

CADTH OPTIMAL USE REPORT

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Table of Contents

Abbreviations.....	5
Summary of Recommendation	6
Technology.....	6
Methods.....	7
Detailed Recommendation	7
Rationale	7
Considerations.....	8
Evidence.....	9
Clinical Evidence.....	9
Economic Evidence.....	10
Patients’ Perspectives and Experiences Evidence.....	10
Implementation Evidence	11
Ethical Analysis	12
Limitations	13
References	14
Appendix 1: Health Technology Review Panel Details.....	16
Appendix 2: CADTH Adaptation of Health Quality Ontario Economic Evaluation.....	17
Tables	
Table 1: Changes to Model Inputs	17
Table 2: CADTH Base Case Re-analyses — Major Depressive Disorder.....	19
Table 3: CADTH Base Case Re-analyses — Anxiety	21
Table 4: CADTH Exploratory Re-analyses — Major Depressive Disorder (Inclusion of Group CBT as a Comparator).....	23
Table 5: CADTH Exploratory Re-analyses — Anxiety (Inclusion of Group CBT as a Comparator)	24
Table 6: Clinical and Baseline Demographic Inputs.....	26
Table 7: Cost and Resource Utilization Inputs	27
Table 8: Utility Inputs.....	28

Figures

Figure 1: Cost-Effectiveness Scatterplot — Major Depressive Disorder (Base Case)	20
Figure 2: Cost-Effectiveness Acceptability Curve — Major Depressive Disorder (Base Case).....	20
Figure 3: Cost-Effectiveness Scatterplot —Anxiety (Base Case).....	21
Figure 4: Cost-Effectiveness Acceptability Curve — Anxiety (Base Case)	22
Figure 5: Cost-Effectiveness Scatterplot — Major Depressive Disorder (Exploratory Analysis)	23
Figure 6: Cost-Effectiveness Acceptability Curve — Major Depressive Disorder (Exploratory Analysis)	24
Figure 7: Cost-Effectiveness Scatterplot — Anxiety (Exploratory Analysis).....	25
Figure 8: Cost-Effectiveness Acceptability Curve — Anxiety (Exploratory Analysis)	25

Abbreviations

CBT	cognitive behavioural therapy
HQO	Health Quality Ontario
HTERP	Health Technology Expert Review Panel
iCBT	Internet-delivered cognitive behavioural therapy
ICUR	incremental cost-utility ratio
MDD	major depressive disorder
QALY	quality-adjusted life-year
RCT	randomized controlled trial

Summary of Recommendation

These CADTH Health Technology Expert Review Panel (HTERP) recommendations aim to address this policy question: Should Internet-delivered cognitive behavioural therapy (iCBT) be offered to people with mild to moderate major depressive disorder or anxiety disorders? iCBT is defined as structured cognitive behavioural therapy (CBT) delivered remotely over the Internet. iCBT can be guided (by a therapist or other practitioner trained in iCBT) or unguided.

The recommendations were developed following HTERP deliberations over multidisciplinary evidence including an overview of systematic reviews of clinical effectiveness and an economic analysis, conducted by Health Quality Ontario (HQO);¹ and two rapid reviews of clinical effectiveness,^{2,3} an adaptation of the HQO economic analysis (in Appendix 2), and a review of patients' perspectives and experiences, implementation issues, and ethical considerations related to the use of iCBT,⁴ conducted by CADTH. Details of the HTERP deliberative process⁵ are available in Appendix 1 and on the CADTH website.⁶

HTERP recommends that guided Internet-delivered cognitive behavioural therapy be offered to adults with mild to moderate major depressive disorder and/or anxiety disorders.

Technology

CBT is the most commonly used form of psychotherapy for the treatment of patients with depression or anxiety disorders.⁷ By combining the principles of cognitive and behavioural therapies, CBT aims to provide patients with the coping strategies and mechanisms for solving current problems and to change dysfunctional thoughts, behaviours, beliefs, and attitudes.⁸

Since the 1960s,⁹ CBT has been the subject of numerous studies investigating its clinical effectiveness for the treatment of depression and anxiety;¹⁰⁻¹² however, despite the apparent clinical effectiveness of CBT, patients suffering from depression or anxiety disorders are frequently unable to access CBT, which is traditionally delivered during face-to-face sessions.^{13,14} Commonly reported barriers to CBT include high cost, perceived stigma, poor access to treatment in rural areas, long wait times, privacy issues, and a lack of trained clinicians. iCBT, which is the delivery of CBT through an online platform, may be an alternative means of providing treatment for people with depression and anxiety to overcome some of the aforementioned barriers.¹⁵ Specific aspects of different iCBT programs vary widely, including but not limited to electronic mode of delivery, cost, number of sessions, and level (or intensity) of practitioner support.¹⁶

Understanding how these characteristics and factors may influence the experience of iCBT is crucial for practitioners and health care facilities looking to offer iCBT to people with depression or anxiety. Broadly speaking, there is a need to clarify current policy and the appropriate use of iCBT in the context of major depressive disorder (MDD) and anxiety disorders in Canada.

Methods

HTERP developed recommendations on iCBT based on information from a number of sources:

- an overview of systematic reviews of the published literature on clinical effectiveness and safety, and an economic analysis, conducted by HQO¹
- a rapid review of evidence from randomized controlled trials (RCTs) on the clinical effectiveness of iCBT, conducted by CADTH²
- a rapid review of abstracts comparing the clinical effectiveness of guided and unguided iCBT, conducted by CADTH³
- an adaptation of HQO's economic analysis, conducted by CADTH (Appendix 2)
- a review of the published literature on patients' perspectives and experiences, and implementation issues, as well as an analysis of ethical issues of iCBT, conducted by CADTH.⁴

HTERP members reviewed the evidence from these sources, discussed all elements of the HTERP deliberative framework,⁵ and developed a recommendation by consensus. Details on the HTERP deliberative process are available in Appendix 1 and on the CADTH website.⁶

Detailed Recommendation

The objective of this recommendation is to provide advice for Canadian health care decision-makers about the use of iCBT.

HTERP recommends that guided Internet-delivered cognitive behavioural therapy be offered to adults with mild to moderate major depressive disorder and/or anxiety disorders.

Rationale

- ICBT was found to be more effective than wait list control (defined as participants receiving iCBT at a later date) for reducing symptoms of depression or anxiety, and improving quality of life.¹
- ICBT may enhance access to mental health services, and was generally found to be acceptable to people seeking treatment. Guided iCBT (through the support of therapists or other trained practitioners) was generally valued by people seeking treatment, although a minority valued the freedom to navigate iCBT on their own, without therapist guidance. Furthermore, studies describing patients' perspectives and experiences indicated that a blended approach with varying levels of therapist support was supported by many people seeking treatment, as they believed a blended approach provided the opportunity for greater tailoring and individual support.⁴
- Given the variation of experiences, preferences, and challenges of iCBT, a tailored approach in terms of content and ongoing support and monitoring may be needed to reflect patients' individual needs. Therapist guidance may help guide appropriate tailoring and ensure intervention "fit."
- This is an area of high unmet need with considerable social burden. Assuming patients have full access to psychotherapies, the incremental cost-utility ratio (ICUR) for guided iCBT compared with usual care (defined as any treatment prescribed by a general practitioner) was under \$50,000 per quality-adjusted life year (QALY) gained in patients

with MDD. For anxiety disorders, the ICUR was higher but under \$100,000 per QALY gained (Appendix 2).

- Therapist support, as offered through guided iCBT, was identified as an important facilitator of uptake and adherence of iCBT by patients.⁴

Considerations

Geographic distance between patients and practitioners can often restrict patients' universal and equitable access to high-quality health care in Canada.¹⁷ A sample of practitioners and providers across Canada believe that iCBT can facilitate access for people in need of mental health care.¹⁷ The economic reanalysis did not consider the impact of capacity restrictions of face-to-face psychotherapy that would result in waiting list to treatment access as part of the evaluation on cost-effectiveness. Even if less cost-effective in treating anxiety than in depression, HTERP recognized that iCBT may offer a viable service option for people with mild to moderate MDD and anxiety disorders who live in remote areas or people who otherwise have limited access to face-to-face CBT.

The factors that influence clinical effectiveness, as well as those that influence uptake and adherence, must be considered when recommending iCBT for persons with mild to moderate MDD or anxiety disorders. Such factors may further impact the potential cost-effectiveness of iCBT.

The clinical effectiveness of iCBT is driven by the willingness and readiness of the person in need of care to participate in the program, as well as the program's "fit" to the person's symptoms and needs. Many other factors influence uptake and adherence to therapy including, for example, expectations of effectiveness, level (or intensity) of practitioners' support, availability of appropriate policies, computer access and literacy, data security, perceptions of confidentiality and privacy, and the presence of disabilities such as visual impairment.

Acceptance of guided iCBT will vary among people diagnosed with mild to moderate MDD and anxiety disorders. For example, while people who are interested in maintaining their privacy and anonymity throughout the treatment process may largely support iCBT, others may dislike the intervention or consider it too impersonal. Furthermore, some people may consider support by a practitioner important, while others may wish to pursue self-directed care without the involvement of a practitioner. These and other points of disjuncture in people's experiences with and perspectives of iCBT underscore the importance of considering individuals' priorities and individual contexts when referring people to iCBT. It may be necessary to offer a variety of programs to ensure that people who are referred to receive iCBT are able to find programs that meet their individual needs, and that the programs are culturally and contextually appropriate.

Consideration of possible harms — for example, intensification of symptoms and detrimental impact on relationships — should be a component of decision-making when referring people to iCBT. Limited information was, however, identified in the reviews on the clinical harms of iCBT, which may be due to the methods used in the studies that were included.

HTERP considered the importance for iCBT to be guided by trained and qualified mental health practitioners;¹⁸ these practitioners should offer services only within the realm of their expertise.¹⁹

Evidence

Clinical Evidence

The clinical evidence is based on the overview of reviews conducted by HQO,¹ and the two rapid response reports (the summary with critical appraisal² and the summary of abstracts³) conducted by CADTH.

Based on an overview of seven systematic reviews of RCTs,¹ it was determined that, compared with waiting list, guided iCBT improves symptoms of mild to moderate MDD and select anxiety disorders. Waiting list is defined as participants receiving iCBT at a later date. Compared with waiting list, guided iCBT is effective and likely results in symptom improvement for mild to moderate MDD and social phobia (moderate quality evidence). Compared with waiting list, guided iCBT may also improve symptoms of generalized anxiety disorder and panic disorder (low-quality evidence). Compared with a combination of usual care (defined as any treatment prescribed by a general practitioner), waiting list, and information control, iCBT may reduce symptom severity and improve quality of life for people with generalized anxiety disorder or panic disorder (low-to-moderate quality evidence). The effectiveness of iCBT as compared with individual or group face-to-face CBT for individuals with MDD is unknown. Limited evidence suggested that compared with face-to-face CBT, iCBT does not significantly improve symptoms of panic disorder (very low-quality evidence) or social phobia (low-quality evidence). For all comparisons, participants across treatment and control groups used medication as prescribed by their health professionals.

A CADTH rapid review² provided an assessment of primary studies published after the latest publication date of the studies that were included in the overview of reviews. Consistent with findings from the overview of reviews, evidence from the nine more recently-published RCTs showed that treatment with iCBT may reduce symptom severity in adult patients with MDD and select anxiety disorders (generalized anxiety disorder, panic disorder with or without agoraphobia, and social anxiety disorder) compared with waiting list. In combination with usual care, iCBT reduced symptom severity compared with usual care alone. Compared with waiting list, iCBT improved quality of life, satisfaction with treatment, and remission and recovery rates. The CADTH rapid review did not identify recent RCTs with information on the comparison of effects between iCBT and face-to-face CBT.

A second CADTH rapid review (summary of abstracts)³ captured published literature evaluating the clinical effectiveness of guided versus unguided iCBT for patients with mild to moderate MDD and anxiety disorders. Eleven of the included abstracts reported no clear difference in symptom severity between people participating in guided and unguided iCBT for the treatment of anxiety, depression, or anxiety and depression. In two abstracts, it was reported that guided iCBT may improve symptom severity compared with unguided iCBT in patients with depression or anxiety disorders. One abstract also reported lower attrition rates in the guided iCBT group compared with unguided iCBT. A review of full texts with critical appraisal was not conducted.

Economic Evidence

HQO constructed a one-year decision tree to compare the cost-effectiveness of guided and unguided iCBT with face-to-face CBT and to usual care from an Ontario Ministry of Health perspective.¹ The primary outcome was cost per QALY gained in 2018 Canadian dollars. The health economic model was adapted by CADTH to:

- align the model with the clinical results noted from the additional CADTH rapid response reviews
- incorporate additional clinical expert validation in order to reflect a pan-Canadian context (Appendix 2).

Costs of iCBT included those related to an initial assessment (for referral to the program by the person's primary care doctor); salaries for regulated non-physician therapists (for guided iCBT, only); maintenance, IT support, and licensing specific to the delivery of iCBT through a central online portal. CADTH's base case compared usual care (defined as any treatment prescribed by a general practitioner), therapist-guided iCBT, unguided iCBT, and individual face-to-face CBT. In the base-case analysis, group CBT was excluded from the comparators because of limited comparative clinical data between iCBT and group CBT.

The cost-effectiveness of treatment strategies was found to be dependent on the clinical condition. In patients with MDD, the efficiency frontier was composed of usual care, guided iCBT (ICUR of \$41,520 per QALY gained compared with usual care), and individual face-to-face CBT (ICUR of \$108,443 per QALY gained compared with guided iCBT). Between a willingness-to-pay threshold of \$50,000 to \$150,000 per QALY gained, therapist-guided iCBT had the highest probability of being cost-effective. For patients with anxiety disorders, the efficiency frontier was composed of the same set of interventions (i.e., ICUR for guided iCBT was \$91,213 per QALY gained compared with usual care; ICUR for individual face-to-face CBT was \$120,250 per QALY gained compared with guided iCBT). However, greater decision uncertainty was present within this model as highlighted by the cost-effectiveness acceptability curve. Unguided iCBT was found to be dominated by usual care for both conditions. Of note, the economic evaluation did not consider the economic impact in light of capacity constraints. Appendix 2 presents the details, as well as the results, of an exploratory analysis to include group CBT as a comparator despite the limited comparative evidence comparing group CBT and iCBT.

Patients' Perspectives and Experiences Evidence

A systematic review and meta-synthesis of published primary qualitative studies on patients' perspectives and experiences was conducted. Once relevant studies were identified, their content was analyzed using a staged coding process similar to grounded theory methodology.

While studies generally reported participant acceptance of iCBT, it was clear that a one-size-fits-all solution is not applicable. As such, the included studies spoke to the importance of individual "fit" of iCBT that could relate to a person's learning style, as well as mental health and engagement needs. This attention to "fit" could come in the form of critically thinking through the interventional relevance for a given user or person, providing ongoing support and monitoring, and tailoring the intervention with respect to the content and the level of support relevant to the person being treated — all which would typically be achieved with therapist support as in guided iCBT.

While a minority of represented people valued the freedom to navigate iCBT by themselves and at their own pace, guided iCBT (i.e., through therapist involvement or support) was generally valued. Furthermore, a blended approach between iCBT and face-to-face therapy with varying levels of therapist support was supported by many people, as it was felt to provide the opportunity for greater tailoring and individual support.

Given the variation of experiences, preferences, and challenges with iCBT, strategies with the aim of optimal person-centred care, as well as careful assessment of patient needs, are required. Such tailoring may be better supported through the involvement of a therapist, as in guided iCBT. Based on the published literature, anticipated strategies may be less about a prescriptive or formulaic approach and rather about a malleable approach that seeks resonance, with considerations for both evidence-based and person-centred care. Continued critical reflection on the need for services in an adequately-funded mental health care system within which iCBT is embedded invites sufficient resources to address the range of patient needs and proactivity in improving experiences and outcomes for service users.

Implementation Evidence

Implementation issues were evaluated using information from the CADTH Environmental Scan report *Internet-Delivered Cognitive Behavioural Therapy for Major Depressive Disorder and Anxiety Disorders*¹⁷ and a literature review of published articles.

While practitioner or administrative staff support was identified as an important facilitator of iCBT for patients, precisely how iCBT is introduced has important implications for uptake and adherence by practitioners and patients. Practitioners favour integrating iCBT into care pathways by offering it as a short-term, alternate option, or offering it in conjunction with face-to-face therapy. Using a stepped care approach when initially integrating iCBT into clinical practice might allow people being treated and their practitioners to experiment with multiple forms of CBT so that they can determine what works best within their specific context.

Potential barriers to offering guided iCBT include practitioners' lack of confidence in facilitating the delivery of care through the Internet, demanding workloads, gaps in technical capability, and legal restrictions to offering cross-province service. Mitigating these risks requires strategies that focus on engaging and collaborating with all stakeholders involved in the delivery of iCBT, including patients, practitioners, insurance companies, regional health authorities, and provincial governments. These strategies include providing practitioners with additional training on using electronic devices to deliver care, investing in supportive managers who promote iCBT, developing policies that foster the use of electronic devices, and supporting the development of transdiagnostic iCBT programs that address multiple mental health conditions.

To facilitate uptake among Indigenous populations, providers of iCBT programs may consider engaging the community in the development of the programs and incorporating content that addresses language of communication and accommodates recognition of regional cultural variation, such as is observed among the Aboriginal and Torres Island Straits people of Australia. Providers may consider including topics such as colonization, intergenerational trauma, and identity, among others that are unique to Indigenous populations. Health professionals could also promote iCBT programs in schools and health centres to increase a community's knowledge of the technology and manage expectations of the effectiveness of iCBT.

Ethical Analysis

An analysis of the empirical and normative bioethics, clinical, and public health literatures was conducted to identify ethical issues related to the implementation of iCBT. The ethical issues identified, the values described, and the solutions proposed in the literature were evaluated using the methods of ethical (applied philosophical) analysis, which includes applying standards of logical consistency and rigour in argumentation, particularly where specific implications are identified and specific solutions advocated; responsiveness to important values of health care and health care policy in the field in which the technology is proposed for implementation; adequacy to the context for which the technology is being considered; and the representation of perspectives from diverse relevant communities, particularly marginalized and vulnerable populations. Themes that emerged from the included literature fell under the following seven broad ethical principles or domains:

- trust and the therapeutic alliance
- privacy and confidentiality in the context of Internet-delivered therapies
- beneficence and the uncertainty of new treatment modalities
- non-maleficence and limitations to client safety
- justice and enhanced access
- respect for autonomy and informed consent
- professional and legal issues.

Ethical issues identified in this review reflect practical, technical, and logistical matters (e.g., compromises to confidentiality because of the spectre of data insecurity; jurisdictional licensing) that may be addressed with appropriate measures and due attention (e.g., data security protocols and informing clients of limits to confidentiality; creative licensing arrangements across jurisdictions). The more intractable ethical concerns raised by iCBT have received relatively scant attention in the literature. The report therefore provides novel ethical analysis of these ethical issues or considerations including the following issues pertaining first to equity and access, and second to therapists' ethical responsibilities, as outlined in the following paragraph.

While iCBT may enhance access to mental health services for some, it may also produce, perpetuate, or exacerbate inequities of access for others. Persons with limited access to or comfort with digital technologies will not be reached by iCBT without due attention to the social determinants of access to technology. The standardization possible with iCBT may appear to contribute to all clients receiving the same standard of care; in reality, it is possible that standardization may simply systematize biases and be insufficiently sensitive and responsive to important client characteristics, such as language, culture, religious beliefs, sex, and gender, which are particularly important in the diverse Canadian context. These justice-enhancing and justice-diminishing features must be carefully considered and balanced.

iCBT may render it challenging for providers to fulfill their ethical obligations of non-maleficence in the face of limitations to client safety that may be inherent to the therapy's mode of delivery. It would be ethically problematic to conclude that this concern can be easily circumvented by simply informing clients of this fact. It may be challenging for iCBT providers to establish a trusting alliance with their clients relative to traditional face-to-face iCBT, which may render them less capable or incapable of effectively fulfilling their ethical obligations.

Considered together, while iCBT has the capacity to enhance access to mental health services, these justice-enhancing features of iCBT may perhaps only be viewed as virtues where the prospect of increased access extends to those less privileged, and where the therapeutic environment doesn't entirely eliminate an alliance between therapist and client where ethical practice is possible.

Limitations

Substantial heterogeneity in definitions used to describe terms like iCBT, guidance, support, or treatment medium, complicated efforts to synthesize information across studies. Without the certainty that each study was working from the same homogenous set of terms, there is a possibility that study findings may have been misinterpreted.

Limitations of the studies included in the rapid review of clinical effectiveness such as their open-label nature and lack of detailed reporting on potential confounders (e.g., patient use of medication) should be considered when interpreting these results. One rapid review was a summary of abstracts and therefore full-text articles were not retrieved or appraised.

The economic analysis did not assess the cost-effectiveness of any specific iCBT programs; input parameters relating to treatment efficacy were based on the clinical review, and costs for iCBT programs were based on plausible but hypothetical assumptions using clinical expert feedback and data identified in the literature. This should be taken into consideration during the selection and implementation of iCBT programs, with careful monitoring of clinical outcomes and actual costs. Additionally, the economic conclusions are based on a one-year time horizon; the lifetime cost-effectiveness of iCBT remains uncertain.

Experiences and opinions of persons being treated and health care providers generally reflected samples of individuals who volunteered to participate in an iCBT intervention. Accordingly, there is a lack of detail related to those who may have been systematically excluded from participation (e.g., those without computer access, those who lack linguistic proficiency in the language of the intervention, and those with cognitive issues that precluded engagement in a CBT intervention). Further consideration of the range of needs of people with depression and anxiety warrants consideration, relative to offering mental health services. Notably, the review was limited to persons 16 years or older, leaving out vulnerable populations of adolescents and children. The literature review of implementation issues is not considered systematic, as a quality assessment of the studies was not performed.

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Appendix 1: Health Technology Review Panel Details

The Health Technology Expert Review Panel (HTERP) is an advisory body to CADTH and is convened to develop guidance or recommendations on non-drug health technologies to inform a range of stakeholders within the Canadian health care system.

HTERP typically consists of up to seven core members appointed to serve for all topics under consideration during their term of office, and up to five expert members appointed to provide their expertise for a specific topic. For this project, the core members included health care practitioners and other individuals with expertise and experience in evidence-based medicine, critical appraisal, health technology assessment, bioethics, and health economics. One public member was also appointed to the core panel to represent the broad public interest. Two expert members with expertise in psychiatry, clinical psychology, and iCBT were also appointed.

HTERP Core Members

Dr. Hilary Jaeger (Chair)

Dr. Jenny Basran

Dr. Lawrence Mbuagbaw

Dr. Jeremy Petch

Dr. Lynette Reid

Ms. Tonya Somerton

Dr. Jean-Eric Tarride

Expert Members

Dr. Vincent Agyapong

Dr. Heather Hadjistavropoulos

Conflict of Interest

HTERP core members' declarations are posted on the CADTH website.

Dr. Heather Hadjistavropoulos is the Founder and Director of the Online Therapy Unit at the University of Regina. Dr. Hadjistavropoulos has received funding for iCBT with The Co-operators and Sun Life Financial, and received grants and research funding for the delivery of iCBT and conducting trials on iCBT. Dr. Agyapong has no conflicts of interest to declare.

CADTH [Conflict of Interest Guidelines](#) are posted on the CADTH website.

Appendix 2: CADTH Adaptation of Health Quality Ontario Economic Evaluation

Methods

Health Quality Ontario (HQO) constructed a one-year decision tree to compare the cost-effectiveness of guided and unguided Internet CBT (iCBT) to face-to-face cognitive behavioural therapy (CBT) and to usual care from an Ontario Ministry of Health perspective. The health economic model was adapted in response to the CADTH Health Technology Expert Review Panel (HTERP)'s requested changes to align with the clinical results noted from the additional rapid responses that were conducted by CADTH and to incorporate additional clinical expert validation in order to reflect a broader Canadian context.

Modifications to Model

Changes made to the model were primarily related to parameter estimation and are listed in Table 1. Details on model parameter values can be found in Table 6, Table 7, and Table 8.

Table 1: Changes to Model Inputs

Change	Rationale	Source ^a
Clinical Inputs		
Baseline medication use was added to the model. The cost of baseline medication was set to the lowest cost of the available first-line pharmacotherapies according to Canadian clinical practice guidelines.	One of the clinical experts consulted by CADTH provided data from their setting based upon a chart review of their patients on iCBT.	Clinical expert
The probability of response with unguided iCBT is the same as that for guided iCBT.	A CADTH Rapid Response comparing guided iCBT to unguided iCBT found inconclusive results in efficacy.	CADTH Rapid Response
The probability of recovery is equal among all psychotherapy interventions.	No comparative data comparing the probability of recovery between psychotherapies was identified in the clinical review. As a result, no difference in recovery was assumed.	HQO Clinical Review, CADTH Rapid Response
The probability of recovery when no medication is added following the failure of psychotherapy was set equal to the probability of self-recovery. (NOTE: As the probability of self-recovery in the original model was a three-month value, it was adjusted to reflect the probability of recovery at 9 months.)	There was limited longitudinal data on the probability of recovery in populations that initially failed to respond to psychotherapy.	Assumption
The probability of recovery when medication is added following the failure of psychotherapy was calculated by multiplying the relative risk of response to medication (vs. no medication) to the probability of self-recovery at 9 months for patients not on medication who have failed psychotherapy.	Clinical experts consulted by CADTH indicated that the initial value was very high, and this approach accounts for the baseline probability of recovery in patients not on additional pharmacotherapy.	Arroll et al. (2016) (MDD) ²⁰ Canton et al. (2012) (Anxiety) ²¹
"Drop out" was defined as the proportion of patients reported to have not completed all sessions (for guided iCBT and individual CBT).	"Drop out" was defined in HQO's model as the proportion of sessions not completed. Given that the model is based on a cohort of individuals, the revised definition would better correspond to the analysis (i.e., proportion of	van Ballegooijen et al. (2014) ²²

Change	Rationale	Source ^a
	patients who would be expected to complete all sessions).	
The probability of drop out with group CBT and individual CBT was assumed to be identical.	No comparative data between individual and group CBT was identified in the clinical review. As a result, no difference in drop outs was assumed.	Assumption based on findings of CADTH's Rapid Response
The probability of drop out for unguided iCBT was adjusted by applying the relative risk of drop out for unguided iCBT (compared with guided iCBT) to the probability of drop out for guided iCBT.	The studies identified within the CADTH Rapid Response showed differences in drop-out rates between guided and unguided iCBT.	CADTH Rapid Response; Berger et al. (2011) ²³
The proportion of patients receiving medication after failing psychotherapy was considered equal to the proportion of patients receiving medication if they do not self-recover after three months on usual care.	The clinical expert consulted by CADTH indicated there would be no difference in these values.	Clinical expert
Cost and Resource Utilization Inputs		
Addition of monthly state-specific medical costs (excluding cost of pharmacotherapy or psychotherapy)	To fully capture the disease cost of depression and anxiety, the monthly cost (related to emergency department and hospitalization) was calculated and applied to the model based on the expected time spent with symptoms.	Chiu et al. (2017) ²⁴
Removal of supervisory and training costs for psychotherapies	The clinical expert consulted by CADTH indicated that supervision is typically required for trainees and that an experienced therapist would not be supervised to that extent. Evidence from the US suggests training costs, per patient, may be as low as US\$0.19 for CBT.	Clinical expert; Okamura et al. (2017) ²⁵
The addition of referral costs for iCBT	The clinical expert consulted by CADTH indicated that 50% to 60% of patients would have been referred by their primary care doctors for iCBT.	Clinical expert
Follow-up costs for patients who have medication added after failing to respond/recover from psychotherapy or usual care were adjusted.	Dispensing fees and markups were removed given that these are not consistent across provinces.	Assumption
Follow-up costs (two physician visits) were applied for patients who do not change their medication after psychotherapy or usual care.	These costs were initially applied to patients who responded to psychotherapy only, which led to them having higher costs than patients who did not respond to psychotherapy and who were not on subsequent medication.	Clinical expert
Utility Weights		
Application of condition and health state-specific utilities	Condition and state-specific utilities were applied rather than treatment-specific utilities. For MDD, it was weighted by the proportion of mild and moderate MDD patients at baseline, as outlined in the HQO report.	Mihalopoulos et al. (2014) ²⁶

CBT = cognitive behavioural therapy; iCBT = Internet-based cognitive behavioural therapy; HQO = Health Quality Ontario; MDD = major depressive disorder.

^a Unless otherwise specified, input parameters were applicable to both MDD and anxiety.

Additional Assumptions to the Model

The CADTH model adheres to most of the assumptions noted in HQO’s original model, which include no issues related to capacity constraints or access to psychotherapy. Two additional changes to the model assumptions were made:

- Costs and utilities were adjusted for time-to-response, assuming response would occur upon initiation of the intervention.
- All psychotherapies are billed up front regardless of drop out, with the exception of individual CBT, which is billed on a per-session basis.

Results

Base Case

Group CBT was excluded from the base-case reanalysis, as limited comparative data between iCBT and group CBT were identified from the clinical review. Results of the CADTH base-case re-analysis, with the revisions previously described, are presented sequentially for major depressive disorder (MDD) (Table 2) and anxiety (Table 3). All results are probabilistic.

For both indications, usual care was the reference intervention given it had the lowest expected costs and unguided iCBT was dominated by usual care; i.e., higher costs and lower quality-adjusted life-years (QALYs). For MDD, the sequential incremental cost-utility ratios (ICURs) for interventions on the efficiency frontier were as follows: \$41,520 per QALY gained for guided iCBT compared with usual care and \$108,443 per QALY gained for individual CBT compared with guided iCBT (Table 2). The cost-effectiveness scatter plot and acceptability curve for the depression model can be found in Figure 1 and Figure 2, respectively. Between willingness-to-pay thresholds of \$50,000 and \$150,000 per QALY gained, guided iCBT had the highest probability of being cost-effective.

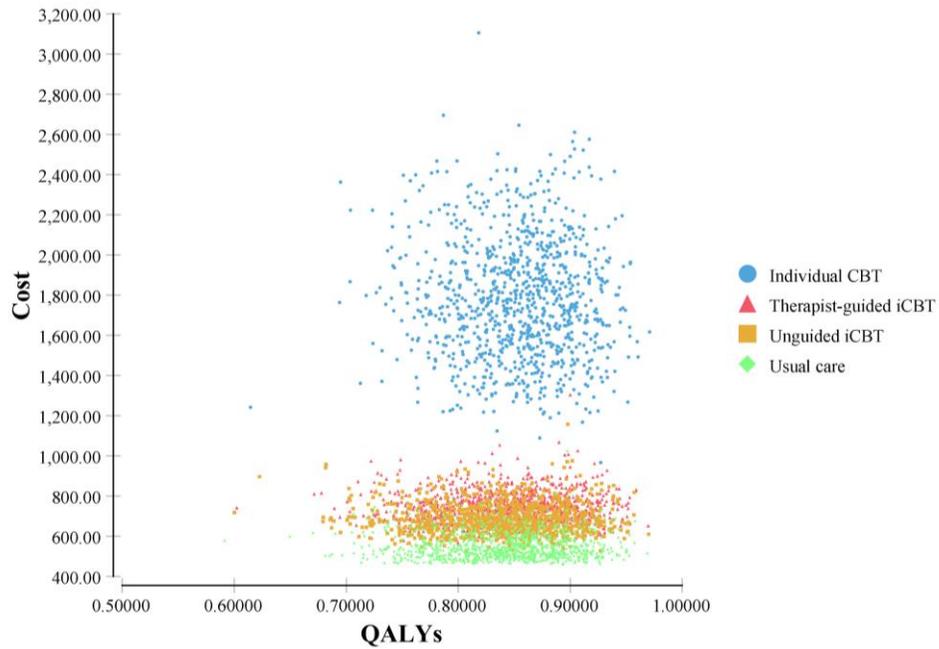
The order of interventions on the efficiency frontier was similar for anxiety, although the associated ICURs were higher (Table 3). The sequential ICURs for interventions on the efficiency frontier for anxiety were, as follows: \$91,213 per QALY gained for guided iCBT compared with usual care and \$120,250 per QALY gained for individual CBT compared with guided iCBT. The cost-effectiveness scatter plot and acceptability curve for the anxiety model can be found in Figure 3 and Figure 4, respectively. It is important to note that, for the anxiety model, a higher degree of decision uncertainty was identified based on the cost-effectiveness acceptability curve.

Table 2: CADTH Base Case Re-analyses — Major Depressive Disorder

Strategies	Expected Costs, \$	Expected QALYs	Incremental Costs, \$	Incremental QALYs	Sequential ICUR, \$/QALY Gained
Usual Care	553.25	0.84091	— Reference —		
Unguided iCBT	688.41	0.83848	135.16	-0.00243	Dominated by usual care
Guided iCBT	745.49	0.84554	192.24	0.00463	41,520
Individual CBT	1,786.25	0.852281	827.7	0	108,443

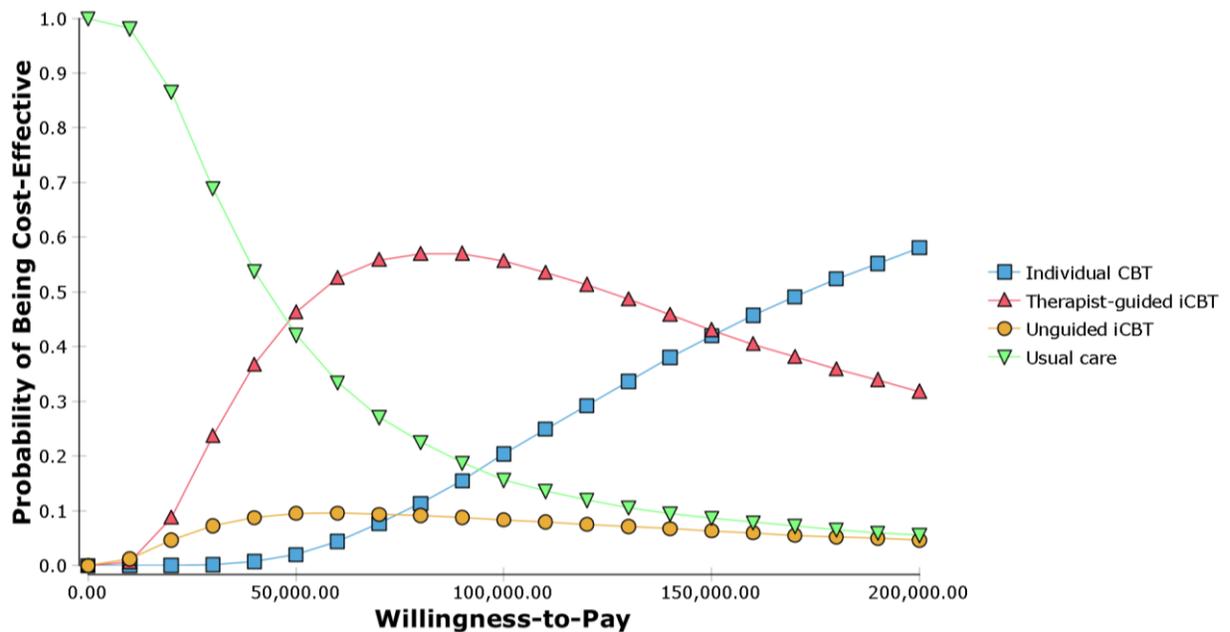
CBT = cognitive behavioural therapy; iCBT = Internet-based cognitive behavioural therapy; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Figure 1: Cost-Effectiveness Scatterplot — Major Depressive Disorder (Base Case)



CBT = cognitive behavioural therapy; iCBT = Internet-delivered cognitive behavioural therapy; QALY = quality-adjusted life-year.

Figure 2: Cost-Effectiveness Acceptability Curve — Major Depressive Disorder (Base Case)



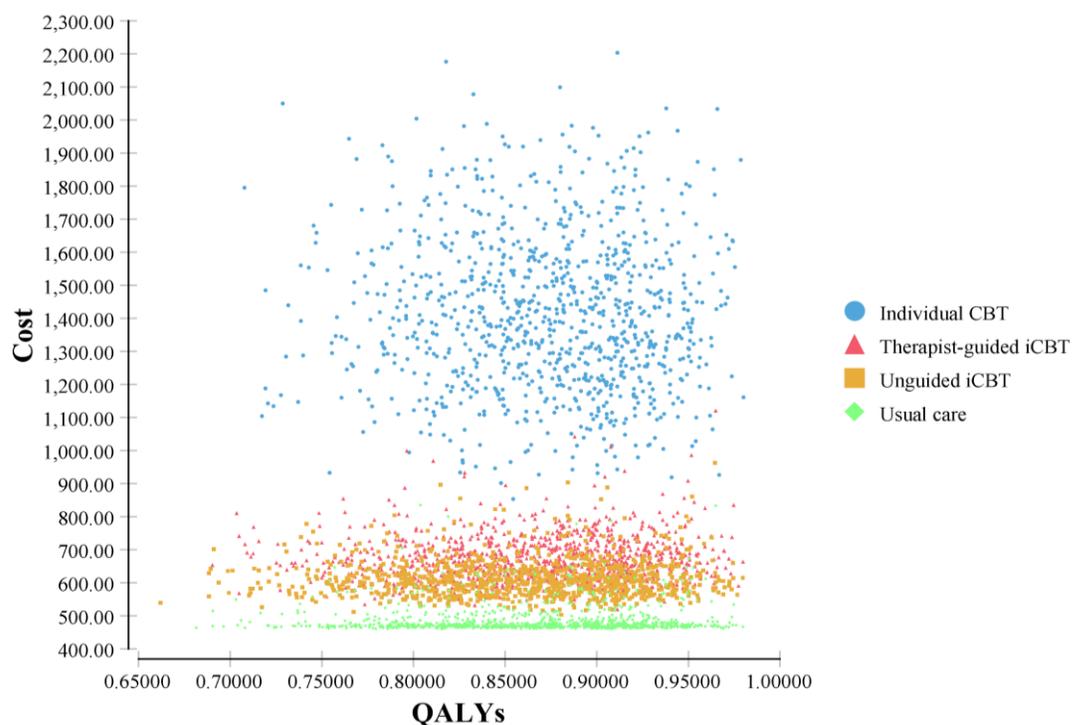
CBT = cognitive behavioural therapy; iCBT = Internet-delivered cognitive behavioural therapy.

Table 3: CADTH Base Case Re-analyses — Anxiety

Strategies	Expected Costs, \$	Expected QALYs	Incremental Costs, \$	Incremental QALYs	Sequential ICUR, \$/QALY Gained
Usual Care	487.23	0.86332	— Reference —		
Unguided iCBT	614.26	0.85870	127.03	-0.00462	Dominated by usual care
Guided iCBT	675.13	0.86538	187.90	0.00206	91,213
Individual CBT	1,414.79	0.87153	589.34	0	120,250

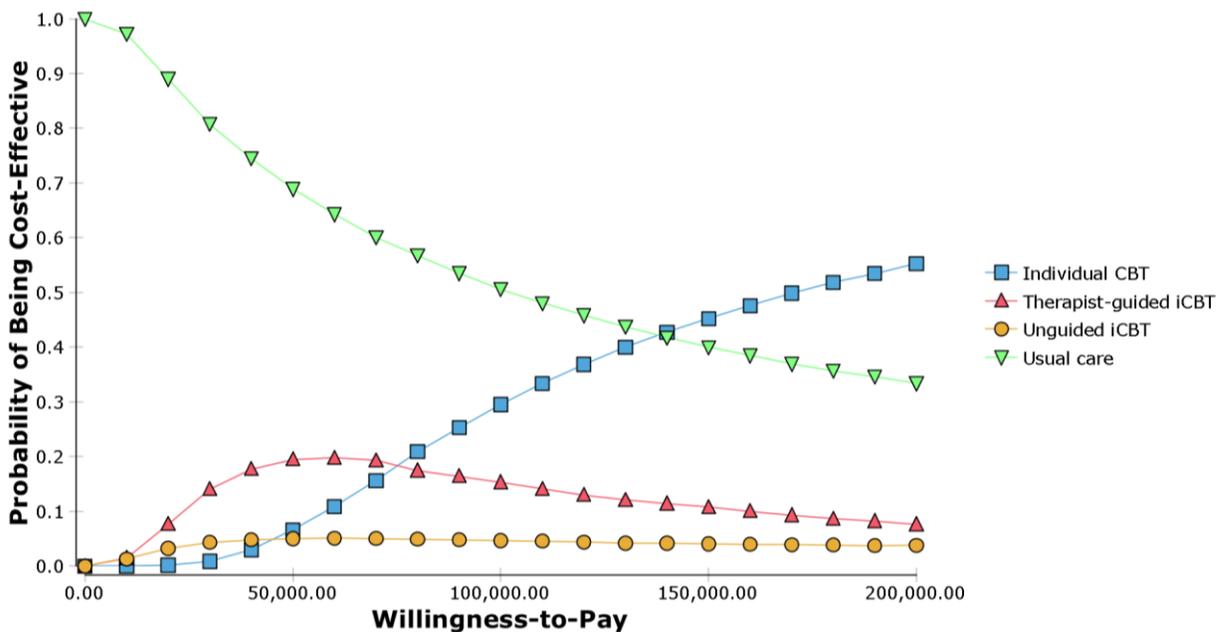
CBT = cognitive behavioural therapy; iCBT= Internet-delivered CBT; ICUR =incremental cost-utility ratio; QALY = quality-adjusted life-year.

Figure 3: Cost-Effectiveness Scatterplot — Anxiety (Base Case)



CBT = cognitive behavioural therapy; iCBT= Internet-delivered CBT; QALY = quality-adjusted life-year.

Figure 4: Cost-Effectiveness Acceptability Curve — Anxiety (Base Case)



CBT = cognitive behavioural therapy; iCBT= Internet-delivered CBT.

Exploratory Analysis

Because of the limited comparative data between iCBT and group CBT, the base-case analyses did not include group CBT. An exploratory analysis including group CBT was, however, conducted in which the clinical outcomes for group CBT were assumed identical to individual CBT. The results, therefore, should be interpreted with a lot of caution. The results of the exploratory analysis are presented sequentially in Table 4 (MDD) and Table 5 (anxiety).

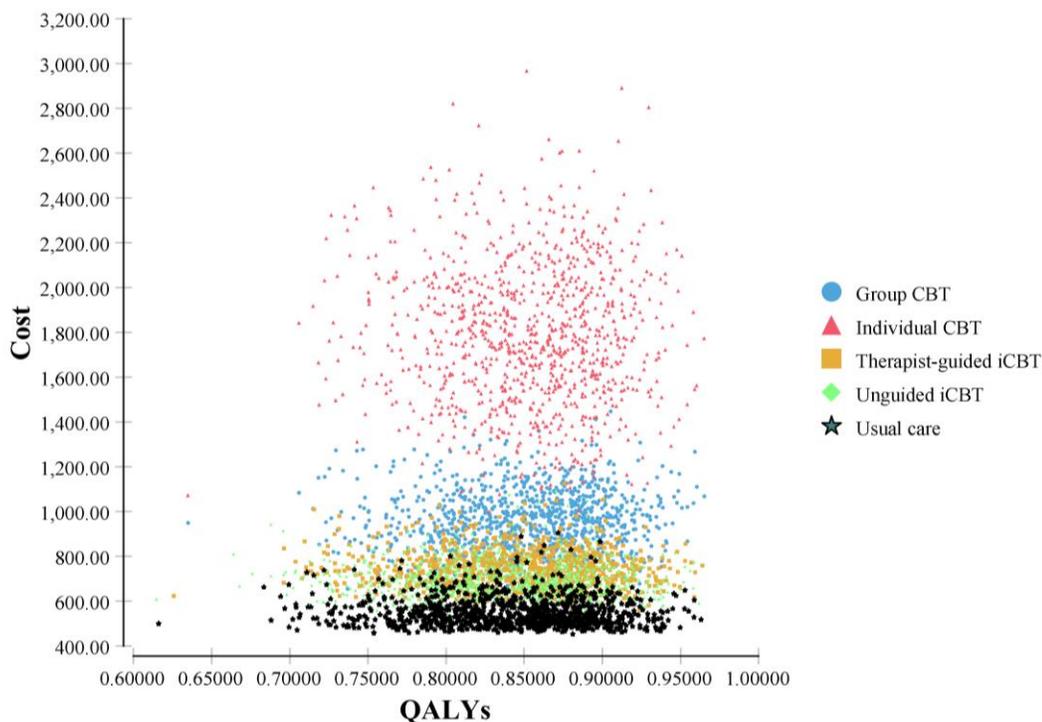
For both indications, unguided iCBT continued to be dominated by usual care, while guided iCBT was subject to extended dominance (i.e., more expensive and provides worse clinical outcomes than a combination of usual care and group CBT). Individual CBT was dominated by group CBT given it was more costly than group CBT and had the same expected QALYs (as these interventions were assumed clinically equivalent). Usual care had the highest probability of being cost-effective up to a willingness-to-pay threshold of \$35,646 and \$41,196 per QALY gained for MDD and anxiety, respectively; group CBT was then considered the most likely cost-effective therapy thereafter. See Figure 5 **Error! Reference source not found.** and Figure 6 and for the cost-effectiveness scatterplot and acceptability curve for MDD, respectively, and Figure 7 and Figure 8 for the cost-effectiveness scatterplot and acceptability curve for anxiety, respectively.

Table 4: CADTH Exploratory Re-analyses — Major Depressive Disorder (Inclusion of Group CBT as a Comparator)

Strategies	Expected Costs, \$	Expected QALYs	Incremental Costs, \$	Incremental QALYs	Sequential ICUR, \$/QALY Gained
Usual Care	553.25	0.84091	— Reference —		
Unguided iCBT	688.41	0.83848	135.16	-0.00243	Dominated by usual care
Guided iCBT	745.49	0.84554	192.24	0.00463	Subject to extended dominance through usual care and group CBT
Group CBT	958.55	0.85228	405.3	0.01137	35,646
Individual CBT	1,786.25	0.852281	827.7	0	Dominated by group CBT

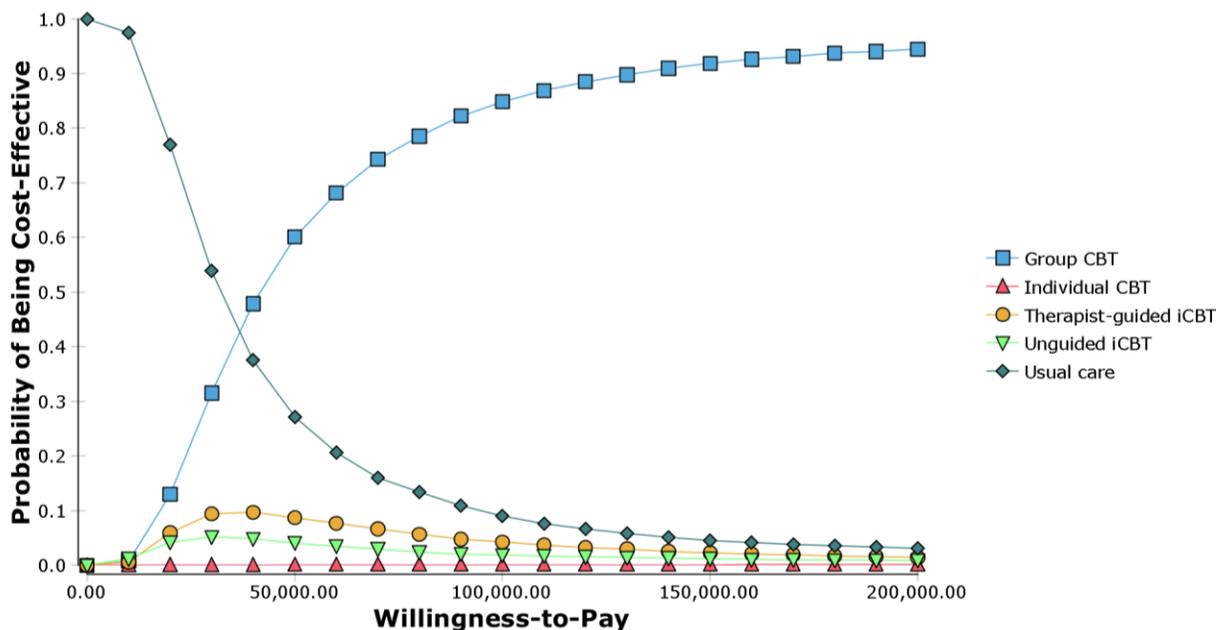
CBT = cognitive behavioural therapy; iCBT = Internet-delivered CBT; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Figure 5: Cost-Effectiveness Scatterplot — Major Depressive Disorder (Exploratory Analysis)



CBT = cognitive behavioural therapy; iCBT= Internet-delivered CBT; QALY = quality-adjusted life-year.

Figure 6: Cost-Effectiveness Acceptability Curve — Major Depressive Disorder (Exploratory Analysis)



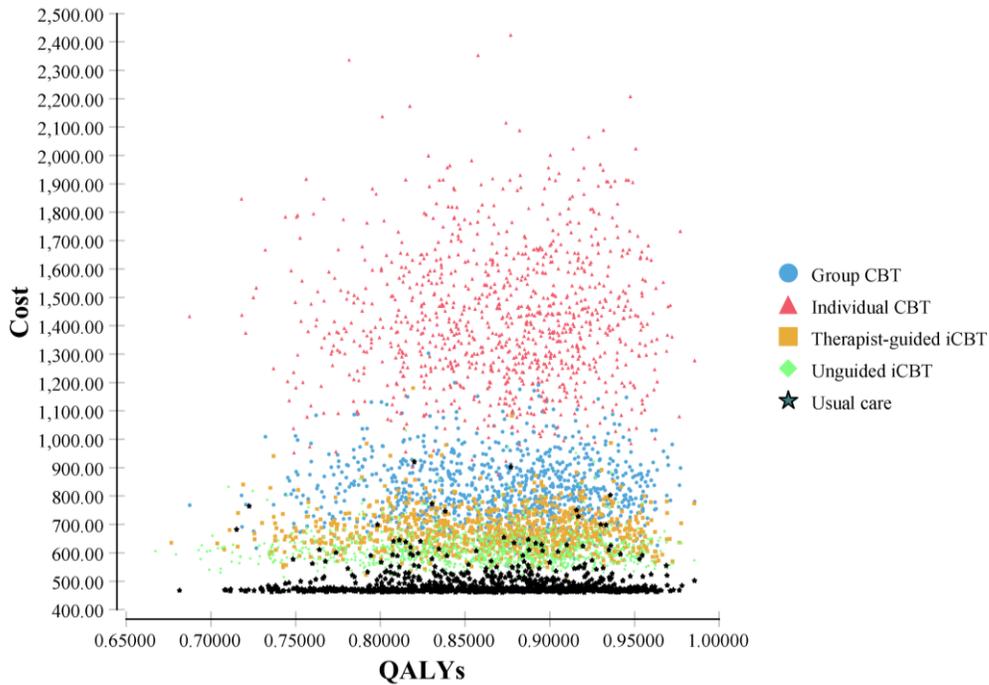
CBT = cognitive behavioural therapy; iCBT= Internet-delivered CBT.

Table 5: CADTH Exploratory Re-analyses — Anxiety (Inclusion of Group CBT as a Comparator)

Strategies	Expected Costs, \$	Expected QALYs	Incremental Costs, \$	Incremental QALYs	Sequential ICUR, \$/QALY Gained
Usual Care	487.23	0.86332		— Reference —	
Unguided iCBT	614.26	0.85870	127.03	-0.00462	Dominated by usual care
Guided iCBT	675.13	0.86538	187.90	0.00206	Subject to extended dominance through usual care and group CBT
Group CBT	825.45	0.87153	338.22	0.00821	41,196
Individual CBT	1,414.79	0.87153	589.34	0	Dominated by group CBT

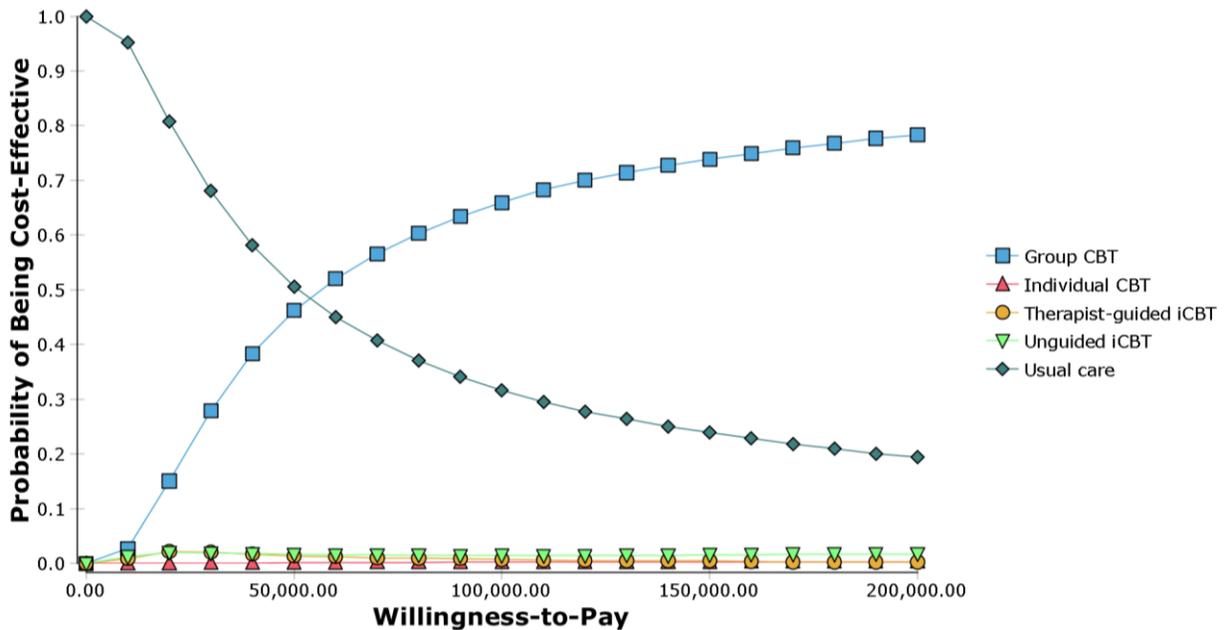
CBT = cognitive behavioural therapy; iCBT= Internet-delivered CBT; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life-year.

Figure 7: Cost-Effectiveness Scatterplot — Anxiety (Exploratory Analysis)



CBT = cognitive behavioural therapy; iCBT - Internet-delivered CBT; QALY = quality-adjusted life-year.

Figure 8: Cost-Effectiveness Acceptability Curve — Anxiety (Exploratory Analysis)



CBT = cognitive behavioural therapy; iCBT = Internet-delivered CBT.

Supplement: Input Tables

Table 6: Clinical and Baseline Demographic Inputs

Input	Value (SD or Alpha, Beta)	Distribution	Source	Value (SD or Alpha, Beta)	Distribution	Source
	MDD			Anxiety		
Baseline medication use	0.63	–	Clinical expert	0.66	–	Clinical expert
Probability of response (on all psychotherapies)	0.73 (0.02)	Beta	CADTH Rapid Response, Arnberg et al. (2014) ²⁷	0.74 (0.02)	Beta	CADTH Rapid Response, Arnberg et al. (2014) ²⁷
3-month probability of response/self-recovery (on usual care)	0.25	–	Clinical expert (HQO)	0.25	–	Clinical expert (HQO)
Probability of recovery conditional on response to psychotherapy (all psychotherapies)	0.52 (668,629)	Beta	Novick et al. (2017) ²⁸	0.51 (26.52, 25.48)	Beta	Springer et al. (2018) ²⁹
Relative risk of recovery with medication vs. no medication	1.33 (0.285,0.0535)	Log Normal	Arroll et al. (2016) ²⁰	1.83 (0.609, 0.0419)	Log Normal	Canton et al., (2012) ²¹
Proportion of patients dropping out (guided iCBT)	0.349 (0.92)	Normal	van Ballegooijen et al. (2014) ²²	0.349 (0.92)	Normal	van Ballegooijen et al. (2014) ²²
Proportion of patients dropping out (all CBT)	0.153 (0.794)	Normal	van Ballegooijen et al. (2014) ²²	0.153 (0.794)	Normal	van Ballegooijen et al. (2014) ²²
Relative risk of drop-out unguided iCBT vs. guided iCBT	1.54 (0.429, 0.284)	Log Normal	Berger et al. (2011) ²³	1.54 (0.429, 0.284)	Log Normal	Berger et al. (2011) ²³
Proportion of patients receiving medication after failure on psychotherapy or after no self-recovery on usual care	0.7	N/A	Clinical experts (CADTH and HQO)	0.7	NA	Clinical expert (CADTH and HQO)

CBT = cognitive behavioural therapy; iCBT = Internet-delivered CBT; HQO = Health Quality Ontario; MDD = major depressive disorder; N/A = not available; SD = standard deviation; vs. = versus.

Table 7: Cost and Resource Utilization Inputs

Input	Value (SD)	Distribution Used	Value (SD)	Distribution Used	Source	Notes ^a
	MDD		Anxiety			
Baseline medication costs	48.62		48.62	–	Clinical expert; ODB	12 months of citalopram
Proportion of patients receiving referral to iCBT	0.50 to 0.60	Uniform	0.50 to 0.60	Uniform	Clinical expert	N/A
Guided iCBT costs (one-time)	\$228 (57.0)	Gamma	\$228 (57.0)	Gamma	Revised from HQO's report as per clinical expert opinion	Includes cost of primary care doctor's referral, licensing, maintenance, and 3 hours of social worker time (from HQO report). Costs are similar to those for publicly administered programs (e.g., Tranquility: \$200 to \$300)
Unguided iCBT costs (one-time)	\$168 (42.0)	Gamma	\$168 (42.0)	Gamma	Revised from HQO's report as per clinical expert opinion	Includes cost of primary care doctor's referral, licence, and maintenance. Costs are similar to those for publicly administered programs (e.g., Tranquility: \$118 to \$177)
Individual CBT (billed per session)	\$1,430.85 (357.71)	Gamma	\$1,085.85 (271.46)	Gamma	Revised from HQO's report as per clinical expert opinion	Includes cost of referral and therapist salary Difference in costs between MDD and anxiety due to differences in number of sessions with therapist
Group CBT (billed one-time)	\$464.85 (116.21)	Gamma	\$395.85 (98.96)	Gamma	Revised from HQO's report as per clinical expert opinion	Includes cost of referral and therapist salary. Difference in costs between MDD and anxiety due to differences in number of sessions with therapist
ED visit costs for patients with symptoms (annual)	\$38.5 (17.2)	Gamma	\$40.99 (12.82)	Gamma	Chiu et al. (2017) ²⁴	Values used are the incremental costs of the condition (compared with the general population). Converted to and inflated to 2018 C\$
Hospitalization costs for patients with symptoms (annual)	\$256.55 (192.33)	Gamma	\$78.02 (166.70)	Gamma	Chiu et al. (2017) ²⁴	Values used are the incremental costs of the condition (compared with the general population). Converted to and inflated to 2018 C\$
Follow-up costs for patients who receive additional medication (9 months)	\$647.73	–	\$647.73	–	Clinical expert; ODB; Ontario Schedule of Benefits and Fees	Includes one physician visit per month and 9 months of sertraline

Input	Value (SD)	Distribution Used	Value (SD)	Distribution Used	Source	Notes ^a
Follow-up costs for patients who do not receive additional medication (9 months)	\$125.5	–	\$125.5	–	Clinical expert; Ontario Schedule of Benefits and Fees	Includes two physician visits

C\$ = Canadian dollars; CBT = cognitive behavioural therapy; iCBT = Internet-delivered CBT; ED = emergency department; HQO = Health Quality Ontario; MDD = major depressive disorder; N/A = not available; ODB = Ontario Drug Benefit (e-Formulary); SD = standard deviation; vs. = versus.

^a Applies to both clinical conditions unless otherwise specified.

Table 8: Utility Inputs

Health State	Mean	Distribution	Source
MDD			
Mild MDD	0.67 (0.19)	Beta	Mihalopoulos et al. (2014) ²⁶
Moderate MDD	0.63 (0.20)	Beta	
Well	0.94 (0.03)	Beta	
Anxiety			
Anxiety	0.65 (0.20)	Beta	Mihalopoulos et al. (2014) ²⁶
Well	0.94 (0.03)	Beta	

MDD = major depressive disorder.