

# Cost-effectiveness of varying degrees and models of therapist-assisted transdiagnostic internet-delivered cognitive behaviour therapy: Evidence from a randomized controlled trial

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## ABSTRACT

In routine care, Internet-delivered Cognitive Behaviour Therapy (ICBT) is often delivered with therapist support via emails/phone calls, but the cost-effectiveness of varying amounts of therapist support or having therapists specialized in ICBT is not known. This study compared the cost-effectiveness of specialized therapists providing ICBT support once-weekly (1WS) versus providing support once-weekly supplemented with a one-business-day response to patient emails (1W/1BD-S). We further compared the cost-effectiveness of 1W support offered by therapists employed in a specialized clinic (1WS) versus community clinics where therapists primarily deliver face-to-face therapy (1WC). Patients were randomly allocated to groups: 1WS group ( $n = 216$ ), 1W/1BD-S group ( $n = 233$ ), and 1WC group ( $n = 226$ ). At baseline, 12, 24 and 52-week follow-up, patients completed the Treatment Inventory of Costs in Patients with Psychiatric Disorders questionnaire (TiC-P) adapted for use in Canada to assess healthcare use and productivity losses. Additionally, to assess Quality Adjusted Life Years (QALYs) gained, patients completed the EQ-5D-5L at the same time periods. We quantified uncertainties by one-way and probabilistic sensitivity analysis and reported Incremental cost-effectiveness ratios (ICER), cost-effectiveness planes and acceptability curves. Cost-effectiveness over 52 weeks was CAD 3072/QALY for 1WC, CAD 3244/QALY for 1W/1BD-S, and CAD 3528/QALY for 1WS. Our model suggests that 1WS is the best strategy since the incremental cost per QALY is below the \$50,000 threshold (ICER is CAD 42,328/QALY compared to the next most effective, 1WC). 1W/1BD-S is dominated by the other strategies. The cost-effectiveness acceptability curves suggest that the 1WS group has a higher probability for cost-effectiveness (38 %) than 1W/1BD-S (30 %) and 1WC (32 %) when the willingness to pay is \$50,000 per QALY. These results have important implications for health policymakers deciding on delivery of ICBT for the treatment of anxiety and/depressive disorders.

## 1. Introduction

Common mental health concerns such as anxiety and depression are associated with significant personal and societal costs and are two of the leading causes of disability worldwide (GBD 2019 Mental Disorders Collaborators, 2022). Direct and indirect costs related to anxiety and depression include medication and healthcare service usage

(Christenson et al., 2020), as well as disability and lost productivity in the workplace (König et al., 2019; Konnopka and König, 2020). The high costs associated with anxiety and depression highlight the need for cost-effective treatments to mitigate the economic burden of these mental health concerns.

There is considerable evidence for the use of Internet-delivered cognitive behaviour therapy (ICBT) as an effective way to treat

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anxiety and depression (Andersson et al., 2019; Carlbring et al., 2018; Karyotaki et al., 2021). ICBT can overcome several of the barriers that patients may face when seeking face-to-face CBT, such as stigma, rural location, mobility or time constraints, or a preference for self-managing symptoms (Andersson et al., 2019). When used in a routine care setting, ICBT also has the potential to reduce healthcare costs, as its use has been associated with decreased therapist time and the ability to offer services to a larger number of patients than in traditional face-to-face CBT (Andersson et al., 2014). Therapists offering ICBT often only spend 10–15 min per patient on a weekly basis, in contrast to a typical 60-minute session in face-to-face CBT (Titov et al., 2018).

While ICBT in routine care is often delivered with brief once-weekly (1W) therapist support (Etzelmueller et al., 2020), it is not uncommon for patients to request additional therapist support during the week (Hadjistavropoulos et al., 2018). In our past research, we explored whether increasing support from 1W to twice-weekly support would confer advantages and found no such benefit in client outcomes (Hadjistavropoulos et al., 2020b). Additionally, we explored if offering 1W with an additional one-business-day response (1W/1BD-S) to any patient emails received would result in improved outcomes (Hadjistavropoulos et al., 2020a). This latter approach was advantageous as it was felt to be more responsive to patients' needs with patients being provided with extra support if they desired it, but allowed to work independently if no such support was requested.

As with twice-weekly support, there was no benefit to 1W/1BD contact in terms of symptom improvement and 1W/1BD contact was associated with greater therapist time per patient (Hadjistavropoulos et al., 2020a). Nevertheless, from the therapists' perspective, some of the benefits of 1W/1BD-S contact included stronger rapport with patients, faster skill development for patients, and greater therapist satisfaction compared to 1W support in terms of having more natural and responsive exchanges between therapist and patient. In the current study, we conducted additional analyses using data from a published trial, including a comparison of the cost-effectiveness of 1W/1BD versus 1W support.

### 1.1. Cost-effectiveness

Although there is substantial evidence for the effectiveness of ICBT in treating anxiety and depression, less work has been published on the cost-effectiveness of ICBT. Policy and health decision makers may be reluctant to support the adoption of ICBT if not enough is known about the cost-effectiveness of this form of service delivery (Lennon et al., 2017). Reviews of cost-effectiveness for ICBT have typically been limited by a lack of information about intervention implementation costs (e.g., Ahern et al., 2018; Kolovos et al., 2018). More recently, Mitchell et al. (2021) reviewed 33 studies that included economic evaluations of internet-based interventions for anxiety ( $n = 13$ ) and depression ( $n = 20$ ), with eight of these studies reporting costs associated with developing the intervention. The cost to deliver the interventions to each participant ranged from \$124 to \$1001 for the interventions targeting anxiety and ranged from \$0 to \$2842 for interventions that focused on depression. Most studies included incremental cost-effectiveness ratios (ICERs) as well as Quality Adjusted Life-Years (QALYs) as part of their cost-effectiveness analysis. The ICERs ranged from -\$19,659 to \$10,298 per QALY for anxiety interventions and from -\$6929 to \$717,530 per QALY for depression interventions. Overall, 81 % of the included interventions were found to be cost-effective, with a greater proportion of anxiety interventions being cost-effective compared to depression interventions (i.e., 100 % vs 69 %).

The findings of the Mitchell et al. (2021) review suggest that most internet interventions for depression and anxiety are cost-effective, although less is known about the cost-effectiveness of transdiagnostic programs. Further, despite the high degree of heterogeneity in comparison conditions (i.e., treatment as usual, waitlist, face-to-face

interventions, or other online interventions), none of the studies compared different amounts of therapist support. This comparison is important for policy-makers and funders, as it is currently unknown whether additional therapist support in ICBT is a cost-effective option. Of note, none of the studies included in the Mitchell et al. (2021) review were from Canada. Given the differences in healthcare costs and public funding for mental healthcare among different countries, it is important to conduct a cost-effectiveness of ICBT within Canada to ascertain whether the results of previous reviews are generalizable to the Canadian context. It is also worthwhile to compare the costs associated with offering ICBT by therapists who specialize in ICBT compared to therapists who primarily offer face-to-face services and secondarily deliver ICBT, as this may inform models for implementing ICBT in routine care. In our past research, we found no differences in ICBT outcomes between specialized versus community mental health clinics when delivering ICBT (Hadjistavropoulos et al., 2016; Hadjistavropoulos et al., 2020a), but cost-effectiveness has not been assessed.

### 1.2. Study purpose

To our knowledge, no previous studies have examined the cost-effectiveness of ICBT with varying amounts of support or when therapists specialize in ICBT versus deliver face-to-face therapy, with ICBT as a secondary job responsibility. This study had two primary aims: 1) to compare the cost-effectiveness of ICBT when delivered with once-weekly support (1WS) compared to once-weekly supplemented with one-business day support (1W/1BD-S) when offered by therapists working in a specialized ICBT clinic, and 2) to compare the cost-effectiveness of ICBT when offered with 1W support when offered by therapists in a community clinic (1WC) versus therapists working in a specialized ICBT clinic (1WS).

Data came from a previously published registered trial (see Hadjistavropoulos et al., 2020a for details) but has not yet been reported. Patients in the trial were randomly assigned to one of three treatment conditions: 1WS, 1W/1BD-S, or 1WC. Hadjistavropoulos et al. (2020a) compared these three groups based on symptom improvement (i.e., anxiety and depression as primary outcomes), treatment engagement (e.g., lessons completed, number of messages patients sent to therapists, and number of log-ins), and treatment experiences (e.g., treatment satisfaction, therapeutic alliance, and negative effects). As noted in Section 1.1, 1W/1BD-S did not result in improved outcomes, engagement, or treatment experiences for patients relative to 1WS, although it was associated with therapists spending more time with each patient over the course of therapy. Although no specific benefits were identified for 1W/1BD-S over 1WS in Hadjistavropoulos et al. (2020a), a cost-effectiveness analysis was considered worthwhile to examine whether 1W/1BD-S resulted in any benefits over 1WS in terms of reduced healthcare costs or productivity loss over a one-year period. Further, previous trials have not found significant differences in outcomes when ICBT is offered by a specialized versus community-based clinic (Hadjistavropoulos et al., 2016; Hadjistavropoulos et al., 2020a), so cost-effectiveness may be a deciding factor in which delivery approach should be implemented.

## 2. Method

### 2.1. Ethics statement and study design

This cost-effectiveness analysis reports additional data from a previously published and registered clinical trial (Clinicaltrials.gov: NCT03304392) that received institutional Research Ethics Board approval. Patients were randomized to one of three groups: 1WS, 1WC, or 1W/1BD-S (see Hadjistavropoulos et al., 2020a for additional details).

**Table 1**  
Per unit direct and indirect cost and associated sources.

	Service	Cost per visit/hour (CAD \$)	Data source
1	General Practitioner	\$67.0 per visit, \$37.0 for the subsequent visit	Payment Schedule for Insured services, Saskatchewan Medical Association <a href="https://www.sma.sk.ca/58/fees-insured.html">https://www.sma.sk.ca/58/fees-insured.html</a>
2	Psychiatrists	\$154.0 per visit, \$52.00 for the subsequent visit	Payment Schedule for Insured services, Saskatchewan Medical Association <a href="https://www.sma.sk.ca/58/fees-insured.html">https://www.sma.sk.ca/58/fees-insured.html</a>
3	Psychologists	\$180 per hour	Psychology Association of Saskatchewan <a href="https://www.psychsask.ca/resources/for-members">https://www.psychsask.ca/resources/for-members</a>
4	Social Worker	\$70 per hour	Canadian Association of Social Workers' <a href="https://www.casw-acts.ca/en/131-getting-paid">https://www.casw-acts.ca/en/131-getting-paid</a>
5	Counsellor	\$125 per hour	<a href="https://www.cpcra-rpc.ca/counsellor-directory.aspx">https://www.cpcra-rpc.ca/counsellor-directory.aspx</a>
6	Nurse/community nurse/ psychiatric nurse?	\$41.62 per hour	Statistics Canada. Table 14-10-0340-01 Employee wages by occupation, annual DOI: doi:10.25318/1410034001-eng
7	Occupational therapist	\$99.86 per hour	Service fee and fee codes for OT's-WCB, Saskatchewan Worker compensation Board <a href="https://www.wcbsask.com/wp-content/uploads/2014/02/Medical-Fees-Occupational-Therapy-Services-Fee-Schedule.pdf">https://www.wcbsask.com/wp-content/uploads/2014/02/Medical-Fees-Occupational-Therapy-Services-Fee-Schedule.pdf</a>
8	Emergency room	\$230 per visit	Email communication from SK health: Average estimated cost for an emergency department visit in SK hospitals for 2018–19 (latest year available) is \$164, plus topped it with ED physician visit costs
9	Medical Specialist (Cardiologists, Neurologists)	\$76.60-Cardiologist \$80.30-Neurology	Payment Schedule for Insured services, Saskatchewan Medical Association <a href="https://www.sma.sk.ca/58/fees-insured.html">https://www.sma.sk.ca/58/fees-insured.html</a>
10	Other Health Professional	\$32.91	Statistics Canada. Table 14-10-0340-01 Employee wages by occupation, annual DOI: doi:10.25318/1410034001-eng
11	Drug cost	Varies by type of medicine and volume	Collected from Sask. formulary <a href="http://formulary.drugplan.ehealthsask.ca/SearchFormulary">http://formulary.drugplan.ehealthsask.ca/SearchFormulary</a>
12	Productivity cost	Average gross hourly wages adjusted for age and gender to value absenteeism, presenteeism, and unpaid cost	Source: Labor Force Survey, Statistics Canada, 2018

## 2.2. Setting, participant recruitment, screening, and randomization

Patients who applied for ICBT through the Online Therapy Unit website ([www.onlinetherapyuser.ca](http://www.onlinetherapyuser.ca)) between October 25, 2017 and September 14, 2018 were included in the cost-effectiveness analysis. The Online Therapy Unit is a government-funded, specialized ICBT clinic that offers free ICBT to residents of Saskatchewan. To be included in the trial, patients had to be at least 18 years of age, be residents of Saskatchewan, endorse symptoms of anxiety and/or depression, have reliable access to a computer with internet, and provide a physician as an emergency contact. Prospective patients were excluded if they had a high suicide risk; had a suicide attempt or were hospitalized for mental health in the previous year; had unmanaged psychosis, alcohol or drug problems, or mania; would not be present in the province during treatment period; or had concerns about participating in ICBT. Patients who were accepted into the trial were randomized to 1WS ( $n = 216$ ), 1WC ( $n = 226$ ), or 1W/1BD-S ( $n = 233$ ) using Research Electronic Data Capture (REDCap) in a 1:1:1 ratio in blocks of 24 without matching. See [Hadjistavropoulos et al. \(2020a\)](#) for additional details regarding participant recruitment, screening, and randomization.

## 2.3. Intervention

All accepted patients were offered the same treatment, namely the *Wellbeing Course* (see [Titov et al., 2015](#) for full details), which is an 8-week transdiagnostic ICBT course that was developed by the eCentreClinic at Macquarie University, Sydney, Australia, and has been used by >30,000 patients across the sites it is offered at. The course consists of five lessons that covers common components of CBT including the cognitive-behavioural model, thought monitoring and challenging, identifying and managing symptoms of under-arousal and over-arousal, graded exposure, and relapse prevention. The core lesson materials are presented in a slideshow format and patients have access to additional content (e.g., patient stories, homework materials) to facilitate learning. Patients can also access a list of additional resources any time during the course (i.e., assertiveness, communication skills, managing beliefs, mental skills, managing panic attacks, managing PTSD, sleep, structured

problem solving). Patients receive automated emails with reminders about upcoming course content. Lessons 1, 2, 3, 4, and 5 are available at the beginning of weeks 1, 2, 4, 5 and 7, respectively. The lessons on thought challenging (Lesson 2) and graded exposure (Lesson 4) are each 2 weeks long to allow patients more time for practice and skill acquisition.

## 2.4. Therapist support

Across all three conditions, patients were encouraged to send messages to their therapist throughout the week and were informed that therapists would respond to any of their messages each week on a set day (e.g., every Tuesday) for the 8-week treatment period. Therapists were instructed to include the following components in each weekly message: express warmth and concern, facilitate patients' understanding of the lesson content, provide feedback on patients' symptoms, highlight lesson content and answer any related questions to assist with developing skills, reinforce skills and patient progress, manage any risk (e.g., suicide risk), and provide information about what to expect in the course. The majority of therapist support was provided by email through the Online Therapy Unit's secure treatment platform. Therapists could make telephone calls to patients in the following situations: (1) if patients' symptoms increased significantly; (2) if therapists perceived an increased suicide risk; or (3) if patients requested a telephone call.

In the 1W/1BD-S condition, patients received the standard weekly message from their therapist and also received additional one-business-day response to any email they sent to their therapist. Therefore, additional therapist contact in the 1W/1BD-S condition was only provided if the patient initiated contact.

## 2.5. Outcomes

Outcome measures for this study were administered at baseline and at 12, 24, and 52-week (w) follow-up after enrollment. All measures were completed on REDCap. Patients received a combination of automated emails and telephone calls as reminders to complete outcome measures. To increase the completion rate at 52-week follow-up,

patients were entered into a draw for a \$150.00 gift card (1 in 50 chance of winning) if they completed the measures.

### 2.5.1. Cost assessment

The analysis was performed from a societal perspective, and therefore, included both direct medical costs and indirect costs resulting from productivity losses. The Trimbos/iMTA questionnaire was used to measure costs associated with psychiatric illness (TiC-P) adapted for use in Canada to collect cost data (Hakkart-van Roijen, 2002). The TiCP is a self-report measure designed to assess direct and indirect costs associated with mental health and has been utilized in previous ICBT research (e.g., Hedman et al., 2016; Klein et al., 2018). The TiC-P has been found to be a feasible and reliable measure for assessing healthcare utilization and productivity losses (Bouwman et al., 2013).

The TiCP consists of three parts. Part I assesses patients' utilization of various healthcare services and their frequency in the past three months. Part II collects information on respondents' workplace absenteeism and/or reduction in productivity in paid or unpaid work due to mental health illnesses in the past month. Part III asks a series of demographic questions such as age, education, and respondent's chronic conditions (e.g., asthma, high blood pressure, diabetes) in the past year. The cost data were collected at baseline, 12w, 24w and 52w.

Direct medical costs included costs for various types of healthcare services and medications. Total direct healthcare cost is the sum of general physician services, medical specialists, psychiatrists, psychologists, social workers, counsellors, nurses, occupational therapists, hospitals, and prescription drugs. The per-unit cost was combined with the healthcare utilization data (quantity x unit cost) to calculate the cost of various healthcare services. The data on per-unit cost of visits and costs of prescription drugs were obtained from Saskatchewan Medical Association Reports, Statistics Canada, the Saskatchewan Worker Compensation Board, Canadian Institute of Health Information, Saskatchewan Ministry of Health, and Saskatchewan Drug Formulary database. Table 1 provides details on sources of per unit cost for each health care service.

Indirect costs refer to productivity losses due to absenteeism and presenteeism in paid work and the inability to perform unpaid domestic tasks, expressed as the number of hours received help from a family member or other personnel to perform those chores. Productivity cost calculations were based on the human capital approach (Drummond et al., 2005). Specifically, the patients were asked whether they had been absent from work during the past month (absenteeism). These absent days were multiplied by their average working hours per day to calculate lost productive hours due to mental health-related illness. The total time absent from work was then multiplied by the average gross hourly wages to calculate absenteeism costs. Similarly, participants were asked to report the number of days that they fell ill while at work during the past month (presenteeism). These days were multiplied by average hours per workday and self-reported inefficiency score, which ranged between 0 and 1 (1 represents totally inefficient, and 0 represents as efficient as when in good health), to calculate lost productive hours at work. Subsequently, their lost productive hours at work were multiplied by the average gross hourly wages to calculate presenteeism costs. Finally, the hours of paid and unpaid help received from family members or other personnel were calculated using the opportunity cost approach by valuing at average gross hourly wages. The data on average gross hourly wages for calculating presenteeism, absenteeism, and unpaid work were obtained from Statistics Canada's 2018 Labour Force Survey and were adjusted for age and gender. Both direct and indirect costs were adjusted for inflation using 2019 dollars and the Saskatchewan health care component of the Consumer Price Index (CPI) from the Canadian Socio-Economic Information Management System (CANSIM). Discounting was not performed because both costs and outcomes occurred within a 1-year time horizon.

Hospitalization costs were excluded from the analysis as very few participants reported hospitalization during the entire study period (<1%), and the cost range was wide for those who had any cost, yielding a

very high standard deviation. Moreover, the 1W/1BD-S group reported no hospitalization in the entire study period. Similarly, participants ( $n = 2$ ) with unusually high indirect cost reporting from unusually high average working hours in a day were excluded. After excluding these outliers, the sample consisted of 673 participants in all three interventions with 215 participants in the 1WS group (one outlier), 233 participants in the 1W/1BD-S group (no outliers) and 225 participants in the 1WC group (one outlier).

We also included per person capital and other overhead expenses directly related to the intervention, such as the costs for developing and hosting the intervention. These overhead costs were calculated for the one-year study period and were distributed over the follow-up period (0-12w, 12-24w, 24-52w). The treatment cost was also included by multiplying the mean therapist time for each intervention with per hour standard therapist wage rate (\$70 per hour). As treatment was for the 8-week period, this cost was only included for the first time period (i.e., 0-12w). On average, therapists from the specialized clinic spent 155 min supporting each patient in the 1W/1BD-S group compared to 109 min for each patient in the 1WS group and 136 min in the 1WC group. It was assumed that all of the participants owned a computer and had internet access, so these costs were not included. Table 1 lists all unit costs and their sources associated with various health care uses.

### 2.5.2. The EuroQol 5-Dimensional Questionnaire (EQ-5D-5L)

We used Quality-adjusted life-years (QALYs) as the primary outcome to measure health effectiveness over 52w. Specifically, a patient's health status was measured through a self-reported EQ-5D-5L questionnaire developed by the EuroQol Group. The EQ-5D-5L questionnaire provides respondents with a descriptive system to classify their health status based on five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is rated on five levels: no problems, slight problems, moderate problems, severe problems, or extreme problems (Herdman et al., 2011). This measurement provides a utility score between 0 and 1 for each of the EQ-5D-5L health states, with 1 representing the perfect health state and 0 the worst state. The utility scores for each EQ-5D-5L health state were obtained from the Canadian standardized value set (Xie et al., 2016). QALYs were then calculated by multiplying the utility scores with the length of time spent in that health state. As the EQ-5D-5L data was collected over four-time periods-baseline, 12w, 24w, and 52w, we calculated the length of time as baseline to 6w (0.12), 7-18w (0.23), 19-30w (0.23), 31 to 52w (0.423). QALYs gained per patient in each intervention during the 52w follow-up period were then calculated using linear interpolation between measurement points and accumulating these points over time using the area under the curve method. Of note, patients also completed the EQ-5D-5L questionnaire at 8w, but it is not included in the present analysis because of the unavailability of the corresponding cost data. However, we used these 8w EQ-5D-5L scores to impute missing data during the 12w period. We imputed the missing QALY values at different periods using the last value carried forward method assuming a linear change.

### 2.5.3. Therapist time

Therapists tracked how much time they spent supporting patients weekly. They were instructed to start timing from the moment they opened the client's file until they finished composing patient messages, calling the patient, or writing contact notes. During that time, therapists could also be reviewing patient progress, outcome measures, and messages from patients.

## 2.6. Data analysis

Data were analyzed using TreeAge Pro Healthcare 2020 (TreeAge Software, Inc). An intention-to-treat approach that considered all participants randomly assigned to different treatment options was applied to the analysis. Decision-analytic modelling was used to evaluate cost-



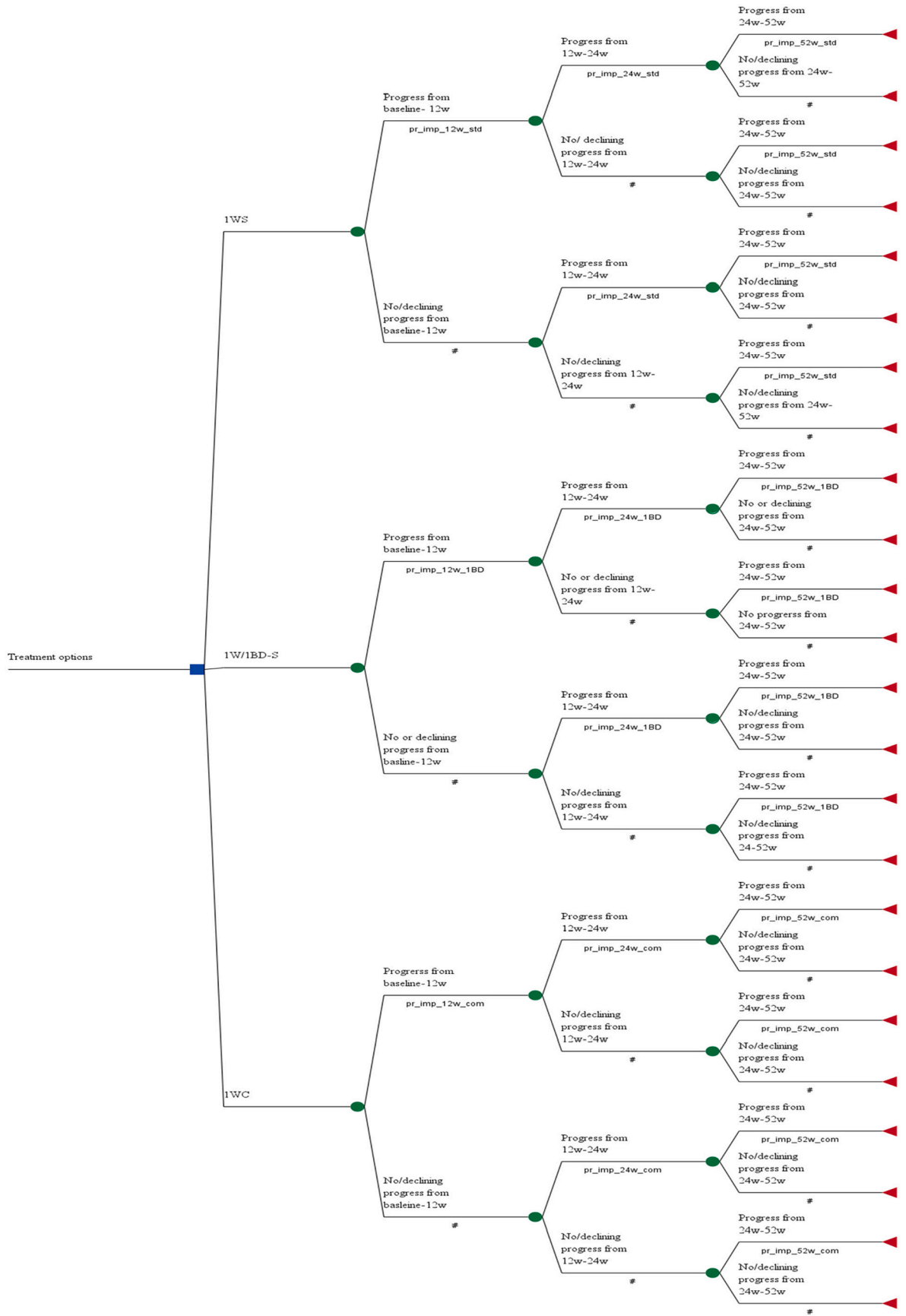


Fig. 1. Decision-tree model.

Note. 1WC = once-weekly community support; 1WS = once-weekly specialized support; 1W/1BD-S = once-weekly supplemented with a one-business-day response specialized support.

**Table 2**  
Baseline demographic and health characteristics of participants.

	Standard (n = 216)		IBD (n = 233)		Community (n = 226)		Total (N = 675)	
Demographic characteristics								
Age								
Mean (SD)	37.03 (13.39)		37.37 (13.15)		36.34 (12.56)		36.92 (13.02)	
Range	18–78		18–84		18–77		18–84	
Gender, n (%)								
Female	155	71.8	179	76.8	179	79.2	513	76.0
Male	61	28.2	54	23.2	47	20.8	162	24.0
Marital status, n (%)								
Single/never married	61	28.2	54	23.2	57	25.2	172	25.5
Married/common law	134	62.0	150	64.4	147	65.0	431	63.9
Separated/divorced/widowed	21	9.7	29	12.4	22	9.7	72	10.7
Education level, n (%)								
Less than high school	5	2.3	7	3.0	7	3.1	19	2.8
High school diploma	36	16.7	39	16.7	34	15.0	109	16.1
Postsecondary college certificate/diploma/some university	94	43.5	102	43.8	107	47.3	303	44.9
Undergraduate degree	61	28.2	61	26.2	53	23.5	175	25.9
Professional/graduate degree	20	9.3	24	10.3	25	11.1	69	10.2
Employment status, n (%)								
Employed part-time/full time	135	62.5	144	61.8	136	60.2	415	61.5
Unemployed	13	6.0	19	8.2	13	5.8	45	6.7
Homemaker/child caregiver	26	12.0	25	10.7	32	14.2	83	12.3
Student	16	7.4	17	7.3	20	8.8	53	7.9
Disability/unfit for work	17	7.9	13	5.6	17	7.5	47	7.0
Retired	9	4.2	15	6.4	8	3.5	32	4.7
Area of residence, n (%)								
Large city (over 200,000)	92	42.6	94	40.3	88	38.9	274	40.6
Small to medium city (10,000 to 20,000)	52	24.1	60	25.8	67	29.6	179	26.5
Small rural location (under 10,000)	72	33.3	79	33.9	71	31.4	222	32.9
Ethnicity/race, n (%)								
White/Caucasian	195	90.3	217	93.1	204	90.3	616	91.3
Indigenous	10	4.6	13	5.6	13	5.8	36	5.3
Black	2	0.9	–	–	2	0.3	–	–
Other	9	4.2	3	1.3	9	4.0	21	3.1
Health characteristics								
Chronic conditions, n (%)								
1	115	53.2	132	56.7	120	53.1	367	54.4
2	39	18.1	44	18.9	41	18.1	124	18.4
3+	62	28.7	57	24.5	65	28.8	184	27.3

effectiveness at one year. Decision tree models evaluate the costs and effectiveness of different strategies relative to each other (Drummond et al., 2005). Fig. 1 shows the decision tree modelled/constructed for this study, with three treatment options emerging from the initial decision node represented by a square. The circular (chance) nodes define the points of uncertainty for a patient in the tree. For each treatment option, a given patient can follow one of the two pathways (progress or no progress) that characterize the outcomes of alternate treatment options at that point in the tree. For instance, for each treatment option, the first chance node relates to whether or not a patient progresses from baseline to 12w. The pathways are built through series of branches representing particular events at three different time frames—baseline to 12w, 12w to 24w, 24w to 52w. The probabilities of improvement and its complement, the cost and QALYs are shown in the respective branches. All pathways were terminated at the 52-week follow-up period.

The cost, QALYs, and probabilities used in the tree assigned to each chance node were determined from the data. For instance, probabilities were estimated using the proportion of people who improved (or not) during a given period for a given intervention. Similarly, costs and QALYs were calculated using the mean values at each chance node for each intervention for each time period.

The incremental cost-effectiveness ratio (ICER) was calculated as the ratio of differences in mean costs and mean number of QALYs. We quantified model variability and parameter uncertainty by one-way and probabilistic sensitivity analysis. Specifically, the mean cost differences and the mean outcome differences were assessed using Monte Carlo simulation, and the results are presented in a cost-effectiveness plane.

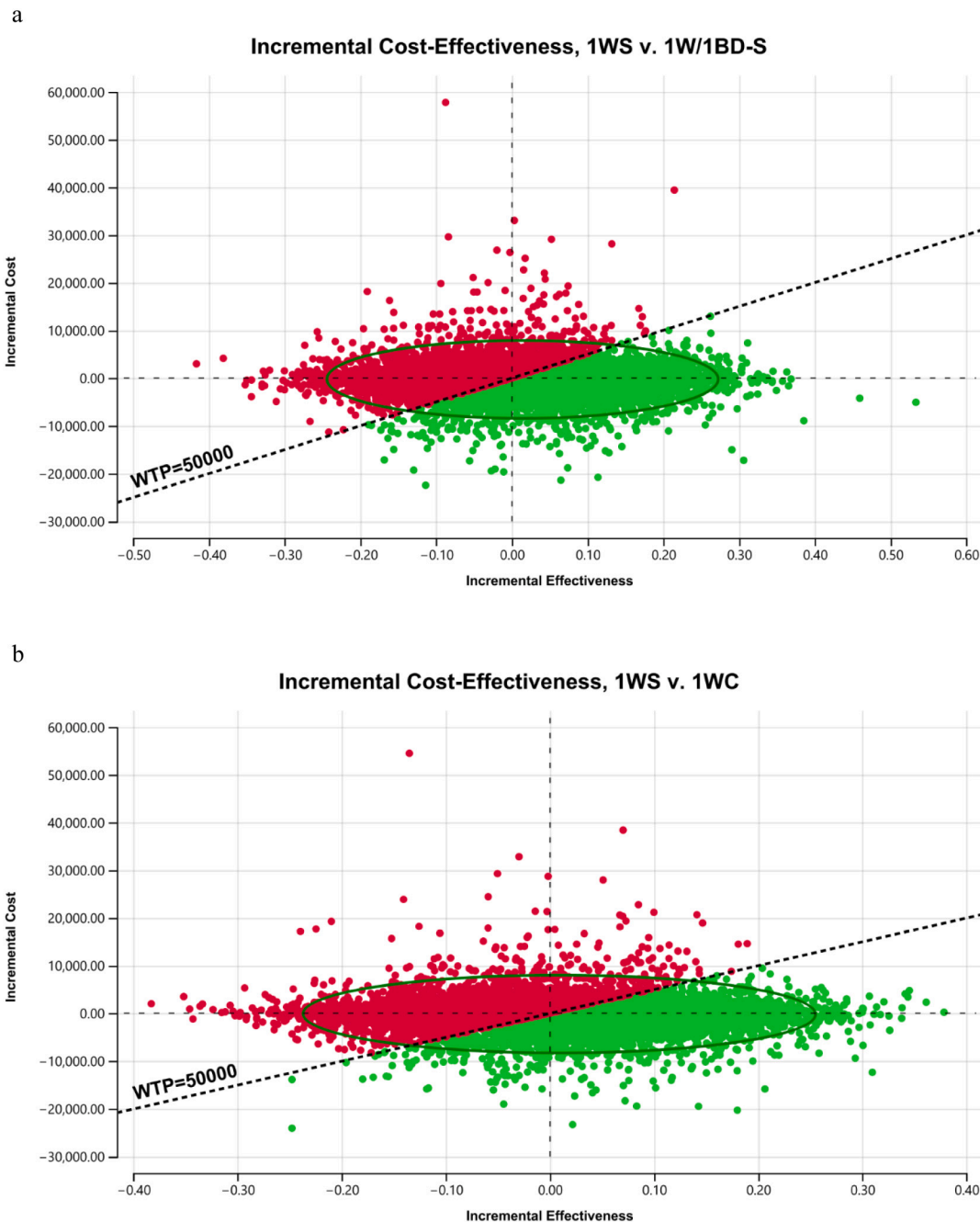
The cost and effectiveness data were repeatedly modelled for 10,000 iterations on the basis of known probability distributions for generating the outcomes. The intervention is acceptable/dominates if lower costs are associated with better outcomes (south-east quadrant). In this case, the intervention ‘dominates’ the active control group. If the ICER/ICUR falls in the northeast quadrant, the intervention is estimated to generate better health for more costs. The intervention is unacceptable/inferior as less health is produced at additional costs (northwest quadrant), and if the ICER/ICUR falls in the southwest quadrant, the intervention is estimated to produce inferior health outcomes for lower costs. Finally, cost-effectiveness acceptability curves were graphed to inform decision-makers on the likelihood that an intervention is deemed to be cost-effective relative to the control group, given a range of willingness-to-pay (WTP) ceilings for gaining additional QALYs.

The main objective in these sensitivity analyses was to investigate how sensitive the ICERs would be to changes of cost and QALYs estimates within a reasonable uncertainty range. In the one-way sensitivity analysis, the analysis was repeated but with average direct and indirect medical cost of ICBT increased to \$1000. An analysis was conducted where QALYs ranged from the low value (0) to the high value (1) depending on the time frame of the follow-up. Probabilities were varied from their lowest to highest value to determine which variables had thresholds where the order of cost and/or effectiveness among the strategies changed. A tornado diagram was used to perform a one-way sensitivity analysis that summarizes the effect of variation in key model parameters one at a time on the model outcome. The parameters are sorted in descending order by their outcome impact and longer bars

**Table 3**  
Cost-effectiveness report for base-case analysis.

Intervention	Mean Cost	Mean QALYs	Cost/effectiveness ratio	ICER	Dominates
1WC	2210.78	0.72	3072.07		
1WS	2568.79	0.73	3528.09	42,327.97	Undominated
1W/1BD-S	2315.99	0.71	3243.84	-18,545.23	Absolutely dominated

Note. 1WC = once-weekly community support; 1WS = once-weekly specialized support; 1W/1BD-S = once-weekly supplemented with a one-business-day response specialized support; QALYs = Quality Adjusted Life Years; ICER = Incremental Cost-Effectiveness Ratios.



**Fig. 2.** Cost-effectiveness plane.

Note. 1WC = once-weekly community support; 1WS = once-weekly specialized support; 1W/1BD-S = once-weekly supplemented with a one-business-day response specialized support.

indicate the most influential parameters. For the probability sensitivity analysis, gamma distributions were used for cost, and beta distributions for QALYs and probabilities as a means of estimating the uncertainty

surrounding the true average value. The mean and SD for distribution parameters were obtained from the observed data. Treatment and capital costs were excluded from the probability sensitivity analysis.

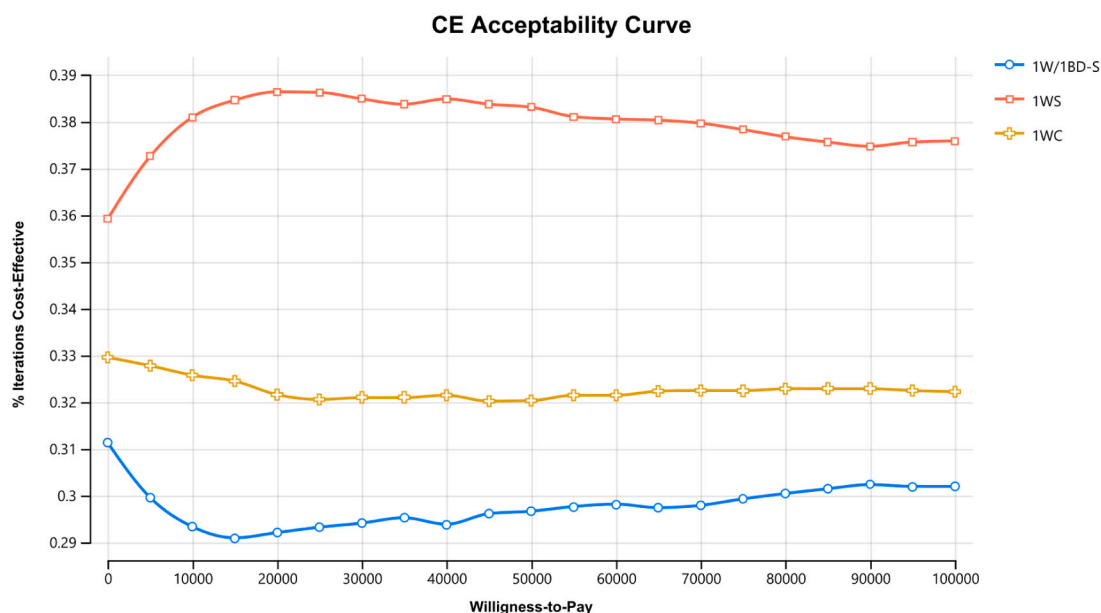


Fig. 3. Cost-effectiveness acceptability curve.

Note. 1WC = once-weekly community support; 1WS = once-weekly specialized support; 1W/1BD-S = once-weekly supplemented with a one-business-day response specialized support.

### 3. Results

On average, patients were 36.92 years of age, the majority (76 %) were women, 63.9 % were married/common-law, 36 % reported having a university undergraduate or professional degree. The majority of patients (54 %) reported at least one chronic condition and 27 % reported having three or more chronic conditions. More information on patient characteristics by intervention group can be found in Table 2 as well as in Hadjistavropoulos et al. (2020a). A flowchart outlining the percentage of patients who completed outcome measures at each time point is also included in Hadjistavropoulos et al. (2020a). Details on per capita cost and QALYs for each intervention at baseline, 12w, 24w and 52w are provided in a supplementary file.

The results of the base case cost-effectiveness analysis are presented in Table 3. Cost-effectiveness over the 52w was CAD 3072/QALY for 1WC, CAD 3244/QALY for 1W/1BD-S, and CAD 3528/QALY for 1WS. 1WS generates the most QALYs (0.73, compared to 0.72 for 1WC, 0.71 for 1W/1BD-S). The model suggests that 1WS is the best strategy since the incremental cost per QALY is below the \$50,000 threshold (ICER is CAD 42,328/QALY compared to the next most effective 1WC). 1W/1BD-S is dominated by the other strategies.

The results of the probabilistic sensitivity analyses are presented in Figs. 2 and 3. Fig. 2 is a cost-effectiveness plane showing 10,000 simulated ICER samples comparing 1WS with 1W/1BD-S and 1WS with 1WC in the cost-effectiveness analysis. Of the ICERs in Fig. 2a, a majority (30 %) of the simulated ICERs lie in the south-east quadrant of the plane given a WTP of \$50,000, where 1WS generates better health outcomes for lower costs than 1W/1BD-S group. 25 % of the simulated ICERs are located in the north-east quadrant of the plane indicating 1WS more often generates better health outcomes compared with 1W/1BD-S group but at a higher cost. Of the remaining ICERs, 20 % lie in the northwest quadrant and 24 % in the southwest quadrant. Similarly, the distribution of ICERs comparing 1WS with 1WC in Fig. 2b in four quadrants is as follows: 28 % are located in the south-east quadrant, 26 % in the northeast quadrant, 22 % in the northwest quadrant, and 24 % in the southwest quadrant. Thus, 1WS in comparison to 1WC and 1W/1BD-S more frequently generates larger improvements in QALYs at a lower societal cost.

Fig. 3 displays the cost-effectiveness acceptability curves. This plots

the probability that each intervention is the most cost-effective for a range of willingness-to-pay thresholds. The results suggest that the 1WS group has a higher probability for cost-effectiveness (38 %) than 1W/1BD-S (30 %) and 1WC (32 %) when the willingness to pay is \$50,000 per QALY.

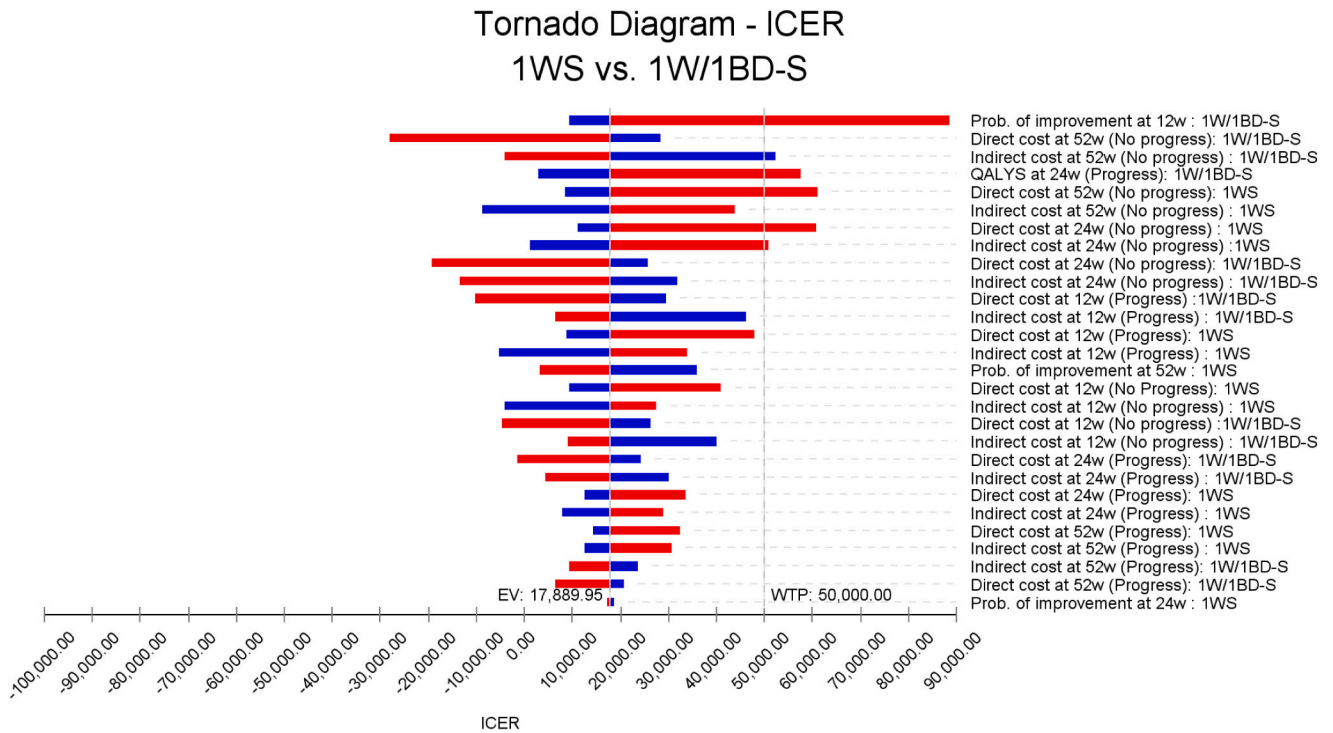
The Tornado diagram in Fig. 4 shows the results of one-way sensitivity analyses, which depicts graphically how variations in costs, probabilities, and QALYs affect the results. Fig. 4a shows that the ICER between 1WS and 1W/1BD-S group was most sensitive to the probabilities of improvement from baseline to 12w for the 1W/1BD-S group, direct and indirect cost at 52w with no progress in QALYs from 24w-52w for the 1W/1BD-S group, and progress in QALYs from 12w-24w for the 1W/1BD-S group. Similarly, Fig. 4b shows that the ICER between 1WS and 1WC group was most sensitive to the probabilities of improvement from baseline to 12w for the 1WC group, probability of improvement at 52w given the progress in QALYs from 24w to 52w for the 1WS group, direct and indirect cost at 52w with no progress in QALYs from 24w-52w for the 1WS group.

### 4. Discussion

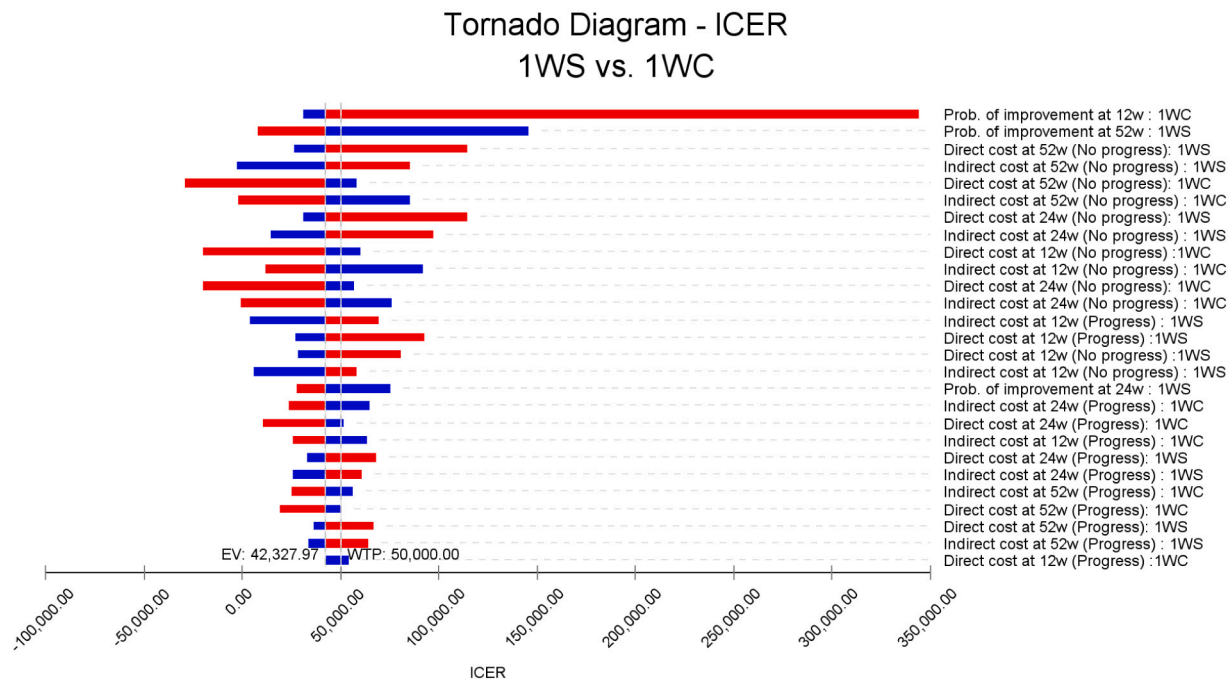
While there is considerable evidence for ICBT being an efficacious treatment for anxiety and depression (Andersson et al., 2019; Carlbring et al., 2018; Karyotaki et al., 2021), less is known about the cost-effectiveness of ICBT in routine care, particularly when ICBT is offered with varying levels of support and by specialized versus community-based therapists who primarily deliver face-to-face psychological services rather than ICBT. Using a decision analysis modelling approach, this study examines the cost-effectiveness of varying levels of therapist-guided ICBT for the treatment of depression or anxiety disorders. The three options generated similar QALYs (1WS: 0.73, 1WC: 0.72, 1W/1BD-S: 0.71). However, when examining ICERs per QALY gained, the results suggest that over a 52-week time period, 1WS may represent an economically attractive option compared to 1WC and 1W/1BD-S (ICER is CAD \$42,328/QALY compared to the next most effective 1WC). 1WS was associated with ICERs less than \$50,000 per QALY gained. Similar results were found comparing 1WS with 1WC. The sensitivity analyses further support the robustness of the base case results. The ICER for 1WS remained robust and at similar probabilities of cost-effectiveness below



a. Comparing 1WS with 1W/1BD-S



b. Comparing 1WS with 1WC



**Fig. 4.** Tornado diagram for one-way sensitivity analysis.  
 Note. 1WC = once-weekly community support; 1WS = once-weekly specialized support; 1W/1BD-S = once-weekly supplemented with a one-business-day response specialized support.

the commonly used willingness to pay value of \$50,000 per QALY gained. While it is challenging to directly compare the results of this study with the existing cost-effectiveness studies, due to differences in study design, sample size, type of interventions, etc., the findings of this study's cost-effectiveness analysis can be considered in light of previously reported comparisons of therapist-guided and unguided ICBT with face-to-face CBT and to usual care within Canada. A report from the Canadian Agency for Drugs and Technologies in Health found that for major depressive disorder, the therapist-guided ICBT was most cost-effective compared to usual care, individual CBT, and unguided ICBT when compared at willingness-to-pay of \$50,000 per QALY gained (CADTH, 2019). The design of therapist-guided ICBT is very similar to the 1WS intervention in this study.

Although in previous analyses, these three approaches did not differ in term of patient outcomes, the current results suggest that overall, 1WS was identified as the most cost-effective method of service delivery, based on the cost per QALY and probability for cost-effectiveness. This finding lends further support for 1WS being the optimal level of support offered in ICBT, based on previous findings that 1WS results in comparable rates of symptom reductions as 1W/1BD-S and 1WC and is associated with fewer organizational challenges (Hadjistavropoulos et al., 2020a). While some patients request additional contact with therapists as part of ICBT (Hadjistavropoulos et al., 2018) and patient-centered care approach would suggest that offering this additional support is beneficial to outcomes (Preference Collaborative Review Group, 2008), the data from this study further suggests that this additional contact does not confer benefits. As discussed by Hadjistavropoulos et al. (2020a) and Schueller et al. (2017), it could be that there is reduced learning and autonomy that happens with increased therapist support, which accounts for reduced cost-effectiveness of the 1W/1BD-S approach. Moreover, therapists themselves suggest that the approach results in therapists feeling they are rushing to respond to increased emails and this at times impacts the quality of their emails.

It is also important to briefly discuss lower cost-effectiveness of the 1WC approach compared to the 1WS approach. In the initial research by Hadjistavropoulos et al. (2020a), these two approaches were not significantly different in terms of patient outcomes. The one difference that was found, however, was that for treatment of depression patients who received 1W support from therapists employed by the community clinics obtained somewhat lower rates of reliable improvement and somewhat higher rates of no change at post-treatment than patients treated offered 1WS. In a previous audit of therapist practice, it was found that some undesirable therapist behaviours (e.g., inadequate detail in therapist emails), were more common among 1WC therapists than 1WS therapists (Hadjistavropoulos et al., 2019) and in yet another study, feedback from therapists from community settings who provided ICBT and face-to-face therapy, often reported challenges delivering ICBT related to competing demands on their time (Hadjistavropoulos et al., 2017). Together these findings suggest that while there may be a desire to have therapists who deliver face-to-face therapy also deliver ICBT, the combined evidence does not support such an approach.

Some study limitations are worth noting. First, cost and QALYs data are based on a self-report questionnaire; hence responses may suffer from recall bias. Therefore, future research should collaborate with local health authorities and employers to access administrative health and productivity data to evaluate clinical outcomes and actual direct and indirect costs. Second, outliers were excluded from the analysis as they could skew average costs. This resulted, however, in the exclusion of only two participants with unusually high indirect cost reporting, and hospitalization costs which were only reported by a few participants. As hospital visits are much more expensive than physician visits, the cost estimates may be on the conservative side. Of note, our sensitivity analysis includes a wide range of direct and indirect cost values, and our results are robust to the high-cost values. Third, estimates are based on a 365-day follow-up. Therefore, the lifetime cost-effectiveness of 1WS compared to other strategies remains unclear and warrants further

investigation. Fourth, while the sensitivity analysis points to the robustness of the results, caution should be exercised in generalizing these results to other Canadian provinces. Regional variations in fee codes for various healthcare services, types of ICBT programs, their availability, accessibility, and delivery methods may affect cost and outcome parameters. Future research should evaluate the cost-effectiveness of alternate ICBT programs in different settings to validate their clinical and economic effectiveness in treating anxiety and depression patients. Finally, the results of this study are only valid in specific settings with low to moderate risk patients (e.g., low suicide risk, no hospitalization in the past year) who are comfortable using technology. Moreover, the majority of our sample consists of patients of white ethnicity. Therefore, further research with a diverse sample, including vulnerable populations, to validate the cost-effectiveness of alternate ICBT programs is recommended.

Despite these limitations, the study has several notable strengths that add to the literature on the cost-effectiveness of ICBT. The study's design and inclusion of data up to one-year post-treatment allowed us to fulfill our primary study aims of comparing the cost-effectiveness of 1WS versus 1WS/1BD-S when offered by a specialized ICBT clinic, as well as to compare the cost-effectiveness of 1WS when offered by therapists in a specialized ICBT clinic compared to therapists in a community clinic. Our findings provide valuable information for health and policy decision-makers who may be considering adding ICBT to their services. Specifically, this study helps answer questions about what frequency of support and what type of clinic result in the most cost-effective delivery of ICBT.

## 5. Conclusions

1WS represents good value for money and could be an economically attractive ICBT alternative for adults with depression or anxiety disorders in Saskatchewan. Adding one-business-day support to once-weekly support is less cost-effective than once-weekly alone over a 52-week follow-up period. Also, having therapists specialize in ICBT is more cost effective than community clinicians who deliver face-to-face therapy and ICBT. These results have important implications for health policymakers deciding on the best possible practices of delivering ICBT for the treatment of anxiety and/depressive disorders. The default strategy in health to implement services through a hybrid service model (therapist treating both face-to-face and ICBT) may not result in a more cost-effective program.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that appear to have influenced the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.invent.2022.100567>.

## References

- Ahern, E., Kinsella, S., Semkova, M., 2018. Clinical efficacy and economic evaluation of online cognitive behavioral therapy for major depressive disorder: a systematic review and meta-analysis. *Expert Rev. Pharmacoecon. Outcomes Res.* 18 (1), 25–41. <https://doi.org/10.1080/14737167.2018.1407245>.
- Andersson, G., Carlbring, P., Titov, N., Lindfors, N., 2019. Internet interventions for adults with anxiety and mood disorders: a narrative umbrella review of recent meta-analyses. *Can. J. Psychiatr.* 64 (7), 465–470. <https://doi.org/10.1177/0706537198393>.
- Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., Hedman, E., 2014. Guided internet-based vs. Face-to-Face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry* 13 (3), 288–295. <https://doi.org/10.1002/wps.20151>.
- Bouwman, C., De Jong, K., Timman, R., Zijlstra-Vlasveld, M., Van der Feltz-Cornelis, C., Tan Swan, S., Hakkaart-van Roijen, L., 2013. Feasibility, reliability and validity of a questionnaire on healthcare consumption and productivity loss in patients with a psychiatric disorder (TIC-P). *BMC Health Serv. Res.* 13, 217. <https://doi.org/10.1186/1472-6963-13-217>.
- Canadian Agency for Drugs and Technologies in Health, 2019. Internet-delivered cognitive behaviour therapy for major depressive disorder and anxiety disorders: recommendations. CADTH optimal use report, 8(2c). <https://www.cadth.ca/interne-t-delivered-cognitive-behavioural-therapy-major-depressive-disorder-and-anxiety-disorders>.
- Carlbring, P., Andersson, G., Cuijpers, P., Riper, H., Hedman-Lagerlof, E., 2018. Internet-based vs. Face-to-Face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. *Cogn. Behav. Ther.* 47 (1), 1–18. <https://doi.org/10.1080/16506073.2017>.
- Christenson, M.K., Lim, C.C.W., Saha, S., Plana-Ripoli, O., Cannon, D., Presley, F., Weyer, N., Momen, N.C., Whiteford, H.A., Iburg, K.M., McGrath, J.J., 2020. The cost of mental disorders: a systematic review. *Epidemiol. Psychiatr. Serv.* 29, 1–8. <https://doi.org/10.1017/S204579602000075X>.
- Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brien, B.J., Stoddart, G.L., 2005. *Methods for the Economic Evaluation of Health Care Programmes*, 3rd ed. Oxford University Press.
- Etzelmüller, A., Vis, C., Karyotaki, E., Baumeister, H., Titov, N., Berking, M., Cuijpers, P., Riper, H., Ebert, D.D., 2020. Effects of internet-based cognitive behavioral therapy in routine care for adults in treatment for depression and anxiety: a systematic review and meta-analysis. *J. Med. Internet Res.* 22 (8), e18100. <https://doi.org/10.2196/18100>.
- GBD 2019 Mental Disorders Collaborators, 2022. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. *Lancet Psychiatry* 19 (2), 137–150. [https://doi.org/10.1016/S2215-0366\(21\)00395-3](https://doi.org/10.1016/S2215-0366(21)00395-3).
- Hadjistavropoulos, H.D., Faller, Y.N., Klatt, A., Nugent, M.N., Dear, B.D., Titov, N., 2018. Patient perspectives on strengths and challenges of therapist-assisted internet-delivered cognitive behaviour therapy: using the patient voice to improve care. *Community Ment. Health J.* 54 (7), 944–950. <https://doi.org/10.1007/s10597-018-0286-0>.
- Hadjistavropoulos, H.D., Gullickson, K.M., Schneider, L.H., Dear, B.F., Titov, N., 2019. Development of the internet-delivered cognitive behaviour therapy undesirable therapist behaviours scale (ICBT-UTBS). *Internet Interv.* 18, 100255. <https://doi.org/10.1016/j.invent.2019.100255>.
- Hadjistavropoulos, H.D., Nugent, M.M., Alberts, N.M., Staples, L., Dear, B.F., Titov, N., 2016. Transdiagnostic internet-delivered cognitive behaviour therapy in Canada: an open trial comparing results of a specialized online clinic and nonspecialized community clinics. *J. Anxiety Disord.* 42, 19–29. <https://doi.org/10.1016/j.janxdis.2016.05.006>.
- Hadjistavropoulos, H.D., Nugent, M.M., Dirkse, D., Pugh, N., 2017. Implementation of internet-delivered cognitive behavior therapy within community mental health clinics: a process evaluation using the consolidated framework for implementation research. *BMC Psychiatry* 17, 331. <https://doi.org/10.1187/s12888-017-1496-7>.
- Hadjistavropoulos, H.D., Peynenburg, V., Nugent, M., Karin, E., Titov, N., Dear, B.F., 2020. Transdiagnostic internet-delivered cognitive behaviour therapy with therapist support offered once-weekly or once-weekly supplemented with therapist support within one-business day: pragmatic randomized controlled trial. *Internet Interv.* 22, 100347. <https://doi.org/10.1016/j.invent.2020.100347>.
- Hadjistavropoulos, H.D., Peynenburg, V., Thiessen, D.L., Nugent, M., Adlam, K., Owens, K.M.B., Karin, E., Dear, B.F., Titov, N., 2020. A pragmatic factorial randomized controlled trial of transdiagnostic internet-delivered cognitive behavioural therapy: exploring benefits of homework reflection questionnaires and twice-weekly therapist support. *Internet Interv.* 22, 100357. <https://doi.org/10.1016/j.invent.2020.100357>.
- Hakkart-van Roijen, L., 2002. *Manual Trimbos/iMTA Questionnaire for Costs Associated with Psychiatric Illness (in Dutch)*. Institute for Medical Technology Assessment, Rotterdam.
- Hedman, E., Andersson, E., Ljótsson, B., Axelsson, E., Lekander, M., 2016. Cost effectiveness of internet-based cognitive behaviour therapy and behavioural stress management for severe health anxiety. *BMJ Open* 6, e009327. <https://doi.org/10.1136/bmjopen-2015-009327>.
- Herdman, M., Gudex, C., Lloyd, A., Janssen, M.F., Kind, P., Parkin, D., Bonsei, G., Badia, X., 2011. Development and preliminary testing of the new five-level version of the EQ-5D (EQ-5D-5L). *Qual. Life Res.* 20 (10), 1727–1736. <https://doi.org/10.1007/s11136-011-9903-x>.
- Karyotaki, E., Efthimiou, O., Miguel, C., Bermpohl, F.M.G., Furukawa, T.A., Cuijpers, P., Individual Patient Data Met-Analyses for Depression (IPDMA-DE) Collaboration, Riper, H., Patel, V., Mira, A., Gemmil, A.W., Yeung, A.S., Lange, A., Williams, A.D., Mackinnon, A., Geraedts, A., van Straten, A., Meyer, B., Björkelund, C., Forsell, Y., 2021. Internet-based cognitive behavioral therapy for depression: a systematic review and individual patient data network meta-analysis. *JAMA Psychiatry* 78 (4), 361–371. <https://doi.org/10.1001/jamapsychiatry.2020.4364>.
- Klein, N.S., Bockting, C.L., Wijnen, B., Kok, G.D., van Valen, E., Riper, H., Cuijpers, P., Dekker, J., van der Heiden, C., Burger, H., Smit, F., 2018. Economic evaluation of an internet-based preventive cognitive therapy with minimal therapist support for recurrent depression: randomized controlled trial. *J. Med. Internet Res.* 20 (11), e105437. <https://doi.org/10.2196/10437>.
- Kolova, S., van Dongen, J.M., Riper, H., Buntrock, C., Cuijpers, P., Ebert, D.D., Geraedts, A.S., Kenter, R.M., Nobis, S., Smith, A., Warmerdam, L., Hayden, J.A., van Tulder, M.W., Bosmans, J., 2018. Cost-effectiveness of guided internet-based interventions for depression in comparison with control conditions: an individual-participant data meta-analysis. *Depress. Anxiety* 35 (3), 209–219. <https://doi.org/10.1002/da.22714>.
- König, H., König, H.-H., Konnopka, A., 2019. The excess costs of depression: a systematic review and meta-analysis. *Epidemiol. Psychiatr. Sci.* 29, 1–16. <https://doi.org/10.1017/S2045796019000180>.
- Konnopka, A., König, H., 2020. Economic burden of anxiety disorders: a systematic review and meta-analysis. *Pharmacoeconomics* 38 (1), 25–37. <https://doi.org/10.1007/s40273-019-00849-7>.
- Lennon, M.R., Bouamrane, M.M., Devlin, A.M., O'Connor, S., O'Donnell, C., Chetty, U., Agbakoba, R., Bikker, A., Grieve, E., Finch, T., 2017. Readiness for delivering digital health at scale: lessons from a longitudinal qualitative evaluation of a national digital health innovation program in the United Kingdom. *J. Med. Internet Res.* 19 (2), e42. <https://doi.org/10.2196/jmir.6900>.
- Mitchell, L.M., Joshi, U., Patel, V., Lu, C., Naslund, J.A., 2021. Economic evaluations of internet-based psychological interventions for anxiety disorders and depression: a systematic review. *J. Affect. Disord.* 284, 157–182.
- Preference Collaborative Review Group, 2008. Patients' preferences within randomised trials: systematic review and patient level meta-analysis. *BMJ* 337, a1864. <https://doi.org/10.1136/bmj.a1864>.
- Schuller, S.M., Tomasino, D.C., Mohr, D.C., 2017. Integrating human support into behavioral intervention technologies: the efficiency model of support. *Clinical Psychology: Science and Practice* 24, 27–45. <https://doi.org/10.1111/cpsp.12173>.
- Titov, N., Dear, B.F., Niessen, O., Staples, L., Hadjistavropoulos, H., Nugent, M., Adlam, K., Nordgreen, T., Hogstad Bruvik, K., Hovland, A., Repål, A., Mathiasen, M., Kraepelien, M., Blom, K., Svanborg, C., Lindfors, N., Kalso, V., 2018. ICBT in routine care: a descriptive analysis of successful clinics in five countries. *Internet Interv.* 13, 108–115. <https://doi.org/10.1016/j.invent.2018.07.006>.
- Titov, N., Dear, B.F., Staples, L.G., Terides, M.D., Karin, E., Sheehan, J., McEvoy, P.M., 2015. Disorder-specific versus transdiagnostic and clinician-guided versus self-guided treatment for major depressive disorder and comorbid anxiety disorders: a randomized controlled trial. *J. Anxiety Disord.* 35, 88–102. <https://doi.org/10.1016/j.janxdis.2015.08.002>.
- Xie, F., Pullenayegum, E., Gaebel, K., Bansback, N., Bryan, S., Ohinmaa, A., Poissant, L., Johnson, J.A., Canadian EQ-5D-5L Valuation Study Group, 2016. A time trade-off-derived value set of the EQ-5D-5L for Canada. *Med. Care* 54 (1), 98–105. <https://doi.org/10.1097/MLR.0000000000000447>.