Early Value Assessment GID-HTE10020 Digital health technologies for management of psychosis: EVA

Final Protocol

Produced by: CEDAR (Centre for Healthcare Evaluation, Device Assessment, and Research)

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Contents

Abbreviations

Term	Definition
CBT	Cognitive behaviour therapy
CMHT	Community mental health team
DTAC	Digital technology assessment criteria
EAG	External assessment group
EIP	Early Intervention in Psychosis
EVA	Early Value Assessment
GP	General practitioner
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
RCT	Randomised controlled trial

Plain English Summary

Psychosis is a state of mind where a person's abilities to understand and test reality are impaired. Primary psychosis is when psychosis is the main feature and these are called psychotic disorders. Secondary psychosis is when psychosis is caused by a medication or substance, or when there is another medical condition or mood disorder present. Psychosis is characterised by "positive" and "negative" symptoms. 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).

There are a number of things that may be linked with psychotic disorders. These include a person's social environment, such as: inner city living, deprivation, population density, social fragmentation and ethnic density or individual life experiences such as childhood adversity and abuse, early experience of alcohol or substance use and abuse, discrimination and adult social (Psychosis Data Report).

There are a number of options to help people treat and manage symptoms of psychosis. To help manage psychosis, options include early intervention in psychosis (EIP) specialist teams for the first episode, or a specialist community mental health team (CMHT) for longer-term psychosis. An acute episode of psychosis may require psychiatric hospitalisation. A person with psychosis could be discharged back to their GP if they have been stable and symptom-free for a long time. Antipsychotic medication and cognitive behavioural therapy (CBT) are used to treat psychosis.

There are also digital technologies that people can use to access therapy and it is important to know how these work and if they are safe before they are made available on the NHS. NICE reviews the evidence for treatment and therapies in England and this assessment will look at a number of digital therapies to determine whether they are safe for use and report how well they work to manage and treat

psychosis. The assessment will also consider the costs of providing digitally enabled therapies and their potential value for money.

1. Background

The primary indication of this early value assessment (EVA) are digital health technologies to help manage symptoms of psychosis, and prevent relapse.

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.

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.

The objective of this Early Value Assessment (EVA) is to identify promising technologies in health and social care where there is greatest need and where the evidence base is still emerging. 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 3 technologies; assess their potential clinical and cost-effectiveness and to identify evidence gaps to help direct data collection and further research.

2. Decision Problem

The decision problem is described in the final scope and summarised here.

2.1. Population

The population of interest is people over the age of 14 living with primary psychosis. Where data permits, subgroups will be considered based on:

- Severity of psychosis
- High risk of relapse
- Age

2.2. Intervention Technologies

Digital health technologies for symptom management and relapse prevention of psychosis were selected. Three criteria were used to identify these technologies:

- Digital health interventions 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.
- 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.
- Available for use in the NHS.

Four digital health technologies were identified which met the selection criteria. These are AVATAR Therapy, CareLoop, SlowMo and gameChange. GameChange is already being evaluated in another EVA, Virtual reality for treating agoraphobia and agoraphobic avoidance, and so was excluded from this EVA.

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 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.

2.3. Potential Alternative Technologies

No other commercially available technologies were identified for this topic. This was clarified with clinical experts.

2.4. Comparators

The comparator for this assessment is standard care for psychosis which is based on NICE clinical guideline for psychosis and schizophrenia treatment and management. Broadly, the comparators can be grouped into two categories and relevant comparators for each technology may differ depending on the purpose of the technology.

For AVATAR and SlowMo, the comparator is standard care for managing symptoms. Access to CBT for psychosis varies depending on location, and some people are on waiting lists to access services. In some areas, other forms of psychological therapy such as group therapy or supportive counselling may be available to people on a waiting list whereas in some areas people may not be offered any form of psychological support. These will also be used as a comparator besides the NICE CG mentioned above.

For CareLoop the comparator is standard care for monitoring people at risk of relapse. 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.

2.5. Outcomes

A number of high priority outcomes related to symptom management and relapse prevention have been identified (Table 1). Additional outcomes relevant to both include healthcare professional acceptance, changes in other psychological symptoms and impact on family and carers.

Table 1: High Priority Outcomes

Symptom Management	Relapse Prevention
Change in targeted psychotic symptoms such as paranoia, agoraphobia, hearing distressing voice etc	Rates of relapse or deterioration
Health related quality of life	Time to relapse or deterioration
Patient experiences and well being	Severity of relapse
Intervention adherence and completion	Intervention adherence and completion
Intervention related adverse events	Patient experience and wellbeing
	Health related quality of life
	Intervention-related adverse events

2.6. 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 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.

Potential place of technologies 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 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. Objective

The purpose of this evidence assessment is to summarise and critically appraise existing evidence of the digital health technologies; AVATAR Therapy, CareLoop, and SlowMo in people over the age of 14, living with primary psychosis. 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. It should be noted that the purpose of the review is not to compare the technologies with each other.

Based on the scope developed by NICE, the following specific research questions are proposed:

- What is the clinical effectiveness of AVATAR Therapy and SlowMo for the treatment and management of symptoms?

- What is the clinical effectiveness of CareLoop for the monitoring of symptoms to aid prediction and prevention of relapse?
- What are the practical implications of introducing the technologies into the current care pathway?
- What are the cost and resource implications relating to the use of the technologies?

4. Methods

The inclusion criteria are described fully in the final scope but are also summarised by the research questions in Table 2 below. The following broad objectives are proposed to address the identified research questions:

Clinical Effectiveness

- Identify and assess relevant evidence. If feasible, also a meta-analysis of the clinical effectiveness of the three digital health technologies
- Identify evidence gaps to support further evidence generation, and highlight the data that may require collection to address these gaps
- Describe any on-going or planned studies to help address evidence gaps
- Report any potential safety issues and identify any risks associated with the use of these technologies in the NHS whilst further evidence is generated
- Highlight any equalities issues not described in the scope
- Outline the potential generalisability and limitations of any evidence identified that is not related to the scope

Cost Effectiveness

- Identify and assess relevant economic evidence
- Develop an early economic model for each of the digital health technologies to determine potential cost-effectiveness of their use in the NHS. If this is not

possible, develop a conceptual economic model that can be used to inform future data collection and research.

- Report available model parameters and any evidence gaps
- Describe any on-going or planned studies to help inform the economic model.

Table 2: Study Eligibility Criteria

Research Question	**What is the clinical effectiveness of AVATAR Therapy and SlowMo for the treatment and management of symptoms?**	**What is the clinical effectiveness of CareLoop for the monitoring of symptoms to aid prediction and prevention of relapse?**	**What are the practical implications of introducing the technologies into the current care pathway?**	**What are the cost and resource implications relating to the use of the technologies?**
Participants	People aged 14 and over living with primary psychosis. Where data permits, subgroups will be considered based on: • Severity of psychosis • Age	People aged 14 and over living with primary psychosis. Where data permits, subgroups will be considered based on: • High risk of relapse		
Setting	Outpatient clinics Inpatient care Home based care	Outpatient clinics Home based care	Outpatient clinics Inpatient care Home based care	Outpatient clinics Inpatient care Home based care
Intervention	AVATAR Therapy for auditory hallucinations SlowMo for paranoia	CareLoop	AVATAR Therapy for auditory hallucinations SlowMo for paranoia CareLoop	AVATAR Therapy for auditory hallucinations SlowMo for paranoia CareLoop
Comparator	Standard psychological care for managing symptoms of psychosis. This may include: • CBT for psychosis. The intervention could be used to replace symptom-specific	Standard care for monitoring people at risk of a relapse of psychosis		

Research Question	What is the clinical effectiveness of AVATAR Therapy and SlowMo for the treatment and management of symptoms?	What is the clinical effectiveness of CareLoop for the monitoring of symptoms to aid prediction and prevention of relapse?	What are the practical implications of introducing the technologies into the current care pathway?	What are the cost and resource implications relating to the use of the technologies?
	components of a CBT for psychosis programme. • Psychological support whilst waiting for CBT for psychosis. • No access to psychological support.			
Outcomes	<u>High priority outcomes</u> • 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	<u>High priority outcomes</u> • 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	• Healthcare professional acceptance • Changes in other psychological symptoms • Impact on carers and family	

Research Question	**What is the clinical effectiveness of AVATAR Therapy and SlowMo for the treatment and management of symptoms?**	**What is the clinical effectiveness of CareLoop for the monitoring of symptoms to aid prediction and prevention of relapse?**	**What are the practical implications of introducing the technologies into the current care pathway?**	**What are the cost and resource implications relating to the use of the technologies?**
	• Intervention-related adverse events			
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.			

4.1. Search Strategy

Searches will be developed in MEDLINE (Ovid) by an experienced Information Specialist. Search terms will include free-text terms and controlled terms from databases (e.g. MeSH, Emtree). Searches will be structured around population and intervention concepts as detailed in the inclusion criteria. A combined search will be conducted for all digital health technologies.

An example search strategy is provided in Appendix A. A single search strategy for clinical evidence will be created and will be peer-reviewed by a second Information Specialist. For economic evidence, evidence will be identified from the clinical evidence search, in addition to a broad scoping search for economic evidence relating to the care pathway.

The EAG will assess the number of results identified in MEDLINE and based on this, will decide whether additional database searches are required. Additional databases that will be searched include:

- Embase (Ovid)
- PsycInfo (Ovid)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- International HTA database (INAHTA)

The following clinical trial registries will be searched:

- ClinicalTrials.gov
- International Clinical Trials Registry Platform (ICTRP)

Relevant guidelines will be identified by searching:

- NICE Guidance
- Scottish Intercollegiate Guidelines Network (SIGN)

Additionally, company websites will be searched to identify relevant publications and ongoing trials, and the MHRA and MAUDE will be searched for any safety notices or adverse events for the technologies.

4.2. Study selection

Retrieved references will be imported into EndNote and deduplicated. EndNote will also be used to record reviewers' screening decisions. Titles and abstracts of identified studies will be screened by one reviewer and a minimum of 20% checked by a second reviewer against pre-specified inclusion and exclusion criteria. Full-text articles of eligible studies will be obtained and screened by one reviewer with final inclusions and a random 20% of exclusions checked by a second reviewer.

4.3. Data extraction

A standardised data extraction form will be created and piloted. Where available, the following data will be extracted from studies: study information (i.e., author, year) study design, study dates, intervention characteristics (i.e., intervention name, therapist delivering intervention), comparator, participant characteristics (i.e., demographics, symptoms of psychosis, psychological symptoms), patient outcomes (e.g., change in symptoms of psychosis, change in psychological symptoms, global functioning, work and social adjustment, reliable recovery, reliable improvement, reliable deterioration, rates of relapse, health-related quality of life, treatment satisfaction). Data extraction will be conducted by one reviewer and checked by a second.

4.4. Quality assessment

Formal quality assessment using checklists will not be conducted. A narrative summary of the key strengths and limitations of the evidence will be presented in the final report. This summary will highlight potential biases in individual studies for example, relevance to scope, potential confounding) and will discuss how these impact on the certainty of the results and how this might impact generalisability to NHS clinical practice.

5. Evidence Synthesis and Evidence Gap Analysis

The EAG will consider meta-analysis methods to synthesis the relevant clinical evidence. However, due to the nature and purpose of an Early Value Assessment, it is not anticipated that there will be enough data available to conduct a meta-analysis.

Results for both clinical and economic literature will therefore be presented in a suitable tabular format accompanied by a narrative synthesis of the data, considering available evidence relating to all aspects of the scope (for example, population, setting, comparators). Methodological problems with included studies will be noted along with any identified risks of bias which may impact study results. A discussion outlining the applicability of the evidence to the scope of the EVA will be included, as well as consideration of the generalisability of evidence to clinical practice in the NHS.

Evidence gaps will be identified and summarised in a suitable tabular format. A traffic light system, or similar may be used to highlight the relative importance of the evidence gaps. The EAG will discuss the identified evidence gaps within the context of the NICE EVA processes to allow expert judgements to be made regarding further evidence generation. Key ideas for evidence generation to fill these gaps will be summarised in tabular format identifying the key outcomes for evidence generation to address.

6. Identification of key economic and purchasing factors

Existing models will be identified from guidance and literature. Suitability of existing models will be assessed, and if applicable access to the models will be requested. This may not be possible in many cases, or may be limited by the available timeframe.

The likely key parameters will be identified from existing literature, company submissions and consultation with clinical experts and patient representatives. Assumptions in the model will be clearly described and informed by evidence or advice from clinical experts.

Availability of data for these parameters will be considered including the use of any real-world data sets that are available. These should be identified as early as possible and access and support to interpret them facilitated by NICE. It is recognised that this type of data cannot always be shared at the required level, and is likely to have limitations.

Whole lifecycle costs will be identified and considered. The implications of reversing a decision to use the technology will also be discussed.

Costs will be considered from an NHS and Personal Social Services perspective and may include:

- Licencing model and costs
- Training of healthcare professionals
- Costs of any hardware required to use the software other than a phone or tablet
- Costs of delivering the intervention
- Administration costs for the programme

In addition, consideration will be made of the cost of providing a phone or tablet and data access for participants who do not have this, in the form of scenario analysis.

7. Development of a conceptual economic model

Where suitable models already exist and can be shared or re-created the EAG will assess the feasibility of populating the model with relevant data for the technologies being assessed.

Where existing models are not available, or not suitable, the EAG will consider creation of a new model. As a minimum this will be a conceptual model that describes the pathways and parameters needed for its population. This may be completed in a software package as an executable model even if the parameters cannot be fully populated. The aim of a conceptual model is to identify model inputs required and the evidence gaps, and form the basis for future economic work.

If there is sufficient evidence available a populated model may be created. For inputs without direct evidence, literature and advice from clinical experts will be used, with all assumptions clearly stated. Ideally the model would cover a long enough time horizon to consider the costs of ongoing health service use, and any relapse treatment including adverse events. Sensitivity analysis would investigate the impact of uncertainty around assumptions and evidence sources.

8. Company Submissions

Information may be sought from companies where appropriate. All data submitted by the company or other stakeholders will be considered by the EAG if received by 05/09/2023. Data received after this date will be considered if practicable and at the discretion of the EAG.

All correspondence with companies will be recorded in a correspondence log for transparency. Any ‘commercial in confidence’ data provided by the company, and specified as such, will be highlighted in blue and underlined in the report and correspondence log. Any ‘academic in confidence’ data provided by the company, and specified as such, will be highlighted in yellow and underlined in the report and correspondence log.

9. Competing Interests of Authors

None

Appendix A Example search strategy

Sample search strategy for the clinical effectiveness review designed in Ovid-MEDLINE

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. (1403)
5	or/1-4 (1594)
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. (289)
10	((prevent* adj relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. (1355)
11	((predict* adj2 relapse) and (digital* or app* or web* or internet or comput* or online or mhealth or smartphone*)).tw. (1503)
12	or/6-11 (3114)
13	avatar.tw. (1448)
14	avatar therapy.in. (0)
15	(digital adj (representation or simulation)).tw. (424)
16	or/13-15 (4978)
17	5 or 12 or 16 (6572)
18	Psychotic Disorders/ (52495)
19	exp Schizophrenia/ (115392)
20	Affective Disorders, Psychotic/ (2317)
21	Paranoid Disorders/ (4278)
22	Delusions/ (8157)
23	Hallucinations/ (11931)
24	psychos#s.tw. (51095)

25 psychotic.tw. (38950)

26 schizophreni*.tw. (138723)

27 paranoi*.tw. (8987)

28 delusion*.tw. (12321)

29 hallucin*.tw. (20250)

30 (hear* adj2 voice*).tw. (1511)

31 or/18-30 (247074)

32 17 and 31 (348)

33 exp animals/ not humans.sh. (5150978)

34 32 not 33 (348)