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Literature review of effectiveness of supported digital mental health interventions (DMHIs)

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List of acronyms and abbreviations

| Abbreviation | Term |
|--------------|--|
| ACT | Acceptance and Commitment Therapy |
| AMSTAR | Assessing the Methodological Quality of Systematic Reviews |
| ATSI | Aboriginal and Torres Strait Islander |
| CALD | Culturally and Linguistically Diverse |
| CBT | Cognitive Behavioural Therapy |
| CCBT | Computer assisted forms of Cognitive Behavioural Therapy |
| CEA | Cost-Effectiveness Analyses |
| CI | Confidence Interval |
| CUA | Cost-Utility Analyses |
| d | Cohen's d |
| DALY | Disability-Adjusted Life Year |
| DMHS | Digital Mental Health Service |
| DMHI | Digital Mental Health Interventions |
| F2F | Face to Face |
| GAD | Generalised Anxiety Disorder |
| GAD-7 | Generalised Anxiety Disorder 7-Item Scale |
| GP | General Practitioner |
| iCBT | internet Cognitive Behavioural Therapy |
| ICER | Incremental Cost-Effectiveness Ratio |
| Int | Intervention |
| LGBTQIA+ | Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, and Asexual |
| m | Mean |
| MA | Meta Analysis |
| max | Maximum |
| MDD | Major Depressive Disorder |
| MR | Meta-Review |
| N | Counts |
| NR | Not Reported |
| n.s. | Not significant |
| oCBT | Online CBT |
| OCD | Obsessive Compulsive Disorder |
| OR | Odds Ratio |
| P | p value |
| PD | Panic Disorder |
| PDT | Psychodynamic Therapy |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| PST | Problem Solving Therapy |
| PTSD | Post Traumatic Stress Disorder |
| QALY | Quality Adjusted Life Year |
| RCT | Randomised controlled trial |
| RR | Relative Risk |
| SAD | Social Anxiety Disorder |
| SD | Standard Deviation |
| SES | Socio Economic Status |
| SMS | Short Message Service |
| SOMS | Secure Online Messaging System |
| SR | Systematic Review |
| TAU | Treatment As Usual |
| vs | Versus |
| WL | Waiting List |
| WTP | Willingness-To-Pay |

Glossary

| Term | Definition |
|-----------------------------|--|
| AMSTAR | This tool provides guidance to rate the overall confidence in the results of a systematic review (high, moderate, low or critically low depending on the number of critical flaws and/or non-critical weaknesses). |
| CI | Confidence interval. The interval in which the population parameter will fall 95% of the time. |
| Cost-benefit analyses | A type of economic evaluation in which both the costs and consequences of different interventions are expressed in monetary units. |
| Cost-consequence | A form of economic evaluation which assesses a wide range of costs and consequences of the products being compared and reports them separately. It includes all types of effects: health, non- health, negative, positive both to consumer and other groups. |
| Cost-effectiveness analyses | A type of economic evaluation in which all costs are related to a single, common effect. Results are usually stated as additional cost expended per additional health outcome achieved. Outcomes are measured using clinically meaningful units of outcome, such as point improvements on depression or anxiety rating scales, or proportion of population that has remitted from a high prevalence disorder. |
| Cost-minimisation | A method of comparing the costs of alternative interventions (including the costs of managing any consequences of the intervention), which are known, or assumed, to have an equivalent medical effect. |
| Cost-utility analyses | A type of cost-effectiveness analysis in which benefits are expressed as the number of life years saved adjusted to account for loss of quality from morbidity of the health outcome or side effects from the intervention. The main unit of outcome are generic health indices that combine both health-related quality of life along with length of life. The best-known generic indices used in CUA are quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs). |
| d | A measure of effect size. See effect size. |
| DALY | Disability Adjusted Life Year. One DALY represents the loss of the equivalent of one year of full health. DALYS for a health condition are the sum of years of life lost due to premature mortality and the years lived with a disability in a population. |
| DMHS | Digital Mental Health Service. DMHSs are delivered online via desktops, mobile devices and applications; or via telephone crisis and counselling services. Some online DMHSs offer automated self-help programs, and others involve support or guidance, typically from clinicians. |
| DMHI | Digital Mental Health Intervention. Refers to a specific DMHI, typically delivered either in an experimental study or as one of several components of what a real-world DMHS offers. |
| Effect size | Measures the strength of relationship between treatment and outcome. An effect size (measured using Cohen's d or Hedge's g) of around 0.2 is considered a small effect size, 0.5 considered medium and 0.8 considered large. |
| GAD-7 | Generalised Anxiety Disorder 7-Item Scale. A measure of the level of worry and anxiety symptoms. |
| n.s. | Not significant. Statistical result indicating insufficient evidence to reject the null hypothesis that there is no difference between the groups. |
| Publication bias | Meaning studies included in a meta-analysis differ systematically from all studies that should have been included, typically due to studies with larger than average effects being more likely to be published. |
| OR | A measure of the odds of an event happening in one group compared to the odds of the same event happening in another group. |
| p | P value. Measure of the strength of the evidence against the null hypothesis. Values around 0.05 indicate weak evidence against the null; values around 0.01 indicate moderate evidence against the null and values around 0.001 indicate strong evidence against the null. |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| QALY | Quality Adjusted Life Year. One QALY is equivalent to one year in perfect health. QALYs are determined by estimating the numbers of years remaining following a treatment and weighting each year with a quality of life score. |

| Term | Definition |
|----------------------------------|---|
| Randomised controlled trials | Randomised control trial. A gold standard research method to measure efficacy of an intervention, whereby one group is exposed to the intervention and another group acts as a control and is not exposed to the intervention. Assignment to each group is based on randomisation and is therefore not influenced by participant characteristics. |
| Reliable change index | Measures whether change unlikely to be due to measurement error, and is an absolute measure of change. |
| Rates of deterioration | Negative effects |
| RR | A measure of the risk of a certain event happening in one group compared to the risk of the same event happening in another group. |
| SD | Standard deviation. A measure of the amount of variation in values within a sample. |
| Within-trial economic evaluation | An economic evaluation that is conducted alongside a clinical trial. |
| WTP | Willingness to pay. An evaluation method used to determine the maximum amount of money an individual is willing to pay for a particular outcome or benefit (e.g., to receive a health care service). |

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Background

The Australian Government funds numerous digital mental health services (DMHSs) ranging from those focusing on promotion and prevention to those focusing on treatment and recovery. The Government's digital mental health gateway, Head to Health (www.headtohealth.gov.au), lists these services.¹

DMHSs are delivered online via desktops, mobile devices and apps; or via telephone crisis and counselling services. They can help improve access to mental health care or complement traditional face-to-face care given their scalability and the ubiquity of desktop, mobile and telephone devices. They are low-cost for end-users and have the potential to reach people who do not or cannot access services (e.g., people in rural/remote and low-income regions) in a convenient setting (home, workplace, schools, through clinicians' workplaces). They are portable and have the added advantage of reducing stigma associated with using mental health services by offering users anonymity and the ability to manage their mental health problems real-time 24/7.²

Some DMHSs offer automated self-help programs and others involve guidance from clinicians, volunteer crisis supporters, teachers, administrators or peers. **Supported DMHSs** are online treatment programs that involve clinician/therapist support or guidance, usually occurring after consumers complete successive online modules.

The Productivity Commission Mental Health Inquiry Report noted the potential benefits of supported DMHSs.³ It recommended that the Australian Government fosters supported DMHSs as a treatment option by: increasing funding to expand their availability; commissioning an evaluation of their performance; and developing information campaigns for people with lived experience of mental illness and health professionals to increase the awareness of this treatment option.³

Purpose of the literature review

The Centre for Mental Health at the University of Melbourne was commissioned by the Department of Health to undertake the independent evaluation of Australian government funded supported DMHSs. This literature review, conducted as one component of the evaluation, uses the term Digital Mental Health Intervention (DMHI) to refer to a specific intervention, typically delivered either in an experimental study or as one of several components of what a real-world DMHS offers (with other service offering examples including assessment and referral). The review aims to address two overarching questions:

- Are supported DMHIs effective?
- Are supported DMHIs cost effective?

The purpose of the overall evaluation (which will address additional evaluation questions) is to inform Australian Government decisions related to future funding for supported DMHSs and activities to increase awareness and utilisation of these services by people with lived experience of mental illness and health professionals.

To collate information in a rigorous and timely manner, we conducted an umbrella review (review of systematic reviews) of relevant national and international peer-reviewed literature published between 2011 and 2021. The focus of the search was on systematic reviews or meta-analyses because they are widely accepted as the highest quality of scientific evidence. This was supplemented by searching for primary studies published since the most recent systematic review on cost-effectiveness. Details of our review methods are provided in the Appendices (A-E). We present our findings from review of the effectiveness and cost-effectiveness of supported DMHIs in this report.

Are supported DMHIs effective?

Our literature search for evidence of effectiveness identified 542 records, with an additional 29 identified from other sources. Once duplicates were removed, 329 records were screened at the title and abstract stage and 72 were assessed for full-text eligibility. Of these, 37 were assessed as eligible but potentially overlapping and 12 were included in the review. Since publications about the effectiveness of DMHIs are prolific, we selected reviews that synthesised evidence for a single mental disorder, typically depression or an anxiety disorder. Consistent with our disorder-specific approach, we did not consider it meaningful to conduct a further meta-analysis⁴ as this was already presented in the reviews we identified, and because a quantitative summary of the summaries would likely contain too much heterogeneity to provide meaningful results. Details of our methods for this component of the review are in Appendix A, the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)⁵ flow diagram is in Appendix B; and reasons for excluding 25 eligible reviews from our synthesis, the characteristics of these reviews and their overlap with other reviews are described in Appendix C.

An overview of the 12 included reviews is presented in Table 1. All reviews were meta-analyses, which means they used statistical methods to systematically synthesise the results of past individual studies to derive conclusions.⁴ Four reviews focused on depression (with or without anxiety) – two were included for effects in adults,^{6, 7} one for effects in youth⁸ and one for its specific focus on negative effects.⁹ One review focused on youth depression and anxiety, but was included only for effects on anxiety.¹⁰ One review each focused on each of the anxiety disorders – generalised anxiety disorder (GAD), social anxiety disorder, obsessive compulsive disorder (OCD), panic disorder and post-traumatic stress disorder (PTSD). Finally, another review focused on negative effects in mostly anxiety disorders¹¹ and one on eating disorders.¹²

Most studies included in each of the reviews were randomised controlled trials, which are the gold standard in research design. Most reviews synthesised findings from 15 or more studies. The exceptions were the reviews that focussed on OCD, PTSD and binge eating disorder, which included 7, 13 and 3 studies, respectively. Most of these studies were conducted in Australia and Europe, suggesting that Australia has a leading role in the growing field of DMHIs. The DMHIs investigated typically provided evidence-based cognitive behavioural therapy (CBT); and the type, format and extent of support or guidance offered were diverse. The length of treatment also varied, ranging from 1 week to 4 months. Ten studies focused on adults and two on youth aged 12-25 years.

We rated the quality of the reviews using the AMSTAR2 (Assessing the Methodological Quality of Systematic Reviews) tool.¹³ Overall, the quality of the reviews varied, with one rated as high, three as moderate, five as low and three as critically low. It should be noted that because the (AMSTAR2)¹³ uses very strict quality criteria, it is difficult for most reviews to attain a high-quality rating. Furthermore, these ratings reflect the quality of the review, rather than the quality of the primary studies themselves. The most common critical weakness was not registering the review protocol, which may indicate the review methods were not planned ahead of conducting the review. Adherence to a well-developed protocol reduces the risk of bias in the review and the lack of review protocols therefore somewhat undermines confidence in review findings.

Table 1: Summary of 12 meta-analyses on effectiveness of supported DMHIs

| Study | Mental health condition(s) | Demographic | Search years | Countries of origin of studies (n) | No. and type of studies and no. participants | Intervention | Support/guidance | Duration | Quality rating (AMSTAR2) |
|------------------------------------|---|--|---------------------|--|--|---|--|---|--------------------------|
| Ahern et al. (2018) ⁷ | Depression (includes one study on postnatal depression) M age = 42.7 in int and 43.2 in control. Female = 70.6% | Adults with MDD or scored above the clinical cut-off standardised measure | Jan 2006 - Dec 2016 | Australia (7) Sweden (7) UK (5) USA (4) Netherlands (3) Germany (2) Spain (1) Norway (1) | 30 in SR (29 in MA; 37 subsamples); 29 RCTs, 1 propensity matched case-control trial; 5429 | 17 CBT interventions; many diverged from traditional CBT. In some instances, CBT supplemented with additional resources and online information forums | 29 of 37 subsamples (24 studies) involved guidance Therapist support – F2F (2) Therapist F2F and email – (1) Therapist support – SOMS (3) Therapist support – phone and email (4) Therapist support – email (7) Therapist support conditionally – email (1) Therapist support – type NR (1) Administrative support – email (3) Administrative support – phone and email (4) Administrative – phone (4) Administrative support – type NR (1) No support (7) | 1 week – 4 months; M, NR | Critically low |
| Christ et al. (2020) ¹⁰ | Anxiety (and depression but only anxiety data extracted; effects on depression in youth extracted from Garrido et al. ⁸) | Youth mean age 12-25 with diagnosis or elevated symptoms University, community and clinical samples | Up to Sept 2019 | Australia (5) UK (3) Spain (1) USA (1) Canada (1) Sweden (2) Ireland (1) Denmark (1) | 15 RCTs (5 in adolescents, 6 young adults, 4 young and older adults); 958 | Mostly iCBT Also, CBT via computer program (or CD-ROM) or smartphone | 11 studies involved guidance Guidance by therapist or researcher by phone and/or email, chat sessions or face to face during module completion Involved monitoring progress and providing support, encouragement and clarification Subgroup analysis on guidance (15 studies) | 2-16 weeks; M, 7.5 (for 24 of 25 total anxiety and depression studies) | Moderate |
| *Ebert et al. (2016) ⁹ | Depression | Adults with diagnosis or elevated symptoms | Up to Jan 2014 | Sweden (5) Germany (1) Australia (4) Netherlands (6) Germany/Switzerland (1) USA (1) | 18 RCTs (21 comparison groups); 2079 | CBT (13) PST (5) ACT (1) PDT (1) | All included professional guided intervention Guidance varied with telephone contact, email, feedback on module answers or homework | 4-13 weeks; M, NR | Low |
| Eilert et al. (2021) ¹⁴ | GAD | Adults with diagnosis Aged 18-81 | Jun 2009 – Apr 2020 | Sweden (5) Australia (9) UK (2) New Zealand (1) Canada (1) Netherlands (1) Switzerland/Germany/Austria (1) | 20 RCTs (24 comparison groups); 1333 | CBT (15) ACT(1) APT (1) CBM (2) other (5) | Only one group did not involve any support Qualified or soon-to-be qualified therapist or clinician (18) Psychological wellbeing practitioner/non-specialist psychologist/technician/researchers (5) Unguided (1) Support consisted of individual feedback, answering questions, and feedback on assignments; through email, telephone, text messaging, webpage messaging, video conferencing, and online discussion forums. | 1.6-12weeks | Moderate |

| Study | Mental health condition(s) | Demographic | Search years | Countries of origin of studies (n) | No. and type of studies and no. participants | Intervention | Support/guidance | Duration | Quality rating (AMSTAR2) |
|---------------------------------------|---|--|-------------------|--|---|--|--|--------------------------------|--------------------------|
| Garrido et al. (2019) ⁸ | Depression (anxiety not included in meta-analysis) | Aged 12-25 more comprehensive than Christ et al. (2020) ¹⁰ for depression in youth | 2007-2017 | Mostly Australia, US and other English-speaking countries. Northern Europe, Asia, South America (based on 41 studies, not available for the 15 RCTs we extracted data for) | MA of 15 RCTs; 3294 | Mostly CBT (11) ACT (1) Referral to care (1) Positive psychology (1) delivered online (9), via mobile MMS (1) or app (1), computer game (1), computer program (2) Details missing for one study | Subgroup analyses for high (n=7), low (n=3), or no therapist support (5). | NR | Low |
| Guo et al (2021) ¹⁵ | Social anxiety disorder (mild to moderate) | Adults M age 34, range 18-79 | Up to Jul 2020 | NR | 20 RCTs; 1743 | All iCBT | Treatment guided by experienced therapists (n=5), inexperienced therapists (n=9) or unguided (n=4). | 9-12 weeks | Moderate |
| Hoppen et al. (2021) ¹⁶ | OCD | Adults | Up to Mar 2021 | Sweden (1) Germany (2) Australia (4) | 7 iCBT; 704 included in our own MA (total 18 RCTs) | All iCBT | <i>Type of therapist contact (total minutes)</i> Feedback via secure web-based communication system (462) Email (max. 180) Contact if needed via messages (129) Twice weekly therapist contact (88.63) Scheduled personal emails (6) Only answers if questions (0) No support (0) | 8-12 weeks; M, 9 weeks | Low |
| *Karyotaki et al. (2018) ⁶ | Depression | Adults with diagnosis Clinical and community samples; age M=42.4 (SD 11.9) | Up to Jan 1, 2016 | Australia (4) Germany (5) Japan (1) Netherlands (6) Sweden (7) Switzerland USA (1) | 24 RCTs (26 comparisons); 4889 | CBT (16) CBM & CBT (1) ACT (1) PST (6) PDT (1) | All studies involved guidance Guidance from therapist, coach, clinician, psychologist or NR Various forms of guidance from phone contact, emails, and feedback on module answers or homework | 5-13 weeks; M, NR | Low |
| Moghimi et al. (2021) ¹² | Binge eating disorder | Aged 18+ M age range 35 (SD 10) - 40 (SD 11) 99% female | Up to Feb 2019 | NR | 3 RCTs; 298 | All based on CBT | All guided to varying extents Weekly contact via email; Internet-based contact with the therapist twice a week; Internet-based contact with therapist when submitting assignments | 15 weeks to 6 months; M, NR | Critically low |

| Study | Mental health condition(s) | Demographic | Search years | Countries of origin of studies (n) | No. and type of studies and no. participants | Intervention | Support/guidance | Duration | Quality rating (AMSTAR2) |
|--------------------------------------|---|--|---|--|--|--|---|--------------------------|--------------------------|
| Polak et al. (2021) ¹⁷ | Panic disorder | Adults who met criteria for panic disorder Other demographics NR | up to Mar 2020 | Sweden (5) Australia (7) Romania (1) | 13 RCTs; 1214 participants | All iCBT | All 13 studies involved guidance. 12 involved email contact with therapist, 3 with phone contact as well. 1 involved videocall with therapist. Therapist time per patient ranged from M = 6.04 mins (SD 10.66) to 376.3 mins (SD 156.8). Guidance provided by postgraduate psychology students, psychologists, clinical psychologists, clinicians, therapists, licensed psychotherapists) | 6-16 weeks; M, NR | Low |
| *Rozenal et al. (2017) ¹¹ | Any (mostly anxiety disorders – 61%, depression – 20 %) | M age 39 (SD 13) 63% female Vast majority samples general population, 1 study each – primary care and students | All trials conducted from 2005-2016 by review authors | Sweden (29) | 29 controlled trials (26 RCTs); 2866 | iCBT (74%) control, mostly waitlist (26%) | 27/29 unguided | 4-12 weeks; M; 8.5 weeks | Critically low |
| Simon et al. (2021) ¹⁸ | PTSD | Adults (>70% met diagnostic criteria) Aged 16+ | up to June 2020 | Sweden (1) UK (1) USA (2) Iraq (1) Australia (2) | 8 RCTs guided; 476 (13 RCTs total; 808) | iCBT in all 8 guided studies | 8 studies involve guidance Maximum 5 hours of therapist guidance, delivered face-to-face or remotely (e.g., phone, email, instant messaging) | 3-10 weeks; M, 7 weeks | High |

*Individual participant data meta-analysis (i.e., used raw scores from each participant, rather than group means and standard deviations)

ACT, acceptance and commitment therapy; **F2F**, face to face; **iCBT**, internet-based CBT; **M**, mean; **MA**, meta-analysis; **MDD**, major depressive disorder; **MR**, meta-review; **NR**, not reported; **oCBT**, online CBT; **PDT**, psychodynamic therapy; **PST**, problem solving therapy; **SR**, systematic review; **RCT**, randomised controlled trial; **SOMS**, secure online messaging system

Depression

Two reviews focused on populations with depression – Karyotaki et al (2018)⁶ and Ahern et al. (2018).⁷

Karyotaki et al (2018)⁶ evaluated the effectiveness of supported DMHIs for depression in adults. The review pooled data from 4,889 adults with depression across 26 samples from 24 RCTs. Most interventions were based on iCBT with six based on problem-solving therapy, and intervention length varied from 5-13 weeks. Guidance varied from telephone contact, emails, and feedback on module answers or homework. The participants tended to be middle-aged (mean age = 42), 59% were female, 48% were married, and a high proportion had comorbid anxiety (56%). The most common comparator was waiting list control (n=13), but in 11 studies, an active comparison (brief scheduled therapist support, web-based discussion groups or treatment as usual) was used as control.

There were higher rates of response in the digital intervention versus the comparison condition (56.2% vs 35.1%), with the odds of response more than double in participants who received the intervention (OR=2.49). Response was defined based on the reliable change index, which measures change unlikely to be due to chance, and is an absolute measure of change (e.g., a reduction of 5 points on a depression scale). An alternative definition of response (50% improvement in symptoms) also showed consistent findings, with higher odds of response in the intervention group (39.6% vs 19.1%, OR=2.83). This response rate is comparable to that reported in a recent meta-analysis of 228 RCTs examining the effects of face-to-face psychotherapies (60% CBT): 41% psychotherapies vs 17% usual care vs 16% waitlist.¹⁹ Karyotaki and colleagues (2018) found similar effects on participants reaching remission, with the odds about 2-2.5 higher in those receiving DMHIs compared to controls. For both response and remission, there was evidence of **publication bias** meaning studies included in the meta-analysis differ systematically from all studies that should have been included, typically due to studies with larger than average effects being more likely to be published. However, the effect was still significant after adjusting for missing studies (OR=2.15 for response, OR=2.17 for remission).

The review investigated whether the effectiveness varied based on intervention or participant characteristics. There was no effect from the number of online sessions, or whether participants had a formal depression diagnosis, comorbid anxiety, or used antidepressants. Effectiveness also did not vary by gender, educational level or employment status. However, there was a higher response in native-born participants vs ethnic minorities (OR=1.66), participants in a relationship vs single (OR=1.33), and older adults vs younger adults (OR=1.01). There was also the suggestion of a better chance of remission in participants with greater depression severity (OR=1.19).

Another review by Ahern (2018)⁷ examined CBT-based DMHIs in adults with depression and examined the effect of type of support. This review included 5,429 adults from 29 RCTs, of which 24 involved some form of guidance. There were 17 studies with interventions that involved support from a therapist providing clinical post-session feedback to patients, and these showed a moderate effect size post-intervention compared to controls ($g=0.56$). There was a small-to-moderate effect size in the 12 studies that involved administrative support (encouraging adherence or providing technical support), $g=0.30$. This difference in effect size across the two modes was not statistically significant ($p=.08$). The mode of communication (e.g., phone, email) used throughout the supported studies did not significantly impact depressive symptoms. Across all the studies there was no difference in effects based on the number of sessions (8 or more vs <8) or intervention duration (10 or more weeks vs <10 weeks).

We rated the quality of these reviews as low (Karyotaki 2018)⁶ and critically low (Ahern 2018)⁷, suggesting they may not provide an accurate and comprehensive summary of the available studies.

Generalised anxiety disorder (GAD)

Eilert (2021)¹⁴ reviewed the evidence for DMHIs for adults with GAD. They included 24 comparisons from 20 RCTs with 1,333 participants. Eighteen interventions were supported in some fashion (ranging from individual feedback, answering questions, and feedback on assignments; through to email, telephone, text messaging, webpage messaging, video conferencing, and online discussion forums). Most interventions were based on CBT and there was a range of intervention lengths (1.6-12 weeks). Only 9 interventions were GAD specific, while 15 were transdiagnostic in approach. Most control comparisons were waitlists rather than active control groups (four studies). Pooling the effects at post-intervention, there was a large reduction in anxiety symptoms ($g=0.79$) and worry ($g=0.75$). Follow-up effects 1 to 6 months after intervention remained significant for anxiety based on six studies ($g=0.84$) but were smaller and no longer significant for worry symptoms based on five studies ($g=0.35$, 95% CI: 0.17 to 0.86). There was a moderate amount of heterogeneity in effects at post-intervention, and the authors investigated whether age, intervention focus (diagnostic specific vs transdiagnostic), intervention basis (CBT vs other), symptom severity, length of treatment, number of intervention modules, completion rates, and time spent by supporters had a role in effects. The only significant moderator was intervention length, whereby a longer intervention length was associated with better outcomes. Overall, methodological quality assessment ratings seemed good across the included studies, and we rated the review quality as moderate, suggesting it is a reasonably accurate summary of the results of available studies.

Social anxiety disorder

Guo (2021)¹⁵ reviewed the evidence for DMHIs in adults with social anxiety disorder. They included 20 RCTs with 1,743 adults who met diagnostic criteria for mild to moderate social anxiety disorder. Most interventions were 9 or 10 weeks long and all were based on CBT, but four did not provide any support. Participants were aged 34 years on average. Pooling results from 14 studies, showed a large reduction in social anxiety symptoms compared to waitlist controls, $g=0.79$. The review also found effects were similar between post-intervention and 6 or 12 months later. Three studies with 213 participants compared digital CBT with face-to-face CBT and found no significant difference in effects. Analyses also showed that effects did not vary depending on the experience level of the therapist providing support, with similar large effects in studies with experienced therapists ($g=0.81$) and inexperienced therapists ($g=0.82$). There was no indication of publication bias and we rated the review quality as moderate, suggesting it is a reasonably accurate summary of the results of available studies.

Panic disorder

Polak (2020)¹⁷ reviewed DMHIs for adults with panic disorder (with or without agoraphobia). There were 13 RCTs included which involved 1,214 adults who met diagnostic criteria for panic disorder. All interventions were supported, with most providing email contact with a therapist. Intervention length ranged from 6-16 weeks and all were based on CBT. Pooling the data from nine studies with 470 participants that compared internet-delivered CBT (iCBT) with controls such as waitlists, there was a large reduction in panic symptoms post-intervention ($g=-0.89$). There were also large effects on comorbid anxiety and depression symptoms ($g=0.72$).

There were 10 studies with 744 participants that compared iCBT with an active comparison based on CBT (such as CBT delivered face to face). This found no difference in effects on symptoms of panic post-intervention between the two types of treatments ($g=0.02$), with 50% in iCBT interventions responding positively versus 46% in the active comparison interventions. A similar result was observed at follow-up ($g=-0.11$). There were also similar results when examining effects on comorbid anxiety and depression symptoms post-intervention ($g=-0.03$) and follow-up ($g=-0.00$).

The authors also investigated whether adherence and symptom severity had an impact on the size of effects. This found larger effects in studies where >80% of participants logged in to the

treatment program compared to studies with fewer than 80% participants. Effects were also larger in studies with participants who had more severe symptoms at the start of the study. Overall, there was no indication of publication bias and there were no included studies with a high risk of bias.

Finally, using three studies with 363 participants, the authors found no significant difference in outcomes of DMHIs based on whether the intervention was guided or self-directed. However, we rated the review quality as low, suggesting it may not provide an accurate summary of the results of available studies.

Post-traumatic stress disorder (PTSD)

The effectiveness of DMHIs for PTSD in adults was reviewed by Simon (2021).¹⁸ They included 13 RCTs of 808 participants aged 16+ where at least 70% met diagnostic criteria for PTSD. Intervention length ranged from 3-14 weeks and all were based on CBT. Of the 13 studies, 8 were supported, which was defined as a maximum of five hours of therapist guidance, delivered face-to-face or remotely (e.g., telephone, email, instant messaging). Pooling results from the 8 studies that were supported (n=439), there was a large reduction in PTSD symptoms post intervention ($g=0.78$). The authors judged there to be very low-certainty evidence for this effect, taking into account the risk of bias of the included studies. We rated this review as high quality, suggesting it provides an accurate summary of the results of available studies.

Obsessive compulsive disorder (OCD)

Hoppen (2021)¹⁶ reviewed the evidence for technology-delivered CBT for OCD and included 18 RCTs, seven of which focused specifically on iCBT. As Hoppen (2021) did not separate the effects of DMHIs from other technologies (e.g., telephone), we performed a meta-analysis on the seven internet-based studies. These included 704 adults with OCD symptoms. Intervention length averaged 8 weeks and, in most studies (5/7), therapists provided support if contacted (typically by email). One study had twice-weekly therapist contact and one study provided no support. Participants tended to be female (77%) and middle-aged (mean age 36 years). Overall, there was a large reduction in symptoms of OCD ($g=0.78$) with high levels of heterogeneity. There was a somewhat larger effect in the three studies with waitlist controls ($g=0.87$) than the 4 studies with active controls such as face-to-face CBT, medication, online non-directive supported therapy ($g=0.69$). Overall, there was no evidence of publication bias and the included studies were mostly judged to be low risk of bias. We rated the review as low quality, suggesting it may not provide an accurate summary of the results of available studies.

Eating disorders

The effectiveness of DMHIs for people with binge eating disorder was reviewed by Moghimi (2021).¹² We identified no other meta-analyses focusing on other eating disorders. This review included three RCTs involving 298 adults with full or subthreshold binge eating disorder. All interventions were based on CBT and were supported by a therapist. Participants were on average middle-aged and the vast majority were female. Compared to waitlist controls, digital interventions reduced binge episodes ($g=0.77$), eating disorder symptoms (0.71), shape concerns (0.61), and weight concerns (0.91). However, there was no significant change in body mass index from these interventions ($g=-0.01$). The studies were rated to have a low risk of bias, but we rated the review quality as critically low, suggesting caution in the accuracy of these findings.

Negative effects

We found two reviews that examined rates of deterioration (negative effects) in recipients of supported DMHIs.

Ebert et al. (2016)⁹ focused on depression in adults. This review pooled data from 2,079 adults across 21 samples from 18 RCTs. Interventions were most commonly based on CBT and varied in length from 4-13 weeks. Compared to controls (mainly waitlist), rates of deterioration in symptoms were approximately half in intervention participants (3.4% vs 7.6%, RR=0.47) at post intervention. This difference was similar at short-term follow-up (1-4 months after intervention), 2.8% vs 6.1% (RR=0.47) but not at longer-term follow-up (6-10 months after intervention), with deterioration observed in 6.0% vs 5.3% participants (RR=n.s.). There was some evidence of publication bias, with 5 studies potentially missing, but the difference in deterioration was still statistically significant at post-intervention (RR=0.58, 95% CI: 0.38 to 0.90). There were no significant moderators that identified participants who were more likely to worsen in the intervention than the control. Although participants with only high-school education had higher rates of deterioration in the intervention group than the control group, this difference was not statistically significant (10.2% vs 6.3%).

Rozenal et al. (2017)¹¹ also examined deterioration rates, but they focused on interventions for a range of mental health conditions conducted in a single country (Sweden). This review pooled data from 2,866 participants across 29 clinical trials (26 RCTs). Most interventions were guided and on average lasted 8.5 weeks. Participants mostly had a diagnosis of anxiety disorder (60%), followed by depression (20%), and other conditions. Participants were aged 39 on average, with 63% female, 68% in a relationship, and 65% with a university degree. There was a small percentage of participants in receipt of a digital intervention who showed a mild deterioration in symptoms (6%) compared with 17% of those in controls (mainly waitlist). There were similar participant characteristics associated with deteriorating across interventions and controls, except for education levels. Participants with a university education were less likely to deteriorate in the intervention group (OR=0.54) compared to those without, but this was not the case in controls where the risk was the same (OR=1.02).

We rated the quality of these reviews as low and critically low, suggesting they may not provide an accurate and comprehensive summary of the available studies.

Youth

There are fewer evaluations of supported DMHIs in youths compared to adults.

Christ et al. (2020)¹⁰ examined the effectiveness of CBT-based DMHIs in youth aged 12-25 with anxiety. Participants were both older and younger than 25 years in 4 of 15 studies. Across all 15 studies involving 958 youth, there was a small-to-moderate effect of guided computerised CBT on anxiety symptoms compared to controls at post-intervention ($g=0.41$). Note that most comparison conditions were passive (involving waiting list), with few active (e.g., face to face) comparators. We rated this review's quality as moderate, suggesting it is a reasonably accurate summary of the results of available studies.

Garrido et al. (2019)⁸ identified 15 RCTs that examined the effect of DMHIs on depression symptoms in 3,294 youth aged 12-25. There were nine studies that compared digital interventions to a waitlist control (seven of which were supported), and these showed a small-to-moderate pooled effect size ($d=0.33$). However, this effect disappeared in studies judged to have a low risk of bias ($d=0.01$ vs $d=0.44$ in other studies). Subsequent analyses showed larger effects in studies with higher levels of interaction. Pooling the data from five studies with high levels of human interaction (direct contact with a therapist or completed in supervised settings such as a lab, clinic or school) showed a moderate effect size ($d=0.52$), whereas two studies with low levels of interaction (regular emails, text messages, or optional opportunities to contact a therapist) showed a smaller, non-significant effect ($d=0.16$, 95% CI -0.06 to 0.38). There were also three studies that compared supported digital interventions to an active control such as usual care or a non-depression specific intervention. These showed no significant difference in interventions with low support (1 study, $d=0.21$, 95% CI: -0.03 to 0.46) and high support (2 studies, $d=0.49$, 95% CI: -0.11 to 1.09). We rated

the quality of this review as low, suggesting it may not provide an accurate summary of the available studies.

Are supported DMHIs cost effective?

As demonstrated in the previous section of this report, there is substantial evidence showing that supported DMHIs are effective. However, an intervention that is effective is not necessarily cost-effective. This section of the report will discuss the findings from a two-stage pragmatic literature review that investigated the cost-effectiveness evidence of DMHIs for depression and anxiety disorders. In the first stage, we completed a desktop search of systematic reviews. In the second stage, we conducted a systematic literature search to identify any new primary studies that had been published since the most recent systematic review. Details of our methods for this component of the review are in Appendix D.

Stage 1: Desktop search of systematic reviews

Our first stage of this literature review was a desktop search through which we identified two recently published systematic reviews, Jankovic et al. (2021)²⁰ and Mitchell et al. (2021).²¹ The former investigated a broader range of mental health problems and the latter focused on anxiety and depressive disorders only. The reference lists of these two reviews yielded an additional six systematic reviews^{7, 22-26} that were published before 2021, with the earliest being 2012.²⁴ Of these six systematic reviews, only one included a meta-analysis component, Kolovos et al. (2018).²⁵

Table 2 summarises the main characteristics of these eight systematic reviews. Most of the search dates reported by the reviews overlapped each other and ranged from 1990 to August 2020. The number of individual studies synthesised across the reviews ranged from 2 to 67 studies with most studies being categorised as economic evaluations of guided/supported interventions. The dominant type of study design of the individual studies comprising the reviews was economic evaluations alongside randomised controlled trials. Depression and anxiety-related disorders were the most frequently investigated mental health conditions. Most economic evaluations were **cost-effectiveness** and **cost-utility analyses** (CEA and CUA). In cost-effectiveness analyses (CEA), outcomes are measured using clinically meaningful units of outcome, such as point improvements on depression or anxiety rating scales, or proportion of population that has remitted from a high prevalence disorder. In cost-utility analyses (CUA), the main unit of outcome are generic health indices that combine both health-related quality of life along with length of life. The best known generic indices used in CUA are quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs).

The interventions evaluated were generally internet-based cognitive behavioural therapy (iCBT)-focused interventions and a minority were based on problem-solving therapy or positive psychology interventions. The guided component of the interventions typically comprised some form of remote contact with a therapist or coach and self-help materials. Intervention delivery costs generally ranged from \$124 to \$2,842 per participant and included cost components such as personnel time, website-related costs and participant time spent in intervention.

Table 2: Summary of 8 recent systematic reviews reporting economic evaluation of DMHIs (identified via desktop search)

| Reviews | Inclusion of meta-analysis | Search dates | Number of studies included | Study designs (number of studies) | Population mean age in years and sample size | Mental health conditions (number of studies) | Economic evaluation type (number of studies) | Reported quality appraisal |
|--------------------------------------|----------------------------|-------------------------------|-----------------------------|--|--|--|--|---|
| Ahern et al. (2018) ⁷ | Yes | Jan 2006 – Dec 2016 | 5 (all guided) | RCT (n=4); Observational study (n=1) | Intervention group - 39.10 years (n=774) Comparator group - 45.19 years (n=3,599) | Depression (n=5) | CEA and CUA (n=4) CEA (n=1) | Drummond and Jefferson Quality Assessment Scale (1996) 4 studies identified as good quality |
| Arnberg et al. (2014) ²² | Yes | Database inception – Mar 2013 | 2 (all guided) | RCT (n=2) | Not reported | Depression (n=1); Social phobia (n=1) | CEA (n=1) CUA (n=1) | Not reported |
| Donker et al. (2015) ²³ | No | 1990 – Jul 2014 | 16 (10 guided, 6 unguided) | RCT (n=15); Partial RCT (n=1) | Mean age not reported (n=14,301) | Depression (n=4); Smoking (n=3); Social phobia (n=3); Harmful alcohol use (n=2); Panic disorder (n=1); Health anxiety (n=1); Anxiety (n=1); Suicidal ideation (n=1) | CEA and CUA (n=10) CEA (n=6) | Drummond and Jefferson Quality Assessment Scale (1996) On average, the 16 studies scored 72% (33/471) of the items positive. |
| Hedman et al. (2012) ²⁴ | No | Database inception – Jun 2012 | 8 (7 guided, 1 unguided) | RCT (n=8) | Mean age not reported (n=1,019) | Depression (n=3); Social phobia (n=2); Severe health anxiety (n=1); Irritable bowel syndrome (n=2) | CEA and CUA (n=5) CEA (n=3) | Not reported |
| Jankovic et al. (2021) ²⁰ | No | 1997 – Dec 2018 | 67 (45 guided, 22 unguided) | RCT (n=51); Pilot trials (n=3); Markov model (n=3); Decision tree | Not reported | Depression (n=20); Anxiety (n=21); Depression and anxiety (n=5); Suicidal ideation | CEA and CUA (n=22) CEA (n=20) CUA (n=21) | Not reported |

| Reviews | Inclusion of meta-analysis | Search dates | Number of studies included | Study designs (number of studies) | Population mean age in years and sample size | Mental health conditions (number of studies) | Economic evaluation type (number of studies) | Reported quality appraisal |
|--------------------------------------|----------------------------|-------------------------------|----------------------------|---|--|--|--|---|
| | | | | (n=4); Observational study (n=1); Others (n=2) | | (n=1); Child disruptive behaviour (n=1); Eating disorders (n=3); Schizophrenia (n=3); Addiction and substance misuse (n=13) | Cost comparison (n=1) Exploratory economic analyses (n=1) | |
| Kolovos et al. (2018) ²⁵ | Yes | Jan 2000 – Jan 2017 | 5 (all guided) | RCT (n=5) | 45 years (n=1,426) | Depression (n=5) | CEA and CUA (n=5) | Cochrane Risk of Bias assessment tool (2011) 4 studies with low risk of bias in all domains |
| Mitchell et al. (2021) ²¹ | No | Jan 2000 – Aug 2020 | 33 (28 guided, 5 unguided) | RCT (n=30); Pilot RCT (n=2); Observational study (n=1) | Mean age not reported (n=12,949) | Depression (n=20); Anxiety (n=13) | CEA (n=5) CUA (n=22) ICER not reported (n=6) | Drummond and Jefferson Quality Assessment Scale On average, the 33 studies scored 0.85. |
| Paganini et al. (2018) ²⁶ | No | Database inception – Jan 2017 | 12 (9 guided, 3 unguided) | RCT (n=12) | 44 years (n=4,060) | Depression (n=12) | CEA and CUA (n=7) CEA (n=1) CUA (n=3) Not clear (n=1) | Checklist of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (2013) The studies scored 93.3% (235/252). |

RCT, randomised controlled trial; **CEA**, cost-effectiveness analysis; **CUA**, cost-utility analysis; **ICER**, incremental cost-effectiveness ratio

Though not definitive, there is considerable evidence across the identified systematic reviews that supported DMHIs for depression and anxiety are cost-effective. Both the reviews by Hedman et al. (2012) and Arnberg et al. (2014) reported that guided iCBT is likely to be cost-effective compared with treatment as usual. Similarly, Ahern et al. (2018) reviewed 5 studies which focused on depression and concluded that, from the healthcare perspective, guided online-based CBT demonstrated a 50-95% probability of being cost-effective compared with controls based on country-specific willingness-to-pay (WTP) thresholds ranging from £20,000/QALY in the UK to \$95,000/QALY in Australia. Donker et al. (2015) also concluded that guided iCBT is likely to be cost-effective for several mental health conditions, including depression and anxiety. In contrast, the review by Kolovos et al. (2018) found that there is a low probability (<35%) of guided Internet-based interventions to treat depressive symptoms being cost-effective compared to the control group based on a WTP threshold of €35,000/QALY. The review by Paganini et al. (2018) presented mixed evidence for the treatment and prevention of depression using Internet- and mobile-based interventions, where only half of the included interventions (6 out of 12) were judged to be cost-effective. Mitchell et al. (2021), the most recent review on the economic evaluations of supported DMHIs for anxiety and depressive disorders, found 81% of the included studies concluded that the interventions evaluated were cost-effective compared to their respective control condition (e.g., treatment as usual, waitlist, another online intervention). Even though Jankovic et al. (2021) provided a qualitative critique of methods for economic evaluation of DMHIs, we decided to include this review in our report because it provided useful observations about the literature. The authors concluded that the evidence surrounding the cost-effectiveness of guided DMHI is not conclusive. They argued that this is mainly due to the challenges associated with the estimation of all costs and outcomes and identification of appropriate comparators for DMHIs, which are often complex and heterogeneous in nature.

Five out of eight reviews reported some form of quality appraisal for their included studies and the method of quality appraisal varied. For these five reviews, the quality of their included studies was good, with a majority of studies assessed positively. While the remaining three reviews did not conduct quality assessment, the number of included studies in two of these reviews was relatively low and another review (i.e., Jankovic et al., 2021) had a focus on methodology evaluation and did not attempt to provide a conclusion on cost-effectiveness of DMHIs. Although the overall findings from our desktop search of systematic reviews were supported by primary studies that generally were of good quality, the small proportion of low-quality studies and their impact on our conclusion was not entirely clear.

The reviews also identified several economic evaluations of supported DMHIs conducted in Australia. One was an economic modelling study by Mihalopoulos et al. (2005), which suggested that an internet-based psychological intervention (Panic Online) was cost-effective when supported by health professionals such as GPs or psychologists. Similarly, two iCBT interventions targeted at Australian adults aged over 60 years to treat depressive and anxiety symptoms were found to be cost-effective compared with a delayed-treatment waitlist control group (Dear et al. (2015); Titov et al. (2015)). The probability of the intervention being cost-effective for both studies was >95% based on a \$50,000 WTP threshold. A more recent study, Lee et al. (2017), evaluated the cost-effectiveness of the MindSpot iCBT program for Australians with anxiety and depressive disorders and concluded that the program is highly cost-effective when compared with usual care.

Stage 2: Systematic literature review of primary studies published since most recent systematic review

The second stage of our literature review, which aimed to update the most recent systematic review by Mitchell et al. (2021),²¹ yielded 1,566 potential articles after removal of duplicates. Of these, six met the inclusion criteria after title, abstract and full text screening. The PRISMA flow diagram is in Appendix E.

Table 3 summarises the key features of these studies. None of the studies was conducted in Australia. The majority were trial based economic evaluations (4/6) and the balance were modelled economic evaluations (2/6). I-CBT was used in most studies to treat depression and anxiety. In terms of evaluation perspective, two studies adopted both healthcare and societal perspective, two adopted a societal perspective and one adopted a healthcare policy perspective while the perspective for the remaining study was unclear. Most of the studies (5/6) were cost-utility analyses and used QALYs. Except for one study that did not report cost-effectiveness based on WTP, all studies generally concluded that their respective supported DMHIs for depression or anxiety-related disorders were cost-effective.

Table 3: Summary of 6 primary studies reporting economic evaluation of supported DMHs since 1 January 2020 (identified via systematic literature review)

| Study | Study design, sample and perspective | Mental health condition | Intervention type | Total costs of intervention and components | Total costs of control and components | Measure of effectiveness | Incremental cost-effectiveness ratio | Willingness-to-pay-threshold |
|--|---|---|---|---|---|--|---|--|
| Axelsson et al. (2020) ²⁷ Sweden | RCT; 204 patients (≥18 years); Societal perspective | Health anxiety or principal diagnosis of DSM-5 somatic symptom disorder | Therapist-guided ICBT (12 weekly sessions) | US\$ 13,113 modelled net total costs from BS to 12months; Components: -Intervention costs -Direct medical costs (Healthcare visits, medication) -Direct non-medical costs -Indirect costs (Unemployment, sick leave, work cutback, domestic) | US\$ 19,240 modelled net total costs from BS to 12months; Components: -Intervention costs -Direct medical costs (Healthcare visits, medication) -Direct non-medical costs -Indirect costs (Unemployment, sick leave, work cutback, domestic) | (1) Clinically significant improvement; (2) QALYs | FTF-CBT vs to ICBT: (1) US\$ 39,057 per additional patient in a clinically significant improvement (2) US\$ 643,516 per QALY gained | Not reported |
| Baumann et al. (2020) ²⁸ Germany | Modelling; Societal perspective | Unipolar depression | Base case scenario: ICBT with waiting time of 3 weeks | Cost per cycle (1week) and state: -Depressed (untreated) €106.25 -Depressed (during CBT) €57.60 -Remission €9.23 Components: -Pharmaceutical -Outpatient -Inpatient -Indirect | Cost per cycle (1week) and state: -Depressed (untreated) €106.25 -Depressed (during CBT) €57.60 -Remission €9.23 Components: -Pharmaceutical -Outpatient -Inpatient -Indirect | QALYs | Base Case: Dominant with Incremental cost of €-1755 and incremental effects of 0.256 | At €0 per QALY gained, 76.0% probability of being cost-effective. Other thresholds does not cause variations of this chance. |

| Study | Study design, sample and perspective | Mental health condition | Intervention type | Total costs of intervention and components | Total costs of control and components | Measure of effectiveness | Incremental cost-effectiveness ratio | Willingness-to-pay-threshold |
|---|---|----------------------------|--|---|--|---|--|---|
| Nordh et al. (2021) Sweden ²⁹ | RCT; 103 children and adolescents aged 10 to 17 years old; Societal and health care professional perspectives | Social anxiety disorder | Therapist-guided internet-delivered cognitive behavioral therapy (ICBT) | €176.84 mean health care cost, €2426.20 mean societal cost; Components: healthcare visits, non-healthcare related support, medication and supplements, absenteeism and presenteeism | €145.36 mean health care cost, €3502.5 mean societal cost; Components: healthcare visits, non-healthcare related support, medication and supplements, absenteeism and presenteeism | QALY gained; differences in remitter status | Societal ICER indicating cost-savings (-€17 900 per differences in remitter status), CUA ICER not calculated due to no difference in utility | Threshold not stated but at €30,000 WTP based on acceptability curve, around 90% probability of cost-effective. |
| Piera-Jimenez et al. (2021) ³⁰ Spain | Economic modelling (Markov); 229 adult patients (18 years and older); Healthcare and societal perspective | Major depressive disorder | Community internet-based cognitive behavioral therapy intervention | Not reported; Costs for health care costs included remission and depression; costs for societal included loss of labor productivity | Not reported; Costs for health care costs included remission and depression; costs for societal included loss of labor productivity | QALY gained | Over a lifetime time horizon (100 years): €29,366.92 per QALY gained for healthcare perspective, €27,783.38 per QALY gained for societal perspective | At WTP of €30,000 intervention is cost-effective (probability of being cost-effective not reported) |
| Richards et al. (2020) ³¹ UK | RCT; 361 patients; Health and social care perspective | Depression and anxiety | A low-density intervention delivered over 8 weeks, Internet-delivered cognitive behavioural therapy (iCBT) | £198.71 per patient over the 8-week intervention period; Components: intervention delivery, health professional visits, health care costs (ambulance and inpatient/day care) | £102.99 per patient at 8 weeks; Components: intervention delivery, health professional visits, health care costs (ambulance and inpatient/day care) | QALY gained | Over an 8-week time horizon, £21,253 per QALY gained | At WTP £20,000, 45.4% probability of cost-effectiveness; at At WTP £30,000, 64.4% probability of cost-effectiveness |
| Thase et al. (2020) ³² USA | RCT; 154 patients; Perspective unclear | Major depressive disorders | Computer-assisted forms of cognitive behavior therapy (CCBT) | Mean (SD) total service costs at 6 months: \$1,247 (\$1423) | Mean (SD) total service costs at 6 months: \$2,164 (\$3,465) | QALYs (CBT: 0.3412; CCBT: 0.3415) | Not reported | At WTP \$50,000, 96% probability of cost-effectiveness |

RCT, randomised controlled trial; QALY, quality-adjusted life years; WTP, willingness-to-pay threshold; iCBT, internet-delivered cognitive behavioural therapy

Summary and conclusions

Are supported DMHIs effective?

Our review of reviews suggests that supported DMHIs are effective for treating all of the disorders we examined – depression, anxiety disorders, and binge eating disorder.

Based on many studies, there is strong evidence of effectiveness of supported DMHIs for depression in adults. Furthermore, the evidence shows that supported DMHIs⁶ and face-to-face psychotherapy³³ for depression result in similar rates of response to treatment, remission and deterioration. There was a tendency towards larger effects with therapeutic rather than administrative support, but this was not statistically significant.⁷ A few characteristics identify who will do better (e.g., those who are native-born, in an intimate relationship, older, and with more severe symptoms).⁶ However, this should be interpreted in the context of the monolithic nature of samples (middle-aged females predominate).

There is a small to moderate effect of supported DMHIs for depression in youth, but a suggestion of publication bias tempers this.⁸ High levels of support may be especially important for youth. Based on a few studies, there seems to be no difference in the effectiveness of supported DMHIs and usual care or other active comparison interventions in treating depression in youth.

There are large effects of supported DMHIs for generalised anxiety disorder (GAD),¹⁴ social anxiety disorder,¹⁵ panic disorder,¹⁷ PTSD¹⁸ and OCD¹⁶ in adults. However, the findings are based on relatively small numbers of studies for PTSD and OCD. In contrast, the effect of supported DMHIs for anxiety in youth is small to moderate.¹⁰

Supported DMHIs seem to be as effective as other active control interventions (e.g., face-to-face treatment) for social anxiety disorder¹⁵ and panic disorder¹⁷ in adults. Outcomes are better with a longer intervention length for GAD in adults.¹⁴ Outcomes are better when the comparison group is passive (e.g., waitlist), adherence is high, and symptoms are more severe for panic disorder in adults.¹⁷ In terms of variation in support or guidance, there was no effect of support time for GAD,¹⁴ therapist experience for social anxiety disorder¹⁵ or therapist time for panic disorder.¹⁷

Finally, rates of deterioration are around half or less in those with depression⁹ and a range of mental disorders,¹¹ respectively, who receive supported DMHI interventions compared with control (mainly waitlist) conditions at post-treatment.

Are supported DMHIs cost effective?

The existing economic evaluation evidence showed that the provision of supported DMHIs is generally low cost and effective. Our review of local and international evidence suggests that these interventions will likely be cost effective compared with usual care across different settings, population groups and policy contexts. Therefore, in addition to improving clinical outcomes, supported DMHIs have the potential to be good value for money.

Strengths and limitations

To our knowledge, this is the first mental disorder specific synthesis of evidence of the effectiveness of supported online DMHIs.

Our review of effectiveness reviews should be interpreted in the context of several limitations. We did not focus on transdiagnostic or mobile-based supported DMHIs, or on the effects of supported DMHIs in the promotion of mental health in well populations and prevention of mental disorders in subclinical populations. Furthermore, our review does not provide evidence for the effectiveness of

DMHIs across the lifespan (e.g., children or the elderly), all mental disorders (e.g., psychotic, bipolar, personality, substance-related/addictive, neurodevelopmental etc.) or disadvantaged groups (e.g., CALD, ATSI, rural and remote, low SES). Finally, most supported DMHIs were based on CBT, which means findings are not generalisable to all other therapeutic approaches.

Our economic evaluation review should also be interpreted in the context of several limitations. The methodology used across the economic evaluation studies was heterogeneous, including aspects such as cost identification, valuation and estimation. Therefore, it can be difficult to make direct comparison between studies, and conclusions about cost-effectiveness need to be considered carefully within the context of each study. In addition, the reliability of cost-effectiveness estimates can be affected by the quality of studies. Although most of the studies covered in this review were of (self-reported) good quality, the small proportion of low-quality studies and their impact on overall cost-effectiveness was unknown. Further research is necessary to investigate the relationship between the quality of included studies and economic evaluation outcomes.

Implications and conclusions

Supported DMHIs for adults with mental disorders, particularly those founded on evidence-based CBT, work – often as well as usual treatment – and have the potential to be good value for money. The evidence base in young people is promising but limited by comparison; more high-quality research in this population, including active treatment control groups and long-term follow up, is needed.¹⁰ DMHIs with varying degrees and types of support are already being delivered in Australia (and internationally), from where much of the evidence has been generated. It should be noted, however, despite favourable evidence for supported online DMHIs, some consumers simply prefer face-to-face services which results in dropping out of DMHI services.³⁴

Several key issues need to be considered when implementing and evaluating DMHIs. First, there are gaps in knowledge about the effectiveness of supported DMHIs involving therapeutic approaches other than CBT; and in children, the elderly and disadvantaged minority groups (e.g., CALD, ATSI, LGBTQIA+). Second, a better understanding of adherence, dosage, type and intensity of guidance or support, and long-term impact of the treatment effect is crucial towards increasing the reliability of the conclusions drawn. Third, using standardised mental health outcome and cost components and comparator groups will enable meaningful comparisons to be made between different interventions in terms of effectiveness and cost-effectiveness. Fourth, using modelled economic evaluation to combine multiple data sources of important parameters such as clinical effectiveness, disease progression, resource use and health-related quality of life may further improve the generalisability of findings. As more evidence of clinical effectiveness emerges from future interventions, a taxonomy for supported DMHIs is likely needed to address the issues above and to overcome the major methodological limitations of the existing evidence base.

Our review supports the recommendations made in the Productivity Commission's Mental Health Inquiry Report to expand (and sustain) supported online DMHIs, particularly those based on CBT targeting depression and anxiety,³ which have the potential to result in at least small benefits for large segments of the community. Funding should be aimed at not only implementation of services, but also ongoing evaluation of effectiveness and cost effectiveness. It should also be directed towards research to fill the existing gaps in knowledge and raising community awareness of supported DMHIs, especially among GPs as the first port of call for mental health problems. This is particularly important in the context of the current pandemic, which has led to nationwide increased distress and increasing remote service use more broadly.³⁵ This area of knowledge and service growth would be supported by a repository for evidence-based DMHIs, such as the Head to Health Gateway or its forthcoming replacement, the National Digital Mental Health Platform. Such a repository would help consumers and health professionals make informed decisions about accessing trustworthy mental health care.

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Appendix A: Method for literature review of effectiveness studies

Eligibility criteria

We included meta-reviews (reviews of reviews) and meta-analyses that reported on the effectiveness of supported DMHIs that met the following criteria:

- Reviews of studies originating primarily from high-income countries with health systems that are comparable to Australia or are known to have implemented or piloted supported DMHIs. These included but were not limited to the United Kingdom, Canada, New Zealand, the Netherlands and the USA.
- Published in peer-reviewed journals between 2011 and 2021.
- Reviewed studies of services in which mental health problems (including suicidality) were the focus of the intervention
- Delivered the intervention via a digital platform.
- The majority (two-thirds or more) of primary studies included in the review involved human support in the form of a therapist, clinician or coach OR the review findings were split by primary studies involving human support and primary studies that were self-directed. All types of support were eligible including therapeutic and administrative forms of support.
- Involved participants of any age.
- Randomised controlled trials and quasi-experimental designs that report on effectiveness, based on samples receiving eligible supported DMHIs.
- Were written in English.

Reviews were excluded if they:

- Were based on qualitative study designs, are editorials, commentaries, discussions, or literature summaries;
- Focused on smartphone apps or therapeutic videogames exclusively or in the majority of primary studies (two-thirds or more);
- Focused on neurological disorders (e.g., dementia) or addiction disorders in the absence of mental health problems;
- Focused on populations with physical health conditions where improving mental health symptoms was a secondary goal OR where these studies were pooled with other eligible studies;
- Focused on nonclinical populations (e.g., employees, university students);
- Focused on prevention of mental disorders or
- Involved studies of DMHIs delivered via email, phone, chat, video in the absence of an online component.

Identification and selection of studies

On 5 August 2021, we searched the academic databases: Medline, PsycINFO, CINAHL and Scopus using the search terms shown in Box 1.

Box 1: Search strategy

OID MEDLINE – 158 RESULTS

1. ((mental health* or psych* or depress* or anxiety) adj5 (digital or online or internet or mHealth or eHealth or desktop or telehealth or telemedicine or e-mental health)).mp.
2. (therapist* or clinician* or coach or personal or supported or guided or counsel* or psychologist* or psychiatrist* or nurse* or social worker*).mp.
3. (treat* or service* or support* or prog* or intervention*).mp.
4. ((systematic adj2 review*) or (meta-analys* or metaanalys*)).mp.
5. 1 and 2 and 3 and 4
6. limit 5 to (english language and yr="2011 - 2021")

OID PSYCINFO – 102 RESULTS

1. ((mental health* or psych* or depress* or anxiety) adj5 (digital or online or internet or mHealth or eHealth or desktop or telehealth or telemedicine or e-mental health)).mp.
2. (therapist* or clinician* or coach or personal or supported or guided or counsel* or psychologist* or psychiatrist* or nurse* or social worker*).mp.
3. (treat* or service* or support* or prog* or intervention*).mp.
4. ((systematic adj2 review*) or (meta-analys* or metaanalys*)).mp.
5. 1 and 2 and 3 and 4
6. limit 5 to (english language and yr="2011 - 2021")

CINAHL – 82 RESULTS

"(("mental health*" or psych* or depress* or anxiety) N5 (digital or online or internet or mHealth or eHealth or desktop or telehealth or telemedicine or "e-mental health") AND (therapist* or clinician* or coach or personal or supported or guided or counsel* or psychologist* or psychiatrist* or nurse* or "social worker*") AND (treat* or service* or support* or prog* or intervention*) AND (((systematic N2 review*) or (meta-analys* or metaanalys*)))
Published Date: 20110101-20211231 on 2021-08-05 01:17 AM"
Limiters - Published Date: 20110101-20211231
Narrow by Language: - english
Search modes - Boolean/Phrase
Academic journals

SCOPUS – 200 RESULTS

(TITLE-ABS-KEY (("mental health*" OR psych* OR depress* OR anxiety) W/5 (digital OR online OR internet OR mhealth OR ehealth OR desktop OR telehealth OR telemedicine OR "e-mental health")) AND TITLE-ABS-KEY (therapist* OR clinician* OR coach OR personal OR supported OR guided OR counsel* OR psychologist* OR psychiatrist* OR nurse* OR "social worker*") AND TITLE-ABS-KEY (treat* OR service* OR support* OR prog* OR intervention*) AND TITLE-ABS-KEY ((systematic W/2 review*) OR (meta-analys* OR metaanalys*))) AND (LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMIT-TO (PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011)) AND (LIMIT-TO (LANGUAGE , "English")))

We also checked the reference lists and citations of included reviews identified through the search. In addition, other relevant literature was identified through previous work undertaken by AM and BB including reviews of the effectiveness of computerised treatments for depression and anxiety.^{36,37}

Search results were imported into the reference manager EndNote, where duplicates were removed. Two reviewers independently screened each title and abstract from the initial literature search against the inclusion criteria. Due to the large number of eligible reviews, we only obtained the full text report for articles that appeared to be meta-analyses. These full-text articles were screened for eligibility by one author and a sample was checked for eligibility by a second author. As there were multiple eligible reviews on the same topic (e.g., internet-based CBT for depression in adults), one author assessed each review for overlap with other reviews and selected the most appropriate to include. Given DMHIs is a rapidly growing area of research we preferenced the most recently published review (or most recent search) then the review with the most comprehensive outcomes relevant to this umbrella review, as is recommended when there are overlapping reviews.³⁸

Data extraction and assessment of review quality

A data extraction template was developed in Excel. Data from each review was extracted by one author. We extracted the following data from each included review: mental health condition, databases searched, search years, publication years of included studies, number of included studies, sample demographics, location of studies, psychological approach of DMHI, description of support/guidance, duration of intervention, risk of bias of included studies, comparison conditions, timepoint of comparison, mental health outcome, pooled effect size, heterogeneity, publication bias and moderators.

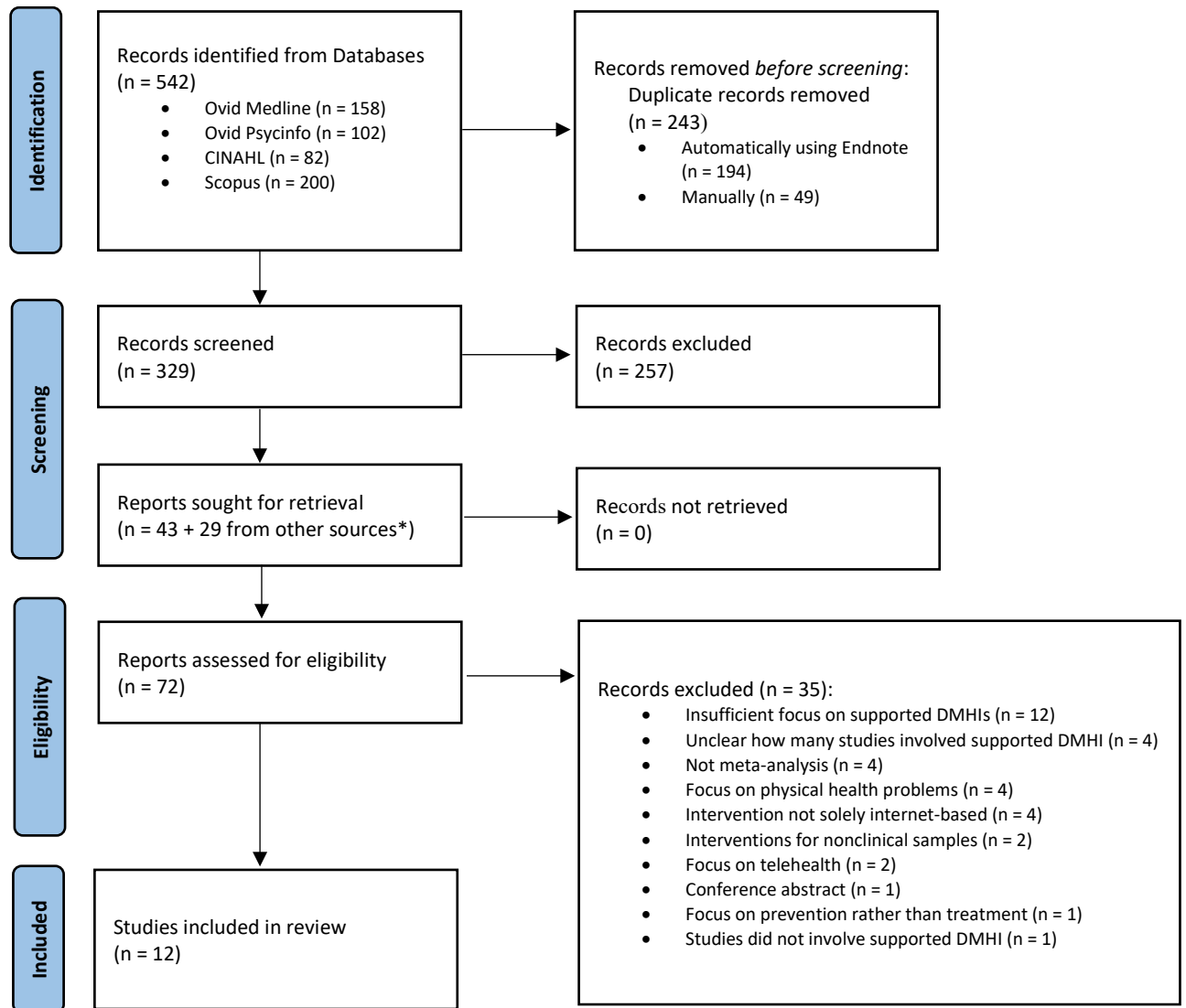
We assessed methodological quality of included meta-reviews and meta-analyses using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR2) tool.¹³ This tool provides guidance to rate the overall confidence in the results of a review (high, moderate, low or critically low depending on the number of critical flaws and/or non-critical weaknesses). The tool includes 16 domains with the following domains judged as critical for this review: protocol registered before start of review; adequacy of literature search; assessment of risk of bias in included studies; appropriateness of meta-analytic methods; consideration of risk of bias when interpreting results; and assessing presence and likely impact of publication bias.

Synthesis method

Data were synthesised narratively, except for obsessive compulsive disorder (OCD). For OCD we could not identify any review where we could extract the effectiveness of supported DMHIs. We therefore performed a meta-analysis on a subset of studies reported in a review by Hoppen et al (2021).

Effect size is a metric used to indicate the magnitude of the difference in a given outcome (e.g., symptoms of mental disorder as assessed using a standardised measurement tool) between two means. An effect size (Cohen's *d* or Hedge's *g*) of around 0.2 is considered small, 0.5 medium and 0.8 large.³⁹

Appendix B: PRISMA flow diagram of search for systematic reviews on effectiveness



Note. DMHI, digital mental health intervention; *other relevant literature was identified through previous work undertaken by AM and BB including reviews of the effectiveness of computerised treatments for depression and anxiety.^{36, 37}

Appendix C: Reasons for excluding 25 eligible review studies

| Study | Type of review | Search years | Demographic | Mental health condition(s) | Comments and reasons for excluding |
|--|----------------|--|--|---|---|
| Andersson et al. (2019). Internet Interventions for Adults with Anxiety and Mood Disorders: A Narrative Umbrella Review of Recent Meta-Analyses. <i>The Canadian Journal of Psychiatry</i> , 64(7), 465-470. | MR | Jan 2014 – Sept 2018 | Adults | PD SAD GAD PTSD MDD | Only includes one effect per review (not comprehensive) and only includes anxiety and depression. Superseded by other reviews that focussed on these disorders. |
| Andrews et al (2018). Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis. <i>Journal of Anxiety Disorders</i> , 55, 70-78. | MA | 2004-2016 | Aged 18+ | MDD GAD PD SAD | 32 studies for MDD. 12 studies for PD. 11 studies for SAD. 9 studies for GAD. All disorders reported separately but combined guided with unguided interventions. Also reports all conditions together. These analyses don't break down disorder by control condition or look at follow-up period. Similar to Olthius et al. (2015) and superseded by Pauley et al. (2021). |
| Baumeister et al. (2014). The impact of guidance on Internet-based mental health interventions - A systematic review. <i>Internet Interventions</i> , 1(4), 205-215. | MA | Up to 4/6/2013 | Adults | Social phobia, Depression Eating disorders, Insomnia PD Anxiety GAD Diagnosis and subthreshold | Pools all disorders together to compare guided vs unguided so not that useful. Also looks at effect of qualification within guided (pooling across disorders) but superseded by Domhardt et al. (2019). |
| Bennett et al. (2020). eHealth to redress psychotherapy access barriers both new and old: A review of reviews and meta-analyses. <i>Journal of Psychotherapy Integration</i> , 30(2), 188-207. | MR | NR (search conducted March/April 2020) | Varied, commonly community, clinical or undergrad participants. Less frequently children and adolescents, caregivers, and employees) *demographics not eligibility criterion, obtained from results | Common mental health problems (e.g., depression, anxiety, substance use, general wellbeing) | Includes reviews of both supported and unsupported interventions, mixed mental health problems, apps, and substance use. |
| Black et al. (2021). The effectiveness of online psychotherapy interventions for the treatment of perinatal mental health disorders: A systematic review. <i>Evidence Based Midwifery</i> , 19(1), 6-18. | MA | Up to July 2020. | Women | Antenatal depression and postnatal depression | Only includes 5 studies. Had to have a clinician-assessed diagnosis so narrower focus. Less comprehensive than the reviews we included for depression. |

| Study | Type of review | Search years | Demographic | Mental health condition(s) | Comments and reasons for excluding |
|---|----------------|-------------------------------------|---|---|---|
| Cowpertwait et al. (2013). Effectiveness of web-based psychological interventions for depression: A meta-analysis. <i>International Journal of Mental Health and Addiction</i> , 11(2), 247-268. | MA | up to October, 2010 | Adults Community, primary and secondary care | Depression | Superseded by newer reviews |
| Domhardt et al. (2019). Internet- and mobile-based interventions for anxiety disorders: A meta-analytic review of intervention components. <i>Depression and Anxiety</i> , 36(3), 213-224. | MA | Up to April 2017 | Adults ≥18 years | Specific phobia, social anxiety disorder, panic disorder (PD), agoraphobia, or generalized anxiety disorder | Pools all anxiety disorders together. Looks at effect of qualification within guided (4 studies). Anxiety disorder specific vs transdiagnostic. CBT vs other therapeutic approaches. Superseded by disorder-specific reviews. |
| Domhardt et al. (2020). Are Internet- and mobile-based interventions effective in adults with diagnosed panic disorder and/or agoraphobia? A systematic review and meta-analysis. <i>Journal of Affective Disorders</i> , 276, 169-182. | MA | Up to June 2019 | Adults | Panic disorder | Overlaps with Polak et al. (2021), ¹⁷ which supersedes it. |
| Grist et al. (2019). Technology Delivered Interventions for Depression and Anxiety in Children and Adolescents: A Systematic Review and Meta-analysis. <i>Clinical Child and Family Psychology Review</i> , 22(2), 147-171. | MA | N/R | Youth 18 years and younger | Depression and anxiety | Includes CBT, ABM and CBM interventions. Overlaps with, and not as comprehensive as, Christ et al. (2020) ¹⁰ and Garrido et al. (2019), ⁸ both of which supersede it. |
| Huguet et al. (2018). A systematic review and meta-analysis on the efficacy of Internet-delivered behavioral activation. <i>Journal of Affective Disorders</i> , 235, 27-38. | MA | Up to June 2017 | Participants from non-clinical settings, adults (18 years or older) | Depression, subthreshold depression, complicated grief and rumination, depression with comorbid diabetes, postpartum depression | Reviews 9 studies on behavioural activation for different types of depression. Not as comprehensive as other reviews on depression. |
| Kampmann et al. (2016). Meta-analysis of technology-assisted interventions for social anxiety disorder. <i>J Anxiety Disord</i> , 42, 71-84. | MA | Up to June 2015 | Adults | Social anxiety disorder | Compares to passive and active controls, and at post and follow-up. Uses g. Overlaps with Pauley et al. (2021) and superseded by Guo et al. (2021). ¹⁵ |
| Karyotaki et al. (2021). Internet-Based Cognitive Behavioral Therapy for Depression: A Systematic Review and Individual Patient Data Network Meta-analysis. <i>JAMA Psychiatry</i> , 78(4), 361-371. | MA | Up to January 1, 2019 | Community, clinical, mixed, other; adult | Depression | Uses individual participant data. Different from Karyotaki et al. (2018) ¹⁹ as it focuses on CBT only. Focuses on relative efficacy of guided vs unguided (also TAU and WL) in a network analysis so less useful. |
| Königbauer et al. (2017). Internet- and mobile-based depression interventions for people with diagnosed depression: A systematic review and meta-analysis. <i>Journal of Affective Disorders</i> , 223, 28-40. | MA | Up to June 2016 | Adults | Depression | Overlaps with Ahern et al. (2018) ⁷ and Wright et al. (2019) and is superseded by them. |
| Lau et al. (2017). Therapist-Supported Internet-Based Cognitive Behavior Therapy for Stress, Anxiety, and Depressive Symptoms Among Postpartum Women: A Systematic Review and Meta-Analysis. <i>Journal of Medical Internet Research</i> , 19(4), e138. | MA | from inception to February 9, 2017. | women with age ≥ 18 years in the postpartum period (≤ 2 years postpartum) | Stress, Anxiety, and Depressive Symptoms | Focuses on symptoms (not disorder) and other reviews we included cover depressive and anxiety disorders, albeit not in this specific population. |

| Study | Type of review | Search years | Demographic | Mental health condition(s) | Comments and reasons for excluding |
|---|----------------|---|---|---|---|
| Lewis et al. (2018). Internet-based cognitive and behavioural therapies for posttraumatic stress disorder (PTSD) in adults. <i>Cochrane Database of Systematic Reviews</i> , 2018(12). | MA | to June 2016, update search on 1 March 2018 | Adults (aged over 16 years or over), in which at least 70% of the participants met the diagnostic criteria for PTSD | PTSD | Superseded by Simon et al. (2021). ¹⁸ |
| Olthuis et al. (2015). Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. <i>Cochrane Database of Systematic Reviews</i> (3). | MA | Up to March 2015 | Adults | Anxiety disorders (pools them together) | Includes panic, agoraphobia, social phobia, acute stress, PTSD, GAD, OCD, specific phobia. Superseded by newer review [Pauley et al. (2021)] for panic/agoraphobia, social phobia, GAD, mixed. |
| Pauley et al. (2021). Two decades of digital interventions for anxiety disorders: a systematic review and meta-analysis of treatment effectiveness. <i>Psychological Medicine</i> , 1-13. | MA | Up to 1 January 2020 | Adults Community, clinical | Anxiety disorders | Includes 42 guided, 11 unguided studies. Pools anxiety disorders for comparison of guided vs unguided. Also has separate analyses for GAD (9), mixed anxiety (9), panic disorder (15), social anxiety disorder (20) but these include unguided studies and they don't look at effect of control group or follow-up period. <u>Panic</u> : overlaps with Polak et al. (2021) ¹⁷ and superseded by it because Pauley 2021 includes unguided and has less detailed comparisons. <u>GAD</u> : overlaps with Richards et al. (2015) and Andrews et al. (2018). Superseded by Eilert et al. (2021). ¹⁴ <u>Social</u> : overlaps with Andrews et al. (2018) and very similar so use this one as more recent. Overlaps with Kampmann 2016. Superseded by Guo et al. (2021). ¹⁵ |
| Podina et al. (2016). A Meta-Analysis on the Efficacy of Technology Mediated CBT for Anxious Children and Adolescents. <i>Journal of Rational-Emotive & Cognitive-Behavior Therapy</i> , 34(1), 31-50. | MA | Up to Sept 2015 | Youth 18 years and younger | Anxiety | Superseded by newer review – Christ et al. (2020). ¹⁰ |
| Richards et al. (2012). Computer-based psychological treatments for depression: a systematic review and meta-analysis. <i>Clinical Psychology Review</i> , 32(4), 329-342. | MA | March 2001- March 2011 | Adults | Depression | Superseded by several newer reviews. |
| Richards et al. (2015). The efficacy of internet-delivered treatment for generalized anxiety disorder: A systematic review and meta-analysis. <i>Internet Interventions</i> , 2(3), 272-282. | MA | Up to June 2013 | Adults | GAD | Includes both disorder specific interventions and transdiagnostic approaches. Superseded by newer review – Pauley et al. (2021). |
| Simblett et al. (2017). A Systematic Review and Meta-Analysis of e-Mental Health Interventions to Treat Symptoms of Posttraumatic Stress. <i>JMIR Mental Health</i> , 4(2), e14. | MA | up to Nov 2016 | Adults | PTSD | Superseded by newer review – Simon et al. (2021) ¹⁸ . |
| Stech et al. (2020). Internet-delivered cognitive behavioral therapy for panic disorder with or without agoraphobia: a systematic review and meta-analysis. <i>Cognitive Behaviour Therapy</i> , 49(4), 270-293. | MA | Up to Nov 2018 | Adults | Panic | Superseded by newer review – Polak et al. (2021) ¹⁷ |
| Twomey et al. (2017). Effectiveness of a freely available computerised cognitive behavioural therapy programme (MoodGYM) for depression: Meta-analysis. <i>Australian and New Zealand Journal of Psychiatry</i> , 51(3), 260-269. | MA | up to Jan 2016 | Adults | Depression, anxiety symptoms | Only included studies involving (a) adults with elevated mental ill health symptoms or (b) adults seeking mental health interventions. Focuses on MoodGYM only. Too niche. |
| Twomey et al. (2020). Effectiveness of a tailored, integrative Internet intervention (deprexis) for depression: Updated meta-analysis. <i>PLoS ONE [Electronic Resource]</i> , 15(1), e0228100. | MA | up to Aug 2019 | Adults | Depression | MA of specific intervention (deprexis) primarily in Germany. Too niche. |

| Study | Type of review | Search years | Demographic | Mental health condition(s) | Comments and reasons for excluding |
|---|----------------|-----------------|--------------------|----------------------------|--|
| Wright et al. (2019). Computer-Assisted Cognitive-Behavior Therapy for Depression: A Systematic Review and Meta-Analysis. <i>J Clin Psychiatry</i> , 80(2). | MA | Up to July 2016 | 16 years and older | Depression | Overlaps with Ahern et al. (2018) ⁷ and is superseded by it (search ended earlier). |

GAD, generalised anxiety disorder; **MA**, meta-analysis; **MDD**, major depressive disorder; **MR**, meta-review; **NR**, not reported; **PD**, panic disorder; **PTSD**, post-traumatic stress disorder; **SAD**, social anxiety disorder; **TAU**, treatment as usual; **WL**, waiting list

Appendix D: Method for literature review of cost effectiveness studies

There were two stages in our pragmatic literature review of cost-effectiveness of supported DMHIs. In the first stage, the research team (AT, LL) conducted a desktop search to identify the most recent systematic reviews of economic evaluations for supported DMHIs. The reference lists of the identified articles from this desktop search were also searched for additional systematic reviews or meta-analyses.

In the second stage, a systematic search was performed to identify additional articles that were published since the most recent systematic review that was identified in the first stage. The following databases were searched from 1 January 2020 to 1 August 2021: MEDLINE, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews. The full MEDLINE search strategy can be found in Box 2. The inclusion criteria included: (i) studies investigating depression or anxiety-related outcomes, (ii) studies with digital-based and guided/supported interventions and (iii) studies that include full economic evaluations (i.e., cost-minimisation, cost-effectiveness, cost-utility, cost-consequence or cost-benefit analyses). There was no restriction on study design – within-trial economic evaluation, modelling studies and administrative data analyses were included. Opinion pieces, editorials, commentaries and studies published in a language other than English were excluded.

After the systematic search was completed, all articles were imported into a reference management software and duplicates were removed. Eligible articles were then identified using a two-stage screening process, first by titles and abstracts and followed by full texts. Data were then extracted from the included articles using a standard template and summarized into a table.

Box 2: MEDLINE Search Strategy

Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily
1 December 2018 to 1 August 2021
Search Strategy:

1 digital*.ti,kf.
2 (android or app or apps or avatar* or blog* or CD-ROM or cell phone* or cellphone* or chat room* or computer* or cyber* or (digital* adj (based or deliver* or media* or medium or platform* or technolog*)) or DVD or eHealth or e-health or electronic health or e-mail* or email* or e-Portal or ePortal or ePsych* or e-Psych* or eTherap* or e-therap* or electronic forum* or gaming or information technolog* or instant messag* or messaging or internet* or ipad or i-pad or iphone or i-phone or ipod or i-pod or podcast or smart phone or smartphone or social network* site* or social networking or mHealth or m-health or mobile or multi-media or multimedia or online* or on-line or personal digital assistant or PDA or SMS or social medi* or software or telecomm* or telehealth* or tele-health* or telemed* or tele-med* or telemonitor* or tele-monitor* or telepsych* or tele-psych* or teletherap* or tele-therap* or text messag* or texting or virtual* or web* or WWW).ti,kf,hw.
3 computer communication networks/ or internet/ or blogging/ or social media/
4 electronic mail/ or cell phones/ or smartphone/ or text messaging/ or videoconferencing/ or webcasts as topic/ or wireless technology/
5 (eLearning or blended learning).ti,kf.
6 (telecomm* or tele-comm*).ti,kf.
7 Telemedicine/
8 (technology based or ((technology or technologies) adj5 (deliver* or wearable or information or communication? or mood or mental or psychiatr*))).ti,kf.
9 Therapy, Computer-Assisted/
10 (gaming or gamification or smartwatch* or wearable device? or wearables or videogame or video game or videoconferenc* or video conferenc*).ti,kf.
11 (synchronous or asynchronous or (electronic adj2 deliver*)).ti,kf.
12 artificial intelligen*.ti,ab,kf.
13 artificial intelligence/ or computer heuristics/ or expert systems/ or knowledge bases/ or machine learning/ or robotics/
14 ((computer* or online or internet* or (web adj (based or deliver*)) or digital* or multimedia or multi-media or blended) adj2 (CBT or cognitive or behavio?ral or therap* or psychotherap* or counsel*)).ti,ab,kf.
15 (bCBT or b-CBT or cCBT or c-CBT or iCBT or i-CBT).ti,ab,kf.
16 ((distance* or remote*) adj2 (CBT or cogniti* or behavio* or therap* or psychotherap*)).ti,ab,kf.
17 ((computer* or online or internet* or (web adj (based or deliver*)) or digital* or multimedia or multi-media or blended) adj3 (intervention* or program* or bibliotherap* or mindful* or mind training or problem solving or psychoeducat* or psychodrama or rational emotive or RET or reality therap* or role play* or self control or schema* or stress manag* or multicomponent* or multi* component* or (acceptance adj2 commitment))).ti,ab,kf.

- 18 (tele* adj2 (cognitive behavi* or CBT)).ti,ab,kf.
- 19 ((computers or computer interface or software or online or internet or (web adj (based or deliver*)) or multimedia) and (psychotherapy or cognitive therapy or behavior therapy or (acceptance and commitment) or bibliotherapy or metacognition or mindfulness or problem solving or psychoeducation or psychodrama or rational emotive or reality therapy or relaxation therapy or role playing or self control)).hw.
- 20 ((audio* or CD or CD-ROM or chat room or computer* or cyber* or digital* or DVD or e-mail or email or eHealth* or e-Health* or electronic health or etherap* or e-therap* or internet* or interactive or mobile or multimedia or multi-media or mHealth or online or on-line or podcast or tape or taped or telemed* or telehealth* or telepsych* or teletherap* or tele-therap* or instant messag* or SMS or social medi* or text messag* or texting or instant messag* or software or technolog* or video* or virtual or (web adj (based or deliver*)) adj5 (self-help or (self adj2 (direct* or guid* or unguid* or non-guid* or minim* guidance or minim* contact*))))).ti,ab,kf. (1169)
- 21 ((audio* or CD or CD-ROM or chat room or computer* or cyber* or digital* or DVD or e-mail or email or eHealth* or e-Health* or electronic health or etherap* or e-therap* or internet* or interactive or mobile or multimedia or multi-media or mHealth or online or on-line or podcast or tape or taped or telemed* or telehealth* or telepsych* or teletherap* or tele-therap* or instant messag* or SMS or social medi* or text messag* or texting or instant messag* or software or technolog* or video* or virtual or (web adj (based or deliver*)) adj5 (cognitive behavi* or CBT)).ti,ab,kf.
- 22 (self care and (computers or internet or software)).sh.
- 23 (Beat* the Blues or Blues Away or BluesBegone or Blues Begone or blended CBT or bCBT or b-CBT or BounceBackNow or Bounce Back Now or BrainMaster or Brain Master or BrainGame or Brain Game or BRAVEOnline or BRAVE-online or Brave for Teen* or Brave for Child* or caCCBT or CaptainsLog or Captains Log or CatchIT or Catch-IT or CATTs or Camp Cope-A-Lot or CogMed or Cool Teens or deprexis or FindMe or GETON Mood Enhancer or GET ON Mood Enhancer or Glasgow Steps or GlasgowSteps or GripOpJeDip or Grip Op Je Dip or Help4Mood or Interapy or MasterYourMoodOnline or Master Your Mood or Mindcheck* or MindReading or Mind Reading or MindWise or Mind Wise or MobileType or Mobilyze or MoodGym or Mood Gym or MoodHacker or Mood Hacker or MoodHelper or Mood Helper or MoodMechanic or Mood Mechanic or Moodivate or MyCompass or My Compass or NetCope or Net Cope or OCFighter or OC-Fighter or ODIN or overcoming depression on the internet or PlayAttention or Play Attention or Pratenonline or Praten Online or RoboMemo or SALUDBN or SALUD BN or SmartBrain or Smart Brain or SPARX or StressBusters or Stress Busters or Stresspac or StudentBodies or Student Bodies or The Journey or Think Feel Do or ThisWayUp or This-Way-Up).ti,ab,kf.
- 24 (CALM or CAVE or ecompared or e-compared or eSmart* or e-Smart*).ti.
- 25 (Bebo or Chatbot or Chat-bot or Club Penguin or Facebook or Franktown or Friendster or Habbo or Jabbersmack or hi5 or iTwixie or MySpace or Orkut or Sweetie High or Kidzworld or Tumblr or Twitter or Sina Weibo or Yoursphere or YouTube).ti,kf.
- 26 or/1-25
- 27 mental disorders/ or anxiety disorders/ or agoraphobia/ or anxiety, separation/ or neurocirculatory asthenia/ or neurotic disorders/ or obsessive-compulsive disorder/ or hoarding disorder/ or panic disorder/ or phobic disorders/ or phobia, social/ or "bipolar and related disorders"/ or bipolar disorder/ or "disruptive, impulse control, and conduct disorders"/ or firesetting behavior/ or gambling/ or trichotillomania/ or dissociative disorders/ or multiple personality disorder/ or "feeding and eating disorders"/ or anorexia nervosa/ or binge-eating disorder/ or bulimia nervosa/ or "feeding and eating disorders of childhood"/ or female athlete triad syndrome/ or pica/ or mood disorders/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or premenstrual dysphoric disorder/ or seasonal affective disorder/ or cyclothymic disorder/ or neurocognitive disorders/ or alcohol amnestic disorder/ or korsakoff syndrome/ or auditory perceptual disorders/ or "attention deficit and disruptive behavior disorders"/ or attention deficit disorder with hyperactivity/ or conduct disorder/ or child development disorders, pervasive/ or asperger syndrome/ or autism spectrum disorder/ or autistic disorder/ or mutism/ or reactive attachment disorder/ or schizophrenia, childhood/ or stereotypic movement disorder/ or tic disorders/ or tourette syndrome/ or paraphilic disorders/ or exhibitionism/ or "fetishism (psychiatric)"/ or masochism/ or pedophilia/ or sadism/ or transvestism/ or voyeurism/ or personality disorders/ or antisocial personality disorder/ or borderline personality disorder/ or compulsive personality disorder/ or dependent personality disorder/ or histrionic personality disorder/ or hysteria/ or paranoid personality disorder/ or passive-aggressive personality disorder/ or schizoid personality disorder/ or schizotypal personality disorder/ or "schizophrenia spectrum and other psychotic disorders"/ or affective disorders, psychotic/ or capgras syndrome/ or delusional parasitosis/ or morgellons disease/ or paranoid disorders/ or psychotic disorders/ or psychoses, substance-induced/ or psychoses, alcoholic/ or schizophrenia/ or schizophrenia, catatonic/ or schizophrenia, disorganized/ or schizophrenia, paranoid/ or shared paranoid disorder/ or sexual dysfunctions, psychological/ or dyspareunia/ or vaginismus/ or sleep wake disorders/ or dyssomnias/ or sleep deprivation/ or sleep disorders, circadian rhythm/ or jet lag syndrome/ or sleep disorders, intrinsic/ or "disorders of excessive somnolence"/ or "sleep initiation and maintenance disorders"/ or parasomnias/ or nocturnal paroxysmal dystonia/ or sleep arousal disorders/ or night terrors/ or somnambulism/ or sleep-wake transition disorders/ or somatoform disorders/ or body dysmorphic disorders/ or conversion disorder/ or factitious disorders/ or munchausen syndrome/ or munchausen syndrome by proxy/ or hypochondriasis/ or neurasthenia/ or substance-related disorders/ or alcohol-related disorders/ or alcohol withdrawal delirium/ or alcoholic intoxication/ or alcoholism/ or binge drinking/ or wernicke encephalopathy/ or amphetamine-related disorders/ or cocaine-related disorders/ or inhalant abuse/ or marijuana abuse/ or opioid-related disorders/ or heroin dependence/ or morphine dependence/ or phencyclidine abuse/ or substance abuse, intravenous/ or "tobacco use disorder"/ or "trauma and stressor related disorders"/ or adjustment disorders/ or stress disorders, traumatic/ or battered child syndrome/ or combat disorders/ or psychological trauma/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/
- 28 Mental Health/
- 29 mental health services/ or community mental health services/
- 30 catatonia/ or child reactive disorders/ or delusions/ or depersonalization/ or depression/ or human coprophagia/ or malingering/ or mental fatigue/ or alert fatigue, health personnel/ or compassion fatigue/ or obsessive behavior/ or stalking/ or paranoid behavior/ or polydipsia, psychogenic/ or problem behavior/ or schizophrenic language/ or self-injurious behavior/ or self mutilation/ or suicide/ or suicidal ideation/ or suicide, attempted/ or stress, psychological/ or wandering behavior/ or dangerous behavior/ or drinking behavior/ or alcohol drinking/ or alcohol drinking in college/ or drug-seeking behavior/ or escape reaction/ or harm reduction/ or impulsive behavior/ or compulsive behavior/ or behavior, addictive/ or "inhibition (psychology)"/ or marijuana smoking/ or hoarding/ or risk-taking/ or gambling/ or social adjustment/ or psychology, social/ or psychosocial deprivation/
- 31 health risk behaviors/ or smoking cessation/ or smoking prevention/ or "tobacco use cessation"/

32 intellectual disability/ or exp learning disorders/ or mentally disabled persons/
33 child behavior disorders/ or juvenile delinquency/ or social behavior disorders/
34 (acute stress or ADHD or addiction or addictive or adjustment disorder* or ADNOS or affective disorder* or agoraphobi* or ((alcohol or tobacco or drug or marijuana or marihuana or cannabis or opioid or opiate or heroin or morphine) adj (user* or abuse* or depend*) or alcoholism or anorexia nervosa or anxiety or asperger* or astheni* or attachment disorder* or attention deficit or autism or autistic or BPD or binge drink* or binge eat* or bingeing or bipolar or body dysmorphi* or bulimi* or catatoni* or college drink* or combat disorder* or compulsi* or conduct disorder* or conversion disorder* or coping behavio* or coprophagi* or cyclothymi* or delusion* or depersonali#ation or depressed or depression or depressive or disruptive behavi* or dissociative disorder* or dyssomni* or dyspareunia* or dysphori* or dysthymi* or dystoni* or eating disorder* or EDNOS or emotional adjustment or emotional trauma or exhibitionism or factitious disorder* or fear or female athlete triad syndrome or fetichis* or firesetting or fire-setting or gambling or gambler* or harm reduction or health anxiety or hoarding or hyperactivity or hypochondri* or hysteri* or impulse control or impulsive or insomnia* or masochis* or medically unexplained or malingering or mania or manic or MDD or mental* or mood? or munchausen* or MUPS or mutism or neurastheni* or neurocognitive disorder* or neurotic or neuros* or nightmare* or night terror* or obsess* or p?edophil* or panic or paranoi* or paraphili* or parasomni* or parasuicid* or passive-aggressive or perceptual disorder* or personality disorder* or phobi* or pica or PND or ((post-trauma* or posttrauma*) adj stress*) or psychiatr* or psychogenic or psychosocial or psychological or psychosomatic or psychotherap* or psychotic or psychos* or PTSD or risk taking or sadis* or schizo* or school adjustment or school refusal or (self adj (injur* or harm or mutilat*)) or sexual dysfunction* or sleep disorder* or smoking cessation or social adjustment or social anxiety or somati* or somatoform or somnambulis* or somnolence or stress disorder* or ((substance or drug or opioid) adj2 (abus* or disorder*)) or SUD or SUDs or suicid* or tic disorder* or tourette* or transvesti* or trichotillomani* or under age drink* or stalking or vaginismus or voyeuris*).ti,kf.
35 ((intellect* and (deficien* or disab* or handicap* or impair*)) or (mental* and (deficien* or disab* or handicap* or impair* or retard*)) or (learning and (difficult* or disab* or disorder* or impair*)) or (down? adj3 syndrome?)).ti,kf.
36 (bullying or (oppositional adj3 (defiant* or disorder*)) or ((conduct or behavi* or antisocial or anti social or dyssocial or emotional* or internal#ing or external#ing) and (disorder* or problem* or difficult* or psychopathol*))).ti,kf.
37 (((aggressive or antisocial or anti-social or runaway or run away) adj3 behavio*) or school dropout or school drop-out or delinquen*).ti,kf.
38 or/27-37
39 ECONOMICS/
40 RESOURCE ALLOCATION/
41 "COSTS and COST ANALYSIS"/ or "cost allocation"/ or cost-benefit analysis/ or "cost control"/ or "cost savings"/ or "cost of illness"/ or "cost sharing"/ or health care costs/ or direct service costs/ or employer health costs/ or hospital costs/ or health expenditures/ or capital expenditures/
42 ECONOMICS, HOSPITAL/ or HOSPITAL CHARGES/ or HOSPITAL COSTS/
43 ECONOMICS, MEDICAL/
44 ECONOMICS, NURSING/
45 economics.mp.
46 economics.fs.
47 (economic* adj2 (analys* or benefit* or consequence* or effect* or evaluat* or minimi#ation or saving*)).ti,ab,kf.
48 MODELS, ECONOMIC/ or MODELS, ECONOMETRIC/
49 ((economic or econometric) adj2 model*).ti,ab,kf.
50 ((cost or costs or costing*) adj2 (analys* or benefit* or consequence* or effective* or estimate* or minimi#ation or saving* or utility or variab*)).ti,ab,kf.
51 (budget* or unit cost).ti,ab,kf.
52 (expenditure* not energy).ti,ab,kf.
53 value for money.ti,ab,kf.
54 or/39-53
55 26 and 38 and 54
56 or/14-16,18
57 54 and 56
58 55 or 57
59 limit 58 to (english language and yr="1997 -Current")

Appendix E: PRISMA flow diagram of studies from the search to update most recent systematic review on economic evaluations of supported DMHIs

