

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Guided Versus Unguided Internet-Delivered Cognitive Behavioural Therapy for Major Depressive Disorder and Anxiety Disorders: Comparative Clinical Effectiveness

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Research Question

What is the comparative clinical effectiveness of guided versus unguided internet-delivered cognitive behavioural therapy for patients with mild-to-moderate major depressive disorder or anxiety disorders?

Key Findings

Three systematic reviews (two with meta-analyses) and ten randomized controlled trials were identified regarding the comparative clinical effectiveness of guided versus unguided internet-delivered cognitive behavioural therapy for patients with mild-to-moderate major depressive disorder or anxiety disorders.

Methods

A limited literature search was conducted on key resources including Ovid Medline, PubMed (for non-Medline records), the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and October 18, 2018. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.



Table 1: Selection Criteria

Population	Adults (aged 16 years and older) with a primary diagnosis of mild or moderate MDD or anxiety disorders (excluding OCD and PTSD) according to a validated diagnostic instrument (e.g., DSM-IV, DSM-V, ICD, Centre for Epidemiological Scale for Depression, Beck Depression Inventory, Patient Health Questionnaire, Structured Diagnostic Interview Schedule) - Participants with a primary diagnosis of anxiety disorders or primary diagnosis of mild to moderate MDD coexisting with other mental health conditions (with the exception of severe depression, OCD, and PTSD) are included - Participants with concurrent pharmacotherapy use are included				
Intervention	Guided internet-delivered CBT (e.g., therapist-guided, clinician-guided, coach-guided) - Both transdiagnostic and disorder-specific programs are included - Non-traditional CBT (e.g., mindfulness CBT), CBT that is delivered via bibliotherapy, and CBT that is described as computerized (e.g., delivered via CD-ROM) with no internet component are excluded				
Comparator	Unguided internet-delivered CBT (e.g., self-guided, self-help)				
Outcomes	Clinical effectiveness (e.g., remission of depression or anxiety symptoms [acute phase], prevention of relapse following a successful acute treatment [maintenance phase], response to therapy [50% reduction in symptoms from baseline], improvement in social function or activities of daily living), time-to-event data (e.g., to response, remission, dropout), changes in use of pharmacotherapy, safety, quality of life, satisfaction with care, and patient adherence				
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies				

CBT = cognitive behavioral therapy; DSM = Diagnostic and Statistical Manual of Mental Disorders; ICD = International Classification of Diseases; MDD = major depressive disorder; OCD = obsessive compulsive disorder; PTSD = post-traumatic stress disorder.

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Three systematic reviews (two with meta-analyses) and ten randomized controlled trials were identified regarding the comparative clinical effectiveness of guided versus unguided internet-delivered cognitive behavioural therapy for patients with mild-to-moderate major depressive disorder or anxiety disorders. No relevant health technology assessments or non-randomized studies were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Three systematic reviews¹⁻³ (two with meta-analyses^{1,3}) and ten randomized controlled trials (RCTs)⁴⁻¹³ were identified regarding the comparative clinical effectiveness of guided versus unguided internet-delivered cognitive behavioural therapy (iCBT) for patients with mild-to-moderate major depressive disorder (MDD) or anxiety disorders. Detailed study characteristics are provided in Table 2.

The identified literature reported varied conclusions regarding the comparative clinical effectiveness of guided versus unguided iCBT for patients with mild-to-moderate MDD or



anxiety disorders. ¹⁻¹³ One systematic review and seven RCTs ^{4,6-8,11-13} included participants with anxiety disorders, one RCT included participants with depression, and two systematic reviews and two RCTs included participants with depression and/or anxiety. The primary outcomes in all included studies ¹⁻¹³ were symptoms of depression or anxiety measured with various symptom assessment scales. The authors of eleven studies ^{1-2,4-12} concluded that there was no clear difference between guided and unguided iCBT for the treatment of symptom severity in patients with anxiety, ^{1-2,4,6-8,11-12} depression, ¹⁰ or anxiety and depression. ^{5,9} However, the authors of one of these RCTs did report lower attrition rates in the guided iCBT group compared to unguided iCBT. Two studies ^{2,13} concluded that guided iCBT outperformed unguided iCBT for symptom severity in patients with depression or anxiety disorders. ¹³ It was not clear from the abstract of one systematic review whether the results indicated if there was a difference in guided and unguided iCBT for the treatment of depression or anxiety disorders.

Table 2: Summary of Included Studies on the Comparative Clinical Effectiveness of Guided Versus Unguided Internet-Delivered Cognitive Behavioural Therapy for Patients with Mildto-Moderate Major Depressive Disorder or Anxiety Disorders

First Author, Year	Study Characteristics and Objectives	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions
		Systematic Rev	iews and Meta-Ar	nalyses	
Olthuis, 2016 ¹	 MA performed 30 included RCTs Adults with anxiety disorders N = 2,181 Objective: to evaluate the effectiveness of iCBT for the treatment of anxiety disorders 	Therapist- supported iCBT	Waiting list control, unguided CBT, or face-to-face CBT	 Anxiety disorder diagnosis Anxiety symptom severity 	One study that compared unguided iCBT to therapist-supported iCBT showed no difference in clinically important improvement in anxiety at post-treatment (54 participants, very low quality evidence) Four studies that compared unguided CBT (2 used bibliotherpy and 2 used iCBT) and therapist-supported iCBT reported no clear differences at post-treatment for disorder-specific anxiety symptoms (253 participants, low quality evidence) or general anxiety symptoms (138 participants, low quality evidence)
Saddichha, 2014 ²	Number of included studies was NR in the abstract Individuals with anxiety or	 Therapist- guided internet- based interventions Unguided internet-based 	NR in the abstract	Symptoms of depression Symptoms of anxiety	"For depression, therapist- guided cognitive behavioral therapy (CBT) had larger effect sizes consistently across studies, ranging from 0.6 to 1.9; while



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First Author, Year	Study Characteristics and Objectives	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions	
	depression N = NR Objective: to review the current research on the effectiveness of internet-based interventions for depression and anxiety	interventions			stand-alone CBT (without therapist guidance) had a more modest effect size of 0.3–0.7." ² "For anxiety disorders, studies showed robust effect sizes for therapist-assisted interventions with effect sizes of 0.7–1.7 (efficacy similar to face-to-face CBT) and stand-alone CBT studies also showed large effect sizes (0.6–1.7)." ² "IBIs for anxiety and depression appear to be effective in reducing symptomatology for both depression and anxiety, which were enhanced by the guidance of a therapist." ²	
Dedert, 2013 ³	MA performed Number of included studies was NR in the abstract Adults with depressive of anxiety disorders N = NR Objective: to evaluate the effectiveness of computerized programs for the treatment of mental health conditions	Web-based programs (including both guided and unguided iCBT)	NR in the abstract	Symptoms of depression Symptoms of anxiety	Computer-based CBT programs have demonstrated effectiveness in reducing symptoms of depression or anxiety Providing support via email, instant messaging, or phone contact may improve attrition rates and treatment response	
	Randomized Controlled Trials					
Ciuca, 2018 ⁴	Individuals meeting the	Guided iCBT (12 week	 Unguided iCBT (12 week 	Severity of self- report panic	Both forms of iCBT showed improvement in	



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First Author, Year	Study Characteristics and Objectives	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions
	diagnostic criteria for panic disorder • N = 111 Objective: to examine the efficacy of guided and unguided iCBT compared to waitlist in patients with PD	intervention)	intervention) • WL	symptoms Diagnostic status Symptoms of depression Functional impairment Catastrophic cognitions Fear of sensations Body vigilance	panic disorder and associated symptoms at post-treatment (guided iCBT vs. WL: Cohen's d=1.04–1.36; unguided iCBT vs. WL: Cohen's d=0.70–1.06) The iCBT groups did not significantly differ for symptom reduction at post-treatment, but the guided treatment was more effective for diagnostic status The guided treatment was superior to the unguided treatment at 6-month follow-up
Dear, 2018 ⁵	Young adults with symptoms of anxiety and depression N = 191 Objective: "to compare the efficacy of an Internet-delivered cognitive behaviour therapy intervention designed for adults aged 18–24 years, when delivered in clinician-guided versus self-guided formats." **Tourising the symptoms of the symptom	Transdiagnostic, clinician-guided iCBT (Mood Mechanic Course)	Transdiagnostic, self-guided iCBT (Mood Mechanic Course)	Symptoms of depression Symptoms of anxiety General psychological distress Satisfaction with life Disability	Compared to baseline, both treatment groups reported improvements in symptoms of anxiety and depression, general psychological distress, satisfaction with life, and disability at post-treatment There were no marked or consistent differences between guided and unguided iCBT at post-treatment, 3-month follow-up, or 12-month follow-up Participants reported high satisfaction with both treatments, although it was slightly higher for clinician guided iCBT
Gershkovich, 2017 ⁶	 Participants with SAD N = 42 Objective: to examine the acceptability and 	Therapist- supported iCBT	Unguided iCBT	Symptoms of SAD Functioning Quality of life Attrition rates	"Both groups experienced a significant reductions in SAD symptoms and improvements in functioning and quality of life, with no significant differences between



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First Author, Year	Study Characteristics and Objectives	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions
	efficacy of a novel iCBT program with and without therapist support				groups in both completer- only and intent-to-treat analyses. However, the therapist support group evidenced lower attrition than the minimal support group (20% vs. 50%)." ⁶
Dear, 2016 ⁷	Participants with SAD N = 233 Objective: to compare transdiagnostic and disorder-specific iCBT programs across clinician-guided and self-guided formats for the treatment of SAD	 Clinician-guided disorder specific iCBT Clinician-guided transdiagnostic iCBT 	 Self-guided disorder specific iCBT Self-guided transdiagnostic iCBT 	Symptoms of SAD Symptoms of depression Symptoms of GAD Symptoms of PD	All treatment groups reported large improvements in symptoms of SAD and moderate-to-large improvements in symptoms of comorbid depression, GAD, and PD at post-treatment and 24-month follow-up compared to pretreatment There were no marked differences in effectiveness between treatment groups
Fogliati, 2016 ⁸	Participants with PD N = 145 Objective: to compare transdiagnostic and disorder-specific iCBT programs across clinician-guided and self-guided formats for the treatment of PD	 Clinician-guided disorder specific iCBT Clinician-guided transdiagnostic iCBT 	Self-guided disorder specific iCBT Self-guided transdiagnostic iCBT	Symptoms of PD Symptoms of depression Symptoms of GAD Symptoms of SAD Symptoms of SAD	All treatment groups reported large improvements in symptoms of PD and moderate-to-large improvements in symptoms of comorbid depression, GAD, and SAD at post-treatment and 24-month follow-up compared to pretreatment There were no marked differences in effectiveness between treatment groups
Titov, 2016 ⁹	 Adults (≥ 60 years) with symptoms of anxiety or depression N = 433 	Transdiagnostic, clinician-guided iCBT with an initial clinician interview	 Transdiagnostic, self-guided iCBT with an initial clinician interview Transdiagnostic, self-guided 	 Symptoms of depression Symptoms of anxiety Satisfaction ratings 	"Large reductions (d ≥1.00) in symptoms of depression and anxiety were observed across groups, and sustained at follow-up. No differences were observed in clinical outcomes or



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First Author, Year	Study Characteristics	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions
i cai	and Objectives				
	Objective: to compared clinician-guided and self-guided versions of an iCBT program for adults aged 60 year and above		treatment without an initial clinician interview		satisfaction ratings."9 "Carefully developed iCBT interventions may significantly reduce symptoms of anxiety and depression in older adults when delivered in either clinician-guided or selfguided formats."9
Montero-Marin, 2016 ¹⁰	Adults from primary care settings with mild or moderate major depression N = 296 Objective: to compare the effectiveness of low-intensity therapist-guided iCBT, completely self-guided iCBT, and improved treatment as usual for individuals with depression	Low-intensity therapist-guided iCBT (Smiling is Fun) + iTAU Completely self-guided iCBT (Smiling is Fun) + iTAU	• iTAU alone	Depression severity (BDI-II score)	Neither iCBT program conferred benefit over iTAU alone after 3 months; however, both iCBT groups outperformed iTAU alone at 6- and 15-month follow-ups Low-intensity therapist-guided iCBT and completely self-guided iCBT did not differ at any time point "An Internet-based intervention for depression combined with iTAU conferred a benefit over iTAU alone in the Spanish primary health care system." Note Table 10 per 10
Dear, 2015 ¹¹	Participants with GAD N = 338 Objective: to compare transdiagnostic and disorder-specific iCBT programs across clinician-guided and self-guided formats for the treatment of GAD	 Clinician-guided disorder specific iCBT Clinician-guided transdiagnostic iCBT 	 Self-guided disorder specific iCBT Self-guided transdiagnostic iCBT 	Symptoms of GAD Symptoms of depression Symptoms of SAD Symptoms of PD	All treatment groups reported large improvements in symptoms of GAD and comorbid depression, SAD, and PD at post-treatment and 24-month follow-up compared to pre-treatment There were no substantive differences in effectiveness between treatment groups
Berger, 2011 ¹²	Individuals	Therapist-	Pure self-help	Symptoms of	"Results showed significant



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First Author, Year	Study Characteristics and Objectives	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions
	meeting the diagnostic criteria for social phobia • N = 81 Objective: to assess the benefits of a self-help iCBT program, the same program with minimal therapist support, and a third group with a flexible level of support for the treatment of social phobia	guided iCBT	(unguided) iCBT • iCBT with flexible levels of support	social phobia Symptoms of depression Interpersonal problems General symptomatology	symptom reductions in all three treatment groups with large effect sizes for primary social phobia measures (Cohen's d = 1.47) and for secondary outcome measures (d = 1.16). No substantial and significant between-groups effects were found on any of the measures (Cohen's d = 0036). Moreover, no difference between the three conditions was found regarding diagnosis-free status, clinically significant change, dropout rates, or adherence measures such as lessons or exercises completed. These findings indicate that Internet-delivered treatment for social phobia is a promising treatment option, whether no support is provided or with two different types of therapist guidance." 12
Titov, 2008 ¹³	Individuals with social phobia N = 98 Objective: to compare the effectiveness of clinician-guided, self-guided, and waitlist control for the treatment of social phobia	Clinician-guided iCBT (the Shyness programme)	Self-guided iCBT (the Shyness programme) Waitlist control	Symptoms of social phobia	Patients who underwent clinician-guided iCBT reported significantly improved symptoms of social phobia compared to the self-guided iCBT and the waitlist control Patients in the self-guided group who completed the treatment did report significant improvement in symptoms of social phobia compared to their baseline (within-group) "The therapist-guided condition, was superior to the self-guided condition,"



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First Author, Year	Study Characteristics and Objectives	Intervention(s)	Comparator(s)	Outcomes	Relevant Conclusions
					but a subgroup of participants still benefited considerably from the latter. These data confirm that self-guided education or treatment programmes for common anxiety disorders can result in significant improvements." 13

BDI-II = Deck Depression Inventory-II; CBT = cognitive behavioral therapy; GAD = generalized anxiety disorder; IBI = internet-based intervention; iCBT = internet-delivered cognitive behavioral therapy; iTAU = improved treatment as usual; MDD = major depressive disorder; NR = not reported; PD = panic disorder; RCT = randomized controlled trial; SAD = social anxiety disorder; SMD = standardized mean difference; WL = waitlist.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

 Olthuis JV, Watt MC, Bailey K, Hayden JA, Stewart SH. Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database Syst Rev.* 2015 Mar 05(3):CD011565.

PubMed: PM25742186

 Saddichha S, Al-Desouki M, Lamia A, Linden IA, Krausz M. Online interventions for depression and anxiety - a systematic review. Health Psychol Behav Med. 2014 Jan 01;2(1):841-881.

PubMed: PM25750823

 Dedert E, McDuffie JR, Swinkels C, et al. Computerized cognitive behavioral therapy for adults with depressive or anxiety disorders. (VA evidence-based synthesis program reports). Washington (DC): Department of Veterans Affairs (US); 2013. PubMed: PM25590119

Randomized Controlled Trials

 Ciuca AM, Berger T, Crisan LG, Miclea M. Internet-based treatment for panic disorder: a three-arm randomized controlled trial comparing guided (via real-time video sessions) with unguided self-help treatment and a waitlist control. PAXPD study results. *J Anxiety Disord*. 2018 May;56:43-55.



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- Gershkovich M, Herbert JD, Forman EM, Schumacher LM, Fischer LE. Internetdelivered acceptance-based cognitive-behavioral intervention for social anxiety disorder with and without therapist support: a randomized trial. *Behav Modif.* 2017 Sep;41(5):583-608.

PubMed: PM28776431

 Dear BF, Staples LG, Terides MD, et al. Transdiagnostic versus disorder-specific and clinician-guided versus self-guided Internet-delivered treatment for Social Anxiety Disorder and comorbid disorders: a randomized controlled trial. *J Anxiety Disord*. 2016 08;42:30-44.

PubMed: PM27261562

 Fogliati VJ, Dear BF, Staples LG, et al. Disorder-specific versus transdiagnostic and clinician-guided versus self-guided Internet-delivered treatment for panic disorder and comorbid disorders: a randomized controlled trial. *J Anxiety Disord*. 2016 Apr;39:88-102.

PubMed: PM27003376

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 PubMed: PM27703754
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PubMed: PM27565118

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PubMed: PM26460536

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 <u>PubMed: PM21255767</u>
- 13. G Titov N, Andrews G, Choi I, Schwencke G, Mahoney A. Shyness 3: randomized controlled trial of guided versus unguided Internet-based CBT for social phobia. Aust N Z J Psychiatry. 2008 Dec;42(12):1030-1040.

PubMed: PM19016091

Non-Randomized Studies

No literature identified.



Appendix — Further Information

Previous CADTH Reports

- 14. e-Therapy interventions for the treatment of anxiety: clinical evidence. (CADTH Rapid response report: summary with critical appraisal). Ottawa (ON): CADTH; 2018: https://www.cadth.ca/sites/default/files/pdf/htis/2018/RC0984%20e-Therapy%20Anxiety%20Final.pdf. Accessed 2018 Oct 26.
- 15. e-Therapy interventions for the treatments of patients with depression: a review of clinical effectiveness. (CADTH Rapid response report: summary with critical appraisal). Ottawa (ON): CADTH; 2018: https://www.cadth.ca/sites/default/files/pdf/htis/2018/RC0983%20-%20E%20therapy%20for%20depression%20Final.pdf. Accessed 2018 Oct 26.
- 16. Self-directed cognitive behavioural therapy for adult patients with a diagnosis of depression: a systematic review of clinical effectiveness, cost-effectiveness, and guidelines. (CADTH Rapid response report: systematic review). Ottawa (ON): CADTH; 2010: https://www.cadth.ca/sites/default/files/pdf/M0014_CBT_for_Depression_L3_e.pdf

Systematic Reviews and Meta-analyses

Alternative Population - Not Restricted to Mild-to-Moderate Major Depression

 Wells MJ, Owen JJ, McCray LW, et al. Computer-assisted cognitive-behavior therapy for depression in primary care: systematic review and meta-analysis. *Prim Care Companion CNS Disord*. 2018 Mar 01;20(2):01.

PubMed: PM29570963

 Twomey C, O'Reilly G, Meyer B. Effectiveness of an individually-tailored computerised CBT programme (Deprexis) for depression: a meta-analysis. *Psychiatry Res.* 2017 10;256:371-377.

PubMed: PM28686935

 Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cogn Behav Ther.* 2009;38(4):196-205.

PubMed: PM20183695

Alternative Intervention - Unclear if iCBT is Included

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PubMed: PM28373153

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PubMed: PM26235445

 Lewis C, Pearce J, Bisson JI. Efficacy, cost-effectiveness and acceptability of self-help interventions for anxiety disorders: systematic review. *Br J Psychiatry*. 2012 Jan;200(1):15-21.

PubMed: PM22215865

 Van't Hof E, Cuijpers P, Stein DJ. Self-help and Internet-guided interventions in depression and anxiety disorders: a systematic review of meta-analyses. CNS Spectr. 2009 Feb;14(2 Suppl 3):34-40.

PubMed: PM19238128

Randomized Controlled Trials

Alternative Comparator - Comparing Different Types of Guidance

 Gilbody S, Brabyn S, Lovell K, et al. Telephone-supported computerised cognitivebehavioural therapy: REEACT-2 large-scale pragmatic randomised controlled trial. Br J Psychiatry. 2017 05;210(5):362-367.

PubMed: PM28254959

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- 28. Brabyn S, Araya R, Barkham M, et al. The second Randomised Evaluation of the Effectiveness, cost-effectiveness and Acceptability of Computerised Therapy (REEACT-2) trial: does the provision of telephone support enhance the effectiveness of computerdelivered cognitive behaviour therapy? A randomised controlled trial. *Health Technol Assess*. 2016 11;20(89):1-64.

PubMed: PM27922448

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Alternative Intervention – Unclear if the Intervention is iCBT

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Alternative Population - Not Restricted to Mild-to-Moderate Major Depression

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 PubMed: PM22060248

Trial Protocols

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PubMed: PM26769021

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Non-Randomized Studies

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