

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

**Early Value Assessment
MT589 Digitally Enabled Therapies for Adults with Anxiety
Disorder
External Assessment Group report**

Produced by: Cedar

Authors: Dr Huey Yi Chong (Senior Researcher)

Dr Laura Knight (Senior Researcher)

Megan Dale (Principal Researcher)

Dr Rhys Morris (Cedar Director)

Simone Willis (Systematic Reviewer)

Dr Susan O'Connell (Principal Researcher)

Correspondence to: Cedar, Cardiff Medicentre, Heath Park, Cardiff CF14 4UJ

Date completed: 27/01/2023

Contains confidential information: Yes

Number of attached appendices: 2

Purpose of the early value 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](#).

Megan Dale and Susan O'Connell hold honorary contracts with Cardiff University, Simone Willis is an employee of Cardiff University and the EAG team as a whole has close working links with Cardiff University. None of the team has worked in any capacity on Spring.

Acknowledgements

The EAG wish to thank all specialist committee members for their valuable input.

Copyright belongs to Cedar Health Technology Research Centre, Cardiff and Vale University Health Board

Responsibility for report

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

Any **'commercial in confidence'** information in the submission document is underlined and highlighted in turquoise.

Any **'academic in confidence'** information in the submission document is underlined and highlighted in yellow.

Contents

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE	1
Early Value Assessment	1
MT589 Digitally Enabled Therapies for Adults with Anxiety Disorder	1
External Assessment Group report	1
Executive summary	5
1 Decision problem	6
2 Overview of the technology	9
2.1 Included Technologies	9
3 Clinical context	17
4 Clinical evidence selection	23
4.1 Evidence search strategy and study selection	23
4.2 Included and excluded studies	23
5 Clinical evidence review	42
5.1 Quality assessment of included studies	42
5.2 Results from the evidence base	44
5.2.1 Health Anxiety, Obsessive Compulsive Disorder, Panic Disorder with or without agoraphobia, Specific Phobia	45
5.2.2 Body Dysmorphic Disorder	45
5.2.3 Generalised Anxiety	48
5.2.4 Post-traumatic Stress Disorder	61
5.2.5 Social Anxiety Disorder	64
6 Adverse events	66
7 Evidence synthesis	66
8 Interpretation of the clinical evidence	68
8.1 Integration into the NHS	69
8.2 Ongoing studies	70
9 Economic evidence	71
9.1 Key economic evidence for anxiety in adults	71
9.2 Key economic evidence for Digitally enabled therapies delivered with support, for anxiety in adults	75
9.3 Conceptual modelling	83
9.4 Results from the economic modelling	98
9.5 Interpretation of the economic evidence	102
10 Evidence gap analysis	104
10.1 Summary and conclusions of evidence gap analysis	111
10.2 Key areas for evidence generation	112
11 Conclusions	113
11.1 Conclusions from the clinical evidence	113
11.2 Conclusions from the economic evidence	114
12 Summary of the combined clinical and economic sections	114
13 References	115
14 Appendices	121
Appendix A: Clinical data search strategy	121
Appendix B: Excluded Studies	158

Abbreviations

Term	Definition
BDD	Body Dysmorphic Disorder
CBT	Cognitive Behavioural Therapy
CBT-TF	Trauma focused CBT
CI	Confidence interval
CT	Cognitive Therapy
dCBT	Digitally enabled CBT
DHSC	Department of Health and Social Care
EAG	External assessment group
EVA	Early Value Assessment
EVPI	Expected Value of Perfect Information
GAD	Generalised Anxiety Disorder
GP	General Practitioner
HIT	High Intensity Therapist
HTA	Health Technology Assessment
IAPT	Improving Access to Psychological Therapies
iCBT	Internet delivered Cognitive Behavioural Therapy
IQR	Interquartile range
ITT	Intention to Treat
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
MTEP	Medical Technologies Evaluation Programme
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
NMB	Net Monetary Benefit
OCD	Obsessive Compulsive Disorder
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSSRU	Personal Social Services Research Unit
PTSD	Post Traumatic Stress Disorder
PWP	Psychological Wellbeing Practitioner
QALY	Quality Adjusted Life Years
QUORUM	Quality of Reporting of Meta-analyses
RCT	Randomised controlled trial
SAD	Social Anxiety Disorder
SD	Standard deviation
SSRI	Selective serotonin reuptake inhibitor
VAS	Visual analogue scale
Vs	Versus
WTP	Willingness to Pay

Executive summary

Digitally-enabled guided therapies can be used within the Improving Access to Psychological Therapies (IAPT) pathway as an intervention for symptoms of anxiety disorders. The clinical evidence (n=19 studies) suggests that guided digital therapies can reduce anxiety symptoms across a range of conditions and that reductions can persist up to 12 months post treatment. Limited comparative evidence indicates the reduction in anxiety symptoms was larger in those using the guided therapies, compared to waiting list or usual care. However, there are some major limitations with the included evidence. Firstly, there are no studies that reported for patients with a diagnosis of Generalised Anxiety Disorder. Further, the majority of this evidence groups participants with those also experiencing depression symptoms. There was a lack of relevant comparators and therapist or 'guided' element which limits applicability of evidence to the scope. Few of the included studies were conducted in a UK/NHS setting, reducing the generalisability of the results.

Wysa, Cerina, Mind District, Iona Mind and Resony technologies and the following conditions; health anxiety, obsessive compulsive disorder, panic disorder and specific phobias had no relevant published evidence.

Economic evidence was available for 4 technologies, reporting cost-effectiveness compared to non-IAPT comparators (n=3), and cost-saving compared to an IAPT comparator (n=1). The EAG created a decision tree model, with a 15 month time horizon, using the IAPT database as a comparator. This indicated the plausibility of digitally enabled therapies being less costly and equally or more effective than other IAPT interventions, but the level of uncertainty means no clear conclusions can be drawn. Where there was no clinical evidence it was not possible to include these technologies in the model, as their cost effectiveness is highly dependent on their clinical effectiveness.

There are significant gaps where technologies and conditions included in the scope had no appropriate evidence to report. To address these gaps and those identified within the included evidence, high-quality randomised controlled trials with appropriate diagnoses and comparators should be conducted within a UK/NHS setting.

1 Decision problem

The target population for this assessment is adults with anxiety disorders including excessive fear, worry and anxiety that is severe enough to cause significant distress or impairment in a person’s functioning and daily living. Anxiety disorders treated in IAPT services include body dysmorphic disorder, generalised anxiety disorder, health anxiety, obsessive compulsive disorder, panic disorder with/without agoraphobia, post-traumatic stress disorder, social anxiety disorder and specific phobias.

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

Table 1: Decision Problem

Decision problem	Scope	EAG comment
Population	Adults (aged 18 years and older) with anxiety disorders <ul style="list-style-type: none"> • Body dysmorphic disorder • Generalised Anxiety Disorder • Health Anxiety • Obsessive Compulsive Disorder • Panic disorder with/without agoraphobia • Post traumatic stress disorder • Social anxiety disorder • Specific phobias 	<p>In some cases, technologies may be described in the evidence as being used to treat symptoms of anxiety with no diagnosis of a specific anxiety disorder. The EAG will consider such evidence on a technology by technology basis and include it only where there is no evidence for use to treat specific anxiety disorders.</p> <p>Some of the included technologies are suitable for use by people under 18 years. If no other evidence is available, the EAG will report the evidence in young people while noting the lack of evidence in adult populations as an evidence gap.</p>
Intervention	Digitally enabled therapies delivered with the support of a practitioner or therapist <ul style="list-style-type: none"> • Beating the Blues (365 Health Solutions) • Cerina • iCT-PTSD for post-traumatic stress disorder • iCT-SAD for social anxiety disorder • Iona Mind • Minddistrict (Minddistrict) • Perspectives • Resony • SilverCloud • Spring • Wysa (Wysa) 	<p>For any studies which include people with depression and anxiety, the EAG will consider the evidence where the technologies are being used for a diagnosed anxiety disorder.</p> <p>Where a study reports on the use of a technology for anxiety without defining or separating specific anxiety related diagnosis, the EAG will consider this on a case by case basis and include a summary of these as a separate subgroup, highlighting the potential limitations.</p> <p>Studies which report results for anxiety and depression combined will be considered for inclusion on case by case basis.</p>

Decision problem	Scope	EAG comment
Comparator(s)	Standard Care within the IAPT care pathway <ul style="list-style-type: none"> • Low intensity (step 2) • High intensity (step 3) 	<p>It is likely that technologies are being used outside of IAPT, particularly in the case of non-UK based studies. The EAG will include any relevant evidence, noting the lack of IAPT specific evidence as a gap.</p> <p>Although excluded from the scope, if evidence comparing with standard interventions is limited, the EAG will consider studies comparing technologies with waitlist controls and other non-standard comparators. This will be done on a technology by technology basis.</p>
Healthcare setting	Improving access to psychological therapies (IAPT) services	
Outcomes	<p>Intermediate measures for consideration may include:</p> <ul style="list-style-type: none"> • Patient choice and preferences • Treatment satisfaction and engagement • Intervention adherence and completion • Referral to treatment time • Assessment to treatment time • Intervention-related adverse events • Inaccessibility to intervention (digital inequalities) <p>Clinical outcomes for consideration may include:</p> <ul style="list-style-type: none"> • Change in anxiety symptoms • Change in other psychological symptoms • Global functioning and work and social adjustment <p>Service level clinical outcomes:</p> <ul style="list-style-type: none"> • Rates of reliable recovery • Rates of reliable improvement • Rates of reliable deterioration • Rates of relapse including relapse rate and time from remission to relapse <p>Patient-reported outcomes for consideration may include:</p> <ul style="list-style-type: none"> • Health-related quality of life • Patient experience 	
Cost analysis	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include:	

Decision problem	Scope	EAG comment
	<ul style="list-style-type: none"> • Costs of the technologies • Cost of other resource use (e.g., associated with managing anxiety, adverse events, or complications): <ul style="list-style-type: none"> ○ GP or IAPT appointments ○ Medication ○ Healthcare professional grade and time 	
Study Design		All study designs will be considered and the decision to include or exclude a study based on design will be made on a technology by technology basis.

2 Overview of the technology

Included in this early value assessment (EVA) are digitally enabled therapies that are intended for use by adults and deliver a therapeutic intervention in line with NICE guidelines. They can be used in IAPT services with practitioner or therapist support. The technology must deliver a substantial portion of the therapy through the technology rather than being platforms to support teletherapy. Any technologies included must have regulatory approval or be actively working towards regulatory approval, specifically DTAC and CE or UKCA mark where required, and be available for use in the NHS. It should be noted that the IAPT manual states that IAPT only supports the delivery of therapies (digital or non-digital) whose content is the same as the content of the treatments recommended in the main NICE guideline for the relevant clinical condition. The purpose of the EVA is to assess the clinical and economic evidence for the included technologies however and will not assess the content of the technologies for compliance. The included technologies are being assessed separately through the IAPT digitally enabled therapies (DET) assessment process, the findings of which will need to be considered alongside the EVA.

Virtual reality therapies are excluded as their use in the care pathway will likely differ from online or app-based therapies.

2.1 *Included Technologies*

In total, 11 digitally-enabled therapies for adults with anxiety disorders were identified as relevant to the assessment (Table 2).

Table 2: Included Technologies

Technology (Company)	Regulatory Status	Delivery	Condition(s) Treated	Key Features	EAG Comments
Beating the Blues	Class 1 under UKCA DTAC: [REDACTED]	Laptop, computer and/or smart device	Mild to moderate <ul style="list-style-type: none"> Anxiety Depression Mixed anxiety and depression 	<ul style="list-style-type: none"> Approved for use as part of the stepped care approach No real-time interface with therapist or helper Collects GAD7 and PHQ9 and can be configured to send results to therapist/clinical helper 	Generalised anxiety disorder mentioned on company website, however not clear whether formal GAD diagnosis required – likely used for GAD or symptom of anxiety.
Cerina (NoSuffering Ltd.)	Class 1 under UKCA DTAC: Not currently, but DTAC requirements have been considered while building the product	Smart Phone (iOS and Android)	Generalised anxiety disorder (GAD)	<ul style="list-style-type: none"> Self-guided Adults only 7 Sessions of CBT Not currently used in the NHS 	<ul style="list-style-type: none"> Low intensity therapy only based on information in company submission Not currently supported by a therapist
iCT-PTSD for post-traumatic stress disorder	Currently uncertified however company state they will shortly be applying for CE/UKCA certificate DTAC: Not yet, but company believe product meets criteria	Can be used on mobile phones but company recommend computer, laptop or tablet	Mild to severe post-traumatic stress disorder (PTSD)	<ul style="list-style-type: none"> Therapist assisted Designed to be a 1st line treatment for PTSD within IAPT Collects PCL-5, GAD-7, PHQ-9, WSAS Used in 11 IAPT services Content of treatment is in line with NICE recommendations Reporting to PC-MIS & IAPTus 	Currently used within the NHS and collects all relevant IAPT measures for PTSD as outlined in the IAPT manual.

Technology (Company)	Regulatory Status	Delivery	Condition(s) Treated	Key Features	EAG Comments
iCT-SAD for social anxiety disorder	Currently uncertified however company state they will shortly be applying for CE/UKCA certificate DTAC: Not yet, but believe product meets criteria	Can be used on mobile phones but company recommend computer, laptop or tablet	Social anxiety disorder (SAD)	<ul style="list-style-type: none"> • Therapist assisted • Designed to be a 1st line treatment for SAD within IAPT • Used in 6 IAPT services • Content of treatment is in line with NICE recommendations • Suitable for use by PWP's and by Hi intensity CBT therapists • Collects all relevant IAPT measures (SPIN, GAD-7, PHQ-9, WSAS) • Reporting to PC-MIS and IAPTus 	Currently used within the NHS and collects all relevant IAPT measures for SAD as outlined in the IAPT manual.
Iona Mind	Unregulated Class 1 certification pending DTAC: Assessment booked for Q1 2023	Mobile App delivered via smart phone or tablet	Generalised anxiety or low mood	<ul style="list-style-type: none"> • Fits step 2 of IAPT pathway • Intervention within the app is recommended by PWP, clinical psychologist or assistant psychologist • Adjunct to usual step 2 treatment • Patient reported outcomes GAD7, PHQ9 can be recorded • Reporting to PCMIS and IAPTUS 	
Minddistrict	Class 1		Generalised Anxiety Disorder	<ul style="list-style-type: none"> • Collects PHQ-9 and GAD-7 • Self-help, guided self-help and 	

Technology (Company)	Regulatory Status	Delivery	Condition(s) Treated	Key Features	EAG Comments
	DTAC: Submitted, awaiting feedback		Obsessive Compulsive Disorder Panic Disorder Phobia Social Anxiety Health Anxiety	blended	
Perspectives (Koa Health)	Unregulated DTAC: Preparing for submission to DTAC	Mobile app for patients Web access for healthcare professionals	Body dysmorphic disorder (BDD)	<ul style="list-style-type: none"> • Replacement for step 3 interventions or as an adjunct to step 4/5 interventions • Supported by a healthcare professional • Adults only • Accessed by referral from a licensed healthcare professional or by self-referral • Cognitive behavioural therapy programme • Training required for healthcare professionals 	<ul style="list-style-type: none"> • Developed by Koa Health/Massachusetts General hospital with a backend data storage element – may present issues for GDPR however company information states data could be held on an NHS server if required • Information provided suggests that the therapist can be a clinician equivalent to high intensity therapist or a coach (equivalent to a PWP). Specialist committee input raised concerns around the impact of therapists delivering interventions they were not trained

Technology (Company)	Regulatory Status	Delivery	Condition(s) Treated	Key Features	EAG Comments
					<p>for</p> <ul style="list-style-type: none"> States the technology is for people with symptoms of BDD – unclear whether a diagnosis of BDD is required
Resony	<p>Class 1</p> <p>DTAC: Currently in progress</p>	Mobile app (iOS or android) for use on smart phones or tablets	Generalised anxiety disorder (GAD) (IFU use state that it is intended for the improvement of worry and anxiety and management of GAD)	<ul style="list-style-type: none"> Adjunct to usual care, to be used while people on IAPT waitlist Healthcare professional supervision if using for GAD Adults Only 6 week programme, used 3 times per day GAD-7 Psychological and physiological techniques such as cognitive behavioural therapy (CBT) exercises, mindfulness exercises, progressive muscle relaxation exercises (PMR) and resonance frequency breathing exercises 	<ul style="list-style-type: none"> Cannot be used for treatment of severe GAD NHS input to the programme content
SilverCloud	Unregulated as not classed as medical device	Cloud hosted Software-as-a-service (SAAS). Available on	<ul style="list-style-type: none"> Depression Anxiety 	<ul style="list-style-type: none"> Used as an alternative or adjunct to current treatment option 	<ul style="list-style-type: none"> Currently being used within the NHS

Technology (Company)	Regulatory Status	Delivery	Condition(s) Treated	Key Features	EAG Comments
	DTAC: accredited	all devices (smartphones, PC, tablets). Uses push notifications and text alerts	<ul style="list-style-type: none"> • Generalised Anxiety Disorder • Health Anxiety • OCD • Panic • Phobia • Social Anxiety • Depression & Anxiety 	<ul style="list-style-type: none"> • Used with supervision of a trained professional provided by the patient's clinical organisation • It is intended that support monitoring would last for 1-2 months • Techniques used focus around a CBT framework with additional aspects of mindfulness, positive psychology and motivational interviewing techniques • SilverCloud has embedded a screening tools depending on the patient group, program type or risk profile etc. These include M3, BDI, PHQ9 (Patient Health Questionnaire 9), GAD7 and WHOQoL. 	
Spring	Unregulated as not classed as medical device DTAC: No, but are planning to apply	Internet based	Mild to moderate post-traumatic stress disorder (PTSD) from a single event	<ul style="list-style-type: none"> • Low intensity CBT treatment delivered with the support of a healthcare professional • Adults only • Delivered over 4 30-minute sessions in 8 weeks • Used as first line treatment for those presenting with PTSD (following standard processes after referral from GP etc) 	<ul style="list-style-type: none"> • Used within NHS Wales • Not to be used for those with complex PTSD or any co-morbidities

Technology (Company)	Regulatory Status	Delivery	Condition(s) Treated	Key Features	EAG Comments
				<ul style="list-style-type: none"> • Seen as an alternative/replacement to current first line treatments 	
Wysa	<p>Class 1 CE marked device</p> <p>DTAC: accredited</p>	<p>Mainly provided via app on a mobile device</p> <p>Wysa's e-triage and therapist companion app are web based and can be used on any computer or tablet.</p>	Mild to moderate anxiety and/or depression	<ul style="list-style-type: none"> • AI enabled chat bot that uses Natural language Processing (NLP) to support a user to reflect on their current experiences and to complete clinician written tools and activities designed to improve mental health outcomes and increase resilience • Uses a collection of IAPT mapped CCBT assisted self-help programmes designed for use alongside PWP support in self-help • Outcome measures can trigger an SOS if words associated with self-harm, abuse or suicidal thoughts are identified. This can also be triggered by the person if needed. • Integrated with patients electronic records • Aimed at stage 2 of the IAPT pathway • Intended for teenagers as well as adults 	<ul style="list-style-type: none"> • Currently used within some NHS England trusts • Is not recommended for individuals who are currently self-harming, are actively suicidal or who have experienced psychosis within the past 6 months

Abbreviations: BDD, body dysmorphic disorder; CBT, cognitive behavioural therapy; DTAC, digital technology assessment criteria; GAD, generalised anxiety disorder; IAPT, Improving Access to Psychological Interventions; IFU, instructions for use; NLP, natural language processing; PTSD, post-traumatic stress disorder; PWP, psychological wellbeing practitioner;

3 Clinical context

This early value assessment will focus on the use of digitally enabled therapies for adults with anxiety disorders within IAPT services. The IAPT programme organises the provision of evidence-based psychological therapies in the NHS to people with anxiety disorders and depression ([National Collaborating Centre for Mental Health 2021](#)). IAPT services follow a stepped care approach as recommended in [NICE's clinical guideline on common mental health problems](#). This means offering the least intrusive, most effective intervention first. If the patient does not respond to treatment at the first level, then they would progress through the IAPT stages.

IAPT services deliver low and high intensity psychological interventions at step 2 and 3 of the care pathway, respectively. Digitally enabled therapies are most commonly offered as a step 2 low intensity intervention. Low intensity interventions are delivered by psychological wellbeing practitioners who facilitate treatment and review progress. There are a number of relevant NICE guidelines covering body dysmorphic disorder, generalised anxiety disorder, obsessive compulsive disorder, panic disorder, post-traumatic stress disorder and social anxiety disorder (Table 3). The EAG note that although the NICE guideline currently has PTSD included at step 2, the IAPT manual states that PTSD and SAD should not use a stepped care approach, instead recommending that high intensity treatment is the first intervention. The EAG has therefore considered PTSD and SAD at step 3 for this assessment. There is currently no NICE guidance on health anxiety. The NHS suggests that people with health anxiety use self-help and see a GP if symptoms do not improve or worries are significantly impacting daily living (NHS 2020).

The NHS advises that specific phobias can be treated using desensitisation or self-exposure therapy with the help of a professional or a self-help programme (NHS 2022). NICE's 4-year surveillance of CG159 (2017) does not recommend computerised CBT for the routine treatment of specific phobias because of a lack of quality evidence at that time.

In IAPT services, digitally enabled therapies may also be offered as high intensity psychological interventions if they include the same therapeutic content as recommended in the NICE guideline. [The IAPT manual](#) states that this should be supported or delivered by a high intensity therapist trained in the specific therapies.

No other relevant guidelines were identified.

Table 3: Relevant NICE Guidelines

Guideline	Condition	Recommendation
NICE CG31	Body Dysmorphic Disorder	<ul style="list-style-type: none"> Individual or group CBT with ERP that addresses key features of BDD for adults with mild functional impairment Adults with moderate functional impairment should be offered either a selective serotonin reuptake inhibitor (SSRI) or more intensive individual CBT with ERP, while those with severe impairment should be offered both an SSRI and CBT with ERP
NICE CG113	Generalised anxiety disorder	<p>Low intensity</p> <ul style="list-style-type: none"> Individual guided self-help, individual unguided self-help, or psychoeducational groups Guided or unguided self-help for GAD should include written or electronic materials based on the principles of CBT Interventions should be completed over at least 6 weeks with guided self-help including 5 to 7 sessions with a trained practitioner. <p>High Intensity</p> <ul style="list-style-type: none"> CBT or applied relaxation if a person chooses a high intensity psychological intervention. This would usually consist of 12 to 15 weekly sessions each lasting an hour Drug treatment may be offered to some people who prefer it to therapy
NICE CG31	Obsessive Compulsive Disorder	<p>Low Intensity</p> <ul style="list-style-type: none"> Low intensity interventions as a first line treatment for people with mild functional impairment and/or who prefer a low intensity approach This includes brief individual CBT including exposure and response prevention (ERP) using structured self-help materials or by telephone, or group CBT with ERP. <p>High Intensity</p> <ul style="list-style-type: none"> SSRI or more intensive CBT with ERP for adults with moderate functional impairment or who have

Guideline	Condition	Recommendation
		<p>not benefited from low intensity treatment</p> <ul style="list-style-type: none"> Adults with severe functional impairment should be offered both an SSRI and CBT with ERP
NICE CG113	Panic Disorder with or without agoraphobia	<p>Low Intensity</p> <ul style="list-style-type: none"> Guided or unguided self-help for people with mild to moderate panic disorder People with moderate to severe panic disorder with or without agoraphobia would usually be offered step 3 interventions <p>High Intensity</p> <ul style="list-style-type: none"> CBT or an antidepressant for people with moderate to severe panic disorder with or without agoraphobia
NICE NG116	Post-traumatic stress disorder	<ul style="list-style-type: none"> Individual trauma-focused CBT as first line treatment Eye movement desensitisation and reprocessing (EMDR) or supported trauma-focused computerised CBT may be offered to some adults who present more than 3 months after a traumatic event if they prefer it to face-to-face treatment. This should be based on a validated programme delivered over 8 to 10 sessions, with guidance and support from a trained practitioner
NICE CG159	Social Anxiety Disorder	<ul style="list-style-type: none"> Individual CBT specifically developed to treat social anxiety disorder as first line treatment CBT-based supported self-help may be offered to people who decline individual CBT. This should include up to 3 hours of support to use CBT-based self-help materials over 3 to 4 months People who decline either treatment may be offered drug treatment or short-term psychodynamic psychotherapy where appropriate

IAPT terminology and database

All appointments and courses of therapy delivered within the IAPT framework are recorded in the IAPT database, with much of the information publicly available via NHS Digital in the form of a dashboard and regular reports. Table 4 shows the total numbers of completed therapy courses recorded in the IAPT database for Depression and Anxiety descriptors. There are slightly more people with anxiety than depression, and within the anxiety group, over half are classified as have GAD.

Table 4: Extract from IAPT database 2021-22

Problem descriptor	Total Courses delivered	Selected therapy types used for economic modelling						
		Stage 2					Stage 3	
		Guided Self Help (Book)	Non-guided Self Help (Book)	Guided Self Help (Computer)	Non-Guided Self Help (Computer)	Psychoeducational peer support	Eye Movement Desensitisation Reprocessing	Cognitive Behaviour Therapy (CBT)
Depression	152,850	27.9%	1%	4.6%	0.2%	5.7%	0.4%	37.2%
Anxiety (all)	210,105	28.1%	0.6%	5.2%	0.3%	5.1%	2.4%	52.5%
Agoraphobia	2,812	37.1%	1%	4.1%	0.1%	4.3%	0.4%	51.7%
Body Dysmorphic disorder	272	1.5%	0%	0.7%	0.0%	1.5%	0.7%	95.2%
Social phobias	13,047	10.0%	0%	2.5%	0.1%	1.0%	0.2%	84.4%
Specific (isolated) phobias	3,845	19.6%	0%	3.0%	0.2%	1.3%	1.7%	72.7%
Panic disorder	9,767	36.8%	1%	6.4%	0.2%	5.9%	0.2%	47.8%
Generalised Anxiety Disorder	107,597	38.5%	1%	7.4%	0.4%	6.6%	0.4%	41.1%
Mixed anxiety and depressive disorder	7,661	21.8%	1%	4.7%	0.1%	4.0%	0.8%	46.6%
Obsessive-compulsive disorder	12,989	8.5%	0%	2.2%	0.1%	0.7%	0.4%	87.0%
Post-traumatic	25,895	2.4%	0%	0.2%	0.0%	1.0%	15.9%	77.4%

stress disorder								
Hypochondriacal disorders	7,778	12.5%	0%	3.8%	0.2%	1.8%	0.4%	80.3%
Other anxiety or stress related disorder	18,442	34.8%	2%	4.5%	0.1%	10.0%	1.1%	25.8%

Reporting of the proportion of people who access each type of therapy is restricted in table 4 to those therapies used within the economic modelling, however the full information is available via NHS digital on the IAPT dashboard. Overall, for people treated for anxiety of any kind, 28% are given guided self-help, in the form of books, 5% receive guided self-help via a computer, and 52.5% receive some form of CBT. A clinical expert did state however that patients will rarely be given books for guided self-help, but will often be offered information sheets, short booklets, videos and website links.

IAPT definitions

Courses are described as completed if the patient has finished a course of treatment and there are 2 or more attended treatment appointments. Patients are described as “*at caseness*” if at least one indicator meets the clinical threshold. For generalised anxiety these are normally PHQ-9 and GAD-7. For other anxiety disorders there are condition specific tools listed in the IAPT manual which should be used in addition to PHQ-9 and GAD-7.

IAPT manual definitions consider a person *recovered* if their scores on PHQ-9 and / or the relevant anxiety measure are above the clinical cut-off on either at the start of treatment, and their scores on both are below the clinical cut-off at the end of treatment. *Reliable improvement* is when scores on the depression and/or the relevant anxiety/MUS measure have reduced by a reliable amount and neither measure has shown a reliable increase. *Reliable recovery* is when a person meets the criteria for both recovery and reliable improvement (IAPT Manual).

Anxiety assessment tools and measurement within IAPT

Generalised Anxiety Disorder Assessment (GAD-7) is the IAPT-recommended tool for assessing anxiety, unless an additional measure is required for specific anxiety disorders such as PTSD or OCD. This tool gives a score between 0 and 21, where 21 represents the maximum level of anxiety. The IAPT definition of “caseness” requires a level of GAD-7 higher than 7. Patients may be described as recovered if they move from caseness to non-caseness, with a reliable recovery also indicating that there was an improvement of at least 4 points on the GAD-7 score. A reliable clinical improvement or deterioration is a movement of at least 4 points on the GAD-7 score without a change from caseness to non-caseness. For condition specific measures, the reliable change values are included in the IAPT manual.

Potential place of digitally enabled therapies in the care pathway

In IAPT services, digitally enabled therapies would be offered after assessment and identification of the appropriate problem descriptor in line with ICD-10. Digitally enabled therapies may be offered as an alternative to existing low intensity or high intensity interventions for adults with anxiety disorders. The place in the care pathway depends on the specific disorder, healthcare professional assessment and clinical judgement, the content of the intervention, patient preferences and risk, and the level of support needed.

Special considerations, including issues related to equality

Scoping workshop participants noted that health inequalities need to be considered as a priority. Specific considerations may include (but are not limited to):

- Anxiety in specific groups (e.g. traveller community, anxiety associated with menopause)
- Some users struggle to focus on digital therapies (e.g. people with ADHD)
- Digital literacy
- Safe space for access
- General accessibility issues (e.g. language / internet / devices)

4 Clinical evidence selection

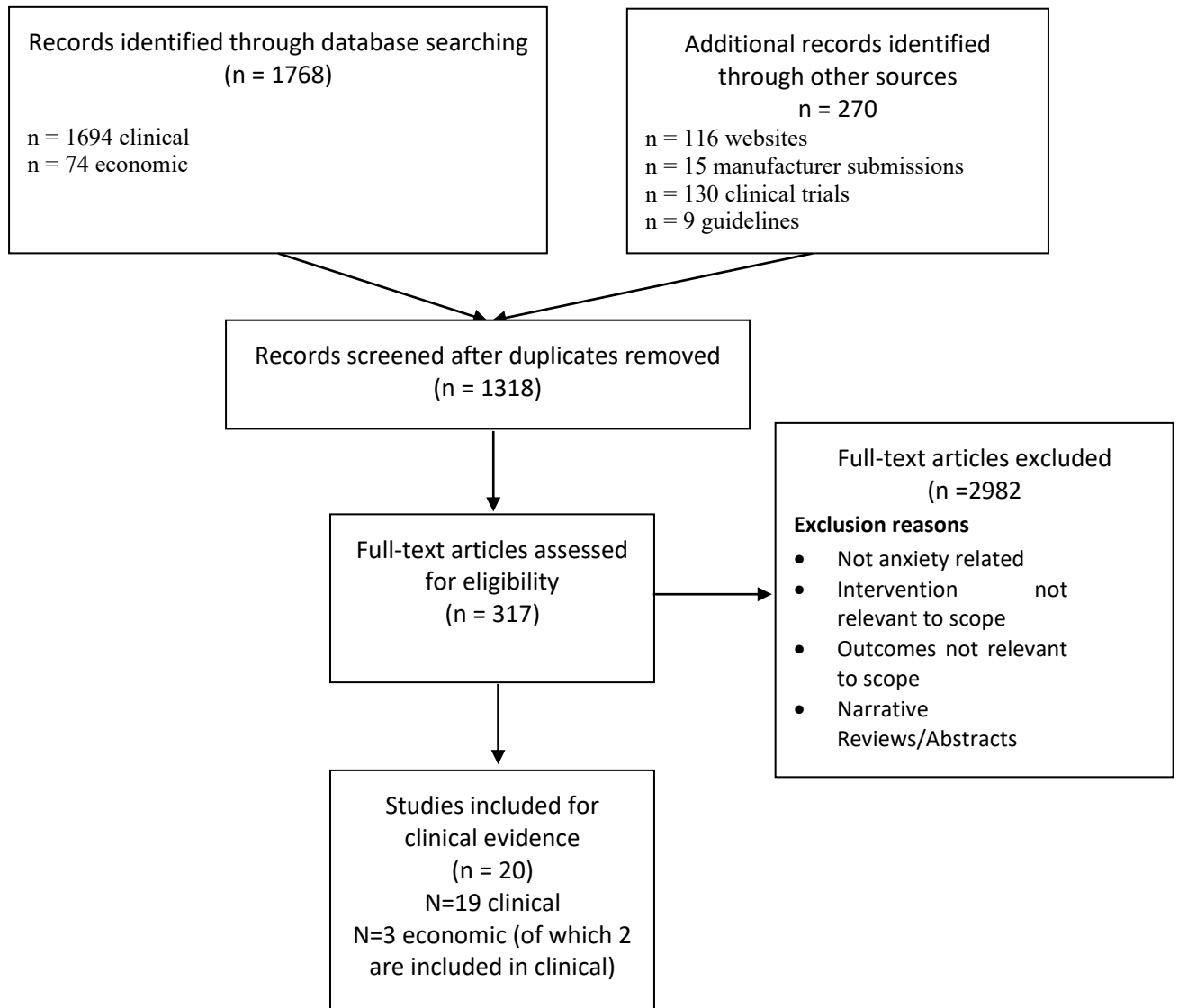
4.1 *Evidence search strategy and study selection*

The EAG conducted literature searches to ensure that all relevant evidence had been identified. The EAG literature searches identified a total of 1250 records. Fifteen studies included in the company submission were not picked up through EAG searches and were added to the database. Details of the EAG searches are provided in [Appendix A](#).

4.2 *Included and excluded studies*

A total of 19 published studies are included in the clinical review and are summarised in Table 5. A rating of **Green** indicates an element that meets the scope fully, **amber** meets the scope partially and **red** indicates does not meet the scope.

Figure 1: Study Selection Flow Chart



Companies also provided some additional, unpublished evidence for their technologies and this has been included and discussed where appropriate.

Due to the volume of studies available, the EAG made some pragmatic decisions around inclusion of studies that did not meet the scope and small number of studies which included technologies named in the scope have been excluded from this review (appendix B).

Table 5: Studies selected by the EAG as the evidence base

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Spring (1 study)				
<p>Study: Bisson 2022</p> <p>Location: UK</p>	<p>Design: Multicentre, pragmatic, randomised controlled non-inferiority trial</p> <p>Aim: To determine if guided internet based cognitive behavioural therapy with a trauma focus (CBT-TF) is non-inferior to individual face-to-face CBT-TF for mild to moderate post-traumatic stress disorder (PTSD) to one traumatic event</p> <p>Comparator: Face to face CBT therapy</p> <p>Therapist Involvement: experienced psychological therapists who received training</p> <p>Green</p>	<p>Participants: N=196 adults with a primary diagnosis of mild to moderate PTSD from one traumatic event</p> <p>Setting: NHS Mental Health Services (IAPT, primary and secondary care)</p> <p>Green</p>	<p>Follow-up at 16 and 52 weeks post-randomisation</p> <p>Primary outcome:</p> <ul style="list-style-type: none"> • Clinician Administered PTSD Scale for DSM-5 (CAPS-5) at 16 weeks <p>Secondary outcomes:</p> <ul style="list-style-type: none"> • CAPS-5 at 52 weeks • Generalised Anxiety Disorder (GAD-7) • Work and Social Adjustment (WASA) Scale • The Patient Health Questionnaire Depression (PHQ-9) • EuroQol (EQ-5D-5L) <p>Green</p>	<p>Good quality study. High number of participants with a very specific and relevant diagnosis. The outcomes are all within scope and there is a guided element to the use of the technology.</p>

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Beating the Blues (6 studies)				
<p>Study: Cavanagh 2011</p> <p>Location: UK</p>	<p>Design: Pragmatic, open trial, pre-post design</p> <p>Aim: To test the generalisability of efficacy and effectiveness findings within the NHS to the implementation of CCBT in a service user-led, third sector Self Help Clinic</p> <p>Comparator: None</p> <p>Therapist Involvement: Therapist involvement not reported. Service volunteer offers support after each session</p> <p>Amber</p>	<p>Participants: N=351 completed baseline assessment (n=295 started BTB program)</p> <p>Setting: NHS Mental Health Services (Self Help Services – third sector)</p> <p>Green</p>	<p>Follow up after each session</p> <ul style="list-style-type: none"> • PHQ-9 • GAD-7 <p>Follow up at end of programme</p> <ul style="list-style-type: none"> • Clinical Outcomes in Routine Evaluation-Outcome Measure (CORE-OM) • WASA • Patient Experience Questionnaire <p>Numbers reaching caseness criteria (depression caseness criteria PHQ-9 ≥ 10; anxiety caseness criteria GAD-7 ≥ 8)</p> <p>Green</p>	<p>Moderate quality study. There is no comparator and therapist time is not reported. However, there is a good sample size and the outcomes are relevant to the scope.</p>
<p>Study: Cavanagh 2009</p>	<p>Design: Naturalistic, open trial</p>	<p>Participants: N=219 with anxiety and/or depression (191 (87%) completed the pre-treatment</p>	<p>Follow-up immediately posttreatment</p>	<p>Moderate quality study. Questionnaires/Measures used in the study do not align with the</p>

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
<p>Location: UK</p>	<p>Aim: Acceptability of beating the blues for those with depression and/or anxiety</p> <p>Comparator: None</p> <p>Therapist Involvement: Programme completed within routine care setting (e.g., GP office, psychology service)</p> <p>Amber</p>	<p>measures and 84 (38%) completed treatment feedback questionnaire)</p> <p>Setting: NHS mental health services (primary and secondary care)</p> <p>Amber</p>	<ul style="list-style-type: none"> Opinions about Psychological Problems Questionnaire (OPP) Attitudes to CCBT Questionnaire (A-CCBT) Patient Feedback Questionnaire for CCBT (PFQ-CCBT) <p>Amber</p>	<p>IAPT measures and there are no clinical outcome measures. The diagnoses of the participants is also unclear. However, it was conducted within an NHS setting and has a good sample size.</p>
<p>Study: Cavanagh 2006</p> <p>Location: UK</p>	<p>Design: Naturalistic, non-randomised, open trial</p> <p>Aim: To establish the generalizability of continuation and outcomes from the controlled setting of efficacy trials to routine care for depression and anxiety and to benchmark health gains associated with using computerized therapy against those achieved and maintained by patients receiving face-</p>	<p>Participants: N=219 with anxiety and/or depression (104 (47%) completed all 8 sessions of BtB and post-treatment measures – referred to as ‘Research completers’)</p> <p>Setting: NHS Mental Health Services (primary and secondary care)</p> <p>Amber</p>	<p>Weekly follow up</p> <ul style="list-style-type: none"> CORE-OM WASA Self-reported anxiety and depression scores <p>Amber</p>	<p>Moderate quality study. The only anxiety measure is a self-report measure and there is no comparator. The diagnosis of participants is also unclear. However, it was conducted within an NHS setting with a good sample size.</p>

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	<p>to-face counselling and psychological therapy</p> <p>Comparator: None</p> <p>Therapist Involvement: Programme completed within routine care setting (e.g., GP office, psychology service)</p> <p>Amber</p>			
<p>Study: Jonassaint 2020</p> <p>Location: USA</p>	<p>Design: Secondary analysis of a three-arm randomized controlled clinical trial</p> <p>Aim: To study race differences in the impact of cCBT use on mental health outcomes among White and African American primary care patients</p> <p>Comparator: BtB plus internet support group (ISG) and usual care</p> <p>Therapist Involvement: Email and telephone</p>	<p>N=704 with anxiety and/or depression randomised to 3:3:1 ratio:</p> <ul style="list-style-type: none"> N=301 cCBT only N=302 CBT+ ISG N=101 Usual care <p>CBT+ISG group not included in these analyses</p> <p>Setting: Primary care (mental health)</p> <p>Amber</p>	<p>Follow up at 3 and 6 months</p> <ul style="list-style-type: none"> Short form health survey (SF-12) PROMIS-Anxiety PROMIS depression <p>Differences in PROMIS-Anxiety change between Caucasians and African Americans</p> <p>Amber</p>	<p>Moderate quality study as the outcome measures do not align with IAPT approved measures.</p> <p>A usual care comparator group was used but not defined.</p> <p>The diagnosis of patients is unclear and it was not conducted in a UK/IAPT setting but does have a good sample size.</p> <p>Acceptability results reported in this study are the same as those in an earlier study (Jonassaint 2020), unclear if same population in both studies but very possible.</p>

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	<p>guidance and support from a care coach with mental health research experience</p> <p>Amber</p>			
<p>Study: Jonassaint 2017</p> <p>Location: USA</p>	<p>Design: Secondary analysis of randomised controlled trial</p> <p>Aim: Examine differences in CCBT use and self-reported change in depression and anxiety symptoms among African Americans and white primary care patients</p> <p>Comparator: No comparator</p> <p>Therapist Involvement: Email and telephone guidance and support from a care manager with research experience</p> <p>Amber</p>	<p>Participants: N=590 with moderate anxiety and/or depression symptoms</p> <ul style="list-style-type: none"> • N=91 African Americans • N=499 White Americans <p>Setting: Primary care</p> <p>Amber</p>	<p>Follow up at 3, 6 and 12 months</p> <ul style="list-style-type: none"> • GAD-7 • PHQ-9 <p>App engagement</p> <p>Green</p>	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
<p>Study: Learmonth 2008</p> <p>Location: UK</p>	<p>Design: Naturalistic study</p> <p>Aims: To evaluate the impact of Beating the Blues for the management of anxiety and depression, within an NHS CBT specialist healthcare centre</p> <p>Comparator: No comparator</p> <p>Therapist Involvement: Participants completed session material alone. Administrator available to manage concerns and alert therapeutic staff where needed</p> <p>Amber</p>	<p>Participants: N=555 (394 completed full follow-up; 'Research completers') with anxiety and/or depression symptoms</p> <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Amber</p>	<p>Follow up at 6 and 8 weeks</p> <p>Reliable and clinically significant changes in:</p> <ul style="list-style-type: none"> • Beck Depression Inventory II (BDI-II) • Beck Anxiety Inventory (BAI) <p>Amber</p>	
<p>SilverCloud (7 studies)</p>				

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
<p>Study: Chien 2020</p> <p>Location: UK</p>	<p>Design: Cohort study</p> <p>Aims: To identify behaviour types based on how people engage with an internet-based cognitive behavioral therapy (iCBT) intervention for symptoms of depression and anxiety.</p> <p>Comparator: None</p> <p>Therapist Involvement: 8 weeks of guidance and feedback via asynchronous messages, monitors programme activity</p> <p>Amber</p>	<p>Participants: N=54604 adult patients assigned to the Space From Depression and Anxiety treatment program</p> <p>Setting: Not reported</p> <p>Green</p>	<p>Follow up at 14 week</p> <ul style="list-style-type: none"> • PHQ-9 • GAD-7 <p>Log data from user interactions with the iCBT program to inform engagement patterns over time.</p> <p>Green</p>	
<p>Study: Duffy 2020</p> <p>Location: UK</p>	<p>Design: Uncontrolled feasibility design</p> <p>Aim: To investigate the potential impacts of using iCBT as a prequel for patients requiring high intensity treatment (HIT;</p>	<p>Participants: N=124 patients who were on the waiting list for high intensity face to face psychological treatment due to anxiety or depression</p> <p>Setting: NHS Mental Health Services</p>	<p>Changes in the following measures from baseline, iCBT exit and service exit:</p> <ul style="list-style-type: none"> • GAD-7 • WSAS • PHQ-9 	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	<p>face-to-face) for depression and anxiety in IAPT</p> <p>Comparators: No comparator</p> <p>Therapist Involvement: Clinicians and Psychological Wellbeing Practitioners (PWPs) monitor clients' progress for 8 weeks and give feedback</p> <p>Amber</p>	<p>(IAPT)</p> <p>Green</p>	<p>Reliable change, recovery and reliable recovery</p> <p>Green</p>	
<p>Study: Jardine 2020</p> <p>Location: UK</p>	<p>Design: Naturalistic randomised controlled trial</p> <p>Aim: To evaluate clients' expectations, experience, and context of usage of iCBT</p> <p>Comparator: Waitlist control</p> <p>Therapist Involvement:</p>	<p>Participants: N=361 randomised (n=183 completed all assessments)</p> <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Green</p>	<p>Follow up at 4 and 8 weeks</p> <p>Patient expectations of their:</p> <ul style="list-style-type: none"> • online treatment • experience of the intervention • context of their use of the intervention • their perception of the aesthetics employed 	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	<p>PWPs provides asynchronous feedback via written messages on the platform or telephone appointment</p> <p>Amber</p>		<p>Green</p>	
<p>Study: Palacios 2022(a)</p> <p>Location: UK</p>	<p>Design: Naturalistic, observational cohort study</p> <p>Aim: To compare treatment effects of three interventions, utilising four years' worth of routine clinical data</p> <p>Comparator: Guided self-help bibliotherapy (GSH) and psychoeducational group therapy (PGT)</p> <p>Therapist Involvement: PWPs provides encouragement, weekly online asynchronous written feedback for 6 – 8 weeks</p> <p>Green</p>	<p>Participants: N=21215 currently on step 2 of IAPT for anxiety and or depression</p> <ul style="list-style-type: none"> • GSH n=12896 • iCBT n=6862 • PGT n=1457 <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Amber</p>	<p>Follow up at end of treatment</p> <ul style="list-style-type: none"> • GAD-7 • WSAS • PHQ-9 <p>Rates of reliable recovery</p> <p>Green</p>	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
<p>Study: Palacios 2022(b)</p> <p>Location: UK</p>	<p>Design: Secondary analyses from pragmatic RCT</p> <p>Aims: To investigate post-treatment relapse and remission rates 3, 6 and 9 months after completion of a clinician-supported internet delivered cognitive-behavioural therapy (iCBT) for anxiety and depressive symptoms, within a routine care setting</p> <p>Comparator: No comparator</p> <p>Therapist Involvement: PWP's trained in low intensity CBT monitors clients' progress, provides online or telephone reviews, feedback and guidance</p> <p>Amber</p>	<p>Participants: N=241 in intervention arm with anxiety and/or depression symptoms</p> <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Amber</p>	<p>Follow up at 3, 6 and 9 months posttreatment</p> <ul style="list-style-type: none"> • PHQ-9 • GAD-7 <p>Durability of treatment effects</p> <p>Predictors of relapse at end of treatment</p> <p>Green</p>	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
<p>Study: Palacios 2018</p> <p>Location: USA</p>	<p>Design: Open, non-randomised feasibility trial</p> <p>Aim: To assess feasibility, acceptability, effectiveness, and satisfaction of a supported iCBT intervention offering 3 programs on depression, anxiety, and stress to university students</p> <p>Comparator: Space from Depression; Space from Stress (SilverCloud)</p> <p>Therapist Involvement: Licensed psychologist or social worker provided web-based welcome message, encouragement, feedback and reviewed progress</p> <p>Amber</p>	<p>Participants: N=102 University students referred from either counselling services, mental health services or the international office</p> <p>Setting: US University mental health services</p> <p>Amber</p>	<p>Follow up at 8 weeks and 3 months</p> <ul style="list-style-type: none"> • GAD-7 • Reliable Change Index (RCI) • PHQ-9 <p>Satisfaction with Treatment</p> <p>Amber</p>	
<p>Study: Richards 2020</p>	<p>Design: Pragmatic randomised controlled trial</p> <p>Aim: To investigate the</p>	<p>Participants: N=361</p> <ul style="list-style-type: none"> • N=169 depressive disorder <ul style="list-style-type: none"> ○ N=111 SilverCloud ○ N=58 waiting list 	<p>Follow up at 8 weeks and 3, 6, 9 and 12 months</p> <ul style="list-style-type: none"> • GAD-7 • PHQ-9 	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Location: UK	<p>effectiveness and cost-effectiveness of iCBT when fully integrated within an IAPT settings</p> <p>Comparator: Waiting list</p> <p>Therapist Involvement: PWP's monitored and reviewed client's progress and provided weekly feedback over 8-weeks</p> <p>Green</p>	<ul style="list-style-type: none"> N= 192 anxiety disorder <ul style="list-style-type: none"> N=130 SilverCloud N=62 waiting list <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Amber</p>	<ul style="list-style-type: none"> M.I.N.I. diagnosis WSAS <p>App usage</p> <p>Safety</p> <p>Green</p>	
iCT-SAD (2 studies)				
<p>Study: Clark 2022</p> <p>Location: UK</p>	<p>Design: Randomised controlled trial</p> <p>Aim: To compare internet and standard face-to-face delivery of individual cognitive therapy for social anxiety disorder (CT-SAD) with the same therapists, assessing the competence with which the face-to-face therapy is delivered and assessing the quality of the</p>	<p>Participants: N=102 patients with social anxiety disorder (SAD) - N=34 in each group (total 102)</p> <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Green</p>	<p>Follow up mid-treatment, post-treatment and at 3 and 12 months</p> <p>Primary outcome: The social anxiety disorder composite - 6 independent assessor and patient self-report scales of social anxiety including ADIS, SPIN, LSAS, SPS, SIAS and FNE.</p>	Waitlist control not in scope

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	<p>therapeutic alliances</p> <p>Comparators: CT-SAD or waitlist control</p> <p>Therapist Involvement: Weekly phone calls to review progress, assign new modules, deepen learning, and plan behavioural experiments</p> <p>Amber</p>		<p>Secondary outcomes:</p> <ul style="list-style-type: none"> • GAD-7 • PHQ-9 • WSAS <p>Recovery rates as defined by IAPT (Proportion of patients rated as meeting SAD criteria by independent assessor (score below cut-off on both PHQ 9 and SPIN)).</p> <p>Green</p>	
<p>Study: Stott 2013</p> <p>Location: UK</p>	<p>Design: Pilot cohort study</p> <p>Aim: To develop an internet-based version of CBT that requires less therapist time</p> <p>Comparator: Face to face CBT</p> <p>Therapist Involvement: Clinical psychologist</p>	<p>Participants: N=11 with DSM-IV diagnosis of social anxiety disorder</p> <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Amber</p>	<p>Follow up posttreatment</p> <ul style="list-style-type: none"> • Liebowitz social anxiety scale (LSAS) • Social Cognitions Questionnaire (SCQ) • Social Behaviour Questionnaire (SBQ) • Social Attitudes Questionnaire (SAQ) • GAD-7 • PHQ-9 	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	<p>monitors clients' progress, uses secure messaging system, phone call once a week, and mobile SMS messages</p> <p>Green</p>		<p>Patient drop-out</p> <p>Rates of response and remission</p> <p>Therapist time</p> <p>Green</p>	
iCT-PTSD (1 study)				
<p>Study: Wild 2016</p> <p>Location: UK</p>	<p>Design: Pilot cohort study</p> <p>Aims: To develop an Internet version of CT-PTSD that significantly reduces therapist contact time without compromising treatment integrity or retention rates</p> <p>Therapist Involvement: Advice, direction, and support via weekly telephone calls, SMS messages and follow-up</p>	<p>Participants: N=10 patients with DSM-IV diagnosis of PTSD</p> <p>Setting: NHS Mental Health Services (IAPT)</p> <p>Amber</p>	<p>Follow up posttreatment</p> <ul style="list-style-type: none"> • PTSD checklist for DSM-V (PCL-5) • PTSD Symptom Scale Interview (PSS-I) • GAD-7 • PHQ-9 • WSAS • Rates of recovery as measured using the Impact of Events Scale – Revised (IES-R) • Rates of remission as defined by a loss of diagnosis on the PSS-I 	

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	emails Green		<ul style="list-style-type: none"> • Therapist time • Programme engagement • Patient drop out Green	
Koa Health (2 studies)				
Study: Wilhelm 2020 Location: USA	Design: Pilot feasibility and acceptability study Aim: To describe the development of the first smartphone-delivered individual CBT for BDD digital service (“Perspectives”) and obtain data on feasibility, acceptability and treatment outcome Comparator: None Therapist Involvement: Participants had remote access to a licensed psychologist during treatment (phone call or	Participants: N=10 adults with primary BDD (based on DSM-5 criteria) Setting: No specific setting, participants recruited nationally through advertisement Green	Follow up at 6 and 12 weeks, and 3 months Feasibility, acceptability and satisfaction CSQ-8 <ul style="list-style-type: none"> • Yale–Brown Obsessive Compulsive Scale, Modified for BDD (BDD-YBOCS)_ • Brown Assessment of Beliefs Scale (BABS) score • PHQ-9 • Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form (Q-LES-Q-S) 	Low quality due to being a feasibility study with no comparator, small sample size and limited applicability of outcomes to the scope.

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
	secure, asynchronous messaging system) Amber		<ul style="list-style-type: none"> Safety Amber	
Study: Wilhelm 2022 Location: USA	Design: Randomised controlled trial Aim: To provide an initial test of the usability and efficacy of coach-supported app-based cognitive behavioural therapy (CBT) for BDD Comparator: Waitlist Therapist Involvement: Coach provided encouragement and feedback, via calls and asynchronous in-app messages. Coaches followed a manual and were supervised by a licensed clinician Amber	Participants: N=80 participants <ul style="list-style-type: none"> N=40 Perspectives N=40 Waitlist Setting: Not reported Green	Follow up at 6 and 12 weeks Primary Outcome <ul style="list-style-type: none"> Intent to treat analysis of difference in BDD-YBOCS scores between treatment and waitlist groups Secondary Outcome <ul style="list-style-type: none"> BABS QIDS-SR (Quick Inventory of Depressive Symptomatology – Self Report) Q-LES-Q Amber	Moderate quality due to generalisability issues but indicative of positive outcomes.

Abbreviations: A-CCBT, Attitudes to CCBT Questionnaire; ADIS, Anxiety Disorders Interview Scale; BABS, Brown Assessment of Beliefs Scale; BAI, Beck Anxiety Inventory; BDD-YBOCS, Yale–Brown Obsessive Compulsive Scale, Modified for BDD; BDI-II, Beck Depression Inventory II; CAPS-5, Clinician Administered PTSD Scale for DSM-5; CORE-OM, Clinical Outcomes in Routine Evaluation-Outcome Measure; EQ-5D-5L, EuroQol; GAD-7, FNE, Fear of Negative Evaluation; Generalised Anxiety Disorder; IES-R, Impact of Events Scale – Revised; LSAS, Liebowitz Social Anxiety Scale; M.I.N.I., Mini-International Neuropsychiatric Interview; OPP, Opinions about Psychological Problems Questionnaire; PCL-5, PTSD checklist for DSM-V; PFQ-CCBT, Patient Feedback Questionnaire for CCBT; PHQ-9, Patient Health Questionnaire Depression; PSS-I, PTSD Symptom Scale Interview; QIDS-SR, Quick Inventory of Depressive Symptomatology – Self Report; Q-LES-Q-S, Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form; RCI, Reliable Change Index; SAQ, Social Attitudes Questionnaire; SBQ, SIAS, Social Interaction Anxiety Scale; Social Behaviour Questionnaire; SPIN, Social Phobia Inventory; SPS, Social Phobia Scale; SF-12, Short form health survey; WASA, Work and Social Adjustment Scale

5 Clinical evidence review

5.1 Quality assessment of included studies

As outlined in the [final protocol](#) for the review, the EAG has taken a pragmatic approach to critical appraisal and quality assessment. This section outlines key information on factors such as study methodologies, potential risks of bias and key strengths and limitations of each of the included studies (Table 6). A summary comment is provided on EAG conclusions on the quality of the evidence for each condition.

There is no evidence for generalised anxiety disorder (as defined by ICD-10) instead much of the evidence relates to ‘generalised anxiety’ or ‘symptoms of depression and anxiety’ (n=13 studies covering 2 technologies only). Broadly the evidence indicates that use of either Beating the Blues or SilverCloud results in improvements in anxiety symptoms and, where reported participants were satisfied with the technologies, the quality of the evidence is variable (study design, interventions, comparators). Evidence for body dysmorphic disorder is limited to one technology (Koa Health) and only 2 studies. Although there is one randomised trial (Wilhelm 2022) showing favourable results for people using the Koa Health technology, the comparator is not within scope (waitlist control) and the measures used to assess BDD are not those used within IAPT. Additionally, although during the study users have access to a coach, the level of qualification for a coach may not meet the requirements set out for use within IAPT where step 2 interventions are supported by a psychological wellbeing practitioner (PWP). For both post traumatic stress disorder and social anxiety disorder the evidence was limited to 2 studies each. For social anxiety disorder, both studies related to iCT-SAD and included 1 RCT, however both were compared with waitlist control. For post-traumatic stress disorder, 1 study related to iCT-PTSD and 1 to Spring thus providing limited evidence for each of these technologies.

Table 6: Methodologies and Quality Assessment

Condition	Technology	Evidence Quality Comments	Quality conclusion
Body Dysmorphic	Koa Health	Randomised trial evidence	Positive results indicative of

Condition	Technology	Evidence Quality Comments	Quality conclusion
Disorder	(Perspectives)	available but <ul style="list-style-type: none"> Overall limited studies available Comparator not within scope. Validated measures are used to assess BDD in study but they not aligned with the IAPT measures. Therapist supported but unclear whether the level of qualification meets with IAPT requirements for step 2 interventions. 	a benefit from using the technology but this should be balanced against the broader generalisability of the evidence to the UK setting however these could be addressed if the technology was used within a UK specific study setting or within an IAPT setting where data collection requirements can be clearly laid out.
Generalised Anxiety	Beating the Blues SilverCloud	13 published studies available however only 2 technologies addressed by published studies.	Positive results indicate a benefit to using Beating the Blues or Silvercloud to manage symptoms of anxiety however the extent of the benefit is difficult to quantify as for most studies, participants were included if they had symptoms of anxiety and depression and it is not possible to know the proportion of participants with anxiety symptoms. There was no evidence relating to generalised anxiety disorder (as defined by ICD-10) which is the condition included in the scope. Therapist time/involvement was not reported in any of the included studies.
Post-Traumatic Stress Disorder	iCT-PTSD Spring	Extremely limited evidence with only 2 published studies each using a different technology. <ul style="list-style-type: none"> 1 non-comparative study including a small sample size 1 study includes a large sample size of adults with PTSD and compares technology to face to face CBT 	Positive findings indicative of a benefit however the evidence base is extremely limited.

Condition	Technology	Evidence Quality Comments	Quality conclusion
Social Anxiety Disorder	iCT-SAD	Two studies available however: <ul style="list-style-type: none"> iCT-SAD compared with face to face CBT or waitlist control. Both studies set in NHS mental health services and include a total of 112 patients though it should be noted that the sample size in one study included only 11 participants 	Positive findings indicate improvements in SAD with iCT-SAD compared with face to face therapy. Evidence comparing the technology with waitlist control is outside of the scope.
Health Anxiety	None	None	None
Obsessive Compulsive Disorder	None	None	None
Panic Disorders with/without agoraphobia	None	None	None
Specific Phobias	None	None	None

5.2 Results from the evidence base

The IAPT manual recommends that PHQ-9 and WSAS tools are used as part of all assessments with condition specific measures recommended depending on the clinical condition being treated. Results for each anxiety disorder included in the scope are presented in this section. Table 7 shows each measure with a brief description.

Table 7: Included measures and description

Condition	IAPT Recommended Measure	Measure used in literature	Description
Body Dysmorphic Disorder	BIQ	BDD-YBCOS	Body dysmorphia disorder symptom scale
Health Anxiety	HAI	No evidence	Health anxiety scale
OCD	OCI	No evidence	Obsessive Compulsive Disorder Scale
Panic Disorder	PDSS	No evidence	Panic Disorder Severity Scale
PTSD	PCL-5	CAPS-5, PCL-5 and	Post-Traumatic Stress disorder symptom and cognition scales

		PSS-I ■	
Social Anxiety Disorder	SPIN	LSAS	Social anxiety symptom scale
Generalised Anxiety	GAD-7	GAD-7, BAI, PROMIS-Anxiety	Anxiety symptom scales
Other Tools used	WSAS	WSAS	Work and social adjustment scale Used to measure the extent to which a person's mental health problem interferes with functioning
		CORE-OM	Global distress scale
		BABS	Delusions symptoms scale

Whilst the PHQ-9 was listed as an outcome in Table 5, the results from this will not be recorded as they relate to depression symptoms which is outside of the scope of this review.

5.2.1 *Health Anxiety, Obsessive Compulsive Disorder, Panic Disorder with or without agoraphobia, Specific Phobia*

Two included technologies (SilverCloud, Mind District) can be used for health anxiety. Two included technologies (SilverCloud, Mind District) can be used for OCD. Two included technologies (SilverCloud, Mind District) can be used for panic disorder. Two included technologies (SilverCloud, Mind District) can be used for phobia.

None of the identified evidence included reported results for health anxiety, OCD, Panic Disorder or specific phobias using any of the technologies of interest.

5.2.2 *Body Dysmorphic Disorder*

One included technology (Perspectives, Koa Health) can be used for BDD. Two relevant publications were identified relating to Perspectives: a pilot feasibility study including 10 participants (Wilhelm 2020) and a randomised trial including 80 participants (Wilhelm 2022). Table 8 summarises these results.

Table 8: Results for Body Dysmorphic Disorder

Study	Technology	Change in BDD scores	Change in BABS scores	Quality of Life	Remission and recovery	Drop out and App usage	Therapist Time
Wilhelm 2020	Perspectives, Koa Health	BDD-YBOCS scores decreased (Mean 45.27%)	BABS scores decreased (mean 67.08%)		90% of participants were treatment responders ($\geq 30\%$ reduction on BDD-YBOCS) Treatment response remained at 90% at follow-up RCI was 5.08 at posttreatment and 5.69 at follow-up (indicating reliable change)	Participants spent a mean of 398 minutes over 12 weeks using the service	
Wilhelm 2022	Perspectives, Koa Health	Mean BDD-YBOCS scores baseline and week 12 Perspectives: 29.9 to 16.8 Waitlist: 30.9 to 26.7, between group difference $p < 0.001$	Mean BABS scores baseline and week 12: Perspectives: 15.1 to 8.3 Waitlist: 14.5 to 13.2	Mean Quality of life scores baseline and week 12: Perspectives: 52.7 to 66.5 Waitlist: 48.3 to 55.2	Response rates for assessment completers at end of treatment: Perspectives: 68% Waitlist: 14% Full or partial remission: Perspectives: 52% (16/31)	Dropout rate: Perspectives: 23% (9/40) Waitlist: 8% (3/40) $p = 0.11$ App usage Mean 130.2 mins in the app	Coach time Mean 26.9 mins speaking to participants on the phone (mean phone calls 2.1) Mean 1.5 mins per participant per week via chat

Study	Technology	Change in BDD scores	Change in BABS scores	Quality of Life	Remission and recovery	Drop out and App usage	Therapist Time
					Waitlist: 8% (3/37)	Mean 30.4 days Satisfaction 86% were very(14/28) or mostly (25/28) satisfied 89% would recommend Perspectives	

5.2.3 Generalised Anxiety

Six of the included technologies can be used for generalised anxiety (Beating the Blues, Cerina, Iona Mind, Resony, SilverCloud, and Wysa). Thirteen studies reported results for high levels of anxiety symptoms. It should be noted here that none of these used an ICD-10 or DSM-V diagnosis of Generalised Anxiety Disorder (GAD) and will be referred to as generalised anxiety for the rest of this review. Table 9 summarises these results for outcomes relevant to the scope. Therapist time was not reported in any of the included studies.

For Cerina, the company provided a short report (unpublished) and results from an unpublished pilot study providing limited information showing that mean GAD-7 scores before and after, completed by 20 out of 43 participants. Change from 10.2 to 9.2.

For Resony, the company provided a list of publications which were reviewed by the EAG and excluded as they were not considered relevant to the scope of this review. A real-world evidence report was also provided

[REDACTED] and is therefore limited in its applicability to the current review. Resony also submitted results from one unpublished study after the final report was completed which included 86 participants. The aim of the study was to assess safety, clinical outcomes and engagement and treatment satisfaction.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Table 9: Results for generalised anxiety

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
Cavanagh 2006	Beating the Blues	<p>Research completers</p> <ul style="list-style-type: none"> Self-reported anxiety score reduced from 5.47 at baseline to 3.64 post-treatment (p<0.001) <p>Intention to treat analysis:</p> <ul style="list-style-type: none"> Self-reported anxiety score reduced from 5.23 at baseline to 4.00 post-treatment (p<0.001) 	<p>Research completers:</p> <ul style="list-style-type: none"> Mean score reduced from 23.14 at baseline to 18.51 post-treatment (p<0.001) <p>Intention to treat analysis:</p> <ul style="list-style-type: none"> Mean score reduced from 22.39 at baseline to 20.05 post-treatment (p<0.001) 	<p>Research completers:</p> <ul style="list-style-type: none"> Mean score reduced from 1.88 at baseline to 1.27 post-treatment (p<0.001) <p>Intention to treat analysis:</p> <ul style="list-style-type: none"> Mean score reduced from 1.81 at baseline to 1.53 post-treatment (p<0.001) 		
Learmonth 2008	Beating the Blues	<p>Research completers: A statistically significant mean BAI score difference was found between pre and post BtB treatment (difference = -5.9, p<0.001)</p> <p>Intention to treat analysis: A statistically significant mean BAI score difference was found between pre and post BtB treatment (difference = -4.9, p<0.001)</p>			<p>Of the 195 completers recording clinical caseness on the BAI measure, 44 (23%) showed reliable and clinically significant improvement, with 46 (19%) in the intention to treat population (n=238)</p> <p>Of the 394 who</p>	

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
					completed the program, 85 were referred on for further treatment. Of the 161 who did not complete the programme, 153 were referred for further treatment	
Cavanagh 2009	Beating the Blues					<p>Mean pre-treatment total for the A-CCBT was 6.3 with all questions rated significantly higher than the midpoint score of 4 ($p<0.001$)</p> <p>Mean scores of CBT credibility were 1.8 which is significantly higher than the midpoint of 0 ($p<0.001$)</p> <p>Mean scores from the PFQ-CCBT showed the usefulness of the programme's introductory video were above the midpoint of 2.5 (Mean=3.3, $p<0.001$). Mean scores of the interactive, multimedia programme features were above the midpoint of 3 (mean = 4.0, $p<0.001$)</p> <p>Eighty-nine per cent of patients</p>

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
						providing feedback rated the programme overall as very (35%) or quite (54%) helpful, and averaged ratings of its usefulness were above the midpoint of 2.5 (mean =3.2, p <0.001)
Cavanagh 2011	Beating the Blues	Over the course of at least 2 treatment sessions mean GAD-7 scores reduced from 12.6 at baseline to 7.6 (p<0.001)	Over the course of at least 2 treatment sessions mean WASA scores reduced from 24 at baseline to 19.2 (p<0.001)	Over the course of at least 2 treatment sessions mean CORE-OM scores reduced from 19.6 at baseline to 14.5 (p<0.001)	At baseline, 226 (85.3%) of those who completed at least two sessions of CCBT (n=265) met caseness criteria for one of (n = 58, 21.9%) or both anxiety and depression (n = 168, 63.4%) Following treatment of at least 2 sessions, 142 (53.6%) no longer met caseness for either depression or anxiety, 41 (15.5%) continued to meet caseness for one, and 82 (30.9%) for both. Therefore 50.0% cases moved to recovery status	

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
Jonassaint 2017	Beating the Blues	<p>African Americans showed a similar level of decline in anxiety (estimated 8-session change: -5.3 vs. -5.6; P=0.80) over the course of the eight BtB sessions compared to white people</p> <p>Pharmacotherapy use at baseline was not a predictor of decline in GAD-7 scores over time (P=0.6713)</p>				<p>African Americans were less likely than white people to start session 1 of the CCBT programme (75% vs. 87%, P=0.01)</p> <p>African Americans completed slightly fewer sessions at 6 months (mean 4.7 vs. 5.5; P=0.03)</p>
Palacios 2018	SilverCloud	Of those in the Space for Anxiety program, mean GAD-7 scores reduced from 10.9 at baseline to 7.5 at 8 weeks and 6.7 at 3 months.			On the GAD-7, for those with 8-week follow-up data, 17/53 (32%) decreased their scores by more than the RCI (4+), classed as reliable change; 30/53 (57%) had no reliable change and 6/53 (11%) had reliable deterioration (increase of 4 or more). At 3 months, 26/50 (52%) had reliable change,	

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
					22/50 (44%) had no reliable change, and 2/50 (4%) had reliable deterioration	
Chien 2020	SilverCloud	Mean GAD-7 scores reduced from 11.85 at baseline to 4.01 at 14 weeks				<p>5 different classes of engagement were suggested:</p> <ul style="list-style-type: none"> • Class 1 – low engagers • Class 2 – late engagers • Class 3 – high engagers with rapid disengagement • Class 4 – high engagers with moderate decrease • Class 5 – high engagers <p>Estimated engagement class specific mean GAD-7 change over 14 weeks:</p> <ul style="list-style-type: none"> • Baseline/Class 1 = -4.72 • Class 2 = -4.18 • Class 3 = -6.36 • Class 4 = -4.98 • Class 5 = -5.56
Duffy 2020	SilverCloud	<p>GAD-7 Post-hoc analysis of the linear mixed model:</p> <ul style="list-style-type: none"> • Baseline to iCBT exit reduction of 3.226 	<p>WSAS Post-hoc analysis of the linear mixed model:</p> <ul style="list-style-type: none"> • Baseline to iCBT 		N=100 participants had full data at all time points. 58 showed reliable improvement from	

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
		<p>(p<0.001)</p> <ul style="list-style-type: none"> iCBT exit to service exit (completers) reduction of 3.985 (p<0.001) iCBT exit to service exit (dropouts) increase of 0.164 (n.s.) 	<p>exit reduction of 2.426 (p<0.001)</p> <ul style="list-style-type: none"> iCBT exit to service exit (completers) reduction of 4.103 (p<0.001) iCBT exit to service exit (dropouts) increase of 0.168 (n.s) 		<p>baseline to iCBT exit</p> <p>Ninety-nine participants were above clinical caseness threshold at baseline; 22 had achieved recovery by iCBT exit and 20 had achieved reliable recovery; 33 were in recovery at point of service exit all of which reliably recovered</p>	
Jardine 2020	SilverCloud					<p>General expectations theme:</p> <ul style="list-style-type: none"> 137 (75%) participants expected to develop self-management skills and learn how to practically deal with their condition/emotions/thoughts through use of the intervention 42 participants (23%) had high or positive expectations of the treatment itself, for example 21 participants reported that they expected to feel supported,

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
						<p>understood and cared for via the online treatment. Fifteen expected it to be convenient and easy to use due to it being accessible in their own time, under their control</p> <ul style="list-style-type: none"> 42 (23%) of clients had negative expectations of the treatment; expected the experience to be challenging, emotionally confronting or feel strange or alien, while others expected online treatment to feel disconnected when compared to face-to-face therapy <p>Practical expectations theme:</p> <ul style="list-style-type: none"> 69 (38%) participants expected to use the online treatment at a specific or routine time. 50% of clients expected to use the platform when they were feeling low or anxious, or needed help or support <p>Experience vs expectations</p>

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
						<p>theme:</p> <ul style="list-style-type: none"> 71 (39%) participants reported that it was more helpful than they expected it to be 11 (6%) of clients felt that their experience of online treatment was generally harder than they expected <p>Experience of online treatment theme:</p> <ul style="list-style-type: none"> Only 66 (36%) participants reported developing self-management skills (compared to the 75% who expected it) 93 (51%) participants stated that their overall experience of using the platform was a positive, enjoyable or pleasant one For more than a third of clients in this sample, the flexibility and autonomy of online treatment were significant positive factors in their experience 31 (17%) participants reported challenges with online treatment, such as

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
						<p>the treatment lacked adequate support and guidance, the platform was difficult to use or the content was repetitive</p> <ul style="list-style-type: none"> 16 (9%) participants felt the flexibility of the platform hindered their engagement with it as the lack of deadlines and structure meant it was easy to put off or forget about <p>Study identified managing expectations, polarised preferences, momentary help-seeking and long-term support as important aspects of the experience to consider in future design</p>
Jonassaint 2020	Beating the Blues	<ul style="list-style-type: none"> African Americans in the cCBT group showed significantly greater decreases in PROMIS-Anxiety scores compared to those in the UC group (difference of 10.46 vs 4.81, $p < 0.01$). No significant difference between cCBT and UC 				<ul style="list-style-type: none"> White participants completed more BtB sessions on average than African Americans (5.5 vs 4.7, $p = 0.03$).

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
		<p>was seen in the white participants' group for PROMIS-Anxiety score (difference of 8.77 vs 7.37).</p> <ul style="list-style-type: none"> • Compared to the white group, African Americans reported a greater benefit of the cCBT programme on PROMIS-Anxiety score only (p=0.05) • For white participants, the number of BtB sessions completed was associated with 6-month improvements PROMIS-Anxiety(p=0.01 - <0.01). For African Americans, more sessions showed a greater benefit on the PROMIS-Anxiety score only (p = 0.014) 				
Richards 2020	Silvercloud	Paired comparisons showed in those who received Silvercloud, GAD-7 scores were reduced from baseline to 8-weeks more than in those who did not:			At 8-week follow-up 46.4% (90/194) of the intervention arm relative to 16.7% (15/90) control-arm participants recovered, with	

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
		<ul style="list-style-type: none"> Silvercloud = 12.7 vs. 8.2 Waitlist = 12.5 vs. 10.8 <p>8-week models suggested significant interaction effects of time-by-intervention-arm for GAD-7 (0.0001)</p>			<p>63.4% (123/194) intervention-arm relative to 34.4% (31/90) control-arm participants showing reliable improvement.</p> <p>Reliable recovery in the intervention-arm was 40.7% (79/194), and 13.3% (12/90) in the control arm. All between-group differences were significant (p < 0.01).</p>	
Palacios 2022 (a)	SilverCloud	<p>Mean GAD-7 score differences (pre, post):</p> <ul style="list-style-type: none"> iCBT = 12.4, 6.2 GSH = 13.4, 7.9 PGT = 11.4, 7.6 <p>All differences between pre and post were significant at p<0.001</p>	<p>Mean WSAS score difference (pre, post)</p> <ul style="list-style-type: none"> iCBT = 15.6, 9.9 GSH = 17.7, 11.9 PGT = 16.8, 12.3 <p>All differences between pre and post were significant at p<0.001</p>		<p>Overall reliable improvement rate was higher in the iCBT group (67%) compared to GSH (59%) and PGT (41%, p<0.001)</p>	
Palacios 2022 (b)		<p>GAD-7 scores decreased over the course of treatment then increased slightly over</p>			<p>Of the 89 participants included in analysis, 70.8% remained in</p>	

Study	Technology	Anxiety measures – GAD-7, BAI and self report measures	WSAS	CORE-OM	Recovery and remission	Acceptability and usage
		9 months follow-up: <ul style="list-style-type: none"> • Baseline = 11.5 • End of treatment = 3.2 • 3 months follow-up = 4.5 • 6 months = 4.2 • 9 months = 4.5 			remission whereas 28.2% had relapsed at the 9-month follow-up Of those who relapsed, 53.8% experienced a relapse of depression and anxiety, 7.7% depression only and 38.4% anxiety only Younger age, having a long-term condition, and residual symptoms of anxiety at end-of treatment were all significant predictors of relapse at end of treatment	

5.2.4 *Post-traumatic Stress Disorder*

Two included technologies can be used for PTSD (iCT-PTSD, Spring). Two relevant publications were included; one in relation to Spring and one in relation to iCT-PTSD. Table 10 summarises these results.

The company provided additional results from an unpublished randomised controlled trial however the study

[REDACTED]

[REDACTED]

[REDACTED]

Comparative results are considered to be outside of the current scope as

[REDACTED]

and not included in the

scope.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Table 10: Result for Post-Traumatic Stress Disorder

Study	Technology	PTSD specific measures: Change in CAPS-5, PCL-5 and PSS-I	Change in GAD-7	Change in WSAS	Rates of recovery and remission	Acceptability and usage	Therapist time
Wild 2016	iCT-PTSD	<p>Mean PCL-5 scores decreased from 47.90 to 15.80 post treatment (p<0.001)</p> <p>Mean PSS-I scores decreased from 31.7 to 12.44 post treatment (p<0.001)</p>	Mean scores decreased from 11.6 to 4.4 post treatment (p<0.01)	Mean scores decreased from 20.8 to 10.58 post treatment (p<0.05)	<p>9 (90%) participants showed reliable change on the PCL-5, achieving a mean drop of 32.10 points</p> <p>8 (80%) participants showed a drop of 20 points or more on the PCL-5, meeting criteria for clinically significant change</p> <p>At the end of the treatment, 8 (80%) participants were assessed as not having PTSD by an independent assessor on the PSS-I. The same eight patients met IAPT recovery criteria</p>	Participants spent a mean of 21.7 hrs over a mean period of 9.6 weeks on the app	<p>Therapists made a mean of 10.5 telephone calls during the course of treatment, which equated to a mean total telephone contact time of 3.2 h</p> <p>A mean of 20.7 emails 8 texts were sent to patients</p> <p>The total number of minutes therapists spent supporting patients in the course of the treatment was mean 4.1 h</p> <p>Indirect time spent reviewing case notes etc was comparable with face to face therapy</p>
Bisson (2022)	Spring	CBT-TF group:	CBT-TF group:	CBT-TF group	Not reported		

Study	Technology	PTSD specific measures: Change in CAPS-5, PCL-5 and PSS-I	Change in GAD-7	Change in WSAS	Rates of recovery and remission	Acceptability and usage	Therapist time
		<p>CAPS-5 scores decreased from a mean score of 35.6 at baseline to 13.0 at 16 weeks and 10.9 at 52 weeks</p> <p>GSH group: CAPS-5 scores decreased from a mean score of 34.6 at baseline to 13.1 at 16 weeks and 12.9 at 52 weeks</p>	<p>GAD-7 scores decreased from a mean of 13.4 at baseline to 5.3 at 16 weeks and 3.8 at 52 weeks</p> <p>GSH group: GAD-7 scores decreased from a mean of 13.9 at baseline to 5.6 at 16 weeks and 5.3 at 52 weeks</p>	<p>WSAS scores decreased from a mean of 20.9 at baseline to 10.4 at 16 weeks to 6.5 at 52 weeks</p> <p>GSH group: WSAS scores decreased from a mean of 21.1 at baseline to 8.9 at 16 weeks to 8 at 52 weeks</p>			

5.2.5 Social Anxiety Disorder

Three included technologies can be used for SAD (iCT-SAD, MindDistrict and SilverCloud). No evidence was identified for the use of MindDistrict or Silvercloud for social anxiety. Two studies relating to iCT-SAD were relevant to this review; one non-comparative study (Stott 2013) and one RCT (Clark 2022). Table 11 summarises these results.

The company provided some limited real world results from

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Table 11: Results for Social Anxiety Disorder

Study	Technology	LSAS	GAD-7	WSAS	Recovery and remission	Drop out/ app usage	Therapist time
Stott 2013	iCT-SAD	LSAS scores reduced significantly from 80 to 39.8 (p<0.001) over the course of the treatment (mean 13.7 weeks)	GAD-7 scores reduced significantly from 9.3 to 4.3 (p<0.01) over the course of the treatment	Not reported	Nine patients (82%) were classified as treatment responders (improvement of 31% on the LSAS) and 7 (64%) were in remission	No patients dropped out during treatment	Mean iCT-SAD therapist time spent supporting the patient was 3.87 hours compared to mean face to face therapist time of 19.14 hours
Clark 2022	iCT-SAD	See therapist time	No significant between group differences found with mean GAD-7 scores at baseline, post treatment and 12 month follow-up: iCT-SAD = 9.82, 3.75, 3.46 CT-SAD = 8.72, 2.48, 2.41	No significant between group differences found with mean WSAS scores at baseline, post treatment and 12 month follow-up: iCT-SAD = 3.45, 1.77, 1.43 CT-SAD = 2.92, 1.14, 1.04	84% of iCT participants lost their SAD diagnosis at 12 months follow-up compared with 87% in the CT group 67% met the IAPT recovery criteria in the iCT group compared to 75% in the CT group	2% (1/50) of patients in the digital therapy arm 0 patients in the face to face therapy arm	Post treatment, iCT patients had dropped 45.5 points on the LSAS after an average of 6.45 h contact with their therapist. In CT, 15.8 h of therapist contact were required to achieve the same drop on the LSAS. iCT is therefore associated with 2.45 times more symptom change per hour of therapist contact time.

6 Adverse events

A search of the MAUDE database and MHRA (field safety notices/device safety information) did not identify any adverse events or safety concerns relating to any of the included technologies. Two included studies listed safety as an outcome (Richards 2020 and Wilhelm 2020). Neither of these reported any adverse events. One specialist committee member noted that digital therapies would not be suitable for moderate or high-risk clients as digital therapy review involves much less detailed safety review compared with one – to – one guided self-help.

7 Evidence synthesis

Where the studies have focused on one specific diagnosis such as PTSD, SAD and BDD, the results are much clearer and may be more reliable. Each condition had 2 relevant studies and reported for the following technologies; PTSD –one iCT-PTSD and one Spring, SAD – both iCT-SAD and BDD – both Perspectives. The non-comparative studies showed that the digital therapies reduced anxiety levels on both general scales such as the GAD-7 but also disorder specific measures. Further, these reductions did persist up to 1-year post treatment albeit with slight increases reported compared to immediately post treatment. Those studies with waitlist control as a comparator showed that these improvements in anxiety symptoms was greater in those that used the technologies. One study reported no difference between the digital therapy (iCT-SAD) group and cognitive therapy group (Clark 2020) indicating that digital therapy can achieve outcomes at least as good as face to face therapy.

Remission rates were also reported for these three conditions. In those with BDD one non-comparative study showed 90% of participants were classed as having responded to treatment (>30% reduction in BDD score) whilst one comparative study showed on 52% were in full or partial remission. However, this was compared to only 8% for the waitlist comparator group. In those with PTSD reporting for the ICT-PTSD technology, one non-comparative study reported 80% (8/10) were classed as in remission. Studies reporting for SAD

showed in the non-comparative study 64% were in remission at end of treatment. However, in the comparative study, levels of remission were slightly higher in the comparative group (face to face cognitive therapy) compared to iCT-SAD users.

There are 13 included studies that focused on generalised anxiety reporting for either Beating the Blues or SilverCloud technologies. Nine of these were non-comparative, 1 compared between African American and white groups, 1 compared between African Americans and white groups and between intervention and comparator, 1 compared with 2 other treatments and 1 compared with a waitlist group. Eleven of these studies reported reduced levels of anxiety, as measured by the GAD-7, BAI and PROMIS-Anxiety, over the treatment sessions. Three studies reported reduction in WSAS scores over time and 2 reported reductions in the CORE-OM measure.

Six studies reported on remission and recovery. All showed reduced levels of 'caseness' or recovery increase following use of the guided technologies. However, Cavanagh 2011 (Beating the Blues) did not split the recovery rates by diagnosis. One study compared SilverCloud with GSH and PGT and another compared SilverCloud with a waitlist group (Richards 2020). Both found reliable recovery was higher in the Silvercloud group compared to the comparator groups.

Two studies looked at differences between African Americans and white participants in relation to anxiety measures and acceptability/usage of the guided technologies. African Americans showed a greater benefit from the Beating the Blues app in anxiety measures compared to usual care than white participants.

All studies that reported rates of drop out and amount of use of the technologies showed that there was little to no drop out when using the technologies. One study stated 89% of participants would recommend the app (Wilhelm, 2022). This suggests high levels of acceptability and ease of use across all patient groups. However, Jonassaint (2017) did find a slight

discrepancy between ethnic groups as white participants completed more sessions of BtB than African Americans in their study.

8 Interpretation of the clinical evidence

Reviewing the clinical evidence as a whole, it would appear that guided digital technologies do reduce anxiety symptoms (as measured by general and condition specific measures) across different anxiety disorders. In those that have a comparator group, the digital technologies create bigger reductions in anxiety symptoms, except in one study reporting results for SAD and iCT-SAD (Clark 2022). The evidence also suggests that the technologies are easy to use as they have high levels of usage and low levels of drop out across conditions, and tend to have comparable if not increased rates of remission and recovery following use, except again in one study reporting for SAD and iCT-SAD (Clark 2022)

The main limitation of the included evidence is that a large number of the populations reported within the studies are not fully aligned with the scope. There were no studies where participants had a clear DSM-V or ICD-10 diagnosis of GAD but had presented with, sometimes via self-referral methods, as having high levels of anxiety symptoms using the GAD-7 and/or depression symptoms on the PHQ-9. This does not constitute a diagnosis of either disorder and this is a major limitation of the included generalised anxiety studies as they cannot be wholly generalised to the IAPT pathway. Further, these studies grouped participants as those with anxiety and/or depression with results not split by either disorder/symptom group. It is therefore not known which participants showed a reduction in the GAD-7 score, those with anxiety symptoms, depression symptoms or both. Again, this makes the results hard to relate to the IAPT pathway.

There is a general lack of comparator groups within the included evidence and therefore it is hard to know whether the effects seen in these studies are typical or superior/inferior to standard practice or other technologies. Those that did have a comparator group generally used a 'Waitlist' comparator which is not within scope and therefore limits the applicability of this evidence.

There is also a lack of therapist or a guided element within the included research and, while for many studies it is indicated that there is a therapist guided element the details are not clearly reported and therapist time is only reported as an outcome in a small number of studies.

In terms of generalisability, the individual technologies have different information, use different methods to interact and apply to different conditions. The EAG considers therefore, it is not appropriate to consider evidence from one technology to be indicative of any clinical effectiveness with a different technology or to use existing data for one condition to infer generalisability to another condition. Many of the studies do not have comparators and do not report aspects such as therapist involvement sufficiently which further limits generalisability. An NIHR HTA report (Gega 2022) reported that to enable the appropriate analysis and meaningful interpretation of evidence syntheses, research studies need to describe in detail the comparators of digital interventions in accordance with existing frameworks for reporting complex interventions, including any support that participants have received in a waitlist or usual care and the EAG would agree with this.

The purpose of the EVA was not to compare technologies with each other, therefore where evidence is available for more than one technology for the same condition, no judgement can be made on which technology (if any) is better.

8.1 *Integration into the NHS*

The adoption of these technologies into the IAPT pathway would not require significant change as IAPT currently facilitates the use of digitally enabled therapies.

Several of the included studies were reporting from within an NHS IAPT setting and these were in relation to specific conditions; PTSD, SAD and BDD. In relation to generalised anxiety, study settings were a mix of NHS-

IAPT and non NHS/UK which makes these some of the included studies much less generalisable.

The main issues to consider when deciding whether to use any of the technologies would be the evidence available, specifically around place in the stepped pathway and therapist time required. If adopted, it is possible that use of digitally guided technologies could reduce the amount of therapist time needed for face to face sessions however this is not currently supported by the available evidence. For generalised anxiety disorder specifically, use of technologies should be weighed against the fact that the evidence available is related to generalised anxiety or symptoms of anxiety and depression.

Limited evidence suggests that digitally enabled therapies are acceptable to patients and therefore adoption of these technologies into IAPT may give patients more control over their treatment.

8.2 Ongoing studies

Searches identified a total of 6 potentially relevant ongoing studies with detailed summaries reported in Table 12.

Table 12: Ongoing Studies

Study	Technology	Condition	Design	EAG Comment
NCT03271645 Internet-delivered Interventions for Stress, Anxiety and Depression in the Workplace	SilverCloud	Stress, anxiety and depression	Open label, non-randomised trial	<ul style="list-style-type: none"> Study has been withdrawn for logistic reasons. Study setting was the workplace
NCT04622930 Waitlist-Control Trial of Smartphone CBT for Social Anxiety Disorder (SAD)	Koa Health Perspectives	SAD	Randomised, open-label, parallel assignment	
NCT04034693 Waitlist-Control Trial of Smartphone CBT for Body Dysmorphic Disorder (BDD)	Koa Health Perspectives	BDD	Randomised crossover assignment	Information from the company suggests this study has been completed and results reported in Whilhelm 2022.

Study	Technology	Condition	Design	EAG Comment
ISRCTN12462559 A study of the implementation of Internet-based Cognitive Therapy for Post-Traumatic Stress Disorder within NHS Improving Access to Psychological Therapies (IAPT) services	iCT-PTSD	PTSD	Interventional multi-centre implementation study	
ISRCTN16806208 A randomised controlled Trial of therapist-assisted Online Psychological therapies for Post-Traumatic Stress Disorder	iCT-PTSD	PTSD	Randomised Controlled Trial	Listed as ongoing, however company has provided confidential results for consideration and are reported in section 5.2.4 and section 10
ISRCTN72832736 A study of the implementation of internet-based cognitive therapy for Social Anxiety Disorder within NHS Improving Access to Psychological Therapies (IAPT) services (Overcome-SAD)	iCT-SAD	SAD	Interventional multicentre non-randomized implementation study	Listed as ongoing, however company has provided confidential results for consideration and are discussed in section 5.2.5 and section 10.

9 Economic evidence

9.1 Key economic evidence for anxiety in adults

A previous early value assessment report has summarised economic evaluations of guided digital therapies for treatment of symptoms of anxiety for both adults and children (GID-MT580). Therefore, any searching outside the topic scope was limited to information on different modelling approaches. In order to consider the optimum modelling approach, a rapid review was carried out to identify key economic evaluations that used a modelling approach for anxiety in adults. We identified 8 published economic modelling studies for any interventions in the management of anxiety (not limited to digital interventions) (You 2022, Baumann 2020, Stiles 2019, Jankovic 2022, Mavranezouli 2015, Najafzadeh 2017, Gega 2022, Health Quality Ontario 2019), including 2 HTA reports (Gega 2022 (NIHR); Health Quality Ontario 2019) These studies were conducted in the UK (n=3), Australia, Germany, US, Canada and Hong Kong.

In addition, the EAG also considered the economic modelling used in the following clinical guidelines:

- CG159 Social anxiety disorder: recognition, assessment and treatment
- CG113 Generalised anxiety disorder and panic disorder in adults: management
- NG222 Depression in adults: treatment and management (in particular the model for treating new episodes of depression).

The economic models varied in terms of the model type and structure. Both decision tree and markov models were seen, as well as modelling that combined both methods, and one discrete event simulation (Najafzadeh 2017). The time horizon varied significantly, from 7 months, 3-5 years to lifetime. Perspectives undertaken were either societal or health system. The acceptance and adherence rate of internet-based CBT was only explicitly incorporated into the decision model by You et al. Many of the models were non-specific to a particular anxiety disorder, and the majority included only one intervention per arm, without referral to an additional intervention, other than medication.

The NIHR HTA report (Gega 2022) undertook a Markov model with 3-month cycles (adapted from Jankovic 2021) over a lifetime horizon to evaluate the cost-effectiveness of digital interventions in GAD. Health states included in the model were: no anxiety, mild, moderate or severe anxiety. However, Health Quality Ontario (2019), considering digital interventions for anxiety, conducted a short-term simplified decision tree model of 12-month time horizon, and subsequently combined this with a Markov microsimulation model.

This approach is more in line with the economic modelling described in NICE clinical and national guidelines for SAD and depression which use a decision tree for short term modelling of the pathway, and links this with a longer-term Markov model to consider the movement between no anxiety and different anxiety levels over a number of years. The EAG consider that this approach had a number of benefits, although most were not implemented within existing models due to lack of data:

- More explicit pathway during early stage of the model
- Ability to model treatment switching during the early stage of the model
- Ability to model changes in effectiveness due to treatment position in pathway (e.g. effectiveness might be different for group therapy delivered as first intervention, or group therapy after digitally enabled therapy)
- Ability to model combined therapies e.g. medication together with therapeutic approach.

A short narrative summary of the key findings and limitations of modelling reported by the two HTA reports and two NICE guidelines for anxiety is presented in Table 13. These report evidence for generic categories of interventions rather than specific technologies, and the Health Quality Ontario (2019) report is across all anxiety disorders. They all consider digital interventions as part of their evaluation. Health Quality Ontario (2019) is the only one that considers a stepped pathway or any treatment switching, and this is reported as a secondary exploratory analysis. Although others models have extended time horizons, up to a lifetime, they are restricted to a single intervention delivered once per pathway arm (with the exception of medication in some cases).

The NIHR HTA report (Gega 2022) considered 76 economic evaluations and found that they did not capture all relevant comparators or long-term impacts, and that the complex nature of the interventions presented significant challenges. In general, the review (work package 1) found that digital interventions were likely to be cost effective if compared to no intervention or non-therapeutic interventions. They reported that this was less clear where the comparator was face to face therapy or printed manuals.

A network meta-analysis of RCTs (work package 2) found that uncertainty was too great to draw conclusions on digital interventions compared to no intervention, non-therapeutic active control or group therapy.

Modelling (work package 3) found that digital interventions (for GAD) had lower NMB than medication or group therapy, but greater NMB than non-

therapeutic interventions or no intervention. They found that this was driven by clinical outcomes rather than intervention costs. Value of Information analysis suggested that treatment effect had the greatest value, at £12.9 Billion.

Table 13: Summary of HTA and NICE Guidance

	Interventions and population	Modelling approach	Key findings	Key limitations
Gega 2022 (NIHR)	GAD Supported and unsupported therapy, face to face individual and group therapy, medication and usual care	Markov model, lifetime horizon (Jankovic 2022)	Effectiveness results were inconclusive due to uncertainty about appropriate comparators. Digital interventions were likely to be cost effective compared to no intervention, or non-therapeutic controls. This was less clear compared to face to face therapy or printed manuals. Cost effectiveness was driven by how effective technologies were, rather than how much they cost. Clinical effectiveness was also a key driver of uncertainty.	Pooled evidence for similar interventions Single treatment only per pathway Likely to be heterogeneity in patient pathway
Ontario HTA	Usual care vs interventions including guided digital CBT and face to face CBT. Depression and anxiety (modelled separately)	Decision tree (12 months) and Markov. 1 week cycle, lifetime horizon	Guided digital CBT was likely to be good value for money compared to waiting list, but effectiveness was uncertain compared to face to face or group CBT. Exploratory analysis of digitally enabled therapies in a stepped care model appeared to present good value for money compared to usual care (including medication and GP follow up)	Pooled evidence for similar interventions Primary modelling was for a single intervention during pathway. Secondary modelling considered a stepped pathway
CG113	GAD Considers low and high intensity psychological interventions. Modelling is for	Cost analysis: decision tree (35 weeks) for low intensity intervention	Digitally delivered CBT was found to be cost effective compared to a waitlist. It was noted that this does not represent routine practice in the NHS for GAD.	Single treatment only per pathway Waitlist comparators in clinical studies Study population with mixed anxiety disorders

	Interventions and population	Modelling approach	Key findings	Key limitations
	low intensity psychological interventions compared to waiting list.	s		Study reporting: use of continuous outcomes and inconsistent definitions of response and remission
CG159	SAD Compares psychological and pharmacological interventions	Hybrid model, decision tree (12 weeks) and Markov (5 years) (Mavranzev et al 2015)	CT (Clark & Wells) was most cost effective due to higher effectiveness and lower risk of relapse compared to medication. For interventions ranked by NMB, Internet based self help ranked 7 th (with support) and 20 th (without support)	Single treatment only per pathway Limited data available for recovery Lack of robust evidence on the relative risk of relapse

9.2 **Key economic evidence for Digitally enabled therapies delivered with support, for anxiety in adults**

The EAG conducted a combined literature search for both clinical and economic evidence (see Section 4.1). Additional economic studies were identified from the references of a similar report: Guided dCBT for CYP with mild to moderate anxiety or low mood: an Early Value Assessment (MT580). The economic searches from this report were updated to identify any literature published since August 2022. The economic literature searches returned a total of 53 records. Details of the EAG economic searches are provided in Appendix A.

Four studies were identified that were for the intervention technologies included in the scope (McCrone 2004, Richards 2020, Bisson 2022, [REDACTED]), however only one reports a comparator that is within the scope. All are within trial analyses, and are grouped by indication and summarised in Table 14. The digitally enabled therapies that were evaluated were cost-effective when compared to usual care, waitlist or a non-IAPT comparator, but were less conclusive compared to face to face therapy.

Generalised anxiety, and non-specified anxiety disorders

Two studies (McCrone 2004, Richards 2020) looked at mixed populations of people with depression, mixed depression and anxiety or anxiety disorders. Neither presented economic results for patients with anxiety alone or with mixed depression and anxiety as sub-group analysis. Both of these found the intervention to be cost-effective compared to either waiting list or usual care. Neither reported cost-effectiveness compared to interventions at a similar stage of the IAPT pathway.

McCrone et al (2004) report within trial cost effectiveness of Beating the Blues in addition to usual care compared to usual care alone for people with a diagnosis of depression (39%), mixed depression and anxiety (49%) or anxiety disorders (12%). The primary outcomes for clinical reporting and for cost-effectiveness are based on outcome measures for depression, and there is no sub group analysis comparing a population with a primary descriptor of anxiety. The paper reports a 99% probability of cost effectiveness, compared to usual care alone, at a £15,000 WTP threshold. This is based on 8 months follow up post randomization, and using depression free days to estimate QALYs. This is unlikely to be the most appropriate outcome for people with anxiety. The use of health care resources is listed for both study arms, however there is no clear description of usual care, and it is unclear if the healthcare resource includes interventions for anxiety or depression. The provision of usual care alongside the digitally enabled therapy is likely to impact effectiveness compared to the use of digitally enabled therapy on its own.

Richards et al (2020) report within trial cost effectiveness of SilverCloud with waiting list for people who are newly referred to IAPT and meet the “caseness” threshold for either GAD-7 or PHQ-9 with 290 people having a diagnosis at baseline (52% major depressive disorder, 64% anxiety, including mixed depression and anxiety). The primary outcomes include GAD-7 and PHQ-9 and cost effectiveness is calculated using QALYs collected from EQ-5D-5L with a cross walk, as recommended in the NICE reference case. The waiting list comparator is not within scope, and will result in a greater incremental effectiveness than comparison to other step 2 interventions. Data

was only collected for 8 weeks in the waiting list group, with longer term results based on extrapolation for the comparator. Data for SilverCloud was collected for 1 year. The authors reported a 47% probability of being cost effective at 8 weeks, with a WTP of £30,000, or a 91% probability of being cost effective at 1 year.

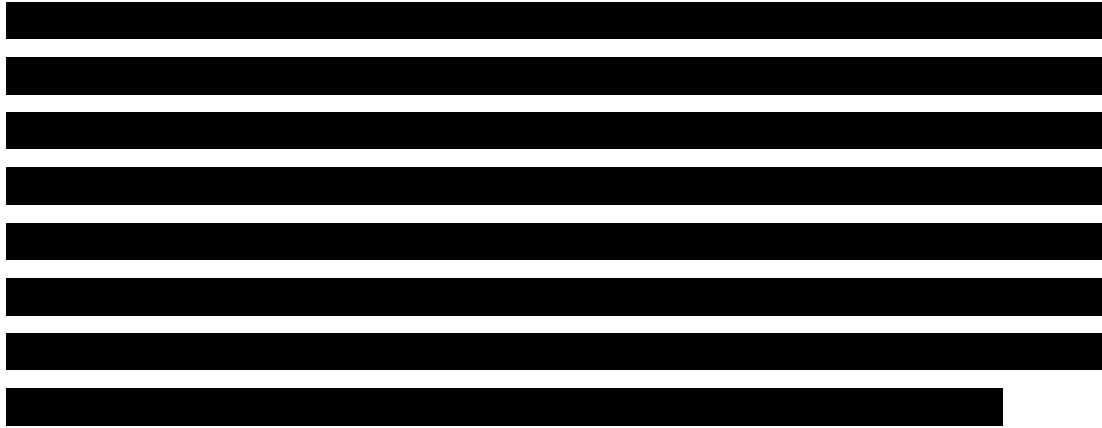
Post Traumatic Stress Disorder

Bisson et al (2022) report within trial cost effectiveness outcomes for an RCT comparing Spring internet delivered trauma focused CBT (CBT-TF) with face to face delivery of similar content. The population was adults with a primary diagnosis of mild to moderate PTSD. The study was a non-inferiority study, and the clinical findings were that the internet delivered CBT-TF was acceptable and non-inferior at 16 weeks, while being inconclusive in favour of face to face CBT at 52 weeks. The study collected EQ-5D-5L data, cross walked to give utilities (NICE reference case), resulting in a non-significant decrease of 0.04 QALYs at 1 year for the internet CBT-TF when compared to face to face delivery. Therefore, although the internet delivery was significantly cheaper than face to face (£277 vs £729 for the two interventions) it resulted in poorer outcomes. Additional unpublished submissions reported that there was a

[REDACTED]

[REDACTED] The authors suggest that the use of guided self help is appropriate due to the reduction in therapist time leading to an increased availability of therapy.


It was noted that all therapy was delivered by experienced psychological therapists working in high intensity IAPT services or psychological services, experience of delivering CBT-TF for PTSD and additional training in the interventions. The company explained that at present in normal practice 50% of therapists delivering Spring are band 5, and not fully accredited face to face cognitive behavioral therapists, and this is expected to increase to 100%. It is possible that this change in delivery could impact on real world effectiveness seen compared to that reported in the paper.



The details of the clinical studies are reported separately in Table 5 to Table 11. Key outcomes from economic analysis are reported in the Table 14, however in most cases there are large amounts of data available either within the paper or as supplementary information that is not included in these tables.

Table 14: Economic Studies

Study name and location	Study Design, intervention(s) and comparator	Economic approach, time horizon	Selected Health Outcomes	Costs	Cost effectiveness	EAG comments
SilverCloud						
Richards 2020. UK <i>(See also tables 5 and 9)</i>	<p>Design: RCT</p> <p>Participants: People with depression, anxiety, and comorbid anxiety and depression</p> <p>Intervention: SilverCloud 8 week, total follow up 1 year (n=241)</p> <p>Comparator: waitlist control limited to 8 week follow up (n=120)</p>	<p>Within trial ITT analysis at 8 weeks.</p> <p>Use of extrapolation to model comparator, allowing comparative analysis of intervention data at 1 year.</p> <p>NHS perspective</p> <p>Complete case reported in addition</p>	<p>GAD-7 mean (SD)</p> <p>Intervention:</p> <p>0 week: 12.66 (4.69)</p> <p>8 week: 8.2 (5.31)</p> <p>1 year: 6.08 (4.81)</p> <p>Waitlist:</p> <p>0 week:: 12.54 (4.18)</p> <p>8 weeks 10.79 (5.12)</p> <p>EQ-5D-5L cross walk mean (SE)</p> <p>Intervention:</p> <p>0 week: 0.657 (0.013)</p> <p>8 week: 0.724 (0.012)</p> <p>1 year: 0.7622 (0.013)</p> <p>Waitlist:</p> <p>0 week: 0.645 (0.020)</p> <p>8 weeks 0.676 (0.024)</p>	<p>Mean cost(SE)</p> <p>Intervention:</p> <p>0 week: £122.91 (£18.24)</p>	<p>For WTP of £30,000/QALY</p> <p>At 8-weeks, 46.6% probability cost-effective</p> <p>At 1 year 91.2% probability cost effective</p>	<p>Limited direct applicability due to comparator choice and heterogenous population.</p> <p>There is no sub-group reporting of patients with a diagnosis of anxiety.</p> <p>Use of waitlist control will result in higher incremental effectiveness than if the comparator were group CBT. This may result in a higher probability of cost effectiveness, as identified by study authors.</p>
Spring						
Bisson	Design: RCT, non-	Within trial	ITT CAPS-5 Mean (SD)	Mean cost (95%	Incremental cost: -£572.55	This paper is within

Study name and location	Study Design, intervention(s) and comparator	Economic approach, time horizon	Selected Health Outcomes	Costs	Cost effectiveness	EAG comments
2022 UK (see also tables 5 and 10)	<p>inferiority</p> <p>Participants: Adults with primary diagnosis of mild to moderate PTSD (n=196)</p> <p>Intervention: Spring internet delivered CBT-TF (and 4 x 30 min Face to face plus 4 phone calls; n=97)</p> <p>Comparator: Face to Face individual CBT-TF (12 x 60-90 min; n=99)</p>	<p>analysis NHS perspective, 1 year time horizon.</p>	<p>Intervention: 0 weeks: 34.6 (6.8) 1 year: 12.9 (11.6)</p> <p>Comparator: 0 weeks: 35.6 (6.7) 1 year: 10.9 (11.1)</p> <p>EQ-5D-5L (utilities) mean (SD) Intervention: 0 weeks: 0.5 (0.3) 1 year: 0.7 (0.3)</p> <p>Comparator: 0 weeks: 0.6 (0.2) 1 year: 0.8 (0.2)</p>	<p>CI)</p> <p>Intervention: £277 (£253 to £301) Comparator: £729 (£671 to £788) P<0.001</p> <p>Total NHS Cost (95% CI) Intervention: £1,325 (£942 to £1,709) Comparator: £1,898 (1,565 to £2,231)</p>	<p>(-£1080.14 to -£64.96) Incremental QALYs -0.04 (-0.10 to 0.01) Incremental NMB(£) at £30kQALY -£460.41 (-£2,143.27 to £1,222.45)</p> 	<p>scope for both the intervention, comparator and population.</p> <p>Therapy was carried out experienced psychological therapists, however in the submission the intervention is described as being delivered by trained therapists at band 4 and 5.</p> <p>Additional information was provided in the form of an accepted HTA report chapter, this is marked AiC</p>
Beating the blues						
<p>McCrone 2004. UK Study reported in Proudfoot 2004</p>	<p>Design: RCT</p> <p>Participants: Adults with depression, anxiety, or mixed depression and anxiety</p> <p>Intervention:</p>	<p>Within trial analysis. 8 month time horizon. Perspective not clearly stated, costs are for healthcare and for loss of</p>		<p>Total NHS cost (1999-2000) Mean (SD) Intervention: 6 months pre: £203 (£262) 8 months post: £397 (£589) Comparator:</p>	<p>Incremental cost £40 at 8 months (excluding employment) Authors report over 99% change of cost effectiveness at a WTP threshold of £15,000</p>	<p>Limited direct applicability due to comparator choice and heterogenous population.</p> <p>There is no sub-group reporting of patients with a diagnosis of anxiety.</p> <p>Quality of life is not</p>

Study name and location	Study Design, intervention(s) and comparator	Economic approach, time horizon	Selected Health Outcomes	Costs	Cost effectiveness	EAG comments
	<p>Beating the Blues, iCBT (n=146)</p> <p>Comparator: Usual care including GP, referral to counselling, practice nurse, or mental health professional, and treatment of physical conditions (n=128)</p>	productivity.		<p>6 months pre: £236 (£404)</p> <p>8 months post: £357 (£575)</p>		<p>directly measured, effectiveness is given per unit of the Beck Depression Inventory, and depression free days are used to estimate QALYs.</p>
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	<p>Limited direct applicability. The comparator is also not a routinely offered treatment for PTSD and is therefore not within scope.</p> <p>There are some difficulties in interpreting the results due to pre-publication summaries without the same level of detail as a full paper. Also, the results are presented in blinded format.</p>

Study name and location	Study Design, intervention(s) and comparator	Economic approach, time horizon	Selected Health Outcomes	Costs	Cost effectiveness	EAG comments
						The EAG were unable to verify ICER calculations from the results presented.

9.3 Conceptual modelling

Existing models have a variety of structures and there is not one single version that is widely accepted. There are however a number of factors that would ideally be included in any model:

- The long-term nature of anxiety disorders
- The possibility that recovery may be followed by relapse or recurrence
- The impact that previous or adjunct treatment may have on the efficacy outcomes (this could be IAPT interventions, medications or others)
- Healthcare and personal social service costs incurred other than direct interventions for anxiety, including those outside the IAPT pathway
- Align with IAPT pathways and definitions, where used for decision making in the IAPT pathway.

Ideally clinical data used in the inputs will:

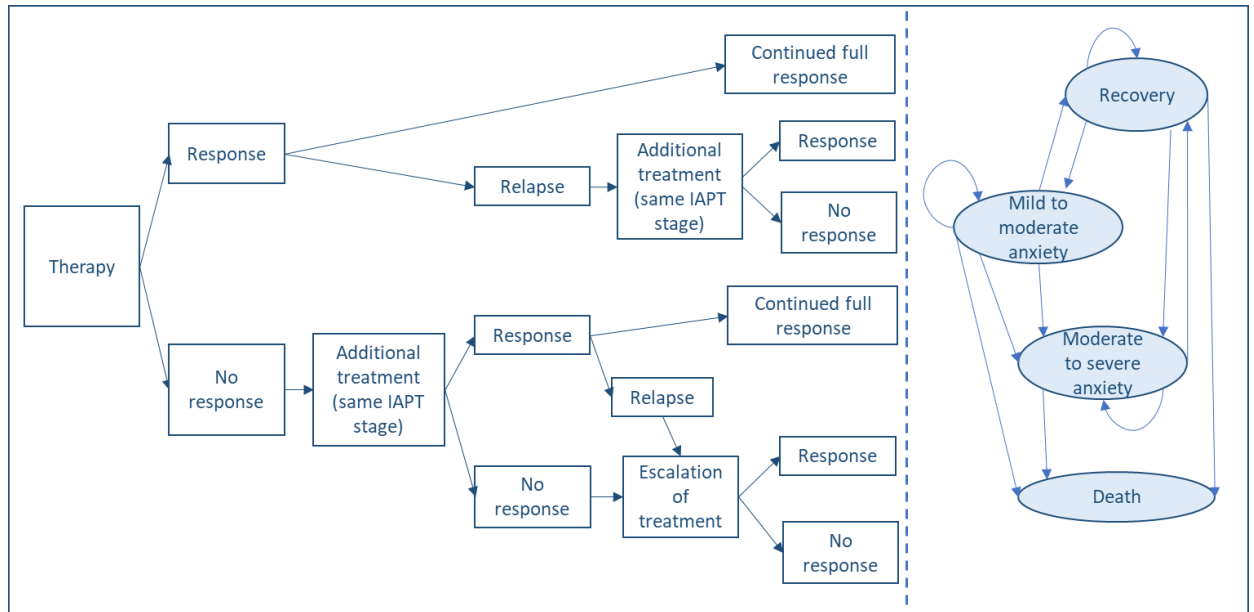
- be for the anxiety descriptor that is under consideration
- use interventions that are delivered in the same way as described by IAPT (e.g therapist guiding time included)
- be reported using IAPT defined terms, such as caseness thresholds, recovery and reliable recovery
- use of longer term data to demonstrate continued recovery or relapse, with reporting at multiple time points (short and longer-term)
- report ITT results, or according to IAPT manual methods, so that those who drop out, or are missing from the final results are assumed not to experience recovery.
- Include comparators that reflect the most appropriate current treatment, or mix of treatments, usually on the IAPT pathway. These should also be reported fully in any clinical studies.

A potential solution to capture the stepped IAPT pathway is to use a decision tree for a fixed duration, and follow this with a markov model over a longer time horizon. This approach has been demonstrated in previous models (You 2022, Mavranouzouli 2015, Health Quality Ontario 2019). Although most previous models have not attempted to include subsequent treatments (either repeating the first intervention, or switching to an alternative approach), the EAG feel this could be used to model one or two subsequent treatments on the pathway. One other model that was identified considered a stepped pathway (Stiles 2019), limiting the time horizon to 12 months and using a decision tree only.

Having captured the initial costs and effectiveness of initial steps on the pathway, the Markov component would consider longer term impacts of future relapses or changes in health state of each intervention, using state based costs, transitions and utilities.

Different modelling approaches could be used to satisfy these requirements, but an example of how such a model may appear is given below. Any new model is unlikely to require the same pathway or approach for all anxiety disorders, as there will be differences in the likelihood of a second or third intervention at the same IAPT stage, or immediate escalation. Preparation of a model for a specific disorder would require further consultation with clinical experts and incorporation of IAPT recommendations specific to that population and pathway.

Figure 2: Theoretical hybrid model for anxiety



Modelling used by EAG for this report

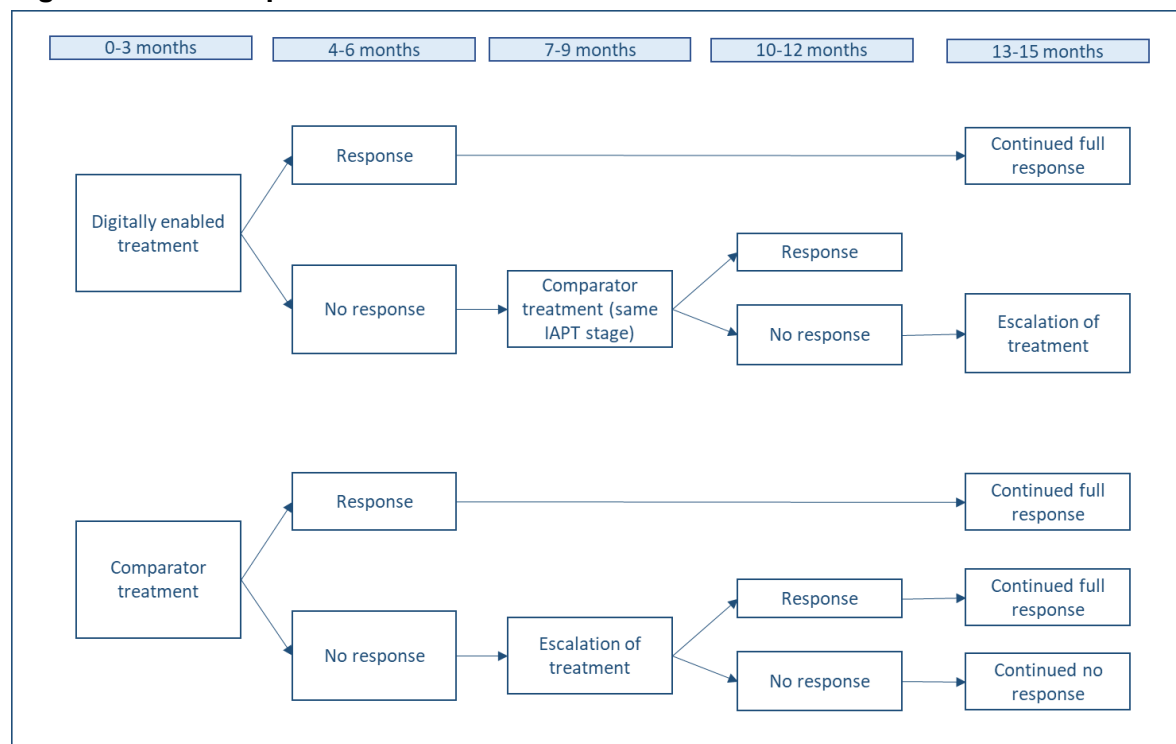
The model used is a 15-month cost effectiveness model using a decision tree structure and taking an NHS and personal social services perspective. The time horizon has been chosen as a short duration that allows progression from the initial intervention, to a second intervention at the same IAPT stage, and further escalation if needed, given the assumptions listed below. The model structure is limited by the amount and type of data available, and numerous assumptions have been made in order to populate it. For these reasons it should be seen as an initial exploration of the economic impact of the technologies, and extreme caution taken in interpreting the results.

The model compares digitally enabled therapy with the alternative therapy that would normally be offered at that stage (i.e. group CBT for stage 2 or individual CBT for stage 3). It assumes that those patients treated with digitally enabled technology either respond, and need no further treatment within the time horizon, or do not respond and are offered the comparator treatment at the same stage. If they do not respond to this then treatment is escalated. The model does not include outcomes from this third treatment due to the short time horizon. The structure is intended to capture the impact of both successful treatments using digitally enabled therapies, and the impact of offering additional treatments to those patients who do not respond.

The model is split into three-month periods, with one intervention occurring within a three-month period, followed by a three-month period of assessment or waiting list during which time there is no intervention, before any additional intervention is provided. Utility values remain static during the intervention period, but then increase if there is a response.

Net benefit was reported at a willingness to pay threshold of £20,000 per QALY and confidence intervals were calculated using probabilistic sensitivity analysis using 10,000 simulations.

Figure 3: EAG simple decision tree model



Assumptions and limitations

A number of simplifications were required to allow the model to be built using available data, and to approximate a number of different pathways. These simplifications may not completely reflect actual patient pathways or clinical realities, and this is discussed in table 15.

Table 15: Assumptions and limitations of the simple model

Assumption	Discussion
Patients are grouped into response and no response	In reality this will be partial responses, some of which will also require additional treatment.

Assumption	Discussion
Patients treated with stage 2 interventions comprise 50% mild and 50% moderate anxiety	The IAPT description is for people with mild to moderate anxiety. This assumption is used to estimate the utility values for this group, which are available for mild, moderate and severe anxiety.
Patients treated with stage 3 interventions comprise 50% moderate and 50% severe anxiety	The IAPT description is for people with moderate to severe anxiety. This assumption is used to estimate the utility values for this group, as in the comment above.
Patients receiving comparator treatments are expected to receive the same benefits regardless of having prior digitally enabled therapies or not	We cannot know the impact of this assumption. It is possible that prior exposure to digitally enabled therapies may make patients more receptive to subsequent treatment. It is also possible that those patients who did not respond to digitally enabled therapies are a subgroup who are also less likely to respond to alternative treatments.
The proportion and impact of patients with other previous or adjunctive treatments is assumed to be the same in each arm.	We know that many patients receive multiple different treatments, and that these include medicines that are prescribed outside the IAPT pathway. There is not sufficient information to group patients according to previous or adjunctive treatment, however it is likely to have an impact on the outcomes experienced.
Study data for interventions reflects real world sufficiently to use the IAPT database as a comparator	Study data may be expected to be somewhat more positive than real world data if patients are engaged with the study having consented, protocols may be more rigorously adhered to and more data collected. Only one intervention had a comparator that was appropriate for modelling, and therefore we have used IAPT data due to the large numbers and availability. This may exaggerate the impact of the intervention. The IAPT database also has limitations, which are discussed in the clinical inputs section
Time durations between treatments are fixed	It is assumed that the initial treatment lasts for 3 months, and if it is not successful then another treatment is offered following a 3 month wait or assessment period.
Treatment response has a duration of at least 1 year	Those people who respond to treatment are assumed to remain at that response level for the remainder of the model. There is no modelling of relapses.
Recovery rates are applicable across different descriptors	For all interventions that can be used for different anxiety descriptors, the recovery rate is obtained from studies that are for a population with mixed anxiety descriptors, and in most cases also depression descriptors (with or without anxiety).
No spontaneous recovery	The model does not allow for patients whose condition may improve without intervention.
Interventions are assumed to be delivered over 3 months	Actual therapist input is based on more detailed data, however for the decision tree process a three month period is assumed, which is used to calculate utilities. There is a 3 month assessment / waiting period before a further intervention is delivered
Utilities change at the end of	In reality utilities may change throughout the intervention

Assumption	Discussion
the intervention period	period, and the modelling is a simplification.
No costs other than those of delivering IAPT interventions are included	Patients who do not experience improved symptoms following the modelled interventions may seek other healthcare resources such as GP appointments, or potentially may deteriorate further and require more intensive interventions.
No costs are included for hardware to support the intervention	It is assumed that services have sufficient internet and computing capability and patients would use existing personal devices and internet connections. There may be situations where devices are provided to enable participation for patients, however this is unlikely to be common practice in the NHS. Inclusion would be unlikely to change any of the report conclusions.

Main clinical parameters

Effectiveness in previous models is either shown by movement between recovery / non-recovery, (which would be defined using the GAD-7 threshold) or by group patients into mild, moderate and severe anxiety states, for which GAD-7 thresholds of 5,10 and 15 are widely accepted. Both have been used in previous models, and lend themselves somewhat to decision tree and Markov model structures respectively (but not exclusively). The EAG has used the recovery / non-recovery approach within the model. Reliable recovery could also be used, and is reported in the IAPT database and some of the clinical studies, but would have reduced the number of technologies with evidence. In designing future studies and modelling, use of reliable recovery may be more robust, however additional clinical advice could be sought for the relevant indication.

Effectiveness for the digitally enabled therapies has been taken from available clinical studies, which share a number of serious limitations.

Many of the trials group patients with anxiety descriptors and depression descriptors together in the results, and also group sub-descriptors of anxiety together. The information in the IAPT database indicates that responses to one therapy type for patients with different descriptors may not be equivalent.

The majority of papers in the clinical evidence use mean cohort score at two time points as their primary outcome, or they may use the mean change per patient between two time points. Both of these are problematic for economic

modelling, as we do not have information on the distribution within the trial population in order to calculate progression to other treatments or appropriate utilities.

The studies used for individual technologies are presented in Table 14, and are also presented in more detail in the clinical evidence section.

Use of IAPT database as a comparator

Only one of the economic analysis papers has an appropriate comparator for the scope of this report. Therefore, the IAPT database has been used as a large source of real-world evidence.

There are limitations in using the IAPT database for this purpose including:

- Studies carried out under trial conditions may experience higher response rates than those reported in real world data, due to strict inclusion criteria, more complete reporting and higher motivation for both staff and participants. As digitally enabled therapies are modelled using trial data, this may increase the resultant cost-effectiveness.
- IAPT data requires two datapoints to be able to report recovery, and therefore patients who don't engage for a first or second appointment are not included in the recovery data. Trial participants will be included in an intention to treat analysis even if they do not engage with the therapy, however they have to have already engaged at some level to have consented to participate. The net effect of this is unknown.
- CBT can be delivered in a group or individual setting; however, these are grouped together within the IAPT database. These have different cost implications and may be delivered within different IAPT stages.

The EAG model is based on supplementary IAPT data that allows us to model a stepped pathway including recovery rates for step 2 and step 3 treatments, but analyses data in a slightly different way.

The main IAPT database and report looks at complete episodes of care and considers changes from the initial assessment to the final appointment. This may involve more than one therapy, and these may be delivered at one or more IAPT steps.

The IAPT data used for the EAG base case analysis breaks down recovery results by therapy type. This data considers only instances within an overall episode of care where there were at least two sessions coded as the same therapy type. This means that the initial assessment is not captured and this may have a therapeutic effect prior to the start of the first recorded therapy session. It is likely that intervention trial data will include this initial assessment at the start of the trial, and this may result in higher clinical effectiveness being shown for the trial data than within the IAPT secondary analysis.

We have included an additional scenario that considers the use of overall recovery rates from the main IAPT database. It should be noted that there are also very significant limitations of this approach. The data is presented for a complete episode, and the model uses the same clinical effectiveness for each treatment iteration. This scenario is an exploration of possible impact, and should not be taken as a final result.

Table 16: Main Clinical Parameters

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
Recovery rate, digitally enabled therapies				
<i>Beating the blues</i>	0.5	B(113, 113)	Cavanagh 2011	Heterogenous population. Intervention was not guided. Overall recovery reported as 50%, however this number may include participants who were not at caseness at baseline
<i>Cerina</i>	n/a		Cerina Short Report	No data available on recovery rate. Unpublished data made available on a small pilot study showing mean GAD-7 scores before and after, completed by 20 out of 43 participants. Change from 10.2 to 9.2
<i>iCT-PTSD</i>	█	█	Company submission, unpublished data	█ Authors note that the recovery criteria require a reduction below the clinical threshold for both PTSD and depression symptoms, and that those who drop out of the study are assume not to have recovered.
<i>iCT-SAD</i>	0.67	B(33, 16)	Clarks et al., 2022	All participants have a diagnosis of SAD. Intervention was guided. IAPT recovery at 12 months, patients who have moved from caseness and below clinical threshold for both SAD (SPIN score) and PHQ-9. Missing data assumed non-recovered
<i>Iona Mind</i>	n/a			There is no available data for this product.
<i>MindDistrict</i>	0.72	B(27, 0.03)	Manufacturer submission	Heterogenous population. Guiding unknown Manufacturer submitted 72% recovery rate based on data from two IAPT providers. This includes all use of MindDistrict supported modules and for all users of the platform. There is no additional data to allow EAG critique. For these reasons, this should be treated with additional caution.
<i>Perspectives</i>	0.516	B(16, 15)	Wilhelm et al., 2022	All participants had a primary diagnosis of BDD. Intervention was guided. This is based on an assessment at 12 weeks of full or partial remission in those who completed the follow up assessment: Perspectives: 52% (16/31) from total of 40 randomised Waitlist: 8% (3/37) from total of 40 randomised This is not an IAPT definition, and we cannot be certain how many would fulfil the

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
				IAPT criteria for recovery, therefore should be treated with additional caution.
<i>Resony</i>	n/a			There is no evidence available that would allow us to complete the model for Resony.
<i>SilverCloud(all)</i>	0.464	B(90, 104)	Richards et al., 2020 (recovery rate at 8 weeks, reliable is available)	Richards: Heterogenous population. Intervention was guided. At 8-week follow-up 46.4% (90/194) of the intervention arm relative to 16.7% (15/90) control-arm participants recovered. Amongst 3-month M.I.N.I. interview completers (total n = 179) 50% (24/48) with anxiety, and 46% (30/65) with comorbid depression and anxiety diagnoses, did not meet diagnostic criteria anymore at 3-months. Alternative, Duffy: N=100 participants had full data at all time points. 99 participants were above clinical caseness threshold at baseline; 22 (22%) had achieved recovery by iCBT exit and 20 (20%) had achieved reliable recovery; 33 were in recovery at point of service exit all of which reliably recovered.
<i>Spring (PTSD)</i>	0.818	B(63, 14)	Bisson et al., 2021 (recovery rate, reliable not available)	All participants had diagnosis of PTSD. Intervention was guided. At 16 weeks, 14 of 77 participants (18%) using iCBT were still classed as PTSD at end, comparator was 12 out of 83 participants (15%). For an ITT approach that assumed no recovery for those who are lost to follow up, this would be 35% (34/97) for intervention and 28% (28/99) for comparator).
<i>Wysa</i>	n/a			There is no evidence available that would allow us to complete the model for wysa.
Recovery rate, IAPT pathway				
<i>IAPT Step 2, GAD</i>	0.511	B(24188, 23157)	IAPT database 2021-2	Weighted recovery rate of each Step 2 interventions for GAD
<i>IAPT Step 2, other</i>	0.396	B(6233, 9493)	IAPT database 2021-2	Weighted recovery rate of each Step 2 interventions
<i>IAPT Step 3, PTSD</i>	0.131	B(2560, 16928)	IAPT database 2021-2	Recovery rate of IAPT CBT for PTSD

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
<i>IAPT Step 3, Social Phobia (SAD)</i>	0.375	B(3903, 6517)	IAPT database 2021-2	Recovery rate of IAPT CBT for Social Phobia
<i>IAPT Step 3, BDD</i>	0.482	B(104,112)	IAPT database 2021-2	Recovery rate of IAPT CBT for BDD (note that the number in database is low)

Resource identification, measurement and valuation of expected key cost drivers

Table 17: Key Cost Parameters

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
dCBT licence cost (per user)				
<i>Beating the blues</i>	████	████	Company	<p>Costs are based on the company submissions in each case, using pricing based on an assumption of 1,000 licences for those that have a volume-based pricing structure, with additional assumptions due to different price structures between devices.</p> <p>Some products are not currently provided commercially, therefore costs are estimated only.</p>
<i>Cerina</i>	████	████	Company	
<i>iCT-PTSD</i>	████	████	Company	
<i>iCT-SAD</i>	████	████	Company	
<i>Iona Mind</i>			Not commercialised in UK	
<i>MindDistrict</i>	████	████	Company	
<i>Perspectives</i>	████	████	Company	
<i>Resony</i>	████	████	Company	
<i>SilverCloud</i>	£49.90	U(40, 50)	Company	
<i>Spring</i>	£40.00	U(40, 50)	Assumption	
<i>Wysa</i>	████	████	Company	

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
Therapist cost calculations				
Therapist unit costs in dCBT (per hour)				
Psychological wellbeing practitioner	£38		PSSRU (2021)	Mean of band 4 (£35) and band 5 (£41), community based scientific and professional staff, not including qualifications.
High Intensity Therapist (HIT)	£60		PSSRU (2021)	Mean of band 6 (£54) and band 6 (£65), community based scientific and professional staff, not including qualifications.
Step 2 interventions, assume delivered by PWP, bands 4 & 5				
Individual non-facilitated self-help	£0		IAPT guidance, PSSRU (2021)	Minimal
Individual guided self-help	£95		IAPT guidance, PSSRU (2021)	IAPT guidance is 5-7 weekly or fortnightly face to face or telephone sessions, each 20-30min. Assume 6 x 25 minutes.
Psychoeducational groups	£38		IAPT guidance, PSSRU (2021)	IAPT guidance is ratio 1 therapist to 12 participants, 6 weekly sessions, each 2 hours.
Brief individual CBT + self-help materials or telephone support	n/a		IAPT guidance, n/a	IAPT guidance is up to 10 therapist hours per patient, assume 10 hours. Not included, as information on uptake not possible to disaggregate from IAPT database.
Group CBT	n/a		IAPT guidance, n/a	May receive >10 hours per patient. Not included, as information on uptake not possible to disaggregate from IAPT database.
Step 3 interventions, assumed delivered by HIT, bands 6 & 7				
GAD	£833		IAPT guidance, PSSRU (2021)	Individual high-intensity psychological intervention, 12-14 sessions x 1 hour. Assume 14 hours
PTSD	£595		IAPT guidance, PSSRU (2021)	Individual high-intensity psychological intervention, 8-12 sessions x 1 hour. Assume 10 hours
SAD	£803		IAPT guidance, PSSRU (2021)	Mean of: book based sessions, support for total of 3 hours, or 14 sessions of 90 min, or

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
				15 sessions of 60 min and 1 of 90 min.
BDD	£595		IAPT guidance, PSSRU (2021), Assumption	Mix of group and individual CBT is offered initially, but no guidance on therapist time or number of sessions. Both individual and group CBT can be offered at approx. 10 hours per patient (see PTSD and Group CBT information above). Therefore, assumption of 10 hours with high intensity psychological intervention.
Mean IAPT costs (therapist time)				
<i>Step 2, GAD</i>	£86	N(88, 9)	IAPT database, 2021-2, NICE GAD guideline	Weighted mean of provided stage 2 interventions (IAPT database) with calculated cost based on estimated therapist time of each intervention NICE GAD guideline, IAPT database)
<i>Step 2, Others</i>	£84	N(84, 8)	IAPT database, 2021-2	Weighted mean of provided stage 2 interventions (IAPT database) with calculated cost based on estimated therapist time of each intervention NICE GAD guideline, IAPT database)
<i>Step 3, PTSD</i>	£595	N(595, 60)		Calculated cost based on estimated therapist time for IAPT Step 3 therapy (NICE PTSD guideline)
<i>Step 3, SAD</i>	£803	N(803, 80)		Calculated cost based on estimated therapist time for IAPT Step 3 therapy (NICE SAD guideline)
<i>Step 3, BDD</i>	£595	N(595, 60)		Calculated cost based on estimated therapist time for IAPT Step 3 therapy using the NICE PTSD guideline, as no guidance for BDD available
<i>Step 3, others</i>	£833	N(833, 83)		Calculated cost based on estimated therapist time for IAPT Step 3 therapy (NICE SAD guideline)
<i>Medication cost per day</i>	£1.13	U(1, 2)	BNF, 2022	Assumed sertraline 100mg per day was prescribed. (50-200mg/day as range) Applied as adjunct to step 3 therapy, following no response to initial step 3 intervention.
Therapist costs as part of guided therapy for intervention arms (adjunct to intervention cost)				
<i>Step 2</i>	£95	U(88, 103)		Estimated using recommended therapist time in IAPT Step 2 guided therapy, delivered by PWP. IAPT guidance is 5-7 weekly or fortnightly face to face or telephone sessions, each 20-30min.

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
				Assume 6 x 25 minutes.
Step 3, PTSD	£238	U(216, 260)	Ehlers et al., 2020	Estimated using trial protocol, 4 hours per participant (iCT-PTSD: 12 weekly phone calls (average 4 hours per participant), Spring: 3 hours face to face + 4 short phone calls), delivered by HIT
Step 3, SAD	£384	U(348, 419)	Clarks et al., 2022	Estimated using trial data (Average 6.45 hours per participant)
Step 3, BDD	£238	U(216, 260)	Assumption	Trial reported 1 hour therapist support, but within IAPT this may be closer to other Step 3 interventions. Therefore the value for PTSD has been assumed.

Table 18: Key Utility Parameters

Variable	Value	Distribution	Source	EAG commentary on availability, quality and reliability of the source/s
Utilities used to calculate model inputs				
No anxiety	0.720	B(14, 5)	NIHR HTA report (Gega 2022)	These are reported in the HTA report (Gega 2022), but are derived from Revicki et al 2012 and Revicki et al. 2008. There is limited information on how the utilities reported in the paper were valued.
Mild anxiety	0.640	B(14, 8)		
Moderate anxiety	0.600	B(14, 9)		
Severe anxiety	0.530	B(13, 11)		
All anxieties other than SAD and PTSD				
Prior to treatment	0.620			Mean of mild and moderate anxiety
Responded to treatment	0.680			Mean of mild and no anxiety
Did not respond to treatment	0.620			Mean of mild and moderate anxiety
PTSD and SAD				
Prior to treatment	0.565			Mean of moderate and severe anxiety
Responded to treatment	0.620			Mean of mild and moderate anxiety
Did not respond to treatment	0.565			Mean of moderate and severe anxiety

9.4 Results from the economic modelling

Exploratory results are presented below, based on a purchase of 1,000 licences, over a 15-month period, and using IAPT database reported recovery to illustrate current normal treatment outcomes. Insufficient evidence on efficacy was available for Cerina, Iona Mind, Resony and Wysa, and therefore their cost-effectiveness could not be modelled, and no conclusions can be drawn for these technologies. Cerina have some small unpublished evidence demonstrating improved clinical scores over time, but these do not include for recovery. Wysa have a number of published studies, but not in applicable patient groups or settings. Beating the Blues, MindDistrict and SilverCloud efficacy data is based on a mixed population with depression, mixed anxiety and depression and other anxiety descriptors. Therefore, the model may not represent outcomes appropriately for the stated anxiety descriptors.

The initial interventions for BDD are group or individual CBT, and the appropriate costs to apply for both the IAPT comparator and the guided element of the intervention are unclear. Assumptions have been stated in the model input tables. Although there is uncertainty in the exact costs, the general direction of the results is likely to be robust.

Table 19: Generalised Anxiety Disorder

GAD	IAPT current pathway	Beating the blues	MindDistrict	Silver Cloud
Cost	£494	■	■	£410
QALYs	0.81	0.81	0.82	0.81
NMB @ £20,000/QALY	£15,771	■	■	£15,811
NMB CI (95%)	12707, 18615	12828, 18724	13357, 19546	12641, 18714

Table 20: Body Dysmorphic Disorder

Body Dismorphic Disorder	IAPT current pathway	Koa Health
Cost	£1,009	■
QALYs	0.74	0.74
NMB @ £20,000/QALY	£13,783	■
NMB CI (95%)	10,639, 16661	10,930, 16,978

Table 21: Other Anxiety Descriptors

Other anxiety descriptors that are initially treated within IAPT Step 2	IAPT current pathway	MindDistrict	Silver Cloud
Cost	£587	█	£459
QALYs	0.81	0.82	0.81
NMB @ £20,000/QALY	£15,538	█	£15,725
NMB CI (95%)	12459, 18455	13306, 19573	12540, 18625

Table 22: Post traumatic stress disorder

PTSD	IAPT current pathway	iCT-PTSD	Spring
Cost	£1,289	█	£496
QALYs	0.72	0.74	0.75
NMB @ £20,000/QALY	£13,044	█	£14,542
NMB CI (95%)	9807, 16214	11167, 17097	11362, 17444

Table 23: Social anxiety Disorder

SAD	IAPT current pathway	iCT-SAD	MindDistrict	Silver Cloud
Cost	£1,433	█	█	£1,168
QALYs	0.73	0.75	0.75	0.74
NMB @ £20,000/QALY	£13,233	█	█	£13,578
NMB CI (95%)	10060, 16141	10938, 17006	11549, 17824	10520, 16519

One-way sensitivity analyses

Net monetary benefit was sensitive to the recovery rate of each intervention, where it varied significantly with the change in recovery rate across all anxiety descriptors (█4).

Scenario analysis

This scenario is based on the use of overall recovery rate from the main IAPT database. The interventions all remain at a lower cost to the comparator, and a similar level of QALY gain, however the uncertainties in the results remain.

Table 24: Generalised Anxiety Disorder

GAD	IAPT current pathway	Beating the blues	MindDistrict	Silver Cloud
Cost	£446	■	■	£384
QALYs	0.82	0.81	0.82	0.81
NMB @ £20,000/QALY	£15,883	■	■	£15,855

Table 25: Body Dysmorphic Disorder

Body Dismorphic Disorder	IAPT current pathway	Koa Health
Cost	£1,008	■
QALYs	0.74	0.74
NMB @ £20,000/QALY	£13,786	■

Table 26: Other Anxiety Descriptors

Other anxiety descriptors that are initially treated within IAPT Step 2	IAPT current pathway	MindDistrict	Silver Cloud
Cost	£517	■	£422
QALYs	0.81	0.82	0.81
NMB @ £20,000/QALY	£15,708	■	£15,789

Table 27: Post traumatic stress disorder

PTSD	IAPT current pathway	iCT-PTSD	Spring
Cost	£1,063	■	£460
QALYs	0.73	0.75	0.75
NMB @ £20,000/QALY	£13,560	■	£14,606

Table 28: Social anxiety Disorder

SAD	IAPT current pathway	iCT-SAD	MindDistrict	Silver Cloud
Cost	£1,457	■	■	£1,179
QALYs	0.73	0.75	0.75	0.74
NMB @ £20,000/QALY	£13,180	■	■	£13,560

Value of information analysis

Estimated population-level value of perfect information (EVPI) was derived based on 330,000 people per year (estimated using the GAD incidence in England, 4.9% and 10% of patients receive intervention) (Jankovic 2022, Kumar 2018) and the lifetime of the intervention was 5 years. The analyses were conducted using SAVI interface (<http://savi.shef.ac.uk/SAVI/>) (Strong 2014).

Table 29: Population EVPI over 5 years

	Population EVPI over 5 years (£)
GAD	
Beating the Blues	4,065,153
MindDistrict	20,015,447
Silver Cloud	26,066,628
Other anxiety descriptors that are initially treated with IAPT Step 2	
MindDistrict	30,069,717
Silver Cloud	517,143
BDD	
Koa	8,037,210
PTSD	
iCT-PTSD	20,651,596
Spring	29,945,591
SAD	
iCT-SAD	1,442,974
MindDistrict	5,518,988
Silver Cloud	108,611

9.5 Interpretation of the economic evidence

Published HTA reports and guidance (Gega 2022, Health Quality Ontario 2019) for guided digital therapies in anxiety found that there was insufficient evidence to draw conclusive results on cost-effectiveness when compared to face to face therapy or printed manuals. It was likely to be cost effective compared to waiting lists. NICE CG113 considered modelling that compared digitally delivered CBT to waitlist for patients with GAD, but noted this did not reflect NHS practices. NICE CG159 reported limitations, but ranked interventions for symptoms of SAD by NMB and found that guided digital therapies were ranked 7th, after different forms of face to face cognitive therapy and some medication.

Economic analysis for technologies within the scope were all within trial analysis. All four studies found the interventions to be cost saving, and three were reported as cost effective; however this is based on either waiting list comparators (Richards, 2020), treatment as usual that is poorly reported and may include waiting list (McCrone, 2004), or other

[REDACTED] These cannot be interpreted as implying cost-effectiveness in the IAPT pathway. Only Bisson (2022) report an economic within study analysis where the comparator is appropriate for treatment within the IAPT pathway. They found cost savings for the intervention, but a slightly lower improvement in QALY values for the intervention compared to face to face CBT.

There are two key limitations to the published economic evidence also apply more widely to the clinical evidence. These are the broad, heterogenous population for unspecified anxiety descriptors (Richards 2020, McCrone 2004), and the inappropriate comparator for IAPT (Richards 2020, McCrone 2004, [REDACTED]).

EAG modelling required simplification of a complex pathway, and was limited by the available evidence. As a result, they should be seen as exploratory only.

Across all the interventions the model finds that they are slightly less costly at 15 months than the modelled IAPT equivalent, with some at stage 3 (PTSD, SAD) having a slightly larger cost saving. The model found similar QALY gains for the interventions and the comparator, with only small differences across the different interventions and technologies. The key driver of the model is clinical effectiveness, meaning that all the limitations noted for the clinical evidence also impact on the model.

Efficacy inputs to the model show the interventions to be more effective than standard IAPT treatment, and this drives a reduced cost, due to fewer additional therapies, and a small increase in accumulated QALYs. However, this should be interpreted with extreme caution, due to the issues discussed in “Main Clinical Parameters”. The IAPT reflects normal care, whereas intervention efficacy is based on trial data, and there are differences in how results are obtained. In addition, there

are limitations in how both IAPT and study data relate to the patient groups being modelled.

The direct cost of providing any of the digitally enabled interventions is the licence cost (and any other fees to the supplier) and therapist time for delivering and guiding the therapy. In all cases the therapist time is the largest element of this cost. For most IAPT stage 2 interventions, therapist time is assumed to be driven by IAPT protocol, and therefore therapist costs are the same for all IAPT stage 2 digitally enabled therapies considered for any given indication. PTSD and SAD therapist time are estimated based on study data, but this the same cost is applied to any digitally enabled therapy used for that indication. This means there is little difference in the cost to deliver each digitally enabled therapy for a given indication, and the key driver for costs is the clinical effectiveness of each intervention.

10 Evidence gap analysis

The primary evidence gap relates to a lack of evidence for specific technologies and for specific conditions included in the scope. Five of the technologies (Cerina, Iona Mind, Mind District, Resony and Wysa) and 4 specific conditions (health anxiety, obsessive compulsive disorder, panic disorder and specific phobias) have no relevant published clinical evidence available. It is therefore not possible to comment on the clinical effectiveness of these technologies or to know whether using digitally enabled technologies can positively impact outcomes for adults with health anxiety, obsessive compulsive disorder, panic disorder and specific phobias. It was also not possible to calculate the cost effectiveness associated with the use of digitally enabled therapies for these specific conditions. Ideally evidence for the economic model would come from a study with a comparator that is relevant to the model i.e. an IAPT pathway intervention.

The EAG identified a number of ongoing studies (table 12) that may contribute to identified evidence gaps.

Table 30 to Table 33 summarises what the evidence gaps are for those conditions and technologies where there was some evidence available.

Table 30: Post traumatic Stress Disorder Evidence Gap Analysis


	iCT-PTSD	Spring
Clinical Studies		
<i>Comparator</i> IAPT pathway	No studies <i>Red</i>	Yes – One RCT <i>Green</i>
<i>Clinical outcome:</i> Symptom severity	Yes – One non-comparative study and data from one unpublished study <i>Amber</i>	Yes – One RCT <i>Green</i>
<i>Clinical outcome:</i> Remission and recovery	Yes – One non-comparative study and data from one unpublished study <i>Amber</i>	Partially reported <i>Amber</i>
<i>Intermediate outcome:</i> Acceptability and usage	Yes – One non-comparative study <i>Amber</i>	No studies <i>Red</i>
<i>Intermediate outcome:</i> Therapist time	Yes – One non-comparative study <i>Amber</i>	No studies <i>Red</i>
<i>Intermediate outcome:</i> Adverse events	No studies <i>Red</i>	No <i>Red</i>
<i>Economic outcome: utilities</i>	Yes <i>Green</i>	Yes – One RCT <i>Green</i>
<i>Economic within trial analysis</i>	One economic analysis of an RCT, comparator is another digital therapy that would not be provided on the IAPT pathway. <i>Amber</i>	One economic analysis of a non-inferiority RCT, with face to face therapy as the comparator. <i>Green</i>
Real World Evidence		
No real world evidence identified for Spring		
		
<i>Amber</i>		
Ongoing studies / Unpublished Studies		
Two ongoing studies were identified by the EAG, both relating to iCT-PTSD. Although these studies have not yet been published in the public domain, the company provided the results to the EAG and these are discussed in the report.		
No additional ongoing studies have been identified.		

Table 31: Social Anxiety Disorder Evidence Gap Analysis

	iCT-SAD	MindDistrict	Silver Cloud
Clinical Studies			
<i>Comparator:</i>	No studies	No studies	No studies


IAPT pathway	<i>Red</i>	<i>Red</i>	<i>Red</i>
<i>Clinical outcome:</i> Symptom severity	Yes – One non-comparative study and one RCT <i>Green</i>	No studies <i>Red</i>	No studies <i>Red</i>
<i>Clinical outcome:</i> Remission and recovery	Yes – One non-comparative study and one RCT <i>Green</i>	No studies <i>Red</i>	No studies <i>Red</i>
<i>Intermediate outcome:</i> Acceptability and usage	Yes – One non-comparative study <i>Amber</i>	No studies <i>Red</i>	No studies <i>Red</i>
<i>Intermediate outcome:</i> Therapist time	Yes – One non-comparative study and one RCT <i>Green</i>	No studies <i>Red</i>	No studies <i>Red</i>
<i>Intermediate outcome:</i> Adverse events	Yes – One RCT <i>Green</i>	No studies <i>Red</i>	No studies <i>Red</i>
<i>Economic outcome:</i> Utilities	No <i>Red</i>	No studies <i>Red</i>	No studies <i>Red</i>
<i>Economic within trial analysis</i>	No <i>Red</i>	No studies <i>Red</i>	No studies <i>Red</i>
Real World Evidence			
No real world evidence identified for MindDistrist or SilverCloud			
			
<i>Amber</i>			
On-going studies / Unpublished Studies			
One ongoing study relating to iCT-SAD was identified. Although this study has not yet been published in the public domain, the company provided the results to the EAG and these are discussed in the report.			
One ongoing study relating to Koa Health (Perspectives) was identified and study completion is anticipated in 2025. The study is randomised but does not use IAPT recommended tools to measure symptoms (LSAS) and the comparator for this study is waitlist which may limit the applicability of evidence from this study.			

Table 32: Body Dysmorphic Disorder Evidence Gap Analysis

Perspectives, Koa Health	
Clinical Studies	
<i>Comparator:</i> IAPT pathway	No studies <i>Red</i>

<i>Clinical outcome:</i> Symptom severity	Yes – One non-comparative study and one RCT Green
<i>Clinical outcome:</i> Remission and recovery	Yes – One non-comparative study and one RCT Green
<i>Intermediate outcome:</i> Acceptability and usage	Yes – One non-comparative study and RCT Green
<i>Intermediate outcome:</i> Therapist time	Yes – One RCT Amber
<i>Intermediate outcome:</i> Adverse events	Yes – one non-comparative study Amber
<i>Economic outcome:</i> Utilities	Quality of life scores are reported (Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form (Q-LES-Q-S)) Amber
<i>Economic within trial analysis</i>	No Red
Real World Evidence No real world evidence identified Red	
On-going Studies / Unpublished Studies One ongoing study relating to Koa Health (Perspectives) was identified with study completion date anticipated to have been January 2022. Information from the company suggests this study has completed and reported in Wilhelm 2022 which is included in the evidence.	

Table 33: Generalised Anxiety Evidence Gap Analysis

	Beating the Blues	Cerina	Iona Mind	Mind District	Resony	Silver Cloud	Wysa
Clinical Studies							
Comparator: IAPT pathway	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes – one study comparing with guided self-help and group therapy. <i>Green</i>	No <i>Red</i>
Clinical outcome: Symptom severity	Yes – 5 studies All included studies reported a baseline anxiety score however this was not specifically reported as a symptom severity outcome and the tools used in each study varied <i>Amber</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes – 6 studies All included studies reported a baseline anxiety score as measured using GAD 7 <i>Green</i>	No <i>Red</i>
Clinical outcome: Remission and recovery	Yes – 5 studies All included studies reported the change from baseline anxiety score in some format. Studies reported changes at different timepoints to indicate change (improvement) over time however this was not specifically reported as remission/recovery <i>Amber</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes – 6 studies All included studies reported the change from baseline anxiety score as measured using GAD 7 Studies reported changes at different follow-up timepoints to indicate change (improvement) over time however this was not specifically reported as remission/recovery	No <i>Red</i>

<i>Intermediate outcome:</i> Acceptability and usage	Yes – 2 studies One randomised trial reporting the acceptability of using the technology in two user groups One non-comparative study reporting patient feedback on usefulness/helpfulness of technology <i>Green</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes – 2 studies One non-comparative study reporting engagement rates One comparative study (comparing to waitlist control) reporting participants expectations of technology including experience versus expectation <i>Green</i>	No <i>Red</i>
<i>Intermediate outcome:</i> Therapist time	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>
<i>Intermediate outcome:</i> Adverse events	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes – one study included adverse events as an outcome. <i>Green</i>	No <i>Red</i>
<i>Economic outcome:</i> Utilities	Yes <i>Green</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes <i>Green</i>	No <i>Red</i>
<i>Economic within trial analysis</i>	Yes, but not relevant comparator <i>Amber</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	No <i>Red</i>	Yes, but not relevant comparator <i>Amber</i>	No <i>Red</i>
Real World Evidence							
No real world evidence identified <i>Red</i>							
Ongoing Studies / Unpublished Studies							
One ongoing study relating to SilverCloud was identified however the trial record indicates this study has been withdrawn due to logistic reasons and will therefore not provide any data to inform the evidence gaps.							

Confidential results from one unpublished study were provided for Resony which report



10.1 Summary and conclusions of evidence gap analysis

The largest volume of evidence was available for Beating the Blues and SilverCloud and related to generalised anxiety. Limited evidence from one technology each was available for body dysmorphic disorder (Koa Perspectives), and Social anxiety disorder (iCT-SAD) and from two technologies for PTSD (iCT PTSD, Spring).

Across all technologies for both clinical and economic evidence, the key relevant clinical outcomes are for remission and recovery, and longer-term outcomes including relapse which require well conducted clinical studies to generate reliable results. Where there is available evidence for specific technologies, a key evidence gap relates to use of a valid comparator within IAPT pathway. For economic analysis, additional data such as costs and utilities may be collected during the study, but may also be based on IAPT guidance and published literature. Real world evidence generation might be possible, particularly within the current IAPT database however currently, the publicly available information does not report on specific details of technologies used where a digital intervention is used. One company provided limited data from real world evidence collection for iCT-PTSD and iCT-SAD which suggests that real world evidence generation is possible and may provide useful and informative results.

Specifically related to generalised anxiety, a second key evidence gap relates specifically to different anxiety descriptors and the separate reporting of depression, anxiety, and separate anxiety descriptors where appropriate.

One additional gap to be considered relates to the use of validated tools / measures to assess conditions. For example, the body dysmorphia studies use BDD-YBCOS to measure symptoms whereas the recommended tool / measure in the IAPT manual is the Body Image Questionnaire.

For many of the technologies, it is impossible to know if the reported effect size is relevant to the anxiety descriptor being discussed, or even to anxiety in its broadest sense.

10.2 **Key areas for evidence generation**

Evidence generation should focus on larger scale randomised controlled trials without a 'Waitlist' comparator group but rather a different technology or ideally a current practice comparator group. They should focus on the technologies with no current evidence and anxiety disorders with no current evidence. Further, those referring to GAD should make it clear whether participants have a defined DSM-V or ICD-10 diagnosis of GAD or are experiencing high levels of anxiety as assessed (usually self-assessed) by the GAD-7 questionnaire. More studies need to be conducted within the UK and preferably within an NHS IAPT setting so that results generated can be readily generalised to the IAPT pathway.

Table 34: Evidence Generation

Population	<ul style="list-style-type: none"> • Studies should clearly report on participant diagnosis - focusing on actual diagnoses of GAD, or differentiating from anxiety symptoms as reported from the GAD-7 • Reporting of results should be split by diagnosis or descriptor – rather than grouping people who are experiencing anxiety and/or depression symptoms • Use of IAPT recommended tools / measures to assess caseness
Interventions	<ul style="list-style-type: none"> • Some interventions are lacking in any clinical evidence, and others have very limited evidence, or no relevant comparative evidence • Clear reporting of therapist involvement and level of qualification • Consistent use of guided element as per IAPT protocol
Comparators	<ul style="list-style-type: none"> • Lack of comparators based on appropriate treatments (rather than waiting list, or treatment as usual that includes waiting list, or has little specification of treatments) •
Outcomes	<ul style="list-style-type: none"> • Reporting of recovery or reliable recovery data • Consistent reporting of ITT, or based on IAPT criteria • Relapse rates and longer term follow up • Consistent use of guided element as per IAPT protocol • Safety/Adverse Events
Economic	<ul style="list-style-type: none"> • Robust clinical evidence as outlined above • Inclusion of quality of life outcomes and utilities

11 Conclusions

11.1 *Conclusions from the clinical evidence*

Where available, the clinical evidence (n=19 studies) suggests that guided digital therapies can reduce anxiety symptoms across a range of conditions and that reductions can persist up to 12 months post treatment. Limited comparative evidence indicates the reduction in anxiety symptoms was larger in those using the guided therapies, compared to waiting list or usual care. There is no evidence that the technologies lead to any adverse events nor is there evidence of any safety concerns with any of the technologies. Where reported, users seem satisfied with the technologies they are using suggesting that digitally enabled technologies are an acceptable however it should be noted that user acceptability measures are largely before and after technology use and therefore it is not clear whether digitally enable technologies are an acceptable alternative to face-to-face CBT.

It is possible that use of digitally enabled technologies may reduce the amount of therapist time needed however studies did not always clearly report whether there was therapist involvement and if so what the role of the therapist and the qualification level of the therapists involved.

None of the identified evidence included reported results for health anxiety, OCD, Panic Disorder or specific phobias using any of the technologies of interest and therefore no conclusion can be made on the effectiveness of these technologies. In addition, it was not the purpose of the review to compare technologies with each other therefore no conclusions can be made on the relative effectiveness of technologies that can be used for the same conditions.

The EAG concludes that digitally enabled technologies show promise but additional evidence is needed for recovery, remission and relapse rates, over longer periods, for a specific population and using appropriate comparators.

11.2 Conclusions from the economic evidence

The economic findings are dependent on clinical evidence for very heterogenous groups, with delivery methods that may not align to the planned IAPT delivery, and comparator data that is not appropriate for an IAPT pathway.

The EAG model attempts to summarise, and standardise, a complex pathway across multiple indications, which, by necessity, involves simplifications and assumptions. The limited quality and applicability of the evidence base, combined with the simplified pathway means that any results should be seen as exploratory, and conclusions should be reached with caution.

Across all the interventions the model finds that they are slightly less costly at 15 months than the modelled IAPT equivalent, with some at stage 3 (PTSD, SAD) having a slightly larger cost saving. The model also calculates a similar QALY gain to the comparator, with only small differences across the different interventions and technologies. It should however be noted that the only economic study that used an appropriate treatment-based comparator found that the digitally enabled therapy for PTSD resulted in a slightly lower QALY gain than the standard face to face intervention.

The key driver for the model is clinical effectiveness, and this is similar to findings from other modelling studies for digitally enabled technologies (Gega 2022). The EAG key evidence gaps are also similar to those identified in previous economic modelling work for interventions for digitally enabled therapies for anxiety (Gega 2022, Health Quality Ontario 2019, CG113).

Additional evidence is needed for recovery, remission and relapse rates, over longer periods, for a specific population and using appropriate comparators.

12 Summary of the combined clinical and economic sections

There is a lack of relevant evidence for some of the included technologies, and a lack of evidence that focuses on specific anxiety descriptors (health

anxiety, obsessive compulsive disorder, panic disorder and specific phobias). Therefore, the EAG are unable to draw any clinical or economic conclusions in these areas.

There are a number of RCTs published, including within trial economic evaluations, for digitally enabled therapies in the unspecified anxiety disorders, PTSD, SAD and BDD. There are no studies that look specifically at GAD, and populations often include depression making interpretation of results difficult. Almost all comparative studies use waiting list or usual care (that may be poorly defined and includes wait list) and are not relevant to a decision based on the IAPT pathway.

Economic evidence is subject to the same limitations and economic modelling is highly driven by the quality of the clinical evidence.

Technologies are likely to be cheaper to deliver than many other IAPT interventions at a similar stage, and are likely to provide better outcomes than waitlist. Modelling shows lower costs and similar outcomes at 15 months compared to IAPT interventions at the same stage, but has a high degree of uncertainty.

Additional evidence is needed for recovery, remission and relapse rates, over longer periods, for a specific population and using appropriate comparators. Other assessments that were not focused on specific technologies, but took a broader view of digitally enabled therapies also noted similar limitations and evidence gaps.

13 References

Baumann M, Stargardt T & Frey S (2020) Cost–Utility of Internet-Based Cognitive Behavioral Therapy in Unipolar Depression: A Markov Model Simulation. *Appl Health Econ Health Policy* 18, 567–578

Bisson, J. I., Ariti, C., Cullen, K., et al. (2022). Guided, internet based, cognitive behavioural therapy for post-traumatic stress disorder: pragmatic,

multicentre, randomised controlled non-inferiority trial (RAPID). *BMJ* 377: e069405

Cavanagh, K., Seccombe, N., & Lidbetter, N. (2011). The implementation of computerized cognitive behavioural therapies in a service user-led, third sector self help clinic. *Behavioural and Cognitive Psychotherapy* 39(4): 427-442

Cavanagh, K., Shapiro, D. A., Van Den Berg, S., et al. (2006). The effectiveness of computerized cognitive behavioural therapy in routine care. *British Journal of Clinical Psychology* 45(4): 499-514

Cavanagh, K., Shapiro, D. A., Van Den Berg, S., et al. (2009). The acceptability of computer-aided cognitive behavioural therapy: a pragmatic study. *Cognitive Behaviour Therapy* 38(4): 235-246

Chien, I., Enrique, A., Palacios, J., et al. (2020). A machine learning approach to understanding patterns of engagement with internet-delivered mental health interventions. *JAMA Network Open* 3(7): e2010791

Clark, D. M., Wild, J., Warnock-Parkes, E., et al. (2022). More than doubling the clinical benefit of each hour of therapist time: a randomised controlled trial of internet cognitive therapy for social anxiety disorder. *Psychological Medicine*: 1-11

Duffy, D., Enrique, A., Connell, S., et al. (2020). Internet-delivered cognitive behavior therapy as a prequel to face-to-face therapy for depression and anxiety: a naturalistic observation. *Frontiers in Psychiatry* 10: 902

Gega L, Jankovic D, Saramago P, Marshall D, Dawson S, Brabyn S, et al. (2022) Digital interventions in mental health: evidence syntheses and economic modelling. *Health Technol Assess* 26(1)

Health Quality Ontario (2019) Internet-delivered cognitive behavioural therapy for major depressive disorder and anxiety disorders: a health technology

assessment. Canada: Canadian Agency for Drugs and Technologies in Health (CADTH)

Jankovic D, Saramago Goncalves P, Gega L, Marshall D, Wright K, Hafidh M, Churchill R, Bojke L (2022) Cost Effectiveness of Digital Interventions for Generalised Anxiety Disorder: A Model-Based Analysis. *Pharmacoecon Open*. 6(3):377-388

Jardine, J., Earley, C., Richards, D., et al. (2020). The experience of guided online therapy: a longitudinal, qualitative analysis of client feedback in a naturalistic RCT. *Proceedings of the 2020 CHI Conference on Human Factors in Computing Systems*: 1-15

Joint Formulary Committee. British National Formulary [Internet]. London: British Medical Association and Royal Pharmaceutical Society of Great Britain. Available from: <https://bnf.nice.org.uk/> Accessed 8 Dec 2022

Jonassaint, C. R., Belnap, B. H., Huang, Y., et al. (2020). Racial differences in the effectiveness of internet-delivered mental health care. *Journal of general internal medicine* 35(2): 490-497

Jonassaint, C. R., Gibbs, P., Belnap, B. H., et al. (2017). Engagement and outcomes for a computerised cognitive-behavioural therapy intervention for anxiety and depression in African Americans. *BJPsych Open* 3(1): 1-5

Jones, Karen C., Burns, Amanda (2021) Unit Costs of Health and Social Care 2021. Personal Social Services Research Unit (PSSRU), University of Kent, Canterbury

Kumar S, Jones Bell M, Juusola JL (2018) Mobile and traditional cognitive behavioral therapy programs for generalized anxiety disorder: A cost-effectiveness analysis. *PLoS ONE* 13(1):e0190554

Learmonth, D., Trosh, J., Rai, S., et al. (2008). The role of computer-aided psychotherapy within an NHS CBT specialist service. *Counselling and Psychotherapy Research* 8(2): 117-123

Mavranetzouli I, Mayo-Wilson E, Dias S, Kew K, Clark DM, Ades AE, et al. (2015) The Cost Effectiveness of Psychological and Pharmacological Interventions for Social Anxiety Disorder: A Model-Based Economic Analysis. PLoS ONE 10(10):e0140704

McCrone, P., Knapp, M., Proudfoot, J., et al. (2004). Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. British Journal of Psychiatry 185(1): 55-62

Najafzadeh M, Garces JA, Maciel A (2017) Economic Evaluation of Implementing a Novel Pharmacogenomic Test (IDgenetix®) to Guide Treatment of Patients with Depression and/or Anxiety. Pharmacoeconomics 35(12):1297-1310

National Collaborating Centre for Mental Health (2018). The Improving Access to Psychological Therapies Manual. London: National Collaborating Centre for Mental Health

NHS Digital (2022) Psychological Therapies: Therapy-based outcomes in IAPT services, 2021-22. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-iapt-services/annual-report-2021-22> Accessed 13 Dec 2022

Palacios, J., Adegoke, A., Wogan, R., et al. (2022). Comparison of outcomes across low-intensity psychological interventions for depression and anxiety within a stepped-care setting: A naturalistic cohort study using propensity score modelling. British Journal of Psychology 00: 1-16

Palacios, J. E., Enrique, A., Mooney, O., et al. (2022). Durability of treatment effects following internet-delivered cognitive behavioural therapy for depression and anxiety delivered within a routine care setting. Clinical Psychology and Psychotherapy 29(5): 1768-1777

Palacios, J. E., Richards, D., Palmer, R., et al. (2018). Supported internet-delivered cognitive behavioral therapy programs for depression, anxiety, and

stress in university students: open, non-randomised trial of acceptability, effectiveness, and satisfaction. *JMIR Mental Health* 5(4): e11467

Proudfoot, J., Ryden, C., Everitt, B., et al. (2004). Clinical efficacy of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *British Journal of Psychiatry* 185(1): 46-54

Revicki DA, Travers K, Wyrwich KW, Svedsäter H, Locklear J, Mattera MS, et al. (2012) Humanistic and economic burden of generalized anxiety disorder in North America and Europe. *J Affect Disord* 140:103–12

Richards, D., Enrique, A., Eilert, N., et al. (2020). A pragmatic randomized waitlist-controlled effectiveness and cost-effectiveness trial of digital interventions for depression and anxiety. *NPJ Digital Medicine* 3: 85

Stiles JA, Chatterton ML, Le LK, Lee YY, Whiteford H, Mihalopoulos C (2019) The cost-effectiveness of stepped care for the treatment of anxiety disorders in adults: A model-based economic analysis for the Australian setting. *J Psychosom Res* 125:109812

Stott, R., Wild, J., Grey, N., et al. (2013). Internet-delivered cognitive therapy for social anxiety disorder: a development pilot series. *Behavioural and Cognitive Psychotherapy* 41(4): 383-397

Strong M, Oakley JE, Brennan A (2014) Estimating multi-parameter partial Expected Value of Perfect Information from a probabilistic sensitivity analysis sample: a non-parametric regression approach. *Medical Decision Making* 34(3):311-26

Wild, J., Warnock-Parkes, E., Grey, N., et al. (2016). Internet-delivered cognitive therapy for PTSD: a development pilot series. *European Journal of Psychotraumatology* 7(1): 31019

Wilhelm, S., Weingarden, H., Greenberg, J. L., et al. (2022). Efficacy of app-based cognitive behavioral therapy for body dysmorphic disorder with coach

support: initial randomized controlled clinical trial. *Psychotherapy and Psychosomatics* 91(4): 277-285

Wilhelm, S., Weingarden, H., Greenberg, J. L., et al. (2020). Development and pilot testing of a cognitive-behavioral therapy digital service for Body Dysmorphic Disorder. *Behavior Therapy* 51(1): 15-26

You JHS, Luk SWC, Chow DYW, Jiang X, Mak ADP, Mak WWS (2022) Cost-effectiveness of internet-supported cognitive behavioral therapy for university students with anxiety symptoms: A Markov-model analysis. *PLoS ONE* 17(5): e0268061

14 Appendices

Appendix A: Search Strategies

Appendix A: Clinical data search strategy.

The EAG conducted a search for both clinical and economic evidence as directed by the scope. Eleven bibliographic databases were searched from inception to 23rd November 2022, using a range of free text terms and, where appropriate, indexed terms. The searches were not restricted by language of publication. Two clinical trial registries were also searched for ongoing and unpublished trials; the companies' websites were also searched for additional literature. The MHRA's medical device alerts and field safety notices and the FDA MAUDE database were searched for adverse events.

Additionally, economic studies were identified from the references of a similar report: Guided dCBT for CYP with mild to moderate anxiety or low mood: an Early Value Assessment (MT580). The economic searches from this report were updated to identify any literature published since August 2022.

Clinical and economic searches

Date	Database Name	Total Number of records retrieved	Total number of records from database after de-duplication
23/11/22	Medline ALL (includes Medline In Process & Medline Epub Ahead of Print)	247	
23/11/22	EMBASE	362	
23/11/22	PsycInfo	398	
23/11/22	Cochrane Library CDSR CENTRAL	89 152	
23/11/22	CRD DARE HTA NHS EED	13 6 1	
23/11/22	INAHTA	13	

Date	Database Name	Total Number of records retrieved	Total number of records from database after de-duplication
23/11/22	PubMed	313	
23/11/22	Epistemonikos	100	
21/06/22	Company websites: Beating the Blues Cerina Iona Mind MindDistrict SilverCloud Spring Wysa Koa Health/Perspectives Oxcadat Resony Deprexis	13 0 0 13 67 0 1 0 14 0 8	
22/06/22	MHRA	0	
27/06/22	FDA MAUDE	0	
21/06/22	Clinical Trials.gov	55	
22/06/22	ICTRP	75	1250 records after manual deduplication

Economic searches

Date	Database Name	Total Number of records retrieved	Total number of records from database after de-duplication
29/11/22	ScHARRHUD	0	
29/11/22	CEA Registry	6	
29/11/22	Medline (ALL)	40	
29/11/22	EMBASE	18	
29/11/22	PsycInfo	10	53 records after manual deduplication

EAG Search strategies

Ovid MEDLINE(R) ALL <1946 to November 22, 2022>

- 1 Anxiety/ 102027
- 2 anxiety disorders/ 39925
- 3 (anxiet* or anxious).tw. 252620
- 4 "generalized anxiety disorder*".tw. 9697
- 5 GAD.tw. 11873
- 6 "social anxiety disorder*".tw. 3217
- 7 phobia*.tw. 9537
- 8 "panic disorder*".tw. 10038
- 9 "posttraumatic stress disorder*".tw. 22077
- 10 PTSD.tw. 30465
- 11 "body dysmorphic disorder*".tw. 1302
- 12 "obsessive compulsive disorder*".tw. 15322
- 13 exp Phobic Disorders/ 12249
- 14 Panic Disorder/ 7237
- 15 Stress Disorders, Post-Traumatic/ 39852
- 16 Body Dysmorphic Disorders/ 1226
- 17 Obsessive-Compulsive Disorder/ 16142
- 18 or/1-17 355241
- 19 Depression/ 145419

20 (depression or depressive or depressed).tw. 509140

21 or/19-20 535264

22 18 or 21 742823

23 "beating the blues".af. 40

24 "365 health solutions".af. 0

25 cerina.af. 157

26 (NoSuffering or "no suffering").af. 20

27 iCT-PTSD.af.3

28 (internet adj2 "cognitive therapy for post traumatic stress disorder").tw.
0

29 iCT-SAD.af. 3

30 (internet adj2 "cognitive therapy for social anxiety disorder").tw. 4

31 OxCADAT.af. 3

32 "iona mind".af. 0

33 Minddistrict.af. 26

34 "mind district".af. 0

35 ("Get.ON" adj2 ("Mood Enhancer" or panic or depression)).af. 10

36 "Koa Health".af. 9

37 (Perspectives adj3 Koa).tw. 3

38 Resony.af. 0

39 "RCube health".af. 0

40 (SilverCloud or "silver cloud").af. 56

41 (space adj2 (anxiety or GAD or "health anxiety" or OCD or panic or phobia)).tw. 40

42 (space adj2 depression).tw. 31

43 Wysa.af. 13

44 Spring.af. and ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt").tw. 120

45 Deprexis.af. 50

46 ("Ethypharm digital" or "gaia group").af. 14

47 23 or 24 or 32 or 33 or 34 or 35 or 36 or 37 or 40 or 43 154

48 22 and 47 114

49 25 or 26 or 27 or 28 or 29 or 30 or 31 or 38 or 39 or 41 or 44 347

50 18 and 49 94

51 42 or 45 or 46 93

52 21 and 51 83

53 48 or 50 or 52 276

54 exp animals/ not humans.sh. 5069381

55 53 not 54 262

56 limit 55 to english language 247

Embase <1974 to 2022 November 22>

1 Anxiety/ 259704

2 anxiety disorder/ 89008

3 (anxiet* or anxious).tw. 355537

4 "generalized anxiety disorder*".tw. 13031

5 GAD.tw. 17664

6 "social anxiety disorder*".tw. 3983

7 phobia*.tw. 12794

8 "panic disorder*".tw. 13048

9 "posttraumatic stress disorder*".tw. 25731

10 PTSD.tw. 39557

11 "body dysmorphic disorder*".tw. 1677

12 "obsessive compulsive disorder*".tw. 20892

13 exp phobia/ 35341

14 panic/ 25681

15 posttraumatic stress disorder/ 74592

16 body dysmorphic disorder/ 3448

17 obsessive compulsive disorder/ 28550

18 generalized anxiety disorder/ 14076

19 social anxiety/ 729

20 or/1-19 555175

21 depression/ 446162

22 (depression or depressive or depressed).tw. 682442

23	or/21-22	816413	
24	20 or 23	1114339	
25	"beating the blues".af.	51	
26	"365 health solutions".af.	0	
27	cerina.af.	193	
28	(NoSuffering or "no suffering").af.	27	
29	iCT-PTSD.af.	2	
30	(internet adj2 "cognitive therapy for post traumatic stress disorder").tw.	0	
31	iCT-SAD.af.	2	
32	(internet adj2 "cognitive therapy for social anxiety disorder").tw.	4	
33	OxCADAT.af.	1	
34	"iona mind".af.	0	
35	Minddistrict.af.	8	
36	"mind district".af.	0	
37	("Get.ON" adj2 ("Mood Enhancer" or panic or depression)).af.	10	
38	"Koa Health".af.	10	
39	(Perspectives adj3 Koa).tw.	2	
40	Resony.af.	0	
41	"RCube health".af.	0	
42	(SilverCloud or "silver cloud").af.	70	

- 43 (space adj2 (anxiety or GAD or "health anxiety" or OCD or panic or phobia)).tw. 51
- 44 (space adj2 depression).tw. 30
- 45 Wysa.af. 3
- 46 Spring.af. and ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt").tw. 213
- 47 Deprexis.af. 60
- 48 ("Ethypharm digital" or "gaia group").af. 29
- 49 25 or 26 or 34 or 35 or 36 or 37 or 38 or 39 or 42 or 45 154
- 50 24 and 49 121
- 51 27 or 28 or 29 or 30 or 31 or 32 or 33 or 40 or 41 or 43 or 46 491
- 52 20 and 51 164
- 53 44 or 47 or 48 111
- 54 23 and 53 95
- 55 50 or 52 or 54 371
- 56 limit 55 to english language 362
-

APA PsycInfo <1806 to November Week 2 2022>

1	Anxiety/	72807
2	anxiety disorders/	20407
3	(anxiet* or anxious).tw.	240939
4	"generalized anxiety disorder*".tw.	9047
5	GAD.tw.	5555
6	"social anxiety disorder*".tw.	3921
7	phobia*.tw.	14047
8	"panic disorder*".tw.	11626
9	"post-traumatic stress disorder*".tw.	33157
10	PTSD.tw.	39717
11	"body dysmorphic disorder*".tw.	1543
12	"obsessive compulsive disorder*".tw.	18225
13	exp phobias/	14015
14	Panic Disorder/	7921
15	posttraumatic stress disorder/	38061
16	body dysmorphic disorder/	1313
17	obsessive compulsive disorder/	15535
18	generalized anxiety disorder/	3451
19	health anxiety/	633
20	social anxiety/	5730

21 or/1-20 309597

22 depression/ 26720

23 (depression or depressive or depressed).tw. 343507

24 or/22-23 344120

25 21 or 24 539329

26 "beating the blues".af. 76

27 "365 health solutions".af. 1

28 cerina.af. 33

29 (NoSuffering or "no suffering").af. 18

30 iCT-PTSD.af.0

31 (internet adj2 "cognitive therapy for post traumatic stress disorder").tw.
0

32 iCT-SAD.af. 1

33 (internet adj2 "cognitive therapy for social anxiety disorder").tw. 3

34 OxCADAT.af. 7

35 "iona mind".af. 0

36 Minddistrict.af. 4

37 "mind district".af. 0

38 ("Get.ON" adj2 ("Mood Enhancer" or panic or depression)).af. 20

39 "Koa Health".af. 2

40 (Perspectives adj3 Koa).tw. 1

41 Resony.af. 1

42	"RCube health".af.	0
43	(SilverCloud or "silver cloud").af.	23
44	(space adj2 (anxiety or GAD or "health anxiety" or OCD or panic or phobia)).tw.	54
45	(space adj2 depression).tw.	18
46	Wysa.af.	23
47	Spring.af. and ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt").tw.	335
48	Deprexis.af.	254
49	("Ethypharm digital" or "gaia group").af.	8
50	26 or 27 or 35 or 36 or 37 or 38 or 39 or 40 or 43 or 46	150
51	25 and 50	98
52	28 or 29 or 30 or 31 or 32 or 33 or 34 or 41 or 42 or 44 or 47	451
53	21 and 52	143
54	45 or 48 or 49	274
55	24 and 54	206
56	51 or 53 or 55	434
57	limit 56 to english language	398

Cochrane Library

- #1 MeSH descriptor: [Anxiety] explode all trees 9306
- #2 MeSH descriptor: [Anxiety Disorders] explode all trees 7991
- #3 (anxiet* or anxious) 68087
- #4 "generalised anxiety disorder*" OR "generalized anxiety disorder*" 3553
- #5 GAD 2999
- #6 "social anxiety disorder*" 1100
- #7 phobia* 2962
- #8 "panic disorder*" 2450
- #9 "posttraumatic stress disorder*" OR "post traumatic stress disorder*". 5971
- #10 PTSD 5518
- #11 "body dysmorphic disorder*" 161
- #12 "obsessive compulsive disorder*" 2939
- #13 MeSH descriptor: [Phobic Disorders] explode all trees 1477
- #14 MeSH descriptor: [Panic Disorder] explode all trees 989
- #15 MeSH descriptor: [Stress Disorders, Post-Traumatic] explode all trees 3190
- #16 MeSH descriptor: [Body Dysmorphic Disorders] explode all trees 81
- #17 MeSH descriptor: [Obsessive-Compulsive Disorder] explode all trees 1159

- #18 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 77725
- #19 MeSH descriptor: [Depression] explode all trees 14311
- #20 (depression or depressive or depressed)102081
- #21 #19 or #20 102081
- #22 #18 or #21 141056
- #23 "beating the blues" 47
- #24 "365 health solutions" 0
- #25 cerina 5
- #26 (NoSuffering or "no suffering") 141
- #27 iCT-PTSD 0
- #28 (internet NEAR/2 "cognitive therapy for post traumatic stress disorder")
0
- #29 iCT-SAD 0
- #30 (internet NEAR/2 "cognitive therapy for social anxiety disorder") 5
- #31 OxCADAT 1
- #32 "iona mind" 0
- #33 Minddistrict 4
- #34 "mind district" 0
- #35 ("Get.ON" NEAR/2 ("Mood Enhancer" or panic or depression)) 29
- #36 "Koa Health" 2
- #37 (Perspectives NEAR/3 Koa) 0

- #38 Resony 0
- #39 "RCube health" 0
- #40 (SilverCloud or "silver cloud") 12
- #41 wysa 3
- #42 Spring AND ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt")33
- #43 deprexis 58
- #44 ("Ethypharm digital" or "gaia group") 4
- #45 (space NEAR/2 (depression or anxiety or GAD or "health anxiety" or OCD or panic or phobia)) 18
- #46 #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 322
- #47 #22 and #46 241
- [152 in CENTRAL 89 in CDSR]

CRD

- 1 MeSH DESCRIPTOR anxiety EXPLODE ALL TREES 314
- 2 MeSH DESCRIPTOR Anxiety Disorders EXPLODE ALL TREES
380
- 3 ((anxiet* or anxious)) 1762
- 4 ("generalised anxiety disorder*") OR ("generalized anxiety disorder*")
95

- 5 (GAD) 32
- 6 ("social anxiety disorder*") 31
- 7 (phobia*) 95
- 8 ("panic disorder*") 121
- 9 ("posttraumatic stress disorder*") OR ("post traumatic stress disorder*")
182
- 10 (PTSD) 106
- 11 ("body dysmorphic disorder*") 6
- 12 ("obsessive compulsive disorder*") 119
- 13 MeSH DESCRIPTOR Phobic Disorders EXPLODE ALL TREES 47
- 14 MeSH DESCRIPTOR Panic Disorder EXPLODE ALL TREES 55
- 15 MeSH DESCRIPTOR Stress Disorders, Post-Traumatic EXPLODE
ALL TREES 139
- 16 MeSH DESCRIPTOR Body Dysmorphic Disorders EXPLODE 1 0
- 17 MeSH DESCRIPTOR Obsessive-Compulsive Disorder EXPLODE 1
57
- 18 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 2001
- 19 MeSH DESCRIPTOR Depression EXPLODE 1 639
- 20 ((depression or depressive or depressed)) 3049
- 21 #19 OR #20 3049
- 22 #18 OR #21 3937
- 23 ("beating the blues")7

- 24 ("365 health solutions") 0
- 25 (cerina) 0
- 26 (NoSuffering) OR ("no suffering") 0
- 27 (iCT-PTSD) 0
- 28 ((internet NEAR2 "cognitive therapy for post traumatic stress disorder")) 0
- 29 (iCT-SAD) 0
- 30 ((internet NEAR2 "cognitive therapy for social anxiety disorder")) 0
- 31 (OxCADAT) 0
- 32 ("iona mind") 0
- 33 (Minddistrict) 0
- 34 ("mind district") 0
- 35 (("Get.ON" adj2 ("Mood Enhancer" or panic or depression))) 0
- 36 ("Koa Health") 0
- 37 ((Perspectives NEAR3 Koa)) 0
- 38 (resony) 0
- 39 ("RCube health") 0
- 40 (silver cloud) OR ("silver cloud") 0
- 41 ((space NEAR2 (anxiety or GAD or "health anxiety" or OCD or panic or phobia))) 0
- 42 ((space NEAR2 depression)) 0
- 43 (wysa)0

- 44 (spring) AND ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt")) 1
- 45 (deprexis) 0
- 46 ("Ethypharm digital") OR ("gaia group"):TI 0
- 47 MeSH DESCRIPTOR Cognitive Behavioral Therapy EXPLODE ALL TREES 28
- 48 #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 36
- 49 #22 AND #48 20

INHATA

- 48 #47 AND #18 13
- 47 #46 OR #45 OR #44 OR #43 OR #42 OR #41 OR #40 OR #39 OR #38 OR #37 OR #36 OR #35 OR #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 106
- 46 "Ethypharm digital" or "gaia group" 0
- 45 Deprexis 0
- 44 (Spring) AND ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt")0
- 43 Wysa 0
- 42 (space) AND (depression)0

41 (space) AND (anxiety or GAD or "health anxiety" or OCD or panic or phobia) 2

40 SilverCloud or "silver cloud" 0

39 "RCube health" 0

38 Resony 0

37 (Koa) AND (Perspectives) 1

36 "Koa Health" 0

35 (Get.ON) AND ("Mood Enhancer" or panic or depression) 8

34 "mind district" 0

33 Minddistrict 0

32 "iona mind" 0

31 OxCADAT 0

30 iCT-SAD 0

29 (internet) AND (cognitive therapy for social anxiety disorder) 0

28 (internet) AND (cognitive therapy for post traumatic stress disorder) 1

27 iCT-PTSD 0

26 NoSuffering or "no suffering" 91

25 Cerina0

24 "365 health solutions" 0

23 "beating the blues" 3

22 #21 OR #18 576

21 #20 OR #19 418

20 depression or depressive or depressed 402

19 "Depression"[mh] 136

18 #17 OR #16 OR #15 OR #14 OR #13 OR #12 OR #11 OR #10 OR #9
OR #8 OR #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 286

17 "Phobia, Social"[mh] 1

16 "Obsessive-Compulsive Disorder"[mh] 8

15 "Panic Disorder"[mh] 5

14 "Stress Disorders, Post-Traumatic"[mh] 36

13 "Body Dysmorphic Disorders"[mh] 0

12 "obsessive compulsive disorder*" 12

11 "body dysmorphic disorder*" 1

10 PTSD 27

9 "post?traumatic stress disorder*" 27

8 "panic disorder*" 4

7 phobia* 11

6 "social anxiety disorder*" 2

5 GAD 4

4 "generalized anxiety disorder*" 0

3 anxiet* or anxious 223

2 "Anxiety Disorders"[mh] 42

1 "Anxiety"[mh] 72

ScHARRHUD

((“cognitive behaviour therapy” or “cognitive behavior therapy” or CBT) and (internet or digital))

CEA Registry

((“cognitive behaviour therapy” or “cognitive behavior therapy” or CBT) and (internet or digital))

PubMed

#28 Search: #4 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 313

#27 Search: (spring AND ("cognitive behavio* therap*" or cbt or dcbt or ccbt or icbt or "digital therapeutic*" or "digital cbt" or "online cbt" or "comput* cbt" or "internet cbt")) AND anxiety 35

#26 Search: "gaia group" 15

#25 Search: "ethypharm digital" 2

#24 Search: deprexis 52

#23 Search: wysa 13

#22 Search: "silver cloud" 3

#21 Search: silvercloud 67

#20 Search: "RCube health" 0

#19 Search: "RCube health" - Schema: all 0

- #18 Search: resony 0
- #17 Search: resony - Schema: all 0
- #16 Search: (perspectives[Title/Abstract] AND koa[Title/Abstract]) 10
- #15 Search: "koa health" 15
- #14 Search: minddistrict 53
- #13 Search: "iona mind" 2
- #12 Search: OxCADAT 3
- #11 Search: iCT-SAD 3
- #10 Search: iCT-PTSD 2
- #9 Search: nosuffering 0
- #8 Search: nosuffering - Schema: all 0
- #7 Search: cerina AND anxiety 2
- #6 Search: "365 health solutions" and (anxiety or depression) 9
- #4 Search: "beating the blues" and (anxiety or depression) 36

Epistemonikos

(title:(title:(("beating the blues" OR "365 health solutions" OR cerina OR nosuffering OR "no suffering" OR iCT-PTSD OR iCT-SAD OR OxCADAT OR deprexis OR "Ethypharm digital" OR "gaia group" OR minddistrict OR "mind district" OR "space from depression" OR "space from anxiety" OR silvercloud OR "silver cloud")) OR abstract:(("beating the blues" OR "365 health solutions" OR cerina OR nosuffering OR "no suffering" OR iCT-PTSD OR iCT-SAD OR OxCADAT OR deprexis OR "Ethypharm digital" OR "gaia group" OR minddistrict OR "mind district" OR "space from depression" OR "space from

anxiety" OR silvercloud OR "silver cloud")) OR abstract:((title:(("beating the blues" OR "365 health solutions" OR cerina OR nosuffering OR "no suffering" OR iCT-PTSD OR iCT-SAD OR OxCADAT OR deprexis OR "Ethypharm digital" OR "gaia group" OR minddistrict OR "mind district" OR "space from depression" OR "space from anxiety" OR silvercloud OR "silver cloud") OR abstract:(("beating the blues" OR "365 health solutions" OR cerina OR nosuffering OR "no suffering" OR iCT-PTSD OR iCT-SAD OR OxCADAT OR deprexis OR "Ethypharm digital" OR "gaia group" OR minddistrict OR "mind district" OR "space from depression" OR "space from anxiety" OR silvercloud OR "silver cloud")))) OR (title:(wysa OR "iona mind" OR "Get.ON" OR "koa health" OR "koa perspectives" OR resony OR "RCube health") OR abstract:(wysa OR "iona mind" OR "Get.ON" OR "koa health" OR "koa perspectives" OR resony OR "RCube health")) OR (title:(space AND (anxiety OR GAD OR "health anxiety" OR OCD OR panic OR phobia OR depression)) OR abstract:(space AND (anxiety OR GAD OR "health anxiety" OR OCD OR panic OR phobia OR depression))) OR (title:((internet OR spring) AND ("cognitive behaviour therapy" OR cbt OR dcbt OR ccbt OR icbt OR "digital therapeutic*" OR "digital cbt" OR "online cbt" OR "comput* cbt" OR wellmind OR "online mindfulness" OR "mindfulness course" OR "mindfulness based cognitive therapy" OR MBCT)) OR abstract:((internet OR spring) AND ("cognitive behaviour therapy" OR cbt OR dcbt OR ccbt OR icbt OR "digital therapeutic*" OR "digital cbt" OR "online cbt" OR "comput* cbt" OR wellmind OR "online mindfulness" OR "mindfulness course" OR "mindfulness based cognitive therapy" OR MBCT))) AND (title:(anxiety OR phobia OR panic OR "post tramatic stress disorder" OR PTSD OR "body dysmorphic disorder" OR "obsessive compulsive disorder") OR abstract:(anxiety OR phobia OR panic OR "post tramatic stress disorder" OR PTSD OR "body dysmorphic disorder" OR "obsessive compulsive disorder")) AND (title:(depression OR depressed OR depressive) OR abstract:(depression OR depressed OR depressive))

ClinicalTrials.gov

Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation
Studies

Search string	Results
beating the blues Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
BtB Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
365 health solutions Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
beating the blues Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	0
BtB Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	0
365 health solutions Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	0
cerina Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
cerina Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Obsessive-Compulsive Disorder	0
nosuffering Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
NoSuffering Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Obsessive-Compulsive Disorder	0

iona mind Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
iona mind Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	0
minddistrict Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0
minddistrict Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Obsessive-Compulsive Disorder	0
minddistrict Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Panic Disorder	0
minddistrict Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies	1
minddistrict Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	0
silvercloud Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	4
silvercloud Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	4
silvercloud Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies	0 additional relevant
Space from depression Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	2
wysa Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	3

wysa Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies	0 additional
wysa Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	3
koa Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	2
koa Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	2
koa health Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies	5
Deprexis Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies	1
Ethypharm Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	0
Gaia Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Depression	2
resony Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies anxiety	0
RCube Health Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies anxiety	0
iCT-PTSD Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies anxiety	0
iCT-PTSD Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Post Traumatic Stress Disorder	0

iCT-SAD Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies anxiety	0
Oxcadat Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies anxiety	0
spring Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation Studies Anxiety	0 relevant (12 total)

Completed, Suspended, Terminated, Withdrawn, Unknown status

Search string	Results
beating the blues Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	3
BtB Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	0 additional
365 health solutions Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	0
beating the blues Completed, Suspended, Terminated, Withdrawn, Unknown status Studies depression	0
BtB Completed, Suspended, Terminated, Withdrawn, Unknown status Studies depression	0
365 health solutions Completed, Suspended, Terminated, Withdrawn, Unknown status Studies depression	0
cerina Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0
cerina Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Obsessive-Compulsive Disorder	0

nosuffering Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0
nosuffering Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Obsessive-Compulsive Disorder	0
iona mind Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	0 relevant
iona mind Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	0 relevant
minddistrict Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	0
minddistrict Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Obsessive-Compulsive Disorder	0
minddistrict Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Panic Disorder	0
minddistrict Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	0
silvercloud Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	6
silvercloud Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	2 additional relevant
Space from depression Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	2 additional relevant (48 total)

wysa Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	2
wysa Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	0 additional
koa Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	0
koa Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	0
Deprexis Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	11
Ethypharm Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	0
Gaia Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Depression	0 additional relevant (4 total)
resony Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0
RCube Health Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0
iCT-PTSD Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0
iCT-PTSD Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Post Traumatic Stress Disorder	0
iCT-SAD Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0

Oxcadat Completed, Suspended, Terminated, Withdrawn, Unknown status Studies anxiety	0 relevant (1 total)
spring Completed, Suspended, Terminated, Withdrawn, Unknown status Studies Anxiety	0 relevant (22)
	26

ICTRP

“beating the blues” 18

365 health solutions 0

cerina 0

nosuffering or “no suffering” 0

iona 0

minddistrict or “mind district” 3

“Silver cloud” or silvercloud 17

“Space from depression” 6

Wysa 5

“koa health” or “koa mindset” or “koa perspectives” 2

Deprexis 17

Ethypharm AND depression 0

Gaia AND depression 3

Resony 0

“RCube Health” 0

iCT-PTSD 2
iCT-SAD 2
Oxcadat 0 relevant (1 total)

Economics searches

Ovid MEDLINE(R) ALL <1946 to November 28, 2022>

1 (computer or computerized or computerised or digital or online or internet\$ or app or apps).ti,ab. 726287

2 (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. 27053

3 1 and 2 3678

4 (dCBT or cCBT).ti,ab. 268

5 ((gaming or gamified or game format or video game\$) and (CBT or cCBT or dCBT or cognitive behavi\$)).ti,ab. 116

6 3 or 4 or 5 3793

7 Anxiety/ or Anxiety Disorders/ 133283

8 exp Depressive Disorder/ or Depression/ 249790

9 (anxiet\$ or anxious or low mood or depress\$).ti,ab. 662705

10 7 or 8 or 9 725340

11 6 and 10 2267

12 economics/ 27477

13 exp "costs and cost analysis"/ 261369

- 14 economics, dental/ 1920
- 15 exp "economics, hospital"/ 25651
- 16 economics, medical/ 9231
- 17 economics, nursing/4013
- 18 economics, pharmaceutical/ 3089
- 19 (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic\$).ti,ab. 990508
- 20 (expenditure\$ not energy).ti,ab. 35481
- 21 (value adj1 money).ti,ab. 40
- 22 budget\$.ti,ab. 34192
- 23 or/12-22 1152950
- 24 ((energy or oxygen) adj cost).ti,ab. 4644
- 25 (metabolic adj cost).ti,ab. 1655
- 26 ((energy or oxygen) adj expenditure).ti,ab. 28278
- 27 24 or 25 or 26 33534
- 28 23 not 27 1145212
- 29 letter.pt. 1200171
- 30 editorial.pt. 627878
- 31 historical article.pt. 368891
- 32 29 or 30 or 31 2175992
- 33 28 not 32 1105779
- 34 11 and 33 413

- 35 limit 34 to english language 408
- 36 limit 35 to yr="2022 - 2023" 40

Embase <1974 to 2022 November 28>

- 1 (computer or computerized or computerised or digital or online or internet\$ or app or apps).ti,ab. 931565
- 2 (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. 37848
- 3 1 and 2 4602
- 4 (dCBT or cCBT).ti,ab. 434
- 5 ((gaming or gamified or game format or video game\$) and (CBT or cCBT or dCBT or cognitive behavi\$)).ti,ab. 176
- 6 3 or 4 or 5 4853
- 7 anxiety/ or anxiety disorder/ 339946
- 8 depression/ 446921
- 9 (anxiet\$ or anxious or low mood or depress\$).ti,ab. 885019
- 10 7 or 8 or 9 1059530
- 11 6 and 10 2751
- 12 health-economics/ 34895
- 13 exp economic-evaluation/ 341870
- 14 exp health-care-cost/ 327275
- 15 exp pharmacoeconomics/ 223818

- 16 (expenditure\$ not energy).ti,ab. 47921
- 17 (value adj2 money).ti,ab. 2838
- 18 budget\$.ti,ab. 44957
- 19 or/12-18 775606
- 20 letter.pt. 1248380
- 21 editorial.pt. 744742
- 22 note.pt. 916306
- 23 20 or 21 or 22 2909428
- 24 19 not 23 656155
- 25 (metabolic adj cost).ti,ab. 1775
- 26 ((energy or oxygen) adj cost).ti,ab. 4899
- 27 ((energy or oxygen) adj expenditure).ti,ab. 35822
- 28 25 or 26 or 27 41313
- 29 24 not 28 655598
- 30 exp animal/ 29411432
- 31 exp animal-experiment/ 2928971
- 32 nonhuman/ 7111933
- 33 (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. 6273170
- 34 30 or 31 or 32 or 33 31572692
- 35 exp human/ 24374590
- 36 exp human-experiment/ 604085

37 35 or 36 24376819
38 34 not (34 and 37) 7196992
39 29 not 38 636636
40 11 and 39 264
41 limit 40 to (english language and yr="2022 -Current") 18

APA PsycInfo <1806 to November Week 3 2022>

1 (computer or computerized or computerised or digital or online or internet\$ or app or apps).ti,ab. 252712
2 (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. 37356
3 1 and 2 2924
4 (dCBT or cCBT).ti,ab. 206
5 ((gaming or gamified or game format or video game\$) and (CBT or cCBT or dCBT or cognitive behavi\$)).ti,ab. 129
6 3 or 4 or 5 3028
7 exp Anxiety/ or exp Anxiety Disorders/ 134889
8 exp "Depression (Emotion)"/ or exp Major Depression/177416
9 (anxiet\$ or anxious or low mood or depress\$).ti,ab. 473455
10 7 or 8 or 9 506849
11 6 and 10 1836
12 "costs and cost analysis"/ 18662

- 13 "Cost Containment"/699
- 14 (economic adj2 evaluation\$.ti,ab.2085
- 15 (economic adj2 analy\$.ti,ab. 1702
- 16 (economic adj2 (study or studies)).ti,ab. 926
- 17 (cost adj2 evaluation\$.ti,ab. 394
- 18 (cost adj2 analy\$.ti,ab. 4251
- 19 (cost adj2 (study or studies)).ti,ab. 996
- 20 (cost adj2 (effectiv\$ or benefit\$ or utili\$ or minimi\$ or consequence\$ or comparison\$ or identificat\$)).ti,ab. 22429
- 21 (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic\$.ti,ab. 243492
- 22 or/12-21 245661
- 23 (task adj2 cost\$.ti,ab,id. 769
- 24 (switch\$ adj2 cost\$.ti,ab,id. 1533
- 25 (metabolic adj cost).ti,ab,id. 112
- 26 ((energy or oxygen) adj cost).ti,ab,id. 309
- 27 ((energy or oxygen) adj expenditure).ti,ab,id. 2998
- 28 or/23-27 5405
- 29 (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. 378653
- 30 editorial.dt. 44328
- 31 letter.dt. 25566

- 32 dissertation abstract.pt. 541765
- 33 30 or 31 or 32 611659
- 34 22 not (28 or 29 or 33) 201241
- 35 11 and 34 263
- 36 limit 35 to (english language and yr="2022 -Current") 10

Appendix B: Excluded Studies

Where a technology had evidence available, the decision to include a study was based on criteria such as outcomes, comparators, sample size and setting. Studies were excluded if the outcomes were not relevant to the scope regardless of whether there was any alternative evidence. For technologies where the outcomes were relevant, inclusion was based on meeting one of the following criteria

- Comparator relevant to the scope
- Sample size <100
- Conducted in UK / IAPT service

Study	Technology	Reason for Exclusion
Beatty 2022	Wysa	The aim and outcomes of the study were not relevant to the scope.
Eilert 2022	SilverCloud	Outcomes were not considered to be within the scope of this review (use of CBT skills following completion of treatment)
Eilert 2022	SilverCloud	Outcomes were not considered to be within the scope of this review (follow-up on use of CBT skills following completion of treatment)
Enrique 2021	SilverCloud	Outcomes were not considered to be within the scope of this review (beliefs in rumination and emotion regulation and their impact on CBT use)
Lawler 2021	SilverCloud	N=15 Results for depression and anxiety cannot be separated
McMurchie 2013	Beating the Blues	Primary indication for use of technology is depression. Depression with co-morbid anxiety is included but EAG considered this not to be relevant to the anxiety

		topic.
Pittaway 2010	Beating the Blues	Outcomes were not considered to be within the scope of this review. N=50 across 3 groups,
Thew 2022	iCT-SAD	N=44, compared with waitlist control and not a UK based study