

# Clinician-guided internet-based psychotherapy compared with face-to-face therapy for people with anxiety or depression

## What were we asked to look at?

NHS Education for Scotland (NES) asked us to review the published evidence on the effectiveness, cost-effectiveness, safety and acceptability of clinician-guided internet-based psychotherapeutic interventions compared with in-person, face-to-face individual or group psychotherapeutic interventions for adult patients with depression or anxiety disorders.

## Why is this important?

This report will support an update of the [NES matrix of psychological therapies](#) commissioned in NHS Scotland. Depression and anxiety disorders are common and it is likely that there have been rapid advances in interactive technologies and changes in digital skills in society since the NES Matrix was published in 2015.

## What was our approach?

An abbreviated SHTG Assessment was undertaken with limited critical appraisal and without peer review.

## What next?

This assessment will inform a comprehensive review process around delivery and demand for psychological therapies which is being undertaken by NES.

## Key findings

Based on a very limited evidence base around CBT it appears that guided internet psychotherapy provides similar outcomes to face-to-face treatment and is acceptable to many patients with depression or anxiety disorders.

Cost-effectiveness estimates vary widely and are limited by a lack of robust input data, many of which vary according to local service delivery parameters.

## Clinical effectiveness

- There is a limited evidence base which suggests that, in the short term, the two modes of delivering cognitive behaviour therapy (guided internet psychotherapy and face-to-face psychotherapy) are similarly effective in improving symptoms of anxiety and depression.
- The evidence base included fewer than ten randomised controlled trials directly comparing guided internet psychotherapy with face-to-face psychotherapy for people with mild to moderate depression or anxiety.
- Trials typically have fewer than 50 participants in each arm and are heterogeneous with respect to participant inclusion criteria, specific psychotherapy used, and the expertise, format, duration and intensity of therapist input. A wide range of outcome measures are used to assess symptoms and symptom change.
- Studies focus on cognitive behaviour therapy (CBT) and recruit participants (mostly from the community rather than clinical settings) who are willing to undergo both face-to-face and internet treatment. These participants may be both more educated and more motivated than the general patient population, and may have less complex conditions.
- Larger non-inferiority trials in clinical populations are required to provide more certainty around this, as are trials examining longer-term recovery.

## Safety

- Safety outcomes are rarely addressed in trials. Individual patient data meta-analyses of people receiving internet-based psychotherapy suggest that the risk for clinical deterioration is greater in people with a low education level.

### Cost effectiveness

- A Canadian HTA which included systematic reviews, primary analyses and a de-novo cost effectiveness model concluded that, for people with major depression and anxiety disorders, guided internet CBT (iCBT) may represent an economically attractive option when used as a one-time, non-repetitive short-term treatment or when combined with face-to-face CBT over a long-term time horizon.
- A predictive model set in Germany found that guided iCBT has the potential to reduce waiting times for patients with depression and increase service capacity without necessarily increasing costs.

### Patient and social aspects

- Participants allocated to face-to-face therapy are more likely to complete all sessions when compared with those allocated to iCBT.
- Experiences of iCBT and face-to-face CBT vary widely according to the expectations and circumstances of participants. The impact of specific anxiety or depression symptoms on factors such as motivation, concentration and ability to travel may influence preferences. Where iCBT is preferred, this may be associated with the flexibility, convenience and accessibility offered, whilst the personalised and collaborative relationship in face-to-face intervention may be more important to others.

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## Research question

The parameters of the research question are outlined in table 1.

Table 1: Parameters of the research question

Patients	Diagnosed with depression and/or anxiety disorders  Depression: include major depressive disorder (MDD), recurrent, chronic and persistent (old/new terms), dysthymia.  Anxiety: generalised anxiety disorder, panic disorder, agoraphobia, social anxiety disorder, specific phobias, obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD) and health anxiety
Intervention	Internet therapy with clinician input (guided) [exclude self-guided, and blended interventions]
Comparators	Face-to-face individual or group interventions
Outcomes	Any validated measures related to the diagnoses for example Patient Health Questionnaire (PHQ9), Hospital Anxiety and Depression Scale (HADS), General Anxiety Disorder-7 (GAD7), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI).
Study methodologies	Systematic reviews Meta-analyses

## Literature search

A systematic search of the secondary and primary literature was carried out between 15 September 2020 and 24 September 2020 to identify systematic reviews, health technology assessments and other evidence based reports. Medline, Embase, PsycInfo and Web of Science Core Collection databases were searched. Results were limited to English language and 2015 onwards.

Key websites were searched for guidelines, policy documents, clinical summaries, economic studies and patient issues material. Concepts used in all searches included: remote, digital, online, internet, telephone, mobile, technology, telemedicine, telehealth/depression, anxiety, PTSD, OCD, trauma, panic / therapy, therapies. A full list of resources searched and terms used is available on request.

## Health technology description

A systematic literature review of electronic mental health interventions for major depressive disorder found that most interventions deliver cognitive behaviour therapy (CBT) techniques via the internet.<sup>1</sup> The review describes a typical electronic mental health intervention as:

“A prototypical system takes a CBT approach and might comprise six modules, one of which is released every week. The modules can be accessed on a website. The participant is made aware of the presence of a new module via email; thus, the participant is reminded to adhere to the treatment. Modules might cover topics such as activity scheduling, learning to detect automatic thoughts, cognitive restructuring, problem solving, psychoeducation concerning depression and the therapeutic approach, and relapse prevention. Each module comes with exercises that are submitted to be checked by a therapist or similar, who again provides feedback via email. The website might include a small calendar application for the purposes of activity scheduling and a diary application for the purposes of thought recording. In these applications, the user can enter and save information. Once a week, the participant is asked to complete a depression scale, and the therapist is notified if suicidal ideation is detected. The remaining questions are averaged and presented to the user as a mood graph on the landing page.”<sup>1</sup>

Example systems include; Living Life to the Full, Beating the Blues, Deprexis, MoodGYM and Help4Mood.

A systematic review comparing internet CBT (iCBT) with face-to-face CBT for anxiety and depression disorders<sup>2</sup> found that therapists spent 7.8 times (standard deviation (SD) 4.5) more time on face-to-face CBT participants than on iCBT participants. There is heterogeneity around how this therapist time is allocated, for example across a mix of email, telephone or text message support.

Blended programmes, which include some face-to-face sessions alongside internet delivered therapy, are excluded from this assessment.

## Clinical effectiveness

A number of important factors should be considered when comparing guided internet therapy with face-to-face therapy. Limitations with the evidence base include:

- variation in the definitions of, and terminology used to describe, both internet therapy and face-to-face therapy
- heterogeneity in features such as number of modules, level of training of those guiding therapy, availability and duration of therapeutic contact and frequency of support
- wide variation in outcome measures used to assess effectiveness, including Hamilton Rating Scale for Depression (HAM-D), Beck Depression Inventory (BDI), Montgomery Asberg Depression Rating Scale—Self-rated (MARDSS), Generalised Anxiety Disorder 7 (GAD 7), Social Phobia Inventory (SPIN), and the Panic Disorder Severity Rating Scale
- many reviews did not distinguish between guided and unguided internet therapy
- reviews frequently combined studies on people with a range of diagnoses and/or mental health symptoms and somatic conditions
- reviews varied as to whether community based, clinical or mixed populations were included
- controlling or adjusting for the use of pharmacological agents was inconsistent
- the clinical significance of statistically significant findings was rarely explored.

Participant selection bias within primary studies should also be taken into account; people who volunteer to take part in studies may be particularly comfortable with internet programmes and not be representative of the general population. There may also be bias in outcome assessment since, for many studies, outcomes are either self-rated or measured by an assessor not blinded to treatment assignment. Blinding of study participants to delivery format is not possible.

The authors of included trials conduct many of the systematic reviews for this topic area. This has the potential to influence their assessment of evidence quality.<sup>3</sup>

## Systematic reviews

### Depression

A comprehensive HTA from Canada examined systematic reviews published prior to February 2018 on the effectiveness of iCBT for adults diagnosed with mild to moderate

major depression.<sup>4</sup> One of the stated comparators of interest was face-to-face CBT. Within the systematic reviews included in the HTA, no trials compared guided iCBT with face-to-face CBT (individual or group). In July 2018, an evidence rapid response was produced to supplement the HTA which examined evidence from primary studies published more recently than the systematic reviews included in the full HTA.<sup>5</sup> No data were available comparing guided iCBT to traditional face-to-face CBT (individual or group format).

Another Canadian rapid response<sup>6</sup> identified a systematic review which conducted a meta-analysis of two studies and found iCBT to have an equivalent effect on post-treatment depressive symptoms when compared with face-to-face CBT ( $g = 0.06$ , 95% CI  $-0.67$  to  $0.79$ ,  $p$  value not reported).<sup>7</sup> The systematic review did not present an appraisal of study quality nor provide data on excluded studies.

A systematic review with a literature search up to February 2017 identified four studies comparing guided (any therapist input) iCBT with face-to-face CBT (including one trial using acceptance and commitment therapy (ACT) in people with depressive symptoms)<sup>8</sup>. The pooled between-group effect size in the four studies targeting depressive symptoms post-treatment (BDI, MADRSS at 6-10 weeks) was  $g=0.02$  (95% CI  $-0.22$  to  $0.19$ ) indicating no evidence of a statistically significant difference. Long-term effects were not examined due to variations in follow-up periods that ranged from three months to three years. All of the trials were in self-referred community populations rather than clinical populations. Two of the trials were designed to assess non-inferiority. One compared iCBT with individual face-to-face CBT ( $n=62$ ) and one with group CBT ( $n=69$ )<sup>9,10</sup>. Both these small trials concluded that guided internet CBT is at least as effective as face-to-face treatment.

A network meta-analysis (NMA) compared the effectiveness of CBT therapy delivery formats in adults with depression.<sup>11</sup> Five delivery formats (guided self-help, unguided self-help, telephone, individual and group) were compared with two control conditions (wait list and care as usual). Of the 155 studies included in the analysis, only seven studies involved direct comparison of guided self-help with individual or group CBT (nine comparisons). Participants were recruited from the community rather than from clinical settings and four of the studies investigated bibliotherapy or psychoeducation interventions rather than internet (two studies) or computer-based (one study) CBT. A sensitivity analysis excluding non-internet based studies mirrored the findings of the main analyses with individual, group, guided self-help, and telephone CBT being statistically significantly more effective than care as usual, waiting list, and unguided self-help. When comparing internet guided self-help with individual therapy no statistically significant difference was identified; standardised mean difference (SMD)  $0.22$ , (95% CI  $-0.08$  to  $0.52$ ). There was no corresponding direct pairwise comparison. There was a small but statistically significant superiority of group CBT compared with internet guided self-help; SMD  $0.37$ , (95% CI  $0.08$  to  $0.66$ ). This finding was not consistent with the direct pairwise meta-analysis of the two small ( $n=69$  and  $n=62$ ) included studies (SMD  $0.20$ , 95% CI  $-0.17$  to  $0.56$ ), so the finding should be treated with

caution. One of the studies was incorrectly classified as group face-to-face delivery rather than individual and it is unclear what effect this had on the analysis.

## Anxiety

An HTA from Canada examined systematic reviews published prior to February 2018 on the effectiveness of iCBT in adults diagnosed with anxiety disorders.<sup>4</sup> The following were excluded: studies of people with drug or alcohol dependence-anxiety, obsessive compulsive disorder, post-traumatic stress disorder and anxiety comorbid with physical disorders. Two overlapping systematic reviews were included.<sup>3, 12</sup>

Based on three randomised controlled trials (total n=248) in one of the systematic reviews<sup>12</sup> included in the HTA, there was no statistically significant difference in symptoms of panic disorder for participants who had undergone iCBT compared with those who had undergone face-to-face CBT (SMD=0.06, 95% CI -0.19 to 0.31, p=0.64). The systematic review authors described the strength of evidence as moderate according to a system based on GRADE (Grading of Recommendations, Assessment, Development and Evaluations).

In the other systematic review,<sup>3</sup> for people with panic disorder, one trial found no difference in symptoms between guided iCBT and live group CBT (non-inferiority not established). A second trial reported no difference in symptoms between guided iCBT and live individual CBT, but was not designed as a non-inferiority trial and the small sample size (n=30) limits the inferences that can be made. For social phobia, the systematic review identified one RCT which reported a statistically significant symptom benefit favouring participants who received iCBT (that included therapist support) compared with group face-to-face CBT (d=0.41, 95% CI 0.03 to 0.78). The systematic review authors rated the strength of evidence as low or very low according to GRADE.

A subsequent rapid response, conducted in July 2018, to supplement the HTA examined evidence from primary studies published more recently than the systematic reviews included in the full HTA.<sup>5</sup> No additional data was identified comparing guided iCBT to traditional face-to-face CBT (individual or group format).

A Cochrane systematic review (with literature search to September 2014) compared therapist-supported iCBT with face-to-face CBT for anxiety disorders in adults.<sup>13</sup> There was no statistically significant difference between the two methods of delivery for clinically important improvements in anxiety (by a standardised interview or clinically accepted measure cut-off score) or anxiety symptom severity (for example Panic Disorder Severity Rating Scale, Social Phobia Inventory) at the end of treatment (four studies) or at follow up (three studies). This is consistent with a more recent systematic review incorporating the

same studies, which included self-referred or mixed community and clinical populations.<sup>8</sup> The review found a small difference between groups favouring iCBT for quality of life post-treatment (SMD=0.26, 95% CI 0.06 to 0.45,) and at follow up (SMD=0.33, 95%CI 0.11 to 0.55). Evidence quality was assessed as low to moderate according to GRADE. Whilst the results suggest that therapist-supported iCBT may not be significantly different from face-to-face individual CBT in treating anxiety disorders, only one of the included studies was designed to assess non-inferiority.

One additional systematic review found that, although symptoms of panic disorder were not statistically significantly different when comparing iCBT with face-to-face CBT (three studies) for agoraphobia symptoms, there was some indication in favour of iCBT ( $g=0.38$ , 95% CI 0.03 to 0.73,  $p=0.03$ ).<sup>14</sup> The review is based on only two studies and so the findings should be treated with caution.

### Post-traumatic stress disorder

A Cochrane systematic review of internet-based cognitive and behavioural therapies for people with post-traumatic stress disorder (PTSD) identified ten studies up to March 2018.<sup>15</sup> No studies compared iCBT with face-to-face group or individual CBT or face-to-face non-CBT. A Canadian HTA updated the Cochrane systematic review to June 2019 and did not identify relevant new evidence for this comparison.<sup>16</sup>

### Obsessive compulsive disorder

Across the systematic reviews examined for this assessment, no directly relevant trials were identified for people with OCD. An ongoing randomised non-inferiority trial in this patient group is due to complete in January 2021 ([NCT02541968](#)).

## Safety

Safety outcome evidence is drawn from a 2018 Norwegian HTA on therapist-supported internet therapy for mental disorders (translated)<sup>17</sup>.

A systematic review specifically sought data on harms or negative effects experienced by participants in studies of internet-delivered therapy for anxiety and depression disorders. In a literature search for all study types up to February 2016, no studies were identified<sup>2</sup>.

Two individual patient data (IPD) meta-analyses were identified which provided information on rates of deterioration in people receiving internet therapies. In the majority of included

studies, the comparator was wait list or treatment as usual, so the relevance of this to comparisons with face-to-face therapy is unclear.

One IPD meta-analysis examined exacerbation of depressive symptoms in RCTs of internet-based guided self-help up to January 2014 (18 studies, 21 comparisons, 2,079 participants).<sup>18</sup> Only studies with therapist guidance were included, and all comparators including wait list and usual care were included. Most of the studies were on CBT or problem solving therapy, one study involved psychodynamic therapy, and one looked at acceptance and commitment therapy. The risk of experiencing exacerbation from baseline to end of intervention was lower in the internet-guided group than in the control group (3.36% compared with 7.60%, relative risk (RR) 0.47 (95% CI 0.29 to 0.75)). The educational level of participants was a moderating factor. Patients with a lower level of education displayed a greater risk for deterioration than patients with higher educational level.

Another IPD also examined deterioration and moderating factors in participants undergoing internet treatment with CBT compared with control conditions.<sup>19</sup> Data from 2,866 participants across 29 studies found that deterioration rates (as measured using the reliable change index) were 5.8% (n=122) for internet CBT compared with 17.4% (n=130) in control conditions. Higher symptom level before treatment was associated with a lower risk of exacerbation in both the intervention groups (odds ratio (OR) 0.62, 95% CI 0.50 to 0.77, p = 0.00) and the control groups (OR 0.51, 95% CI 0.51 to 0.80, p = 0.00).

A consensus statement provided recommendations for identifying, classifying and measuring negative effects in research on internet delivery of psychotherapeutic interventions compared with face-to-face delivery.<sup>20</sup>

## Patient and social aspects

### Acceptability

The acceptability of internet therapy is assessed using a range of measures. Indirect measures include take-up rates, adherence or completion rates, and direct measures include questionnaires, focus groups or qualitative interviews to measure satisfaction rates and explore experiences and preferences.<sup>21</sup>

### Quantitative studies

A NMA of 155 studies compared the acceptability (defined as rate of study drop-out at any time and for any reason) of CBT therapy delivery formats in adults with depression. Guided self-help was statistically significantly less acceptable than individual (relative risk of drop out, RR=1.44; 95% CI, 1.09-1.89) and group (RR of drop out=1.38; 95% CI, 1.06-1.80) CBT.

Findings remained consistent in sensitivity analysis excluding studies of non-internet based guided self-help. The NMA authors suggest that the reduced personal contact may make it easier for participants to disengage.

A meta-analysis identified by a Canadian HTA as a reference source for an economic evaluation provided comparative data on adherence to face-to-face individual CBT (14 studies) and guided iCBT (12 studies) in trials with participants with depression recruited from community settings.<sup>22</sup> A major limitation of the analysis was that none of the trials directly compared the two modes of CBT delivery. Face-to-face CBT ranged in length from 12 to 28 sessions and iCBT ranged from five to ten sessions. Three measures of adherence were analysed; proportion of sessions completed, proportion of participants completing all sessions and proportion of participants completing 80% or more of the allocated sessions. The findings are set out in table 2. The level of heterogeneity was high for all comparisons.

There was no statistically significant difference between the interventions in the proportion of allocated sessions completed, although statistically significantly fewer of those allocated to guided iCBT fully completed their treatment or completed over 80% of their treatment.

Table 2: Adherence to face-to-face CBT and iCBT<sup>22</sup>

	Guided iCBT	Face-to-face CBT	p	I <sup>2</sup>
	% (95% CI)	% (95% CI)		
Proportion of sessions completed	80.8% (73.0% to 88.7%)	83.9% (75.7% to 92.1%)	0.59	86.5%
Number of study groups participating	8 groups	7 groups		
Completers (100%)	65.1% (55.3% to 73.8%)	84.7% (78.0% to 89.6%)	<0.001	78.4%
Number of study groups participating	9 groups	11 groups		
Completers (≥80%)	67.5% (56.8% to 76.6%)	85.2% (78.1% to 90.4%)	0.003	79.3%
Number of study groups participating	9 groups	11 groups		

A systematic review of computer therapy for anxiety and depression disorders identified 50 trials where data on adherence to iCBT was measured.<sup>2</sup> Adherence was defined as the proportion of participants who finished the course. The median adherence was 66% (interquartile range 52% to 80%). Across 24 trials that measured patient satisfaction the proportion of people reporting being satisfied or very satisfied was 86% (range 62% to 100%). There was a wide range of comparators in the review so the applicability of these data to the comparison with face-to-face intervention is limited.

### Qualitative studies

A qualitative synthesis explored the acceptability and usability of digital health interventions (DHIs) for adults with depression, anxiety, and somatoform disorders.<sup>23</sup> The majority of the included studies 19/24 (79%) involved treatment according to CBT principles and the same proportion involved some form of support. The meta-synthesis generated three main themes: initial motivations and approaches; personalisation of treatment; and the value of personal support. The meta-synthesis highlighted variability within individuals' experiences of DHIs depending on expectations, attitudes and preferences. Usability can be influenced by the degree of personalisation and extent of responsive support offered.

Digital interventions were perceived to be helpful in increasing accessibility, flexibility and choice, though some people had negative expectations around whether a therapeutic relationship could be established through a computer-based intervention. There was a difference in approach between participants who found the intervention difficult, stressful, impersonal and isolating, and those who expressed a sense of obligation to complete the therapy. The former preferred face-to-face sessions. The value of the treatment was linked to the degree to which the interventions were personalised to the needs of the participants. For some, the accessibility and flexibility around time and place was valued, whilst for others the lack of structure and protected time led to disengagement. Similarly, for some, the privacy was helpful and led to reduced stigma and perceived judgement, whilst for others the lack of a private space away from home was a downside. Participants who engaged with DHIs were surprised at how quickly a relationship could be formed remotely with a person and sometimes likened the DHI to a face-to-face session. For those who did not engage, the lack of face-to-face contact felt cold and unfriendly and the use of written communication with time delays between responses was unwelcomed. Technical competence was only a potential barrier in three studies in the synthesis.

A systematic review (incorporating studies overlapping with the qualitative synthesis) identified 24 studies with qualitative data addressing the experiences of iCBT (guided and unguided) in people with depression and anxiety disorders.<sup>24</sup> A wide range of qualitative approaches were used including focus groups, questionnaires, and face-to-face interviews,

and there was variation in methodological quality and the depth to which data analysis was explored. Many of the findings related to CBT in general rather than relating to the mode of receipt of the therapy, for example, perceived benefits such as improved mood and wellbeing, greater recognition of thought patterns, and better understanding and acceptance of one's condition. Some experiences were related to the use of the technology, for example the need for improved responsiveness to patients and greater or more consistent therapist input. Issues around problems with the iCBT platform, such as passwords and difficulty saving work/losing data led to frustration and confusion in some study participants. An affinity for iCBT in those who are private or reserved was highlighted, as was the appeal for people who did not want to or were unable to attend face-to-face therapy. The disinhibiting effect of not being seen in person was for some a benefit. For some respondents face-to-face therapy was preferred or desired in that they found iCBT more superficial, less intensive and less helpful. Several papers noted risk with iCBT for some individuals based on the severity of their condition, for example heightened risk for patients engaging in iCBT during severe symptomatic episodes. Issues around time, rurality or remoteness, and stigma were identified as reasons for preferring iCBT even if face-to-face treatment was available. The overall summary from this review of a wide spectrum of experiences highlighted the need for tailoring interventions flexibly to fit with individual patient need, learning style, circumstances, and preference.

## Cost effectiveness

A 2018 Canadian HTA identified nine systematic reviews on the cost-effectiveness of iCBT, spanning mixed study populations and a range of controls.<sup>4</sup> Most reviews suggested that iCBT could represent an economically viable treatment alternative over control. There was large variability in cost-effectiveness estimates across these reviews. One review that included individual-level participant data and conducted a meta-analysis, did not find guided iCBT to be a cost-effective option compared with control.

The HTA authors conducted their own systematic review of 29 studies, the findings of which are summarised in table 3. The authors concluded that guided iCBT probably offered good value for money for the short-term management of mild to moderate major depression or anxiety disorders, when compared with usual care. It is unclear whether these results can be extended to comparisons against face-to-face CBT due to the limited use of individual or group based face-to-face CBT as the comparator intervention in the majority of studies and the potential for biased results.

Table 3: Summary of systematic review of economic evaluations of iCBT<sup>4</sup>

	Mild to moderate major depression	Anxiety disorders
Number of primary studies	12 conducted alongside trials (six UK, one Spain, one Australia, three Netherlands); Three model-based (two Australia, one UK)	11 conducted alongside trials (seven Sweden, two Australia, one US, one UK); Five model-based (one US, three UK, one Australia)
Analysis perspective	UK studies – health sector; Spain, Australia, Netherlands – societal	UK, Australia and US – health sector; Sweden - societal
Time horizon	8 weeks to 12 months in most studies	Varied according to type of anxiety disorder. Generally 6 weeks to 18 months.
Intervention	Nine studies examined therapist guided iCBT (6-16 sessions); Six studies examined unguided iCBT (4-8 sessions)	13 studies examined guided iCBT; three studies examined unguided iCBT
Comparator(s)	Seven compared with usual care (most often GP); One compared with problem solving therapy; One compared with unguided iCBT; One compared with face-to-face CBT	Six included comparisons with stress management, usual care or wait list; Seven included a comparison with group or individual face-to-face CBT
Overall methodological quality	Eight studies had potentially serious limitations	12 studies had potentially serious limitations and three had very serious limitations
Example limitations	<ul style="list-style-type: none"> <li>- Short time frame of iCBT (usually 3 months or less)</li> <li>- Study populations were exposed to prior treatments (medications or psychotherapies)</li> <li>- Co-intervention of iCBT with other case management approaches</li> <li>- Small sample sizes and missing data</li> <li>- Did not account for repetitive use of iCBT for the treatment of recurrent episodes of major depression and anxiety</li> </ul>	

Overall findings as reported by the HTA	<p>In 11 studies, guided or unguided iCBT were cost-effective treatment delivery options because incremental cost-effectiveness ratio estimates were below country-specific willingness-to-pay thresholds.</p> <p>In four studies, guided or unguided iCBT was said to be economically unattractive.</p>	Most studies found guided iCBT represented good value for money (cost-saving or cost-effective at a country-specific willingness-to-pay threshold) when compared with control. In many studies, the probability of iCBT being cost-effective versus control was high and ranged from 70% to over 95%.
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Only one of the studies included face-to-face CBT as a comparator for the management of mild to moderate major depression. The cost-utility analysis found unguided iCBT to have lower total costs compared to face-to-face CBT and pharmacotherapy, but also resulted in fewer quality-adjusted life years (QALYs) versus face-to-face CBT. Unguided iCBT was concluded to be not cost-effective at the level of the national willingness to pay threshold in Australia. Seven studies included either individual or group based face-to-face CBT as a comparator for management of anxiety disorders, but conclusions were mixed. Guided iCBT was cost effective versus group based face-to-face CBT in three studies, cost effective versus individual face-to-face CBT in one study, less costly and less effective versus group CBT in one study and not cost effective versus individual CBT in two studies.

The Canadian HTA also included the development of a de-novo economic model to assess the cost effectiveness of guided or unguided iCBT compared with face-to-face CBT. A decision tree model was developed to estimate cost-effectiveness of iCBT as a one-time intervention to treat a single episode of depression or anxiety, and a second Markov microsimulation model was developed to estimate its cost effectiveness as part of a stepped-care model to account for repetitive use of iCBT with recurrent episodes of the disorder. The stepped-care approach involved therapist-guided iCBT followed by group or individual face-to-face CBT upon disease recurrence or progression.

The analyses included usual care, group CBT and individual CBT as the three comparator treatments. The models were populated with parameters related to the effectiveness of interventions (including probabilities of response and recovery), health state utilities, and direct medical costs. Important characteristics of the model and the values applied to key parameters in relation to the different treatments are summarised in table 4.

Table 4: Summary of model characteristics and parameter values<sup>4</sup>

Health Quality Ontario Model	
Country	Canada
Intervention	Unguided iCBT (6-8 weekly sessions) Guided iCBT (8-10 weekly sessions)
Comparators	Usual care (medication) Individual face-to-face CBT Group face-to-face CBT
Perspective	Healthcare
Time horizon	One off treatment – 1 year horizon Stepped-care model – Lifetime horizon
Probability of response (major depression / anxiety disorders)	Face-to-face CBT: 0.73 / 0.73 Unguided iCBT: 0.50 / 0.67 Guided iCBT: 0.73 / 0.74 Medication: 0.70 / 0.70
Probability of recovery	Face-to-face CBT: 0.66 (individual), 0.63 (group) Unguided iCBT: 0.38 Guided iCBT: 0.48 Medication: 0.62
Probability of drop-out	Face-to-face CBT: 0.16 Unguided iCBT: 0.32 Guided iCBT: 0.19
Baseline utilities	Mild depression: 0.79 Moderate depression: 0.67 Anxiety: 0.77 Normal health: 0.94
Guided iCBT utilities	4 months: 0.82 6-12 months: 0.85 12+ months: 0.83
Individual CBT utilities	4 months: 0.85 6-12 months: 0.85 12+ months: 0.83
Group CBT utilities	4 months: 0.80 6-12 months: 0.81 12+ months: 0.80

Reference case results for iCBT as a one-time intervention in patients with mild to moderate major depression found that total mean costs for guided iCBT were higher than usual care but lower than both group and individual CBT. Guided iCBT generated the same number of QALYs as individual CBT (0.826 QALYs), but more QALYs than those of unguided iCBT (0.778), usual care (0.787) and group CBT (0.817). Guided iCBT therefore dominated (better outcomes and lower cost) the group CBT and was cost-minimising versus individual face-to-face CBT. The probability of cost effectiveness for guided iCBT was 63% at a willingness-to-pay value of \$50,000/QALY and 67% at a willingness-to-pay value of \$100,000/QALY.

For the treatment of anxiety disorders, total costs for guided iCBT were higher than usual care and group CBT but lower than individual CBT. Guided iCBT generated more QALYs (0.834) than all three comparators. Guided iCBT dominated individual CBT and produced an incremental cost-effectiveness ratio (ICER) of \$23,000/QALY versus group CBT.

Results for the stepped-care model of unguided followed by guided iCBT in patients with mild to moderate major depression found that total mean costs were higher than usual care but lower than both group and individual CBT. Stepped care iCBT generated more QALYs (0.803) than usual care (0.787), but fewer QALYs than group CBT (0.817) or individual CBT (0.827). Over a lifetime time horizon using a stepped-care model, guided iCBT followed by individual face-to-face CBT represented an economically attractive option when compared with guided iCBT followed by group CBT (ICER of \$1,100/QALY gained).

Based on the results of the model, guided iCBT may represent an economically attractive option when used as a one-time, non-repetitive short-term treatment and is estimated to be the optimal strategy over a patient's lifetime when delivered as part of a stepped-care model followed by in-person CBT for people who have recurrent episodes of anxiety or major depression.

A more recent attempt (2020) at modelling the cost-effectiveness of iCBT compared with face-to-face CBT for treating depression, suggests that guided iCBT has the potential to generate greater QALY gains and reduce healthcare expenditure in Germany.<sup>25</sup> This study was not identified systematically but is included due to its direct relevance to the research question.

Baumann *et al* developed a Markov model to simulate costs and QALYs associated with guided iCBT over a 3-year period. The model included six health states through which patients could transition based on probabilities obtained through the literature. Key parameter values are listed in table 5. Effectiveness of CBT/iCBT was defined as the proportion of patients who entered remission after treatment. An additional feature of this model was the inclusion of waiting time prior to treatment initiation, to more accurately reflect the impact of remaining in the depressed health state for varied lengths of time.

Base case results indicated that guided iCBT was the dominant treatment, generating a 0.26 QALY incremental gain and saving €2,536 per patient compared with face-to-face CBT. On

average, patients in the iCBT cohort spent 55% of their time in remission (CBT: 35%) and 12% of their time depressed (CBT: 34%). iCBT avoided 0.50 deaths per 1,000 patients compared with face-to-face CBT. After accounting for higher dropout rates for iCBT, the shorter waiting time increased the number of patients who completed treatment across the three year period by 70%. Although substantially more patients were treated in the iCBT cohort, total costs were lower than in the CBT patient cohort.

Table 5: Summary of model characteristics and parameter values<sup>25</sup>

Baumann et al model	
Country	Germany
Intervention	Guided iCBT (12 weekly sessions)
Comparators	Face-to-face CBT (unspecified)
Perspective	Societal
Time horizon	3 years
Transition probabilities	CBT to remission: 0.609 iCBT to remission: 0.517 Depressed to spontaneous remission: 0.012 Spontaneous remission to depressed: 0.0202 Remission to depressed: 0.0064
Probability of drop-out	CBT: 0.0145 iCBT: 0.0201
Average waiting time for treatment	CBT: 20 weeks iCBT: 3 weeks
Baseline utilities	Depressed untreated: 0.29 Depressed mild: 0.45 Depressed moderate: 0.33 Depressed severe: 0.15 Remission: 0.85
Treatment utilities	Depressed on CBT: 0.47 Remission mild: 0.74 Remission moderate: 0.44 Remission severe: 0.30
Treatment costs	CBT: €1303 iCBT: €737

Despite the economic results presented here, there remains a high level of uncertainty with respect to the cost-effectiveness of guided iCBT compared with face-to-face CBT. The estimates of treatment response applied to models are not considered to be robust and can be affected by a range of variables and treatment conditions such as waiting times, severity

of illness and number of previous episodes. The results of the predictive models can be transferred across countries as treatments costs, waiting times, referral pathways and stepped-care plans may differ substantially.

## Conclusion

Based on a very limited evidence base around CBT it appears that guided internet psychotherapy provides similar outcomes to face-to-face treatment and is acceptable to many patients with depression or anxiety disorders.

Cost-effectiveness estimates vary widely and are limited by a lack of robust input data, many of which vary according to local service delivery parameters.

There is a need for large randomised non-inferiority trials, which include safety outcomes.

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