NICE National Institute for Health and Care Excellence

Medical Technologies Evaluation Programme

Guided self-help digital cognitive behavioural therapy for children and young people with mild to moderate symptoms of anxiety or low mood

Committee Papers

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

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Contents:

Any information supplied to NICE which has been marked as confidential has been redacted. All personal information has also been redacted.

Document cover sheet

Assessment report: Guided dCBT for CYP with mild to moderate anxiety/low mood: an Early Value Assessment.

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[MT580]: Guided self-help digital cognitive behavioural therapy for children and young people with mild to moderate symptoms of anxiety and low mood

External Assessment Group report

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Early Value Assessment Programme

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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.

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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.

Contents

Abbreviations

Term	Definition
ASD	Autism spectrum disorder
CAMHS	Child and Adolescent Mental Health Services (synonym for CYPMHS)
CGAS	Children's Global Assessment Scale
dCBT	(Digital) cognitive behavioural therapy
CE mark	Conformity with European health, safety, and environmental protection standards
CI	Confidence interval
CSRI	Client Services Receipt Inventory
CYP	Children and young people
CYPMHS	Children and young people's mental health services (synonym for CAMHS)
DHSC	Department of Health and Social Care
DTAC	Digital Technology Assessment Criteria
EAG	External assessment group
HoNOSCA	Health of the Nation Outcome Scales for Children and Adolescent mental health
HRQoL	Health-related quality of life
IQR	Interquartile range
GP	General practitioner
MAIC	Matching-adjusted indirect comparisons
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
MHST	Mental health support team
MTEP	Medical Technologies Evaluation Programme
N/A	Not applicable
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NICE CG	NICE clinical guideline
NICE MTG	NICE medical technology guidance
NICE QS	NICE quality standard
NMA	Network meta-analysis
OSCA	Online Social anxiety Cognitive therapy for Adolescents
OSI	Online support and intervention for child anxiety
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

QUORUM	Quality of Reporting of Meta-analyses
RCT	Randomised controlled trial
SCM	Specialist Committee Member
SD	Standard deviation
VAS	Visual analogue scale
Vs	Versus

Executive summary

Quality and relevance of clinical evidence

There are a number of evidence gaps in respect of the clinical evidence base as it pertains to the decision problem. Currently, there is no evidence on some technologies of interest; where evidence is available, there is very little comparative data and no evidence including active comparators in the published literature. Comparative evidence, including comparisons with active controls, was identified among ongoing studies, but only for a single technology. There was no evidence for the effectiveness of technologies for low mood, and also no evidence for the effectiveness of technologies in young people aged 12 to 18 years. No information is available on the incidence of suicidal ideation or behaviours, which are considered to be important adverse event signals. No prospective or ongoing work to address these gaps was identified.

While reported outcomes relating to symptom severity and impairment were reported heterogeneously, some measures were common to most. Included studies mostly suffered from methodological limitations, and bias in effect estimates could not be ruled out as a result.

Quality and relevance of economic evidence

Whilst there is a *prima facie* weak case for guided dCBT to be cost-effective compared with no treatment, there is a lack of evidence to determine whether one dCBT intervention is more cost-effective than another, or whether any guided dCBT intervention is more or less cost-effective than other active treatments such as face to face dCBT. Duration of the intervention appears to have the biggest impact on cost-effectiveness.

Evidence Gap Analysis

Key evidence requirements are assessment of the most appropriate health related quality of life tool on which to measure health state utility, estimates of the relative effect of the interventions over the short and long (12 months +) term, and whether the 'guidance' in guided dCBT can be provided equally well by a mental health support worker as by a trained clinical psychologist or other specialist.

1 Decision problem

Table 1 details the final scope issued by NICE for this EVA, defined per element of assessment.

Table 1 Summary scope of the assessment

Element of assessment	Final scope issued by NICE	Clinical advice to the EAG comment
Population	Children and young people with mild to moderate symptoms of anxiety or low mood that are significantly interfering with their ability to function in their daily lives • Children aged 5 to 11 • Young people aged 12 to 18	Clinical advice to the EAG suggested the presence of considerable heterogeneity in the clinical characteristics, risk factors and care pathway of young people aged 12 to 18, and that this subgroup may be too broad.
Interventions (proposed technologies)	Guided self-help digital cognitive behavioural therapy technologies supported by healthcare professionals aimed at children and young people with mild to moderate symptoms of anxiety or low mood as a first line treatment: • Space from anxiety for teens, Space from low mood for teens, Space from anxiety and low mood for teens • Online support and intervention (OSI) • OSCA (Online Social anxiety Cognitive therapy for Adolescents) • Lumi Nova and standard care that may include education, advice, support and signposting	None
Comparator	Standard care that may include education, advice, support and signposting	SCM advice to the EAG suggested that face-to-face therapy should be included as a comparator as the current standard of care. SCM advice further suggested that the active comparator should be online-supported psychoeducation without CBT content.
Healthcare setting	Mental health support teams, including those based in schools and primary care	SCM advice to the EAG suggested that CAMHS/CYPMHS as MHST only cover one third of the UK, with the balance covered by CYPMHS.
Outcomes	Intermediate measures for consideration may include: • Intervention-related adverse events	None

Element of assessment	Final scope issued by NICE	Clinical advice to the EAG comment
	• Rates of and reasons for attrition • Treatment satisfaction and engagement	
	Clinical outcomes for consideration may include: • Measures of symptom severity (self-, parental- or practitioner reported) • Social, behavioural, and functional outcomes (self, parental or practitioner reported) • Suicidal thoughts and behaviour • Global functioning • Rates of remission	SCM advice to the EAG suggested that school and social functioning should be considered along with global functioning.
	Patient-reported outcomes for consideration may include: • Health-related quality of life, including well-being • Patient experience	None

	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:
	• Costs of the technologies including licensing fees
	• Cost of other resource use (e.g., associated with managing anxiety, adverse events or complications):
	  ○ GP, mental health support team or CYPMHS appointments
	  ○ Health care professional training, grade and time for providing regular support and guidance for the users of the dCBT technologies
		SCM advice to the EAG suggested that school-related costs should also be considered.

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.	None

Abbreviations: CAMHS, Child and Adolescent Mental Health Services; CBT, cognitive behavioural therapy; CE mark, conformity with European health, safety, and environmental protection standards; CYPMHS, children and young people's mental health services; DTAC, Digital Technology Assessment Criteria; EAG, External Assessment Group; GP, general practitioner; MHST, mental health support teams; N/A, not applicable; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, online support and intervention for child anxiety; SCM, Specialist Committee Member

2 Overview of the technology

2.1 *Purpose of the medical technology*

Guided digital CBT may provide an alternative and more accessible treatment option for anxiety and low mood in children and young people when compared to face-to-face CBT. This could be very important development in mental health and improve care by engaging people in treatment in a different way as well as providing greater patient choice. In addition, mental health services are in high demand and access varies widely across the country: the availability of effective mental health treatments is limited, with a shortage of qualified staff, long waiting times and access to treatment depending on the severity of symptoms.[1] Early research suggests that the pandemic and subsequent measures have had a significant impact on the mental health of children and young people and subsequently intensified these issues related to accessing effective mental health treatments.[2] It is estimated that only 1 in 3 children with a mental health condition get access to NHS care and treatment.[3] In 2019/20, the reported average waits across England ranged from 8 days to 82 days, and only 20% of children referred to services started treatment within 4 weeks[3] – the ambition set out in the Government's Green Paper on children's mental health.

Given the prevalence of the condition and importance of early treatment, children and young people's mental health services are NHS priorities for care and outcome improvements. Publications including the NHS Long Term Plan (2019)[4] and the Green Paper for Transforming children and young people's mental health[5] detail the investment and proposed expansion of services in particular in the community and school settings. Guided self-help digital CBT, describing the use of self-help materials with some professional guidance (for example, goal setting before a session)[6] in a digital format, is a treatment offered for children and young people to help with negative feelings, including mild to moderate symptoms of anxiety and/or low mood that is delivered via mobile phones, tablets, and computers. It is based on the principles of face-to-face CBT which is a talking therapy that can help a person learn new skills to manage problems by understanding how thoughts can affect how they feel and

behave and includes various components including psychoeducation and cognitive restructuring. Digital CBT can be accessed remotely and can be used as a standalone intervention with guidance from a health care professional. It can potentially improve access to mental health services by offering greater flexibility, more choice and self-management through remote online interventions.

2.2 *Product properties*

This scope focuses on guided self-help digital CBT technologies that meet the following criteria:

- Has appropriate regulatory approval or is actively working towards regulatory approval – for example, CE mark and DTAC.
- Available to children or young people with symptoms of anxiety and/or low mood. Interventions can support children and young people directly, or parents or carers to help them support their child.
- Based on the principles of CBT with a guided element built into the intervention including scheduled (weekly) follow up, for example a phone or video call, with mental health practitioners affiliated to the company or the NHS.
- Available for use in the NHS.

In total, four guided self-help digital CBT technologies designed to treat children and young people with symptoms of anxiety and/or low mood are included in the scope.

Space from anxiety for teens, Space from low mood for teens, Space from low mood & anxiety for teens (SilverCloud)

Internet-based (computer, tablet or smart phone) intervention for teens aged 15 to 18 years old with symptoms of anxiety, low mood, or both. However, according to CAMHS protocols and clinical judgement, it can be used in a younger age group. It has seven core modules structured around the principles of traditional CBT which include: understanding anxiety and/or low mood, noticing feelings, facing your fears, spotting thoughts, challenging thoughts, managing worry and reflections on learnings. The supported model has online

support from psychologists and online cognitive behavioural therapy co-ordinators to assess the needs of the person. After each module, they check in to help the person progress through the CBT content and send motivational messages. It is used in several services in the NHS.

Online support and intervention for child anxiety (OSI)

OSI is an internet based (computer, tablet and smart phone), parent-led and therapist supported psychological intervention for children aged 5 to 12 years old with symptoms of anxiety. It comprises three components, a parent's website, a clinician case management website and an optional game app for children (Monster's Journey: Facing Fears). It comprises seven core modules that include interactive worksheets, videos and quizzes. Parents or carers have weekly telephone appointments with the therapist to review the work they have done over the previous week, after which the next week's weekly module is released.

OSCA (Online Social anxiety Cognitive therapy for Adolescents)

OSCA is an internet programme of cognitive therapy for social anxiety in adolescents aged 14 to 18 years old. All users receive a core set of modules to work through at the beginning of the programme which is then individualised for each user. The therapist will carry out a 15-minute phone call with the user each week and releases modules that will be most helpful to that person, depending on their concerns. They will receive encouragement and support via secure messaging within the online programme and SMS texts. Parents are involved by receiving regular emails on their child's progress. This is explained to children aged 14 to 15 and consented from young people aged 16 to 18 years old.

Lumi Nova (BfB Labs)

Lumi Nova: Tales of Courage is a CE marked class 1a medical device digital therapeutic intervention in the form of a game available on Android and iOS for children and young people aged between 7 and 12 with symptoms of mild to moderate anxiety. It combines evidence-based therapeutic content (exposure therapy, a form of CBT) and psychoeducational content within an intergalactic

role-playing game. Access to Lumi Nova is provided through a secure web-based platform, VitaMind Hub (BfB Labs Ltd), which is a point of access for practitioners that allow them to track and monitor player progress with the game. Practitioners also check in with users and guardians provide support to their child (app user) when needed and can receive SMS notifications when their child uses the app.

3 Comparator

Guided self-help digital CBT technologies could be a first line and alternative treatment for children and young people demonstrating mild to moderate symptoms of anxiety and/or low mood. The comparator is standard care which may include education, advice, support and signposting. Clinical advice to the EAG suggested that active comparators such as face to face CBT are also relevant.

4 Clinical context

The target population for this assessment is children and young people with mild to moderate symptoms of anxiety and/or low mood.

Anxiety disorders are one of the most common types of mental health disorders in children and young people. In 2017, 3.9% of 5- to 10-year-old children were identified as having an anxiety disorder, 7.5% of 11- to 16-year-olds and 13.1% of 17- to 19-year-olds.[7] Anxiety in children and young people may negatively impact education, social functioning and family life. Anxiety disorders can have a lifelong course of relapse and remission and can persist into adulthood if left untreated. The worldwide prevalence of anxiety disorders in children and adolescents is estimated at 6.5%,[8] with the median age of onset of 11 years.[9]

Depression is also a common mental health problem and can present itself in different symptoms, including low mood. Other symptoms in children include being irritable, not being interested in things they used to enjoy, feeling tired, having trouble sleeping or sleeping more than usual, not being able to concentrate, being indecisive, not having much confidence, changes in eating

habits and weight, talking about feeling guilty or worthless.[10] The point prevalence of dysthymia in adolescents is estimated to be 4%[11] and is one of the most common mental health problems facing young people.[1] Depression in adolescence can have a negative effect on relationships, development trajectory, schooling, and educational attainment and increases the risk of suicide.[12-14]

4.1 *Care pathway*

Symptoms of anxiety and/or low mood may be identified by the child or young person themselves, their parents or carer, GPs and in community care, social workers or in school. Children and young people can be assessed and treated in a range of settings, including school mental health support teams, single point of access teams (SPA), voluntary sector teams and children and young people's mental health services (CYPMHS). Not all children and young people with mild to moderate symptoms of anxiety and/or low mood will meet the severity threshold to be seen by CYPMHS and are treated within mental health support teams (MHSTs). SCM advice to the EAG indicated that it is not clear whether MHSTs have the training to identify levels of severity of anxiety and/or low mood to direct different types of treatment. Across these settings the professionals will have varying levels of specialist mental health training and expertise to provide targeted outcome-focused help. These professionals might include nurses, therapists, psychologists, child and adolescent psychiatrists, support workers, social workers, health visitors, school nurses, education mental health practitioners.

Children and young people's mental health services (CYPMHS), sometimes known as Child and adolescent mental health services (CAMHS), are services that support children and young people with their mental health. Care is personalised and varied, and provided across a range of settings. The THRIVE framework can be used to determine a care package based on the needs of the child or young person.[15 16] The framework integrates a person centred, and needs led approach to delivering mental health services for children, young people and families which conceptualises need in 5 categories: thriving, getting advice and signposting, getting help, getting more help, and getting risk

support. Guided self-help digital CBT may be offered as a first line treatment for children and young people identified as having mild to moderate symptoms of anxiety and/or low mood, who are considered as 'getting help' or 'getting more help' based on the THRIVE framework, to improve access to treatment. Users may then continue to further support such as face to face CBT.

4.2 *Patient issues and preferences*

Digital CBT is delivered via mobile phones, tablets, or computers and can thus be accessed remotely. Digital CBT provides more treatment options, flexible access, greater privacy and anonymity, increased convenience and increases therapist capacity and support for patients requiring face-to-face CBT. It may be particularly appealing to children and young people who are typically regular users of digital technologies such as smartphones and tablets. In 2020, 61% of 5- to 15-year-olds had their own tablet and 55% their own smartphone. The latter increased to 91% in the 12- to 15-year-old age group.[17] The use of guided self-help digital technologies may create the supportive and motivating therapeutic relationship that reduces the rates of attrition that is a concern for unguided technologies. There may also be concerns around data security and quality control.

5 Special considerations, including issues related to equality

A number of potential equality issues have been identified. There are multiple equality considerations for this class of technologies which are addressed in more detail in NICE's guideline on depression in children and young people: identification and management.[18] Key aspects include:

- Children and young people from certain socio-economic backgrounds and those with disabilities are disproportionately affected by higher risk of mental health issues.
- Children and young people from high-risk disadvantaged socio-economic groups likely have differential access to devices and data plans when compared to those in different socio-economic circumstances.

- Patient-facing digital health technologies may be unsuitable for those with cognitive impairment, problems with manual dexterity or learning disabilities. Carer or advocate assistance may be required to navigate the programme and consideration of this should be made by the company as well as the referring practitioner when considering appropriate intervention for the child or young person. Further considerations can be found in NICE Guidance on mental health problems in people with learning disabilities.[19]
- Patient-facing digital health technologies should ensure their programme is accessible for screen readers (people with visual impairments) and those with hearing impairments.
- Children and young people with English as a second language may have difficulties navigating digital technologies provided in English.
- The way that children and young people with symptoms of anxiety and/or depression and their families view mental health problems may be affected by their ethnic, religion and cultural background.
- Children and adolescents may in general have increased autonomy in accessing therapy using digital formats. However, specific groups may particularly benefit from improved access to CBT online, for example:
    - Adolescents may have increased engagement with this format of intervention. However, younger children may require higher levels of parental support or engagement with the intervention.
    - Those living in rural areas might have problems with travelling to face-to-face appointments if public transport is sporadic and unreliable, and their parents are unable to drive them there.
    - Those living in more remote rural areas may not have access to mobile internet connections.
    - Children and young people from lower socioeconomic groups may lack the financial support required to ensure that they attend face to face sessions. These families may also be less likely to seek help in the first place and or be less able to navigate the healthcare system.
    - Children and young people with more chaotic home lives may lack the family support required to ensure that they attend face to face sessions. These families may also be less likely to seek help in the first place and or be less able to navigate the healthcare system.

- Children and young people from abusive homes may be prevented from seeking help and or attending face to face therapy sessions by controlling parents or carers.
- Looked after children and young people may lack support needed to engage with mental health services.

However, accessibility would not be improved for those who are unable to engage with a digital service due to a lack of equipment, unavailability of internet connection, lack of experience with computers or lack the privacy needed to complete the intervention. Age, disability, race and religion or belief are protected characteristics under the Equality Act (2010).

6 Potential implementation issues

A potential barrier to implementation is the need for children and young people to be assessed and a need to determine the appropriateness of guided self-help digital CBT interventions. Patients also need to be assessed to determine the correct level of intervention required based on severity, impairment and co-morbidity.

7 Other issues for consideration

Characteristics of digital technologies

The digital CBT technologies included in the scope are heterogeneous in terms of delivery mode (computer, app) and access (referred or self-referrals), content or active components, intended population and condition (anxiety vs low mood vs both), practitioner or parental support, data collected and regulatory status.

8 Clinical evidence selection

8.1 *Evidence search strategy and study selection*

Search strategy

Search strategies used were those devised during the initial scoping searches by NICE Information Services, with some amendments. The search strategies used relevant search terms, comprising a combination of indexed keywords (e.g., Medical Subject Headings, MeSH) and free-text terms appearing in the

titles and/or abstracts of database records and were adapted according to the configuration of each database. No date or publication status (published, unpublished, in-press, and in-progress) limits were applied. The searches were limited to English language studies.

Following deduplication, a total of 1,215 records of potentially relevant evidence on clinical effectiveness, 451 records of potentially relevant economic evaluations and 304 trial registry entries were retrieved. Further details relating to databases searched and exact search terms for clinical and cost-effectiveness evidence are presented in Appendix A and B (Section 17), respectively.

Study selection

A single reviewer screened all 1,970 titles and abstracts of potentially relevant records, simultaneously screening for clinical and economic evidence using Bond University's Systematic Review Accelerator.[20] A total of 155 potentially relevant full-text articles were identified during title and abstract screening. Of these, seven full-text publications and four trial registry entries detailing eligible studies were identified and included in the clinical evidence base. Furthermore, a total of 28 articles reporting on cost-effectiveness or economic evaluations were identified and included.

Eligibility criteria were based on the scope, but were slightly adapted in consultation with the NICE technical team during the process. This related exclusively to criteria for the population of interest. For clinical evidence all studies reporting on adults were excluded, though the EAG intended to include studies if they reported on an eligible subsample of participants (e.g., a mix of adolescents (eligible) and young adults (ineligible) receiving the intervention). Studies in children with underlying conditions, such as cancer and other chronic diseases, were excluded; however, following consultation with the NICE technical team and clinical experts the EAG considered studies in children with neurodevelopmental conditions (for example, autism spectrum disorder; ASD) to be eligible. Children with comorbid depression and insomnia were also initially excluded; this was later amended to consider studies in children with a

primary condition of interest and comorbid insomnia. Finally, the EAG initially excluded all studies in children experiencing anxiety and/or low mood in the face of specific stressors, such as natural disasters or trauma. Following consultation with the NICE technical team, the EAG amended this to include children who may have developed symptoms in the context of COVID-19.

The EAG screened clinical effectiveness evidence strictly according to the scoped technologies of interest, but included economic evidence of any guided self-help digital CBT interventions. All studies were screened for comparators as per scope, but no restrictions related to outcomes were applied during screening.

The EAG considered this approach to be appropriate and in line with the NICE scope, with deviations resulting in over-inclusivity rather than the potential exclusion of relevant evidence.

In addition, the EAG contacted company representatives for all the included technologies to enquire about any additional research that may not have been included in the search, or any not in the public domain, to ensure the maximum evidence representation in the review.

The study selection flowchart is available as Figure 3 in Appendix C (Section 17.3).

8.2 *Included and excluded studies*

The EAG considered studies by Hill et al. (2022a),[21] Hill et al. (2022b),[22] Leigh & Clark (2022),[23] Lockwood et al. (2022)[24] and Williamson et al. (2022)[25] as completed included studies with available data; protocols by Leigh et al. (2019), Reardon et al. (2022a),[26] Reardon et al. (2019),[27] Reardon et al. (2022a),[26] Reardon et al. (2022b),[28] Reardon et al. (2022c),[29] Taylor et al. (2022)[30] and Williamson et al. (2021)[31], a statistical analysis plan by Jones et al. (2022)[32] as well as five trial registry entries (all linked to published studies) are considered eligible ongoing or prospective works with no available data. One eligible unpublished study by Green et al. (2022), provisionally accepted for publication, was identified by a company representative and included in the review. It was

not clear to the EAG whether the qualitative information included in Williamson et al. (2022)[25] originated from the same sample as that reported in Green et al. (2022), since both cite Williamson et al. (2021)[31] as protocol. As such, the EAG would like to flag the potential for duplication in reporting of results, as well as overlap in terms of scoping, stemming from this uncertainty. Two additional ongoing studies on Lumi Nova, '[redacted]' and '[redacted]', were identified by a company representative and included in the review as ongoing studies.

Table 2 details comprehensive information on the six eligible completed studies, as well as a summary of stated intentions of eligible ongoing or prospective works.

A full list of excluded full-text records, with reasons for exclusions, is provided in Table 34 and Table 35, Appendix D (Section 17.4).

Table 2. Studies selected by the EAG as the clinical evidence base

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Hill, Chessell, Percy, et al. (2022)[22] UK	Single-arm case series Intervention: OSI (therapist-supported, parent-led) Comparator: None Intervention: **GREEN** Comparator: **RED**	Inclusion criteria: Children aged 7–12 years assessed as having a primary anxiety problem associated with significant functional impairment; parents having access to the internet, and the ability to read in English language in order to access the OSI content. Exclusion criteria: The research clinic does not provide treatment to children with an autism diagnosis, significant learning disability, or where there are substantial risk/safeguarding concerns. 23 children aged between 7 and 12 years were offered the intervention (20 children met per-protocol criteria for participation) 17 girls (73.9%) and 6 boys (26.1%) with mean age 9.65 (SD 1.19) years Ethnicity of participants was predominantly white British (n=15; 65.2%), while the remainder did not specify ethnicity (n=8; 34.8%). Primary anxiety problem was specific phobia (n=6; 26.1%), social phobia (n=3; 13%), generalised anxiety (n=7; 30.4%), separation anxiety (n=7; 30.4%) Clinical risk level was low for all participants 18 families (all of children meeting per-protocol criteria) completed all treatment modules	• Attrition (rates and reasons) • Treatment satisfaction (SRS) • Treatment engagement (treatment engagement and understanding) • Measures of symptom severity (RCADS-P) • Social behavioural and functional outcomes (GBO and CAIS-P) • Global functioning (CORS) • Rates of remission • Patient experience Outcomes reported by subgroups: whole sample and those with RCADS-P score above the clinical cut-off at baseline Outcomes: **GREEN**	The included paediatric population does not fall exactly into either of the pre-specified subgroups, but is more representative of the children aged 5 to 11 years grouping. Exclusion of children with diagnosed autism or significant learning disability limits generalisability and may impact equity. Scoped outcomes not included: • Intervention-related adverse events • Suicidal thoughts and behaviour • Health-related quality of life • Cost of technology • Cost of other resource use

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		NHS research clinic Participants: **GREEN** Setting: **GREEN**		
Hill, Reardon, Taylor, et al. (2022)[21] UK	Single arm formative research Intervention: OSI (beta version) Comparator: None Intervention: **RED** Comparator: **RED**	Inclusion criteria: Parents, children and clinicians familiar with the face-to-face version of the treatment, either having received this treatment through local child and adolescent mental health service or as part of a research trial[33] including children with current anxiety disorder whose primary caregiver did not meet criteria for current anxiety disorder. Exclusion criteria: None stated. 7 parents and 4 children aged 9-12 years were recruited (of which 5 parents and 4 children had recently received the brief face-to-face, parent-led treatment); 11 clinicians with experience of delivering face-to-face treatment were also recruited Usability testing was conducted with 2 girls (50%) and 2 boys (50%) with mean age 9.50 (SD 0.58) years; 6 female (86%) and 1 male (14%) parent(s) with mean age 45.86 (SD 9.84) years; 4 female (50%) and 4 male (50%) clinicians with mean age 41.88 (SD 9.42). Ethnicity of children participating in the usability testing phase was predominantly white British (n=3; 75%), while the remaining	Patient experience of OSI beta version Outcomes reported by subgroups: N/A Outcomes: **RED**	Research was not conducted on the final version of OSI, therefore the EAG does not consider the available evidence on patient experience with the beta version to have utility for the current EVA. The EAG noted, however, that an inclusive and formative process is the preferred approach to development of technologies of this nature. The included paediatric population does not fall exactly into either of the pre-specified subgroups, but is more representative of the children aged 5 to 11 years grouping. None of the scoped outcomes, with the exception of patient

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		child was report as of mixed ethnicity (n=1; 25%). Two NHS clinics Participants: **GREEN** Setting: **GREEN**		experience, are addressed.
Leigh & Clark (2022)[23] Linked references: Leigh & Clark (2019);[27] ISRCTN15079139 (2019)[34] UK	Two-arm RCT Intervention: OSCA (therapist-guided) Comparator: Waitlist control Intervention: **GREEN** Comparator: **AMBER**	Inclusion criteria: Young people aged 14–18 years with a primary diagnosis of DSM-5 SAD. Exclusion criteria: Diagnosis of autism, learning disability, psychosis, current alcohol or substance dependence, previous receipt of CT/CBT for SAD, suicidal intent or recurrent self-harm, or active safeguarding concerns. 22 participants were randomised to OSCA, 21 participants were randomised to waitlist control Young people in the intervention and control groups were 91% (n=20) and 90% (n=19) female, respectively. Mean ages in the intervention and control groups were 16.04 (SD 1.03) and 16.42 (SD 1.11), respectively. The intervention group included participants with historical peer victimisation (n=5; 23%), ongoing peer victimisation (n=4; 18%), previous psychological therapy (n=5; 23%), comorbidity (n=11; 50%); current suicidal ideation (n=10; 46%) and deliberate self-harm (n=8; 36%). Mean ADIS CSR for SAD diagnosis was 5.23 (SD 0.97).	• Intervention-related adverse events • Attrition (rate only) • Treatment satisfaction (treatment credibility) • Treatment engagement (patient activity) • Measures of symptom severity (LSAS-CA-SR, SPWSS, SMFQ, RCADS, RCADS-P) • Social, behavioural and functional outcomes (SCQ domains, SBQ, SAQ, concentration, participation, satisfaction, CALIS, CALIS-P) • Rates of remission Outcomes reported by subgroups: No	The included paediatric population falls into the pre-specified subgroup of young people aged 12 to 18 years. Exclusion of children with diagnosed autism or significant learning disability limits generalisability and may impact equity. Scoped outcomes not included: • Suicidal thoughts and behaviour • Global functioning • Health-related quality of life • Patient experience • Cost of technology

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		The comparator group included participants with historical peer victimisation (n=6; 29%), ongoing peer victimisation (n=6; 29%), previous psychological therapy (n=9; 43%), comorbidity (n=13; 62%); current suicidal ideation (n=5; 24%) and deliberate self-harm (n=4; 19%). Mean ADIS CSR for SAD diagnosis was 5.62 (SD 1.28). 20 participants completed OSCA, 21 participants completed waitlist control Four secondary schools in the Southeast of England Participants: **GREEN** Setting: **GREEN**	Outcomes: **GREEN**	• Cost of other resource use
Lockwood, Williams, Martin, et al. (2022)[24] UK	Single-arm evaluation study Intervention: Lumi Nova (guardian-led) Comparator: None Intervention: **GREEN** Comparator: **RED**	Inclusion criteria: Children, identified by school-based staff in 12 participating schools as experiencing difficulties with anxiety and not concurrently receiving psychological treatment, and their guardians, who completed demographic and anxiety measures. Exclusion criteria: None stated. 120 children aged between 7 and 12 years were assessed for the intervention, 95 were offered the intervention The sample of participants with baseline and follow-up (T1-T2) measures comprised 18 girls (60%) and 12 boys (40%) with mean age 9.81 (SD 1.70) years; the sample with gameplay	• Intervention-related adverse events • Attrition (rate only) • Treatment satisfaction (participant quotes) • Treatment engagement (gameplay data) • Measures of symptom severity (SCAS-P and RCADS-P) • Social, behavioural and functional outcomes (CAIS-P)	The included paediatric population does not fall exactly into either of the pre-specified subgroups, but is more representative of the children aged 5 to 11 years grouping. The EAG noted one child was older than the stated target range. No specific exclusions stated, but the school setting likely excludes children with severe

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		data comprised 35 girls (52%) and 31 boys (46%) with mean age 9.61 (SD 1.53). Authors report "2 (1.7%) children were marginally outside the target age range of 7-12 years (aged 6.97 and 13.0 years) at the point of entering the study and were retained in the analysis." Ethnicity of the sample of participants with T1-T2 measures was predominantly white British (n=24; 80%); the remainder were Asian, of mixed ethnicity, of another ethnic group (n=1 each; 3% each), or black (n=3; 10%). The sample of participants with gameplay data were white British (n=42; 63%), black (n=8; 12%), of mixed ethnicity (n=4; 6%), Asian (n=2; 3%), or of another ethnic group (n=1; 1%). Most participants in the T1-T2 sample had not had other treatment for anxiety (n=25; 83%), CAMHS contact for anxiety (n=23; 77%), or GP/nurse contact for anxiety (n=25; 83%). The sample had mean scores of 8.33 (SD 4.56) for SCAS-P, 30.30 (SD 16.92) for RCADS-P, and 20.57 (SD 15.40) for CAIS-P. Most participants in the gameplay sample also had not had other treatment for anxiety (n=53; 79%), CAMHS contact for anxiety (n=46; 69%), or GP/nurse contact for anxiety (n=48; 72%). The sample had mean scores of 7.83 (SD 3.71) for SCAS-P, 28.97 (SD 14.45) for RCADS-P, and 18.39 (SD 13.25) for CAIS-P. 74 participants activated the game keys, 67 generated gameplay data	Outcomes reported by subgroups: sample with T1-T2 anxiety measures and sample with gameplay data Outcomes: **GREEN**	autism or significant learning disability. This may limit generalisability and may impact equity. Scoped outcomes not included: • Suicidal thoughts and behaviour • Global functioning • Rates of remission • Health-related quality of life • Patient experience • Cost of technology • Cost of other resource use

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		Primary and secondary schools in Southeast England Participants: **GREEN** Setting: **GREEN**		
Williamson et al. (2022)[25] Linked reference: Williamson, Larkin, Reardon, et al. (2021)[31] UK	Single-arm feasibility study Intervention: OSI (parent-led) Comparator: None Intervention: **GREEN** Comparator: **RED**	Inclusion criteria: Children will be eligible to participate if they are in Y4 (i.e. aged 5-11 years) in a mainstream primary school in England, with parent/carer consent for their participation. A child will be considered to have screened 'positive' for likely anxiety difficulties if they score above the cut-off on the SCAS-8 on the basis of any reporter (score of 7.5 for parents, 6.5 for children and 4.5 for teachers) and/or indicate that anxiety interferes at least 1 'only a little' on any of the interference items. Exclusion criteria: None stated. The study aims to recruit 165 children across all stages of the project Mainstream primary schools in England Participants: **GREEN** Setting: **GREEN**	• Patient experience (not clear) Outcomes reported by planned subgroups: None stated • Outcomes: **RED**	The included paediatric population falls into the pre-specified subgroup of children aged 5 to 11 years. No specific exclusions stated, but the school setting likely excludes children with severe autism or significant learning disability. This may limit generalisability and may impact equity. Scoped outcomes not included: • Intervention-related adverse events (not clear) • Attrition (not clear) • Treatment satisfaction (not clear)

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
				• Treatment engagement (not clear) • Measures of symptom severity (not clear) • Social, behavioural and functional outcomes (not clear) • Suicidal thoughts and behavior (not clear) • Global function (not clear) • Rates of remission (not clear) • Health-related quality of life (not clear) • Cost of technology (not clear) Cost of other resource use (not clear)
Green et al. (2022) [redacted]	[redacted] Intervention: OSI (parent-led) [redacted]	[redacted]	[redacted]	[redacted]

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
[redacted]	Intervention: **GREEN** Comparator: **RED**	[redacted] Participants: **GREEN** Setting: **GREEN**	[redacted] Outcomes: **GREEN**	[redacted]
Ongoing or prospective work				

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Protocol: Reardon, Ball, Breen, et al. (2022a)[28] Linked reference: ISRCTN30032471 (2021)[35] Trial end date: 30/11/2021 UK	Single-arm feasibility trial Intervention: OSI (parent-led with telephone support from a CWP) Comparator: None Intervention: **GREEN** Comparator: **RED**	Inclusion criteria: Children who 'screen positive' (score ≥3 on parent-report 2-item child anxiety questionnaire) on a 2-item parent-report child anxiety screen at baseline will be the target population. Further criteria: • Child: in year 4 (aged 8-9 years) in a participating class, their parent/carer does not opt out, and child provides assent; sufficient English to give assent and complete questionnaires, with assistance if necessary. • Parents: child in year 4 in a participating class, and they provide consent. Where a parent/carer has more than one eligible child, they will be invited to consent/participate for each child; sufficient English to give consent and to complete questionnaires, with assistance if necessary. • Teachers: class teacher of participating child or nominated member of support staff who works regularly with the child. Exclusion criteria: None stated. The study aims to recruit 360 children from six primary/junior schools (30 children per class, two classes per school) Mainstream primary or junior schools in England	• Attrition • Measures of symptom severity (SCAS, RCADS-C and -P) • Social, behavioural and functional outcomes (SDQ-C and -P and school attendance) • Global functioning • Health-related quality of life (CHU 9D, EQ-5D-Y and EQ-5D-5L) • Patient experience (acceptability) • Cost of other resources (individual resource use, therapist-reported time spent on intervention delivery) Outcomes reported by planned subgroups: None stated Outcomes: **GREEN**	The intended paediatric population would fall into the pre-specified subgroup of children aged 5 to 11 years. No specific exclusions stated, but the school setting likely excludes children with severe autism or significant learning disability. This may limit generalisability and may impact equity. Scoped outcomes not planned include: • Intervention-related adverse events (not clear) • Treatment satisfaction • Treatment engagement • Suicidal thoughts and behaviour • Rates of remission • Cost of technology

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		Participants: **GREEN** Setting: **GREEN**		
Protocol: Reardon, Dodd, Hill, et al. (2022b)[26] Linked references: Jones et al. (2022);[32] ISRCTN82398107 (2021)[36] Trial end date: 31/08/2023 UK	Two-arm RCT Intervention: OSI (parent-led) Comparator: Usual school practice (any usual support available at school) Intervention: **GREEN** Comparator: **AMBER**	Inclusion criteria: Child in Reception, Year 1 or Year 2 in a participating school (aged 4-7 years), screening positive on child anxiety symptoms, and/or behavioural inhibition, and/or parent/carer anxiety symptoms. One parent/carer will complete screening questionnaires for each child. Exclusion criteria: Parent/carer does not have sufficient use of English to provide consent, complete measures and/or take part in the intervention, or does not have frequent access to the internet, either at home or elsewhere. The study aims to recruit 1080 children (540 per arm) from at least 60 infant or primary schools. This is based on a power calculation for a sample large enough to detect a reduction in the presence of anxiety disorders at 12 months (primary outcome) from 50% (control arm) to 35% (intervention arm) with 90% power at the 5% (two-sided) level. An ITT analysis will be conducted, accounting for missing data using multiple imputation. Mainstream infant or primary schools in England	• Measures of symptom severity (ADIS-P and preschool anxiety scale) • Social, behavioural and functional outcomes (CALIS-P preschool version, parent-reported SDQ Externalising Scale, parent-reported behavioural avoidance, coping efficacy and intolerance of uncertainty) • Health-related quality of life (CHU 9D, EQ-5D-Y and EQ-5D-5L) • Patient experience • Cost of other resource use (individual resource use and therapist-reported time spent on intervention delivery) Outcomes: **GREEN**	The intended paediatric population would fall roughly into the pre-specified subgroup of children aged 5 to 11 years, though the EAG noted that inclusion criteria would result in the inclusion of children younger than those specified in the scope. No specific exclusions stated, and the infant or primary school setting is likely not yet excluding children with milder autism or learning disability. Scoped outcomes not planned include: • Intervention-related adverse events • Attrition • Treatment satisfaction • Treatment engagement

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		Participants: **GREEN** Setting: **GREEN**		• Suicidal thoughts and behavior • Global functioning • Rates of remission • Cost of technology
Protocol: Reardon, Ukoumunne, Violato, et al (2022c)[29] Linked reference: ISRCTN76119074 (2021)[37] Trial end date: 30/11/2024 UK	Two-arm RCT Intervention: OSI (parent-led) Comparator: Usual school practice (any usual support available at school) Intervention: **GREEN** Comparator: **AMBER**	Inclusion criteria: • Child: screening positive (score ≥ 3 out of 6) on the brief parent-report child anxiety screening questionnaire in Year 4 (aged 8 to 9) in a participating class, on the class register during recruitment and baseline data collection up to school randomisation, not opted out by parent or caregiver. • Parent/caregiver: caring for a target child in Year 4 (aged 8 to 9) in a participating class, providing written consent. • Teachers: current class teacher or member of school staff who works regularly with target children in a participating class. Exclusion criteria: • Children who do not have sufficient English language or comprehension skills to complete measures, even with support, will not complete child-report questionnaires. • Parents/caregivers who do not have sufficient English language or	• Treatment engagement (logs to record time spent on activities) • Measures of symptom severity (iCATS-2, SCAS-C/P/T, RCADS-C/P, RCADS-C/P-Depression scale) • Social, behavioural and functional outcomes (interference related to child anxiety additional items alongside SCAS, SDQ-C/P, school attendance, punctuality and academic attainment) • Patient experience (qualitative interviews and acceptability questionnaires) • Health-related quality of life (CHU-9-C/PQ-5D-Y-C/P) • Cost of other resource use (CSRI and therapist-reported time spent on delivery)	The intended paediatric population would fall into the pre-specified subgroup of children aged 5 to 11 years. No specific exclusions stated, but the school setting likely excludes children with severe autism or significant learning disability. This may limit generalisability and may impact equity. Scoped outcomes not planned include: • Intervention-related adverse events (not clear) • Attrition • Treatment satisfaction • Suicidal thoughts and behaviour • Global functioning

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
		comprehension skills to provide consent, complete measures, and/or take part in the intervention, even with support and/or translated study information, will not take part. The study aims to recruit 398 children (199 per arm) from at least 80 primary or junior schools. This is based on a power calculation to detect an increase in the remission of anxiety problems from 50% ('usual school practice' arm) to 70% ('screening and intervention' arm). Mainstream primary or junior schools in England Participants: **GREEN** Setting: **GREEN**	Outcomes reported by planned subgroups: None stated Outcomes: **GREEN**	• Rates of remission • Cost of technology
Protocol: Taylor et al (2022)[30] Linked reference: ISRCTN12890382 (2020)[38] Trial end date: 31/03/2023	Two-arm RCT Intervention: OSI (parent-led, therapist-supported) Comparator: TAU for children with anxiety in clinical CAMHS in the	Inclusion criteria: • Child: aged 5-12 years at intake, primary problem is anxiety, willing and able to assent. • Parent/caregiver: sufficient English language to complete measures/access interventions, family access to the internet and willing and able to provide consent. Exclusion criteria:	• Measures of symptom severity (RCADS-C, RCADS-P, SCAS-P, parent-reported COVID-19-specific worries, SDQ-P) • Social, behavioural and functional outcomes (CAIS-P and CAIS-C) • Global functioning (parent-reported overall functioning)	The intended paediatric population does not fall exactly into either of the pre-specified subgroups, but would be more representative of the children aged 5 to 11 years grouping. Exclusion of children with autism or learning

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
UK	COVID-19 context (C-TAU) Intervention: **GREEN** Comparator: **GREEN**	• Child: co-morbid conditions that are likely to interfere with treatment delivery (established ASD condition/learning disability, suicidal intent/recurrent or potentially life-limiting self-harm), or identified by social services due to child protection concerns. • Parent/caregiver: significant intellectual impairment or severe mental health problem that is likely to interfere with treatment delivery, or unable to access or understand the written English language materials necessary for the interventions. Oxford Health NHS Foundation Trust Participants: **GREEN** Setting: **GREEN**	• Health-related quality of life (EQ-5D-5L parent self-report and CHU-9D proxy version) • Cost of other resources (parent-reported use of services and therapist-reported time spent on treatment delivery) Outcomes reported by planned subgroups: None stated Outcomes: **GREEN**	disability. This may limit generalisability and may impact equity. The COVID-19 context, while currently very valid, may not have good generalisability in future. Scoped outcomes not planned include: • Intervention-related adverse events • Attrition • Treatment satisfaction • Treatment engagement • Suicidal thoughts and behavior • Rates of remission • Cost of technology
Ongoing manufacturer data collection: [redacted]	[redacted] Intervention: Lumi Nova (guardian-led) [redacted]	[redacted]	[redacted]	[redacted]

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
[redacted]	Intervention: **GREEN** Comparator: **RED**	[redacted] Participants: **GREEN** Setting: **GREEN**	[redacted] • Outcomes: **GREEN**	[redacted]
Ongoing manufacturer data collection: [redacted]	[redacted] Intervention: Lumi Nova (guardian-led) [redacted] Intervention: **GREEN** Comparator: **RED**	[redacted]	[redacted] • Outcomes: **RED**	[redacted]

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
[redacted]		[redacted] Participants: **GREEN** Setting: **GREEN**		[redacted]

Abbreviations: ADIS(-P) CSR, Anxiety Disorders Interview Schedule for children and adolescents (-parent report) Clinical Severity Rating; CAIS-C/P, Child Anxiety Impact Scale (– child/parent report); CALIS(-P), Child Anxiety Life Interference Scale (– parent report); CAMHS, Children and Adolescent Mental Health Service; CBT, cognitive behavioural therapy; CHU-9D(-C/P), Child Health Utilty instrument nine-dimension (-child/parent version); CORS, Child Outcome Rating Scale; CSRI, Client Services Receipt Inventory; CT, cognitive therapy; CWP, Child Wellbeing Practitioner; DSM-5, Diagnostic and Statistical Manual of Mental Disorders Fifth Edition; EAG, External Assessment Group; EQ-5D-5L, EuroQoL five-dimension five-level; EQ-5D-Y(-C/P), EuroQoL five-dimension for youth (-child/parent version); GBO, goal-based outcomes; iCATS-2, identifying Child Anxiety Through Schools-2; LSAS-CA-SR, Liebowitz Social Anxiety Scale for Children and Adolescents – Self-Report version; N/A, not applicable; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, online support and intervention for child anxiety; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– child/parent report); RCT, randomised controlled trial; SAD, social anxiety disorder; SAQ, Social Attitudes Questionnaire; SBQ, Social Behaviour Questionnaire; SCAS(-P), Spence Child Anxiety Scale(-P) (– parent report); SCQ, Social Cognitions Questionnaire; SD, standard deviation; SDQ(-C/P), Strengths and Difficulties Questionnaire (– child/parent report); SMFQ, Short Mood and Feelings Questionnaire; SPWSS, Social Phobia Weekly Summary Scale; SRS, Session Rating Scale; T1, time one; T2, time two; TAU, treatment as usual; Y4, year four

9 Clinical evidence review

9.1 *Overview of methodologies of all included studies*

All relevant studies described in Table 2 had some methodological limitations or misalignment with the scope of the NICE decision problem.

Study design, intervention and comparator

The majority of completed studies (Hill et al. (2022a),[21] Hill et al. (2022b),[22] Lockwood et al. (2022),[24] Williamson et al. (2022)[25] and Green et al. (2022)) and one protocol and its linked trial registry entry (Reardon et al. (2022a)[29]; ISRCTN30032471 (2021)[35]) were single-arm designs with no direct comparator. Only four studies, three ongoing studies investigating OSI (Taylor et al. (2022);[30] ISRCTN12890382 (2020);[38] Reardon et al. (2022b)[26]; ISRCTN82398107 (2021);[36] and Reardon et al. (2022c)[29]; ISRCTN76119074 (2021)[37]) and one completed study investigating OSCA (Leigh & Clark (2022)[23]; also described in the protocol by Leigh & Clark (2019)[27] and ISRCTN15079139 (2019)[34]), were two-arm RCT designs. Furthermore, only one of these (Taylor et al. (2022);[30] ISRCTN12890382 (2020)[38]) had an active comparator. The EAG considered this lack of comparative evidence to cause methodological limitations due to lack of information on baseline risk as well as misalignment with the NICE scope, though it noted that prospective and ongoing work had greater representation of comparative evidence. All included studies included the appropriate intervention, though the EAG noted that Hill et al. (2022a)[21] reported formative work on a beta-version of OSI that was still undergoing iterative development. Any experiential evidence from this work was considered by the EAG to have limited alignment with the NICE scope.

Evidence gap: No published comparative evidence for Lumi Nova was found. In addition, no active comparators were found among completed research for OSI and OSCA; only one ongoing study reported an active comparator for OSI, with two others comparing OSI with usual available school support. No published evidence for the SilverCloud interventions (Space from anxiety for teens, Space from low mood for teens, or Space from low mood & anxiety for teens) was found.

Participants and setting

All included studies described participants and settings that fit within the NICE scope, though the EAG noted that populations in Hill et al. (2022a),[21] Hill et al. (2022b)[22] and Lockwood et al. (2022),[24] as well as Taylor et al. (2022)[30] (ISRCTN12890382 (2020)[38]) and two ongoing studies investigating Lumi Nova, had slight overlap between age subgroups specified by NICE. Furthermore, Reardon et al. (2022b)[26] (ISRCTN82398107 (2021)[36]) included some reception year children younger than the NICE scope. The EAG considered these deviations minor, and considered that the majority of participants in these studies would fall into the subgroup of children aged 5 to 11 years. Only one study, investigating OSCA (Leigh & Clark 2022),[23] included young people fitting the NICE-scoped subgroup of young people aged 12 to 18 years. Sample sizes across interventions were small (ranging from 23 to 360 participants) and presented a risk of spurious chance findings and underpowered analyses. The EAG could not fully assess the risk of the latter, since only three studies reported on power calculations (Reardon et al. (2022b),[26] Reardon et al. (2022c)[29] and one ongoing study investigating Lumi Nova ('[redacted]')). The EAG noted that none of the studies described participants with low mood; it considered this to be a serious evidence gap. However, the EAG further noted that all interventions, with the exception of the SilverCloud interventions, were intended for anxiety indications.

The EAG considered generalisability to the UK setting to be well-aligned, given all studies were conducted in UK settings and the ethnic mix of participants is broadly reflective of that of the country. Population generalisability of all studies, with the exception of Reardon et al. (2022b)[26] (ISRCTN82398107 (2021)[36]) and one ongoing study investigating Lumi Nova ([redacted]), was considered to be limited by the explicit or implicit exclusion of children with ASD or learning disability, a group of patients that represents a considerable proportion of the target population. Furthermore, clinical advice to the EAG suggested that children with neurodevelopmental

conditions, in particular, might prefer online modes of delivery over face-to-face therapy interactions.

Evidence gap: No published evidence for CYP with low mood was found. No published evidence for children aged 5 to 11 years was found for OSCA or the SilverCloud interventions. No published evidence for young people aged 12 to 18 years was found for OSI, Lumi Nova or the SilverCloud interventions.

Methodological gap: Small sample sizes in included studies present a risk of spurious chance findings and underpowered analyses.

Generalisability gap: No evidence for children and young people with ASD or learning disability.

Outcomes

None of the included studies reported on all outcomes included in the NICE scope, but all reported some outcomes of interest. The EAG noted that patient experience outcomes reported in the formative work of Hill et al. (2022a)[21] were not well-aligned with the NICE scope, as these were not derived from the finalised intervention. The EAG considered outcomes to be heterogeneously measured, particularly in terms of symptom severity (RCADS-C and -P, LSAS-CA-SR, SPWSS, SCAS, SDQ-P, SMFQ, COVID-19-specific worries, and ADIS-P) as well as social, behavioural and functional outcomes (GBO, CAIS-C and -P, CALIS-P, SAQ, SBQ, SCQ, concentration, participation, satisfaction, SDQ-C and –P, and school attendance). However, most studies reported (or intend to report) symptom severity as RCADS (Hill et al. (2022b),[22] Leigh & Clark (2022),[23] Lockwood et al. (2022),[24] Reardon et al. (2022a),[26] Reardon et al. (2022c),[29] Taylor et al. (2022),[30] Green et al. (2022) and one ongoing study investigating Lumi Nova (‘[redacted]’) and social, behavioural and functional outcomes as CAIS (Hill et al. (2022b),[22] Lockwood et al. (2022),[24] Reardon et al. (2022),[26] and Taylor et al. (2022)[30]). This suggests using these measures in any future studies would be most useful for comparability and homogeneity in the evidence base.

SCM advice to the EAG indicated that while RCADS and CAIS are appropriate measures for symptom severity and impairment, respectively, self-report of these measures would be preferable for adolescents; particularly for internalising symptoms. The EAG noted that none of the available evidence reports on the subgroup of young people aged 12 to 18 years, which may account for the lack of self-report measures of severity. SCM advice to the EAG also noted that CAIS is a broad measure of impairment, and suggested that the Children's Global Assessment Scale (CGAS) and Health of the Nation Outcome Scales for Children and Adolescent mental health (HoNOSCA) might also be appropriate.

Evidence gap: No published evidence for the outcomes of suicidal thoughts or behaviour, or cost of technology was found.

Heterogeneity issue: Clinical measures are reported heterogeneously, though some measures are frequently reported across studies. These measures were identified by SCM advice to the EAG as broadly appropriate.

9.2 *Critical appraisal of studies*

All studies with eligible and available outcome data (Green et al. (2022), Hill et al. (2022b),[22] Leigh & Clark (2022),[23] Lockwood et al. (2022)[24] and Williamson et al. (2022)[25]) had aspects that the EAG considered to be threats to internal validity. Full assessment of the risk of bias of these studies is presented in Table 36 of Appendix E (Section 17.5).

Random sequence generation and allocation concealment was logically not possible in the single-arm studies (Green et al. (2022), Hill et al. (2022b),[22] Lockwood et al. (2022)[24] and Williamson et al. (2022)[25]), but was judged to be unclear for Leigh & Clark (2022)[23] due to a lack of explicit reporting. The EAG noted that blinding of participants is not possible due to the nature of the intervention. As a consequence, all studies had a high risk of performance bias. Four studies were also at high risk of detection bias (Green et al. (2022), Hill et al. (2022b),[22] Lockwood et al. (2022)[24] and Williamson et al. (2022)[25]) as

outcomes were assessed by participants and/or their parents, while a third (Leigh & Clark (2022)[23]) was considered unclear due to some outcomes being assessed by participants.

Green et al. (2022), Hill et al. (2022b)[22] and Lockwood et al. (2022)[24] were also considered to be at high risk of attrition bias considering high rates of attrition with a lack of appropriate accounting for missing data. Selective outcome reporting was not identified in any of the studies. Green et al. (2022), Hill et al. (2022b)[22] and Lockwood et al. (2022)[24] were judged at high risk of other bias due to a lack of reporting regarding unbiased recruitment. These studies were not judged to be at high risk of intervention misclassification, or deviations from intended intervention.

Methodological gap: More high-quality randomised controlled trials are required. These trials need clear reporting of efforts to minimise selection bias; blinded participants (if possible) and outcome assessors; as well as proper statistical management of missing data, such as multiple imputation.

9.3 *Results from the evidence base*

The EAG summarises the results from the evidence base in this section, arranged by outcomes as per the NICE scope.

Attrition

OSI. A total of three (3/23; 13%) families did not meet the 'per protocol' criteria for participation in OSI (Hill et al. (2022b)[22]). These families dropped out; one each after module 1, 2, and 3; citing technical difficulties, anxiety resolved, and family disengaged from service (n=1 each). Other families meeting the 'per protocol' criteria (n=20) discontinued treatment after module 4 (n=1, difficulty in managing treatment alongside home schooling and work during lockdown), after module 5 (n=1, difficulty managing treatment alongside domestic issues and lockdown). Two families meeting the 'per protocol' criteria are reported as not attending the 4-week follow-up session for unknown reasons. Six families attended the 4-week follow-up session but did not complete the measures on OSI. It is not clear if there was overlap, i.e. whether families who did not attend follow-up may have been the same families who did not complete measures on

OSI, therefore true numbers of attrition are difficult to assess. Authors also report that "Only two participants completed the Session Rating Scales (SRS) after the final follow-up session so this time-point was omitted, and technical issues meant that SRS data were inaccurate for eight participants so these cases were removed."

OSCA. Two participants (2/22; 9%) discontinued OSCA, no participants (0/21) discontinued the waitlist control in the study by Leigh & Clark (2022).[23] No reasons for attrition were provided.

Lumi Nova. For the Lumi Nova intervention, a total of 30 guardians (30/95; 32%) reported anxiety outcome measures for their children after the intervention. Gameplay data were generated by 67 families (67/95; 71%) (Lockwood et al. (2022)[24]). No reasons for attrition were provided.

Treatment satisfaction

OSI. Hill et al. (2022b)[22] reported treatment satisfaction using a Session Rating Scale (SRS). The authors reported that participants appeared highly satisfied with both the OSI treatment material and the therapist support telephone review sessions. Participants consistently rated telephone review sessions with their therapist very positively and above the cut-off score. These results are summarised in Table 3.

Table 3. Mean (SD) feedback ratings for each OSI module

Item[a]	Module 0 (n=22)	Module 1 (n=21)	Module 2 (n=20)	Module 3 (n=19)	Module 4 (n=20)	Module 5 (n=18)	Module 6 (n=18)
The module was easy to understand	4.77 (.43)	4.52 (.51)	4.55 (.61)	4.26 (.81)	4.60 (.50)	4.39 (.70)	4.67 (.49)
Was there a part you found particularly difficult to understand and would like to discuss with your therapist? (%yes (n))	4.5 (n=1)	9.5 (n=2)	15.0 (n=3)	31.6 (n=6)	5.0 (n=1)	22.2 (n=4)	11.1 (n=2)
The module took an appropriate	4.59 (.59)	4.48 (.60)	4.35 (.81)	4.26 (.93)	4.55 (.51)	4.44 (.51)	4.56 (.51)

Item[a]	Module 0 (n=22)	Module 1 (n=21)	Module 2 (n=20)	Module 3 (n=19)	Module 4 (n=20)	Module 5 (n=18)	Module 6 (n=18)
amount of time to complete							
The module was helpful	4.41 (.67)	4.38 (.50)	4.65 (.49)	4.53 (.61)	4.60 (.50)	4.39 (.61)	4.56 (.51)
The tone of the material was sensitive for parents seeking help for their child's anxiety	4.64 (.49)	4.43 (.51)	4.45 (.95)	4.63 (.50)	4.65 (.49)	4.50 (.52)	4.56 (.62)
The material was relevant for parents seeking help for their child's anxiety	4.59 (.59)	4.52 (.51)	4.70 (.47)	4.58 (.51)	4.60 (.50)	4.50 (.51)	4.56 (.51)
The module was easy to navigate	4.68 (.48)	4.67 (.48)	4.65 (.49)	4.63 (.50)	4.55 (.61)	4.50 (.51)	4.67 (.49)
Each screen had the right amount of information	4.64 (.49)	4.62 (.50)	4.65 (.49)	4.53 (.61)	4.60 (.50)	4.50 (.51)	4.61 (.50)
The module was visually pleasing to me	4.50 (.60)	4.52 (.51)	4.45 (.51)	4.42 (.61)	4.55 (.51)	4.50 (.51)	4.56 (.51)
It was always clear what to do next in this module	4.50 (.60)	4.62 (.50)	4.45 (.61)	4.37 (.76)	4.60 (.50)	4.39 (.70)	4.56 (.51)
I would recommend this module to other parents of anxious children	4.24 (.83)	4.48 (.60)	4.65 (.59)	4.42 (.69)	4.55 (.51)	4.50 (.62)	4.61 (.50)

Source: Hill et al. (2022a) supplementary Table S2.
Abbreviations: OSI, Online support and intervention for anxiety; SD, standard deviation
Note:
[a] Rated on a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree)

OSCA. Leigh & Clark (2022)[23] reported high credibility, with a mean rating of 8.70 (SD 0.91). In a linear regression, credibility did not predict post-treatment Liebowitz Social Anxiety Scale for Children and Adolescents - Self-report version (LSAS-CA-SR) scores, controlling for baseline LSAS-CA-SR and gender (b=-2.84, p=0.662). The authors further reported that mean participant-rated alliance was 75.00 (SD=4.97) and mean therapist-rated alliance was 69.25 (SD=5.39). In a linear regression, neither participant-rated alliance (b=-

0.126, p=0.919) nor therapist-rated alliance (b=1.097, p=0.205) predicted post-treatment LSAS-CA-SR scores, controlling for baseline LSAS-CA-SR and gender.

Lumi Nova. Lockwood et al. (2022)[24] reported qualitative as well as quantitative findings for satisfaction. Caregivers were reported as stating the following:

"*When she did the challenge, getting an answer wrong, that gave her a bit of confidence that [a] little mistake doesn't put one in trouble by teachers*." [guardian of a girl, aged 12 years]

"*He seems more willing to talk about feeling anxious, he asks questions about anxiety*" [guardian of a boy, aged 9 years]

"*She liked knowing that she could take small steps towards a recognised fear and liked remembering that she coped with all those steps comfortably*." [guardian of a girl, aged 7 years]

"*He took to the game very well and I think it helped him rationalise one of his fears – staying away from home...I definitely think the game put in some excellent groundwork for him to draw on going forward*." [guardian of a boy, aged 12 years]

"*My daughter lost interest in the game and thought it was more aimed at younger children. She has specific worries that weren't covered*." [guardian of a girl, aged 7 years]

"*The feelings bit at the beginning was good, but the tasks following this could be repetitive*." [guardian of a boy, aged 9 years]

Guardians also provided comments to open-response feedback fields. The summary of these findings are presented in Table 4.

Table 4. Guardian open-response comments summarised by research domain (from n=16 guardians reporting on Lumi Nova)

Research domain and summarised content	n (%)
Effectiveness	
Increased confidence and bravery to tackle challenges	6 (38)
Increased appreciation that taking small steps is helpful	3 (19)
Perceived progression in relation to goal choice	2 (13)
Facilitated discussion about anxiety	1 (6)
Beneficial in conjunction with other support	1 (6)
Engagement and experience	
Neutral endorsement of use	5 (31)
Laudatory comments	4 (25)
Barriers to adoption (design and process)	6 (38)
Barriers to adoption (technical barriers)	2 (13)
Increased frustration	1 (6)

Treatment engagement

OSI. Hill et al. (2022b)[22] reported that parents used desktop computers or laptops (39.1%), smartphones (22.4%), or both (39.1%) to log onto OSI. No parents used a tablet for this purpose. The total number of 376 logins to OSI from the whole sample (n=23) over the duration of the intervention were recorded, with a mean 16.35 (SD 8.38; range 4 to 37) logins per participant. The authors further reported that the mean number of page views per module substantially exceeded the total number of pages in the module, suggesting that parents revisited and engaged with module material more than once.

OSCA. In addition to core modules of OSCA, authors report that an additional 7.20 (range 5 to 11) optional modules were released (Leigh & Clark (2022)[23]). The authors further reported that patients logged onto OSCA for a mean total of 26.14 (SD 11.32) hours and logged a mean 25 (SD 10.75) completed behavioural experiments.

Lumi Nova. Lockwood et al. (2022)[24] reported results of ten of the 67 players (15%) with Lumi Nova gameplay data who rated how easy they found the intervention. Eight of these players (80%) provided positive or neutral

evaluations, with most (60%) finding the game easy or very easy and two (20%) finding the game neither easy nor hard. The remaining two players (20%) found the game very hard to play.

Lockwood et al. (2022)[24] also reported average frequency and duration of gameplay with Lumi Nova. These results, stratified by the gameplay sample and the sample of participants with anxiety measures at the start and end of the intervention, are presented in Table 5.

Table 5. Average frequency and duration of gameplay with Lumi Nova

	Gameplay sample (n=67)	T1-T2 sample
Frequency (times played)		
Value, mean (SD)	11.22 (9.41)	12.16 (10.45)
Value, median (range)	8 (1-46)	8 (1-46)
Duration[a] (days played)		
Value, mean (SD)	18.37 (14.75)	18.28 (14.60)
Value, median (range)	15 (1-53)	16 (1-53)

Abbreviations: T1, time 1 (before the intervention); T2, time 2 (after the intervention)
Note:
[a] Duration of play from the first recorded date to the last date of gameplay per participant

Measures of symptom severity

All three included studies reported results for the Revised Child Anxiety and Depression Scale – parent report (RCADS-P). The results for all RCADS-P measures are summarised in Table 6.

Table 6. Summary of changes in RCADS-P total (anxiety) scores reported across included studies

Study	Measure	n	Pre-treatment; mean (SD)	Post-treatment; mean (SD)	Pre- vs post-treatment; p-value, Cohen's *d* (OSI only)	Follow-up; mean (SD) (OSI only)	Pre-treatment vs follow-up; p-value, Cohen's *d* (OSI only)	Post-treatment vs follow-up; p-value, Cohen's *d* (OSI only)
Hill et al. (2022a) (OSI)	RCADS-P total anxiety (raw score)	18	48.83 (18.99)	35.67 (18.3)	*p*=0.01, *d*=0.88	31.83 (18.13)	*p*<0.001, *d*=1.10	*p*=0.07, *d*=0.51
Hill et al. (2022a) (OSI)	RCADS-P total anxiety (*t*-score)	18	74.67 (16.76)	63.5 (16.17)	*p*=0.01, *d*=0.86	60.39 (16.25)	*p*=0.001, *d*=1.10	*p*=0.08, *d*=0.51
Hill et al. (2022a) (OSI)	RCADS-P total score (raw score)	18	58.61 (23)	43 (23.77)	*p*=0.01, *d*=0.84	38.72 (23.82)	*p*=0.001, *d*=1.05	*p*=0.15, *d*=0.50
Hill et al. (2022a) (OSI)	RCADS-P total score (*t*-score)	18	74.56 (16.39)	63.61 (17.03)	*p*=0.01, *d*=0.81	60.94 (17.23)	*p*=0.001, *d*=1.03	*p*=0.18, *d*=0.48
Leigh & Clark (2022) (OSCA)[a]	RCADS-P total score (unadjusted for time)	22	41.50 (16.95)	29.09 (14.86)	NR	N/A	N/A	N/A
Leigh & Clark (2022) (OSCA waitlist)[b]	RCADS-P total score (unadjusted for time)	21	42.53 (16.25)	52.99 (17.13)	NR	N/A	N/A	N/A

Study	Measure	n	Pre-treatment; mean (SD)	Post-treatment; mean (SD)	Pre- vs post-treatment; p-value, Cohen's *d* (OSI only)	Follow-up; mean (SD) (OSI only)	Pre-treatment vs follow-up; p-value, Cohen's *d* (OSI only)	Post-treatment vs follow-up; p-value, Cohen's *d* (OSI only)
Lockwood et al. (2022) (Lumi Nova)	RCADS-P total anxiety	30	30.73 (13.94)	30.30 (16.92)	p=0.20	N/A	N/A	N/A

OSCA vs waitlist

Study	Measure	n	Adjusted difference (SE) [95% CI], p value[c]		Effect size Cohen's *d* [95% CI]			
			Mid	Post	Between group at mid	Between group at post	Within group pre-post[d]	
							OSCA[a]	Waitlist[b]
Leigh & Clark (2022) (OSCA vs waitlist)	RCADS-P total score (Bonferroni adjusted for time)	43	-	22.56 (6.32) [9.87, 35.25], p<0.001	-	1.37 [0.60, 2.14]	1.32 [0.64, 2.00]	0.39 [-0.08, 0.87]

Abbreviations: CI, confidence interval; N/A, not applicable; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, Online support and intervention for anxiety; RCADS-P, Revised Child Anxiety and Depression Scale – parent report; SD, standard deviation; SE, standard error; vs, versus

Note:

[a] In the OSCA group, 22 participants provided complete data at baseline, 21 at mid-treatment and 20 at post-treatment

[b] In the wait group, 21 participants provided data at baseline, 20 at mid-treatment and 21 at post-treatment

[c] All linear mixed effects models included baseline LSAS and gender as covariates, and a random effect of participant. The RCADS were completed at baseline and post-treatment/wait, not at mid-treatment/wait.

[d] Within-group effect sizes obtained from separate linear mixed effects models including baseline score as a timepoint.

OSI. Hill et al. (2022b)[22] additionally reported on reliable and clinically significant changes in RCADS-P for OSI. The results of these, reported for the total anxiety and total score subscales, are reported in Table 7.

Table 7. Reliable and clinically significant changes in RCADS-P at post-treatment and follow-up after OSI

	RCADS total anxiety subscale		RCADS total score	
	Post-treatment; mean (SD)	**Follow-up; mean (SD)**	**Post-treatment; mean (SD)**	**Follow-up; mean (SD)**
Reliable change				
Whole sample (n=18)				
Reliable improvement	44.4 (8)	55.6 (10)	44.4 (8)	61.1 (11)
No reliable change	55.6 (10)	44.4 (8)	55.6 (10)	38.9 (7)
Reliable deterioration	0 (0)	0 (0)	0 (0)	0 (0)
Above clinical threshold at baseline[a] (n=13)				
Reliable improvement	61.5 (8)	76.9 (10)	61.5 (8)	84.6 (11)
No reliable change	38.5 (5)	23.1 (3)	38.5 (5)	15.4 (2)
Reliable deterioration	0 (0)	0 (0)	0 (0)	0 (0)
Recovery (n=13)[b]				
Recovered	38.5 (5)	69.2 (9)	46.2 (6)	61.5 (8)
Non-recovered	61.5 (8)	30.8 (4)	53.8 (7)	38.5 (5)
Reliable recovery (n=13)[b]				
Recovered	30.8 (4)	61.5 (8)	30.8 (4)	61.5 (8)
Non-recovered	69.2 (9)	38.5 (5)	69.2 (9)	38.5 (5)

Abbreviations: OSI, Online support and intervention for anxiety; RCADS-P, Revised Child Anxiety and Depression Scale – parent report; SD, standard deviation
Note:
[a] Number of participants above the clinical cut-off for this subscale at baseline (i.e. t-score of 65 or higher for their school year and gender based on developer norms)
[b] Results presented for those above clinical cut-off for this subscale at baseline

Lumi Nova. Lockwood et al. (2022)[24] additionally reported symptom outcomes Spence Child Anxiety Scale - parent report (SCAS-P) for Lumi Nova. These changed from mean 8.33 (SD 4.56) before the intervention to mean 7.43 (SD

3.28) after (t29=2.79; P=.009; Cohen d=0.35). The authors report that statistical significance remained after Bonferroni correction at p<.01.

OSCA. Leigh & Clark (2022)[23] additionally reported on the LSAS-CA-SR, Social Phobia Weekly Summary Scale (SPWSS), Short Mood and Feelings Questionnaire (SMFQ), and RCADS for OSCA. This was done without adjustment for the effect of time (Table 8) as well as for the intention-to-treat (ITT) population, adjusting values using Bonferroni adjustment for the effect of time (Table 9).

Table 8. Unadjusted changes in LSAS-CA-SR, SPWSS, SMFQ, RCADS total scores reported at various timepoints during the OSCA intervention

Measure	Waitlist[a]		OSCA[b]	
	Mean	SD	Mean	SD
LSAS-CA-SR				
Baseline	93.29	22.43	86.59	25.43
Mid	89.55	28.54	52.48	28.08
Post	86.52	35.37	15.11	15.15
3 months follow-up	-	-	11.75	10.57
6 months follow-up	-	-	16.45	13.64
SPWSS				
Baseline	37.22	7.66	31.61	8.27
Mid	28.17	10.00	21.44	8.04
Post	32.50	9.23	14.12	5.43
3 months follow-up	-	-	10.75	6.96
6 months follow-up	-	-	12.60	7.36
SMFQ				
Baseline	13.81	7.22	13.59	7.01
Mid	13.86	8.29	7.05	4.97
Post	13.10	7.37	4.05	3.72
3 months follow-up	-	-	4.00	3.48
6 months follow-up	-	-	4.85	4.84
RCADS				
Baseline	70.86	23.02	66.09	20.15
Mid	-	-	-	-
Post	63.62	25.56	21.52	16.57
3 months follow-up	-	-	-	-

Measure	Waitlist[a]		OSCA[b]	
	Mean	SD	Mean	SD
6 months follow-up	-	-	23.58	14.72

Abbreviations: LSAS-CA-SR, Liebowitz Social Anxiety Scale for Children and Adolescents – Self-Report version; OSCA, Online Social anxiety Cognitive therapy for Adolescents; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– child/parent report); SD, standard deviation; SDQ(-C/P), Strengths and Difficulties Questionnaire (– child/parent report); SMFQ, Short Mood and Feelings Questionnaire; SPWSS, Social Phobia Weekly Summary Scale

Notes:

[a] In the wait group, 21 participants provided data at baseline, 20 at mid-treatment and 21 at post-treatment

[b] In the OSCA group, 22 participants provided complete data at baseline, 21 at mid-treatment and 20 at post-treatment

Table 9. Bonferroni-adjusted changes in LSAS-CA-SR, SPWSS, SMFQ, RCADS total scores reported at various timepoints during the OSCA intervention for the ITT population

Measure	Adjusted difference (SE) [95% CI], p value[a]		Effect size Cohen's *d* [95% CI]			
	Mid	Post	Between group at mid	Between group at post	Within group pre-post	
					Treatment[b]	Waitlist[c]
LSAS-CA-SR	31.01 (6.29) [18.28, 43.74], p<0.001	64.92 (6.29) [52.19, 77.65], p<0.001	1.07 [0.63, 1.51]	2.31 [1.86, 2.76]	2.94 [2.39, 3.49]	0.22 [-0.05, 0.50]
SPWSS	6.07 (2.63) [0.80, 11.34], p<0.05	64.92 (6.29) [52.19, 77.65], p<0.001	0.64 [0.09, 1.22]	2.24 [1.57, 2.92]	1.75 [0.93, 2.57]	0.54 [-0.06, 1.03]
SMFQ	6.66 (1.29) [4.07, 9.25], p<0.001	9.00 (1.29) [6.41, 11.59], p<0.001	0.96 [0.58, 1.33]	1.49 [1.06, 1.92]	1.55 [1.09, 2.01]	0.10 [-0.35, 0.16]
RCADS	-	35.44 (4.83) [25.66, 45.22], p<0.001	-	1.60 [1.16, 2.04]	1.87 [1.35, 2.38]	0.29 [0.02, 0.56]

Abbreviations: CI, confidence interval; ITT, intention-to-treat; LSAS-CA-SR, Liebowitz Social Anxiety Scale for Children and Adolescents – Self-Report version; OSCA, Online Social anxiety Cognitive therapy for Adolescents; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– child/parent report); SE, standard error; SDQ(-C/P), SMFQ, Short Mood and Feelings Questionnaire; SPWSS, Social Phobia Weekly Summary Scale

Notes:

[a] All linear mixed effects models included baseline LSAS and gender as covariates, and a random effect of participant. The RCADS were completed at baseline and post-treatment/wait, not at mid-treatment/wait

[b] In the OSCA group, 22 participants provided complete data at baseline, 21 at mid-treatment and 20 at post-treatment

[c] In the wait group, 21 participants provided data at baseline, 20 at mid-treatment and 21 at post-treatment

Social, behavioural and functional outcomes

Both Hill et al. (2022b)[22] and Lockwood et al. (2022)[23] reported pre- and post-treatment scores of the Child Anxiety Impact Scale – parent report (CAIS-P) as part of this outcome, for OSI and Lumi Nova, respectively; but found contradictory results. Hill et al. (2022b)[22] additionally reported this measure at four weeks follow-up. The results for the two studies are summarised in Table 10.

Table 10. Change in CAIS-P total score of participants treated with OSI and OSCA pre- and post-treatment and at follow-up (OSI only)

Study	n	Pre-treatment; mean (SD)	Post-treatment; mean (SD)	Pre- vs post-treatment; p-value, Cohen's *d* (OSI only)	Follow-up; mean (SD) (OSI only)	Pre-treatment vs follow-up; p-value, Cohen's *d* (OSI only)	Post-treatment vs follow-up; p-value, Cohen's *d* (OSI only)
Hill et al. (2022a)[a] (OSI)	18	21.56 (15.12)	13.72 (14.46)	p=0.03, *d*=0.58	13.44 (14.62)	p=0.02, *d* =0.58	p=0.66, *d* =0.10
Lockwood et al. (2022)[b] (Lumi Nova)	30	20.57 (15.40)	20.97 (15.49)	p=0.80	N/A	N/A	N/A

Abbreviations: CAIS-P, Child Anxiety Impact Scale – parent report; N/A, not applicable; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, Online support and intervention for anxiety; SD, standard deviation

Note:

[a] Data presented are from the primary analysis using the last observation carried forward approach only (the per-protocol sample is the same as paired data are from modules 0 and 6 when the full CAIS-P was administered)

[b] Significance testing was based on Wilcoxon signed-rank tests for the Child Anxiety Impact Scale–Parent version home and social subscales; otherwise, significance was based on paired sample t tests

OSI. Hill et al. (2022b)[22] additionally reported on goal-based outcomes (GBO) at pre- and post-treatment with OSI as well as four weeks follow up. Highly significant improvements were observed between pre- and post-treatment, as well as pre-treatment and follow-up; no significant increases were found between post-treatment and follow-up. The results of this measure are presented in Table 11. Green et al. (2022) [redacted].

Table 11. Change in GBO of participants treated with OSI pre- and post-treatment and at follow-up

Analysis	n	Pre-treatment; mean (SD)	Post-treatment; mean (SD)	Follow-up; mean (SD)	Pre- vs post-treatment; p-value, Cohen's *d*	Pre-treatment vs follow-up; p-value, Cohen's *d*	Post-treatment vs follow-up; p-value, Cohen's *d*
Primary	22[a]	2.42 (1.91)	6.58 (2.53)	7.02 (2.76)	*P*<0.001, *d*=-1.67	*p*<0.001, *d*=-1.81	*p*=0.15, *d*=-0.45
Per protocol	20	2.57 (1.92)	6.85 (2.46)	7.33 (2.66)	*p*<0.001, *d*=-1.73	*p*<0.001, *d*=-1.92	*p*=0.05, *d*=-0.47

Abbreviations: GBO, goal-based outcomes; OSI, Online support and intervention for anxiety; SD, standard deviation
Note:
[a] n = 22 for this analysis because data must be available for three modules (modules 0, 1 and 2) as GBO is rated from module 1 onwards

OSCA. The study by Leigh & Clark (2022)[23] reported on the frequency and belief domains of the Social Cognitions Questionnaire (SCQ), the Social Behaviour Questionnaire (SBQ), Social Attitudes Questionnaire (SAQ), concentration, participation, satisfaction and the Child Anxiety Life Interference Scale (CALIS; both child- and parent-reported) with OSCA. The results of these, unadjusted for the effect of time, are presented in Table 12.

Table 12. Unadjusted means and standard deviations for continuous outcome measures at various timepoints during the OSCA intervention

Measure	Waitlist[a]		OSCA[b]	
	Mean	SD	Mean	SD
SCQ - frequency				
Baseline	3.40	0.60	3.02	0.74
Mid	3.09	1.01	1.87	0.59
Post	3.62	0.88	1.25	0.31
3 months follow-up	-	-	1.22	0.27
6 months follow-up	-	-	1.28	0.41
SCQ - belief				
Baseline	58.18	19.82	53.96	19.12
Mid	51.28	20.98	23.02	14.95
Post	53.86	23.80	7.43	7.77
3 months follow-up	-	-	6.38	6.56

Measure	Waitlist[a]		OSCA[b]	
	Mean	**SD**	**Mean**	**SD**
6 months follow-up	-	-	7.64	9.88
SBQ				
Baseline	1.48	0.18	1.45	0.13
Mid	1.77	0.18	1.02	0.47
Post	1.45	0.15	0.40	0.24
3 months follow-up	-	-	0.48	0.34
6 months follow-up	-	-	0.45	0.23
SAQ				
Baseline	3.26	0.92	3.39	0.71
Mid	3.45	1.12	4.08	0.89
Post	3.45	0.93	5.23	0.69
3 months follow-up	-	-	5.32	0.80
6 months follow-up	-	-	5.25	0.74
Concentration				
Baseline	3.67	2.01	4.50	1.71
Mid	4.00	1.81	5.19	1.94
Post	3.71	1.76	6.25	1.29
3 months follow-up	-	-	6.05	1.43
6 months follow-up	-	-	5.50	2.01
Participation				
Baseline	50.32	15.06	48.20	13.98
Mid	48.10	12.78	55.30	8.57
Post	48.73	16.07	69.26	8.22
3 months follow-up	-	-	68.85	9.29
6 months follow-up	-	-	66.70	11.73
Satisfaction				
Baseline	15.81	4.85	15.98	3.61
Mid	16.90	4.70	20.55	3.36
Post	18.41	5.05	22.63	3.50
3 months follow-up	-	-	22.45	3.46
6 months follow-up	-	-	21.80	3.43
CALIS				
Baseline	19.57	6.61	16.59	8.18
Mid	-	-	-	-
Post	17.81	6.90	7.16	5.25
3 months follow-up	-	-	7.70	4.74

Measure	Waitlist[a]		OSCA[b]	
	Mean	SD	Mean	SD
6 months follow-up	-	-	6.80	5.86
CALIS - parent				
Baseline	22.00	10.79	20.11	11.50
Mid	-	-	-	-
Post	26.69	9.93	12.53	11.32
6 months follow-up	-	-	-	-

Abbreviations: CALIS(-P), Child Anxiety Life Interference Scale (– parent report); SAQ, Social Attitudes Questionnaire; SBQ, Social Behaviour Questionnaire; SCQ, Social Cognitions Questionnaire; SD, standard deviation

Notes:

[a] In the wait group, 21 participants provided data at baseline, 20 at mid-treatment and 21 at post-treatment

[b] In the OSCA group, 22 participants provided complete data at baseline, 21 at mid-treatment and 20 at post-treatment

OSCA. Leigh & Clark (2022)[23] additionally reported on the frequency and belief domains of the Child and Adolescent Social Cognitions Questionnaire (CASCQ), Child and Adolescent Social Attitudes Questionnaire (CASAQ), Child and Adolescent Social Behaviour Questionnaire (CASBQ), concentration, participation, satisfaction, and CALIS (child- and parent-reported) for the intention-to-treat (ITT) population receiving OSCA or waitlist control, adjusting values using Bonferroni adjustment for the effect of time. The results of these are presented in Table 13.

Table 13. Adjusted differences and effect sizes for continuous measures for intention to treat sample during the OSCA intervention

Measure	Adjusted difference (SE) [95% CI], p value[a]		Effect size Cohen's *d* [95% CI]			
	Mid	Post	Between group at mid	Between group at post	Within group pre-post	
					OSCA[b]	Waitlist[c]
CASCQ – frequency	1.08 (0.21) [0.66, 1.53], p<0.001	1.65 (0.22) [1.21, 2.09], p<0.001	1.28 [0.78, 1.78]	2.41 [1.77, 3.05]	2.42 [1.66, 3.16]	0.43 [-0.03, 0.83]
CASCQ – belief	25.29 (4.62) [16.04, 34.54], p<0.001	42.98 (4.62) [33.73, 52.23], p<0.001	1.36 [0.86, 1.86]	2.34 [1.84, 2.85]	2.75 [2.09, 3.40]	0.19 [-0.12, 0.51]

Measure	Adjusted difference (SE) [95% CI], p value[a]		Effect size Cohen's *d* [95% CI]			
	Mid	Post	Between group at mid	Between group at post	Within group pre-post	
					OSCA[b]	Waitlist[c]
CASAQ	-0.51 (0.21) [-0.93, -0.09], p<0.05	-1.52 (0.21) [-1.94, -1.10], p<0.001	0.53 [0.09, 0.97]	1.99 [1.44, 2.55]	2.29 [1.70, 2.90]	0.20 [-0.11, 0.52]
CASBQ	0.71 (0.09) [0.53, 0.89], p<0.001	1.01 (0.09) [0.83, 1.19], p<0.001	1.93 [1.44, 2.42]	4.95 [4.07, 5.83]	5.22 [4.25, 6.20]	0.18 [-0.94, 0.59]
Concentration	-0.89 (0.51) [-1.91, 0.13], p=0.09	-2.22 (0.51) [-3.24, -1.20], p<0.001	0.46 [0.07, 0.99]	1.40 [0.76, 2.04]	1.08 [0.27, 1.89]	0.03 [-0.43, 0.49]
Participation	-6.65 (3.24) [-0.16, -13.14], p<0.05	-21.67 (3.20) [-15.26, -28.08], p<0.001	0.60 [0.01, 1.18]	1.64 [1.16, 2.13]	1.92 [1.33, 2.51]	0.10 [-0.40, 0.21]
Satisfaction	-3.08 (1.14) [-0.79, -5.37], p<0.01	-3.91 (1.14) [-1.62, -6.20], p<0.01	0.74 [0.19, 0.29]	0.87 [0.36, 1.39]	1.09 [0.42, 1.75]	0.51 [0.18, 0.85]
CALIS	-	7.41 (2.02) [3.32, 11.50], p<0.001	-	1.18 [0.53, 1.82]	1.04 [0.45, 1.62]	0.25 [-0.16, 0.66]
CALIS – parent	-	12.21 (4.12) [3.92, 20.50], p<0.01	-	2.07 [0.91, 3.23]	0.88 [0.37, 1.40]	0.09 [-0.33, 0.51]

Abbreviations: CALIS(-P), Child Anxiety Life Interference Scale (– parent report); CASAQ, Child & Adolescent Social Attitudes Questionnaire; CASBQ, Child & Adolescent Social Behaviour Questionnaire; CASCQ, Child & Adolescent Social Cognitions Questionnaire (mean scores); CI, confidence interval; SE, standard error; LSAS-CA-SR, Liebowitz Social Anxiety Scale for Children and Adolescents – Self-Report version; OSCA, Online Social anxiety Cognitive therapy for Adolescents

Notes:

[a] All linear mixed effects models included baseline LSAS and gender as covariates, and a random effect of participant. The RCADS were completed at baseline and post-treatment/wait, not at mid-treatment/wait

[b] In the OSCA group, 22 participants provided complete data at baseline, 21 at mid-treatment and 20 at post-treatment

[c] In the wait group, 21 participants provided data at baseline, 20 at mid-treatment and 21 at post-treatment

Suicidal thoughts and behaviour

No studies with published data available reported on this outcome.

Global functioning

OSI. Hill et al. (2022b)[22] reported on the Child Outcome Rating Scale (CORS), a four-item scale measuring psychosocial functioning through parent-report of visual analogue scale outcomes on a scale of 0 to 10. The results of CORS for the primary and per-protocol populations treated with OSI are presented in Table 14. Green et al. (2022)

[redacted].

Table 14. CORS total score of participants treated with OSI pre- and post-treatment and at follow-up

Analysis	n	Pre-treatment; mean (SD)	Post-treatment; mean (SD)	Follow-up; mean (SD)	Pre- vs post-treatment; p-value, Cohen's *d*	Pre-treatment vs follow-up; p-value, Cohen's d	Post-treatment vs follow-up; p-value, Cohen's d
Primary[a]	23	24.93 (8.53)	32.25 (7.39)	33.15 (6.42)	p=0.001, *d*=-0.87	p=0.004, *d* =-0.96	p=0.37, *d* =-0.20
Per protocol[b]	20	26.58 (7.43)	32.71 (7.68)	33.75 (6.51)	p=0.002, *d* =-0.83	p=0.003, *d* =-0.92	p=0.37, *d* =-0.22

Notes:
[a] Data presented are from the primary analysis using the last observation carried forward (LOCF) approach
[b] Data presented are from the per-protocol analysis

The studies by Leigh & Clark (2022)[23] and Lockwood et al. (2022)[24] did not report on this outcome for OSCA and Lumi Nova, respectively.

Rates of remission

OSI. Hill et al. (2022b)[22] reported that the majority of participants who completed OSI (15/18; 83.3%) were discharged from the service, based on the view of both parents and clinicians that no further psychological input was needed.

OSCA. Leigh & Clark (2022)[23] reported that, at post-intervention, it could be demonstrated that 17 participants (17/22; 77%) of the OSCA group no longer met criteria for DSM-5 diagnosis of SAD. DSM-5 diagnosis of SAD was an eligibility criterion for the study.

Lumi Nova. The study by Lockwood et al. (2022)[24] did not report on this outcome.

Health-related quality of life

No studies with published data available reported on this outcome.

Patient experience

OSI. Hill et al. (2022b)[22] reported that mean feedback scores on the OSI feedback questionnaire were consistently in the 'agree' to 'strongly agree' range for each module. These results are summarised in Table 3, under the section on Treatment satisfaction.

Two included studies, Green et al. (2022) and Williamson et al. (2022)[25] reported on treatment experience with OSI. As discussed in Section 8.2, the EAG could not rule out duplication of these perspectives on treatment experience, as both studies cite Williamson et al. (2021)[31] as protocol. Williamson et al. (2022)[25] found that parents were influenced by the COVID-19 context, and felt more comfortable working remotely. Therefore, the online intervention was seen as more acceptable and accessible and weekly phone calls from CWP were considered to be an essential part of the intervention. Parents noted that the COVID-19 context did not allow them to speak with friends or school staff informally about their experiences with the pathway; while it was generally perceived and experienced as positive and helpful, parents expressed concern about the availability about follow-up support and the potential for bullying as an unintended consequence of screening. Green et al. (2022) reported themes indicating that [redacted], [redacted], and that [redacted].

The studies by Leigh & Clark (2022)[23] and Lockwood et al. (2022)[24] did not report on this outcome for OSCA and Lumi Nova, respectively.

Cost of technologies

No studies with published data available reported on this outcome.

Cost of other resource use

No studies with published data available reported on this outcome.

10 Adverse events

The study by Hill et al. (2022b)[22] did not measure, monitor for or report any adverse events with OSI. Leigh & Clark (2022)[23] reported that no adverse events or serious adverse events were identified with OSCA. Lockwood et al. (2022)[24] reported safety using the RCADS-P subscale for major depressive disorder (MDD), which showed non-significant change in scores from the start to the end of the Lumi Nova intervention (Table 15).

Table 15. Safety measured as change in RCADS-P subscale for MDD during the Lumi Nova intervention

Safety	T1, mean (SD)	T2, mean (SD)	p-value
RCADS-P (MDD subscale)	7.07 (4.91)	6.60 (3.94)	0.46

Abbreviations: MDD, major depressive disorder; RCADS-P, Revised Child Anxiety and Depression Scale – parent report; SD, standard deviation, T1, time 1 (start of intervention); T2, time 2 (end of intervention)

Evidence gap: No published safety evidence for OSI or the SilverCloud interventions was found. No published evidence for suicidal thoughts or behaviour with any of the interventions was found.

11 Evidence synthesis

Given the heterogeneity in the evidence base as it pertains to outcomes, a lack of completed studies with available data, as well as the absence of comparative evidence (with the exception of OSCA, reported in Leigh & Clark (2022)[23]), it was not possible to synthesise findings within or across intervention categories.

Even if synthesis was to be attempted, small sample sizes would result in underpowered analyses and the risk of spurious findings.

Addressing the identified evidence gaps and heterogeneity issues should improve the feasibility of future evidence syntheses, while addressing identified generalisability gaps would improve the external validity and, consequently, utility of such analyses.

12 Economic evidence

12.1 *Published economic evidence*

The search for economic evidence was conducted alongside the search for clinical evidence and is detailed in Section 8 and Section 17.2 (Appendix B). A total of 28 articles of relevance to the economic analysis was identified.

Due to the anticipated scarcity of evidence in the target population (CYP), economic studies on adults were included as they are highly likely to provide information of indirect relevance. Studies of direct and indirect relevance to the decision problem are summarized in Table 16. Directly relevant studies are those providing inputs into the decision model, or previous models in the relevant patient population. Indirectly relevant studies are those reporting economic analyses in a related area or patient group as these may provide useful background on, for example, model structure or other insight into input parameters. The reporting of economic evaluations (decision models and piggybacked-studies alongside RCTs) was quality-assessed using the CHEERS checklist[39] (Appendix B).

Evidence for economic outcomes in children and young people

Seven systematic reviews were identified summarising economic evidence for CBT in children or adults for either anxiety, depression or both. Only the Ophuis 2017[40] review found any evidence on the cost-effectiveness of digital health interventions for anxiety, low mood or depression in children and young people. This review found 3 studies none of which were directly relevant to this

assessment: two were in the wrong populations (PTSD and sexually abused children)[41 42] and the other compared family vs individual CBT.[43]

Only one economic evaluation was identified which assessed the cost-effectiveness of parent-delivered cognitive behavioural therapy and face-to-face solution-focused brief therapy for treatment of childhood anxiety disorders in children aged 5-12 alongside an RCT conducted in 4 centres in Oxfordshire (n=136, 6 month follow-up post treatment completion).[44] Little difference in QALYs was found (mean (95%CI) QALY difference of 0.006, (–0.009 to +0.02); p=0.42); brief guided parent-delivered CBT was, however, associated with lower costs. The mean societal cost for children was £1,494 (SD 1107.79) for those in the brief guided parent-delivered CBT and the mean difference versus face-to-face therapy was –£448 (95% CI –934 to 37; p=0.070). Taking into account sampling uncertainty, brief guided parent-delivered CBT was considered likely to represent a cost-effective use of resources compared with solution-focused brief therapy. The quality and generalisability of this study is, however, questionable given the location of the study and the fact that the key driver of the difference in cost savings was therapist time and travel costs associated with the treatment delivery which was not expected by the authors.

Evidence for economic outcomes in adults

Evidence for adults was considerably more prevalent with the most recent systematic reviews in anxiety and depressive disorders both identifying a sizeable evidence base and concluding that ICBT was most likely cost-effective.[40 45]

In adults, the Li 2022[45] systematic review provides the most up to date summary for depression. A total of 15 studies reported the cost-utility of ICBT in the treatment of depression (mostly mild to moderate) from a social or health system perspective, with a time horizon of 3 to 60 months. Eleven studies showed that ICBT alone or combined with usual care was more cost-effective than usual care alone; of the 11 studies, 7 studies focused on guided ICBT, and the other 3 studies focused on unguided or minimally supported ICBT. Two

studies showed that guided ICBT did not seem to be any more cost-effective than usual general practice care. Another 2 studies compared the cost-effectiveness of guided ICBT with unguided ICBT for depression; 1 study showed guided ICBT was more cost-effective than unguided ICBT (guided ICBT was dominated), whereas the other study indicated that guided CBT was not more cost-effective than unguided informational websites. The authors concluded that there was fair or high-quality evidence that CBT monotherapy or combination therapy for adult depression was cost-effective.

In adults, the Ophuis 2017[40] systematic review provides the most up to date summary for anxiety disorders. Thirty-nine studies were identified in adults or older patients. The studies were heterogeneous, and the quality was variable. The authors concluded that iCBT appeared to be cost-effective in comparison with the control conditions and that four out of five studies comparing psychological interventions with pharmacological interventions showed that psychological interventions were more cost-effective than pharmacotherapy.

Learnings relating to model structure and key issues impacting cost-effectiveness

Review papers indicated that key issues in interpreting the cost-effectiveness evidence available included the transferability of trial results to routine clinical practice, the effectiveness of blended formats and stepped care models, the appropriate comparator (active treatment such as face to face therapy or waiting list). Results from the ongoing IAPT-based study should prove useful in examining issues around real-world application in the UK.

The economic models identified focused on adult populations.[46-48] Learnings from the models presented include: the wide variety of potential approaches to costing ICBT dependent on how the programme is set up and charged to the NHS,[48] the need to consider continuation with / adherence to treatment;[47 48] the wider treatment pathway (e.g. medication, stepped care[48]); potential approaches to consideration of differential wait times between internet-based and face to face care[46] and spontaneous remission,[46] and finally the general

paucity of health economic data for model population and complete lack of data for the impact of interventions on caregivers.[46-48]

Table 16 Narrative summary of economic studies of direct and indirect relevance

Study ID	Title	Study type	Narrative summary
Palmqvist 2007 [49]	Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost?	editorial	Discusses the Kaltenhalter systematic review and advises that other costs than licensing associated with CCBT in general practice are the hardware/computer costs, the costs of screening for suitable clients and the cost for clinical support where applicable. The cost of the clinical support will vary greatly according to the profession of the supporting staff (e.g., a licensed psychologist will cost more than a nurse, who in turn costs more than a psychology student). Given the availability of CBT principles in published self-help books and the accelerating computer literacy among staff and the general public, it is possible that in the future healthcare companies and institutions might prefer to develop their own CCBT or internet-delivered programs, thus avoiding the licence cost in the long run. However, the costs of providing clinical support will continue to play a role in future applications. This will make CCBT less cost effective. In conclusion, at present it is premature to draw any firm conclusions regarding the cost-effectiveness of internet-delivered CCBT.
Creswell 2017 [44]	Clinical outcomes and cost-effectiveness of brief guided parent-delivered cognitive behavioural therapy and solution-focused brief therapy for treatment of childhood anxiety disorders: a randomised controlled trial	EE alongside RCT	Economic evaluation alongside an RCT (n=136, 6 month follow-up post treatment completion) for children aged 5-12 years conducted in 4 centres in Oxfordshire referred for anxiety difficulties. Compares brief guided parent-delivered CBT with face-to-face solution-focused brief therapy, with minimisation for age, sex, anxiety severity, and level of parental anxiety. Mean QALY difference of 0·006, –0·009 to 0·02; p=0·42. Brief guided parent-delivered CBT was associated with lower costs (mean difference –£448; 95% CI –934 to 37; p=0·070) and, taking into account sampling uncertainty, was considered likely to represent a cost-effective use of resources compared with solution-focused brief therapy. Results based on a restricted health-care provider perspective confirmed the main finding with the key driver of the difference in costs being savings which occurred in the therapists' time and travel costs associated with the treatment delivery which was not expected by the authors.
Duarte 2017 [50]	Cost-effectiveness of computerized cognitive–behavioural therapy for the treatment of depression in primary care: findings from the	EE alongside RCT	First study based on a large (n=691) NIHR-funded independent pragmatic trial in the UK (REEACT) to assess the cost-effectiveness of cCBT (one free and one commercial programme) for depression in adults as an adjunct to GP care with 2-year follow-up. Neither cCBT programme was found to be cost-effective compared with usual GP care alone. Adherence was found to be low (less than 20% of patients on cCBT completed the treatment). At a £20 000 per QALY

Study ID	Title	Study type	Narrative summary
	Randomised Evaluation of the Effectiveness and Acceptability of Computerised Therapy (REEACT) trial		threshold, usual GP care alone had the highest probability of being cost-effective (0.55) followed by MoodGYM (0.42) and Beating the Blues (0.04).
Gerhards 2010 [51]	Economic evaluation of online computerised cognitive–behavioural therapy without support for depression in primary care: randomised trial	EE alongside RCT	Economic evaluation of online computerised cognitive–behavioural therapy (CCBT) without support for adults with depression in primary care based on an RCT (n=303) with 12 month follow-up alone or in combination with treatment as usual vs treatment as usual in the Netherlands. Study used a societal perspective and found that costs were lowest in the CCBT group and there were no significant group differences in effectiveness or quality of life. The authors comment that all treatments showed low adherence rates and modest improvements in depression and quality of life. In fact the EQ-5D remains around 0.70 for all 3 arms for all timepoints. Adherence to treatment was low which may mean that outcomes reflect the natural course of the disease rather than treatment received.
Hedman 2011 [52]	Cost-effectiveness of Internet-based cognitive behaviour therapy vs. cognitive behavioural group therapy for social anxiety disorder: Results from a randomized controlled trial	EE alongside RCT	Cost-effectiveness alongside a non-inferiority RCT (n=126; max follow-up 6 months post treatment, single centre in Sweden) of internet based cognitive behavioural therapy (ICBT) vs cognitive behavioural group therapy (CBGT) from a societal perspective using a prospective design for social anxiety disorder. Results showed that the gross total costs were significantly reduced at six month follow-up, compared to pre-treatment in both treatment arms. As both treatments were equivalent in reducing social anxiety and gross total costs, ICBT was more cost-effective due to lower intervention costs. Both treatments generated savings that exceeded the intervention cost of respective treatment within one year
Hollinghurst 2010 [53]	Cost-effectiveness of therapist-delivered online cognitive–behavioural therapy for depression: randomised controlled trial	EE alongside RCT	Economic evaluation of online CBT vs usual care for adult depression at 8 months alongside an RCT in the UK (n=297). Online CBT was more expensive than usual care, although the outcomes for the CBT group were better. Cost per QALY gain based on complete case data was £17 173, and £10 083 when missing data were imputed (NHS perspective).
Jolstedt 2018[54]	Efficacy and cost-effectiveness of therapist-guided internet cognitive behaviour	EE alongside RCT	Economic evaluation of ICBT vs internet-delivered child-directed play for paediatric anxiety disorders based on a single-blind RCT of children ages 8-12 conducted in a single site in Stockholm (n=131; max follow-up 3 months post treatment and cross-over allowed immediately post treatment to ICBT). ICBT resulted in an average societal cost saving of €493·05 (95% CI

Study ID	Title	Study type	Narrative summary
	therapy for paediatric anxiety disorders: a single-blind randomised controlled trial		477·17 to 508·92) per participant. The authors concluded that ICBT is a cost-effective treatment for paediatric anxiety disorders that should be considered for implementation in routine clinical care.
Kraepelien 2018 [55]	Cost-effectiveness of internet-based cognitive–behavioural therapy and physical exercise for depression	EE alongside RCT	Economic evaluation of a randomised controlled trial (N=945) in Sweden comparing ICBT with physical exercise and treatment as usual (TAU). The primary analysis (3 month, health care provider perspective) showed that incremental cost per QALY gained was €8817 for ICBT and €14 571 for physical exercise compared with TAU. At the established willingness-to-pay threshold of €21 536 (£20 000) per QALY, the probability of ICBT being cost-effective is 90%, and for physical exercise is 76%, compared with TAU.
Warmerdam 2010 [56]	Cost-Utility and Cost-Effectiveness of Internet-Based Treatment for Adults With Depressive Symptoms: Randomized Trial	EE alongside RCT	This study aims to evaluate the relative cost-utility and cost-effectiveness of (1) Internet-based cognitive behavioural therapy, (2) Internet-based problem-solving therapy, and (3) a waiting list for adults with depressive symptoms based on an RCT (n=263, 12 weeks). Cost-utility analysis showed that cognitive behavioural therapy and problem-solving therapy had a 52% and 61% probability respectively of being more cost-effective than waiting when the willingness to pay is €30,000 per QALY. Comparing both Internet-based treatments showed no clear preference for one or the other of the treatments. This study showed that a brief intervention based on problem-solving therapy seems to be a good alternative for Internet-based cognitive behavioural therapy in terms of cost-effectiveness. The generic nature of problem-solving therapy makes it suitable as a first step in a stepped care model. This would enable therapists to free up their limited resources and direct these to people presenting with more complex and severe symptomatology.
Baumann 2020 [46]	Cost–Utility of Internet-Based Cognitive Behavioral Therapy in Unipolar Depression: A Markov Model Simulation	EE decision model	This study reports the outcomes from a Markov model comparing internet based CBT with face to face CBT (FCBT) in Germany considering differential waiting times (3 vs 20 weeks) using a societal perspective. The authors modelled a time horizon of 3 years using six states (remission, depressed, spontaneous remission, undergoing treatment, treatment finished, death) with transition probabilities using meta-regression per transition which is then essentially used within a naïve comparison. QoL and cost data are obtained from the literature. ICBT generated 0.260 QALYs and saved €2536 per patient compared to FCBT. PSA suggested that ICBT is highly likely to be more effective (91.5%), less costly (76.0%), and the dominant strategy (69.7%) compared to FCBT. Scenario analysis revealed that the base-case results are robust to variations in time-to-treatment differences with the factor having the most impact being wait times.

Study ID	Title	Study type	Narrative summary
You 2022 [47]	Cost-effectiveness of internet-supported cognitive behavioural therapy for university students with anxiety symptoms: A Markov model analysis	EE decision model	Exploratory model-based evaluation of the cost-effectiveness of guided low-intensity i-CBT vs face to face CBT (f-CBT) for university students with mild anxiety symptoms from the societal perspective of Hong Kong (5 year time horizon). In the base-case analysis, i-CBT gained higher QALYs (2.9956 versus 2.9917) at lower total cost (US$6,101 versus US$6,246) than f-CBT.
Stein 2009 [57]	The precision of health state valuation by members of the general public using the standard gamble	health state valuation	Vignette study using SG with UK general population for five comparisons of the outcomes of treatments, based on health state descriptions (n=27 to 59). The mean utility differences between groups was: 0.23 for computerised cognitive behavioural therapy for depression (n=41, P<0.001). The computerised CBT for depression exemplar was based on the parallel group RCT by Selmi et al. This showed a significant difference of 7.5 points between treatment and control groups on the Beck Depression Inventory (BDI). Health states were developed for the BDI categories of moderate, mild and minimal depression, targeting the mid-point in the ranges within each BDI category. The vignettes were reviewed by a consultant psychiatrist and a family physician, who confirmed that they depicted the target condition and appropriately described levels of severity. The outcomes according to the original health states are not reported.
Health Quality, Ontario 2019 [48]	Internet-Delivered Cognitive Behavioural Therapy for Major Depression and Anxiety Disorders: A Health Technology Assessment	HTA assessment	HTA of internet-delivered CBT for Major Depression and Anxiety Disorders conducted by Health Quality Ontario. Concluded that compared with waiting list, guided iCBT improves symptoms of mild to moderate major depression and select anxiety disorders and guided iCBT represents the most economical option for the short-term treatment of adults with mild to moderate major depression or anxiety disorders. For adults with mild to moderate major depression, guided iCBT was associated with increases in both quality-adjusted survival (0.04 quality-adjusted life-years [QALYs]) and cost ($1,257), yielding an ICER of $31,575 per QALY gained when compared with usual care. In adults with anxiety disorders, guided iCBT was also associated with increases in both quality-adjusted survival (0.03 QALYs) and cost ($1,395), yielding an ICER of $43,214 per QALY gained when compared with unguided iCBT. In this population, guided iCBT was associated with an ICER of $26,719 per QALY gained when compared with usual care. The probability of cost-effectiveness of guided iCBT for major depression and anxiety disorders, respectively, was 67% and 70% at willingness-to-pay of $100,000 per QALY gained. Guided iCBT delivered within stepped-care models appears to represent good value for money for the treatment of mild to moderate major depression and anxiety disorders.

Study ID	Title	Study type	Narrative summary
			However, participants reported important barriers and limitations to using iCBT, including the need for a computer, internet access, and computer literacy, as well as the ability to understand complex written information. Participants found that the cost of treatment, the number of sessions in a course of treatment, and the lack of follow-up support were also substantial drawbacks for iCBT.
Foroushani 2011 [58]	Meta-review of the effectiveness of computerised CBT in treating depression	Meta-analysis	A thorough search and analysis of reviews of efficacy of computerised cognitive behaviour therapy (cCBT) published between 1999 and February 2011. The search yielded twelve systematic reviews from ten studies covering depression. The meta-review supports the efficacy of cCBT for treatment of depression; however there is limited information on different approaches, whose relative cost-effectiveness remains to be demonstrated. Only one study Kaltenthaler et al. 2006 was found which addressed cost-effectiveness for the Beating the Blues package (£1,250 per QALY estimate from a review which excluded 'commercially-sensitive' information).
Marks 2003 [59]	Pragmatic evaluation of computer-aided self-help for anxiety and depression	Open pragmatic evaluation	Provides a "rough" cost comparison based solely on assumed unit costs and assumptions around admin and overheads within taking into account outcomes
Antle 2019 [60]	Dissemination of computer-assisted cognitive-behaviour therapy for depression in primary care	Protocol	Planned RCT with 240 patients randomly assigned to computer-assisted cognitive-behaviour therapy or treatment as usual based on patients >18 yrs old from 5 primary care clinics in Kentucky. Planned follow-up up to 6 months including CCBT program completion and satisfaction rates, CSQ-8, PHQ-9, Automatic Thoughts Questionnaire, Computer Attitudes Questionnaire, Satisfaction with Life Scale and cost effectiveness analysis with a societal perspective. Enrolment was planned to continue until March 2019 but the study does not yet appear to have reported.
Richards 2018 [61]	Digital IAPT: the effectiveness & cost-effectiveness of internet-delivered interventions for depression and anxiety disorders in the Improving Access to Psychological Therapies programme: study	Protocol	Protocol for a study which aims to evaluate the clinical and cost-effectiveness of internet-delivered interventions for symptoms of depression and anxiety disorders in IAPT. The study is a parallel-groups, RCT examining the effectiveness and cost-effectiveness of iCBT interventions for depression and anxiety disorders, against a waitlist control group. The iCBT treatments are of 8 weeks duration and will be supported by regular post-session feedback by Psychological Wellbeing Practitioners. Assessments will be conducted at baseline, during, and at the end of the 8-week treatment and at 3, 6, 9, and 12-month follow-up. Participants in the waitlist control group will complete measures at baseline and week 8, at which point they will receive access to the treatment. All adult users of the Berkshire NHS Trust IAPT Talking Therapies Step 2 services will be approached to participate and measured against set eligibility criteria (score of ≥9 on PHQ-9

Study ID	Title	Study type	Narrative summary
	protocol for a randomised control trial		and/or a score of ≥8 on GAD-7 and internet suitability). Recruitment was supposed to being in June 2017 and last for 9 months. The EQ-5D-5L and Re-QOL questionnaires are included as well as clinical outcomes. The protocol states that: "Resource-use and subsequent costs will be estimated over the 12-month time horizon for the intervention group and for the 8-week waiting list time period for the control group. Healthcare resource will be valued using unit costs derived from available data sources." The Client Service Receipt Inventory (CSRI) is included which collects individuals' use of health and social care resources comprising questions about health care utilization including inpatient and outpatient hospital services, community-based day services, primary and community care contacts and employment status.
Kumar 2017 [62]	The Effectiveness of Internet-Based Cognitive Behavioral Therapy in Treatment of Psychiatric Disorders	Review	Literature search using PubMed and Google Scholar investigating ICBT's role in treating and controlling psychiatric illnesses which concludes that ICBT is useful in treating mental health and medical illnesses with psychiatric comorbidities and has also been found to be cost-effective for patients and society. The date of the search and methodology used is not clear. The review is focused on the implications for the rural US and of low relevance considering this. The cost-effectiveness papers included are Romero-Sanchez 2017 for major depression and Lenhard 2017 for paediatric OCD.
Lehtimaki 2021 [63]	Evidence on Digital Mental Health Interventions for Adolescents and Young People: Systematic Overview	Review	This review aimed to synthesize the current evidence on digital health interventions targeting adolescents and young people with mental health conditions, aged between 10-24 years, with a focus on effectiveness, cost-effectiveness, and generalizability to low-resource settings (e.g., low- and middle-income countries). The authors searched MEDLINE, PubMed, PsycINFO, and Cochrane databases between January 2010 and June 2020 for systematic reviews and meta-analyses. The authors included 18 systematic reviews and meta-analyses and found evidence on the effectiveness of computerized cognitive behavioural therapy on anxiety and depression, whereas the effectiveness of other digital mental health interventions remained inconclusive. Data on cost-effectiveness were not reported in any of the systematic reviews and meta-analyses in their sample. They concluded that widespread adoption and scale-up of digital mental health interventions, especially in settings with limited resources for health, will require more rigorous and consistent demonstrations of effectiveness and cost-effectiveness vis-à-vis the type of service provided, target population, and the current standard of care.
Peck 2007 [64]	Computer-guided cognitive– behavioural	Review	Narrative review which concludes that all the RCTs and other trials conducted to date indicate that outcomes using CCBT are comparable to those obtained with FTF treatment. CCBT programmes also appear to be cost-effective (based on the NICE review of TA51). However more

Study ID	Title	Study type	Narrative summary
	therapy for anxiety states		trials are needed, with greater numbers of participants and with FTF therapy as a comparator, to examine outcomes and cost-effectiveness in more detail.
Schroder 2016 [65]	Internet interventions for depression: new developments	Review	This review summarizes the current body of evidence and highlights pros and cons of Internet interventions. It considers that despite profound evidence for the efficacy of Internet interventions, it is yet to be shown that results can be transferred into routine clinical and that more research on the cost effectiveness of blended formats is needed.
Arnberg 2014 [66]	Internet-Delivered Psychological Treatments for Mood and Anxiety Disorders: A Systematic Review of Their Efficacy, Safety, and Cost-Effectiveness	SR	Systematic review funded by the Swedish Council on Health Technology Assessment of efficacy, safety and cost-effectiveness of internet delivered psychological treatments for mood and anxiety disorders. Searches conducted in March 2013 and used PubMed, Cochrane Library, CINAHL, PsycINFO, Psychology and Behavioural Sciences Collection (PBSC), TRIP database and CRD. Identified 52 RCTs of which 12 were excluded due to high risk of bias. Five cost-effectiveness studies were identified and three were excluded due to high risk of bias due to incomplete information on costs (Bergstrom 2010, Mihalopoulos 2005 and Titov 2009, none of which are included in the current review). The included trials mainly evaluated internet-delivered cognitive behavioural therapy (I-CBT) against a waiting list in adult volunteers and were primarily conducted in Sweden or Australia. For adults, the quality of evidence was graded as moderate for the short-term efficacy of I-CBT vs. waiting list for mild/moderate depression (d = 0.83; 95% CI 0.59, 1.07) and social phobia (d = 0.85; 95% CI 0.66, 1.05), and moderate for no efficacy of internet-delivered attention bias modification vs. sham treatment for social phobia (d =20.04; 95% CI 20.24, 0.35). The quality of evidence was graded as low/very low for other disorders, interventions, children/adolescents, noninferiority, adverse events, and cost-effectiveness. The two cost-effectiveness studies included were Hedman 2011 and Hollinghurst 2010 (assessed separately here) both of which were found to have a moderate risk of bias
Donker 2015 [67]	Economic evaluations of Internet interventions for mental health: a systematic review	SR	Systematic review funded by the Black Dog Institute, University of New South Wales, and VU University Amsterdam, of economic evaluations alongside RCTs for internet interventions for mental health. Searches covered 1990 - 2014 and used Medline, EMBASE, the Cochrane Central Register of Controlled Trials, NHS Economic Evaluations Database, NHS Health Technology Assessment Database, Office of Health Economics Evaluations Database, Compendex and Inspec. 16 papers met the inclusion criteria, 4 of which described treatment for depression (Warmerdam 2010, Hollinghurst 2010, Gerhards 2010 and Phillips 2014) and 4 of which described treatment or anxiety or panic disorders (Hedman 2011, Hedman 2012a, Bergstrom 2010 and Nordgren 2014).

Study ID	Title	Study type	Narrative summary
			In terms of quality the authors considered that ten of the included studies (62.5%) adhered to >=75% of the guidelines and therefore achieved a rating of good quality using the Drummond checklist rather than CHEERS (which the authors considered difficult to use). The authors conclude that "Results of guided Internet interventions being cost-effective are promising with most studies adhering to publication standards, but more economic evaluations are needed in order to determine cost-effectiveness of Internet interventions compared to the most cost-effective treatment currently available."
Halldorsson 2021 [68]	Annual research review: immersive virtual reality and digital applied gaming interventions for the treatment of mental health problems in children and young people: the need for rigorous treatment development and clinical evaluation	SR	Systematic review which found no studies providing data on the health economic outcomes for immersive virtual reality and digital applied gaming interventions for the treatment of mental health problems in children and young people with a cut-off publication date of 5th November 2019.
Hollis 2017 [69]	Annual research review: digital health interventions for children and young people with mental health problems - a systematic and meta-review	SR	Systematic review which found no studies providing data on the cost-effectiveness of digital health interventions in children and young people for anxiety and depression with a cut-off publication date of 1st November 2015.
Li 2022 [45]	Economic Evaluation of Cognitive Behavioural Therapy for Depression: A Systematic Review	SR	This review aimed to aimed to conduct a systematic review of cost-utility studies of internet-based and face-to-face cognitive behavioural therapy (CBT) for depression from childhood to adulthood. A structured search for cost-utility studies concerning CBT for depression was performed in 7 databases from their inception to July 2020. Two reviewers independently screened the literature, abstracted data, and assessed quality using the Consolidated Health Economic Evaluation Reporting Standards and Quality of Health Economic Studies checklists.

Study ID	Title	Study type	Narrative summary
			The primary outcome was the incremental cost-effectiveness ratio (ICER) across all studies. Cost data were inflated to the year 2020 and converted into US dollars. Thirty-eight studies were included in this review, of which 26 studies (68%) were deemed of high methodological quality and 12 studies (32%) of fair quality. Despite differences in study designs and settings, the conclusions of most included studies for adult depression were general agreement; they showed that face-to-face CBT monotherapy or combination therapy compared with antidepressants and usual care for adult depression were cost-effective from the societal, health system, or payer perspective (ICER 2$241 212.4/quality-adjusted life-year [QALY] to $33 032.47/QALY, time horizon 12-60 months). Internet-based CBT regardless of guided or unguided also has a significant cost-effectiveness advantage (ICER $37 717.52/QALY to $73 841.34/QALY, time horizon 3-36 months). In addition, CBT was cost-effective in preventing depression (ICER $23 932.07/QALY to $26 092.02/QALY, time horizon 9-60 months). A total of 15 studies reported the cost-utility of ICBT in the treatment of adults' depression from a social or health system perspective, with the time horizon from 3 to 60 months. The depressive symptoms of most participants were mild/moderate. Eleven studies showed that ICBT alone or combined with usual care was more cost-effective than usual care alone; of the 11 studies, 7 studies focused on guided ICBT, and the other 3 studies focused on unguided or minimally supported ICBT. In addition, 2 studies showed that guided ICBT did not seem to be any more cost-effective than usual general practice care. Another 2 studies compared the cost-effectiveness of guided ICBT with unguided ICBT for depression; 1 study showed guided ICBT was more cost-effective than unguided ICBT (guided ICBT was dominated), whereas the other study indicated that guided CBT was not more cost-effective than unguided informational websites. The evidence for the cost-effectiveness of CBT for children and adolescents was ambiguous. No ICBT studies were identified in children.
Musiat 2014 [70]	Collateral outcomes in e-mental health: a systematic review of the evidence for added benefits of computerized cognitive behaviour therapy interventions for mental health.	SR	Systematic review of the evidence for added benefits of computerized cognitive behaviour therapy interventions for mental health conducted in January 2013 using Medline and Web of Science. Thirteen of the included studies included some form of economic evaluation of the tested intervention 3 of which were for depression (Gerhards 2010, Hollinghurst 2010 and McCrone 2004). The first 2 are included separately in our review, the latter reported a comparison of iCBT + TAU with TAU which found that at $6168 per QALY: iCBT was cost-effective with 85% probability, at $18503 per QALY: iCBT cost-effective with 99% probability based on an economic evaluation alongside a RCT (n=174, 8 month follow-up, 12 general practices in SE England). The authors conclude that: "On balance, the results from the economic evaluation of e-mental health

Study ID	Title	Study type	Narrative summary
			interventions suggest that cCBT is a cost-effective alternative to usual care, achieving results that are similar to, or better than, usual care, at lower direct costs." Limitations noted were that studies did not include in their calculations those costs that are required to be met by the patients and none of the studies reported the development costs of the intervention nor license costs nor incorporated them into the cost-effectiveness analysis despite these being potentially significant.
Ophuis 2017 [40]	Cost-effectiveness of interventions for treating anxiety disorders: A systematic review	SR	This systematic review aimed to provide an overview of the evidence regarding the cost-effectiveness of interventions for anxiety disorders. The review was conducted using PubMed, PsycINFO, NHS-EED, and the CEA registry. They included full economic evaluations on interventions for all anxiety disorders published before April 2016, with no restrictions on study populations and comparators. Preventive interventions were excluded. The quality of the studies was appraised using the Consensus on Health Economic Criteria. 42 studies were included. The studies were heterogeneous and the quality was variable. Internet-delivered cognitive behavioural therapy (iCBT) appeared to be cost-effective in comparison with the control conditions. Four out of five studies comparing psychological interventions with pharmacological interventions showed that psychological interventions were more cost-effective than pharmacotherapy. Comparability was limited by heterogeneity in terms of interventions, study design, outcome and study quality. The majority of the studies (n=38) targeted adult patients, although four studies focused on other age categories. Bodden et al. (2008) included children aged 8–18 years, Gospodarevskaya and Segal (2012) included sexually abused children in a hypothetical cohort with a baseline age of 10 years. One study included both adults and children younger than 16 years (Mihalopoulos et al., 2015).

Abbreviations: CCBT, Computerised Cognitive Behavioural Therapy; CHEERS, Consensus on Health Economic Evaluation Reporting Standards; EE, Economic Evaluation; FCBT, Face-to-Face Cognitive Behavioural Therapy; FTF, Face to Face; HTA, Health Technology Assessment; iCBT, Internet Cognitive Behavioural Therapy; ICER, Incremental Cost-Effectiveness Ratio; NIHR, National Institute for Health and Care Research; OCD, Obsessive-Compulsive Disorder; QALY, Quality Adjusted Life Year; RCT, Randomised Controlled Trial; SG, Standard Gamble

12.2 *Conceptual modelling*

Following is an early cost utility analysis and value of information analysis of four dCBT interventions and treatment as usual / status quo to treat Children and Young People with mild/moderate anxiety and low mood. The primary purpose is to assess whether there is a plausible *prima facie* case for cost-effectiveness of the dCBT technologies in CYP with mild/moderate anxiety and low mood, and to identify where there is greatest value in future research to reduce uncertainty.

This highly simplified decision analysis draws heavily on a previous modelling study comparing the cost-effectiveness of pharmacotherapy and CBT in adults with moderate to severe depression.[71] This includes relapse at various time points and so allows the impact of this to be quantified both on point estimate cost-effectiveness and on decision uncertainty.

The model structure is shown in Figure 1. Briefly, there are three branches from each node, defined according to RCADS-P t-score. The RCADS-P authors[72] suggest that a t score >70 indicates a referral threshold, a score of 65-69 is borderline and below 65 normal functioning. As RCADS-P was measured across all source studies, the model is driven by this, with a t-score above 70 analogous to 'full response', 65-69 to 'partial response' and below 65 to 'no response'. The model assesses response at three time points: 3, 6 and 12 months. The interventions are scheduled to last between 8-14 weeks, thus a 3-month (12 week) time point approximates an evaluation at the end of the intervention. The overall time horizon of the model is 12 months.

The model does not explicitly analyse discontinuations / drop-out from the dCBT courses. This is because data in the available RCT[23] is analysed on the intention to treat basis. It is unclear how available cohort studies[22 24] accounted for drop-outs in their analyses. It was therefore considered expedient for the purposes of this early model to draw on ITT data, without separate modelling of discontinuations.

Figure 1 Model structure

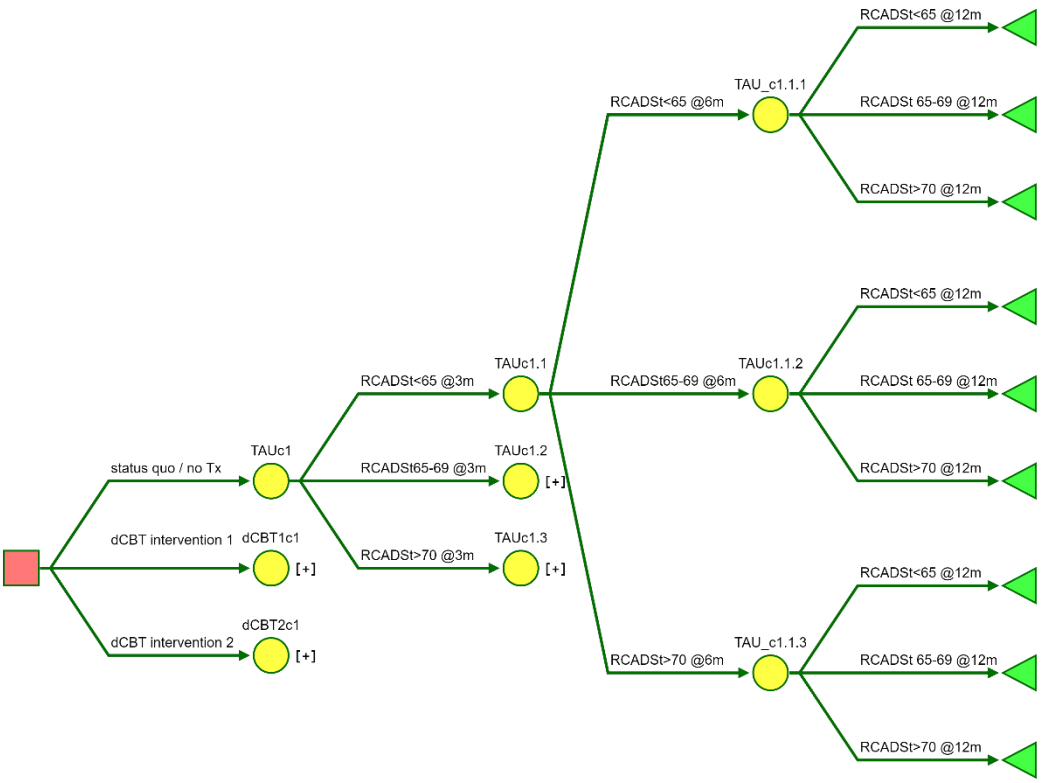

Figure shows decision node with TAU (status quo / no treatment), and two possible dCBT comparators. Chance nodes are labelled TAUc1, TAUc1.1 etc for ease of modelling. RCADSt refers to RCADS-P t-score at each time point (3, 6 and 12months). RCADSt<65 represents full response, t65-69 partial response and t>=70 no response. [+] indicates tree is identical to section above but is collapsed for clarity. Figure drawn with Silver Decisions.[73]

12.2.1 Comparators

We conduct an early economic evaluation of four dCBT interventions and 'treatment as usual' / status quo (TAU, assumed to be no intervention). Due to a lack of comparative data, face to face CBT is not included in this analysis, but noted as a critical evidence gap. SilverCloud and OSCA are aimed at adolescents aged 14 or 15 to 18 years, whereas OSI and Lumi Nova are aimed at children ages 5-12 and 7 to 12 respectively. We therefore divide the population into two groups as per the NICE scope: child (nominally 5-11 years) and adolescent (nominally 12-18 years). The analysis compares TAU vs OSI vs Lumi Nova in the child age group and TAU vs SilverCloud vs OSCA in the adolescent group.

12.2.2 Model Inputs

12.2.2.1 Clinical Parameters

Clinical parameters required in the model are the proportion of participants with full, partial and no response at 3, 6 and 12 months post baseline. As described above, all source studies used in the economic model collected the RCADS-P t-score as part of their outcomes suite. We therefore focus on this as the definition of full, partial and no response. The most robust approach to comparing each intervention would be a single, long term, multi-arm RCT. However, failing this a network meta-analysis would enable indirect comparisons adjusting for differences in the enrolled populations. As there is only one RCT in the evidence base, this is not possible. Furthermore, a matching adjusted indirect comparison (MAIC) is also not possible without individual patient data (IPD). Our analysis is therefore based on a crude naïve comparison of changes in RCADS-P t-scores over time (Table 17), from which the proportion of participants expected to be in full, partial and no response was estimated.

Briefly, for the TAU arm, the probabilities of the t score exceeding 70, being between 65-69 and below 65 at post treatment (assumed to be 3 months) were evaluated assuming a Normal distribution with a mean and standard deviation as reported in Leigh and Clark.[23] A Dirichlet distribution was assigned around this, based on the sample size in the waiting list arm.

For example, at post treatment, 21 patients had a mean (SD) RCADS-P of 52.99 (17.13). A Normal distribution with these parameters has a 75.8% probability of t<65, 8.1% probability of 65>t<70, and 16.0% probability of t>69. A Dirichlet distribution with these mean probabilities and overall sample size of 21 has the parameters (15.93, 1.71, 3.37).

Leigh & Clark[23] reported an adjusted mean (standard error) difference in RCADS-P between control and the OSCA arm of -22.56 (6.32). The mean in the OSCA arm was therefore assumed to be (52.99 – 22.56 =) 30.43. The standard deviation was assumed the same in the OSCA arm as per the waitlist control. Assuming a Normal distribution, the proportions of participants with

RCADS-P in the three cut-off zones is (97.8%, 1.1%, 1.0%). For a sample size of 22 patients, this yields a Dirichlet distribution of (21.52, 0.25, 0.23).

As no data are available for six- and 12-month follow up, Dirichlet distributions were assigned with the parameters divided by an arbitrary factor of 10 to represent the added uncertainty.

A cohort study of the OSI software[22] showed a difference in RCADS-P t score from baseline to follow up of -13.62. This was subtracted from the baseline score observed in the waitlist control arm of Leigh and Clark[23] of 42.53 to yield an adjusted mean of 28.91 post treatment in the OSI cohort. The standard deviation was assumed the same as at baseline (16.39). Assuming a Normal distribution and sample size of 18, this yielded a Dirichlet(17.75, 0.14, 0.11). As above, due to the lack of longer term data, the same means but with Dirichlet parameters divided by 10 were assigned to the 6 and 12 month follow-up points.

We were unable to extract appropriate data from the cohort study of the Lumi Nova software,[24] and to date no data are published for the SilverCloud software. We therefore assumed equal point estimate effectiveness for these as the OSI software, but with parameters of Dirichlet distributions divided by 10 reflecting the lack of data.

Evidence gap: Preferably directly comparative data of TAU vs OSI vs Lumi Nova in children and TAU vs SilverCloud vs OSCA in adolescents (new trials required). In interim, individual patient data of existing studies would allow a patient level meta-analysis.

Evidence gap: How should the decision model incorporate discontinuations / withdrawals?

Evidence gap: Is the RCADS-P the most appropriate tool on which to base health related quality of life?

Critique: All studies have different follow-up times, but these are equated to 3m for the model.

Critique: No comparative data are available. Comparisons are crudely adjusted between the studies.

Table 17 Main clinical parameters

Variable	Mean (%)	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
Full, partial and no response at 3m, TAU	(76%, 8%, 16%)	Dirichlet (15.93, 1.71, 3.37)	Extrapolated from clinical evidence[23]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 6m, TAU	(76%, 8%, 16%)	Dirichlet (1.593, 0.171,0.337)	Extrapolated from clinical evidence [23]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 12m, TAU	(76%, 8%, 16%)	Dirichlet (1.593, 0.171,0.337)	Extrapolated from clinical evidence [23]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 3m, OSCA	(99%, 1%, 0%)	Dirichlet (21.52, 0.25, 0.023)	Extrapolated from clinical evidence [23]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 6m, OSCA	(98%, 1%, 1%)	Dirichlet (2.152, 0.025, 0.023)	Extrapolated from clinical evidence [23]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 12m, OSCA	(98%, 1%, 1%)	Dirichlet (2.152, 0.025, 0.023)	Extrapolated from clinical evidence [23]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 3m, OSI	(99%, 1%, 0%)	Dirichlet (17.75, 0.14, 0.11)	Extrapolated from clinical evidence[22]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 6m, OSI	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	Extrapolated from clinical evidence[22]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 12m, OSI	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	Extrapolated from clinical evidence[22]	Naïve, unadjusted comparison. Very high risk of bias

Variable	Mean (%)	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
Full, partial and no response at 3m, LumiNova	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	Estimated, unable to extract data from source[24]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 6m, LumiNova	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	Estimated, unable to extract data from source[24]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 12m, LumiNova	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	Estimated, unable to extract data from source[24]	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 3m, SilverCloud	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	No published data. Estimated.	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 6m, SilverCloud	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	No published data. Estimated.	Naïve, unadjusted comparison. Very high risk of bias
Full, partial and no response at 12m, SilverCloud	(99%, 1%, 0%)	Dirichlet (1.775, 0.014, 0.011)	No published data. Estimated.	Naïve, unadjusted comparison. Very high risk of bias

12.2.2.2 Resource use and cost

All dCBT interventions by definition require access to computing equipment and an internet connection. In order to address equity concerns around digital exclusion, the cost of a tablet computer and mobile internet connection for the duration of the interventions is included as a resource use item for all interventions.

SilverCloud comprises seven core modules, based on a previously developed adult dCBT intervention. A check-in session is included after each module with a psychologist or CBT co-ordinator. The time span over which the modules are to be completed is unclear, but for the purposes of this analysis we assume an

eight week 'treatment period'. **OSI** comprises eight weekly modules (numbered zero to 6, plus final follow-up), each taking around 30 minutes of the child's time, completed over the 8 week treatment period. Each module includes a 20 minute telephone session between parent/guardian and a therapist.[22] **OSCA** is a 14 week course, with eight modules to be worked through in the first two weeks, and up to 16 additional modules over the remaining 12 weeks, tailored to the needs of the user. Participants have weekly 20-minute phone calls with their therapist, supplemented with tailored SMS messaging and within-software messaging. Support within the clinical trial[23] was provided by clinical psychologists, but it is unknown whether this can be delivered by a less specialist therapist. **Lumi Nova** is a game-centred app that can be downloaded onto a tablet or mobile phone, with parent/guardian involvement through SMS notifications triggered by the child's progress through the game. Time spent on the game by the child is limited to 40 minutes per day after the initial tutorial session. Progress summaries are available through the 'VitaMind Hub' to authorised professionals for monitoring and guiding care. A pilot prospective cohort study evaluated outcomes after an 8-week period of game play.[24] Frequency of interactions with health care professionals are not stated, but for the purpose of this analysis we assume a weekly 20 minute contact.

Licensing costs per user are not finalised for some of the software packages. We therefore assume all are of a similar price, varied between [redacted] and [redacted] per user per programme.

Based on the descriptions above, resource use assumptions for each intervention are summarised in Table 18 and unit costs presented in Table 19.

Table 18. Resource items and quantities for interventions

	SilverCloud	OSI	OSCA	Lumi Nova
Duration of intervention	8 weeks	8 weeks	14 weeks	8 weeks
Resource items	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone
	Internet connection (8 wks)	Internet connection (8 wks)	Internet connection (16 wks)	Internet connection (8 wks)

	SilverCloud	OSI	OSCA	Lumi Nova
	8x20minute telephone call with therapist	8x20minute telephone call with therapist	14x20 minute telephone call with clinical psychologist	8x20 minute telephone call with therapist.

Abbreviations: OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, Online support and intervention for anxiety

Table 19. Unit costs

Item	Point estimate Cost	Distribution	Source / Notes
Per user licence, software	[redacted]	U[redacted]	Notional per user costs.
Tablet computer or smart phone	£80	N(80,8)	Representative cost from large online retailer, September 2022. 10" Android tablet with sim card slot. A basic smart phone is similar cost
Data sim card, per month	£20	N(20,2)	Representative cost from price comparison website, September 2022. Unlimited 5G data-only plan, 1m contract
Telephone consultation with therapist	£33.67	N(33.67,3,37)	Unit Costs of Health and Social Care 2021, Section 6.10 (p80). Reported cost per client-related hour £101 to provide counselling service for children with mental or emotional difficulties. Assuming 20 minute consultation (prep included within the 20 minutes)
Telephone consultation with clinical psychologist	£41	N(41,4.1)	Unit Costs of Health and Social Care 2021, Section 14 (p141). Cost per working hour, psychiatric consultant £123 (assumed same cost as clinical psychologist). Assuming 20 minute consultation.

Abbreviations: N, Normal distribution; U, Uniform distribution

12.2.2.3 Health State Utilities

A search of the Tufts CEA database[74] with the terms 'mild' and 'depression' yielded no directly relevant health state utility data in the population of interest. However, an economic evaluation of St. John's Wort in mild to moderate depression,[75] drawing on health state valuations from a previous study[76] was identified. The difference between response and remission in the Solomon study was a utility gain of 0.13. We therefore assumed the utility of full response

to be 1, of no response to be 0.83, and partial response 0.9. Arbitrary standard errors were assigned around these (Table 20).

Evidence gap: Health state utility data for mild/moderate anxiety and low mood in children and young people.

Methods gap: What is the most appropriate HRQoL tool for estimating health state utilities in children and young people with mild/moderate anxiety and low mood?

Table 20 Health State Utilities

Health State	Mean (SE)	Distribution	Source
Full response	1 (0)	[Constant]	Assumption
Partial response	0.9 (0.1)	B(7.2, 0.8)	Adapted from Soloman 2013 and Sapin 2004.
No response	0.83 (0.2)	B(2.1, 0.43)	Adapted from Soloman 2013 and Sapin 2004.

Abbreviations: B, Beta distribution; SE, standard error

12.2.3 Approach to Analysis

The decision model is written in R.[77] We conduct a cost utility analysis reporting net benefit at a willingness to pay threshold of £20,000 per QALY gained, analysis of uncertainty and value of information analysis (conducted using the Sheffield Accelerated Value of Information Analysis package[78]). Probabilistic analyses are presented in all cases with 100,000 simulations from input distributions.

12.3 *Results from the economic modelling*

Mean cost, QALYs and net benefit (+/-95%CI) at a willingness to pay threshold of £20,000/QALY are reported in section 12.3.1. One way sensitivity analyses exploring the impact of the cost of a telephone consultation with low and high cost staff, and the per-user licence cost of the dCBT interventions are in Section 12.3.2. Finally, a value of information analysis reporting the per-participant EVPI and EVPPI for outcomes data, unit costs and health state utilities are in

Section 12.3.3. A brief commentary follows in Section 12.3.4. Results are presented for the child and adolescent populations.

12.3.1 Base Case Results

Table 21 Base case results - Child

	TAU	OSI	Lumi Nova
Cost	[redacted]	[redacted]	[redacted]
QALYs	[redacted]	[redacted]	[redacted]
Mean NB@£20,000	[redacted]	[redacted]	[redacted]
95%CI	[redacted]	[redacted]	[redacted]

Abbreviations: CI, confidence interval; NB, net benefit; OSI, Online support and intervention for anxiety; QALY, quality-adjusted life years; TAU, treatment as usual

Table 22 Base case results - Adolescent

	TAU	SilverCloud	OSCA
Cost	[redacted]	[redacted]	[redacted]
QALYs	[redacted]	[redacted]	[redacted]
Mean NB@£20,000	[redacted]	[redacted]	[redacted]
95%CI	[redacted]	[redacted]	[redacted]

Abbreviations: CI, confidence interval; NB, net benefit; OSCA, Online Social anxiety Cognitive therapy for Adolescents; QALY, quality-adjusted life years; TAU, treatment as usual

12.3.2 One-way sensitivity & scenario analyses

Table 23 Scenario analysis, cost of telephone consultations - Child

	TAU	OSI	Lumi Nova
Base	[redacted]	[redacted]	[redacted]
Low therapist cost	[redacted]	[redacted]	[redacted]
High therapist cost	[redacted]	[redacted]	[redacted]

Abbreviations: OSI, Online support and intervention for anxiety; TAU, treatment as usual

Table 24 Scenario analysis, cost of telephone consultations - Adolescent

	TAU	SilverCloud	OSCA
Base	[redacted]	[redacted]	[redacted]
Low therapist cost	[redacted]	[redacted]	[redacted]
High therapist cost	[redacted]	[redacted]	[redacted]

Abbreviations: OSCA, Online Social anxiety Cognitive therapy for Adolescents; TAU, treatment as usual

Figure 2 Net Benefit as a function of per-user licence cost

[redacted]

12.3.3 Value of information analysis

Table 25 Value of Information Analysis - Child

Parameters	Per person EVPPI	Approx. Standard error
EVPPI, Effectiveness	157.41	7.50
EVPPI, Unit costs	4.35	4.77
EVPPI, Health state utilities	119.19	1.42
EVPI	181.30	-

Abbreviations: EVPPI, Expected Value of Perfect Parameter Information; EVPI, Expected Value of Perfect Information

Table 26 Value of Information Analysis - Adolescent

Parameters	Per person EVPPI	Approx Standard error
EVPPI, Effectiveness	109.12	7.65
EVPPI, Unit costs	0.00	0.20
EVPPI, Health state utilities	118.58	1.45
EVPI	170.50	-

Abbreviations: EVPPI, Expected Value of Perfect Parameter Information; EVPI, Expected Value of Perfect Information

12.3.4 Commentary

The evidence base in this early value assessment is too uncertain to draw any inferences around whether one dCBT intervention is more or less cost-effective than another. However, the EAG notes that there is a trend towards their being more effective than TAU, and that this is probably achieved at a cost that would

be considered value for money given conventional willingness to pay thresholds (generally yielding a higher net benefit than TAU, Section 12.3.1). OSCA is a longer course than the other dCBT interventions (14 weeks vs 8), thus explaining the higher cost. However, the evidence is too uncertain to know whether the longer course leads to higher effectiveness. The EAG notes that OSCA is the only intervention with an RCT, and the cohort studies are not adjusted for drop-out whilst the OSCA results are based on ITT, and therefore the relative effectiveness estimates are at very high risk of bias.

The one-way sensitivity analyses (Section 12.3.2) show that the results are relatively insensitive to whether a therapist or clinical psychologist provides telephone support, or the per participant licence cost (within the bounds considered). The key driver is the longer course length with one of the interventions. Finally, the value of information analysis is consistent with the evidence gap analysis: future research is of value into the relative effects of the dCBT interventions, as well as health state utilities.

13 Interpretation of the evidence

13.1 *Interpretation of the clinical and economic evidence*

Currently there is an absence of evidence to assess whether one dCBT intervention is more or less effective than another. The single RCT[23] suggests the OSCA intervention is more effective than a waiting list control in terms of anxiety symptom severity (indeed, waiting list controls showed a deterioration over time), and before-and-after cohort analyses of OSI and Lumi Nova[22 24] suggest an improvement in anxiety symptom severity over time. At present there is no peer-reviewed evidence published on the SilverCloud interventions.

In summary, there is weak evidence to suggest the guided dCBT interventions may better than TAU, but it is unknown whether there is a difference between individual interventions. The effectiveness compared with active controls (e.g. face to face CBT) is unknown.

Costs of the different interventions are broadly similar and fairly minimal, the key components being licensing costs and mental health professional contact

time for weekly telephone calls. It is unknown whether the qualifications of the professional affect effectiveness (e.g., mental health team member vs clinical psychologist), although exploring the impact on cost alone does not appear to lead to a large impact on cost-effectiveness (at least within the ranges considered and within this early, crude model).

The biggest issue affecting cost-effectiveness is the duration of the intervention. OSCA is scheduled over a 14-week period, whilst Lumi Nova, OSI and the SilverCloud interventions are scheduled over 8 weeks. It is unknown whether the shorter duration of the latter three lead to poorer outcomes, or whether the longer duration of the former simply increases cost.

13.2 *Integration into the NHS*

The EAG identified two completed studies (Hill et al. (2022a)[21] and Hill et al. (2022b)[22]) and two ongoing studies, Taylor et al. (2022, ISRCTN12890382)[30] and

‘[redacted]’ (Lumi Nova), that provided direct evidence of use in the NHS. These studies describe research conducted in several NHS clinics, one Foundation Trust and NHS-funded mental health services for CYP. Some patients were selected on the basis of having previously received face-to-face versions of the technology (Hill et al. (2022b)[22]), but most were selected based on their presentation to NHS clinics and subsequent diagnosis following routine clinical assessment or within CAMHS following a diagnosis of anxiety as the primary presenting problem.

All other studies were conducted in school settings, though the EAG noted that these were all conducted, or planned to be conducted, in England. Therefore, it considered these to be indirect but reasonably generalisable settings to indicate integration into the NHS.

The EAG did not identify any significant barriers to adoption of dCBT for children and young people with symptoms of mild/moderate anxiety and low

mood, and could be readily added to existing CAMHS provision. The major limitation would be availability of therapists / mental health workers to provide the weekly contacts all the interventions require. If a school mental health team member or similar is able to provide support to the required level, this will be less of a barrier than if the specialist skills of, say, a clinical psychologist are required.

Those providing the support will require training in the specific dCBT interventions. The level of training provided by suppliers of the systems is varied, but would need to be clarified prior to any supply contract being enacted.

13.3 *Ongoing studies*

The EAG identified four ongoing studies from the literature, all investigating OSI (Reardon et al. (2022a), Reardon et al. (2022b), Reardon et al. (2022c), and Taylor et al. (2022)),[26 28-30] as well as two ongoing studies investigating Lumi Nova. Full details are available in Table 2.

The EAG noted that these studies were generally more aligned with the NICE scope, mostly including comparators and, in one case, an active comparator (Taylor et al. (2022)[30]). Participants, settings and outcomes were considered to map well to the NICE scope, though one study did not state the intention to measure RCADS-P and one did not state the intention to report on any scoped outcomes. These studies, arranged in order of relevance in terms of scope and availability of RCADS-P outcome data that can be used in economic modelling, are presented in Table 27 along with the indicated end dates.

Table 27 Ongoing studies investigating OSI and Lumi Nova, arranged in descending order of relevance in terms of scope and availability of data for economic modelling

Intervention	Ongoing study	Alignment with scope	Outcome data for economic model	Indicated trial end date
OSI	Protocol: Taylor et al (2022) Linked reference:	Intervention: **GREEN** Comparator: **GREEN** Participants: **GREEN**	Yes	31/03/2023

Intervention	Ongoing study	Alignment with scope	Outcome data for economic model	Indicated trial end date
	ISRCTN12890382 (2020)	Setting: **GREEN** Outcomes: **GREEN**		
OSI	Protocol: Reardon, Ukoumunne, Violato, et al (2022c) Linked reference: ISRCTN76119074 (2021)	Intervention: **GREEN** Comparator: **AMBER** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	Yes	30/11/2024
OSI	Protocol: Reardon, Dodd, Hill, et al. (2022b) Linked references: Jones et al. (2022); ISRCTN82398107 (2021)	Intervention: **GREEN** Comparator: **AMBER** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	No	31/08/2023
Lumi Nova	Ongoing manufacturer data collection: [redacted]	Intervention: **GREEN** Comparator: **RED** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	Yes	[redacted]
OSI	Protocol: Reardon, Ball, Breen, et al. (2022a) Linked reference: ISRCTN30032471 (2021)	Intervention: **GREEN** Comparator: **RED** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	Yes	30/11/2021
Lumi Nova	Ongoing manufacturer data collection: [redacted]	Intervention: **GREEN** Comparator: **RED** Participants: **GREEN** Setting: **GREEN** Outcomes: **RED**	No	[redacted]

Abbreviations: ISRCTN, International Standard Randomised Controlled Trial Number; OSI, Online support and intervention for anxiety

In addition, the EAG was made aware of the following studies in progress for SilverCloud:

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

13.4 *Evidence gap analysis*

A summary of evidence gaps, pertaining to the intermediate and final outcomes from the scope, and those pertaining to decision modelling are summarised in Table 28.

Table 28 Evidence Gap Analysis

Outcomes	SilverCloud interventions	OSCA	OSI	Lumi Nova
Clinical trials				
Intermediate outcome: Intervention-related adverse events	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	No **RED**	Yes, single-arm evaluation **RED**
Intermediate outcome: Rates of and reasons for attrition	No studies **RED**	Yes, rates only, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, rate only, single-arm evaluation **RED**
Intermediate outcome: Treatment satisfaction and engagement	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series, feasibility study and formative research **RED**	Yes, single-arm evaluation **RED**
Clinical outcome: Symptom severity (self/parent/practitioner reported)	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, single-arm evaluation **RED**
Clinical outcome: Social, behavioural and functional outcomes (self/parent/practitioner reported)	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, single-arm evaluation **RED**

Clinical outcome: Suicidal thoughts and behaviour	No studies **RED**	No **RED**	No **RED**	No **RED**
Clinical outcome: Global functioning	No studies **RED**	No **RED**	Yes, single-arm case series and feasibility study **RED**	No **RED**
Clinical outcome: Rates of remission	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series **RED**	No **RED**
Patient reported outcomes: HRQoL	No studies **RED**	No **RED**	Yes, single-arm feasibility study **RED**	No **RED**
Patient reported outcomes: Patient experience	No studies **RED**	No **RED**	Yes, single-arm case series and feasibility study **RED**	No **RED**
Resource use and costs	No studies **RED**	No **RED**	Yes, use and cost of other resources, single-arm feasibility study **RED**	No **RED**
Real-world evidence				
Intermediate outcome: Intervention-related adverse events	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Intermediate outcome: Rates of and reasons for attrition	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Intermediate outcome: Treatment satisfaction and engagement	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Symptom severity (self/parent/practitioner reported)	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome:	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**

Social, behavioural and functional outcomes (self/parent/practitioner reported)				
Clinical Outcome: Suicidal thoughts and behaviour	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Global functioning	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Rates of remission	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Patient reported outcomes: HRQoL	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Patient reported outcomes: Patient experience	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Resource use and costs	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Models and economic outcomes				
Effectiveness evidence: Comparative data	No direct or indirect comparisons of effect of the target interventions (and TAU). Is one dCBT intervention more effective than another and TAU? **RED**			
Effectiveness evidence: Comparative data	Is one dCBT intervention more effective than another and face to face CBT? **RED**			
Effectiveness evidence: Follow-up times and lengths	Follow-up times vary across the source studies, which are crudely equalized to 3m in the decision model. Common FU times are required, along with longer term follow-up data (to 12m+). **RED**			
Effectiveness evidence: Discontinuations / withdrawals	Withdrawals are currently accounted for via ITT analyses of RCADS-P. Should they be modelled specifically? **AMBER**			
Clinical outcome and costs: Qualifications of mental health contact	Is a mental health support worker as effective as a clinical psychologist at providing weekly contacts? **AMBER**			
HRQoL: Estimating health state utilities	Is RCADS-P the most appropriate tool on which to base health state utilities for CYP? What other tools are there for measuring and valuing mild/moderate anxiety and low mood in CYP? **RED**			

Abbreviations: (d)CBT, (digital) cognitive behavioural therapy; CYP, children and young people; FU, follow-up; HRQoL, health-related quality of life; ITT, intention to treat; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, online support and intervention for child anxiety; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– child/parent report); RCT, randomised controlled trial; TAU, treatment as usual

13.5 *Summary and conclusions of evidence gap analysis*

Several evidence gaps were identified by the EAG, as summarised below.

Study design gaps:

- Two (or multi-) arm randomised controlled trials for all technologies. Three ongoing studies have been identified to address this gap for OSI.
- Blinding of outcome assessors in studies of all technologies. No ongoing studies have been identified to address this gap.
- Appropriate accounting for missing data due to attrition using intention-to-treat analyses and multiple imputation of missing data. One study has been identified to address this gap for OSI.

Population gaps:

- Evidence for the effectiveness of technologies on low mood. One ongoing study has been identified to address this gap for OSI.
- Evidence for the effectiveness of technologies on anxiety and/or low mood in young people aged 12 to 18 years. No ongoing studies have been identified to address this gap.
- Evidence for the effectiveness of technologies on anxiety and/or low mood in children and young people with neurodevelopmental conditions. No ongoing studies have been identified to address this gap.

Intervention gaps:

- Clinical trial evidence for the SilverCloud interventions. No ongoing studies have been identified to address this gap.
- Real-world evidence for all technologies. No ongoing studies have been identified to address this gap.

Comparator gaps:

- Comparative evidence using active comparators for all outcomes across technologies. One ongoing study has been identified to address this gap for OSI.
- Comparative evidence for all outcomes across technologies. Two ongoing studies have been identified to address this gap for OSI.

Outcome gaps:

- Evidence on suicidal thoughts and behaviour for all technologies. No ongoing studies have been identified to address this gap.

- Homogeneity in reported outcome measures. RCADS-P has been identified as a common outcome for symptom severity in completed studies. Three out of four ongoing studies for OSI and two ongoing studies for Lumi Nova have been identified as measuring RCADS-P.

Decision modelling gaps:

- The most appropriate approach to measuring and valuing health states is unclear. The early decision model makes use of RCADS-P due to it being reported across relevant studies. However, other HRQoL tools may be more appropriate.

- It is unknown whether a mental health support worker or similar is as effective as a clinical psychologist in delivering the 'guidance' in guided dCBT. The impact on cost-effectiveness is unclear.

13.6 *Key areas for evidence generation*

The EAG identified a number of evidence generation recommendations. These are summarised in Table 29.

Table 29 Evidence generation recommendations

Research question	Recommended study design	Outcomes
1. What is the most appropriate tool to measure health related quality of life in CYP with mild/moderate anxiety and/or low mood that can be mapped to a health state utility for decision modelling purposes?	Systematic review, structured interviews with relevant experts.	Summary of strengths and weaknesses of different tools, ability to map to health state utilities. Recommendations for data collection in clinical trials.
2. What is the relative effectiveness of all dCBT interventions compared with each other, active control (e.g., face to face CBT) and no treatment control for anxiety and/or low mood?	Ideally a multi-arm RCT with all comparators. Failing this series of RCTs comparing technologies with active comparators can be meta-analysed. Evidence against active comparators is needed, in particular, for OSCA, Lumi Nova and the SilverCloud interventions. Follow-up of 12 months or longer.	Existing standard tools plus health-related quality of life tool identified in (1) above. Discontinuations and adverse events, particularly suicidal

	Studies should be conducted in children as well as adolescents, or include both these groups and explore subgroup effects.	ideation and behaviours.
3. Is a mental health support worker as effective as a clinical psychologist at providing weekly contacts?	Ideally RCT of all dCBT interventions with two different support. However, this could be conducted as part of a service evaluation or stepped-wedge study design	As per (2)

Abbreviations: (d)CBT, (digital) cognitive behavioural therapy; CYP, children and young people; FU, follow-up; OSCA, Online Social anxiety Cognitive therapy for Adolescents; RCT, randomised controlled trial

14 Conclusions

14.1 *Conclusions from the clinical evidence*

Among completed studies, there is a paucity of evidence to assess whether dCBT interventions are better than comparator treatment, with only one study on OSCA suggesting a modest effect compared to waitlist control. No current evidence is available to assess the effectiveness of dCBT compared to an active comparator, though the EAG noted that one such study on OSI is due to be completed in the first quarter of 2023. No prospective studies with comparator arms, active or not, were identified for any of the other technologies. No existing or planned analyses of important subgroup effects were identified, with the exception being stated intent [redacted] in an ongoing study investigating Lumi Nova. The EAG noted, however, that all included evidence fits broadly into the NICE-scoped subgroup of children aged 5 to 11.

No evidence investigating the SilverCloud interventions (Space from anxiety for teens, Space from low mood for teens, Space from anxiety and low mood for teens) was identified in the literature, although the EAG was alerted to several in-progress evaluations and a pilot RCT due to begin recruitment in September 2022. No evidence regarding the effect of any included technology on low mood, or evidence of the effect of any included technology on anxiety and/or

low mood in young people aged 12 to 18, were identified. The EAG also did not identify any planned or ongoing studies that would address this research gap.

Included studies with available data generally suffered from methodological limitations, therefore the possibility of biased estimates of treatment effect could not be ruled out.

14.2 *Conclusions from the economic evidence*

There is weak evidence to suggest dCBT interventions in CYP may be more effective than TAU. Costs of implementing are minimal, the key factor being the provision of the weekly follow-up calls with the CYP. The greatest value is to be obtained from research into the effectiveness of dCBT interventions relative to one another and to either no treatment or active control (such as face to face CBT), and health state utilities.

Other key research requirements are around assessing most-appropriate tool for measuring health related quality of life in CYP. The decision model draws on RCADS-P for expedience as it was measured across all interventions. However, a generic tool such as EQ-5DY or CHU-9D would increase comparability with other diverse interventions, although these may be less sensitive to changes in condition-specific dimensions. The longer-term (to 12m) effectiveness of all interventions is unknown, therefore any RCTs should plan follow-up to at least this length.

15 Summary of the combined clinical and economic sections

The only RCT of guided dCBT in children and young people is for OSCA, compared to a waiting list control. This suggests evidence of effectiveness, but there are no comparative studies of different dCBT interventions: the evidence base is limited to prospective cohort studies. Studies are underway on OSI, and the EAG has been made aware of a number of service evaluations and a pilot RCT of SilverCloud.

Early decision modelling suggests there is a *prima facie* case for guided dCBT interventions to be cost-effective compared with do-nothing / TAU, but it is unknown whether one intervention is more cost-effective than another.

Key evidence requirements are assessment of the most appropriate health related quality of life tool on which to measure health state utility, estimates of the relative effect of the interventions over the short and long (12 months +) term, and whether the 'guidance' in guided dCBT can be provided equally well by a mental health support worker as by a trained clinical psychologist or other specialist.

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17 Appendices

17.1 *Appendix A: Searches for clinical effectiveness evidence*

A summary of the resources searched for clinical effectiveness evidence is presented in Table 30.

Table 30. Resources searched for clinical effectiveness studies

Database/Resource	Host	Date range	Date Searched	Results
MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily	Ovid	1946 to August 25, 2022	26.8.22	704
Embase	Ovid	1974 to 2022 Week 33	26.8.22	722
APA PsycINFO	Ovid	1806 to August Week 3 2022	26.8.22	423
CDSR	Cochrane Library: Wiley	Issue 8 of 12, August 2022	26.8.22	12
CENTRAL	Cochrane Library: Wiley	Issue 7 of 12, July 2022	26.8.22	498
INAHTA HTA database	https://database.inahta.org/	up to 26 August 2022	26.8.22	15
KSR Evidence	www.ksrevidence.com	Database last updated 26 August 2022	26.8.22	91
Epistemonikos	https://www.epistemonikos.org	up to 26 August 2022	26.8.22	157
ClinicalTrials.gov	http://www.clinicaltrials.gov/	up to 26 August 2022	26.8.22	245
WHO ICTRP	https://trialsearch.who.int/	up to 26 August 2022	26.8.22	81
Total records retrieved			**2948**	
Total records after deduplication			**1519**	

The exact search strategies for identifying clinical effectiveness evidence are presented below.

MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid): 1946 to August 25, 2022; Searched: 26.8.22

1 ("online support and intervention" or iCATS or MY CATS or Co CAT).ti,ab. (45)
2 (("Online Social anxiety Cognitive" adj2 adolescent$) or (OSCA adj3 (anxiet$ or anxious or low mood or depress$))).ti,ab. (1)
3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud).ti,ab. (4)
4 (ThinkNinja or Haelios).ti,ab. (0)
5 ("clear fear" or stem4).ti,ab. (6)
6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs).ti,ab. (4)
7 (SPARX or ((Smart or Positive or Active or Realistic) adj2 X factor)).ti,ab. (39)
8 (stressbusters or stress busters or mindstead).ti,ab. (18)
9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi$ or mood tracker or mood diary)).ti,ab. (16)
10 (Competent Adulthood Transition adj3 (Cognitive or Humanistic or interpersonal)).ti,ab. (14)
11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579).ti,ab,sa. (17)
12 or/1-11 (135)
13 (computer or computerized or computerised or digital or online or internet$ or app or apps).ti,ab. (706776)
14 (cognitive adj2 behavio$ adj3 (therap$ or intervention$ or treatment$ or psychotherap$ or programme$1 or program$1 or method$1 or approach$1)).ti,ab. (26513)
15 13 and 14 (3537)
16 (dCBT or cCBT).ti,ab. (264)
17 ((gaming or gamified or game format or video game$) and (CBT or cCBT or dCBT or cognitive behavi$)).ti,ab. (113)
18 or/15-17 (3650)
19 Anxiety/ or Anxiety Disorders/ (131387)
20 exp Depressive Disorder/ or Depression/ (247208)
21 (anxiet$ or anxious or low mood or depress$).ti,ab. (651212)
22 or/19-21 (713687)
23 Child/ (1859705)
24 Adolescent/ (2185996)
25 (child$ or adolescen$ or kid or kids or youth$ or youngster$ or minor or minors or young person$ or young people or pre adolescen$ or preadolescen or pre teen$ or preteen or teen or teens or teenager$ or juvenile$ or boy or boys or boyhood or girl or girls or girlhood or schoolchild$ or school age$ or schoolage$).ti,ab. (2213167)
26 (CYPMH or CYPMHS).ti,ab. (6)
27 or/23-26 (4035279)
28 18 and 22 and 27 (610)
29 12 or 28 (714)

30 limit 29 to english language (704)

Embase (Ovid): 1974 to 2022 week 33; Searched: 26.8.22

1 ("online support and intervention" or iCATS or MY CATS or Co CAT).ti,ab,dv,dm. (60)
2 (("Online Social anxiety Cognitive" adj2 adolescent$) or (OSCA adj3 (anxiet$ or anxious or low mood or depress$))).ti,ab,dv,dm (1)
3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud).ti,ab,dv,dm. (4)
4 (ThinkNinja or Haelios).ti,ab,dv,dm. (0)
5 ("clear fear" or stem4).ti,ab,dv,dm. (8)
6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs).ti,ab,dv,dm. (4)
7 (SPARX or ((Smart or Positive or Active or Realistic) adj2 X factor)).ti,ab,dv,dm. (45)
8 (stressbusters or stress busters or mindstead).ti,ab,dv,dm. (22)
9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi$ or mood tracker or mood diary)).ti,ab,dv,dm. (20)
10 (Competent Adulthood Transition adj3 (Cognitive or Humanistic or interpersonal)).ti,ab,dv,dm. (19)
11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579).ti,ab,cn. (20)
12 or/1-11 (168)
13 (computer or computerized or computerised or digital or online or internet$ or app or apps).ti,ab. (905177)
14 (cognitive adj2 behavio$ adj3 (therap$ or intervention$ or treatment$ or psychotherap$ or programme$1 or program$1 or method$1 or approach$1)).ti,ab. (37011)
15 13 and 14 (4404)
16 (dCBT or cCBT).ti,ab. (423)
17 ((gaming or gamified or game format or video game$) and (CBT or cCBT or dCBT or cognitive behavi$)).ti,ab. (165)
18 or/15-17 (4648)
19 anxiety/ or anxiety disorder/ (329824)
20 depression/ (433752)
21 (anxiet$ or anxious or low mood or depress$).ti,ab. (867470)
22 or/19-21 (1037649)
23 child/ (1962174)
24 adolescent/ (1688668)
25 (child$ or adolescen$ or kid or kids or youth$ or youngster$ or minor or minors or young person$ or young people or pre adolescen$ or preadolescen or pre teen$

or preteen or teen or teens or teenager$ or juvenile$ or boy or boys or boyhood or girl or girls or girlhood or schoolchild$ or school age$ or schoolage$).ti,ab. (2768596)
26 (CYPMH or CYPMHS).ti,ab. (6)
27 or/23-26 (4036080)
28 18 and 22 and 27 (598)
29 12 or 28 (732)
30 limit 29 to english language (722)

APA PsycINFO (Ovid): 1806 to August Week 3 2022; Searched: 26.8.22

1 ("online support and intervention" or iCATS or MY CATS or Co CAT).ti,ab. (13)
2 (("Online Social anxiety Cognitive" adj2 adolescent$) or (OSCA adj3 (anxiet$ or anxious or low mood or depress$))).ti,ab. (0)
3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud).ti,ab. (3)
4 (ThinkNinja or Haelios).ti,ab. (0)
5 ("clear fear" or stem4).ti,ab. (2)
6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs).ti,ab. (0)
7 (SPARX or ((Smart or Positive or Active or Realistic) adj2 X factor)).ti,ab. (17)
8 (stressbusters or stress busters or mindstead).ti,ab. (3)
9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi$ or mood tracker or mood diary)).ti,ab. (8)
10 (Competent Adulthood Transition adj3 (Cognitive or Humanistic or interpersonal)).ti,ab. (6)
11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579).af. (3)
12 or/1-11 (48)
13 (computer or computerized or computerised or digital or online or internet$ or app or apps).ti,ab. (246740)
14 (cognitive adj2 behavio$ adj3 (therap$ or intervention$ or treatment$ or psychotherap$ or programme$1 or program$1 or method$1 or approach$1)).ti,ab. (36926)
15 13 and 14 (2854)
16 (dCBT or cCBT).ti,ab. (204)
17 ((gaming or gamified or game format or video game$) and (CBT or cCBT or dCBT or cognitive behavi$)).ti,ab. (127)
18 or/15-17 (2958)
19 exp Anxiety Disorders/ or exp Anxiety/ (133130)
20 exp "Depression (Emotion)"/ or exp Major Depression/ (175148)
21 (anxiet$ or anxious or low mood or depress$).ti,ab. (467562)
22 or/19-21 (500671)
23 18 and 22 (1795)

24 limit 23 to (100 childhood <birth to age 12 yrs> or 120 neonatal <birth to age 1 mo> or 140 infancy <2 to 23 mo> or 160 preschool age <age 2 to 5 yrs> or 180 school age <age 6 to 12 yrs> or 200 adolescence <age 13 to 17 yrs>) (285)
25 (child$ or adolescen$ or kid or kids or youth$ or youngster$ or minor or minors or young person$ or young people or pre adolescen$ or preadolescen or pre teen$ or preteen or teen or teens or teenager$ or juvenile$ or boy or boys or boyhood or girl or girls or girlhood or schoolchild$ or school age$ or schoolage$).ti,ab. (1031088)
26 (CYPMH or CYPMHS).ti,ab. (4)
27 or/25-26 (1031088)
28 23 and 27 (394)
29 24 or 28 (433)
30 12 or 29 (461)
31 limit 30 to english language (423)

Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 8 of 12, August 2022 and Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): Issue 7 of 12, July 2022; Searched: 26.8.22

#1 ("online support and intervention" or iCATS or "MY CATS" or "Co CAT" or MY-CATS or Co-CAT):ti,ab,kw 3
#2 (("Online Social anxiety Cognitive" near/2 adolescent*) or (OSCA near/3 (anxiet* or anxious or "low mood" or depress*))):ti,ab,kw 1
#3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud):ti,ab,kw 5
#4 (ThinkNinja or Haelios):ti,ab,kw 1
#5 ("clear fear" or stem4):ti,ab,kw 1
#6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs):ti,ab,kw 0
#7 (SPARX or ((Smart or Positive or Active or Realistic) Near/3 "X factor")):ti,ab,kw 20
#8 (stressbusters or "stress busters" or mindstead):ti,ab,kw 5
#9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or "cognitive behavi*" or "mood tracker" or "mood diary")):ti,ab,kw 3
#10 ("Competent Adulthood Transition" Near/3 (Cognitive or Humanistic or interpersonal)):ti,ab,kw 13
#11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579)26
#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 61
#13 (computer or computerized or computerised or digital or online or internet* or app or apps):ti,ab,kw 93170
#14 (cognitive Near/2 behavio* Near/3 (therap* or intervention* or treatment* or psychotherap* or programme* or program* or method* or approach*)):ti,ab,kw 21232

#15 #13 and #14 4194
#16 (dCBT or cCBT):ti,ab,kw 174
#17 ((gaming or gamified or "game format" or "video game*") and (CBT or "cognitive behavi*")):ti,ab,kw 32
#18 #15 or #16 or #17 4238
#19 MeSH descriptor: [Anxiety] this term only 8688
#20 MeSH descriptor: [Anxiety Disorders] this term only 4546
#21 MeSH descriptor: [Depression] this term only 14144
#22 MeSH descriptor: [Depressive Disorder] explode all trees 13398
#23 (anxiet* or anxious or "low mood" or depress*):ti,ab,kw 127303
#24 #19 or #20 or #21 or #22 or #23 127358
#25 MeSH descriptor: [Child] explode all trees 61756
#26 MeSH descriptor: [Adolescent] explode all trees 110478
#27 (child* or adolescen* or kid or kids or youth* or youngster* or minor or minors or "young person*" or "young people" or pre-adolescen* or preadolescen or "pre teen*" or preteen or teen or teens or teenager* or juvenile* or boy or boys or boyhood or girl or girls or girlhood or schoolchild* or "school age*" or schoolage*):ti,ab,kw 292441
#28 (CYPMH or CYPMHS):ti,ab,kw 0
#29 #25 or #26 or #27 or #28 292441
#30 #18 and #24 and #29 722
#31 #12 or #30 762
#32 #12 or #30 in Cochrane Reviews, Cochrane Protocols 12
#33 (clinicaltrials or trialsearch):so 407924
#34 #31 not #33 in Trials 498

International HTA Database (INAHTA): up to 26 August 2022; https://database.inahta.org/; Searched: 26.8.22

(((CYPMH or CYPMHS) OR (child* or adolescen* or kid or kids or youth* or youngster* or minor or minors or "young person*" or "young people" or pre-adolescen* or preadolescen* or pre-teen* or preteen* or teen or teens or teenager* or juvenile* or boy or boys or boyhood or girl or girls or girlhood or schoolchild* or "school age*" or school-age* or schoolage*) OR ("Adolescent"[mhe]) OR ("Child"[mhe])) AND ((anxiet* or anxious or "low mood" or depress*) OR ("Depressive Disorder"[mhe]) OR ("Depression"[mhe]) OR ("Anxiety Disorders"[mhe]) OR ("Anxiety"[mhe])) AND ((gaming or gamified or "game format" or "video game*") OR (dCBT or cCBT) OR (((cognitive and behavio* and therap*) or (cognitive and behavio* and intervention*) or (cognitive and behavio* and treatment*) or (cognitive and behavio* and psycotherap*)) AND (computer or computerized or computerised or digital or online or internet* or app or apps)))) OR (("Competent Adulthood Transition") OR (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or "cognitive behavi*" or "mood tracker" or "mood diary")) OR (stressbusters or "stress busters" or mindstead) OR (SPARX or "Smart Positive Active Realistic X-factor") OR ("lumi nova" or "star atlas" or "bfb labs" or bfblabs) OR ("clear fear" OR stem4) OR (ThinkNinja OR Haelios) OR ("space from anxiety for teens" or "space from low mood

for teens" or "space from low mood and anxiety for teens" or SilverCloud) OR ("Online Social anxiety Cognitive adolescen*" or OSCA) OR ("online support and intervention" OR iCATS OR "MY CATS" OR "Co CAT" OR MY-CATS OR Co-CAT))
Language; Customize; English
15 records

KSR Evidence (Internet): Database last updated 26 August 2022; www.ksrevidence.com; Searched: 26.8.22

1 "online support and intervention" or iCATS or "MY CATS" or "Co CAT" in All text 0 results
2 ("Online Social anxiety Cognitive" near/3 adolescent*) or (OSCA near/3 (anxiet* or anxious or low mood or depress*)) in All text 0 results
3 "space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud in All text 0 results
4 ThinkNinja or Haelios in All text 0 results
5 "clear fear" or stem4 in All text 0 results
6 "lumi nova" or "star atlas" or "bfb labs" or bfblabs in All text 0 results
7 SPARX or ((Smart or Positive or Active or Realistic) near/2 "X factor") in All text 0 results
8 stressbusters or "stress busters" or mindstead in All text 0 results
9 ("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi or mood tracker or mood diary) in All text 0 results
10 Competent Adulthood Transition near/3 (Cognitive or Humanistic or interpersonal) in All text 0 results
11 in All text 0 results
12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 in All text ...
13 computer or computerized or computerised or digital or online or internet* or app or apps in All text 15258 results
14 cognitive near/2 behavio* near/3 (therap* or intervention* or treatment* or psychotherap* or programme* or program* or method* or approach*) in in All text 3321 results
15 #13 and #14 in All text 541 results
16 dCBT or cCBT in All text 24 results
17 (gaming or gamified or "game format" or "video game*") and (CBT or cCBT or dCBT or "cognitive behavi*") in All text 24 results
18 #15 or #16 or #17 in All text 550 results
19 anxiet* or anxious or "low mood" or depress* in All text 16103 results
20 #19 and #18 in All text 325 results
21 child* or adolescen* or kid or kids or youth* or youngster* or minor or minors or "young person*" or "young people" or "pre adolescen*" or preadolescen or "pre-teen*" or preteen or teen or teens or teenager* or juvenile* or boy or boys or boyhood or girl or girls or girlhood or schoolchild* or "school age*" or schoolage* in All text 34138 results
22 #20 and #21 in All text 91 results

Epistemonikos (Internet): up to 26 August 2022; https://www.epistemonikos.org/en/; Searched: 26.8.22

(title:((title:("online support AND intervention" OR iCATS OR MY-CATS OR Co-CAT OR "Online Social anxiety Cognitive adolescent*" OR "space from anxiety for teens" OR SilverCloud OR "clear fear" OR stem4 OR "lumi nova" OR "bfb labs" OR SPARX OR "Smart, Positive, Active, Realistic, X-factor thoughts" OR stressbusters OR stress-busters OR mindstead OR "catch it" OR "grasp the opportunity" OR "Competent Adulthood Transition With Cognitive, Humanistic AND Interpersonal Teaching") OR abstract:("online support AND intervention" OR iCATS OR MY-CATS OR Co-CAT OR "space from anxiety for teens" OR SilverCloud OR "clear fear" OR stem4 OR "lumi nova" OR "bfb labs" OR SPARX OR "Smart, Positive, Active, Realistic, X-factor thoughts" OR stressbusters OR stress-busters OR mindstead OR "catch it" OR "grasp the opportunity" OR "Competent Adulthood Transition With Cognitive, Humanistic AND Interpersonal Teaching")) AND (title:(CBT OR cCBT OR dCBT OR "cognitive behavi*") OR abstract:(CBT OR cCBT OR dCBT OR "cognitive behavi*"))) OR abstract:((title:("online support AND intervention" OR iCATS OR MY-CATS OR Co-CAT OR "space from anxiety for teens" OR SilverCloud OR "clear fear" OR stem4 OR "lumi nova" OR "bfb labs" OR SPARX OR "Smart, Positive, Active, Realistic, X-factor thoughts" OR stressbusters OR stress-busters OR mindstead OR ThinkNinja OR Haelios OR "catch it" OR "grasp the opportunity" OR "Competent Adulthood Transition With Cognitive, Humanistic AND Interpersonal Teaching") OR abstract:("online support AND intervention" OR iCATS OR MY-CATS OR Co-CAT OR "space from anxiety for teens" OR "space from anxiety for teens" or "space from low mood for teens" OR "space from low mood and anxiety for teens" OR SilverCloud OR SilverCloud OR "clear fear" OR stem4 OR "lumi nova" OR "bfb labs" OR SPARX OR "Smart, Positive, Active, Realistic, X-factor thoughts" OR stressbusters OR stress-busters OR mindstead OR "catch it" OR "grasp the opportunity" OR "Competent Adulthood Transition With Cognitive, Humanistic AND Interpersonal Teaching")) AND (title:(CBT OR cCBT OR dCBT OR "cognitive behavi*") OR abstract:(CBT OR cCBT OR dCBT OR "cognitive behavi*")))) OR (title:((title:(computer OR computerized OR computerised OR digital OR online OR internet-based) OR abstract:(computer OR computerized OR computerised OR digital OR online OR internet-based)) AND (title:("cognitive behaviour" OR "cognitive behavior" OR "cognitive behavioural" OR "cognitive behavioral") OR abstract:("cognitive behaviour" OR "cognitive behavior" OR "cognitive behavioural" OR "cognitive behavioral")) AND (anxiety* OR anxious OR "low mood" OR depress*)) OR abstract:((title:(computer OR computerized OR computerised OR digital OR online OR internet-based) OR abstract:(computer OR computerized OR computerised OR digital OR online OR internet* OR app OR apps)) AND (title:("cognitive behaviour" OR "cognitive behavior" OR "cognitive behavioural" OR "cognitive behavioral") OR abstract:("cognitive behaviour" OR "cognitive behavior" OR "cognitive behavioural" OR "cognitive behavioral")) AND (anxiety* OR anxious OR "low mood" OR depress*))) AND (child* OR adolescen* OR kid OR kids OR youth* OR youngster* OR "young person" OR "young persons" OR "young people" OR pre-adolescen* OR preadolescen OR pre-teen* OR preteen OR teen OR teens OR teenager* OR juvenile* OR boy OR boys OR boyhood OR girl OR girls OR

girlhood OR schoolchild* OR "school age" OR "school aged" OR schoolage* OR CYPMH OR CYPMHS)
Total: 157

Clinicaltrials.gov (Internet): up to 26 August 2022; http://clinicaltrials.gov/ct2/search/advanced; Searched: 26.8.22

("online support and intervention" OR iCATS OR "MY CATS" OR "Co CAT" OR "Online Social anxiety Cognitive adolescent" OR "space from anxiety for teens" OR "space from low mood for teens" OR "space from low mood and anxiety for teens" OR SilverCloud OR "clear fear" OR stem4 OR ThinkNinja OR Haelios OR "lumi nova" OR "star atlas" OR "bfb labs" OR bfblabs OR SPARX OR "Smart x factor" OR "Positive x factor" OR "Active x factor" OR "Realistic x factor" OR stressbusters OR "stress busters" OR mindstead OR ("catch it" OR "grasp the opportunity") AND (CBT OR cCBT OR dCBT OR "cognitive behaviour" OR "cognitive behavior" OR "mood tracker" OR "mood diary") OR ("Competent Adulthood Transition" AND (cognitive OR humanistic OR interpersonal)) OR ISRCTN15079139 OR ISRCTN82398107 OR ISRCTN30032471 OR ISRCTN12890382 OR NCT03655067 OR NCT04290754 OR NCT05203198 OR ChiCTR2100048079 OR NCT01893749 OR NCT00145912 OR NCT01228890 OR NCT01783652 OR ACTRN12619000855123 OR NTR3737 OR NCT02169960 OR ACTRN12614000316606 OR ACTRN12613000811707 OR ACTRN12609000814279 OR NCT02186730 OR ISRCTN83507297 OR ISRCTN31219579 OR ((computer OR computerized OR computerised OR digital OR online OR internet OR gaming OR gamified OR "game format" OR "video game") AND ("cognitive behaviour" OR "cognitive behavior" OR CBT) OR dCBT OR cCBT) AND (anxiety OR anxieties OR anxious OR "low mood" OR depression OR depressive OR depressed))
Applied Filters: Child (birth-17)
245 Studies found

WHO International Clinical Trials Register Portfolio (ICTRP) (Internet): up to 26 August 2022; http://www.who.int/ictrp/search/en/; Searched: 26.8.22

The search strategy for the WHO International Clinical Trials Register Portfolio is presented in Table 31.

Table 31 Search strategy for the WHO International Clinical Trials Register Portfolio

	Results
ISRCTN15079139 OR ISRCTN82398107 OR ISRCTN30032471 OR ISRCTN12890382 OR NCT03655067 OR NCT04290754 OR NCT05203198 OR ChiCTR2100048079 OR NCT01893749 OR NCT00145912 OR NCT01228890 OR NCT01783652 OR ACTRN12619000855123 OR NTR3737 OR NCT02169960 OR	(21 records for) 21 trials found

ACTRN12614000316606 OR ACTRN12613000811707 OR ACTRN12609000814279 OR NCT02186730 OR ISRCTN83507297 OR ISRCTN31219579	
"online support intervention" OR iCATS OR "MY CATS" OR "Co CAT"	(5 records for) 5 trials found
"online social anxiety cognitive adolescent"	(0 records for) 0 trials found
"space from anxiety for teens" OR "space from low mood for teens" OR "space from low mood and anxiety for teens" OR SilverCloud OR "clear fear" OR stem4 Search for *clinical trials in children*	(0 records for) 0 trials found
ThinkNinja OR Haelios	(1 records for) 1 trials found
"lumi nova" OR "star atlas" OR "bfb labs" OR bfblabs	(0 records for) 0 trials found
SPARX OR "Smart x factor" OR "Positive x factor" OR "Active x factor" OR "Realistic x factor" Search for *clinical trials in children*	(8 records for) 8 trials found
stressbusters OR "stress busters" OR mindstead OR "catch it" OR "grasp the opportunity" Search for *clinical trials in children*	(10 records for) 10 trials found
"Competent Adulthood Transition" cognitive	(2 records for) 2 trials found
Advanced search option *Condition*: anxiety OR anxieties OR anxious OR depression OR depressive OR depressed *Intervention*: (computer OR computerized OR computerised OR digital OR online OR internet OR gaming OR gamified OR "game format" OR "video game" OR app OR apps OR smartphone) AND ("cognitive behaviour" OR "cognitive behavior" OR CBT) Search for *clinical trials in children*	(56 records for) 56 trials found
Total records retrieved	**103**
Total after deduplication	**81**

17.2 *Appendix B: Searches for cost-effectiveness evidence*

A summary of the resources searched for cost-effectiveness effectiveness evidence is presented in Table 32Table .

Table 32 Resources searched for cost-effectiveness

Database/Resource	Host	Date range	Date Searched	Results
MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily	Ovid	1946 to August 25, 2022	26.8.22	412
Embase	Ovid	1974 to 2022 Week 33	26.8.22	527
APA PsycINFO	Ovid	1806 to August Week 3 2022	26.8.22	148
NHS EED	CRD interface	up to 26 August 2022	26.8.22	16
CEA Registry	www.cearegistry.org	up to 26 August 2022	26.8.22	24
RePEc	http://repec.org/	up to 26 August 2022	26.8.22	52
ScHARRHUD	www.scharrhud.org/	up to 26 August 2022	26.8.22	0
Total records retrieved			**1179**	
Total records after deduplication			**637**	

MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid): 1946 to August 25, 2022; Searched: 26.8.22

1 ("online support and intervention" or iCATS or MY CATS or Co CAT).ti,ab. (45)
2 (("Online Social anxiety Cognitive" adj2 adolescent$) or (OSCA adj3 (anxiet$ or anxious or low mood or depress$))).ti,ab. (1)
3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud).ti,ab. (4)
4 (ThinkNinja or Haelios).ti,ab. (0)
5 ("clear fear" or stem4).ti,ab. (6)
6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs).ti,ab. (4)
7 (SPARX or ((Smart or Positive or Active or Realistic) adj2 X factor)).ti,ab. (39)
8 (stressbusters or stress busters or mindstead).ti,ab. (18)
9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi$ or mood tracker or mood diary)).ti,ab. (16)
10 (Competent Adulthood Transition adj3 (Cognitive or Humanistic or interpersonal)).ti,ab. (14)

11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579).ti,ab,sa. (17)
12 or/1-11 (135)
13 (computer or computerized or computerised or digital or online or internet$ or app or apps).ti,ab. (706776)
14 (cognitive adj2 behavio$ adj3 (therap$ or intervention$ or treatment$ or psychotherap$ or programme$1 or program$1 or method$1 or approach$1)).ti,ab. (26513)
15 13 and 14 (3537)
16 (dCBT or cCBT).ti,ab. (264)
17 ((gaming or gamified or game format or video game$) and (CBT or cCBT or dCBT or cognitive behavi$)).ti,ab. (113)
18 or/15-17 (3650)
19 Anxiety/ or Anxiety Disorders/ (131387)
20 exp Depressive Disorder/ or Depression/ (247208)
21 (anxiet$ or anxious or low mood or depress$).ti,ab. (651212)
22 or/19-21 (713687)
23 18 and 22 (2172)
24 12 or 23 (2275)
25 economics/ (27463)
26 exp "costs and cost analysis"/ (259795)
27 economics, dental/ (1920)
28 exp "economics, hospital"/ (25620)
29 economics, medical/ (9218)
30 economics, nursing/ (4013)
31 economics, pharmaceutical/ (3077)
32 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (967544)
33 (expenditure$ not energy).ti,ab. (34852)
34 (value adj1 money).ti,ab. (40)
35 budget$.ti,ab. (33698)
36 or/25-35 (1129122)
37 ((energy or oxygen) adj cost).ti,ab. (4597)
38 (metabolic adj cost).ti,ab. (1621)
39 ((energy or oxygen) adj expenditure).ti,ab. (27960)
40 or/37-39 (33141)
41 36 not 40 (1121483)
42 letter.pt. (1191221)
43 editorial.pt. (616231)
44 historical article.pt. (368666)
45 or/42-44 (2155196)
46 41 not 45 (1082252)
47 24 and 46 (417)

48 limit 47 to english language (412)

Economics terms based on Costs filter:
Centre for Reviews and Dissemination. Search strategies: NHS EED MEDLINE using OvidSP (economics filter) [Internet]. York: Centre for Reviews and Dissemination; 2014 [accessed 24.8.22]. Available from: http://www.crd.york.ac.uk/crdweb/searchstrategies.asp#nhseedmedline

Embase (Ovid): 1974 to 2022 week 33; Searched: 26.8.22

1 ("online support and intervention" or iCATS or MY CATS or Co CAT).ti,ab,dv,dm. (60)
2 (("Online Social anxiety Cognitive" adj2 adolescent$) or (OSCA adj3 (anxiet$ or anxious or low mood or depress$))).ti,ab,dv,dm (1)
3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud).ti,ab,dv,dm. (4)
4 (ThinkNinja or Haelios).ti,ab,dv,dm. (0)
5 ("clear fear" or stem4).ti,ab,dv,dm. (8)
6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs).ti,ab,dv,dm. (4)
7 (SPARX or ((Smart or Positive or Active or Realistic) adj2 X factor)).ti,ab,dv,dm. (45)
8 (stressbusters or stress busters or mindstead).ti,ab,dv,dm. (22)
9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi$ or mood tracker or mood diary)).ti,ab,dv,dm. (20)
10 (Competent Adulthood Transition adj3 (Cognitive or Humanistic or interpersonal)).ti,ab,dv,dm. (19)
11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579).ti,ab,cn. (20)
12 or/1-11 (168)
13 (computer or computerized or computerised or digital or online or internet$ or app or apps).ti,ab. (905177)
14 (cognitive adj2 behavio$ adj3 (therap$ or intervention$ or treatment$ or psychotherap$ or programme$1 or program$1 or method$1 or approach$1)).ti,ab. (37011)
15 13 and 14 (4404)
16 (dCBT or cCBT).ti,ab. (423)
17 ((gaming or gamified or game format or video game$) and (CBT or cCBT or dCBT or cognitive behavi$)).ti,ab. (165)
18 or/15-17 (4648)
19 anxiety/ or anxiety disorder/ (329824)
20 depression/ (433752)
21 (anxiet$ or anxious or low mood or depress$).ti,ab. (867470)

22 or/19-21 (1037649)
23 18 and 22 (2634)
24 12 or 23 (2766)
25 health-economics/ (34571)
26 exp economic-evaluation/ (337548)
27 exp health-care-cost/ (322653)
28 exp pharmacoeconomics/ (221187)
29 or/25-28 (714908)
30 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab. (1276952)
31 (expenditure$ not energy).ti,ab. (47078)
32 (value adj2 money).ti,ab. (2790)
33 budget$.ti,ab. (44235)
34 or/30-33 (1318770)
35 29 or 34 (1670023)
36 letter.pt. (1235405)
37 editorial.pt. (734328)
38 note.pt. (903367)
39 or/36-38 (2873100)
40 35 not 39 (1540481)
41 (metabolic adj cost).ti,ab. (1746)
42 ((energy or oxygen) adj cost).ti,ab. (4839)
43 ((energy or oxygen) adj expenditure).ti,ab. (35384)
44 or/41-43 (40795)
45 40 not 44 (1532116)
46 exp animal/ (28947445)
47 exp animal-experiment/ (2879376)
48 nonhuman/ (6992450)
49 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (6205065)
50 or/46-49 (31082249)
51 exp human/ (23961249)
52 exp human-experiment/ (589380)
53 51 or 52 (23963405)
54 50 not (50 and 53) (7119950)
55 45 not 54 (1388744)
56 24 and 55 (532)
57 limit 56 to english language (527)

Economics terms based on Costs filter:
Centre for Reviews and Dissemination. Search strategies: NHS EED Embase using OvidSP (economics filter) [Internet]. York: Centre for Reviews and Dissemination; 2014 [accessed 25.8.22]. Available from: http://www.crd.york.ac.uk/crdweb/searchstrategies.asp#nhseedmedline

APA PsycINFO (Ovid): 1806 to August Week 3 2022; Searched: 26.8.22

1 ("online support and intervention" or iCATS or MY CATS or Co CAT).ti,ab. (13)
2 (("Online Social anxiety Cognitive" adj2 adolescent$) or (OSCA adj3 (anxiet$ or anxious or low mood or depress$))).ti,ab. (0)
3 ("space from anxiety for teens" or "space from low mood for teens" or "space from low mood and anxiety for teens" or SilverCloud).ti,ab. (3)
4 (ThinkNinja or Haelios).ti,ab. (0)
5 ("clear fear" or stem4).ti,ab. (2)
6 ("lumi nova" or "star atlas" or "bfb labs" or bfblabs).ti,ab. (0)
7 (SPARX or ((Smart or Positive or Active or Realistic) adj2 X factor)).ti,ab. (17)
8 (stressbusters or stress busters or mindstead).ti,ab. (3)
9 (("catch it" or "grasp the opportunity") and (CBT or cCBT or dCBT or cognitive behavi$ or mood tracker or mood diary)).ti,ab. (8)
10 (Competent Adulthood Transition adj3 (Cognitive or Humanistic or interpersonal)).ti,ab. (6)
11 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579).af. (3)
12 or/1-11 (48)
13 (computer or computerized or computerised or digital or online or internet$ or app or apps).ti,ab. (246740)
14 (cognitive adj2 behavio$ adj3 (therap$ or intervention$ or treatment$ or psychotherap$ or programme$1 or program$1 or method$1 or approach$1)).ti,ab. (36926)
15 13 and 14 (2854)
16 (dCBT or cCBT).ti,ab. (204)
17 ((gaming or gamified or game format or video game$) and (CBT or cCBT or dCBT or cognitive behavi$)).ti,ab. (127)
18 or/15-17 (2958)
19 exp Anxiety Disorders/ or exp Anxiety/ (133130)
20 exp "Depression (Emotion)"/ or exp Major Depression/ (175148)
21 (anxiet$ or anxious or low mood or depress$).ti,ab. (467562)
22 or/19-21 (500671)
23 18 and 22 (1795)
24 12 or 23 (1823)
25 "costs and cost analysis"/ (18429)
26 "Cost Containment"/ (690)
27 (economic adj2 evaluation$).ti,ab. (2040)
28 (economic adj2 analy$).ti,ab. (1680)
29 (economic adj2 (study or studies)).ti,ab. (907)
30 (cost adj2 evaluation$).ti,ab. (388)
31 (cost adj2 analy$).ti,ab. (4188)
32 (cost adj2 (study or studies)).ti,ab. (981)
33 (cost adj2 effective$).ti,ab. (17319)

34 (cost adj2 benefit$).ti,ab. (3859)
35 (cost adj2 utili$).ti,ab. (1481)
36 (cost adj2 minimi$).ti,ab. (407)
37 (cost adj2 consequence$).ti,ab. (128)
38 (cost adj2 comparison$).ti,ab. (198)
39 (cost adj2 identificat$).ti,ab. (29)
40 (pharmacoeconomic$ or pharmaco-economic$).ti,ab. (337)
41 or/25-40 (39268)
42 (task adj2 cost$).ti,ab,id. (757)
43 (switch$ adj2 cost$).ti,ab,id. (1517)
44 (metabolic adj cost).ti,ab,id. (112)
45 ((energy or oxygen) adj cost).ti,ab,id. (306)
46 ((energy or oxygen) adj expenditure).ti,ab,id. (2969)
47 or/42-46 (5349)
48 (animal or animals or rat or rats or mouse or mice or hamster or hamsters or dog or dogs or cat or cats or bovine or sheep or ovine or pig or pigs).ab,ti,id,de. (376272)
49 editorial.dt. (44313)
50 letter.dt. (25212)
51 dissertation abstract.pt. (535925)
52 or/49-51 (605450)
53 41 not (47 or 52) (34557)
54 24 and 53 (154)
55 limit 54 to english language (148)

Economics terms based on Costs filter:
Centre for Reviews and Dissemination. Search strategies: NHS EED PsycINFO using OvidSP (economics filter) [Internet]. York: Centre for Reviews and Dissemination; 2014 [accessed 25.8.22]. Available from: http://www.crd.york.ac.uk/crdweb/searchstrategies.asp#nhseedmedline

NHS Economic Evaluation Database (NHS EED) (CRD): up to 31 March 2015; http://www.crd.york.ac.uk/CRDWeb/; Searched: 26.8.22

1 (online support near1 intervention or iCATS or MY CATS or Co CAT or MY-CATS or Co-CAT) 0
2 ((Online Social anxiety Cognitive near2 adolescent*) or (OSCA near3 (anxiet* or anxious or low mood or depress*))) 0
3 (space near2 anxiety near2 teens or SilverCloud or clear fear or stem4) 0

4 ((lumi nova or star atlas or bfb labs or bfblabs)) 0
5 (ThinkNinja or Haelios) 0
6 (SPARX or ((Smart or Positive or Active or Realistic) near3 X factor)) 0

7 (stressbusters or stress busters or mindstead) 0

8 ((catch it or grasp near2 opportunity) near5 (CBT or cCBT or dCBT or cognitive behavi* or mood tracker or mood diary)) 0
9 (Competent Adulthood Transition near5 (Cognitive or Humanistic or interpersonal))0
10 (ISRCTN15079139 or ISRCTN82398107 or ISRCTN30032471 or ISRCTN12890382 or NCT03655067 or NCT04290754 or NCT05203198 or ChiCTR2100048079 or NCT01893749 or NCT00145912 or NCT01228890 or NCT01783652 or ACTRN12619000855123 or NTR3737 or NCT02169960 or ACTRN12614000316606 or ACTRN12613000811707 or ACTRN12609000814279 or NCT02186730 or ISRCTN83507297 or ISRCTN31219579)0
11 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 0
12 ((computer or computerized or computerised or digital or online or internet* or app or apps) near3 (cognitive near3 behavio*)) 58
13 (dCBT or cCBT) 13
14 ((gaming or gamified or game format or video game*) near4 (CBT or (cognitive near3 behavi*))) 1
15 #12 OR #13 OR #14 60
16 MeSH DESCRIPTOR Anxiety EXPLODE ALL TREES 314
17 MeSH DESCRIPTOR Anxiety Disorders EXPLODE ALL TREES 380
18 MeSH DESCRIPTOR Depression EXPLODE ALL TREES 639
19 MeSH DESCRIPTOR Depressive Disorder EXPLODE ALL TREES 1030
20 (anxiet* or anxious or low mood or depress) 1765
21 #16 OR #17 OR #18 OR #19 OR #20 2993
22 #15 AND #21 46
23 #11 OR #22 46
24 * IN NHSEED 17613
25 #23 AND #24 16

Cost-Effectiveness Analysis (CEA) Registry (Internet): up to 26 August 2022; www.cearegistry.org; Searched: 26.8.22

Cognitive behaviour computer

Cognitive behavior computer

Cognitive behavioural computer

Cognitive behavioural computer

Cognitive behaviour internet

Cognitive behavior internet

Cognitive behavioural internet

Cognitive behavioural internet

Cognitive behaviour electronic

Cognitive behavior electronic

Cognitive behavioural electronic

Cognitive behavioural electronic

Cognitive behaviour digital

Cognitive behavior digital

Cognitive behavioural digital

Cognitive behavioural digital

Cognitive behaviour online

Cognitive behavior online

Cognitive behavioural online

Cognitive behavioural online

24 Records retrieved

RePEc (Internet): up to 26 August 2022; http://repec.org/; Searched: 26.8.22; IDEAS search interface

(computer | computerized | computerised | digital | online | internet | gaming | gamified | game format | video game | video games | app | apps) + ((cognitive behaviour | cognitive behavior | cognitive behavioural | cognitive behavioral) + (therapy | therapies | intervention | interventions | treatment | treatments | psychotherapy | psychotherapies)) + (anxiety | anxieties | anxious | low mood | depressed | depression | depressive)
In: Abstract

Records retrieved 52

ScHARR Health Utilities Database (ScHARRHUD)(Internet): up to 26 August 2022; www.scharrhud.org/; Searched: 26.8.22

The search strategy for the ScHARR Health Utilities Database is presented in Table 33.

Table 33 Search strategy for the WHO International Clinical Trials Register Portfolio

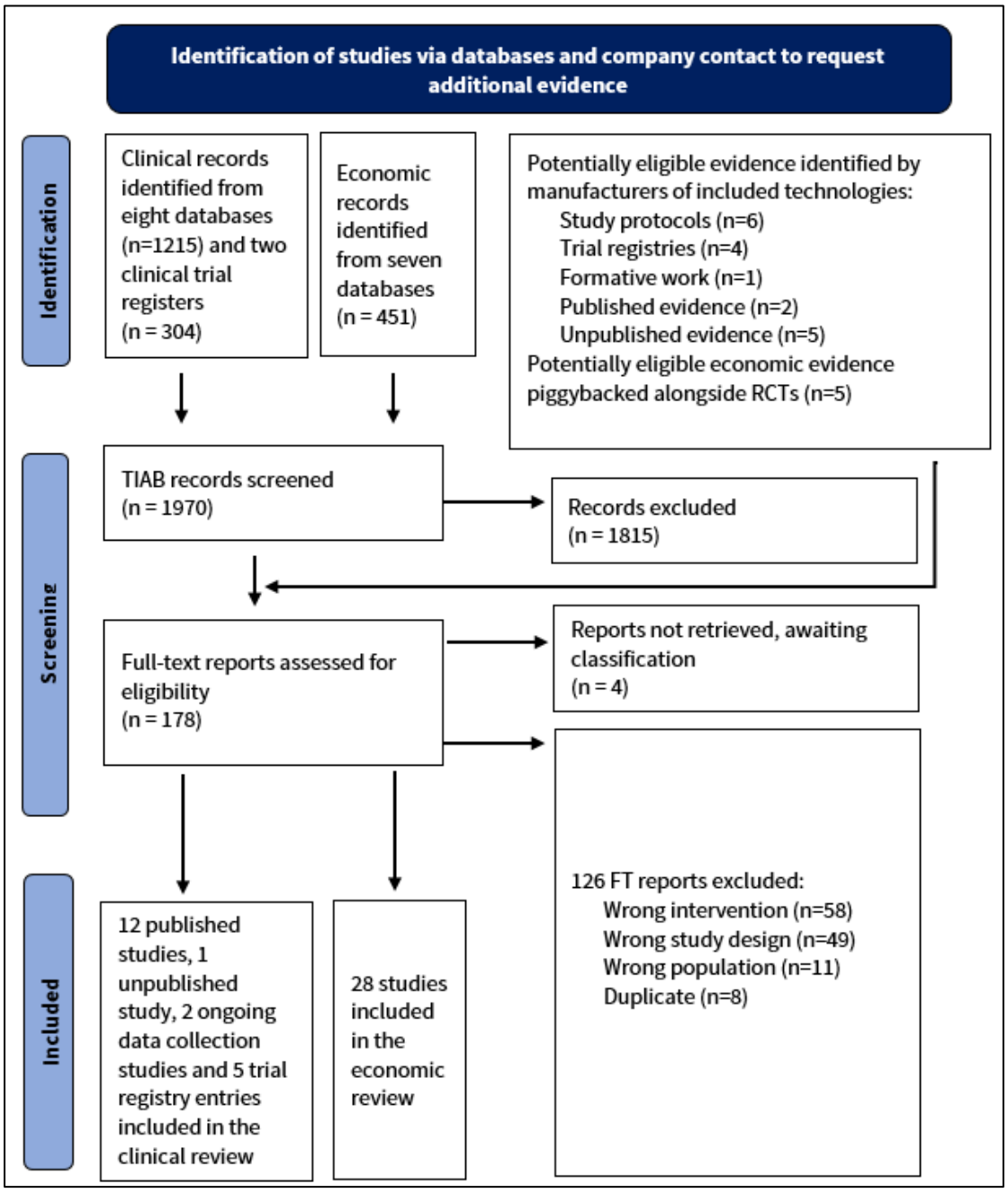
Search terms	Results
(computer OR computerized OR computerised OR digital OR online OR internet OR gaming OR gamified OR game format OR video game OR video games OR app OR apps) AND (cognitive behaviour OR cognitive behavior OR cognitive behavioural OR cognitive behavioral) AND (anxiety OR anxieties OR anxious OR low mood OR depressed OR depression OR depressive)	0
Total	0
Total after removal of duplicates	0

CHEERS checklist quality assessment for included economic evaluations

Economic studies CHEERS checklist.xlsx

17.3 *Appendix C: PRISMA flow diagram*

Figure 3. PRISMA diagram detailing the searches for eligible clinical and economic evidence



Template adapted from Page et al. 2021[79]

17.4 *Appendix D: List of excluded studies and studies awaiting assessment*

Table 34 List of excluded full-text studies with reasons

Excluded study	Reason for exclusion
Aboujaoude et al. 2016	Wrong study design
ACTRN12606000142538 2006	Wrong intervention
Adelman et al. 2014	Wrong study design
Ahern et al. 2018	Wrong study design
Anderson et al. 2012	Wrong intervention
Andersson et al. 2006	Wrong intervention
Andrews et al. 2010	Wrong study design
Antle et al. 2019	Wrong intervention
Barnes et al. 2018	Wrong study design
Barth et al. 2013	Wrong study design
Berry et al. 2014	Wrong study design
Bhattacharya et al. 2012	Wrong study design
Bunge et al. 2016	Wrong study design
Calear et al. 2010	Wrong study design
Christ et al. 2020	Wrong study design
Clarke et al. 2015	Wrong study design
Cox et al. 2015	Wrong study design
CTRI/2012/10/003043 2012	Wrong intervention
Das et al. 2016	Wrong study design
de Graaf et al. 2009	Wrong intervention
Do et al. 2021	Wrong intervention
Drissi et al. 2020	Wrong study design
Duarte et al. 2017	Wrong intervention
Dubicka et al. 2020	Wrong study design
Duffy et al. 2020	Wrong population
Ebert et al. 2015	Wrong study design
Ferrari et al. 2022	Wrong study design
Frazier et al. 2016	Wrong population
Frechette-Simard et al. 2018	Wrong study design
Gega et al. 2004	Wrong intervention
Griffiths et al. 2010	Wrong study design
Grist et al. 2019	Wrong study design
Gujjar et al. 2019	Wrong study design

Excluded study	Reason for exclusion
Gupta et al. 2021	Wrong intervention
Hallgren et al. 2015	Wrong intervention
Hallym University Medical 2015	Wrong intervention
Health Quality, Ontario; Canada 2019	Duplicate
Hedman et al. 2011	Wrong intervention
Hetrick et al. 2015	Wrong study design
Hill et al. 2022a	Duplicate (company provided)
Hill et al. 2022b	Duplicate (company provided)
Hoifodt et al. 2011	Wrong study design
ISRCTN79652741 2012	Wrong intervention
ISRCTN30032471 2021	Duplicate (company provided)
ISRCTN82398107 2021	Duplicate (company provided)
ISRCTN12890382 2020	Duplicate (company provided)
Ivlev et al. 2022	Wrong study design
Jakobsen et al. 2017	Wrong population
Jolstedt et al. 2021	Wrong intervention
Jolstedt et al. 2018	Wrong intervention
Karbasi et al. 2018	Wrong intervention
Karolinska Institutet 2010	Wrong intervention
Karolinska Institutet 2015	Wrong intervention
Karolinska Institutet 2020	Wrong intervention
Kenardy et al. 2003	Wrong population
Kim et al. 2012	Wrong intervention
Klein et al. 2011	Wrong population
Kraepelien et al. 2018	Wrong population
Leykin et al. 2014	Wrong population
Li et al. 2021	Wrong study design
Li, Achilles, et al. 2022	Wrong study design
Liang et al. 2021	Wrong study design
Limbix Health, Inc. 2023	Wrong intervention
Linardon et al. 2019	Wrong study design
Linkoeping University 2018	Wrong intervention
Loucas et al. 2014	Wrong study design
March et al. 2009	Wrong intervention
Marks et al. 2003	Wrong intervention
Martinez et al. 2014	Wrong intervention

Excluded study	Reason for exclusion
Martinez et al. 2019	Wrong intervention
McCashin et al. 2019	Wrong study design
Medeiro et al. 2012	Wrong study design
Merry et al. 2009	Wrong intervention
Mewton et al. 2015	Wrong intervention
Nakao et al. 2021	Wrong study design
Newall et al. 2012	Wrong intervention
Newby et al. 2014	Wrong intervention
Nicolaidou et al. 2021	Wrong intervention
Palmqvist et al. 2007	Wrong study design
Peck et al. 2007	Wrong study design
Pennant et al. 2015	Wrong study design
Pratt et al. 2017	Wrong study design
Radomski et al. 2019	Wrong study design
Reardon et al. 2022	Duplicate (company provided)
Renton et al. 2014	Wrong study design
Richards et al. 2018	Wrong population
Richardson et al. 2010	Wrong study design
Robinson et al. 2010	Wrong intervention
Ruwaard et al. 2009	Wrong population
Salloum et al. 2015	Wrong intervention
Salloum et al. 2016	Wrong intervention
Schmitt et al. 2022	Wrong intervention
Sethi et al. 2010	Wrong intervention
Shechner et al. 2014	Wrong intervention
Short et al. 2017	Wrong intervention
Sikorski et al. 2011	Wrong study design
Smart et al. 2021	Wrong intervention
Spence et al. 2017	Wrong intervention
Spence et al. 2019 Social support	Wrong intervention
Spence et al. 2020	Wrong intervention
Stjerneklar et al. 2019	Wrong intervention
Szigethy et al. 2020	Wrong intervention
Tillfors et al. 2011	Wrong intervention
Tindall et al. 2016	Wrong intervention
Topooco et al. 2019	Wrong intervention

Excluded study	Reason for exclusion
Topooco et al. 2018	Wrong intervention
Topooco et al. 2017	Wrong intervention
Topper et al. 2017	Wrong intervention
Twomey et al. 2013	Wrong study design
Twomey et al. 2015	Wrong study design
University of Aarhus 2016	Wrong intervention
University of British Columbia 2017	Wrong population
University of Chile 2016	Wrong intervention
University of Pittsburgh 2023	Wrong intervention
University of South Florida 2015	Wrong intervention
University of Turku 2020	Wrong intervention
Van Wingerden et al. 2021	Wrong study design
Vigerland et al. 2022	Wrong study design
Vigerland, Lenhard, et al. 2016	Wrong study design
Vigerland, Ljotsson, et al. 2016	Wrong intervention
Vigerland et al. 2017	Wrong intervention
Webb et al. 2017	Wrong study design
Wickersham et al. 2022	Wrong study design
Williamson et al. 2021	Duplicate (company provided)
You et al. 2022	Wrong population
Zou et al. 2017	Wrong study design

Table 35 List of studies awaiting assessment

Excluded study	Reason for exclusion
Center for Psychological Consultation 2015	Awaiting assessment
Lindefors et al. 2013	Awaiting assessment
Seoul National University 2021	Awaiting assessment
Shin et al. 2020	Awaiting assessment

17.5 *Appendix E: Risk of bias of included studies*

Cochrane's Risk of Bias tool was used to assess the methodological quality of included studies with eligible and available data. The results of these assessments are presented in Table 36.

Table 36 Summary of risk of bias assessments of included studies with eligible and available data

Domain	Green et al. (2022)		Hill et al. (2022b)		Leigh & Clark (2022)		Lockwood et al. (2022)		Williamson et al. (2022)	
	Judgment	Comment	Judgment	Comment	Judgment	Comment	Judgment	Comment	Judgment	Comment
Random sequence generation	[redacted]	[redacted]	N/A	Single-arm study.	Unclear	Method of sequence generation not described.	N/A	Single-arm study.	N/A	Single-arm study.
Allocation concealment	[redacted]	[redacted]	N/A	Single-arm study.	Unclear	It is not reported how the randomisation sequence was protected at allocation.	N/A	Single-arm study.	N/A	Single-arm study.
Blinding of participants and personnel	[redacted]	[redacted]	High	Single-arm study, no blinding reported.	High	Blinding is not described, but very unlikely given that intervention and control participants attended the same schools.	High	Single-arm study, no blinding reported.	High	Single-arm study, no blinding reported.

Domain	Green et al. (2022)		Hill et al. (2022b)		Leigh & Clark (2022)		Lockwood et al. (2022)		Williamson et al. (2022)	
	Judgment	Comment	Judgment	Comment	Judgment	Comment	Judgment	Comment	Judgment	Comment
Blinding of outcome assessors	[redacted]	[redacted]	High	Parents as assessors, no blinding reported.	Unclear	SAD diagnosis was determined by a blinded assessor, but other measures were completed by unblinded participants using self-report instruments.	High	Participants and parents as assessors, no blinding reported.	High	Parents as assessors, no blinding reported.
Incomplete outcome data	[redacted]	[redacted]	High	Disengagement was fairly high (13%) with some modules not completed by families who remained in the program, and some children not assessed at all time points. Missing data for some outcomes were addressed using LOCF.	Low	Attrition was relatively low and ITT analyses were conducted, though there is no detail on how missing data were handled.	High	Very high attrition for anxiety symptoms and gameplay sample with no reasons provided.	Unclear	Attrition is not reported, but given the nature of the study this is considered to be minimal.

Domain	Green et al. (2022)		Hill et al. (2022b)		Leigh & Clark (2022)		Lockwood et al. (2022)		Williamson et al. (2022)	
	Judgment	Comment	Judgment	Comment	Judgment	Comment	Judgment	Comment	Judgment	Comment
Selective outcome reporting	[redacted]	[redacted]	Low	All outcomes specified in the Methods section are reported in the Results section.	Low	All outcomes specified in the Methods section are reported in the Results section.	Low	All outcomes specified in the Methods section are reported in the Results section.	Low	All outcomes specified in the protocol are reported in the full paper.
Other bias	[redacted]	[redacted]	High	Lack of reporting regarding unbiased recruitment.	Low	None identified.	High	Lack of reporting regarding unbiased recruitment.	Low	None identified.

Abbreviations: ITT, intention-to-treat; [redacted] SAD, social anxiety disorder

[MT580] Guided self-help digital cognitive behavioural therapy for children and young people with mild to moderate symptoms of anxiety and low mood

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Early Value Assessment Programme

Addendum #1

Inclusion of additional scoped technology

October 2022

Produced by
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1. INTRODUCTION

The purpose of this addendum is to include an additional technology not included in the final scope published by NICE. The ThinkNinja digital cognitive behavioural therapy (dCBT) application is used for the remote treatment of young people with anxiety alongside text chat and video calls, and is manufactured by Healios.

2. EVIDENCE SELECTION

2.1. Search strategy

An additional search was conducted to account for the misspelling of the company Healios, originally included in the NICE draft scope as 'Haelios'. Details of additional search strategies are provided in Section 7 (Appendix I).

A total of 14 records of potentially relevant evidence on clinical effectiveness and nine trial registry entries were retrieved. No potentially relevant economic evaluations were found. Following deduplication from this additional search as well as against the original search results, a total of 17 records were included.

2.2. Study selection

A single reviewer screened all 17 titles and abstracts of potentially relevant records, using Bond University's Systematic Review Accelerator.[1] One potentially relevant full-text article was identified during title and abstract screening and was subsequently included in the clinical evidence base. Eligibility criteria were applied during screening in a manner that was consistent with that described in Section 8.1 of the main report.

In addition, the EAG received additional research and information that may not have been included in the search, or available in the public domain, from a Healios representative. These sources were considered to ensure an unbiased approach with maximum evidence representation in the review.

2.3. Included and excluded studies

The EAG considered the formative study by Burbach & Stiles (2021)[2] as the only completed included study from the published literature on Healios. Two eligible conference presentation reporting data on a pilot samples (Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022))[4] as well as one

[redacted] by Healios (2022) were identified from submissions by the company representative, and included in this addendum. These studies are summarised in Table 1.

No records were excluded at the full-text review stage.

Table 1 Studies selected by the EAG as the clinical evidence base for ThinkNinja/Bytesize (Healios)

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Formative work: Burbach & Stiles (2021) [2] UK	Single arm formative research Intervention: Healios (Bytesize/ ThinkNinja not specified) Comparator: None Intervention: **AMBER** Comparator: **RED**	Inclusion criteria: Patients younger than 16 years of age who had completed their full course of treatment or assessment, and whose case had been closed by Healios. Specific exclusion criteria are not specified. Cases (n=9) were selected from relevant NHS contracts Participants: **GREEN** Setting: **GREEN**	• Treatment satisfaction • Measures of symptom severity (RCADS-C, RCADS-P and YP-CORE) • Social, behavioural and functional outcomes (SDQ-C, SDQ-P, GBO) • Suicidal thoughts and behaviour • Rates of remission • Patient experience Outcomes reported by planned subgroups: None stated Outcomes: **GREEN**	The included paediatric population does not fall, exactly or approximately, into either of the pre-specified subgroups, though included participants are more representative of the young people aged 12 to 18 years grouping. No specific exclusions are stated and no systematic exclusions are anticipated from the setting. The EAG noted that young people autism, ADHD, anger, aggression, self-esteem issues and self-harm behaviours were included in addition to participants with anxiety or low mood. This suggests reasonable generalisability. Scoped outcomes not included: • Intervention-related adverse events • Attrition • Treatment engagement • Global functioning • Health-related quality of life

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
				• Cost of technology • Cost of other resources
Conference presentation: Burbach, Galloghly & Snaith (2021)[3] Location not repoted	Single-arm feasibility study Intervention: CBT Bytesize Comparator: None Intervention: **GREEN** Comparator: **RED**	No inclusion or exclusion criteria reported. The sample included n=6 CYP with a mean age of 15 (SD=0.63; range 14-16) years. The primary presentation for all cases was anxiety. Mean YP-CORE score at baseline was 20 ('moderate') with 83% of the sample having scores in the clinical range. Mean RCADS score at baseline was 68 (in the 'high' but non-clinical range) with 33% of the sample having scores in the clinical range. Mean SDQ-C score at baseline was 20 (in the 'very high' range) with 83% of the sample having scores in the clinical range. Setting not reported Participants: **GREEN** Setting: **could not be assessed**	• Attrition (rates only) • Treatment satisfaction • Measures of symptom severity (YP-CORE) Outcomes reported by planned subgroups: None stated Outcomes: **GREEN**	The included paediatric population falls into the pre-specified subgroup of young people aged 12 to 18 years. No setting or specific inclusion or exclusion criteria are stated. Therefore, the EAG could not assess the impact on generalisability. Scoped outcomes not included: • Intervention-related adverse events • Treatment engagement • Social, behavioural and functional outcomes • Suicidal thoughts and behaviour • Global functioning • Rates of remission • Health-related quality of life • Patient experience • Cost of technology

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
				• Cost of other resources
Conference presentation: Galloghly, Haselton & Burbach (2022)[4] UK	Two-arm non-randomised study Intervention: CBT Bytesize Comparator: CBT at Healios Intervention: **GREEN** Comparator: **GREEN**	'…broad inclusion criteria, regardless of tier of service' are reported, but not further specified. The sample included 41 CYP with a mean age of 14.4 (range 11-17) years, n=21 (75%) female with top presenting problems listed as social anxiety and/or generalised anxiety, comorbid low mood, panic, selective mutism, emetophobia and OCD. A total of n=15 CYP were from tier 3 services (with mean age 14.3 (range 11-17) years; 67% female); n=13 CYP were from tier 2 services (with mean age 14.5 (range 12-17) years; 85% female). CYP offered a choice, 68% opted for CBT Bytesize, 32% declined or did not respond. CYP were accessed through CAMHS Participants: **GREEN** Setting: **GREEN**	• Attrition (rates and reasons) • Treatment satisfaction • Measures of symptom severity (RCADS-C and YP-CORE) • Social, behavioural and functional outcomes (GBO) • Suicidal thoughts and behaviour (risk to self) • Rates of remission Outcomes reported by planned subgroups: completers analysis and subgroups analysis by tier 2 and tier 3 completers Outcomes: **GREEN**	The included paediatric population does not fall exactly into either of the pre-specified subgroups, though included participants are more representative of the young people aged 12 to 18 years grouping. No specific exclusions are stated and no systematic exclusions are anticipated from the setting. The EAG noted that CYP with panic, selective mutism, emetophobia and OCD were included in addition to participants with anxiety and/or low mood. This suggests reasonable generalisability. Scoped outcomes not included: • Intervention-related adverse events • Treatment engagement • Global functioning • Health-related quality of life

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
				• Patient experience • Cost of technology • Cost of other resources
Ongoing or prospective work				
[redacted] Healios (2022) [redacted]	[redacted] Intervention: CBT Bytesize [redacted] Intervention: **GREEN** Comparator: **GREEN**	[redacted] Participants: **GREEN** Setting: **GREEN**	[redacted] Outcomes: **could not be assessed**	[redacted]

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CAMHS, Children and Adolescent Mental Health Service; CBT, cognitive behavioural therapy; CYP, children and young people; EAG, External Assessment Group; GBO, goal-based outcomes; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; NR, not reported; OCD, obsessive-compulsive disorder; PMHSS, primary mental health support service; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– parent report); SDQ(-C/P), Strengths and Difficulties Questionnaire (– child/parent report); YP-CORE, Young Person's Clinical Outcomes in Routine Evaluation

3. CLINICAL EVIDENCE REVIEW FOR BYTESIZE (HEALIOS)

3.1. Overview of methodologies of all included studies

Most relevant studies described in Table 1 had some methodological limitations or misalignment with the scope of the NICE decision problem, or had attributes that could not be assessed due to a lack of information.

Study design, intervention and comparator

Two of the included studies were single-arm designs with no direct comparator (Burbach & Stiles (2021)[2] and Burbach, Galloghly & Snaith (2021)[3]). One included study (Galloghly, Haselton & Burbach (2022)[4]) and [redacted]. The EAG considered [redacted] in most completed studies to cause methodological limitations, though it noted that [redacted].

Evidence gap: Very little published [redacted] evidence for Bytesize was found.

Participants and setting

Most included studies described participants and settings that fit within the NICE scope, though the EAG could not assess the exact setting in Burbach, Galloghly & Snaith (2021).[3] Furthermore, the EAG noted that populations in Burbach & Stiles (2021)[2], Galloghly, Haselton & Burbach (2022)[4] and Healios (2022) had overlap between age subgroups specified by NICE – the EAG considered these deviations to be minor for Galloghly, Haselton & Burbach (2022)[4] as the majority of participants in these studies would fall into the subgroup of young people aged 12 to 18 years. Populations in the other two studies, however, were considered to be [redacted]. The EAG considered the lack of data for Bytesize in the group [redacted] to be a serious evidence gap.

Sample sizes across interventions were small (ranging from six to 41 participants) and presented a risk of spurious chance findings and underpowered analyses. The EAG could not fully assess the risk of the latter, since none of the studies reported on power calculations.

The EAG noted that two of the studies (Burbach & Stiles (2021)[2] and Galloghly, Haselton & Burbach (2022)[4]) explicitly described including participants with low mood; this could not be assessed for two others. Generalisability to the UK setting was considered to be well-aligned, given that three studies (Burbach & Stiles (2021)[2], Galloghly, Haselton & Burbach (2022)[4] and Healios (2022)) explicitly reported UK settings. Population generalisability of two studies (Burbach & Stiles (2021)[2] and Galloghly, Haselton & Burbach (2022)[4]) was considered to be reasonably representative of the population due to the inclusion of a number of participants with comorbid mental health or neurodevelopmental conditions; specific inclusion and exclusion criteria were not reported for two other studies (Burbach, Galloghly & Snaith (2021)[3] and Healios (2022)) and population generalisability could therefore not be assessed. None of the studies explicitly included children with learning disabilities.

Evidence gap: Some published evidence for CYP with low mood was found for Bytesize, but this population may be underrepresented. No published evidence exclusively in [redacted], or subgroups to investigate effects in this group, was found for Bytesize.

Methodological gap: Small sample sizes in included studies on Bytesize present a risk of spurious chance findings and underpowered analyses.

Generalisability gap: Some published evidence for children and young people with neurodevelopmental conditions, but no specific evidence for children and young people with learning disability.

In terms of integration into the NHS, the EAG identified two completed studies (Burbach & Stiles (2021) and Galloghly, Haselton & Burbach (2022)) and one

prospective or ongoing studies by Healios (2022) that provided direct evidence of use in the NHS. These studies describe research conducted in cases selected from relevant NHS contracts, cases accessed through CAMHS and CYP recruited from [redacted]. One other study (Burbach, Galloghly & Snaith (2021)[3]) did not specify its setting, and could not be assessed for its ease of integration.

Outcomes

None of the included studies reported on all outcomes included in the NICE scope, but most reported some outcomes of interest. The EAG noted that the prospective or ongoing work by Healios (2022) did not specify discrete outcomes, and consequently could not assess this study against NICE-scoped outcomes. The EAG considered symptom severity outcomes to be heterogeneously measured (RCADS-C and -P, and YP-CORE); the majority of studies reported RCADS-C (self-report) and all studies reported YP-CORE. The reporting of YP-CORE was highly variable across studies with some reporting on actual changes in scores, some on changes in dichotomised outcomes based on these scores, while others reported only trends. Social, behavioural and functional outcomes were also reasonably heterogeneous in terms of reporting measures (SDQ-C and –P, and goal-based outcomes (GBO)), though both studies reporting on this class of outcomes measured GBO. One of these studies (Galloghly, Haselton & Burbach (2022)[4]) indicated GBO as a routine outcome measure, but did not report any results for this measure.

SCM advice to the EAG indicated that RCADS and GBO are broadly appropriate measures for symptom severity and impairment, respectively. Due to a lack of time, the EAG could not obtain SCM advice on the appropriateness of YP-CORE. SCM advice, however, indicated that self-report of these measures are preferable for adolescents, particularly for internalising symptoms; YP-CORE is one of these self-report measures, along with RCADS-C and GBO. As most of the available evidence reports on the subgroup of young people aged 12 to 18 years, the EAG considered the selection of measures for these outcomes to be appropriate.

Evidence gap: No published evidence for the outcomes of intervention-related adverse events, treatment engagement, global functioning, health-related quality of life, cost of technology or cost of other resources was found.

Heterogeneity issue: Clinical measures are reported heterogeneously, though some measures are frequently reported across studies. Some of these measures were identified by SCM advice to the EAG as broadly appropriate.

3.2. Critical appraisal of studies

All studies with eligible and available outcome data (Burbach & Stiles (2021),[2] Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022)[4]) had aspects that the EAG considered to be threats to internal validity. Full assessment of the risk of bias of these studies is presented in Table 17 of Appendix II (Section 8).

Random sequence generation and allocation concealment was logically not possible in the single-arm studies (Burbach & Stiles (2021)[2] and Burbach, Galloghly & Snaith (2021)[3]), but was judged to be high for the two-arm study by Galloghly, Haselton & Burbach (2022)[4] due to its non-randomised design offering participants the choice of allocation. The EAG noted that blinding of participants is not possible due to the nature of the intervention. As a consequence, all studies had a high risk of performance bias. All studies were also at high risk of detection bias (Burbach & Stiles (2021),[2] Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022)[4]) as outcomes were assessed by participants and/or their parents.

Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022)[4] were also considered to be at high risk of attrition bias considering high rates of attrition with no reported accounting for missing data. Selective outcome reporting could not be assessed in two studies (Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022)[4]) due to a lack of *a priori* stated outcomes. These two studies were also judged at high risk of other bias due to a lack of reporting regarding unbiased recruitment; they were not judged to be at high risk of intervention misclassification, or deviations from intended intervention.

Methodological gap: More high-quality randomised controlled trials of Bytesize with *a priori* stated outcomes are required. These trials need clear reporting of efforts to minimise selection bias; blinded participants (if possible) and outcome assessors; as well as proper statistical management of missing data, such as multiple imputation.

3.3. Results from the evidence base

The EAG summarises the results from the evidence base in this section, arranged by outcomes as per the NICE scope.

Attrition

Burbach, Galloghly & Snaith (2021)[3] reported that two (33%) of the included six participants withdrew from the program, but did not provide reasons. Galloghly, Haselton & Burbach (2022)[4] reported that seven (25%; n=3 from tier 2 and n=4 from tier 3) of the included 28 children and young people receiving Bytesize completed at least four weeks of the programme, but left early. Reasons included non-attendance or disengagement (n=3), referred back to CAMHS due to complexity (n=1), moved to another intervention within Healios (n=2), and a request to finish early due to reportedly feeling better (n=1). Two (7%) tier 3 participants receiving Bytesize completed less than four weeks before being discharged and returned to CAMHS due to risk.

Treatment satisfaction

Burbach & Stiles (2021)[2] reported effective client engagement and therapeutic alliance using the Healios post-session ratings (HPSR), with the client rating four statements on a scale from 0 to 100 following each session. Average scores by case are reported in Table 2.

Table 2 Average HPSR scores with Healios by case

Scales	Case					
	1	2	3	4	5	6
Listened to (0=Did not listen to me, 100=Listened to me)	100.00	99.03	100.00	85.64	100.00	99.90
Importance (0=What we did and talked about was not really that important to me, 100=What we did and talked about were important to me)	100.00	93.18	99.72	74.87	100.00	99.97
What we did (0=I did not like what we did today, 100=I liked what we did today)	100.00	87.47	99.62	78.13	100.00	100.00
Overall (0=I wish we could do something different, 100=I hope we do the same kind of things next time)	100.00	88.83	98.93	68.53	100.00	100.00

Abbreviation: HPSR, Healios post-session ratings

Children and young people included in the study by Galloghly, Haselton & Burbach (2022)[4] reported the following:

"*Have a way of communicating with your therapist easily between sessions like texting*."

"*Would have benefited from more sessions, once a week seemed a long time in-between*."

"*[Would prefer] 2 sessions a week. Things are forgotten by the next week. More than 10 sessions would help a lot*."

"*I think having some form of direct communication with the clinician we are seeing would be helpful, such as if anything were to happen in the time between sessions I could have contacted her directly*."

One young person included in the study by Burbach, Galloghly & Snaith (2021) reported the following:

""*I like being able to text my therapist, I feel like my therapist is helping me and giving me ideas to improve and things I can do in the moment on the app*."

Measures of symptom severity

All included studies (Burbach & Stiles (2021),[2] Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022)[4]) reported results for the Young Person's Clinical Outcomes in Routine Evaluation (YP-CORE), though there was considerable variability in reporting.

Burbach, Galloghly & Snaith (2021)[3] reported dichotomous outcomes based on YP-CORE as well as Revised Child Anxiety and Depression Scale (RCADS) scores; this study defines clinical improvement (or 'recovery') as "*when the young person moves from above the clinical threshold to the non-clinical range on at least 1 measure (YP-CORE or RCADS-47), and both measures also finish in the non-clinical range*", reliable improvement as "*when the young person makes a specific amount of movement in scores on a scale… To be considered reliably improved, the YP needs to improve in at least one measure (YP-CORE, RCADS or GBO) with no reliable deterioration on any measure*", and clinical and reliable improvement as "*When a change in scores on at least 1 measure indicates both reliable and clinical improvement, with no reliable or clinical deterioration on any other measure*". Results from this study are summarised in Table 3; results of subgroup analyses for completers in both arms and by tier 2 and 3 are reported in Table 4 and Table, respectively.

Table 3 Summary of clinical change, reliable change and clinical and reliable change with Bytesize

Measure	Number (%)
Clinical change	
Improved	9 (35%)
No change	15 (58%)
Deteriorated on at least one routine outcome measure	2 (8%)
Reliable change	
Improved	17 (65%)

No change	6 (23%)
Deteriorated on at least one routine outcome measure	3 (12%)
Clinical and reliable change	
Improved	8 (31%)
No change	17 (65%)
Deteriorated on at least one routine outcome measure	1 (4%)

Table 4 Summary of clinical improvement, reliable improvement and clinical and reliable improvement with Bytesize and CBT with Healios

Measure	Number (%)	
	Bytesize (total n=19)	CBT with Healios (total n=717)
Clinical improvement	9 (60%)	166 (31%)
Reliable improvement	17 (89%)	512 (71%)
Clinical and reliable improvement	8 (53%)	135 (25%)

Table 5 Summary of clinical change, reliable change and clinical and reliable change with Bytesize

Measure	Number (%)	
	Bytesize participants from tier 2 (total n=10)	Bytesize participants from tier 3 (total n=9)
Clinical change		
Improved	5 (50%)	4 (44%)
No change	4 (40%)	4 (44%)
Deteriorated on at least one routine outcome measure	1 (10%)	1 (11%)
Reliable change		
Improved	10 (100%)	7 (78%)
No change	0 (0%)	0 (0%)
Deteriorated on at least one routine outcome measure	0 (0%)	2 (22%)
Clinical and reliable change		
Improved	4 (40%)	4 (44%)
No change	6 (60%)	4 (44%)
Deteriorated on at least one routine outcome measure	0 (0%)	1 (11%)

Changes in individual YP-CORE scores reported in Burbach & Stiles (2021)[2] are summarised in Table 6.

Table 6 Summary of changes in YP-CORE scores with Healios reported in Burbach & Stiles (2021)[2]

Timepoint	Cases			
	1	2	3	4
Before treatment	18 (moderate)	11 (mild)	36 (severe)	18 (moderate)
End of treatment	8 (low-level problems) [a,b]	0 (healthy)[a,b]	19 (moderate) [a,b]	20 (moderate)

Abbreviation: YP-CORE, Young Person's Clinical Outcomes in Routine Evaluation
Notes:
[a] clinical improvement
[b] reliable improvement (statistically significant change and clinical improvement as scores changing from above to below the clinical cut-off)

Burbach, Galloghly & Snaith (2021)[3] reported YP-CORE outcomes narratively for only one participant in the sample who withdrew, stating that the patient's score was more than halved and demonstrated reliable improvement from her baseline score in the 'severe' range.

Two included studies (Burbach & Stiles (2021)[2] and Galloghly, Haselton & Burbach (2022)[4]) reported results for the Revised Child Anxiety and Depression Scale – child report (RCADS-C), while Burbach & Stiles (2021)[2] additionally reported the parent-reported measure (RCADS-P). The RCADS results reported in Burbach, Galloghly & Snaith (2021)[3] were reporting indirectly through dichotomous outcomes of clinical improvement, reliable improvement as well as clinical and reliable improvement, based on YP-CORE as well as RCADS scores, as described earlier in this section and summarised in Table 3 above. The results for RCADS measures reported in Burbach & Stiles (2021)[2] are summarised in Table 7.

Table 7 Summary of changes in RCADS scores with Healios reported in Burbach & Stiles (2021)[2]

Measure	Timepoint	Cases				
		1	2	3	4	5
RCADS-C	Before treatment	73 (clinical)	61 (normal)	69 (borderline clinical)	78 (clinical)	62 (normal)
	End of treatment	54 (normal) [a,b]	53 (normal)	33 (normal) [a,b]	61 (normal) [a,b]	54 (normal)
RCADS-P	Before treatment	65 (borderline clinical)	67 (borderline clinical)	77 (clinical)	NR[c]	87 (clinical)
	End of treatment	NR	NR	51 (normal)	79 (clinical)	79 (clinical)

Abbreviation: NR, not reported; RCADS(-C/P), Revised Child Anxiety and Depression Scale (- child/parent report)
Notes:
[a] clinical improvement
[b] reliable improvement (statistically significant change and clinical improvement as scores changing from above to below the clinical cut-off)
[c] the questionnaire had not been completed

Social, behavioural and functional outcomes

The study by Burbach & Stiles (2021)[2] reported on the Strengths and Difficulties Questionnaire (SDQ), measuring changes in both the child- and parent-reported version. The results for SDQ measures reported in Burbach & Stiles (2021)[2] are summarised in Table 8.

Burbach & Stiles (2021)[2] as well as Galloghly, Haselton & Burbach (2022)[4] measured goal-based outcomes (GBO), though only the full paper by Burbach & Stiles (2021)[2] reported results for this measure. The results for GBO measures reported from this paper are summarised in Table 9.

Table 8 Summary of changes in SDQ scores with Healios reported in Burbach & Stiles (2021)[2]

Measure	Timepoint	Cases				
		1	2	3	4	5
SDQ-C	Before treatment	20 (very high)	21 (very high)	22 (very high)	23 (very high)	NR
	End of treatment	9 (average) [a,b]	NR	8 (average) [a,b]	17 (raised) [a]	NR
SDQ-P	Before treatment	12 (average)	13 (average)	22 (very high)	NR	24 (very high)
	End of treatment	NR	NR	13 (average) [a,b]	18 (high)	26 (very high)

Abbreviation: NR, not reported; SDQ(-C/P), Strengths and Difficulties Questionnaire (- child/parent report)
Notes:
[a] clinical improvement
[b] reliable improvement (statistically significant change and clinical improvement as scores changing from above to below the clinical cut-off)

Table 9 Summary of changes in GBO scores with Healios reported in Burbach & Stiles (2021)[2]

Goals	Cases					
When set-end of treatment	1	2	3	4	5	6
1	6-9[a]	3-8 [a]	0-10 [a]	GBI-goal 1: 0-2	CBT-goal 1: 2-3	1-6 [a]
2	7-8	2-7 [a]	4-10 [a]	0-1	3-4	NR
3	NR	NR	0-3 [a]	4-10 [a]	4-2	NR
4	NR	NR	NR	0-2	5-3	NR
5	NR	NR	NR	1-1	0-0	NR
6	NR	NR	NR	0-0	NR	NR
7	NR	NR	NR	0-1	NR	NR
8	NR	NR	NR	0-0	NR	NR

Abbreviation: CBT, cognitive behavioural therapy; GBI, goal-based intervention; GBO, goal-based outcomes; NR, not reported
Notes:
[a] reliable improvement (statistically significant change and clinical improvement as scores changing from above to below the clinical cut-off)

Suicidal thoughts and behaviour

The full paper by Burbach & Stiles (2021)[2] reported that all nine included participants had undergone a risk assessment prior to treatment, but that only one participant (11%) disclosed previous self-harm, suicidal thoughts and a current plan to end her life but no intent to do so. The authors report that no action was taken at this stage, but that risk was monitored in each session. This participant experienced a drop in mood in the middle of treatment; at this stage her mother disclosed worries of risk to self and the participant expressed feelings of worthlessness and suicidal ideation, though she reported no intent to act on these thoughts. The participant remained in the study and was closely monitored for the remaining sessions; her mother was also provided with details for the local CAMHS crisis team.

The conference presentation by Galloghly, Haselton & Burbach (2022)[4] reported on 'risk to self over the last week' as part of the YP-CORE assessment through crude reporting of attrition. This study reported that two (7%) of the 28 CYP receiving Bytesize, both from tier 3, completed less than four weeks of treatment before being discharged and returned to CAMHS due to risk. One participant had completed four sessions over 1.6 weeks, the other only attended the baseline measures session.

Rates of remission

The full paper by Burbach & Stiles (2021)[2] reported 'reliable improvement', defined as a statistically significant change and clinical improvement as scores changing from above to below the clinical cut-off. This outcome is detailed per outcome in the footnotes to Table 6, Table 7, Table 8 and Table 9. Broadly, on completed before-after measures of symptom severity, three of five (60%) of participants showed clinical and reliable improvement on RCADS-C; one of two (50%) showed clinical and reliable improvement on RCADS-P.

The conference presentation by Galloghly, Haselton & Burbach (2022)[4] reported on 'clinical improvement', 'reliable improvement' and 'clinical and reliable improvement'

as discussed under 'Measures of symptom severity' and reported in Table 3. Broadly, the study reported that 35% of participants were clinically improved, 65% were reliably improved and 31% were clinical and reliably improved.

Patient experience

Burbach & Stiles (2021)[2] reported results of the Healios Experience of Service Questionnaire (HESQ), stating that all cases reported satisfaction with the services. The HESQ responses related to CBT are summarised in Table 10.

Table 10 HESQ responses to Healios from young people and parents

Case	HESQ (maximum score of 24 if all 12 questions are completed	
	Young person	Parent
1	22/22 (18/18 + 4/4)	NR
2	24/24 (18/18 + 6/6)	24/24 (18/18 + 6/6)
3	NR	24/24 (18/18 + 6/6)

Abbreviation: HESQ, Healios Experience of Service Questionnaire; NR, not reported

3.4. Adverse events

None of the studies with eligible and available outcome data (Burbach & Stiles (2021),[2] Burbach, Galloghly & Snaith (2021)[3] and Galloghly, Haselton & Burbach (2022)[4]) reported on specific adverse events. Both Burbach & Stiles (2021)[2] and Galloghly, Haselton & Burbach (2022)[4] reported on suicidal thoughts and behaviour; the former as instances of self-harm or suicidal thoughts, the latter on 'risk to self'. These are summarised under 'Suicidal thoughts and behaviour' in Section 3.3.

3.5. Evidence synthesis

Given the heterogeneity in the evidence base as it pertains to outcomes as well as the absence of comparative evidence (with the exception of Galloghly, Haselton & Burbach (2022)[4]), it was not possible to synthesise findings; neither for Bytesize nor or across intervention categories reported here and in the main report. Even if synthesis was to be attempted, small sample sizes would result in underpowered analyses and the risk of spurious findings.

Addressing the identified evidence gaps and heterogeneity issues should improve the feasibility of future evidence syntheses, while addressing identified generalisability gaps would improve the external validity and, consequently, utility of such analyses.

3.6. Ongoing studies

The EAG identified one prospective or ongoing study by Healios (2022) investigating Bytesize. Full details are available in Table 11.

The EAG noted that this study was well-aligned with the NICE scope, including an active comparator as well as participants and settings considered to map well to the NICE scope. Outcomes, however, were not specified and therefore it is not clear whether this study intends to report on RCADS-C or RCADS-P, the outcome that would most likely be used in any economic modelling for all scoped interventions, or YP-CORE, the outcome that is common to most Bytesize interventions.

Table 11 Ongoing study investigating Bytesize, indicating relevance in terms of scope and availability of data for economic modelling

Ongoing study	Alignment with scope	Outcome data for economic model	Indicated trial end date
[redacted] Healios (2022) [redacted]	Intervention: **GREEN** Comparator: **GREEN** Participants: **GREEN** Setting: **GREEN** Outcomes: **could not be assessed**	[redacted]	[redacted]

Abbreviation: [redacted]

4. ECONOMIC EVIDENCE REVIEW FOR BYTESIZE (HEALIOS)

4.1. Published Evidence

No additional economic evidence of relevance over and above that described in Section 12.1 of the main report was identified.

4.2. Resource use and cost

Bytesize provides in-house therapists and coaches alongside the ThinkNinja app, accessible via text and videocall, scaled according to clinical need (that is, coach followed by trained CBT therapist). The programme lasts over an 8-12 week period. As per assumptions in Section 12.2.2 of the main report, CYP require access to a mobile phone or tablet computer plus internet connection. Table 12 reproduces Table 18 from the main report with the addition of ThinkNinja Bytesize for comparison.

Table 12 Resource items and quantities for interventions

	Silvercloud	**OSI**	**OSCA**	**Lumi Nova**	**ThinkNinja Bytesize**
Duration of intervention	8 weeks	8 weeks	14 weeks	8 weeks	8-12 weeks
Resource items	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone
	Internet connection (8 wks)	Internet connection (8 wks)	Internet connection (16 wks)	Internet connection (8 wks)	Internet connection (8-12 wks)
	8x20minute telephone call with therapist	8x20minute telephone call with therapist	14x20 minute telephone call with clinical psychologist	8x20 minute telephone call with therapist.	[included within licence cost]

Abbreviations: OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, online support and intervention for child anxiety

The company reports a per-user licence fee of [redacted].

4.3. Commentary on relative cost-effectiveness vs other dCBT interventions

The company reports that they do not yet have the evidence to establish whether ThinkNinja Bytesize is cost-effective. They position themselves as an alternative to face to face CBT delivered via videoconference. The EAG agrees that this is a relevant comparator but also considers whether it may have a place alongside the other dCBT interventions considered in this evaluation, that is, as an initial 'step 1' intervention, prior to face to face (d)CBT:

The EAG notes (1) that the per user cost is higher than the indicative per-user cost of the other interventions, and (2) the current lack of data on the relative effectiveness of ThinkNinja Bytesize with any other dCBT intervention. Whilst the licence cost is partially offset by in-house provision of therapist text/video support, the EAG considers it unlikely that any additional effectiveness would be sufficient to justify ThinkNinja alongside the other dCBT interventions as a 'step 1'. However, it is likely to compare favourably with face to face CBT. The evidence base supporting the EAG comments above is, however, extremely weak, and therefore should be considered speculative and not definitive.

5. INTERPRETATION OF THE EVIDENCE

5.1. Evidence gap analysis

A summary of evidence gaps for all scoped interventions, pertaining to the intermediate and final outcomes from the scope, and those pertaining to decision modelling are summarised in Table 13. Evidence available for OSCA is considered AMBER due to the lack of an active comparator, evidence for Bytesize is considered AMBER due to the non-randomised design of the study.

Table 13 Evidence Gap Analysis

Outcomes	SilverCloud interventions	OSCA	OSI	Lumi Nova	Bytesize
Clinical trials					
Intermediate outcome: Intervention-related adverse events	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	No **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Intermediate outcome: Rates of and reasons for attrition	No studies **RED**	Yes, rates only, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, rate only, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Intermediate outcome: Treatment satisfaction and engagement	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series, feasibility study and formative research **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Symptom severity (self/parent/practitioner reported)	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist	Yes, single-arm case series and feasibility study **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active

		control) **AMBER**			control) **AMBER**
Clinical outcome: Social, behavioural and functional outcomes (self/parent/practitioner reported)	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Suicidal thoughts and behaviour	No studies **RED**	No **RED**	No **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Global functioning	No studies **RED**	No **RED**	Yes, single-arm case series and feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Rates of remission	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Patient reported outcomes: HRQoL	No studies **RED**	No **RED**	Yes, single-arm feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Patient reported outcomes: Patient experience	No studies **RED**	No **RED**	Yes, single-arm case series and feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Resource use and costs	No studies **RED**	No **RED**	Yes, use and cost of other resources, single-arm	No **RED**	Yes, evidence from one two-arm NRS (active

			feasibility study **RED**		control) **AMBER**
Real-world evidence					
Intermediate outcome: Intervention-related adverse events	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Intermediate outcome: Rates of and reasons for attrition	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Intermediate outcome: Treatment satisfaction and engagement	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Symptom severity (self/parent/practitioner reported)	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Social, behavioural and functional outcomes (self/parent/practitioner reported)	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical Outcome: Suicidal thoughts and behaviour	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Global functioning	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Clinical outcome: Rates of remission	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Patient reported outcomes: HRQoL	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Patient reported outcomes: Patient experience	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Resource use and costs	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**	No studies **RED**
Models and economic outcomes					

Effectiveness evidence: Comparative data	No direct or indirect comparisons of effect of the target interventions (and TAU). Is one dCBT intervention more effective than another and TAU? **RED**
Effectiveness evidence: Comparative data	Is one dCBT intervention more effective than another and face to face CBT? **RED**
Effectiveness evidence: Follow-up times and lengths	Follow-up times vary across the source studies, which are crudely equalized to 3m in the decision model. Common FU times are required, along with longer term follow-up data (to 12m+). **RED**
Effectiveness evidence: Discontinuations / withdrawals	Withdrawals are currently accounted for via ITT analyses of RCADS-P. Should they be modelled specifically? **AMBER**
Clinical outcome and costs: Qualifications of mental health contact	Is a mental health support worker as effective as a clinical psychologist at providing weekly contacts? **AMBER**
HRQoL: Estimating health state utilities	Is RCADS-P the most appropriate tool on which to base health state utilities for CYP? What other tools are there for measuring and valuing mild/moderate anxiety and depression in CYP? **RED**

Abbreviations: (d)CBT, (digital) cognitive behavioural therapy; CYP, children and young people; FU, follow-up; HRQoL, health-related quality of life; ITT, intention to treat; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, online support and intervention for child anxiety; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– child/parent report); RCT, randomised controlled trial; TAU, treatment as usual

6. REFERENCES

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3. Burbach FR, Galloghly E, Snaith M. CBT BYTESIZE: Assessing the feasibility of a novel multimodal intervention for anxiety. [Available from: https://394uad4bz4ay1u40s3479p6q-wpengine.netdna-ssl.com/wp-content/uploads/2022/07/CBT-Bytesize-%E2%80%93-assessing-the-feasibility-of-a-novel-multimodal-intervention-for-anxiety.pdf accessed 09/10/2022.
4. Galloghly E, Haselton PA, Burbach FR. Encouraging results from an initial evaluation of CBT bytesize - a novel multimodal digital intervention for anxiety. BABCP 5-th Annual Conference. London, 2022.

7. APPENDIX I. SEARCH STRATEGIES

A summary of the resources searched for clinical effectiveness evidence is presented in Table 14.

Table 14 Resources searched for the additional HEALIOS search

Database/Resource	Host	Date range	Date Searched	Results
MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily	Ovid	1946 to October 03, 2022	4.10.22	2
Embase	Ovid	1974 to 2022 Week 39	4.10.22	9
APA PsycINFO	Ovid	1806 to September Week 4 2022	4.10.22	1
CDSR	Cochrane Library: Wiley	Issue 10 of 12, October 2022	4.10.22	0
CENTRAL	Cochrane Library: Wiley	Issue 01 of 12, October 2022	4.10.22	0
INAHTA HTA database	https://database.inahta.org/	up to 4 October 2022	4.10.22	0
KSR Evidence	www.ksrevidence.com	Database last updated 4 October 2022	4.10.22	0
Epistemonikos	https://www.epistemonikos .org	up to 4 October 2022	4.10.22	2
ClinicalTrials.gov	http://www.clinicaltrials.gov/	up to 4 October 2022	4.10.22	5
WHO ICTRP	https://trialsearch.who.int/	up to 4 October 2022	4.10.22	4
NHS EED	CRD interface	up to 4 October 2022	4.10.22	0
CEA Registry	www.cearegistry.org	up to 4 October 2022	4.10.22	0
RePEc	http://repec.org/	up to 4 October 2022	4.10.22	0
ScHARRHUD	www.scharrhud.org/	up to 4 October 2022	4.10.22	0

Database/Resource	Host	Date range	Date Searched	Results
Total records retrieved			**23**	
Total records after deduplication			**17**	

MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily (Ovid): 1946 to October 03, 2022; Searched: 4.10.22

1 Healios.ti,ab. (2)

Embase (Ovid): 1974 to 2022 week 39; Searched: 4.10.22

1 Healios.ti,ab. (9)

APA PsycINFO (Ovid): 1806 to September Week 4 2022; Searched: 4.10.22

1 Healios.ti,ab. (1)

Cochrane Database of Systematic Reviews (CDSR) (Wiley): Issue 10 of 12, October 2022 and Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): Issue 10 of 12, October 2022; Searched: 4.10.22

#1 Healios 0

International HTA Database (INAHTA): up to 4 October 2022; https://database.inahta.org/; Searched: 4.10.22

healios 0 records

KSR Evidence (Internet): Database last updated 4 October 2022; www.ksrevidence.com; Searched: 4.10.22

1 haelios in All text 0 results

Epistemonikos (Internet): up to 4 October 2022; https://www.epistemonikos.org/en/; Searched: 4.10.22

healios Total: 2

Clinicaltrials.gov (Internet): up to 4 October 2022; http://clinicaltrials.gov/ct2/search/advanced; Searched: 4.10.22

healios 5 Studies found

WHO International Clinical Trials Register Portfolio (ICTRP) (Internet): up to 4 October 2022; http://www.who.int/ictrp/search/en/; Searched: 4.10.22

The search strategy for the WHO International Clinical Trials Register Portfolio is presented in Table 15.

Table 15 Results of WHO ICTRP search

	Results
healios	(4 records for) 4 trials found

NHS Economic Evaluation Database (NHS EED) (CRD): up to 31 March 2015; http://www.crd.york.ac.uk/CRDWeb/; Searched: 4.10.22

1 healios 0

Cost-Effectiveness Analysis (CEA) Registry (Internet): up to 4 October 2022; www.cearegistry.org; Searched: 4.10.22

healios 0 Records retrieved

RePEc (Internet): up to 4 October 2022; http://repec.org/; Searched: 4.10.22; IDEAS search interface

healios Records retrieved 0

ScHARR Health Utilities Database (ScHARRHUD)(Internet): up to 4 October 2022; www.scharrhud.org/; Searched: 4.10.22

The search strategy for the ScHARR Health Utilities Database is presented in Table 16.

Table 16 Results of ScHARRHUD search

Search terms	Results
healios	0
Total	0

8. APPENDIX II. RISK OF BIAS OF INCLUDED STUDIES

Cochrane's Risk of Bias tool was used to assess the methodological quality of included studies with eligible and available data. The results of these assessments are presented in Table 17.

Table 17 Summary of risk of bias assessments of included studies with eligible and available data

Domain	Burbach & Stiles (2021)[2]		Burbach, Galloghly & Snaith (2021)[3]		Galloghly, Haselton & Burbach (2022)[4]	
	Judgment	Comment	Judgment	Comment	Judgment	Comment
Random sequence generation	N/A	Single-arm study.	N/A	Single-arm study.	High	Two-arm non-randomised study offering participants a choice of allocation.
Allocation concealment	N/A	Single-arm study.	N/A	Single-arm study.	High	Two-arm non-randomised study offering participants a choice of allocation.
Blinding of participants and personnel	High	Single-arm study, no blinding reported.	High	Single-arm study, no blinding reported.	High	Two-arm study offering participants a choice of allocation.
Blinding of outcome assessors	High	Parents and participants as assessors, no blinding reported.	High	Participants as assessors, at least for the primary outcome, with no blinding reported.	High	Participants as assessors.
Incomplete outcome data	Low	No obvious attrition reported or identified.	High	A fairly high proportion (33%) of young people completed four weeks or less of Bytesize. It is not reported if, or how, missing data were addressed.	High	A fairly high proportion (32%) of CYP completed four weeks or less of Bytesize. No information on attrition in the CBT with Healios arm. It is not reported if, or how,

Domain	Burbach & Stiles (2021)[2]		Burbach, Galloghly & Snaith (2021)[3]		Galloghly, Haselton & Burbach (2022)[4]	
	Judgment	**Comment**	**Judgment**	**Comment**	**Judgment**	**Comment**
						missing data were addressed.
Selective outcome reporting	Low	All outcomes specified in the Methods section are reported in the Results section.	Unclear	Could not be assessed due to a lack of *a priori* stated outcomes.	Unclear	Could not be assessed due to a lack of *a priori* stated outcomes.
Other bias	Low	None identified.	High	Lack of reporting regarding unbiased recruitment.	High	Lack of reporting regarding unbiased recruitment.

Abbreviations: CBT, cognitive behavioural therapy; CYP, children and young people

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health technology evaluation

Assessment report overview

Guided self-help digital cognitive behaviour therapy for children and young people with mild to moderate symptoms of anxiety or low mood

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

Key issues for consideration by the committee are described in section 6, following the brief summaries of the clinical and cost evidence.

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

This overview also contains:

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

1 The technology

Guided self-help digital cognitive behavioural therapy (CBT), describing the use of self-help materials in a digital format with some professional guidance, is a treatment that is delivered via mobile phones, tablets, and computers. It is based on the principles of face-to-face CBT which is a talking therapy that can help a person learn new skills to manage problems by understanding how thoughts can affect how they feel and behave and includes various components including psychoeducation and cognitive restructuring.

In total, 5 guided self-help digital CBT technologies designed to treat children and young people with symptoms of anxiety or low mood are included in this assessment.

Space from anxiety for teens, Space from low mood for teens, Space from low mood & anxiety for teens (SilverCloud)

Internet-based (computer, tablet or smart phone) intervention for teens aged 15 to 18 years old with symptoms of anxiety, low mood, or both. However, according to CAMHS protocols and clinical judgement, it can be used in a younger age group. It has seven core modules structured around the principles of traditional CBT which include: understanding anxiety or low mood, noticing feelings, facing your fears, spotting thoughts, challenging thoughts, managing worry and reflections on learnings. The supported model has online support from psychologists and online cognitive behavioural therapy co-ordinators to assess the needs of the person. After each module, they check in to help the person progress through the CBT content and send motivational messages. It is used in several services in the NHS.

Online support and intervention for child anxiety (OSI)

OSI is an internet based (computer, tablet and smart phone), parent-led and therapist supported psychological intervention for children aged 5 to 12 years old with symptoms of anxiety. It comprises three components, a parent's website, a clinician case management website and an optional game app for children (Monster's Journey: Facing Fears). It comprises seven core modules

that include interactive worksheets, videos and quizzes. Parents or carers have weekly telephone appointments with the therapist to review the work they have done over the previous week, after which the next week's weekly module is released.

OSCA (Online Social anxiety Cognitive therapy for Adolescents)

OSCA is an internet programme of cognitive therapy for social anxiety in adolescents aged 14 to 18 years old. All users receive a core set of modules to work through at the beginning of the programme which is then individualised for each user. The therapist will carry out a 15-minute phone call with the user each week and releases modules that will be most helpful to that person, depending on their concerns. They will receive encouragement and support via secure messaging within the online programme and SMS texts. Parents are involved by receiving regular emails on their child's progress. This is explained to children aged 14 to 15 and consented from young people aged 16 to 18 years old.

Lumi Nova (BfB Labs)

Lumi Nova: Tales of Courage is a CE marked class 1a medical device digital therapeutic intervention in the form of a game available on Android and iOS for children and young people aged between 7 and 12 with symptoms of mild to moderate anxiety. It combines evidence-based therapeutic content (exposure therapy, a form of CBT) and psychoeducational content within an intergalactic role-playing game. Access to Lumi Nova is provided through a secure web-based platform, VitaMind Hub (BfB Labs Ltd), which is a point of access for practitioners that allow them to track and monitor player progress with the game. Practitioners also check in with users and guardians provide support to their child (app user) when needed and can receive SMS notifications when their child uses the app.

ThinkNinja CBT Bytesize (Healios)

ThinkNinja CBT-Bytesize is intended for children and young people aged 11 years and older with anxiety or low mood, and related problems. It is an app

that contains psychoeducational, and CBT based content which is delivered in a semi-structured 8-to-12-week programme with wrap around clinician support in the form of text messaging in the app and video calls via a secure platform on the computer or tablet. The coaches and CBT therapists providing the support are employed by Healios. The protocol specifies at least 3 short clinical contacts per week (text or video calls), but children and young people are encouraged to get in touch via text at any time. The team has extended working hours to provide responses promptly.

2 Proposed use of the technology

2.1 Disease or condition

Anxiety disorders are one of the most common types of mental health disorders in children and young people. In 2017, 3.9% of 5- to 10-year-old children were identified as having an anxiety disorder, 7.5% of 11- to 16-year-olds and 13.1% of 17- to 19-year-olds. Anxiety in children and young people may negatively impact education, social functioning and family life. Anxiety disorders can have a lifelong course of relapse and remission and can persist into adulthood if left untreated. The worldwide prevalence of anxiety disorders in children and adolescents is estimated at 6.5%, with the median age of onset of 11 years.

Depression is also a common mental health problem and can present itself in different symptoms, including low mood. Other symptoms in children include being irritable, not being interested in things they used to enjoy, feeling tired, having trouble sleeping or sleeping more than usual, not being able to concentrate, being indecisive, not having much confidence, changes in eating habits and weight, talking about feeling guilty or worthless. The point prevalence of dysthymia in adolescents is estimated to be 4% and is one of the most common mental health problems facing young people. Depression in adolescence can have a negative effect on relationships, development trajectory, schooling, and educational attainment and increases the risk of suicide.

2.2 Patient group

Guided self-help digital CBT can be used to provide an alternative and more accessible treatment option for children aged 5 to 11 and young people aged 12 to 18 with mild to moderate symptoms of anxiety or low mood that are significantly interfering with their ability to function in their daily lives. Early research suggests that the pandemic and subsequent measures have had a significant impact on the mental health of children and young people. This has subsequently intensified issues related to accessing effective mental health treatments including limited availability because of shortage of qualified staff, long waiting times and access to treatment depending on the severity of symptoms. It is estimated that only 1 in 3 children with a mental health condition get access to NHS care and treatment. In 2019/20, the reported average waits across England ranged from 8 days to 82 days, and only 20% of children referred to services started treatment within 4 weeks – the ambition set out in the Government's Green Paper on children's mental health.

2.3 Current management

Symptoms of anxiety or low mood may be identified by the child or young person themselves, their parents or carer, GPs and in community care, social workers or in school. Children and young people can be assessed and treated in a range of settings, including school mental health support teams, single point of access teams (SPA), voluntary sector teams and children and young people's mental health services (CYPMHS). Not all children and young people with mild to moderate symptoms of anxiety or low mood will meet the severity threshold to be seen by CYPMHS and are treated within mental health support teams (MHSTs). SCM advice to the EAG indicated that it is not clear whether MHSTs have the training to identify levels of severity of anxiety or low mood to direct different types of treatment. Across these settings the professionals will have varying levels of specialist mental health training and expertise to provide targeted outcome-focused help. These professionals might include nurses, therapists, psychologists, child and adolescent

psychiatrists, support workers, social workers, health visitors, school nurses, education mental health practitioners.

Children and young people's mental health services (CYPMHS), sometimes known as Child and adolescent mental health services (CAMHS), are services that support children and young people with their mental health. Care is personalised, varied and provided across a range of settings. The THRIVE framework can be used to determine a care package based on the needs of the child or young person. The framework integrates a person centred, and needs led approach to delivering mental health services for children, young people and families which conceptualises need in 5 categories: thriving, getting advice and signposting, getting help, getting more help, and getting risk support.

2.4 Proposed management with new technology

Guided self-help digital CBT may be offered as a first line treatment for children and young people identified as having mild to moderate symptoms of anxiety or low mood, who are considered as 'getting help' or 'getting more help' based on the THRIVE framework, to improve access to treatment. Users may then continue to further support such as face to face CBT.

3 The decision problem

Details of the decision problem from the scope are described in Table 1. The clinical experts have provided advice to the EAG for some elements of the decision problem, however the EAG made no changes to the decision problem.

Table 1. Decision problem

Elements of assessment	Final scope issued by NICE	Clinical expert advice
Population	Children and young people with mild to moderate symptoms of anxiety or low mood that are	Expert advice to the EAG suggested the presence of considerable heterogeneity in the clinical characteristics, risk factors

	significantly interfering with their ability to function in their daily lives • Children aged 5 to 11 • Young people aged 12 to 18 • Children and young people with neurodevelopmental disorders	and care pathway of young people aged 12 to 18, and that this subgroup may be too broad. Expert advice noted that the target population has high neurodiversity and this needs to be addressed.
Interventions (proposed technologies)	Guided self-help digital cognitive behavioural therapy technologies supported by healthcare professionals aimed at children and young people with mild to moderate symptoms of anxiety or low mood as a first line treatment: • Space from anxiety for teens, Space from low mood for teens, Space from anxiety and low mood for teens • Online support and intervention (OSI) • OSCA (Online Social anxiety Cognitive therapy for Adolescents) • Lumi Nova • CBT Bytesize and standard care that may include education, advice, support and signposting	None
Comparator	Standard care that may include education, advice, support and signposting	Expert advice to the EAG suggested that face-to-face therapy should be included as a comparator as the current standard of care. Expert advice further suggested that the active comparator should be online-supported psychoeducation without CBT content.
Healthcare setting	Mental health support teams, including those based in schools and primary care	Expert advice to the EAG suggested that CAMHS/CYPMHS as MHST only cover one third of the UK, with the balance covered by CYPMHS.
Outcomes	Intermediate measures for consideration may include:	None

	• Intervention-related adverse events • Rates of and reasons for attrition Treatment satisfaction and engagement	
	Clinical outcomes for consideration may include: • Measures of symptom severity (self-, parental- or practitioner reported) • Social, behavioural, and functional outcomes (self, parental or practitioner reported) • Suicidal thoughts and behaviour • Global functioning Rates of remission	Expert advice to the EAG suggested that school and social functioning should be considered along with global functioning.
	Patient-reported outcomes for consideration may include: • Health-related quality of life, including well-being • Patient experience	None

Costs	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:
	• Costs of the technologies including licensing fees
	• Cost of other resource use (e.g., associated with managing anxiety, adverse events or complications):
	  ○ GP, mental health support team or CYPMHS appointments
	  ○ Health care professional training, grade and time for providing regular support and guidance for the users of the dCBT technologies
		Expert advice to the EAG suggested that school-related costs should also be considered.

Time horizon	The time horizon for estimating the clinical and economic value should be sufficiently long to reflect any differences in costs or outcomes	Expert advice confirmed that the 1-year time horizon was clinically relevant because these interventions can have a

	between the technologies being compared.	sustained benefit. It is thus important to follow up longer term to capture this. Three months is considered short term, 6 months medium term and 12 months long term. However, expert advice also noted that long term follow up can be difficult because things can change, and other interventions may come in after this one is completed.

4 The evidence

4.1 Summary of evidence of clinical benefit

The EAG included 5 publications (Hill et al., 2022a; Hill et al., 2022b; Leigh & Clark, 2022; Lockwood et al., 2022; Williamson et al., 2022), 2 conference abstracts (Burbach et al., 2021; Galloghly et al., 2022) and 2 unpublished studies (Green et al., 2022; provisionally accepted for publication; [redacted]) as evidence. Of the included studies, 7 were single arm designs with no direct comparator (Burbach et al., 2021; Green et al., 2022; Hill et al., 2022a; Hill et al., 2022b; Lockwood et al., 2022; [redacted]; Williamson et al., 2022). Only 1 study had a RCT design (Leigh & Clark, 2022) and 1 study had a two-arm nonrandomised design (Galloghly et al., 2022). All studies included the appropriate intervention, though the EAG noted that Hill et al., (2022a) reported formative work on a beta-version of OSI that was still undergoing iterative development. Because this research was done on a previous and not final version of OSI the EAG does not consider the available evidence on patient experience with the beta version to have value for the current EVA. Further study protocols and trial registry entries are discussed under ongoing research (section 5). The rationale for the selection of these studies can be found in section 8.1 and 8.2 of the EAG's external assessment report.

Table 2. Included published and unpublished studies in the assessment

	Published and unpublished studies
CBT Bytesize	2 conference abstracts • 1 two-arm non-randomised study (Galloghly et al., 2022) • 1 single arm feasibility study (Burbach et al., 2021)
Lumi Nova	1 publication • 1 single arm evaluation study (Lockwood et al., 2022)
OSCA	1 publication • 1 RCT (Leigh & Clark, 2022)
OSI	4 publications, of which 1 is unpublished • 1 single arm case series (Hill et al., 2022a) • 1 single arm formative research (Hill et al., 2022b) • 1 single arm feasibility study (Williamson et al., 2022) • [redacted] (Green et al., 2022)
Silvercloud	1 unpublished study • [redacted]

The EAG assessed the quality of the 1 unpublished (Green et al., 2022), 4 published studies (Hill et al., 2022b; Leigh & Clark, 2022; Lockwood et al., 2022; Williamson et al., 2022) and 2 conference abstracts (Burbach et al., 2021; Galloghly et al., 2022). All studies with eligible and available outcome data had aspects that the EAG considered to be threats to internal validity. All single arm studies were at risk of performance bias because blinding of participants was not possible (Burbach et al., 2021; Green et al., 2022; Hill et al., 2022b; Lockwood et al., 2022; [redacted]; Williamson et al., 2022). This can be problematic as knowledge of receiving an active intervention may have caused participants to behave or think in a different way than they would have, had they not known they were receiving an active intervention. It may cause them to adhere better or engage more with the content. There was also risk of detection bias and attrition bias. Random sequence generation and allocation concealment, and risk of detection bias was judged to be unclear for the RCT (Leigh & Clark, 2022) due to a lack of explicit reporting and some outcomes being assessed by participants, respectively. Selective outcome reporting was not identified in any of the studies. For further detail see section 9.2 and appendix E of the external assessment report.

The RCT (Leigh & Clark, 2022) suggests the OSCA intervention is more effective than a waiting list control in terms of anxiety symptom severity, waiting list controls showed a deterioration over time. Before-and-after cohort analyses of OSI and Lumi Nova suggest an improvement in anxiety symptom severity over time (Hill et al., 2022b; Lockwood et al., 2022). There is very weak evidence that CBT bytesize results in clinical and reliable improvements over time and that Bytesize may be more effective than CBT with Healios for these outcomes (Burbach et al., 2021; Galloghly et al., 2022). At present there is no peer-reviewed evidence published on the Silvercloud interventions. See section 9.3 of the external assessment report for further detail.

Hill et al. (2022b) did not measure, monitor for or report any adverse events with OSI. For CBT Bytesize, none of the studies with eligible and available outcome data, Burbach et al., (2021) and Galloghly et al., (2022) reported on specific adverse events. Leigh & Clark (2022) reported that no adverse events or serious adverse events were identified with OSCA. Lockwood et al. (2022) reported safety using the RCADS-P subscale for major depressive disorder which showed non-significant change in scores from the start to the end of the Lumi Nova intervention.

The EAG made the following overarching comments regarding the evidence base:

- Sample sizes across interventions were small (ranging from 23 to 360 participants) and presented a risk of spurious chance findings and underpowered analyses.

- None of the studies described participants with low mood. However, the EAG further noted that Silvercloud is the only technology that is intended for this population. The other interventions were intended for anxiety indications.

- The generalisability to the UK setting was well-aligned, given all studies were conducted in UK settings and the ethnic mix of participants is

broadly reflective of that of the country. Population generalisability of all included studies was considered to be limited by the explicit or implicit exclusion of children with ASD or learning disability, a group of patients that represents a considerable proportion of the target population. Furthermore, clinical advice to the EAG suggested that children with neurodevelopmental conditions might prefer online modes of delivery over face-to-face therapy interactions.

- None of the included studies reported on all outcomes included in the NICE scope, but all reported some outcomes of interest. The EAG considered outcomes to be heterogeneously measured, particularly in terms of symptom severity and social, behavioural and functional outcomes. However, most studies reported (or intend to report) symptom severity as RCADS and social, behavioural and functional outcomes as CAIS. This suggests using these measures in any future studies would be most useful for comparability and homogeneity in the evidence base. Clinical advice confirmed RCADS and CAIS to be appropriate measures for symptom severity and impairment and that self-report of these measures would be preferable for adolescents. For impairment, they suggested that the Children's Global Assessment Scale (CGAS) and Health of the Nation Outcome Scales for Children and Adolescent mental health (HoNOSCA) were also appropriate as CAIS is a broad measure.

In summary, the EAG concluded that there is some evidence to suggest the guided dCBT interventions may be better than treatment as usual. The EAG also concluded that addressing the identified evidence gaps and heterogeneity issues should improve the feasibility of future evidence syntheses, while addressing identified generalisability gaps would improve the external validity and, consequently, utility of such analyses. This can help decision-making about using dCBT interventions as a first-line treatment.

Table 3: general details of the peer-reviewed studies included in the assessment report

Study name, design & location	Participants and setting	Intervention & comparator	Outcome measures	EAG comments
OSI				
Hill, Chessell, Percy, et al. (2022b) Single arm case series UK	23 children aged between 7 and 12 years old assessed as having a primary anxiety problem associated with significant functional impairment **Setting:** NHS research clinic	**Intervention**: OSI (therapist-supported, parent-led) **Comparator**: None	• Attrition (rates & reasons) • Treatment satisfaction (SRS) • Treatment engagement and understanding • Measures of symptom severity (RCADS-P) • Social behavioural and functional outcomes (GBO and CAIS-P) • Global functioning (CORS) • Rates of remission • Patient experience	The included population does not fall exactly into either of the pre-specified subgroups but is more representative of the children aged 5 to 11 years grouping. Exclusion of children with diagnosed autism or significant learning disability limits generalisability and may impact equity. This study did not report on every outcome included in the scope.
Hill, Reardon, Taylor, et al. (2022a) Single arm formative research UK	Seven parents, 4 children aged 9 to 12 years old and 11 clinicians familiar with the face-to-face version of the treatment either through receiving or delivering treatment **Setting:** 2 NHS clinics	**Intervention**: OSI (beta version) **Comparator**: None	Patient experience of OSI beta version	Research was not conducted on the final version of OSI, therefore the EAG does not consider the available evidence on patient experience with the beta version to have utility for the current EVA. However, the EAG noted that an inclusive and formative process is the preferred approach to development of technologies of this nature. The included paediatric population does not fall exactly into either of the pre-specified subgroups but is more representative of the children aged 5 to 11 years grouping.

				Patient experience is the only outcome that is addressed.
Williamson et al. (2022) Linked reference: Williamson, Larkin, Reardon, et al. (2021) Single arm feasibility study UK	The study aims to recruit 165 children in Year 4 (aged 8 to 9 years old) with likely anxiety difficulties assessed using the SCAS-8 and/ or indicate that anxiety interferes at least 1 'only a little' on any of the interference items **Setting:** mainstream primary schools in England	**Intervention:** OSI (parent-led) **Comparator:** None	• Patient experience (not clear)	The intended population falls into the pre-specified subgroup of children aged 5 to 11 years. No specific exclusions stated, but the school setting likely excludes children with severe autism or significant learning disability. This may limit generalisability and may impact equity. It is unclear is other outcomes included in the scope are planned to be collected.
Green et al. (2022) [redacted]	[redacted]	**Intervention**: OSI (parent-led) [redacted]	[redacted]	[redacted]

	[redacted]		[redacted]	
OSCA				
Leigh & Clark (2022) Linked references: Leigh & Clark (2019); ISRCTN15079139 (2019) Two-arm RCT UK	43 young people aged 14–18 years with a primary diagnosis of DSM-5 SAD. **Setting:** 4 secondary schools in the Southeast of England	**Intervention**: OSCA (therapist-guided) (n=22) **Comparator**: Waitlist control (n=21)	• Intervention-related adverse events • Attrition (rate only) • Treatment satisfaction (treatment credibility) • Treatment engagement (patient activity) • Measures of symptom severity (LSAS-CA-SR, SPWSS, RCADS, RCADS-P) • Social, behavioural and functional outcomes (SCQ domains, SBQ, SAQ, concentration, participation, satisfaction, SMFQ, CALIS, CALIS-P) • Rates of remission	The included population falls into the pre-specified subgroup of young people aged 12 to 18 years. Exclusion of children with diagnosed autism or significant learning disability limits generalisability and may impact equity. This study did not report on every outcome included in the scope.
Lumi Nova				

Lockwood, Williams, Martin, et al. (2022) Single arm evaluation study UK	95 children aged between 7 and 12 years that experienced difficulties with anxiety and not concurrently receiving psychological treatment **Setting:** primary and secondary schools in Southeast England	**Intervention**: Lumi Nova (guardian-led) **Comparator**: None	• Intervention-related adverse events • Attrition (rate only) • Treatment satisfaction (participant quotes) • Treatment engagement (gameplay data) • Measures of symptom severity (SCAS-P and RCADS-P) • Social, behavioural and functional outcomes (CAIS-P)	The included population does not fall exactly into either of the pre-specified subgroups but is more representative of the children aged 5 to 11 years grouping. The EAG noted one child was older than the stated target range. No specific exclusions stated, but the school setting likely excludes children with severe autism or significant learning disability. This may limit generalisability and may impact equity. This study did not report on every outcome included in the scope.
ThinkNinja CBT Bytesize				
Conference presentation: Burbach, Galloghly & Snaith (2021) Single-arm feasibility study Location not reported	Six children and young people with a mean age of 15. The primary presentation was anxiety. **Setting:** not reported	**Intervention:** CBT Bytesize **Comparator:** none	• Attrition (rates only) • Treatment satisfaction • Measures of symptom severity (YP-CORE)	The included paediatric population falls into the pre-specified subgroup of young people aged 12 to 18 years. No setting or specific inclusion or exclusion criteria are stated. Therefore, the EAG could not assess the impact on generalisability. This study did not report on every outcome included in the scope.
Conference presentation: Galloghly, Haselton & Burbach (2022) Two-arm non-randomised study	41 children and young people with a mean age of 14.4 years old with top presenting problems listed as	**Intervention:** CBT Bytesize **Comparator:** CBT at Healios	• Attrition (rates and reasons) • Treatment satisfaction • Measures of symptom severity (RCADS-C and YP-CORE) • Social, behavioural and functional outcomes (GBO)	The included paediatric population does not fall exactly into either of the pre-specified subgroups, though included participants are more representative of the young people aged 12 to 18 years grouping.

UK	social anxiety and/or generalised anxiety, comorbid low mood, panic, selective mutism, emetophobia and OCD **Setting:** children and young people were accessed through CAMHS		• Suicidal thoughts and behaviour (risk to self) • Rates of remission	No specific exclusions are stated and no systematic exclusions are anticipated from the setting. The EAG noted that CYP with panic, selective mutism, emetophobia and OCD were included in addition to participants with anxiety and/or low mood. This suggests reasonable generalisability. This study did not report on every outcome included in the scope.
Silvercloud				
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations used: **CAIS-C/P,** Child Anxiety Impact Scale (– child/parent report); **CALIS(-P),** Child Anxiety Life Interference Scale (– parent report); **CAMHS**, child and adolescent mental health services; **CBT**, cognitive behavioural therapy; **CHU-9D (-C/P),** Child Health Utility instrument nine-dimension (-child/parent version); **CORS,** Child Outcome Rating Scale; **DSM-5,** Diagnostic and Statistical Manual of Mental Disorders Fifth Edition; **EAG,** External Assessment Group; **EQ-5D-5L,** EuroQoL five-dimension five-level; **GAD-7**, generalised anxiety disorder 7 item scale; GBO**,** goal-based outcomes; **LSAS-CA-SR,** Liebowitz Social Anxiety Scale for Children and Adolescents – Self-Report version; **NHS,** National Health Service; **OSCA,** Online Social anxiety Cognitive therapy for Adolescents; **OSI,** online support and intervention for child anxiety; **RCADS(-C/P),** Revised Child Anxiety and Depression Scale (– child/parent report); **SAD,** social anxiety disorder; **SAQ,** Social Attitudes Questionnaire; **SBQ,** Social Behaviour Questionnaire; **SCAS(-P),** Spence Child Anxiety Scale(-P) (– parent report); **SCQ,** Social Cognitions Questionnaire; **SDQ(-C/P),** Strengths and Difficulties Questionnaire (– child/parent report); **SMFQ,** Short Mood and Feelings Questionnaire; **SPWSS,** Social Phobia Weekly Summary Scale; **SRS,** Session Rating Scale

4.2 Summary of economic evidence

The EAG searches identified 28 publications that were relevant to the economic analysis. Most studies were of indirect relevance, which reported on economic analyses in a related area or patient group including in adults, as these may provide useful background, for example model structure or other insights into input parameters. The studies with direct relevance or previous models in the relevant patient population provided inputs for the decision model. For full details on the published economic evidence, see section 12.1 of the assessment report.

Conceptual modelling

The EAG developed a simple decision analysis (see Figure 1, section 12.2 of the assessment report). The primary purpose of this analysis is to assess whether there is a plausible case for cost-effectiveness of the dCBT technologies in CYP with mild or moderate anxiety or low mood, and to identify where there is greatest value in future research to reduce uncertainty. There are 3 decision nodes with treatment as usual (status quo or no treatment), and 2 possible dCBT comparators (OSI and Lumi Nova for children aged 5 to 11 years; and Silvercloud and OSCA for adolescents aged 12 to 18 years). Following each node are 3 branches that are defined according to the RCADS-P t-score with a t-score above 70 analogous to ‘full response’, 65 to 69 to ‘partial response’ and below 65 to ‘no response’. The RCADS-P authors suggest that a t score >70 indicates a referral threshold, a score of 65-69 is borderline and below 65 normal functioning. The model assesses response at 3 time points: 3, 6 and 12 months. The interventions are scheduled to last between 8 to14 weeks, thus a 3-month (12 week) time point approximates an evaluation at the end of the intervention. The overall time horizon of the model is 12 months. The model does not explicitly analyse discontinuations or drop-out from the dCBT courses.

Model inputs

Clinical parameters

A key clinical parameter in the model is the proportion of participants with full, partial and no response at 3-, 6- and 12-months post baseline. All source studies used in the economic model collected RCADS-P t-score as part of their outcomes. The analysis was based on a crude naïve comparison of changes in RCADS-P t-scores over time, from which the proportion of participants expected to be in full, partial and no response was estimated. This is because it was not possible to do a network meta-analysis with only 1 RCT in the evidence base or a matching adjusted indirect comparison without individual patient data. For more details, see section 12.2.2.1 in the assessment report.

Costs and resource use

All dCBT interventions need access to computing equipment and an internet connection. To address equity concerns around digital exclusion, the cost of a tablet computer and mobile internet connection for the duration of the interventions is included as a resource use item for all interventions. The resource use assumptions for each of the technologies are described in table 4 and the unit costs in table 5.

Table 4. Resource items and quantities for interventions

	Silvercloud	**OSI**	**OSCA**	**Lumi Nova**	**ThinkNinja CBT Bytesize**
Duration of intervention	8 weeks	8 weeks	14 weeks	8 weeks	8 to 12 weeks
Resource items	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone	Tablet computer or smartphone
	Internet connection (8 wks)	Internet connection (8 wks)	Internet connection (14 wks)	Internet connection (8 wks)	Internet connection (8 to 12 wks)

	8x20minute telephone call with therapist	8x20minute telephone call with therapist	14x20 minute telephone call with clinical psychologist	8x20 minute telephone call with therapist.	[included within licence cost]

Table 5. Unit costs

Item	Point estimate Cost	Distribution	Source / Notes
Per user licence, software	[redacted]	U[redacted]	Notional per user costs.
Tablet computer or smart phone	£80	N(80,8)	Representative cost from large online retailer, September 2022. 10" Android tablet with sim card slot. A basic smart phone is similar cost
Data sim card, per month	£20	N(20,2)	Representative cost from price comparison website, September 2022. Unlimited 5G data-only plan, 1m contract
Telephone consultation with therapist	£33.67	N(33.67,3,37)	Unit Costs of Health and Social Care 2021, Section 6.10 (p80). Reported cost per client-related hour £101 to provide counselling service for children with mental or emotional difficulties. Assuming 20-minute consultation (prep included within the 20 minutes)
Telephone consultation with clinical psychologist	£41	N(41,4.1)	Unit Costs of Health and Social Care 2021, Section 14 (p141). Cost per working hour, psychiatric consultant £123 (assumed same cost as clinical psychologist). Assuming 20-minute consultation.

Abbreviations: N, Normal distribution; U, Uniform distribution.

Health state utilities

No directly relevant health state utility data in the population of interest was found using the terms 'mild' and 'depression' in the Tufts CEA database (Neumann & Cohen, 2022). However, an economic evaluation of St. John's Wort in mild to moderate depression (Solomon et al., 2013), drawing on health

state valuations from a previous study was identified (Sapin et al., 2004). The difference between response and remission in the Solomon study was a utility gain of 0.13. The EAG therefore assumed the utility of full response to be 1, of no response to be 0.83, and partial response 0.9. Arbitrary standard errors were assigned around these. See table 20 in section 12.2.2.3 of the external assessment report for further detail.

Approach to analysis

The EAG conducted a cost utility analysis reporting net benefit at willingness to pay threshold of £20,000 per QALY gained, analysis of uncertainty and value of information analysis. Probabilistic analyses are presented in all cases, with 100,000 simulations from input distributions.

Results

The base case results are presented separately for the child and adolescent populations (table 6 and table 7). The EAG notes that there is a trend towards the dCBT interventions being more effective compared with treatment as usual, and that this is probably achieved at a cost that would be considered value for money given conventional willingness to pay thresholds. But the mean net benefit of ThinkNinja Bytesize is below TAU, driven by the per-user licence cost.

OSCA is a longer course than the other dCBT interventions (14 weeks vs 8 weeks), thus explaining the higher cost. However, the evidence is too uncertain to know whether the longer course leads to higher effectiveness. The EAG notes that OSCA is the only intervention with an RCT, and the cohort studies are not adjusted for drop-out whilst the OSCA results are based on ITT, and therefore the relative effectiveness estimates are at very high risk of bias.

Table 6. Base case results - Child

	TAU	OSI	Lumi Nova
Cost	[redacted]	[redacted]	[redacted]
QALYs	[redacted]	[redacted]	[redacted]

Mean NB@£20,000	[redacted]	[redacted]	[redacted]
95%CI	[redacted]	[redacted]	[redacted]

Table 7. Base case results - Adolescent

	TAU	Silvercloud	OSCA	ThinkNinja CBT Bytesize
Cost	[redacted]	[redacted]	[redacted]	[redacted]
QALYs	[redacted]	[redacted]	[redacted]	[redacted]
Mean NB@£20,000	[redacted]	[redacted]	[redacted]	[redacted]
95%CI	[redacted]	[redacted]	[redacted]	[redacted]

One way sensitivity analyses

The one-way sensitivity analyses shows that the results are relatively insensitive to whether a therapist or clinical psychologist provides telephone support, or to the per participant licence cost (within the bounds considered; table 8 and table 9). The net benefit of ThinkNinja is insensitive to the cost of a therapist contact as this is included within the license cost. The key driver is the longer treatment duration with one of the interventions, which is because of the additional therapist contact and the cost of the SIM card.

Table 8. Scenario analysis, cost of telephone consultations - Child

	TAU	OSI	Lumi Nova
Base	[redacted]	[redacted]	[redacted]
Low therapist cost	[redacted]	[redacted]	[redacted]
High therapist cost	[redacted]	[redacted]	[redacted]

Table 9. Scenario analysis, cost of telephone consultations - Adolescent

	TAU	Silvercloud	OSCA	ThinkNinja CBT Bytesize

Base	[redacted]	[redacted]	[redacted]	[redacted]
Low therapist cost	[redacted]	[redacted]	[redacted]	[redacted]
High therapist cost	[redacted]	[redacted]	[redacted]	[redacted]

Value of information analysis

The value of information analysis is consistent with the evidence gap analysis: future research is of value into the relative effects of the dCBT interventions, as well as health state utilities (See table 25 and table 26 in section 12.3.3 of the external assessment report for further detail).

5 Ongoing research

Ongoing research for OSI

The EAG identified four ongoing studies from the literature for OSI (Reardon et al. (2022a), Reardon et al. (2022b), Reardon et al. (2022c), and Taylor et al. (2022)). Full details are available in table 2, section 8.2 of the external assessment report.

The EAG noted that these studies were generally more aligned with the NICE scope, mostly including comparators and, in one case, an active comparator (Taylor et al. (2022)). Participants, settings, and outcomes were considered to map well to the NICE scope, though one study did not state the intention to measure RCADS-P. These studies, arranged in order of relevance in terms of scope and availability of RCADS-P outcome data that can be used in economic modelling, are presented in table 10 along with the indicated end dates.

Table 10. Ongoing studies investigating OSI, arranged in descending order of relevance in terms of scope and availability of data for economic modelling

Ongoing study	Alignment with scope	Outcome data for	Indicated trial end date

		economic model	
Protocol: Taylor et al (2022) Linked reference: ISRCTN12890382 (2020)	Intervention: **GREEN** Comparator: **GREEN** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	Yes	31/03/2023
Protocol: Reardon, Ukoumunne, Violato, et al (2022c) Linked reference: ISRCTN76119074 (2021)	Intervention: **GREEN** Comparator: **AMBER** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	Yes	30/11/2024
Protocol: Reardon, Dodd, Hill, et al. (2022b) Linked references: Jones et al. (2022); ISRCTN82398107 (2021)	Intervention: **GREEN** Comparator: **AMBER** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	No	31/08/2023
Protocol: Reardon, Ball, Breen, et al. (2022a) Linked reference: ISRCTN30032471 (2021)	Intervention: **GREEN** Comparator: **RED** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	Yes	30/11/2021

Ongoing research for ThinkNinja CBT Bytesize

The EAG identified the following study in progress for CBT Bytesize. [redacted]

Table 11. Ongoing study investigating ThinkNinja CBYT Bytesize, indicating relevance in terms of scope and availability of data for economic modelling

Ongoing study	Alignment with scope	Outcome data for economic model	Indicated trial end date
[redacted] Healios (2022) [redacted]	Intervention: **GREEN** Comparator: **GREEN** Participants: **GREEN** Setting: **GREEN** Outcomes: **could not be assessed**	[redacted]	[redacted]

Abbreviation: [redacted]

Ongoing research for Silvercloud

The EAG was made aware of the following studies in progress for Silvercloud:

[redacted]

Table 12. Ongoing study investigating Silvercloud, indicating relevance in terms of scope and availability of data for economic modelling

Ongoing study	Alignment with scope	Outcome data for economic model	Indicated trial end date
Company provided: [redacted]	Intervention: GREEN Comparator: AMBER Participants: GREEN Setting: AMBER Outcomes: GREEN	[redacted]	[redacted]
Company provided: [redacted]	Intervention: GREEN Comparator: RED Participants: GREEN Setting: AMBER Outcomes: GREEN	[redacted]	[redacted]

Abbreviations: [redacted]

Ongoing research for Lumi Nova

The EAG was made aware of the following studies in progress for Lumi Nova:

[redacted]

[redacted]

Table 13. Ongoing study investigating Lumi Nova, indicating relevance in terms of scope and availability of data for economic modelling

Ongoing study	Alignment with scope	Outcome data for economic model	Indicated trial end date
Ongoing manufacturer data collection: [redacted]	Intervention: **GREEN** Comparator: **RED** Participants: **GREEN** Setting: **GREEN** Outcomes: **GREEN**	[redacted]	[redacted]
Ongoing manufacturer data collection: [redacted]	Intervention: **GREEN** Comparator: **RED** Participants: **GREEN** Setting: **GREEN** Outcomes: **RED**	[redacted]	[redacted]

6 Evidence gap analysis

The EAG presented a summary of the evidence gaps, relating to intermediate and final outcomes from the scope, and those related to the decision modelling, which can be found in table 12.

There is no published real-world evidence with relevant outcome data for any of the interventions. There is no published evidence with relevant outcome data for the interventions from Silvercloud. There are large gaps in most of the outcomes for OSI and Lumi Nova. There is some evidence for some of the outcomes for OSCA and ThinkNinja CBT Bytesize. For the model and economic outcomes, the main evidence gaps are related to the effectiveness

of the interventions compared with treatment as usual, follow up times, withdrawals, level of psychological support and health related quality of life.

Table 12. Evidence Gap Analysis

Outcomes	SilverCloud interventions	OSCA	OSI	Lumi Nova	ThinkNinja CBT Bytesize
Clinical trials					
Intermediate outcome: Intervention-related adverse events	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	No **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Intermediate outcome: Rates of and reasons for attrition	No studies **RED**	Yes, rates only, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, rate only, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Intermediate outcome: Treatment satisfaction and engagement	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series, feasibility study and formative research **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Symptom severity (self/parent/practitioner reported)	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Social, behavioural and functional outcomes (self/parent/practitioner reported)	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series and feasibility study **RED**	Yes, single-arm evaluation **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome:	No studies **RED**	No **RED**	No **RED**	No **RED**	Yes, evidence

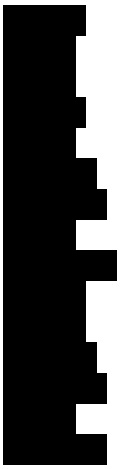
Suicidal thoughts and behaviour					from one two-arm NRS (active control) **AMBER**
Clinical outcome: Global functioning	No studies **RED**	No **RED**	Yes, single-arm case series and feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Clinical outcome: Rates of remission	No studies **RED**	Yes, evidence from one two-arm RCT (waitlist control) **AMBER**	Yes, single-arm case series **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Patient reported outcomes: HRQoL	No studies **RED**	No **RED**	Yes, single-arm feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Patient reported outcomes: Patient experience	No studies **RED**	No **RED**	Yes, single-arm case series and feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**
Resource use and costs	No studies **RED**	No **RED**	Yes, use and cost of other resources, single-arm feasibility study **RED**	No **RED**	Yes, evidence from one two-arm NRS (active control) **AMBER**

Models and economic outcomes	
Effectiveness evidence: Comparative data	No direct or indirect comparisons of effect of the target interventions (and TAU). Is one dCBT intervention more effective than another and TAU? **RED**
Effectiveness evidence: Comparative data	Is one dCBT intervention more effective than another and face to face CBT? **RED**
Effectiveness evidence:	Follow-up times vary across the source studies, which are crudely equalized to 3m in the decision model. Common FU times are required, along with longer term follow-up data (to 12m+). **RED**

Follow-up times and lengths	
Effectiveness evidence: Discontinuations / withdrawals	Withdrawals are currently accounted for via ITT analyses of RCADS-P. Should they be modelled specifically? **AMBER**
Clinical outcome and costs: Qualifications of mental health contact	Is a mental health support worker as effective as a clinical psychologist at providing weekly contacts? **AMBER**
HRQoL: Estimating health state utilities	Is RCADS-P the most appropriate tool on which to base health state utilities for CYP? What other tools are there for measuring and valuing mild/moderate anxiety and depression in CYP? **RED**

Abbreviations: (d)CBT, (digital) cognitive behavioural therapy; CYP, children and young people; FU, follow-up; HRQoL, health-related quality of life; ITT, intention to treat; OSCA, Online Social anxiety Cognitive therapy for Adolescents; OSI, online support and intervention for child anxiety; RCADS(-C/P), Revised Child Anxiety and Depression Scale (– child/parent report); RCT, randomised controlled trial; TAU, treatment as usual

Table 13. Evidence gaps that could be addressed by the ongoing research

Key evidence gap	**Silvercloud interventions**	**OSCA**	**OSI**	**Lumi Nova**	**ThinkNinja CBT Bytesize**
Evidence for CYP with low mood	None	None	Reardon T, Ukoumunne O, Violato M, et al. 2022	None	Healios 2022 
Evidence for CYP with neurodevelopmental conditions		None	Reardon, Dodd, Hill, et al. 2022 Two-arm RCT Reardon, Ball, Breen, et al. 2022 Reardon, Ukoumunne, Violato, et al. 2022		Healios 2022 
Measures of symptom severity using RCADS		None	Reardon, Ball, Breen, et al. 2022		Healios 2022 

Assessment report overview: Guided self-help digital cognitive behavioural therapy for children and young people with mild to moderate symptoms of anxiety or low mood

	[redacted]		Reardon, Ukoumunne, Violato, et al. 2022 Taylor et al. 2022	[redacted]	
Measures of impairment using CAIS-P	None	None	Taylor et al. 2022	None	Healios 2022 [redacted]
Measures of impairment using SDQ	[redacted]	None	Reardon, Ball, Breen, et al. 2022 Reardon, Dodd, Hill, et al. 2022 Two-arm RCT Reardon, Ukoumunne, Violato, et al. 2022 Taylor et al. 2022	None	Healios 2022 [redacted]

Abbreviations: CAIS, Child Anxiety Impact Scale; CBT, cognitive behavioural therapy; [redacted]; N/A, not applicable; [redacted]; RCADS, Revised Children's Anxiety and Depression Scale; RCT, randomised controlled trial

Summary and conclusions of evidence gap analysis

The EAG identified several evidence gaps. The evidence gaps most relevant to the early value assessment are presented below.

<u>Population</u>

- Evidence for the effectiveness of technologies on anxiety or low mood in children and young people with neurodevelopmental conditions. No ongoing studies have been identified to address this gap.

Outcomes

- Homogeneity in reported outcome measures. The EAG considered measures of symptom severity to be the most important clinical outcome, followed by measures of impairment which are called social, behavioural, and functional outcomes in the scope.
    - RCADS-P has been identified as a common outcome for symptom severity in completed studies. Three ongoing studies have been identified as measuring RCADS-P for OSI, 3 for Silvercloud interventions, and 1 for Lumi Nova.
    - Measures of impairment were even more heterogeneously reported, but there was some overlap in reporting of the Child Anxiety Impact Scale (CAIS) and the Strengths and Difficulties Questionnaire (SDQ) in the studies. One ongoing study has been identified as measuring CAIS for OSI. Several ongoing studies have been identified as measuring SDQ, 1 for Silvercloud interventions and 1 for OSI.

Decision modelling

- The most appropriate approach to measuring and valuing health states is unclear. The early decision model makes use of RCADS-P due to it being reported across relevant studies. However, other HRQoL tools may be more appropriate.
- It is unknown whether a mental health support worker or similar is as effective as a clinical psychologist in delivering the 'guidance' in guided dCBT. The impact on cost-effectiveness is unclear.

7 Equalities considerations

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

been identified. There are multiple equality considerations for this class of technologies which are addressed in more detail in NICE's guideline on depression in children and young people: identification and management. Key aspects include:

- Children and young people from certain socio-economic backgrounds and those with disabilities are disproportionately affected by higher risk of mental health issues.
- Children and young people from high-risk disadvantaged socio-economic groups likely have differential access to devices and data plans when compared to those in different socio-economic circumstances.
- Patient-facing digital health technologies may be unsuitable for those with cognitive impairment, problems with manual dexterity or learning disabilities. Carer or advocate assistance may be required to navigate the programme and consideration of this should be made by the company as well as the referring practitioner when considering appropriate intervention for the child or young person. Further considerations can be found in NICE Guidance on mental health problems in people with learning disabilities.
- Patient-facing digital health technologies should ensure their programme is accessible for screen readers (people with visual impairments) and those with hearing impairments.
- Children and young people with English as a second language may have difficulties navigating digital technologies provided in English.
- The way that children and young people with symptoms of anxiety or depression and their families view mental health problems may be affected by their ethnic, religion and cultural background.
- Children and adolescents may in general have increased autonomy in accessing therapy using digital formats. However, specific

groups may particularly benefit from improved access to CBT online, for example:

- Adolescents may have increased engagement with this format of intervention. However, younger children may require higher levels of parental support or engagement with the intervention.
- Those living in rural areas might have problems with travelling to face-to-face appointments if public transport is sporadic and unreliable, and their parents are unable to drive them there.
- Those living in more remote rural areas may not have access to mobile internet connections.
- Children and young people from lower socioeconomic groups may lack the financial support required to ensure that they attend face to face sessions. These families may also be less likely to seek help in the first place and or be less able to navigate the healthcare system.
- Children and young people with more chaotic home lives may lack the family support required to ensure that they attend face to face sessions. These families may also be less likely to seek help in the first place and or be less able to navigate the healthcare system.
- Children and young people from abusive homes may be prevented from seeking help and or attending face to face therapy sessions by controlling parents or carers.
- Looked after children and young people may lack support needed to engage with mental health services.

However, accessibility would not be improved for those who are unable to engage with a digital service due to a lack of equipment, unavailability of internet connection, lack of experience with computers or lack the privacy needed to complete the intervention. Age, disability, race and religion or belief are protected characteristics under the Equality Act (2010).

8 Implementation

The NICE adoption team identified potential factors that could encourage implementation of dCBT interventions to treat children and young people with mild to moderate symptoms of anxiety or low mood:

- Increasing treatment options and reducing waiting times is a priority as it can address an unmet need
- Potential for increased access, rates of attrition and greater reach to groups which 'traditional' services have low uptake within

Potential adoption barriers include:

- There may be limited appetite for another new product because there is currently a lot of transformation work going on in the NHS
- Acceptance of new digital technologies. Some clinicians see digital CBT as second-rate options compared with traditional practitioner led face-to-face CBT. EVA may help overcome this barrier
- It may require changes the current care pathway. There is a need for children and young people to be assessed and to determine the appropriateness of guided self-help digital CBT interventions. Effective discharge or referral for further support following digital CBT is also needed
- Limited evidence. NHS services and pilot sites will need some assurance that each treatment is effective. NHS providers and commissioners are risk averse, especially with services for children and young people
- Accessibility of digital CBT. There may be technical and language barriers and issues for those with additional needs

- Funding for evidence generation, as well as the evidence generation itself.

9 Issues for consideration by the committee

Unmet need

- Mental health services are in high demand and access varies widely across the country: the availability of effective mental health treatments is limited, with a shortage of qualified staff, long waiting times and access to treatment depending on the severity of symptoms. Early research suggests that the pandemic and subsequent measures have had a significant impact on the mental health of children and young people and subsequently intensified these issues related to accessing effective mental health treatments. It is estimated that only 1 in 3 children with a mental health condition get access to NHS care and treatment. The committee may wish to consider that digital CBT interventions with guidance from mental health practitioners may address an unmet need in children and young people with mild to moderate symptoms of anxiety or low mood by providing an accessible first line treatment option.

Population

- Evidence on children and young people with neurodevelopmental conditions was identified as an evidence gap. Effectiveness of the dCBT interventions may differ in this subgroup and this group may benefit from this more remote method of delivering therapy.

Clinical evidence

- There is some evidence to suggest the guided dCBT interventions may be better than treatment as usual. The evidence base consists of 5 published studies, 2 conference abstracts and 2 unpublished studies, of which 1 is an RCT, 1 is a nonrandomised study, while the others are single arm studies.

- The RCT suggests the OSCA intervention is more effective than a waiting list control in terms of anxiety symptom severity with waiting list controls showed a deterioration over time (Leigh & Clark, 2022).
- Before-and-after cohort analyses of OSI and Lumi Nova suggest an improvement in anxiety symptom severity over time (Hill et al., 2022b; Lockwood et al., 2022).
- There is very weak evidence that CBT bytesize results in clinical and reliable improvements over time and that Bytesize may be more effective than CBT with Healios for these outcomes (Burbach et al., 2021; Galloghly et al., 2022).
- At present there is no peer-reviewed evidence published on the Silvercloud interventions.

Economic evidence

- The preliminary results of the simple decision analysis showed a trend towards dCBT being more effective compared with treatment as usual, at a cost that would be considered value for money given conventional willingness to pay thresholds. Based on the analysis the biggest issue affecting cost-effectiveness is the duration of the intervention and the per user license cost. It is unknown whether the shorter duration of the latter three lead to poorer outcomes, or whether the longer duration of the former simply increases cost.

Key gap analysis conclusions

- The outcomes identified as those to be prioritised are symptom severity and measures of impairment.
- No evidence regarding the effect of any included technology on low mood in children or young people were identified.

- The EAG identified several ongoing studies for all interventions that aligned in part with the decision problem such as population and intervention. However, the ongoing or planned studies only partly address the research gaps.

- For the model and economic outcomes, the main evidence gaps are:
    - The effectiveness of the interventions compared with treatment as usual
    - Longer follow up (up to 12 months)
    - Level of qualifications of mental health professionals. Is a mental health support worker as effective as a trained clinical psychologist?
    - Health related quality of life including which is the most appropriate tool (i.e., RCADS, EQ-5DY or CHU-9D)

  Are there any other relevant resource or cost parameters relevant for future economic modelling for which data should be collected?

10 Authors

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NICE Medical Technologies Evaluation Programme

October 2022

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

Details of assessment report:

- Brand A, Duffy S, Lee D, et al. Guided self-help digital cognitive behavioural therapy for children and young people with mild to moderate symptoms of anxiety and low mood. October 2022

For a list of the organisations that accepted the invitation to participate in this assessment as stakeholders and the Expert Adviser Specialist Committee members, see the published project documents. They were invited to attend the scoping workshop and to comment on the external assessment report.

Manufacturers and developers of technologies included in the final scope:

- BfB Labs
- Silvercloud
- Healios
- Universities of Reading and Oxford (OSI)
- University of Oxford (OSCA)

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Reardon T, Dodd H, Hill C, et al. Minimising young children's anxiety through schools (MY-CATS): protocol for a cluster randomised controlled trial to evaluate the effectiveness and cost-effectiveness of an online parent-led intervention compared with usual school practice for young children identified as at risk for anxiety disorders. Trials 2022b;**23**(1):149. DoI: https://dx.doi.org/10.1186/s13063-022-06010-8

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Appendix B: Additional analyses carried out by the EAG

Additional analysis of ThinkNinja CBT Bytesize was carried out after the External Assessment Report was initially submitted to NICE. Please see the addendum for the External Assessment Report for further details.

Adoption report: MTEP EVA Pilot: Guided self-help digital cognitive behavioural therapy for children and young people with mild to moderate symptoms of anxiety or low mood

Summary

Adoption levers identified by contributors

- The draft unmet need identified within the draft scope (to help increase treatment options and reduce wait times) was agreed as being a priority by all. It was also reported by two contributors to fill a gap in CAMHS services particularly as access to these services typically requires more severe symptoms.
- In terms of implementation of the EVA after publication (if a positive recommendation) the advice was to start small by having a limited amount of pilot sites (reflective of different area types e.g. rural, inner city, affluent, deprived etc) to get the process right. ICS size as a geographical area to test is too big.
- Potential for increased access, rates of attrition and greater reach to groups which 'traditional' services have low uptake within
- The concept of EVAs generally was reported by two contributors to hopefully fill the gap between research and NICE recommendations which presents a barrier to innovation.

Adoption barriers identified by contributors

Issue date: October 2022

- Limited Awareness about EVA. To be expected but good to be aware of. Only one contributor was aware of the upcoming EVA product.
- Clinical resistance- All were positive about the concept of an EVA in this area but were concerned that issues around acceptance of new technologies and of digital ones, may present barriers. Some clinicians see digital CBT as 2nd rate options to traditional practitioner led face to face CBT. Some commented that this is exactly what EVA may help to overcome.
- There is a lot of transformation work going on in the NHS at the moment. There may be limited appetite for another new product.
- Implementation of this EVA will require changes to be made to current care pathways.
- Limited evidence may present a barrier. NHS services/pilot sites will need some assurance that each treatment is effective. NHS providers and commissioners are risk adverse- especially with services for CYP.
- AHSN and other innovators were described as being too 'pushy' by one contributor, wanting to drive use tech/approaches with limited evidence bases and this may present barriers to implementation of the published EVA.
- Accessibility of this type of treatment was reported by all to be a potential barrier. There may be technical and language barriers and issues for those with additional needs.
- Funding for evidence generation was reported by all to be a barrier as was the evidence generation itself.

1 Introduction

The adoption team has collated information from healthcare professionals working within NHS organisations. This report has been developed for the medical technologies advisory committee (MTAC) to provide context from current practice and an insight into the potential levers and barriers to adoption within the EVA pilot sites. It does not represent the opinion of NICE or MTAC.

The adoption team spoke to 8 colleagues working within NHS services, 5 of whom have experience of referring people for digital CBT treatment.

Contributors

Details of contributing individuals are listed in the below table.

Job title	Organisation	Digital CBT part of current service provision?
Strategic Lead Clinical Commissioner – Mental Health and Disabilities	NHS Greater Manchester Integrated Care	Yes
NHSE Associate National Clinical Director for Children and Young People's Mental Health and Consultant Child and Adolescent Psychiatrist	Pennine Care NHS Foundation Trust.	Yes
Highly Specialised Oncology Pharmacist and commissioner	Calderdale and Huddersfield NHS Foundation Trust	No
Consultant Psychiatrist (adults)	Health Education Thames Valley	Yes
Commissioning and Contract Manager	East Suffolk and North Essex NHS Foundation Trust	No
Mental Health Lead	Health Innovation Network (South London AHSN)	No
Head of commissioning, mental health and learning disabilities	Isle of Wight CCG	Yes
High intensity CBT therapist		Yes

2 Early Value Assessment Audience

The potential end users/audience for this EVA have been described as wide ranging.

- CAMHS services who want to use or fund digital CBT through their respective research and development departments.

- Companies who may want to fund use of digital CBT within NHS services as part of an EVA pilot
- Public partners (AHSNs, NHSE, AAC) who are looking be to or are already involved in using digital CBT as part of a pilot.
- Defined pilot sites were cited by all but one contributor as being a good idea as long as funded appropriately and delivered by NHS frontline services.

3 Insights from the NHS

Care pathway

Implementation of this EVA (if recommended with evidence generation) will require changes to be made to current care pathways. An initial assessment prior to provision of guided CBT to assess suitability for this type of therapy and effective discharge or referral for further support following digital CBT is needed. Establishing where in the care pathway this is best placed will hopefully come out of the evidence generated if this EVA recommendation type is made.

Clinician confidence/acceptance

Clinician acceptance came up frequently as a probable barrier for this EVA. This issue is very problematic for digital innovations particularly. There is a lot of work to do to encourage different views on this. In this case, contributors reported that it is important for practitioners to see guided CBT as a treatment option and not a less effective alternative.

Funding

All contributors reported funding to put EVAs into practice and thus generate the required evidence as a barrier. It was suggested that we should be transparent about the fact there isn't any funding assigned to this (if hat is the case) and also to highlight any agreed partnership working for example with AHSNs if this has been agreed.

Evidence generation

This was reported by all to be a challenge. Baseline data collection alone was reported as being important and difficult to obtain from NHS systems. Contributors reported that integration of the digital platforms with NHS systems with help overcome this but that each technology will need to be assessed to ensure it collects the data needed. The EVA document should be quite prescriptive about what data is needed to generate the required evidence.