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Systematic Literature Review

Cost-Effectiveness of Different Formats for Delivery of Cognitive Behavioral Therapy for Depression: A Systematic Review Based Economic Model

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ABSTRACT

Objectives: Cognitive behavioral therapy (CBT) is an effective treatment for depression. Different CBT delivery formats (face-to-face [F2F], multimedia, and hybrid) and intensities have been used to expand access to the treatment. The aim of this study is to estimate the long-term cost-effectiveness of different CBT delivery modes.

Methods: A decision-analytic model was developed to evaluate the cost-effectiveness of different CBT delivery modes and variations in intensity in comparison with treatment as usual (TAU). The model covered an average treatment period of 4 months with a 5-year follow-up period. The model was populated using a systematic review of randomized controlled trials and various sources from the literature.

Results: Incremental cost-effectiveness ratios of treatments compared with the next best option after excluding all the dominated and extended dominated options are: £209/quality-adjusted life year (QALY) for 6 (sessions) × 30 (minutes) F2F-CBT versus TAU; £4 453/QALY for 8 × 30 F2F versus 6 × 30 F2F; £12 216/QALY for 8 × 60 F2F versus 8 × 30 F2F; and £43 072/QALY for 16 × 60 F2F versus 8 × 60 F2F. The treatment with the highest net monetary benefit for thresholds of £20 000 to £30 000/QALY was 8 × 30 F2F-CBT. Probabilistic sensitivity analysis illustrated 6 × 30 F2F-CBT had the highest probability (32.8%) of being cost-effective at £20 000/QALY; 16 × 60 F2F-CBT had the highest probability (31.0%) at £30 000/QALY.

Conclusions: All CBT delivery modes on top of TAU were found to be more cost-effective than TAU alone. Four F2F-CBT options (6 × 30, 8 × 30, 8 × 60, 16 × 60) are on the cost-effectiveness frontier. F2F-CBT with intensities of 6 × 30 and 16 × 60 had the highest probabilities of being cost-effective. The results, however, should be interpreted with caution owing to the high level of uncertainty.

Keywords: cognitive behavioral therapy, cost-effectiveness, decision-analytic model, depression.

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Introduction

Depression is a common mental health problem associated with a substantial reduction in quality of life.[1-3] It is also a chronic relapsing condition and heightens the risk of suicidal behavior.[4-8] According to the Adult Psychiatric Morbidity Survey, the prevalence of depression in people aged 16 and older was about 3.3% in England in 2014.[9] Using population estimates from mid-2017, this equates to around 1.6 million people with depression in the United Kingdom in 2017.[10]

Depression is associated with an increased economic burden for both individuals and society. The estimated annual cost of health services for depression in England was £1.7 billion in 2007, with an additional £235 million spent on antidepressant drugs.[11-13] Cognitive behavioral therapy (CBT) has been shown to be an effective psychological treatment for people with depression.[14] CBT has been widely used as an alternative or adjunct to pharmacological treatments alone, with some evidence of a longer-lasting effect compared with drug treatments.[15,16] Despite increased investment in psychological services, it is difficult to meet the demand for CBT.[17,18] To expand access to CBT, improve the efficiency of service delivery, and reduce waiting time for both therapists and patients, alternative modes of CBT delivery have been developed based on modern technology such as the telephone, computer, and mobile devices.[18-20]

Apart from the delivery modes, the intensity (ie, amount of treatment/dose) of CBT constitutes another key factor in the use of

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health resources and may affect treatment outcomes.[21,22] According to the National Institute of Health and Care Excellence (NICE) Clinical Guidelines 90, adults with depression should be offered psychological interventions such as CBT.[11] Exactly what constitutes the optimal intensity (duration and frequency) of CBT, however, remains unknown.[11,21]

We performed a comprehensive systematic review and network meta-analysis (NMA) to compare the effectiveness of different delivery modes of CBT interventions for adults with a primary diagnosis of depression and for whom CBT was considered by their general practitioner. The NMA included 68 randomized controlled trials (RCTs) using standardized diagnostic criteria such as DSM-III, DSM-IV-TR, DSM-5, ICD-10, or validated depression symptom questionnaires to identify depression. The details of the review and the results can be found in a separate paper published in 2019.[23]

The delivery modes included were: traditional face-to-face (F2F-CBT) (either individually or in groups); CBT conducted solely via multimedia (MM) platforms (eg, self-help books, telephone, audio/video recordings, computer programs, computer applications, email); and hybrid-CBT interventions, which involved a mixture of F2F sessions and MM features. The NMA found that MM and hybrid CBT might be as effective as F2F-CBT. The review also examined the impact of intensity on the effectiveness of different CBT strategies based on the average number and length of CBT sessions. The aim of the current study is to evaluate the cost-effectiveness of different CBT delivery modes and variations in intensity in addition to treatment-as-usual (TAU) in comparison with TAU alone.

Methods

Model Structure

A decision-analytic model was constructed to evaluate the cost-effectiveness of the different CBT options in addition to TAU in comparison with TAU alone. For brevity, CBT options plus TAU will be referred to by their CBT elements. The model has two phases: a decision tree to assess the short-term cost-effectiveness of the various CBT interventions during a four-month treatment period, followed by a Markov model with a cycle of 1 month to extrapolate the longer-term cost-effectiveness over the subsequent 5-year period. The time horizon was selected based on the best available data for long-term follow-ups for CBT and is supported based on discussions with clinical experts.[23,24]

Figure 1 illustrates the structure of the decision tree. Intervention options included in the model are TAU alone, F2F-CBT, hybrid CBT, and MM-CBT. The intensities of F2F and hybrid CBT were defined in terms of prespecified combinations of number and length of sessions delivered by a therapist. Based on clinical opinions and the systematic review, the number of sessions was specified as 6, 8, 10, 12, 14, or 16. The length of each session was specified as either 30 or 60 minutes. This allowed for 24 possible intervention combinations (6(sessions)×30(minutes) F2F, 8(sessions)×60(minutes) hybrid, etc.). MM-CBT consisted mainly of self-guided or minimally supported CBTs, and therefore intensity was not measured.

After patients were provided with CBT, they could either complete the intervention or withdraw from therapy. We do not

Figure 1. Structure of the decision tree.

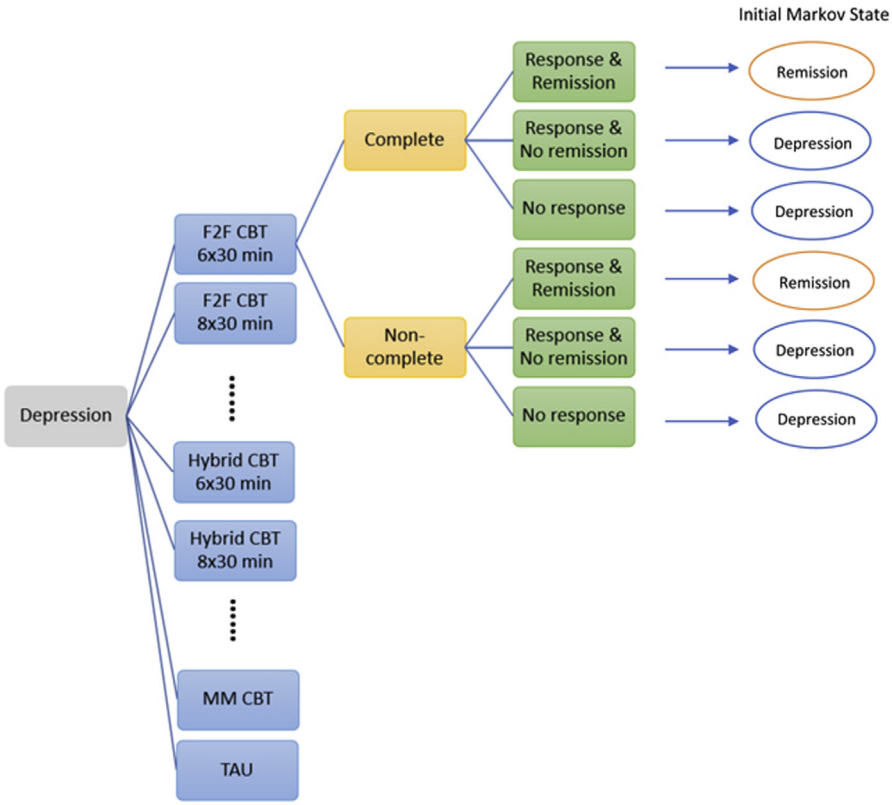
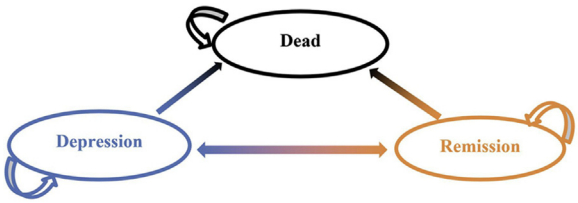


Figure 2. Structure of the Markov model.



model withdrawals from TAU, as TAU is included in all intervention options and these effects would therefore cancel out in an incremental analysis. We assumed that patients who completed the CBT intervention would incur the full course costs while those who withdrew would incur zero costs of CBT. At the end of the 4-month treatment period, under all options patients were classified as responders in remission, responders without achieving remission, or nonresponders. Response was defined as 50% reduction in the Beck Depression Inventory (BDI) from baseline, whereas remission was defined as a BDI score of less than 10 points, commonly used outcomes in previous depression trials.[25,26] It was assumed that all the patients would receive no further depression treatment after the 4-month treatment period.

Figure 2 illustrates the structure of the Markov model that follows the decision tree. The model and the health-state transitions, including remission and relapse beyond the treatment period, take into account the high risk of relapse or a recurrence of depression even after a successful treatment.[7,27,28] In the model, each patient can be in 1 of 3 mutually exclusive health states: depression, remission, or dead.

The proportion of responders in remission at the end of the decision tree was applied to a hypothetical cohort of patients with depression in the initial remission state. Responders who did not achieve remission (including both responders without achieving remission and nonresponders) at the end of the decision tree were classified as being in the depression state. We used a simulated cohort of 10 000 patients with depression, with an average age of 45 based on the trial data from which most of the model parameters were derived.[25,26] The cohort entered the Markov model after the end of treatment and could change their health state following the direction of the arrows at the end of each monthly cycle for 60 cycles. The model was programmed and run using Microsoft Excel®2016.

Model Parameters

Transition probabilities

The decision tree required estimates of the probabilities of withdrawals, response and remission, response without remission, and nonresponse at end of treatment. Response and remission probabilities were derived by assuming a bivariate normal distribution for baseline and follow-up depression scores on the BDI scale for each intervention, and then applying the definitions of response and remission to obtain the proportion of patients with response with or without remission (see Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008). The estimated BDI at baseline and follow-up for TAU were obtained from the control arm of a randomised controlled trial of Internet based cognitive behavioural psychotherapy for depression (IPCRESS) trial, which was felt to best represent contemporary current TAU in the UK setting (see Appendix 2, Tables A1 and A2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008). Relative effects were obtained by reanalyzing the data from the systematic review and jointly synthesizing data of all depression outcomes reported in the papers to obtain mappings between intervention effects on the different depression scales (see Appendix 3, Tables A3 and A4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008). This enabled us to combine all evidence and obtain intervention effects on the BDI scale for use in the economic model.

Intensity of intervention was defined as the product of number of sessions by average session length. We estimated a linear effect of intensity on the BDI scale for F2F and hybrid-CBT interventions with slope −0.496 (95% CI [confidence interval], −0.922 to −0.063), indicating a larger reduction with increasing intensity (see Appendix 3 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008). Owing to a lack of evidence on hybrid CBT, we assumed a common slope for F2F and hybrid CBT.[23]

The NMA found no difference between interventions in withdrawal probability, but there was a high degree of heterogeneity in these figures.[23] We therefore assumed withdrawal to be equal for CBT interventions and fitted a random effects single arm meta-analysis of all CBT arms on the log-odds scale to estimate withdrawal probabilities for the model. The results were summarized in two ways: the mean of the random effects distribution (used in our base-case) and the predictive effect in a new population from the random effects distribution (used in a sensitivity analysis).[29]

The probability of remission and relapse in the posttreatment Markov model was derived from the long-term follow-up data of the CoBalT study, an RCT of CBT conducted in the United Kingdom with the longest follow-up period (average of 46 months).[24] In the Markov model, based on the long-term follow-up data extracted from the CoBalT trial, instead of estimating transition probabilities for each intensity, we assumed that after the end of treatment, the transition probabilities, as well as costs and utilities, only differ between CBT arms and TAU arms.

Based on the CoBalT trial data, the relapse rates were assumed to differ from the period of 0 to 6 months to the 7-month to 5-year period after the end of treatment. Each patient has a risk of dying in either the depression or remission state. We assume that patients in remission have the same mortality rate as the general population. The general population mortality rate was obtained from the deaths registered in England and Wales in 2016.[30] The relative risk of mortality (RR) in depressed people relative to nondepressed people was estimated as 1.52 (95% CI = 1.45-1.59) from a meta-analysis that included 293 studies and 1.8 million participants.[31]

Resource use and costs

The health economic analysis was carried out from the UK National Health Service and personal social services perspectives.[32] All costs are presented in pound sterling at 2016/2017 prices. The resources used during the treatment period were: staff time (including therapist and supervisor time), supplementary materials such as booklets, and remote delivery methods such as telephone and internet. We used a middle-point National Health Service pay grade (band-7) (£36 612 per year) to account for CBT therapists and Band-8a (£44 310 per year) for supervisors.[33] Taking into account the salary oncosts and overheads, the hourly cost of a band-7 and band-8a staff member was estimated at £51 and £62, respectively. For the MM component in hybrid and MM-CBT, unit costs of materials such as books and internet are given in Appendix 4, Table A5 (in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008.) They were estimated using the weighted average cost of materials used in the studies identified by the systematic review.

The 5-year posttreatment costs were obtained from the CoBalT trial,[24] which collected data on health service resource use for patients at 6-, 12-, and 46-month follow-ups and derived costs for

primary and community care, hospital care, and the direct costs of personal social services. Using CoBalT data, we derived the monthly costs for patients who were in remission state and those who were in depression state, respectively.

Utility

The primary outcome measure used in the model was quality-adjusted life years (QALYs). The instrument recommended by NICE to calculate QALYs is the EQ-5D measure.[32] We used data from two large UK–based studies (IPCRESS and CoBalT), with a total sample of 766 patients with depression to compute the EQ-5D utility values for different health states before and after treatment.[24,26] The long-term utility values used in the Markov model were derived solely from the CoBalT follow-up study.[24] QALY estimates were calculated by multiplying the utility value for each health state with the time spent in that state using the area under the curve.[34]

Cost-Effectiveness Analysis and Sensitivity Analysis

An incremental cost-effectiveness analysis was conducted to establish the value for money of different CBT options over and above TAU. We assumed that all patients in the intervention and control groups received TAU. The difference in mean costs between the interventions and the control was divided by the difference in mean health outcomes (QALYs) to generate incremental cost-effectiveness ratios (ICERs) with a time horizon of 5 years after the end of treatment. Based on the maximum acceptable ICER range of £20 000 to £30 000 per QALY gained used by NICE, ICERs below this range suggest that the intervention is considered to be cost-effective compared with the control.[32] Meanwhile, the net monetary benefit of the interventions was calculated for thresholds of £20 000 or £30 000 per QALY. All costs and QALYs were discounted to a present value at an annual discount rate of 3.5%.[32]

Probabilistic sensitivity analysis (PSA) was performed to evaluate the uncertainty surrounding the results. The model was probabilistic in that all parameters were assigned probability distributions to reflect their sample variability.[35] For the short-term decision tree probabilities were estimated using the Markov chain Monte Carlo model; the simulated Markov chain Monte Carlo values were sampled directly to propagate uncertainty in the input parameters throughout the model. Random values of input parameters were drawn from the assumed distributions: beta distribution for probabilities and gamma distribution for both QALYs and costs.[35] The expected costs and QALYs for each option were calculated using combinations of parameter values.[36] This process was repeated 10 000 times, and the results of these simulations were reported in the form of a cost-effectiveness acceptability curve. We performed an extra sensitivity analysis to test the impact of RR of mortality in the model. An extreme value of RR = 1 was used in the sensitivity analysis, that is, we assumed there is no increased risk of mortality in depressed people compared to nondepressed people.

Results

We identified 65 intervention arms with 2210 patients who received F2F-CBT. There were only 7 hybrid-CBT arms identified in the systematic review, with 401 participants in total. Another 18 study arms were identified as MM-CBT, involving 1480 patients. The treatment period was 4 months, in line with most of the included studies.

Transition Probabilities

Appendix Table A4 lists the estimated response and remission probability for each comparator at the end of treatment based on Appendices 1-3 (in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008). The withdrawal probability for CBT interventions estimated as the random effects mean was (0.18, 95% CI: 0.15-0.21), whereas the predictive distribution was (0.20, 95% CI: 0.04-0.50), which reflects the uncertainty as to where the UK population effects would lie in the random effects distribution. Posttreatment transition probabilities used in the Markov model are presented in Appendix 5, Table A6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008.

Costs and Utilities

Table 1 summarizes the cost per person for F2F (range £180-£907) and hybrid CBTs (range £205-£953) by various combinations of number and length of therapy sessions. For the same intensity, the treatment cost was higher for hybrid CBT than F2F-CBT given the additional MM components. The weighted mean cost for MM-CBT across the studies included in the systematic review was estimated to be £148/person (SD £141).

After the treatment period, for those who received CBT, the monthly cost of people in remission was estimated at £22 (SE £5), and that of people who remained depressed was estimated at £79 (SE £20). For those who received TAU, the monthly cost of people in remission was estimated at £41 (SE £12) and that of people who remained depressed was estimated at £67 (SE £13) (see Appendix 5, Table A6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008).

The estimated EQ-5D utility scores are listed in Table 2. The mean baseline utility score for people with depression was 0.65 (SD 0.23). At the end of the treatment period, for people treated

Table 1. Total cost per person of a full course treatment (2016/2017 price).

Number of sessions	F2F-CBT (30 minutes per session)	F2F-CBT (60 minutes per session)	Hybrid CBT (30 minutes per session)	Hybrid CBT (60 minutes per session)
6	£180	£358	£205	£389
8	£234	£468	£262	£501
10	£289	£577	£318	£614
12	£344	£687	£374	£727
14	£399	£797	£431	£840
16	£454	£907	£487	£953
MM-CBT	£148 (average cost per person)			

CBT indicates cognitive behavioral therapy; F2F, face-to-face; MM, multimedia.

Table 2. Utility scores at baseline and at the end of 4-month treatment period.[24,26]

EQ-5D utility scores	Mean	SD
Baseline	0.65	0.23
At the end of 4 months, with TAU treatment		
• Response and remission	0.93	0.09
• Response, no remission	0.80	0.14
• No response, no remission	0.74	0.19
At the end of 4 months, with CBT intervention		
• Response and remission	0.92	0.16
• Response, no remission	0.84	0.12
• No response, no remission	0.74	0.15

CBT indicates cognitive behavioral therapy; SD, standard deviation; TAU, treatment as usual.

with any CBT option, the EQ-5D utility scores for those meeting the criteria for response and remission, response and no remission, no response and no remission were 0.92, 0.84, and 0.74, respectively. The corresponding utility scores for patients treated with TAU were 0.93, 0.80, and 0.74.

During the 5 years after the end of treatment, former patients in remission had a mean monthly QALY of 0.076 in the CBT groups and 0.077 in the TAU groups. For those who remained depressed, the mean monthly QALYs for CBT and TAU groups were 0.064 and 0.058, respectively (see Appendix 5, Table A6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008).

Cost-Effectiveness Analysis

Base-case analysis

Table 3 presents a summary of the base-case results of the incremental cost-effectiveness analysis based on the Markov model over the 5-year time horizon. The second and third columns in Table 3 list the mean costs and QALYs of each intervention. Given the same treatment intensity, hybrid-CBTs appeared to be more expensive and less effective compared with F2F-CBTs. Hence, all the hybrid-CBTs are dominated by their F2F counterparts. Column 4 lists ICERs of all the CBT options compared with TAU, while column 5 shows ICERs of some options compared with the next best option after excluding all the dominated (more costly but less effective than the comparator) and extended dominated (less cost-effective than the next option) options. Appendix 5, Figure A2 illustrates the base-case cost-effectiveness plane (in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008). The CBT options on the cost-effectiveness frontier (the red line in Fig. A2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008) are 6 (sessions) × 30 (minutes) F2F, 8 × 30 F2F, 8 × 60 F2F, and 16 × 60 F2F. The ICER of 6×30 F2F compared with TAU is £209/QALY. The estimated ICER for the comparison between 8 × 30 F2F and 6 × 30 F2F is £4453/QALY. When the length of the 8-session F2F-CBT was extended from 30 minutes to 60 minutes, the ICER increased to £12 216/QALY. The16 × 60 F2F option was the costliest and most effective F2F intervention, resulting in an ICER of £43 072 per additional QALY for 16 × 60 F2F versus 8 × 60 F2F. Columns 6-7 in Table 3 indicate that 8 × 30 F2F has the highest net monetary benefit for thresholds of £20 000 and £30 000 per QALY.

PSA incorporated uncertainty in the parameter estimates to provide estimates of the probability that each intervention would be cost-effective at different acceptable ICER values. The cost-effectiveness acceptability curve in Figure 3 illustrates that for acceptable ICER values less than £25 290/QALY gained, the optimal option is 6 × 30 F2F. The probability of 6×30 F2F being the most cost-effective option declines as the acceptable value increases. At ICER values higher than £25 290/QALY, 16 × 60 F2F becomes the optimal option, with the highest probability of being cost-effective. Figure 3 also shows that, using the NICE decision-making thresholds, 6 × 30 F2F has the highest probability (32.8%) of being cost-effective at £20 000/QALY, and 16 × 60 F2F has the highest probability (31.0%) of being cost-effective at £30 000/QALY. But the probability of these two CBTs being the most cost-effective option never exceeded 50%, indicating a high level of uncertainty.

Sensitivity analyses

We repeated the process for base-case analysis using the predicted effect mean for withdrawal rate. The overall results and findings (especially the cost-effectiveness of different CBT options) were comparable with the random effects mean model, and there were relatively trivial changes to the values of the ICERs. Sensitivity analyses show the 6 × 30 F2F had the highest probability (32.5%) of being cost-effective at £20 000/QALY, and that 16 × 60 F2F had the highest probability (31.1%) of being cost-effective at £30 000/QALY. Appendix 6 lists the results of the sensitivity analysis, where RR of mortality was assumed equal to 1 and the results remained robust (see Appendix 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2020.07.008).

Discussion

The base-case analysis found that the TAU arm yielded 3.501 QALYs over a 5-year horizon at a cost of £3325/person. When compared with TAU, F2F-CBT, hybrid-CBT, and MM-CBT, all might be considered cost-effective given the NICE maximum acceptable ICER range of £20 000-£30 000 per QALY gained. This is consistent with findings of many recent systematic reviews for different forms of CBT.[37,38] Four F2F-CBT options—6 × 30, 8 × 30, 8 × 60, and 16 × 60—were on the cost-effectiveness frontier, which describes the optimal pathway of moving from one strategy to a more costly one with highest increased outcome. The strategy that generated the maximum net monetary benefits for thresholds of £20 000 and £30 000 per QALY was 8 × 30 F2F.

After taking into account uncertainty surrounding the decision, the PSA illustrates that the least costly strategy (6 × 30 F2F) had the highest probability of being the most cost-effective strategy for lower thresholds (less than £25 290/QALY). As the threshold increases, however, the most effective strategy (16 × 60 F2F) becomes the preferred option. These results should be interpreted with caution, however, as none of the options reached a 50% probability of being most cost-effective, indicating a high level of uncertainty.

On the other hand, although we identified 65 F2F-CBT intervention arms with over 2000 patients with depression and 18 MM-CBT with 1480 participants, there were only 7 hybrid CBTs arms identified in the systematic review. The sample size for hybrid CBT was therefore much smaller than for F2F and MM-CBT, adding another layer of uncertainty.

Akin to the dose-response relationship in pharmacological interventions, the intensity of CBT can influence treatment effectiveness; however, the optimal intensity of CBT is not clear.[14,21] In addition, treatment intensity also influences healthcare resource

Table 3. ICERs and net monetary benefit (5 years after intervention).

Interventions	Cost	QALYs	ICERs compared to		Net monetary benefit	
			Lowest cost (TAU)	Next best option	£20 000 per QALY	£30 000 per QALY
TAU	£3325	3.501	-		£66 695	£101 705
F2F 6 × 30	**£3400**	**3.859**	**£209/QALY**	**£209/QALY**	£73 780	£112 370
MM	£3420	3.847	£275/QALY	Dominated	£73 520	£111 990
F2F 8 × 30	**£3424**	**3.864**	**£273/QALY**	**£4453/QALY**	£73 856	£112 496
Hybrid 6 × 30	£3431	3.856	£299/QALY	Dominated	£73 689	£112 249
Hybrid 8 × 30	£3457	3.861	£367/QALY	Dominated	£73 763	£112 373
F2F 10 × 30	£3483	3.861	£439/QALY	Dominated	£73 737	£112 347
F2F 12 × 30	£3500	3.868	£477/QALY	Extended Dominated	£73 860	£112 540
Hybrid 10 × 30	£3518	3.858	£541/QALY	Dominated	£73 642	£112 222
F2F 6 × 60	£3525	3.864	£551/QALY	Dominated	£73 755	£112 395
Hybrid 12 × 30	£3536	3.865	£580/QALY	Dominated	£73 764	£112 414
Hybrid 6 × 60	£3562	3.861	£658/QALY	Dominated	£73 658	£112 268
F2F 14 × 30	£3566	3.862	£668/QALY	Dominated	£73 674	£112 294
F2F 8 × 60	**£3572**	**3.875**	**£660/QALY**	**£12 216/QALY**	**£73 928**	**£112 678**
F2F 16 × 30	£3576	3.872	£677/QALY	Dominated	£73 864	£112 584
Hybrid 14 × 30	£3603	3.859	£777/QALY	Dominated	£73 577	£112 167
Hybrid 8 × 60	£3612	3.872	£774/QALY	Dominated	£73 828	£112 548
Hybrid 16 × 30	£3614	3.869	£785/QALY	Dominated	£73 766	£112 456
F2F 10 × 60	£3699	3.866	£1025/QALY	Dominated	£73 621	£112 281
F2F 12 × 60	£3738	3.879	£1093/QALY	Extended Dominated	£73 842	£112 632
Hybrid 10 × 60	£3740	3.863	£1146/QALY	Dominated	£73 520	£112 150
Hybrid 12 × 60	£3783	3.876	£1221/QALY	Dominated	£73 737	£112 497
F2F 14 × 60	£3872	3.868	£1490/QALY	Dominated	£73 488	£112 168
F2F 16 × 60	**£3903**	**3.883**	**£1513/QALY**	**£43 072/QALY**	£73 757	£112 587
Hybrid 14 × 60	£3919	3.865	£1632/QALY	Dominated	£73 381	£112 031
Hybrid 16 × 60	£3953	3.880	£1657/QALY	Dominated	£73 647	£112 447

ICER indicates incremental cost-effectiveness ratio; F2F, face-to-face; MM, multimedia; QALY, quality-adjusted life-year; TAU, treatment as usual.

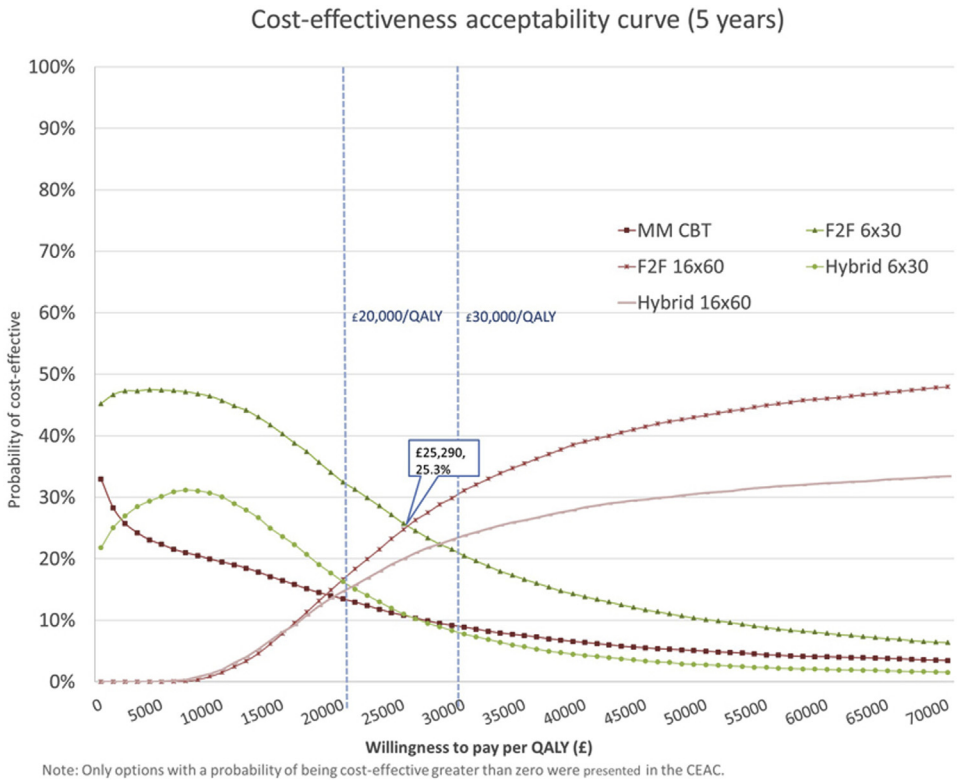
usage, thereby affecting the cost-effectiveness of CBT. In this study, a decision-analytic model was designed to compare the cost-effectiveness of F2F-CBT, hybrid-CBT, and MM-CBT of various intensities with TAU. MM-CBT, although less intensive in resources demand, did not appear to be cost-effective in comparison with the alternatives. The optimal intensity of F2F-CBT appeared to be at the two ends of the spectrum considered. The alternatives in between, while incurring higher cost due to increased intensity, did not appear to produce sufficiently improved outcomes to justify the additional investment, although note that this finding is likely a result of the assumed linear model for intensity. To the best of our knowledge, this study was the first to provide a separate comparison of cost-effectiveness for different CBT delivery modes and intensities with TAU.[38-40]

This study has several limitations. We used a loosely defined TAU as the common comparator in the analysis, but reality is more complicated in that TAU is not a homogeneous service among different countries or over time. For example, the latest NICE Clinical Guidelines recommend both pharmacological and psychological treatments in usual practice.[23] This makes CBT part of the current TAU in the United Kingdom. Therefore, some of the earlier studies might be less comparable than later and especially future ones. Similarly, potential differences in clinical settings and effectiveness between countries were not explored in this analysis. To extract as much data as possible to estimate resource use, the analysis made use of all studies, regardless of country, and valued the resources using cost estimates based on UK practices. However, some studies may have used treatment methods not typically used in the UK, which would bias toward unrealistically high costs.

We simplified the cost of CBT by using full-course costs for the completers and null costs for the noncompleters. This may underestimate the cost of noncompleters, as in practice, patients might withdraw in the middle of a course of treatment. On the other hand, this may also have a chance to overestimate the cost of completers, as completers who attended the final assessment may not attend all the sessions. Given the lack of empirical evidence of the actual number of sessions each group attended, we made the above assumption and assume a similar effect of withdrawal among all the intervention arms. We have also assumed that patients who do not achieve remission have the same long-term outcomes, regardless of whether they responded or not in the short term. Relaxing this assumption is likely to improve the cost-effectiveness of interventions that had higher response rates for a given remission rate.

Third, the cost and utility scores for the posttreatment period were mainly derived from the CoBalT trial. Although this study provides the best available data for long-term follow-up after CBT

Figure 3. Cost-effectiveness acceptability curve (CEAC).



and TAU treatment, the study only included patients with treatment-resistant depression who were taking antidepressant medication for at least 6 weeks. Our model adopted a broader population that included adults with a primary diagnosis of depression and for whom CBT was considered by their general practitioner, including these patients with treatment-resistant depression. Costs and utilities for the broader population might differ from those found in CoBalT; however, because costs and utilities from the same population were used for all the intervention arms, we do not expect the qualitative findings to be sensitive to this, although the magnitude of differences may change. Further studies that measure costs and utilities with sufficiently long follow-up on less severely depressed populations are required for future models.

Within the hybrid-CBTs, the materials used varied from books to smartphones, which is a source of heterogeneity. Their effects on reducing human involvement in therapy delivery could be very different. Moreover, for MM and hybrid-CBTs, the analysis based on trials is unable to take into account the effect of potential improvement in accessibility and flexibility of the service. For example, it would prove cost-effective if hybrid-CBT could reach those who would not have received treatment otherwise, or if the therapist time saved by 1 patient taking up MM-CBT could be used to treat another patient who is less amenable to MM.

Finally, we assumed a linear effect of intensity on the BDI scale. This was well estimated for F2F-CBT (based on 55 studies ranging in intensity from 1.6 to 19.8). We had insufficient evidence, however, to estimate the effect of intensity for hybrid (5 studies ranging in intensity from 1.2 to 3.8), and instead assumed the effect of intensity was the same for hybrid and F2F. We may expect the effect of intensity to differ for hybrid and F2F due to the added MM components, in which case we could find that hybrid interventions were more cost-effective. Further studies exploring hybrid-CBT at different intensities would be required to explore this further.

Conclusion

Financial constraints dictate that healthcare providers need to explore the integration of technology as a part of services in order to increase access to, and effectiveness of, interventions such as CBT. Although the rapid development in technology has resulted in a proliferation of computer applications and online interventions for the self-management of chronic conditions, including depression, few are evidence-based. Moreover, previous work has shown that in order to increase engagement with, and maximize benefit from, computerized forms of CBT, human support is needed. By developing hybrid interventions that combine therapist input with use of technology to deliver tailored treatment, there is a potential for long-term gain. Future research that evaluates both clinical- and cost-effectiveness of such approaches is needed in order to inform provision and development of services. Meanwhile, the model constructed in this study can be easily adapted for use in future studies to explore the long-term cost-effectiveness of other depression treatments.

Supplemental Material

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REFERENCES

1. Ferrari AJ, Charlson FJ, Norman RE, et al. Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010. *PLoS Med*. 2013;10(11):e1001547.
2. Kessler RC, Berglund P, Demler O, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*. 2003;289(23):3095–3105.
3. Ustun TB, Ayuso-Mateos JL, Chatterji S, Mathers C, Murray CJ. Global burden of depressive disorders in the year 2000. *Br J Psychiatry*. 2004;184:386–392.
4. Ng CW, How CH, Ng YP. Depression in primary care: assessing suicide risk. *Singapore Med J*. 2017;58(2):72–77.
5. Angst J, Angst F, Stassen HH. Suicide risk in patients with major depressive disorder. *J Clin Psychiatry*. 1999;60(suppl 2):57–116.
6. Gaynes BN, West SL, Ford CA, et al. Screening for suicide risk in adults: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2004;140(10):822–835.
7. Burcusa SL, Iacono WG. Risk for recurrence in depression. *Clin Psychol Rev*. 2007;27(8):959–985.
8. Kessler RC, Nelson CB, McGonagle KA, Liu J, Swartz M, Blazer DG. Comorbidity of DSM-III-R major depressive disorder in the general population: results from the US National Comorbidity Survey. *Br J Psychiatry Suppl*. 1996;(30):17–30.
9. McManus S, Bebbington P, Jenkins R, Brugha T. *Mental Health and Wellbeing in England: Adult Psychiatric Morbidity Survey 2014*. Leeds, England: NHS Digital; 2016.
10. UK Office for National Statistics. Population estimates for UK, England and Wales, Scotland and Northern Ireland, mid-2017; 2018. https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/bulletins/annualmidyearpopulationestimates/mid2017. Accessed August 30, 2020.
11. National Institute for Clinical Excellence (NICE). Depression in Adults: Recognition and Management. London, England: National Institute for Health and Care Excellence; 2009 [Updated April 2016]. https://www.nice.org.uk/guidance/CG90. Accessed August 30, 2020.
12. McCrone P, Dhanasiri S, Patel A, Knapp M, Lawton-Smith S. *Paying the Price: The Cost of Mental Health Care in England to 2026*. London, England: King's Fund; 2008.
13. Health and Social Care Information Centre. Prescription Cost Analysis, England – 2017; 2018. https://digital.nhs.uk/data-and-information/publications/statistical/prescription-cost-analysis/prescription-cost-analysis-england-2017. Accessed August 30, 2020.
14. Cuijpers P, Berking M, Andersson G, Quigley L, Kleiboer A, Dobson KS. A meta-analysis of cognitive-behavioural therapy for adult depression, alone and in comparison with other treatments. *Can J Psychiatry*. 2013;58(7):376–385.
15. DeRubeis RJ, Gelfand LA, Tang TZ, Simons AD. Medications versus cognitive behavior therapy for severely depressed outpatients: mega-analysis of four randomized comparisons. *Am J Psychiatry*. 1999;156(7):1007–1013.
16. Cuijpers P, Gentili C. Psychological treatments are as effective as pharmacotherapies in the treatment of adult depression: a summary from Randomized Clinical Trials and neuroscience evidence. *Res Psychother*. 2017;20(2):147–152.
17. Kaltenthaler E, Brazier J, De Nigris E, et al. Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation. *Health Technol Assess*. 2006;10(33):iii–168.
18. Shapiro DA, Cavanagh K, Lomas H. Geographic Inequity in the Availability of Cognitive Behavioural Therapy in England and Wales. *Behav Cogn Psychother*. 2003;31(2):185–192.
19. Proudfoot J, Goldberg D, Mann A, Everitt B, Marks I, Gray JA. Computerized, interactive, multimedia cognitive-behavioural program for anxiety and depression in general practice. *Psychol Med*. 2003;33(2):217–227.
20. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cogn Behav Ther*. 2009;38(4):196–205.
21. Cuijpers P, Huibers M, Ebert DD, Koole SL, Andersson G. How much psychotherapy is needed to treat depression? A metaregression analysis. *J Affect Disord*. 2013;149(1-3):1–13.
22. Stulz N, Lutz W, Kopta SM, Minami T, Saunders SM. Dose-effect relationship in routine outpatient psychotherapy: does treatment duration matter? *J Couns Psychol*. 2013;60(4):593–600.
23. Lopez-Lopez JA, Davies SR, Caldwell DM, et al. The process and delivery of CBT for depression in adults: a systematic review and network meta-analysis. *Psychol Med*. 2019;49(12):1937–1947.
24. Wiles NJ, Thomas L, Turner N, et al. Long-term effectiveness and cost-effectiveness of cognitive behavioural therapy as an adjunct to pharmacotherapy for treatment-resistant depression in primary care: follow-up of the CoBalT randomised controlled trial. *Lancet Psychiatry*. 2016;3(2):137–144.
25. Wiles N, Thomas L, Abel A, et al. Cognitive behavioural therapy as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression: results of the CoBalT randomised controlled trial. *Lancet*. 2013;381(9864):375–384.
26. Kessler D, Lewis G, Kaur S, et al. Therapist-delivered Internet psychotherapy for depression in primary care: a randomised controlled trial. *Lancet*. 2009;374(9690):628–634.
27. Hardeveld F, Spijker J, De Graaf R, Nolen WA, Beekman ATF. Prevalence and predictors of recurrence of major depressive disorder in the adult population. *Acta Psychiatr Scand*. 2010;122(3):184–191.
28. Yiend J, Paykel E, Merritt R, Lester K, Doll H, Burns T. Long term outcome of primary care depression. *J Affect Disord*. 2009;118(1-3):79–86.
29. Ades AE, Lu G, Higgins JP. The interpretation of random-effects meta-analysis in decision models. *Med Decis Making*. 2005;25(6):646–654.
30. UK Office for National Statistics. Deaths registered in England and Wales: 2016; 2017. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsregistrationsummarytables/2016. Accessed August 30, 2020.
31. Cuijpers P, Smit F. Excess mortality in depression: a meta-analysis of community studies. *J Affect Disord*. 2002;72(3):227–236.
32. National Institute for Health and Care Excellence. *Guide to the Methods of Technology Aappraisal 2013*. London, England: National Institute for Health and Care Excellence; 2013.

33. Health Careers. Agenda for change - pay rates; 2017. https://www.healthcareers.nhs.uk/about/careers-nhs/nhs-pay-and-benefits/agenda-change-pay-rates. Accessed August 21, 2017.
34. Richardson G, Manca A. Calculation of quality adjusted life years in the published literature: a review of methodology and transparency. *Health Econ*. 2004;13(12):1203–1210.
35. Briggs A, Sculpher M, Claxton K. *Decision Modelling for Health Economic Evaluation*. Oxford, England: Oxford University Press; 2006.
36. Fenwick E, Marshall DA, Levy AR, Nichol G. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation. *BMC Health Serv Res*. 2006;6:52.
37. Paganini S, Teigelkotter W, Buntrock C, Baumeister H. Economic evaluations of internet- and mobile-based interventions for the treatment and prevention of depression: a systematic review. *J Affect Disord*. 2018;225:733–755.
38. Brettschneider C, Djadran H, Harter M, Lowe B, Riedel-Heller S, Konig HH. Cost-utility analyses of cognitive-behavioural therapy of depression: a systematic review. *Psychother Psychosom*. 2015;84(1):6–21.
39. Barrett B, Byford S, Knapp M. Evidence of cost-effective treatments for depression: a systematic review. *J Affect Disord*. 2005;84(1):1–13.
40. Pirraglia PA, Rosen AB, Hermann RC, Olchanski NV, Neumann P. Cost-utility analysis studies of depression management: a systematic review. *Am J Psychiatry*. 2004;161(12):2155–2162.