Digitally enabled therapies for adults with depression [MTG588]

Final protocol

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Date completed 01/09/2022

Declared competing interests of the authors None.

Acknowledgments The authors acknowledge the administrative support provided by Mrs Sue Whiffin and Ms Jenny Lowe (both PenTAG).

Medical Technologies Evaluation Programme

Final Protocol

November 2022

PROJECT TITLE

Digitally enabled therapies for adults with depression

1.1 Plain English Summary

This project assesses what evidence there is that digitally enabled therapies are effective and cost effective for adults with depression. Based upon the final scope, seven digitally enabled therapies will be compared with alternative options offered in Improving Access to Psychological Therapies (IAPT) services to adults with depression.

1.2 Decision Problem

1.2.1 Purpose

The topic has been identified by NICE for consideration for early value assessment (EVA). The objective of EVA is to identify promising technologies in health and social care where there is greatest need and enable earlier conditional access while informing further evidence generation. The evidence developed will demonstrate if the expected benefits of the technologies are realised and inform a final NICE evaluation and decision on the routine use of the technology in the NHS.

1.2.2 The interventions

Seven guided digital therapies were eligible for inclusion:

- Space from Depression (Silvercloud) – an online CBT programme for adults with low mood comprising 7 interactive modules. Can be supported or self-guided.

- Minddistrict (Minddistrict) – an app-based CBT programme with a catalogue of modules for all psychological and some physical health conditions. Can be self-help or therapist-guided. The IAPT depression module is suitable for adults with mild-to-moderate depression.
- Beating the Blues (365 Health Solutions Ltd) – an online CBT programme for adults with mild-to-moderate depression and anxiety. A combination of reading materials and practical hands-on tools.
- Deprexis (Ethypharm Digital Therapy) – an online programme based on elements of CBT to help those with unipolar depression or depressive disorders. Intended as a supplement to usual care. Ten modules on topics related to depression.
- Wysa (Wysa Ltd) –an artificial intelligence-based app for people with mild to moderate depression. Offers a collection of CBT-based self-help programmes designed to be used with professional human support.
- Iona Mind (Iona Mind) - an app-based CBT programme for people with depression or generalised anxiety disorder designed to be used alongside therapist support. It creates personalised support plans using guided exercises and tools to provide insight into patterns of thinking. It monitors mood and goal progression and has functionality to identify crisis events and provide signposting.
- Perspectives (Koa Health) - an app-based CBT programme for adults with depression designed to be used alongside therapist support. It includes a web-based admin portal that lets practitioners and therapists review a person's progress and allows messaging with health care providers between appointments

1.2.3 Care pathways

The NICE clinical guideline on depression in adults: treatment and management recommends the following factors should be taken into account when determining care pathways:

- assessment of need
- any physical health problems

- any coexisting mental health problems
- factors that would make the person most likely to engage with treatment
- previous treatment history
- barriers to the delivery of treatments because of any disabilities, language or communication difficulties

It is also recommended to match the treatment to individual needs and preferences and to use the least intrusive and most resource efficient treatment that is appropriate for individual clinical needs.

The following options are recommended for less severe depression:

- Guided self-help
- Group cognitive behavioural therapy (CBT)
- Group behavioural activation (BA)
- Individual CBT
- Individual BA
- Group exercise
- Group mindfulness and meditation
- Interpersonal psychotherapy
- Selective serotonin reuptake inhibitors
- Counselling
- Short-term psychodynamic psychotherapy

The following options are recommended for more severe depression:

- Combination of individual CBT and an antidepressant
- Individual CBT
- Individual BA
- Antidepressant medication
- Individual problem-solving
- Counselling
- Short-term psychodynamic psychotherapy
- Interpersonal psychotherapy
- Guided self-help
- Group exercise

Guided self-help is recommended as an option for treating less and more severe depression but should be the first option for less severe depression, while interventions with more therapist contact are likely to be preferred for more severe depression. Digital therapies may help address capacity and resource issues.

1.2.4 Population

The relevant population for this appraisal is adults aged 18 or over with depression.

1.2.5 Comparators

The relevant comparators for this appraisal are other treatments on the list recommended by NICE, as above, or waitlist control.

1.2.6 Outcomes to be examined

Intermediate measures for consideration may include:

- 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)
- Rates of attrition (drop-outs) and engagement

Clinical outcomes for consideration may include:

- Change in depression symptoms
- Change in other psychological symptoms
- Global functioning and work and social adjustment

Service level clinical outcomes:

- Rates of reliable recovery
- Rates of reliable improvement

- Rates of reliable deterioration
- Rates of relapse (including relapse rate and time from remission to relapse)

Patient-reported outcomes for consideration may include:

- Health-related quality of life
- Patient experience

1.2.7 Sub-groups to be examined

Subject to availability of appropriate evidence, the population will be split into subthreshold, mild, moderate and severe. A binary split between less severe and more severe depression was considered unfeasible as it was unlikely that clinical evidence would be aligned to these groups due to the NICE clinical guideline being recently updated.

1.3 Objective

The purpose of the Early Value Assessment is to summarise and critically appraise existing evidence on the clinical-effectiveness and cost-effectiveness of guided digital therapies for adults with depression. The following objectives are proposed:

1.3.1 Clinical Effectiveness

- Identify and assess evidence relating to the use and clinical effectiveness of the included technologies as it pertains to the scope
- For evidence not directly related to the scope, outline the potential generalisability and limitations of the evidence
- Report on any potential safety issues
- Report the evidence gaps, highlighting what data may need to be collected to inform these gaps

*1.3.2 **Cost Effectiveness***

- Identify and assess economic evidence relating to the use of the included technologies within the scope
- Develop a conceptual economic model, related to the scope, that can be used to inform future research and data collection
- Report available model inputs and evidence gaps
- Report on the technology costs and use modelling with available inputs to estimate the plausibility of cost effectiveness

1.4 Methods of synthesis of evidence of clinical effectiveness

The review will be undertaken following the general principles published by the NHS Centre for Reviews and Dissemination.

1.5 Search strategy

Refer to Appendix 1 for the draft search strategy for MEDLINE.

Searches will be conducted jointly for adults with depression and for anxiety disorders, in conjunction with Cedar.

The search strategy will comprise the following main elements:

- Searching of electronic databases, including MEDLINE, Pre-Medline, EMBASE and Cochrane
- Scrutiny of bibliographies of included studies
- Contact with experts in the field
- Searching of major conference proceedings
- Economics sources such as NHS EED, ScHARR HUD and CEA Registry
- Current research will be identified through searching the WHO International Clinical Trials Registry Platform (ICTRP) and the US National Library of Medicines registry at clinicaltrials.gov.

- MHRA field safety notices and the MAUDE database will be searched for adverse events.
- In addition, any industry submissions to NICE, as well as any relevant systematic reviews identified by the search strategy, will be scrutinised in order to identify additional relevant studies. Study selection criteria and procedures

1.5.1 Types of study to be included

This assessment will look across a range of evidence types including RCTs, real world evidence and benchmarking against NHS Digital published metrics. Evidence considered will include evidence of clinical effectiveness.

1.5.2 Types of study to be excluded

- Animal models
- Pre-clinical and biological studies
- Narrative reviews, editorials, opinions
- Reports published as meeting abstracts only, where insufficient methodological details are reported to assess the study and its outcomes. . Information provided by the companies that is considered relevant will be considered regardless
- Studies not available in the English language.

1.5.3 Study selection

The abstracts and titles of references retrieved by the electronic searches will be screened for relevance. Full paper copies of potentially relevant studies will be obtained. The retrieved articles will be assessed for inclusion by one reviewer and a minimum of 10% will be independently checked by a second, using the pre-specified inclusion/exclusion criteria. Discrepancies will be resolved by discussion, with involvement of a third reviewer, where necessary. All duplicate papers will be double checked and excluded.

1.5.4 Quality assessment strategy

The quality of individual studies will be assessed by one reviewer and checked by a second reviewer. Any disagreement will be resolved by consensus and if necessary a third reviewer will arbitrate.

The quality of the clinical effectiveness studies will be assessed using the Cochrane Risk of Bias tool for the appropriate study design.

1.5.5 Data extraction strategy

Data will be extracted from included studies by one reviewer into a bespoke database and checked by another reviewer. Key sources of risk of bias will be discussed. The generalisability of findings to clinical practice in the NHS will be considered. Discrepancies will be resolved by discussion, with the involvement of a third reviewer if necessary.

1.5.6 Methods of analysis / synthesis

Data will be tabulated and discussed in a narrative review. Where appropriate, meta-analysis will be employed to estimate summary measures of effect on relevant outcomes, based on intention to treat analyses. It is not expected that this will be possible for this EVA.

1.6 EAG team economic evaluation

The Evidence Assessment Group (EAG) team will endeavour to perform an independent early economic evaluation from the perspective of the UK NHS and PSS, consistent with the methods recommended in the NICE reference case. Any deviation from the NICE reference case will be identified and discussed as appropriate.

1.6.1 Systematic review of cost effectiveness studies

A systematic review of economic evaluations of eligible interventions in the treatment of adults with depression will be conducted as part of the searches described in section

1.5 above. Full economic evaluations will be included where they meet the inclusion criteria set out for the review of clinical effectiveness (see section □).

Methods and findings from included economic evaluations will be summarised in a tabular format and synthesised in a narrative review. Economic evaluations carried out from the perspective of the UK NHS and Personal Social Services (PSS) perspective will be presented in greater detail.

1.6.2 Systematic literature search for other data related to cost effectiveness

A targeted search of the broader literature on adult depression will be undertaken to identify the evidence base on HRQoL (i.e. health state utility values), resource use and costs for treatment and side-effects (UK studies only if available), and the methods available for the modelling of depression to inform cost-effectiveness analyses. The search strategies employed will be reported, and findings from these explorative searches will be presented in summary format, using a tabular approach and narrative text.

1.6.3 Economic modelling

If data allows, an economic model will be constructed either by adapting an existing model (such as the model developed for MT580 guided self-help dCBT for children and young people with anxiety or low mood) or developing a new model using available evidence and following guidance on good practice in decision analytic modelling for HTA.

The structure of any model will be determined on the basis of research evidence and clinical expert advice about:

- Appropriate assumptions to make where no suitable data is identified for effectiveness for some of the interventions:
- Appropriate assumptions to make if there are data gaps in the information available to populate resource use or quality of life information per health state

All assumptions applied in the modelling framework will be clearly stated. All data inputs and their source will be clearly identified.

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

- Costs of the technologies
- Cost of other resource use (e.g., associated with managing depression, adverse events, or complications):
    - GP or IAPT appointments
    - Medication
    - Healthcare professional grade and time

Where appropriate and if data allow, sensitivity analyses will be undertaken to explore uncertainty. These may include one-way and multi-way sensitivity analyses, use of probabilistic sensitivity analyses (PSA) and value of information analyses where modelling permits. The use of PSA involves sampling of parameter inputs from distributions that characterise uncertainty in the mean estimate of the parameter. PSA is used to characterise uncertainty in a range of parameter inputs simultaneously, to consider the combined implications of uncertainty in parameters. Value of Information analysis helps identify where future research can be most efficiently targeted to reduce uncertainty.

Where probabilistic modelling is undertaken, results will be presented using the cost effectiveness plane, and cost effectiveness acceptability curves/frontier (CEACs/CEAF).

1.7 Gap Analysis

Evidence gaps identified pertaining to the intermediate and final outcomes from the scope and those pertaining to the economic modelling will be summarised in tabular and narrative form. If appropriate, a ‘traffic light’ scheme will be used to highlight relative importance of the gap. Key areas for evidence generation will be summarised in tabular form.

1.8 Handling the company submissions

If the data meet the inclusion criteria for the review they will be extracted and quality assessed in accordance with the procedures outlined in this protocol. Data provided

(e.g. cost and resource use data) will be assessed against NICE's manual (2022), reasonableness of assumptions made and appropriateness of the data used.

Any academic or commercial in confidence data taken from a company submission will be underlined and highlighted as appropriate in the report.

1.9 Additional considerations

This EVA forms one of a pair being conducted in parallel – the anxiety review is being conducted by Cedar. Searches will be conducted in collaboration across the two institutions. Screening and analysis will then be conducted separately, although checking will be conducted by members of the other team.

1.10 Competing interests of authors

None.

Appendix 1 Sample Search Strategy

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

1	Anxiety/	102027
2	anxiety disorders/	39925
3	(anxiet* or anxious).tw.	252620
4	"generali?ed anxiety disorder*".tw.	9697
5	GAD.tw.	11873
6	"social anxiety disorder*".tw.	3217
7	phobia*.tw.	9537
8	"panic disorder*".tw.	10038
9	"post?traumatic 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 "Koa Health".af. 9

36 (Perspectives adj3 Koa).tw. 3

37 Resony.af. 0

38 "RCube health".af. 0

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

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

41 (space adj2 depression).tw. 31

42 Wysa.af. 13

43 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

44 Deprexis.af. 50

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

46 23 or 24 or 32 or 33 or 34 or 35 or 36 or 39 or 42 144

47 22 and 46 104

48	25 or 26 or 27 or 28 or 29 or 30 or 31 or 37 or 38 or 40 or 43	347
49	18 and 48	94
50	41 or 44 or 45	93
51	21 and 50	83
52	47 or 49 or 51	266
53	exp animals/ not humans.sh.	5069381
54	52 not 53	252
55	limit 54 to english language	237