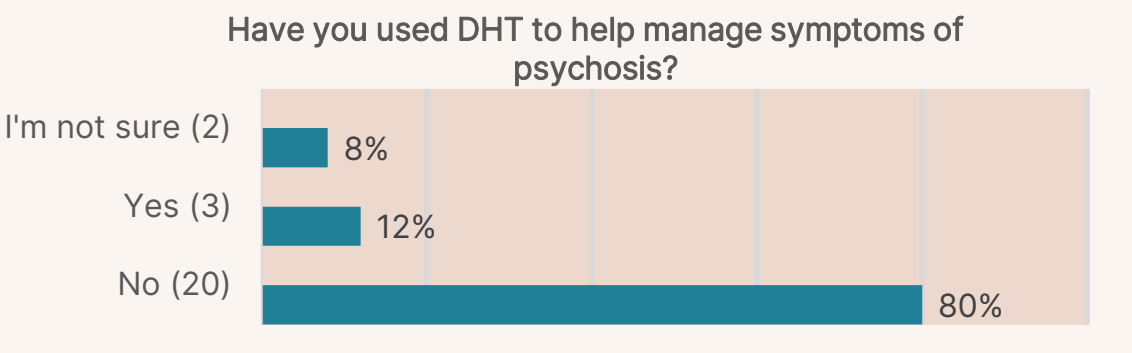
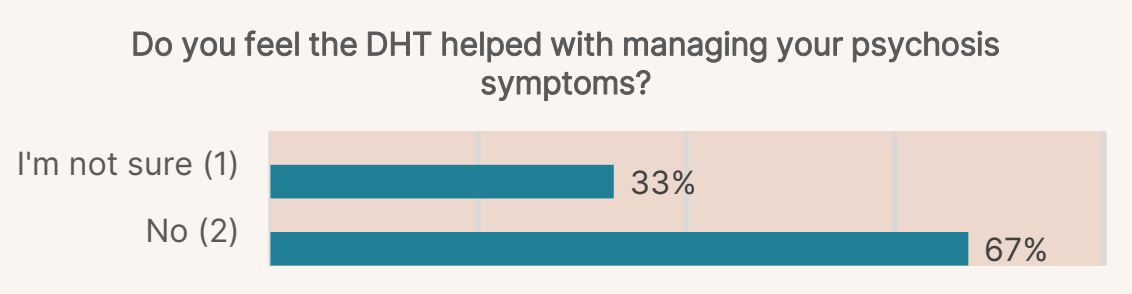
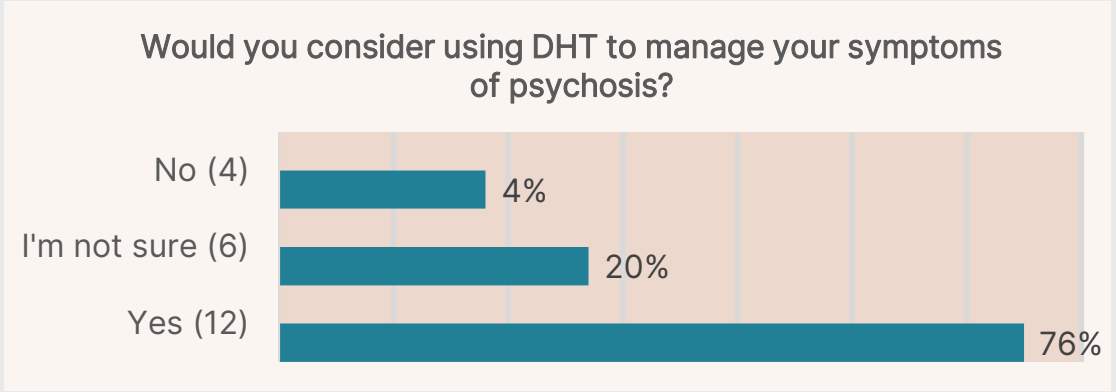
For further details see patient survey report

Patient survey – views on digital health technology



- 3 people reported to have used a DHT to help manage symptoms of psychosis
- There were 2 users of SlowMo and 1 for AVATAR Therapy





- 4 people with no experience of using DHT would not consider using. Reasons provided include:

"My psychosis involves thinking I am being monitored and tracked on my phone and laptop"

"Not helpful need people"

NICE

For further details see patient survey report

Clinical effectiveness

Digital health technologies to help manage symptoms of psychosis and prevent relapse

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Clinical evidence: AVATAR Therapy

Study and location	Design	Population and setting	Key outcomes
(Leff 2013), UK	Single centre, partial crossover RCT	N=26 people aged 14-75 from a single CMHT hearing persecutory voices for at least 6 months, with no adequate response to antipsychotic medication NHS CMHT	PSYRATS BAVQ-R CDS
(Craig 2018), UK	Single centre RCT	N=150 people receiving care for psychosis, that have experienced distressing auditory verbal hallucinations for at least 12 months NHS Psychiatric services	Total score of PSYRATS-AH at 12 weeks
(Rus-Calafell 2020), UK	Observational sub-study of Craig 2018	N=39 people that participated in Craig (2018) NHS CHMT	PSYRATS-AH, BAVQ-R State Social Paranoia Scale Sense of Presence Scale Anxiety VAS
(Rus-Calafell 2022), UK	Semi-structure interviews sub-study of Craig 2018	N=14 people that completed AVATAR Therapy as part of the Craig (2018) study NHS psychiatric services	Subjective experience of AVATAR Therapy
AVATAR2 [Garety 2021a - Study protocol], UK	Multi-site parallel group RCT	N=345 people receiving care for psychosis, that have current frequent and distressing voices NHS psychiatric services	Distress dimension of Psychotic Symptom Rating Scales, auditory hallucinations subscale (PSYRATS-AH) at 16 and 28 weeks

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CHMT: community mental health services

For further details about the selected studies see table 3 of the EAR

Clinical evidence: SlowMo

Study and location	Design	Population and setting	Key outcomes
(Garety 2021b), UK	Parallel-arm RCT	N=362 people diagnosed with schizophrenia spectrum psychosis with distressing, persistent paranoia Community health setting	Green et al Paranoid Thoughts Scale (GPTS) score at 24 weeks
(Greenwood 2021), UK	Qualitative sub-study of RCT	N=22 people that took part in Garety (2021b) who had completed 1 session of SlowMo, and the 24 week follow up Community health setting	Develop and validate theme structure from qualitative interviews
(Hardy 2022), UK	Observational sub-study of RCT	Those that took part in Garety (2021b) Community health setting	Digital literacy, adherence and engagement
(Ward 2022)	Narrative account of SlowMo: sub-study of RCT	N=181 people that took part in Geraty (2021b)	Therapy engagement and withdrawals, session adherence, behavioural work adherence

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RCT: randomised controlled trial

For further details about the selected studies see table 3 of the EAR

Clinical evidence: CareLoop

Study and location	Design	Population and setting	Key outcomes
(Lewis 2020), UK	Open RCT	N=81 people diagnosed with schizophrenia or related disorders aged 16-65 NHS CHMT and EIP team	• PANSS • GAF • ERS
(Gumley 2022a), (Gumley 2022b), UK and Australia	Multicentre feasibility cluster RCT	N=74 people diagnosed with schizophrenia or related disorders aged 16+ NHS CHMT	Feasibility, acceptability, usability and safety
(Allan 2023), UK	Qualitative semi-structured 1-2-1 interviews	N=16 people that participated in Gumley (2022), N=6 mental health staff, and N=1 carer NHS CHMT	Themes derived from the interview data in relation to the implementation of the intervention

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EIP: early intervention in psychosis

For further details about the selected studies see table 3 of the EAR

Clinical evidence: EAG critique (1)

The EAG conducted a qualitative appraisal of the 10 peer-reviewed full-text publication for the included technologies

AVATAR Therapy

- The EAG considers Craig (2018) study to be of high quality. The study was powered to detect an effect with a large sample size and included a larger number of relevant outcome measures that are within the scope. However, the EAG noted that supportive counselling is not necessarily standard care for psychosis.
- The qualitative studies for AVATAR Therapy Rus-Calafell (2020) and Rus-Calafell (2022) were also considered to be of good quality. They both had small sample size but provided useful insights on the subjective experience of using the technology not otherwise captured in the RCT (Craig 2018)
- The EAG felt the RCT (Leff 2013) was of moderate quality because the sample size was small. In the partial crossover section, participants in the AVATAR group did not crossover to TAU. The outcomes reported in the study were all within scope. The EAG noted that the diagnosis was not reported, and so the study could include participants with non-primary psychosis diagnosis.

TAU: treatment as usual

For further details about the critique of the evidence see section 5.1 of the EAR

Clinical evidence: EAG critique (2)

SlowMo

- Garety (2021b) was considered a high-quality study with a large sample size, outcomes within the EVA scope and participants who had been diagnosed with primary psychosis. The EAG noted that primary outcome was self-reported and not observer rated, however 2 standard observer rated assessments of the same outcome were included. Also, in the TAU group, the effects of time with therapist were not controlled for.
- The EAG considered Greenwood (2021) and Hardy (2022) to be good qualitative studies that provided insight into the subjective experience and usability of SlowMo as well as its impact on quality of life. The EAG noted that it was unclear if those that volunteered to be interviewed in Greenwood (2021) were more positive about therapy

TAU: treatment as usual

For further details about the critique of the evidence see section 5.1 of the EAR

Clinical evidence: EAG critique (3)

CareLoop

- The EAG considers Gumley (2022a and b) to be a good feasibility study with moderate sample size and long follow-up period. The study showed clinical efficacy of CareLoop's relapse prevention however it was not fully powered. The EAG noted that the study showed the feasibility of a larger powered RCT and acceptability and usability of the CareLoop app
- Lewis (2020) was an RCT of an earlier iteration (ClinTouch) of CareLoop and the results from the study led to improvements of the intervention. The EAG noted that the study had a short follow up period of 12 weeks and results did not show any impact of ClinTouch to predict relapse in psychosis
- The EAG noted that Allan (2023) provides qualitative data regarding how well CareLoop was implemented as well as the thoughts and opinions of people and staff using CareLoop

TAU: treatment as usual

For further details about the critique of the evidence see section 5.1 of the EAR

Abbreviated outcome measures used in studies

	Abbreviation	Outcome measures
1	PSYRATS	Psychotic Symptom Rating Scales
2	BAVQ-R	Revised Beliefs about Voices Question
3	CDS	Calgary Depression Scale
4	PSYRATS-AH	Psychotic Symptom Rating Scales, auditory and hallucination
5	VAS	Visual analogue scale
6	GPTS	Green et al., Paranoid Thoughts Scale
7	PANSS	Positive and Negative Syndrome Scale
8	GAF	Global Assessment of Functioning
9	ERS	Empowerment rating scale
10	VAAS	Voice Acceptance and Action Scale
11	PSYRATS-DEL	Psychotic Symptoms Rating Scale – Delusions
12	BDI	Beck Depression Inventory-II
13	DASS-21	Depression Anxiety and Stress Scales
14	EQ-5D-5L	EuroQol-5 Dimensions-5 Levels
15	VPDS	Voice Power Differential Scale
16	CHOICE	Choice of Outcome in CBTp
17	ITQ	International Trauma Questionnaire
18	MAP	Maudsley Addiction Profile
19	SAPS and SANS	Scale for Assessment of Positive and Negative Symptoms
20	MANSA	Manchester Short Assessment of Quality of Life

Clinical evidence: results (1)

AVATAR Therapy	
Craig (2018)	• At 12 weeks, there was significant decrease in PSYRATS-AH for the AVATAR group compared with the control group. This was maintained in the AVATAR group at 24 weeks but decreased in the control group resulting in no significant difference between the groups at 24 weeks • Same pattern was observed for BAVQ-R, VPDS and VAAS scores
Leff (2013)	• There was a significant decrease in PSYRATS–AH for the AVATAR group compared with the control group post-treatment. Also, a significant decrease within the control group before and after receiving AVATAR therapy • Same pattern was observed for BAVQ-R scores • These improvements were maintained at 3 months post-treatment
• There was no effect of AVATAR Therapy on more general symptoms of psychosis in both Craig (2018) and Leff (2013)	
Rus-Calafell (2020)	There was a significant decrease in anxiety symptoms and paranoid thoughts between the first and last sessions of AVATAR therapy
AVATAR2 (Unpublished)	• [redacted] •

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For further details about AVATAR Therapy results see page 38 - 41 of the EAR

Clinical evidence: results (2)

SlowMo	
Garety (2021b)	• At 12 weeks, results showed a significant decrease in GPTS score (part A and B) for the SlowMo group compared to the control group. This was not maintained at 24 weeks • There was a significant decrease in PSYRATS-DEL and SAPS score for the SlowMo group compared with control at 12 weeks, and this significant decrease was maintained at 24 weeks
Greenwood (2021)	• The study identified six core themes from the qualitative interviews: starting the SlowMo journey, central role of supportive therapist relationship, slowing things down, value and learning from social connections, approaches and challenges of technology, and Improvements in paranoia and wellbeing
Hardy (2022)	• Engagement findings showed that 80.7% of therapy completers met the a priori analytics adherence criteria and this did not differ by demographics. • High rates of user experience were reported overall (mean 75%). No differences in user experience were found for ethnicity, age, or paranoia severity, although self-reported app use, enjoyment, and usefulness were higher in women than in men. • Results for computer access, smartphone ownership and confidence showed the existence of a 'digital divide' between subgroups of the population related to age and ethnicity.
Ward (2022)	• 85% of patients that attended the first session went on to complete therapy • Fidelity in the delivery of SlowMo was achieved for 95% of people, with fidelity ratings of 90% for each of the 8 modules

For further details about SlowMo results see page 42-44 of the EAR

Clinical evidence: results (3)

CareLoop	
Lewis (2020)	• Between baseline and 12 weeks, there were no significant difference between control and CareLoop for any of the outcome measures • For individual site analysis, a significant decrease was observed in the CareLoop arm compared to control for the PANSS positive score for the EIP site, but not the CMHT site • The frequency of early warning signs documented in patient records was less in the ClinTouch (CareLoop) group (33%) than it was in the control group (46%) • ClinTouch was suboptimal in terms of ClinTouch alerts vs documented early warning signs. Sensitivity was 75%, specificity 8%, giving a predictive value of 29%
Gumley (2022b)	• A lower proportion of people relapsed in the CareLoop arm compared with the control arm with a longer time to relapse in the CareLoop arm • Participants in the CareLoop arm were less fearful of having a relapse compared with the control arm. • At 12 months, there was a larger decrease in PANSS positive score for those in the control arm compared with the CareLoop arm. However, there was a larger decrease in total PANSS score in the CareLoop arm compared with the control arm • Usage of the app was high, 91% of participants met the a priori criterion of acceptable engagement with the app (>33%). The median time of discontinuation of acceptable engagement(>33%) was 32 weeks

For further details about CareLoop results see page 44-45 of the EAR

Clinical evidence: adverse events

Four studies reported adverse events: 1 for AVATAR Therapy, 2 for CareLoop and 1 for SlowMo. The EAG also included unpublished results from AVATAR2 study

- Craig (2018) reported a total of 22 adverse events. There were no recorded incidents of self-harm or suicide attempts and none of the adverse events were found to be attributable to AVATAR Therapy or supportive counselling
- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- Garety (2021b) reported 28 AEs (25 SAEs) for SlowMo and 26 SAEs for TAU. Of the 25 SAEs for SlowMo, 1 was classed as 'possibly related' to SlowMo and 1 'unlikely related'. For the SAEs for TAU, 1 was classed as 'definitely related'
- Gumley (2022a and b) reported 29 adverse events for CareLoop (9 classed as severe and 2 serious) 25 for TAU (15 classed as severe). Of the AEs for CareLoop, 1 was classed as related to the app and 1 to the study procedure. None of the AEs for TAU were related to the app or study procedure. Lewis (2020) reported 3 adverse events related to CareLoop

SAE: serious adverse event; AE: adverse event

For further details about adverse events see section 6 of the EAR

Clinical evidence: EAG overview and interpretation (1)

AVATAR Therapy

- The clinical evidence suggests that AVATAR Therapy effectively reduces auditory hallucination symptoms in people with psychosis
- Qualitative evidence suggests that AVATAR therapy is acceptable for use by those willing to engage with the therapy. However, the EAG propose that more qualitative evidence is needed from those that either turned down the therapy or did not complete the whole course.

The EAG noted that the effectiveness of AVATAR Therapy versus established NHS treatments like CBTp remains unknown. There is also a lack of evidence relating to longer-term effectiveness (beyond 12 months)

The EAG considers AVATAR Therapy generalisable for use within the NHS as it could be used in addition to currently available psychological therapies

For further details about interpretation of clinical evidence see section 9 of the EAR

Clinical evidence: EAG overview and interpretation (2)

SlowMo

- The clinical evidence indicates that SlowMo effectively reduces symptoms of delusion and paranoia in people with psychosis over the medium term (up to 24 weeks) and it also improves quality of life. However, there is lack of evidence regarding its longer-term effectiveness (beyond 12 months)
- The qualitative evidence suggests that the therapy provided by the SlowMo app can provide people with new skills to help manage their symptoms
- There is also data that supports the acceptability of SlowMo for use by people with psychosis with high fidelity for those receiving SlowMo therapy

The EAG considers SlowMo generalisable for use within the NHS and can be used in addition to currently available psychological therapy particularly for those with symptoms of paranoia and delusion. Additionally, SlowMo does not require a data package for use and a paper option is available for those who are unable or unwilling to use the app.

For further details about interpretation of clinical evidence see section 9 of the EAR

Clinical evidence: EAG overview and interpretation (2)

CareLoop

- The clinical evidence indicates that CareLoop effectively reduces the number of people experiencing relapse, and for those that do experience a relapse, it increases the time until a relapse. However, there is lack of evidence for the efficacy of CareLoop in the longer-term (beyond 12 months)
- There is some evidence that shows CareLoop can reduce symptoms of psychosis compared with treatment as usual and acceptability of the app by patients
- Although Gumley (2022) was a feasibility RCT and not fully powered to detect an effect, the findings indicate the feasibility, safety and acceptability of conducting a fully powered RCT

The EAG noted that there is no formal relapse prevention process in the NHS and considers CareLoop generalisable for use within the NHS

For further details about interpretation of clinical evidence see section 9 of the EAR

Issues for consideration: Clinical evidence

Clinical effectiveness

- Evidence suggests that AVATAR Therapy reduces auditory hallucination symptoms and SlowMo reduces the symptoms of delusion and paranoia in people with psychosis. However, the evidence for SlowMo did not show a reduction in paranoia at 24 weeks.
- There is no evidence comparing their use compared with CBT for psychosis. The comparators used were TAU or supportive counselling.
- CareLoop showed a reduction in the number of people experiencing relapse and increases time to relapse in a feasibility study.
- There is no evidence of long-term effectiveness for all 3 technologies
- All clinical studies were conducted in the UK

Unmet need

- Less than 3% of people outside of EIP services will get access to CBTp
- DHTs may not be suitable for everyone

Adverse events

- There is evidence reporting adverse events for all 3 technologies and some of these were classed as likely related to the technology

Cost effectiveness

Digital health technologies to help manage symptoms of psychosis and prevent relapse

NICE National Institute for Health and Care Excellence

Economic evidence

A rapid literature search was completed to identify economic modelling on psychosis.

The aim of the search was to identify key modelling strategies used in the literature and find relevant UK cost information to inform model inputs

12 relevant systematic reviews by title and abstracts were found and from full texts this was narrowed to 6

One additional paper was found through reference searching

The most common modelling techniques were decision tree and Markov models

The health states for the Markov models varied with stable and relapse states being the most common states

The models varied in time horizon from 1 year to lifetime

For further details about searching for economic evidence see page 57 of the EAR

Published economic evidence

The EAG identified 2 cost effectiveness studies related to the technologies (Gumley, 2022b and Morris, unpublished)

- Both studies were done at least partially in the UK.
- Gumley (2022b) study compared CareLoop with treatment as usual over a 12-month period. A limitation of the study is that it was based on a feasibility study that was not powered to show effectiveness and patient data and costs were included from UK and Australia.
- Morris, unpublished based on the Craig (2018) RCT. Analysis was over a 24-week period and compared AVATAR to supportive counselling in an NHS site in London. A limitation of the study was that EQ-5D-5L value set was used and is not part of the NICE reference case.
- Both studies showed a cost saving for the healthcare system.

For further details about published economic evidence see page 53-56 of the EAR

Economic evidence – Cost effectiveness studies (1)

AVATAR Therapy

Morris (unpublished)

- A cost-effectiveness analysis based on an RCT that compared AVATAR to supportive counselling over 24 weeks
- Utility values measured using EQ-5D-5L showed a greater improvement in the AVATAR arm
- Data from Craig 2018 study was used to inform the analysis
- The study found AVATAR costs were slightly higher than the comparator, however when controlled for baseline costs there was a saving of [redacted]

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For further details on economic evidence see table 12 of the AR

Economic evidence – Cost effectiveness studies (2)

CareLoop

Gumley (2022b)

- A cost-effectiveness analysis that compared CareLoop (delivered as EMPOWER) with treatment as usual (TAU) in the UK and Australia. Cost effectiveness analysis was conducted alongside an RCT
- Study included n=42 for CareLoop (delivered as EMPOWER) and n=31 for TAU
- The study reported an incremental QALY of 0.056 (95% CI -0.031 to 0.143)
- The cost effectiveness study found that CareLoop (delivered as EMPOWER) was dominant when compared to TAU and costed less than TAU over a period of one year, from a health services perspective and resulted in improved utilities measured by EQ-5D-5L which were then mapped to EQ-5D-3L
- A limitation was the feasibility study was small and mixed costs and resource use for UK and Australian participants were used
- It was unclear how reported relapses were calculated

For further details on economic evidence see table 12 of the AR

Economic evidence – conceptual modelling

The EAG's conceptual model structure includes an initial phase and maintenance phase:

Initial phase: A decision analytic model structure was developed for AVATAR and SlowMo

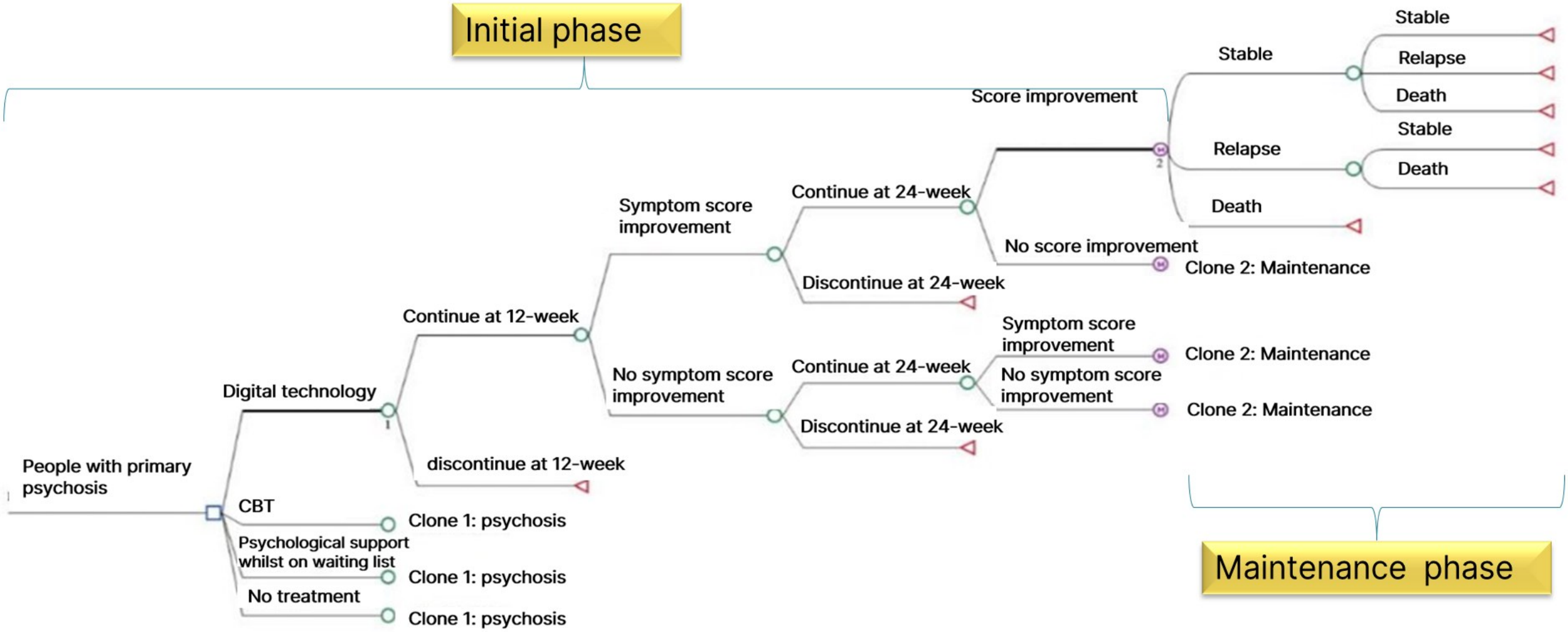
- The EAG noted that it was not currently possible to fully populate the model due to lack of evidence linking short term symptom improvement to long term relapse outcome and downstream changes in health care resource use. Psychological scoring tools were also not mapped to utility values or healthcare resource use.
- A cost consequences approach was used as a result for this part of the model.

Maintenance phase: A Markov model with 1 year cycle was developed with 3 health states: 'stable', 'relapse' and 'death'

- After 24 weeks in the initial phase patients move to a Markov model comparing standard care without monitoring and standard care with CareLoop remote monitoring.
- Patients enter the Markov model through the stable state, and transition between health states over time. A time horizon of 3 years was used in the base case, to reflect the length of an EIS, based on expert opinion.

For further details on model structure see section 10.2 of the AR

Economic model structure: Initial phase



For further details on model structure see section 10.2 of the AR

Economic model assumptions

The EAG made the following assumptions:

- For AVATAR and SlowMo it was advised that 10 clinicians are trained in one site and 100 patients per year will be treated (the per patient cost of training was included in the model)
- Median referrals to EIP was 85 patients per CCG
- IT hardware would be required for AVATAR and SlowMo, and for CareLoop normal office equipment would be sufficient
- For CareLoop, 1000 patients are followed up for a year based on 50% take up from an organisation with 2000 eligible patients
    - 100 care coordinators would be trained per purchasing organisation (based on expert opinion and company statement)
- For model simplicity patients can only have one relapse per year and after that year they revert to being stable. In reality some patients may have recurrent relapses.

For further details on model assumptions see section 10.2 of the EAR

Clinical parameters & utilities

- Effectiveness is indicated by a change in psychological rating scales and utility values in the EAG analyses for AVATAR and SlowMo.
- PSYRATS-AH and PSYRATS-DEL are the main outcomes in the EAG cost consequence analyses because these outcomes were the common measures across the studies
- The EAG conducted a rapid literature search to identify effectiveness evidence for other comparators in the scope. Systematic review and meta-analysis conducted by Van der Gaag (2014) was selected in the EAG cost consequence analysis because findings were pooled from UK papers.
- Effectiveness in CareLoop is indicated by change of relapse risk and hospitalisation following a relapse. A 3-year relapse rate in standard care was sourced from Alvarez-Jimenez (2012) - a systematic review and meta-analysis of longitudinal studies. The relapse rate for CareLoop was estimated using the relative risk reported in Gumley (2022b).

Further details on literature search see page 68-71 of the EAR

Clinical parameters & utilities

Utility effect

- AVATAR effect on utility was sourced from Morris (unpublished) and the EAG obtained a mean utility at each timepoint and mean QALY over 24 weeks which was derived from EQ5D-5L.
- SlowMo additional data from the company was provided with the breakdown of patients with different R-GPTS persecution and references score ranges at each time point (Garety, 2021b). Mean utility value at each timepoint was calculated using utility values of PANSS-generated health states derived from US general population (Lenert 2004). Total QALYs were estimated from area under the curve, using linear extrapolation between timepoints
- CareLoop utility values of relapse and stable health states were sourced from Lenert (2004).

Further details on literature search see page 68-71 of the EAR

Clinical parameters & utilities: AVATAR and SlowMo

Utility	Average utility	Source	Notes
Average	0.89	Jin 2020b, Fusar-Poli 2013	EAG applied weighted average of general population utility values (Fusar-Poli) based on mean age and % male in Garety 2021
Elevated	0.88	Lenert 2004	Assumed to be mild
Moderately severe	0.75	Lenert 2004	Average of different moderate severity categories
Severe	0.61	Lenert 2004	Average of different severe severity categories
Very severe	0.42	Lenert 2004	

Standardised mean difference of CBTp vs control:	Value	Source	Notes
Hallucination	-0.44	Van der Gaag 2014	Paper reported positive effect sizes reported in favour of CBTp, comparability and consistency with other papers EAG reported effect sizes as negative
Delusion	-0.36	Van der Gaag 2014	

For further details on clinical parameters see table 16 of the EAR

Clinical parameters & utilities: CareLoop

Relapse rate of standard care per year (%)	Value	Source
1-year follow up	28	Alvarez-Jimenez 2012
2-year follow up	43	
3-year follow up	54	
Relative risk of relapse of CareLoop vs standard care	0.5	Gumley 2022b
Proportion of patients requiring hospital admission following a relapse (%)		
CareLoop	25	Gumley 2022b
Standard Care	69	
Utility		
Relapse	0.67	Lenert 2004
Stable	0.80	
Death	0	
SMR for people with psychosis		
30-44 years	5.80	Jin 2020b, Reininghaus 2015
45-49 years	2.50	
Starting age (year)	43	Gumley 2022b

For further details on clinical parameters see table 16 of the EAR

Costs & resources: Set up costs

- AVATAR currently has no system set up costs, these costs were not yet determined for SlowMo and for CareLoop [redacted]
- Training time for AVATAR is 7.5 hrs plus supervision of 2 cases, SlowMo 1 day training time dependent upon experience (1 day with experience, 2-3 days otherwise) plus 1 supervised case, CareLoop training is 2 hrs

	AVATAR	SlowMo	CareLoop
Supporting hardware (not included)	Laptop for therapist, laptop for patient, including speakers/headset etc	Laptop for therapy sessions, mobile phone if not using their own	Laptop/PC/ patient mobile phone
Training costs	Not included, cost not known	Included in set up costs	Training cost included

For further details on costs and resources see table 13 of the EAR

Costs & resources: Per patient costs

- Set up time per patient is generally included for all three technologies
- HCP time per session for AVATAR is 50 minutes, SlowMo 60-90 mins and not applicable for CareLoop

	AVATAR	SlowMo	CareLoop
Licensing costs	£100 +VAT 15 sessions over 12 months	£50-£100 + VAT 2-3 year duration	[redacted]
HCP band	Trained therapist broad range of bands, [redacted]	Doctoral level psychologist, other bands being investigated	Band 6 care coordinator
Total HCP hours	[redacted]	10 hrs with mean session time 75 min	n/a

Further details on costs and resources for each technology see table 13 of the EAR

Key cost parameters (1)

Parameter	AVATAR	SlowMo	CareLoop
Total set up costs per system	£1,034	£399	[redacted]
Total training costs per trained clinician	£548	£548	£106
Total delivery costs per patient	£548	£826	[redacted](per patient per year)
Comparator	**Cost**	**Descriptor**	
CBTp	£1,752.83	Cost of £109.55 per session (PSSRU 2016 £97 per session inflated to 2022 values). 16 sessions	
Family intervention	£1,264.93	£97 per session based on multi-systemic therapy inflated to 2022 values. 10 sessions	
Psychological support	£38	6 sessions, 2 hours each (IAPT guidance) staff cost mean band 4 £34 and band £41 PSSRU 2022	
Waiting list	£0	Patients may need to access additional healthcare	
Supportive counselling	[redacted]	Included as comparator for AVATAR. Cost based on Morris (unpublished)	

For further details on key cost parameters see table 17 of the EAR

Key cost parameters (2)

Relapse and remission costs	Cost	Descriptor
Remission	£16,456	Inflated from CG178, using PSSRU 2022
Relapse:	Total cost comprised of outpatient, primary and community care, residential and long-term hospital care plus either acute admission or care at home for psychosis	
Outpatient, primary and community care	£5,590	Inflated from CG178, using PSSRU 2022
Residential and long-term hospital care	£7,010	Inflated from CG178, using PSSRU 2022
Acute hospital admission	£28,300	Inflated from CG178, using PSSRU 2022
Care at home for Psychosis	£3,181	8 weeks support from CRHTT at £341 per week Inflated from CG178, using PSSRU 2022

For further details on the key cost parameters see table 17 of the AR

Base case results AVATAR Therapy & SlowMo

	AVATAR	Supportive counselling	CBTp	Adjusted mean difference between groups (95%)CI)	
				AVATAR vs supportive counselling	Group or individual CBTp vs TAU /Std Care
Costs per person	£548	[redacted]	£1753	£218	N/A
Utility (EQ5D-5L) Total QALYs over 24 weeks	[redacted]	[redacted]	NA	[redacted]	N/A

	SlowMo + TAU	TAU	CBTp	Adjusted mean difference between groups (95%)CI)	
				SlowMo vs TAU	Group or individual CBTp vs TAU /Std Care
Costs per person	£826	£0	£1753	£826 (unadjusted)	N/A
Utility (derived from R-GPTS scores)					
R-GPTS social reference Total QALYS over 24 weeks	0.366	0.352	N/A	0.014 (unadjusted)	N/A
R-GPTS persecution Total QALYS over 24 weeks	0.305	0.292	N/A	0.013 (unadjusted)	N/A

For further details on the results see section 10.3 of the AR

Base case results CareLoop

Intervention	Total Costs (£)	Total QALYs	Incr. costs	Incr. Qalys	Mean NMB @ £20,000)
CareLoop monitoring with standard care	[redacted]	2.27	[redacted]	0.03	[redacted]
Standard care	£56,802	2.24			

- The base case results show that CareLoop is more effective and less costly than standard care without monitoring, therefore a cost-saving strategy.

For further details on the results see section 10.3 of the AR

Sensitivity analysis: AVATAR Therapy & SlowMo

- For AVATAR therapy and SlowMo costs were considered if delivery was by a band 6 or band 7 member of staff
- For SlowMo the provision of 50% patients with a mobile phone was used for an additional scenario

Analyses	AVATAR	SlowMo
Base case	£548	£826
Delivered by band 6 staff (£53 per hour, PSSRU 2022)	£426.57	£620.77
Delivered by band 7 staff (£64 per hour PSSRU 2022)	£492.09	£731.16
50% patients receive mobile phones (EAG assumption £70 per phone, £10 per month for data)		£921

For further details on sensitivity analysis see section 10.4 of the AR

Sensitivity analysis: CareLoop (1)

For CareLoop, the EAG varied a few model inputs and conducted deterministic sensitivity analysis on each variation. A threshold analysis was also conducted

- The results from deterministic sensitivity analysis scenarios suggest that the cost saving results are robust to the variations in the model inputs
- The threshold analysis shows that CareLoop base case results would change from being cost-saving (less costly and more effective) based on the willingness-to-pay threshold of £20,000 per QALY gained, when CareLoop costs increase from [redacted] per year (with all other inputs remaining the same)

For further details on sensitivity analysis see section 10.4 of the AR

Sensitivity analysis: CareLoop (2)

	Standard care		Standard care with CareLoop monitoring		Incremental	
Analyses	Total Cost (£)	Total QALYs	Total Costs (£)	Total QALYs	Costs (£)	QALYs
Base Case	56,802	2.24	[redacted]	2.27	[redacted]	0.03
CareLoop, including 50% provision of pre-installed mobile handset with CareLoop app	56,802	2.24	[redacted]	2.27	[redacted]	0.03
RR relapse of CareLoop using lower 95% CI (0.26)	56,802	2.24	[redacted]	2.29	[redacted]	0.05
RR relapse of CareLoop using upper 95% CI (0.98)	56,802	2.24	[redacted]	2.24	[redacted]	0.00
Probability of hospitalisation following relapse with CareLoop +50% (0.375)	56,802	2.24	[redacted]	2.27	[redacted]	0.03
Relapse rate per year with standard care, using lower 95% CI (Year 1 12%, Year 2 35%, Year 3 40%)	54,200	2.26	[redacted]	2.28	[redacted]	0.02
Relapse rate per year with standard care, using upper 95% CI (Year 1 47%, Year 2 54%, Year 3 63%)	59,497	2.21	[redacted]	2.25	[redacted]	0.04
Threshold analysis CareLoop costs per year [redacted]	56,802	2.24	[redacted]	2.27	[redacted]	0.03

Economic model: EAG review

AVATAR and SlowMo:

- The key drivers of the intervention costs are staff time. In the research setting, both interventions were delivered by staff at a similar or higher level of qualification to those who would typically deliver CBTp, but over fewer sessions than are recommended by NICE for CBTp. Both companies are developing training to allow a range of staff to deliver interventions in future
- No evidence that would allow modelling of a link between the reported symptom improvement to changes in healthcare resource and long-term relapse outcome
- Neither has sufficient information to allow utilities to be included in a more detailed model
- A cost consequence approach had to be used and information from systematic reviews comparing CBTp or psychological support to TAU was used. The population and settings may not be equivalent to the intervention studies, and no direct comparisons with interventions under consideration. Difficult to make firm conclusion on outcomes comparing AVATAR or SlowMo with CBTp

CareLoop model is based on a pilot RCT which isn't fully powered to show clinical effectiveness

Key economic considerations

AVATAR Therapy & SlowMo

- Both interventions may improve the specific symptoms they are designed to address
- Key driver of the cost for both AVATAR Therapy and SlowMo is staff time needed to deliver it
- The exploratory decision analytic model could not be fully populated due to a lack of evidence linking short term symptom improvement to long term relapse outcome

CareLoop

- Exploratory modelling result showed CareLoop to be cost saving compared with standard care
- Key drivers were cost of the licence fee, number of relapse avoided and number of relapse that can be treated in the community avoiding hospitalisation
- Initial set up cost is relatively high and unrecoverable if adoption is reversed

HRQoL: health related quality of life

Evidence gaps

		Symptom management		Relapse prevention
	Outcomes	AVATAR Therapy	SlowMo	CareLoop
Comparator	CBTp and/or family intervention	RED		NR
	Psychological support	GREEN	AMBER	NR
	No psychological support	GREEN	RED	NR
	Standard care	NR	NR	AMBER
High priority outcome	Change in targeted psychotic symptoms	GREEN		NR
	Intervention adherence and completion	AMBER	GREEN	AMBER
	Health related quality of life	GREEN		AMBER
	Patient experiences and well being	GREEN		GREEN
	Intervention-related adverse events	GREEN		AMBER
	Rates of relapse or deterioration	NR		AMBER
	Time to relapse or deterioration	NR		AMBER
Other outcomes	Healthcare professional acceptance	RED		GREEN
	Changes in other psychological symptoms	GREEN		AMBER
	Impact on carers and family			RED

NICE

GREEN = 1-3 powered RCTs, 1 qualitative/observational study

AMBER = 1-2 RCTs (not powered/limited data)

RED = No studies

NR: not reported

Evidence gaps: Models and economic outcomes

	Outcomes	AVATAR Therapy	SlowMo	CareLoop
Costs	Technology (including licence fees and training)	AMBER		AMBER
		(provided by company, some details not yet finalised)		
	Healthcare professional time	AMBER		AMBER
		(1 RCT, real world implementation may differ)		
Others	Health care resources associated with changes in symptom severity	AMBER (1 RCT, aggregated mean utility)	RED	NR
	Utilities associated with changes in symptom severity	AMBER (1 RCT, aggregated mean utility)	RED	NR
	Avoidance and severity of relapse	NR		AMBER (2 RCTs, not powered)
	Health care resources associated with relapse and remission	NR		AMBER (1 RCT, not powered)
	Utilities associated with relapse and remission	NR		AMBER (1 RCT, aggregated mean utility)
	Longer term impact	RED		RED

NR: not reported

RED = no studies

Issues for consideration: Clinical evidence

Clinical effectiveness

- Evidence suggests that AVATAR Therapy reduces auditory hallucination symptoms and SlowMo reduces the symptoms of delusion and paranoia in people with psychosis
- There is no evidence comparing their use with current psychological therapies used in the NHS (i.e CBTp)
- CareLoop showed a reduction in the number of people experiencing relapse and increases time to relapse in a feasibility study
- There is no evidence of long-term effectiveness for all 3 technologies
- All clinical studies were conducted in the UK

Unmet need

- Less than 3% of people outside of EIP services will get access to CBT
- DHT may not be suitable for everyone which could make symptoms worse

Adverse events

- There is evidence reporting adverse events for all 3 technologies and some of these were classed as likely related to the technology

Key economic considerations

AVATAR Therapy & SlowMo

- Both interventions may improve the specific symptoms they are designed to address
- Key driver of the cost for both AVATAR Therapy and SlowMo is staff time needed to deliver it
- The exploratory decision analytic model could not be fully populated due to a lack of evidence linking short term symptom improvement to long term relapse outcome

CareLoop

- Exploratory modelling result showed CareLoop to be cost saving compared with standard care
- Key drivers were cost of the licence fee, number of relapse avoided and number of relapse that can be treated in the community avoiding hospitalisation
- Initial set up cost is relatively high and unrecoverable if adoption is reversed

HRQoL: health related quality of life

Possible recommendations

Conditionally recommended for use while further evidence is generated

- Likely that the technology will solve the unmet need and it is acceptable for the technology to be used in practice while further evidence is generated

Recommended only in a research context

- Uncertain if the technology has the potential to solve the unmet need, or it is not acceptable to be widely used in practice while further evidence is generated

Not recommended for use

- Unlikely that a technology has the potential to meet the unmet need, or where there are concerns about the potential harms associated with using the technology even in a research context

NICE National Institute for Health and Care Excellence

Thank you.

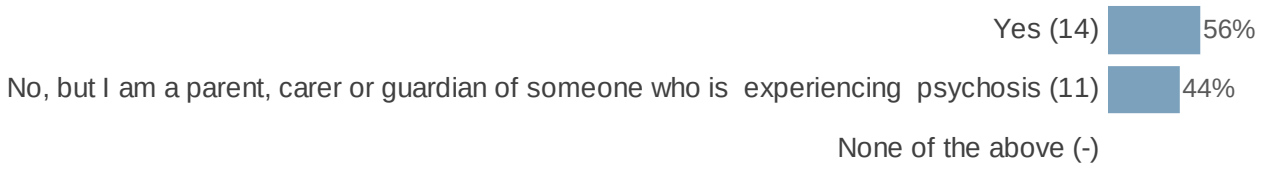
EVA Psychosis survey

This report was generated on 20/11/23. Overall 25 respondents completed this questionnaire. The report has been filtered to show the responses for 'All Respondents'. A total of 25 cases fall into this category.

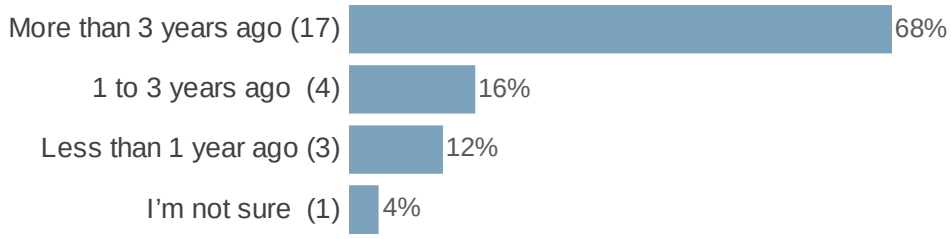
The following charts are restricted to the top 12 codes. Lists are restricted to the most recent 100 rows.

Are you (the person completing the survey) 14 years or over? Please tick one box only

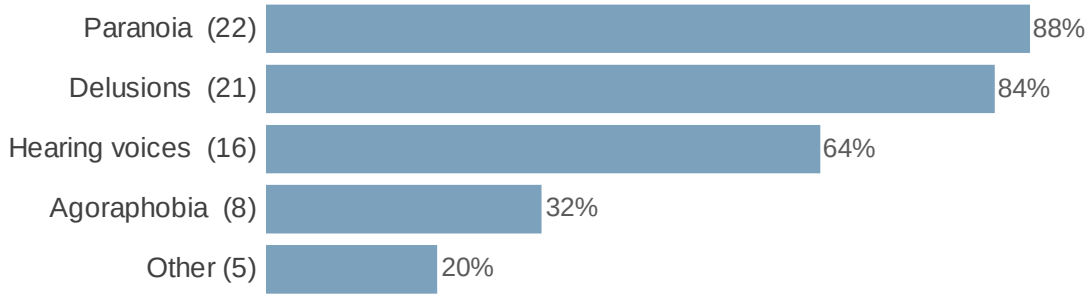
Are you (the person completing the survey) a person who is experiencing psychosis?



When was your first experience of psychosis?



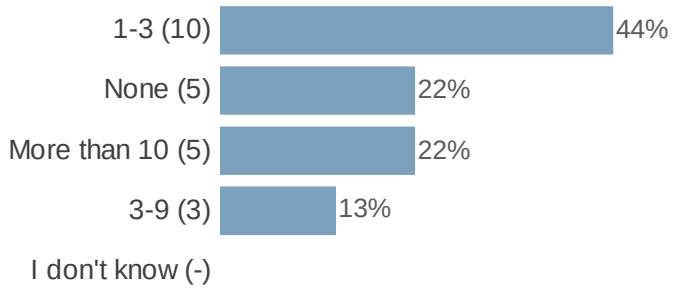
What symptoms of psychosis have you experienced in your life?



Please can you describe what other symptoms of psychosis you have experienced in the box below? (Please can you describe what other symptoms of psychosis...)

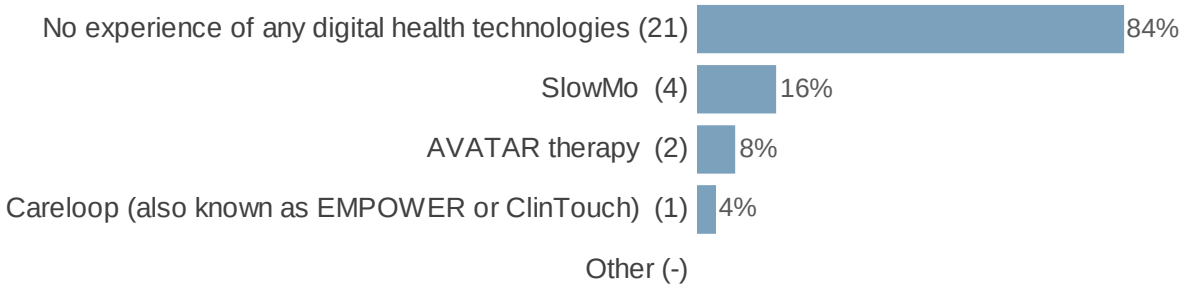
Delusions that people were coming to harm them. Hallucinating and hearing music that was not being played. Displaying towards loved ones and believing they needed to be hurt.
Seeing figures
Anxiety. Poor sleep. Self-medicating. Disordered and conflicting thoughts.

How many relapses of psychosis have you had in the last 3 years?

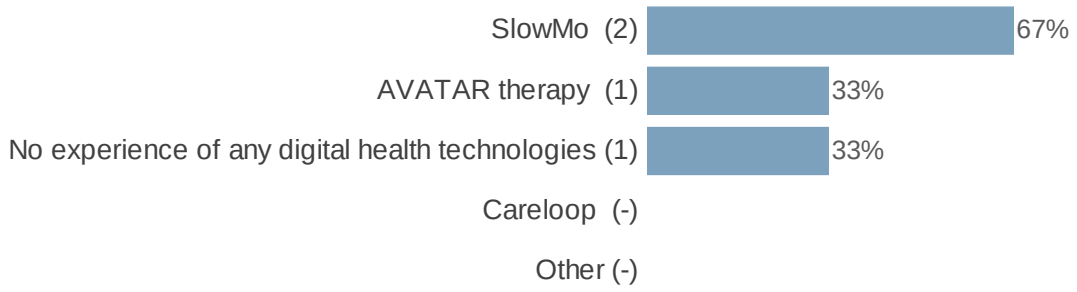


Have you used any digital health technologies to help manage symptoms of psychosis?

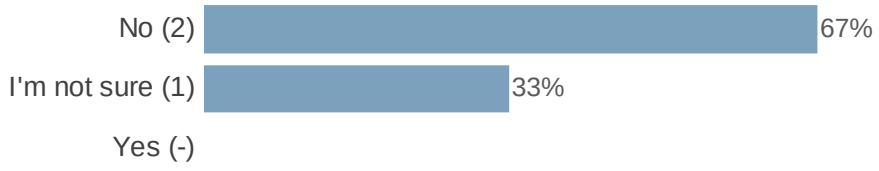
Which of these digital health technologies used in psychosis do you know of? Select all that apply



Which of these digital health technologies have you used for psychosis? Select all that apply



Do you feel like the digital health technology helped with managing your psychosis symptoms?

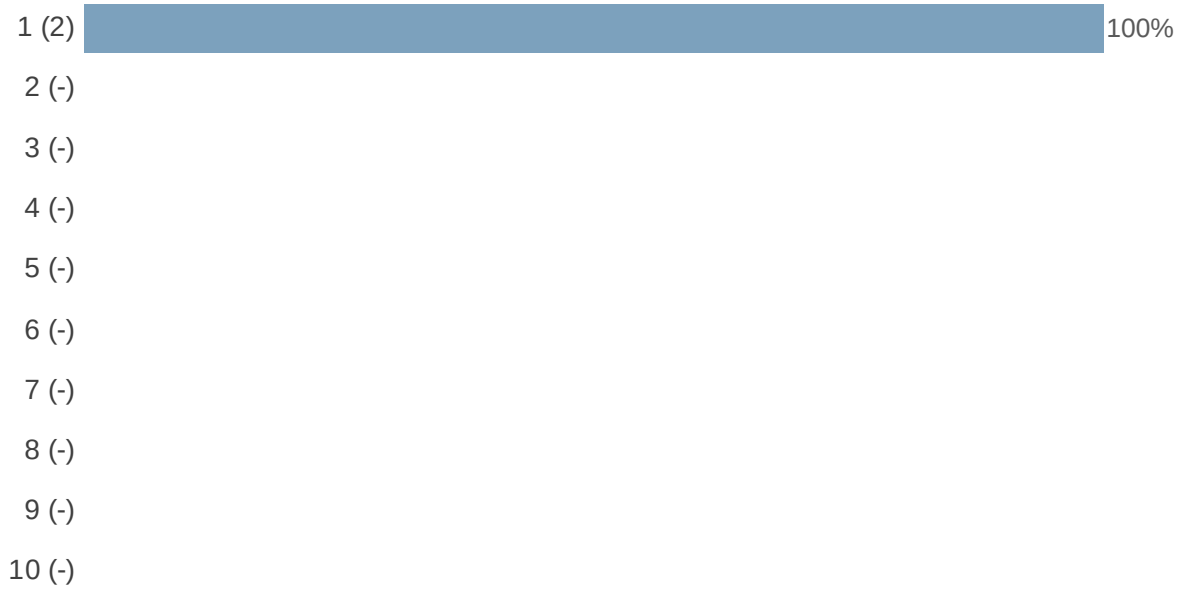


Please explain the reason for your answer

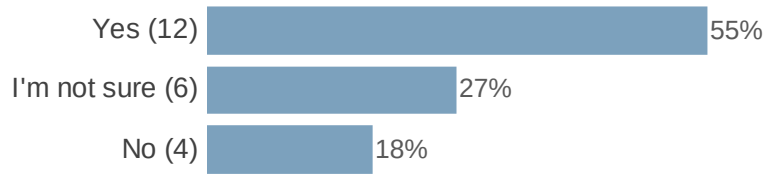
SlowMo was a disaster; it exacerbated my psychosis.

SlowMo exacerbated my psychotic symptoms

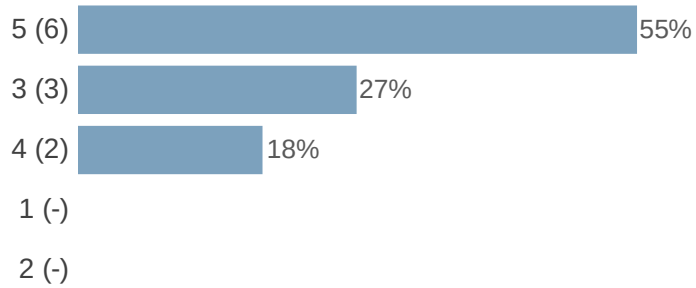
(On a scale of 1 to 10 how likely are you to recommend use of the technology to other people living with psychosis? (1 = not at all likely, 10 = very likely))



Would you consider using digital health technologies to manage your psychosis symptoms?



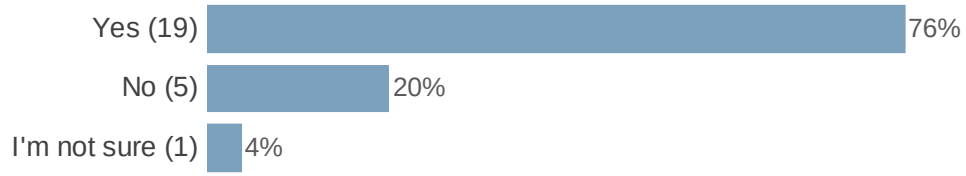
(How likely are you to use digital health technologies to manage your psychosis symptoms? (1 = not at all likely, 10 = very likely))



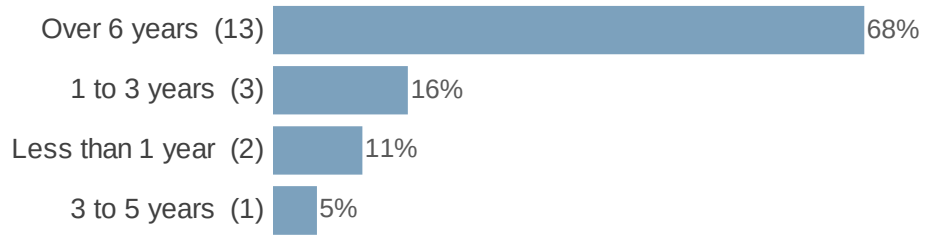
Please explain the reason for your answer

My psychosis involves thinking i am being monitored and tracked on my phone and laptop
Part of the paranoid delusions my mother experiences involve hacking of technology.
Paranoid about technology enough Big Brother syndrome
Not helpful need people

Do you currently take medication for the symptoms of psychosis prescribed by a doctor?



How long have you used the medication for?

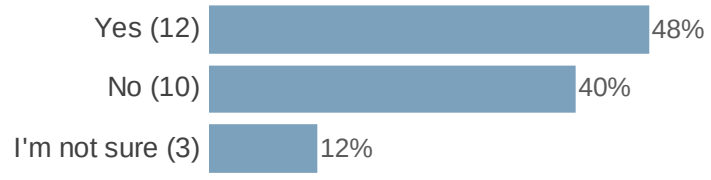


What has the impact on your life been from taking this medication?

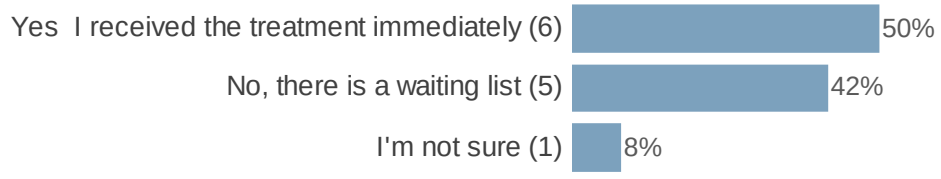
Co-morbidity with Huntington's Disease so it is hard to accurately measure the impact because of HD.
Very positive, it has helped me to feel safer in myself and lead a reasonably normal life
It’s helped a lot, but it’s slowed me down a bit too.
The medication has helped enormously and I could not manage without it.
Allowed me to function and luve my life
It helps but lots of side effects.
Loss of motivation, weight gain.
Prevented most symptoms of psychosis
I have been trying to get off qutipine for more than 13 years,I was put on it after have a psychotic episode around that time ,I have been able to reduce to100mgs a day,I think the side have had a detrimental on my brain,but I am hopeful that I will be off them in the near future.
It has varied.
Fatigue, appetite changes, brain fog, difficulty concentrating, memory loss, bad short term memory, lethargy, slow responses, droopy eyes, heart palpatations
Makes symptoms more bearable
Weight gain. Some fatigue.
Weight gain. Lack of motivation. Concentrate better. Have a job.
Calming symptoms
She takes them and doesn’t mention affects
Extream weight gain

Have you been offered Cognitive Behavioural Therapy (CBT) for psychosis?

(Cognitive behavioural therapy (CBT) for psychosis aims to help people make sense of their experiences. CBT may help to approach goals, such as reducing your distress, returning to work, education or training, or regaining a sense of control.)



Did you receive the treatment immediately or is there a waiting list for Cognitive Behavioural Therapy (CBT) for psychosis?



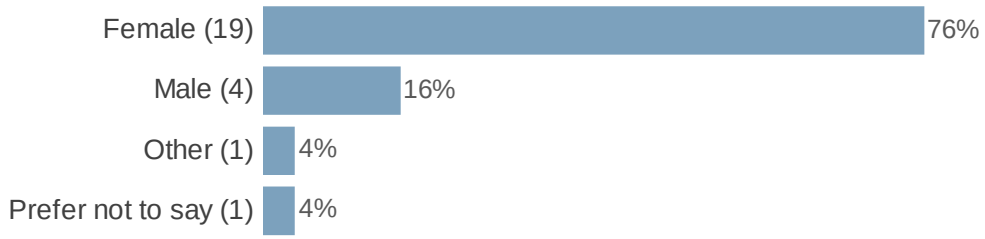
How long do you expect to be on the waiting list? Is there any other psychological support available to you whilst you are on the waiting list

Over 6 months. There was no other psychological support made available. CBT didn't work as health needs are too complex for this form of therapy
Been waiting for over 2 years
There was a waiting list of a few months before I received it
Long time probably 12 months
8 months

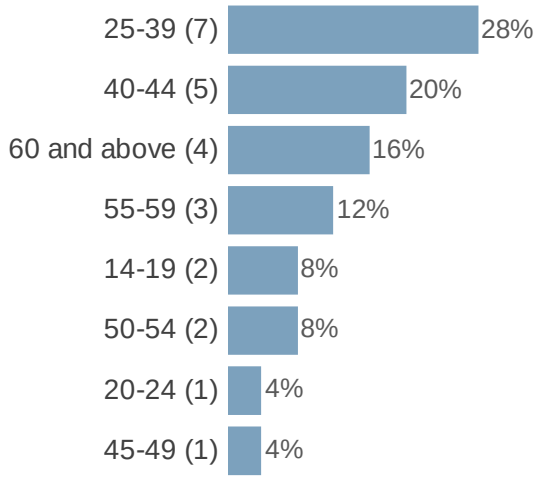
Please use the box below if you would like to tell us about any other types of psychological treatment that you have been offered or received

N/A
DBT - this as a somewhat interesting experience.
I have tried CBT, but I found it very overwhelming to engage.
Although my child experiences these symptoms, they have not been formally diagnosed and are still seeing a psychiatrist about them
Private psychotherapy
Also trauma CBT
I have been having therapy since the age of 14 ,psychotherapist mostly private and through n.h.s.what I really need is trumuor therapy
CBT for psychosis exacerbated my psychotic symptoms
I meet often with my psychiatrist and use the Early Intervention Psychosis service offered by the NHS
Trauma therapy with a real person was invaluable
NA
I have had years of Cognitive therapy: both individual therapy & group therapy led by Psychologists.
Psych-dynamic psychological therapy
Feeling Safe Therapy
She’s paying for a therapist and has a CMHT
Psychedelics

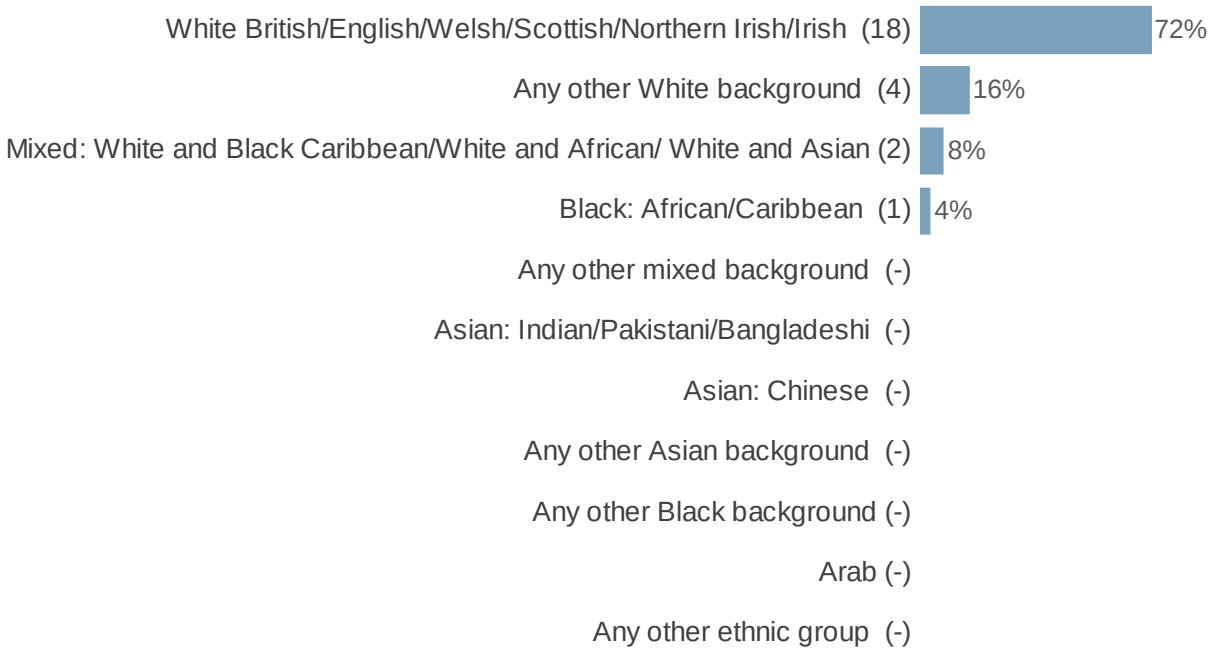
What is your gender identity? Please tick one box only



What is your age range?



What is your ethnicity? Please tick one box only



NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technologies evaluation programme

Equality impact assessment: Guidance development

Digital health technologies to help manage symptoms of psychosis and prevent relapse: early value assessment

The impact on equality has been assessed during this early value assessment (EVA) according to the principles of the NICE Equality scheme.

Draft guidance consultation

1. Have the potential equality issues identified during the scoping process been addressed by the committee, and, if so, how?
The committee thoroughly considered the potential equality issues that were identified during scoping. Key issues included: • People may need regular access to a smart device or computer with internet access to use digital health technologies. Additional support and resources may be needed for people who are unfamiliar with digital technologies or do not have access to smart devices or the internet. Other treatment options may be more appropriate for some people who have limited access to digital technologies or who prefer face-to-face treatment. • People with visual or cognitive impairment, problems with manual dexterity, a learning disability or who have difficulty reading or understanding health-related information may need additional support to use digital health technologies. This should be considered when selecting and delivering these interventions. Further considerations can be found in NICE's guideline on mental health problems in people with learning disabilities. • People with English as a second language may have difficulties navigating digital health technologies provided in English. Some people will benefit from digital health technologies in languages other than English. Digital health technology developers and mental health services should consider how to translate these interventions or provide additional support as needed. • Digital health technologies may increase access to treatment and address a clinically unmet need. Access to mental health care will not increase for

those who are unable to engage with a digital service due to a lack of equipment, unavailability of internet connection or lack of experience with computers to complete the intervention. Treatment options should be discussed by healthcare professionals, patients and (where appropriate) carers and should consider clinical assessment, patient preferences and needs, the level of support needed and the suitability of the treatment to match these considerations.

- People's views of mental health problems or interventions may be influenced by their ethnic, religious and cultural background. People have the right to make informed decisions about their care, including the use of digital health technologies. Healthcare professionals should discuss the language and cultural content of the technologies with patients before use.

Additionally, the committee discussed potential equality considerations related to mental health problems and specifically symptoms of psychosis that are related to technology. People facing social inequality and disadvantage, discrimination and social exclusion are at higher risk of mental health problems. Black men are more likely to be diagnosed with psychosis than white men and less likely to have cognitive behavioural therapy for psychosis for first episode psychosis. These should be considered when selecting and delivering digital health technologies for people with psychosis and steps taken to reduce health inequalities. Age, disability, race and religion or belief are protected characteristics under the Equality Act (2010).

2. Have any other potential equality issues been highlighted in the company's submission, or patient and carer organisation questionnaires, and, if so, how has the committee addressed these?

Patient experts advised that people with mental health conditions face a lot of stigma and discrimination. Some people from some ethnic backgrounds may also experience shame or have negative views of mental health treatment. This may affect their ability or willingness to seek treatment. The committee considered that some people with psychosis may prefer digital health technologies over standard care. Use of these technologies as an alternative option may help promote greater engagement and access to treatment for some people. However, adequate and timely professional support should be provided to react to alerts and outputs from using the technologies.

3. Have any other potential equality issues been identified by the committee and, if so, how has the committee addressed these?
No other potential equality issues or considerations were identified by the committee.

4. Do the preliminary recommendations make it more difficult in practice for a specific group to access the technology compared with other groups? If so, what are the barriers to or difficulties with access for the specific group?
Adults with limited access to the necessary technologies or who are less skilled or comfortable or skilled at using digital technologies may be less likely to benefit from digital health technologies. Additional support may be needed for people with additional accessibility needs or who are unable to read or understand English. The committee considered that other treatment options may be more appropriate for some adults with psychosis. This is discussed in section 3.12 of the draft guidance.

5. Is there potential for the preliminary recommendations to have an adverse impact on people with disabilities because of something that is a consequence of the disability?
No.

6. Are there any recommendations or explanations that the committee could make to remove or alleviate barriers to, or difficulties with access identified in questions 4 or 5, or otherwise fulfil NICE's obligations to promote equality?
Other treatment options including face-to-face treatment may be more appropriate for some adults with psychosis. This is discussed in section 3.9 and 3.11 of the draft guidance.

7. Have the committee's considerations of equality issues been described in the medical technology consultation document, and, if so, where?

Yes, these have been discussed in sections 3.10, 3.11 and 3.12 of the draft guidance.

Approved by Associate Director: Anastasia Chalkidou

Date: 13 December 2023

NICE National Institute for Health and Care Excellence

Medical Technologies Advisory Committee Interests Register

Topic: Digital health technologies to help manage symptoms of psychosis and prevent relapse (provisional title)

NICE's declaration of interest policy can be accessed here

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Dr Isabel Ellory	Specialist Committee Member	Financial Interest	Nothing to declare		7.8.2023		
Dr Isabel Ellory	Specialist Committee Member	Non-Financial Professional and Personal Interest	Nothing to declare		7.8.2023		
Dr Isabel Ellory	Specialist Committee Member	Indirect Interest	The trust within which I work (Greater Manchester Mental Health NHS FT) is currently involved with research projects that relate to digital interventions. This includes a study to test a smoke free app within Early Intervention Services and a second study of service user and staff views on digital remote monitoring for psychosis.		7.8.2023	Ongoing	Declare in the meeting and participate
Dr Jihad Malasi	Specialist Committee Member	Financial Interest	Kent and Medway ICB Clinical Lead in Mental Health and Dementia	March 2023	7.8.2023		

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Dr Jihad Malasi	Specialist Committee Member	Financial Interest	GP Tutor (East Kent) Health Education England (Now NHSE)	November 2021	7.8.2023		
Dr Jihad Malasi	Specialist Committee Member	Financial Interest	Locum GP	indefinite	7.8.2023		
Dr Jihad Malasi	Specialist Committee Member	Financial Interest	Invited Speaker to 'GP Best Practice' Event, held by CloserStill Media - Topic ' Severe Mental Illness' and policy discussion. Will be paid an honorarium, transport and hotel accommodation	November 2023	7.8.2023	November 2023	Declare in the meeting and participate
Dr Jihad Malasi	Specialist Committee Member	Non-Financial Professional and Personal Interest	Post Graduate Student London School of Economics and Political Science- Auditing student 2024 Graduated 7/2023 Executive MSc Health Economics, Policy and Management	2020	7.8.2023	December 2024	I have graduated, but staying on to 'audit' 2 further courses in June 2024. (Audit means attend but no exam requirement)
Dr Jihad Malasi	Specialist Committee Member	Non-Financial Professional and Personal Interest	Post Graduate Student Keele University (MSc Global Healthcare Leadership)	2022	7.8.2023	July 2024	

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Dr Jihad Malasi	Specialist Committee Member	Non-Financial Professional and Personal Interest	British Medical Association- Standard Member, recently rejoined.	July 2023	7.8.2023		
Dr Jihad Malasi	Specialist Committee Member	Non-Financial Professional and Personal Interest	Gurkha Welfare Trust - Volunteer Medical Advisor (Medical Education/Mentorship)	October 2023	7.8.2023		
Dr Jihad Malasi	Specialist Committee Member	Non-Financial Professional and Personal Interest	Associate (student) Member of RSPH	April 2023	7.8.2023		
Dr Jihad Malasi	Specialist Committee Member	Indirect Interest	Wife - Marthe Enger Malasi; GP at Whitstable Medical Practice	2023	7.8.2023		
Dr Lisa Wood	Specialist Committee Member	Financial Interest	Nothing to declare		4.8.2023		
Dr Lisa Wood	Specialist Committee Member	Non-Financial Professional and Personal Interest	Nothing to declare		4.8.2023		
Dr Lisa Wood	Specialist Committee Member	Indirect Interest	Nothing to declare		4.8.2023		
Prof Philip McGuire	Specialist Committee Member	Financial Interest	Nothing to declare		7.8.2023		
Prof Philip McGuire	Specialist Committee Member	Non-Financial Professional and Personal Interest	Involvement in ongoing or scheduled non-commercial trials of novel treatments for psychosis		7.8.2023		Declare in the meeting and participate

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Prof Philip McGuire	Specialist Committee Member	Non-Financial Professional and Personal Interest	STOP – Trial of novel psychological intervention in psychosis (MRC)	2022	7.8.2023		Declare in the meeting and participate
Prof Philip McGuire	Specialist Committee Member	Non-Financial Professional and Personal Interest	STEP – Trials of Cannabidiol in psychosis (Wellcome Trust)	2022	7.8.2023		Declare in the meeting and participate
Prof Philip McGuire	Specialist Committee Member	Non-Financial Professional and Personal Interest	FOCUS – Trial of KatXT in psychosis (Wellcome Trust)	2022	7.8.2023		Declare in the meeting and participate
Prof Philip McGuire	Specialist Committee Member	Indirect Interest	Nothing to declare		7.8.2023		
Anthony Middleton	Lay Member	Financial Interest	Nothing to declare		2.8.2023		
Anthony Middleton	Lay Member	Non-Financial Professional and Personal Interest	Service User, and non-decision making member in a number of related charities to psychosis and mental health, including Bi-Polar UK --Member		2.8.2023 and extra info 24.11.2023		
Anthony Middleton	Lay Member	Indirect Interest	Nothing to declare		2.8.2023		
Karen Persaud	Lay Member	Financial Interest	Nothing to declare		2.8.2023		
Karen Persaud	Lay Member	Non-Financial Professional and Personal Interest	Nothing to declare		2.8.2023		

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Karen Persaud	Lay Member	Indirect Interest	Nothing to declare		2.8.2023		
Catarina Sacadura	Professional Expert	Financial Interest	Nothing to declare		15.9.2023		
Catarina Sacadura	Expert Adviser	Non-Financial Professional & Personal Interests	I was a therapist and site coordinator for the SlowMo trial in Sussex (Sussex partnership NHS Foundation trust), this is how I got experience of using the SlowMo intervention. I was also a co-author is the trial paper, as this is part of the role. I have not been involved in the trial since it finished and the paper has been published. My current research work in the NHS is no longer connected with SlowMo.	2018	15.09.2023	2019	Declare in the meeting and participate
Catarina Sacadura	Professional Expert	Indirect Interest	Nothing to declare		15.09.2023		
Hannah Ball	Professional Expert	Financial Interest	Full time employment in NHS Mental Health services (Greater Manchester Mental Health NHS Foundation Trust)	26/09/2016	23.11.2023	Ongoing	

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Hannah Ball	Professional Expert	Financial Interest	Employed as Trial Therapy Coordinator on the AVATAR2 RCT investigating AVATAR therapy for distressing voices	07/12/2020	23.11.2023	Ongoing	Declare in the meeting and participate
Hannah Ball	Professional Expert	Non-Financial Professional and Personal Interest	Involved in the AVATAR2 research trial which is investigating the effectiveness of AVATAR therapy for people who hear voices.	07/12/2020	23.11.2023	Ongoing	Declare in the meeting and participate
Hannah Ball	Professional Expert	Indirect Interest	Nil		23.11.2023		
Zera Brittenden	Professional Expert	Financial Interest	Nothing to declare		12.8.2023		
Zera Brittenden	Professional Expert	Non-Financial Professional and Personal Interest	Expert directly involved in providing AVATAR therapy	2022	12.8.2023	Ongoing	Declare in the meeting and participate
Zera Brittenden	Professional Expert	Indirect Interest	Nothing to declare		12.8.2023		
Neil Hawkins	Committee Member	Financial Interest	I am a named director of a company that provides HTA consultancy services to the pharmaceutical and biotech industries. No services have been provided to named stakeholders in these assessments.				

Name	Role with NICE	Type of interest	Description of interest	Interest arose	Interest declared	Interest ceased	Comments
Neil Hawkins	Committee Member	Non-Financial Professional and Personal Interest	Nothing to declare				
Neil Hawkins	Committee Member	Indirect Interest	Nothing to declare				