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

Running title: Cost-Effectiveness Model for CBT delivery modes

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**Abstract**

***Objectives***

Cognitive behavioural therapy (CBT) is an effective treatment for depression. Different CBT delivery formats (face-to-face (F2F), multimedia (MM) 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 four-month with a 5-year follow-up period. The model was populated using a systematic review of randomised controlled trials and various sources from the literature.

***Results***

Incremental cost-effectiveness ratios (ICERs) of treatments compared with the next best option after excluding all the dominated and extended dominated options are: £209/QALY for 6(sessions)×30(minutes) F2F-CBT vs TAU; £4,453/QALY for 8×30 F2F vs 6×30 F2F, £12,216/QALY for 8×60 F2F vs 8×30 F2F; £43,072/QALY for 16x60 F2F vs 8×60 F2F. 8×30 F2F-CBT has the highest net monetary benefit for thresholds of £20,000-£30,000/QALY. 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. However, the results should be interpreted with caution due to the high level of uncertainty.

**Highlights**

Depression is a common mental health problem associated with a substantial reduction in quality of life. Cognitive behavioural therapy (CBT) is an effective psychological treatment for people with depression and may have a longer-lasting effect compared with pharmacological treatment alone. Different CBT delivery formats (face-to-face (F2F), multimedia (MM) and hybrid CBT) and intensities have been used to expand access to the treatment.

A decision-analytic model was developed to evaluate the long-term 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-month with a 5-year follow-up period and was populated using a systematic review of randomised controlled trials. This model can be easily adapted for use in future studies, to explore the long-term cost-effectiveness of other depression treatments.

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. However, the results should be interpreted with caution due to the high level of uncertainty.

**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 behaviour 4-8. According to the Adult Psychiatric Morbidity Survey, the prevalence of depression in people aged 16 and above 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 UK 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 behavioural 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. In order 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 telephone, computer and mobile devices 18-20.

Apart from the delivery modes, the intensity (i.e. amount of treatment/dose) of CBT constitutes another key factor in the use of health resources and may affect treatment outcomes 21,22. According to the National Institute of Health and Care Excellence (NICE) Clinical Guidelines 90 (CG90), adults with depression should be offered psychological interventions such as CBT 23. Exactly what constitutes the optimal intensity (duration and frequency) of CBT, however, remains unknown 21,23.

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 GP. The NMA included 68 randomised controlled trials (RCTs) using standardised diagnostic criteria such as DSM-III, DSM-IV-TR, DSM-5, ICD-10, or validated depression symptom questionnaires to identify depression were included. The details of the review and the results can be found in a separate paper published in 2019 24.

The delivery modes included were: traditional face-to-face (F2F-CBT) (either individually or in groups); CBT conducted solely via multimedia (MM) platforms (e.g. self-help books, telephone, audio/video recordings, computer programmes, apps, e-mail); and hybrid-CBT interventions, which involved a mixture of face-to-face sessions and multimedia 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 one 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 supported based on discussions with clinical experts 24,25.

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 pre-specified 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 of mainly 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 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 either: responders in remission, responders without achieving remission, or non-responders. Response was defined as 50% reduction in the Beck Depression Inventory (BDI) from baseline, while remission was defined as a BDI score of less than 10 points, commonly used outcomes in previous depression trials 26,27. It is assumed that all the patients will receive no further depression treatment after the 4-month treatment period.

Figure 2 illustrates the structure of the Markov model which 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 7,28,29. In the model, each patient can be in one of three 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 depressive patients in the initial remission state. Responders who didn’t achieve remission (including both responders without achieving remission and non-responders) at the end of the decision tree were classified as being in the depression state. We used a simulated cohort of 10,000 depressive patients, with an average age of 45 based on the trial data where most of the model parameters derived from 26,27. The cohort enter 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 non-response 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 proportion of patient with response with or without remission (Appendix-1). The estimated BDI at baseline and follow-up for TAU was obtained from the control arm of the IPCRESS trial which was felt to best represent contemporary current TAU in the UK setting (Appendix-2, Table A1 & Table A2). Relative effects were obtained by re-analysing the data from the systematic review jointly synthesising data an all depression outcomes reported in the papers to obtain mappings between intervention effects on the different depression scales (Appendix-3, Table A3 & Table A4). 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% CrI: -0.922 to -0.063) indicating a larger reduction with increasing intensity (Appendix-3). Due to lack of evidence on Hybrid CBT, we assumed a common slope for F2F and Hybrid CBT 24.

The NMA found no difference between interventions in withdrawal probability, but there was a high degree of heterogeneity in these figures 24. 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 summarised 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) 30 .

The probability of remission and relapse in the post-treatment Markov model was derived from the long-term follow-up data of the CoBalT study, an RCT of CBT conducted in the UK with the longest follow-up period (average of 46 months) 25. 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 0-6 months period, to the 7-month-5-years period, following 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 31. The relative risk of mortality in depressed relative to non-depressed 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 32.

*Resource use and costs*

The health economic analysis was carried out from the UK National Health Service (NHS) and personal social services perspectives 33. All costs are presented in Pound sterling at 2016/17 prices. The resources used during the treatment period were: staff time (including therapist and supervisor time), supplementary materials such as booklets, remote delivery methods such as telephone and internet. We used a middle-point NHS pay grade (Band-7) (£36,612 per year) to account for CBT therapists and Band-8a (£44,310 per year) for supervisors34. Taking into account the salary on-costs and overheads, the hourly cost of a Band-7 and Band-8a staff member was estimated at £51 and £62 respectively. For the multimedia component in hybrid and MM-CBT, unit costs of materials such as books and internet are given in Appendix-4, Table A5. They were estimated using the weighted average cost of materials used in the studies identified by the systematic review.

The 5-year post-treatment costs were obtained from the CoBalT trial 25 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 European Quality of Life-5 Dimensions (EQ-5D) measure 33. 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 25,27. The long-term utility values used in the Markov model were derived solely from the CoBalT follow-up study 25. 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 35.

***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-£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 33. Meanwhile, 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% 33.

Probabilistic sensitivity analysis (PSA) were 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 36. For the short-term decision tree probabilities estimated using Markov Chain Monte Carlo (MCMC), the simulated MCMC 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 36. The expected costs and QALYs for each option were calculated using combinations of parameter values 37. This process was repeated 10,000 times, and the results of these simulations were reported in the form of cost-effectiveness acceptability curve (CEAC). 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, i.e. assuming there is no increased risk of mortality in depressed people compared to non-depressed people.

**Results**

We identified 65 intervention arms with 2,210 patients who received F2F-CBT, of which 35 comprised group therapy. There were only seven hybrid-CBT arms identified in the systematic review, with 401 participants in total. Another 18 study arms were identified as MM-CBT, involving 1,480 patients. The treatment period was four months, in line with most of the included studies.

***Transition probabilities***

Table A4 lists the estimated response and remission probability for each comparator at the end of treatment based on Appendices 1-3. 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. Post-treatment transition probabilities used in the Markov model are presented in Appendix-5, Table A6.

***Costs and utilities***

Table 1 summarises 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 multimedia 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 remained depressed was estimated at £79 (SE £20). For those who received TAU, monthly cost of people in remission was estimated at £41 (SE £12) and that of people remained depressed was estimated at £67 (SE £13) (Appendix-5, Table A6).

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 treatment period, for people treated 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 QALY for CBT and TAU groups were 0.064 and 0.058, respectively (Appendix-5, Table A6).

***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. Columns 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. The CBT options on the cost-effectiveness frontier (the red line in Figure A2) 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 £4,453/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 most costly 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 CEAC 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 one and the results remained robust.

**Discussion**

The base-case analysis found that the TAU arm yielded 3.501 QALYs over a five-year horizon at a cost of £3,325/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 38,39. 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. 8×30 F2F generated the maximum net monetary benefits for thresholds of £20,000 and £30,000 per QALY.

However, 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, though, the most effective strategy (16×60 F2F) becomes the preferred option. These results should be interpreted with caution, however, since none of the options reached a 50% probability of being most cost-effective, indicating a high level of uncertainty.

On the other hand, while we identified 65 F2F-CBT intervention arms with over 2,000 depression patients and 18 MM-CBT with 1,480 participants, there were only seven hybrid CBTs arms identified in the systematic review. The sample size for hybrid-CBT was therefore much smaller than 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 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 incurred 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 39-41.

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 recommends both pharmacological and psychological treatments in usual practice 23. This makes CBT part of the current TAU in the UK. 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. In order 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 towards unrealistically high costs.

We simplified the cost of CBT by using full-course costs for the completers and null costs for the non-completers. This may underestimate the cost of non-completers, 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 which had higher response rates, for a given remission rate.

Thirdly, the cost and utility scores for the post-treatment period were mainly derived from the CoBalT trial. Although this study provides the best available data for long-term follow-up after CBT 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 which includes adults with a primary diagnosis of depression and for whom CBT was considered by their GP, 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 wouldn’t have received treatment otherwise, or if the therapist time saved by one patient taking up MM-CBT could be used to treat another patient who is less amenable to multimedia.

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). However, we had insufficient evidence 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 multimedia 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.

Financial constraints dictate that health care providers need to explore the integration of technology as part of services in order to increase access to, and effectiveness of, interventions such as CBT. Whilst the rapid development in technology has resulted in a proliferation of apps 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 maximise benefit from, computerised 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.

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**Tables and figures**

**Table 1 Total cost per person of a full course treatment (2016/17 price)**

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

**Table 2 Utility scores at baseline and at the end of 4-month treatment period (Source:25,27 )**

|  |  |  |
| --- | --- | --- |
| EQ-5D utility scores | Mean | SD |
| Baseline | 0.65 | 0.23 |
| At the end of 4-month, 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-month, 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 |

**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 | £3,325 | 3.501 | - |  | £66,695 | £101,705 |
| **F2F 6x30** | **£3,400** | **3.859** | **£209/QALY** | **£209/QALY** | £73,780 | £112,370 |
| MM | £3,420 | 3.847 | £275/QALY | Dominated | £73,520 | £111,990 |
| **F2F 8x30** | **£3,424** | **3.864** | **£273/QALY** | **£4,453/QALY** | £73,856 | £112,496 |
| Hybrid 6x30 | £3,431 | 3.856 | £299/QALY | Dominated | £73,689 | £112,249 |
| Hybrid 8x30 | £3,457 | 3.861 | £367/QALY | Dominated | £73,763 | £112,373 |
| F2F 10x30 | £3,483 | 3.861 | £439/QALY | Dominated | £73,737 | £112,347 |
| F2F 12x30 | £3,500 | 3.868 | £477/QALY | Extended Dominated | £73,860 | £112,540 |
| Hybrid 10x30 | £3,518 | 3.858 | £541/QALY | Dominated | £73,642 | £112,222 |
| F2F 6x60 | £3,525 | 3.864 | £551/QALY | Dominated | £73,755 | £112,395 |
| Hybrid 12x30 | £3,536 | 3.865 | £580/QALY | Dominated | £73,764 | £112,414 |
| Hybrid 6x60 | £3,562 | 3.861 | £658/QALY | Dominated | £73,658 | £112,268 |
| F2F 14x30 | £3,566 | 3.862 | £668/QALY | Dominated | £73,674 | £112,294 |
| **F2F 8x60** | **£3,572** | **3.875** | **£660/QALY** | **£12,216/QALY** | **£73,928** | **£112,678** |
| F2F 16x30 | £3,576 | 3.872 | £677/QALY | Dominated | £73,864 | £112,584 |
| Hybrid 14x30 | £3,603 | 3.859 | £777/QALY | Dominated | £73,577 | £112,167 |
| Hybrid 8x60 | £3,612 | 3.872 | £774/QALY | Dominated | £73,828 | £112,548 |
| Hybrid 16x30 | £3,614 | 3.869 | £785/QALY | Dominated | £73,766 | £112,456 |
| F2F 10x60 | £3,699 | 3.866 | £1,025/QALY | Dominated | £73,621 | £112,281 |
| F2F 12x60 | £3,738 | 3.879 | £1,093/QALY | Extended Dominated | £73,842 | £112,632 |
| Hybrid 10x60 | £3,740 | 3.863 | £1,146/QALY | Dominated | £73,520 | £112,150 |
| Hybrid 12x60 | £3,783 | 3.876 | £1,221/QALY | Dominated | £73,737 | £112,497 |
| F2F 14x60 | £3,872 | 3.868 | £1,490/QALY | Dominated | £73,488 | £112,168 |
| **F2F 16x60** | **£3,903** | **3.883** | **£1,513/QALY** | **£43,072/QALY** | £73,757 | £112,587 |
| Hybrid 14x60 | £3,919 | 3.865 | £1,632/QALY | Dominated | £73,381 | £112,031 |
| Hybrid 16x60 | £3,953 | 3.880 | £1,657/QALY | Dominated | £73,647 | £112,447 |

Figure 1 Structure of the decision tree

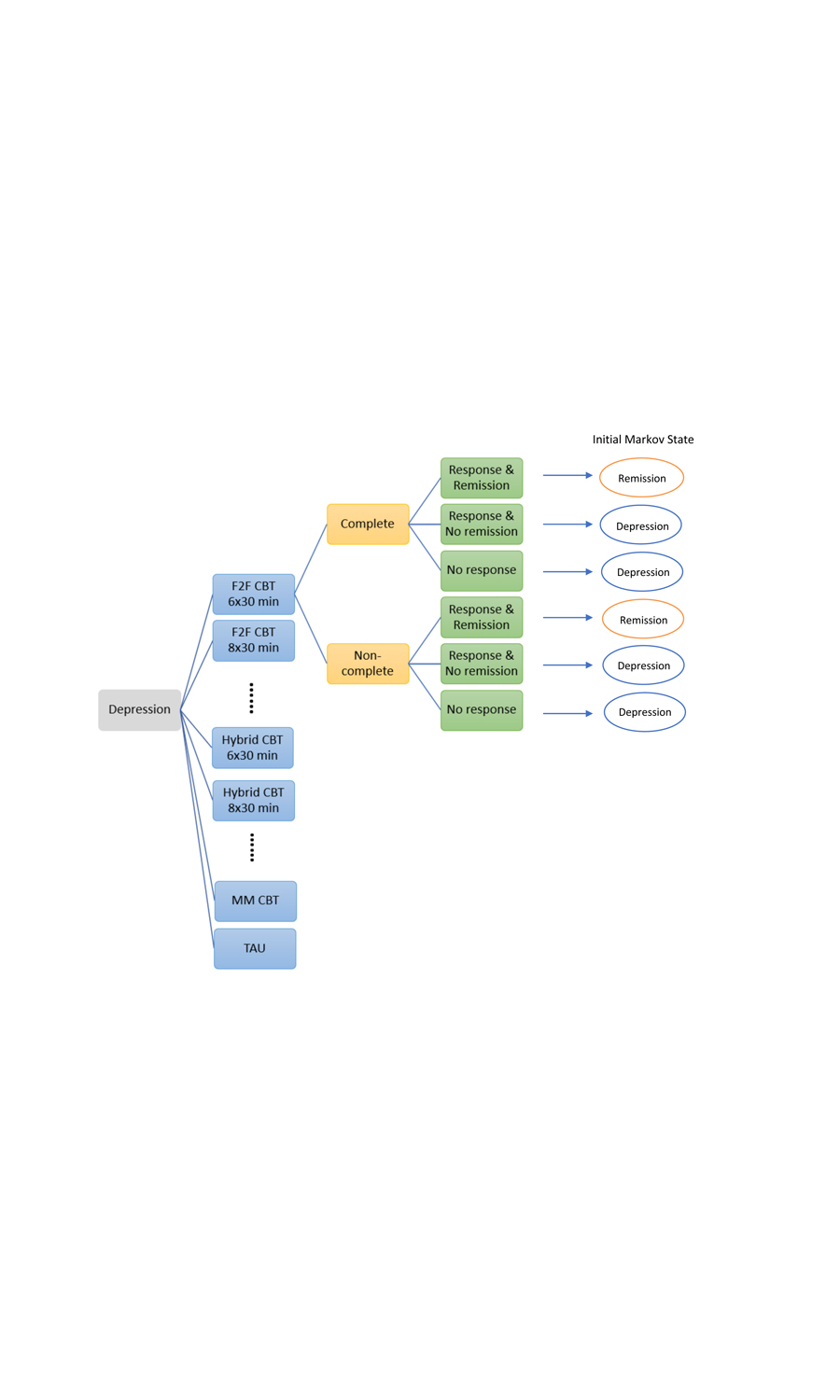


Figure 2 Structure of the Markov model

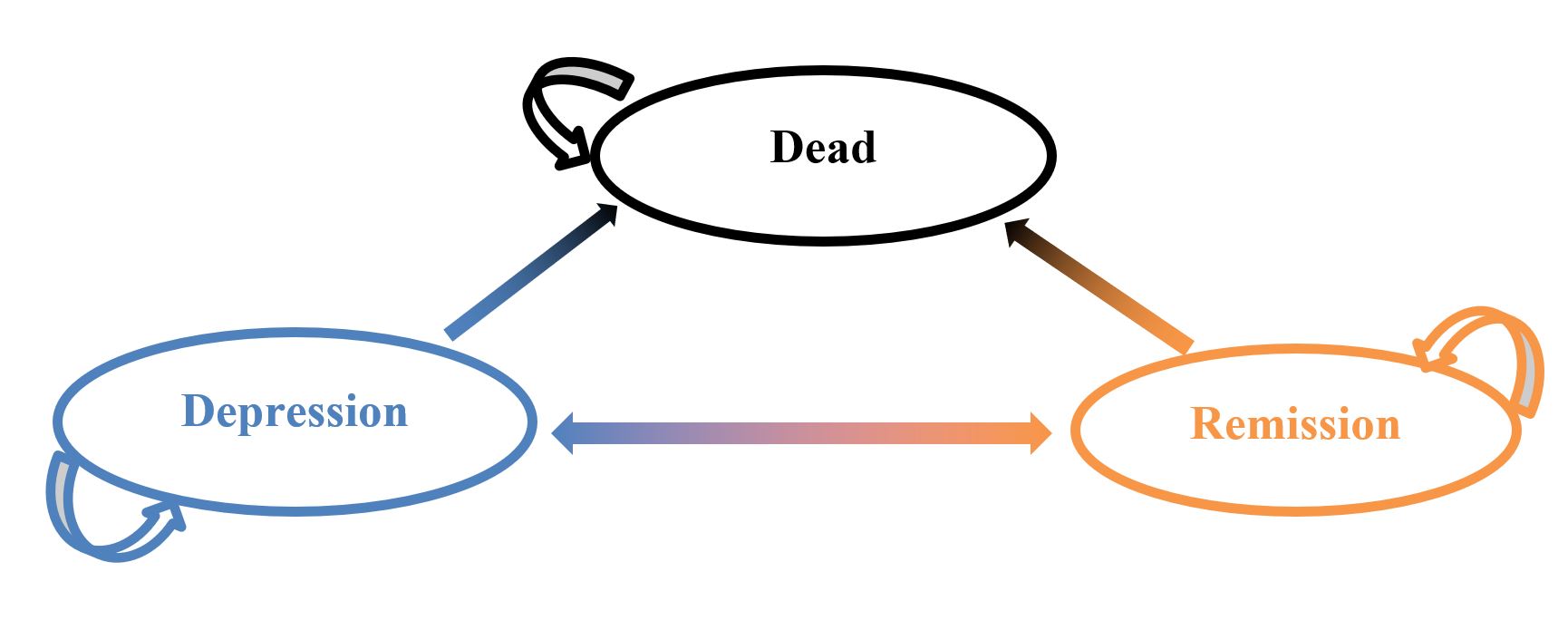
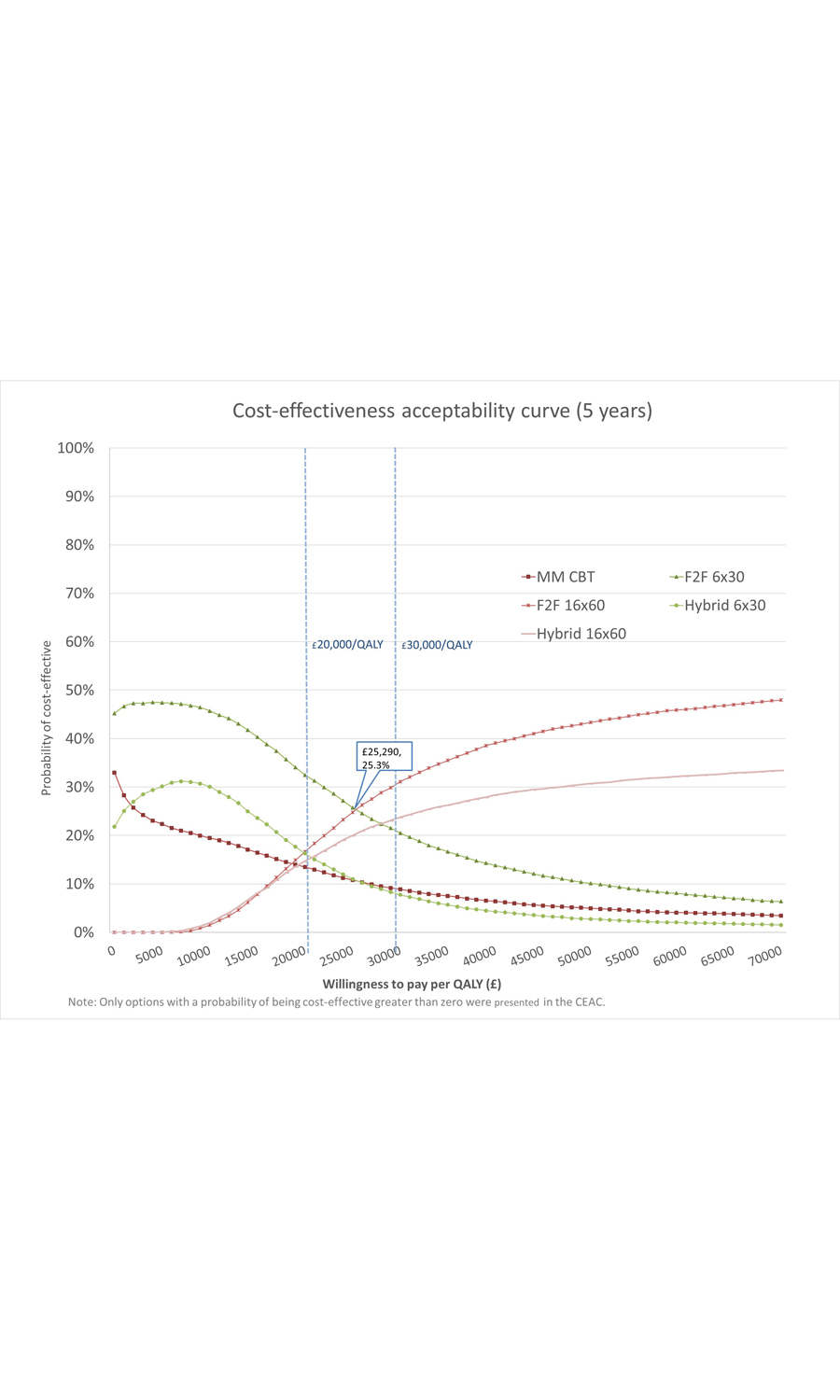


Figure 3 Cost-effectiveness acceptability curve (CEAC)



Appendices

Appendix 1: Method for predicting Remission and Response Probabilities from Continuous Outcomes

The short-term economic model requires estimates of the probabilities of remission, response (without remission), and non-response, at end of treatment. Based on discussions with our project team we defined remission as a score of less than 10 points on the BDI. We define response as 50% reduction of BDI score at baseline. The RCTs identified in our systematic review primarily report continuous outcome measures of depression, on a variety of scales (BDI, HAMD, etc.), whereas reporting of response and remission outcomes was rare 1. This makes the estimation of absolute probabilities of response, and remission for each of our decision options challenging. We chose to maximise our use of the available evidence by estimating response and remission probabilities from the outcomes on the BDI scale, the most commonly reported scale (see Appendix 3 for details). We used a bivariate Normal approximation to the baseline and follow-up score on the BDI for each intervention to obtain estimates of remission and response probabilities as follows.

Let  be the baseline score and  the follow-up score. We define the change score . Response is defined as 50% reduction in score so



Remission is defined as a follow-up score less than a threshold value  (we assume ), so

.

If we assume a multivariate Normal likelihood for the baseline and follow-up scores, then



where  are the mean scores at baseline and follow-up respectively,  are the standard deviation at baseline and follow-up respectively, and  is the correlation between baseline and follow-up measures.

Given an estimated mean change from baseline under TAU, , and relative effect for intervention  compared with TAU, , then the mean at follow-up is:

 (1)

The probability of remission using a threshold  is therefore:

 (2)

Response is more complicated because it is a function of baseline score, and the follow-up score required to achieve response differs between individuals who differ in their baseline scores. We therefore condition on baseline score,  . Under a multivariate Normal assumption, the distribution for follow-up score, conditional on baseline score is



The probability of response conditional on baseline score is therefore



Averaging over the marginal distribution for baseline scores, , gives:



Using the relationship:  when  has a Normal distribution, it can be verified that



Substituting equation (1) for  gives:

 (3)

For TAU baseline and follow-up scores on BDI were estimated from an RCT chosen to be representative of UK practise (see Appendix 2 for details). For all other interventions relative effects on mean change in BDI scores compared with TAU were obtained from a re-analysis of the data from the systematic review described in Appendix 3 1. These relative effects were applied to the follow-up BDI score for TAU to obtain absolute BDI follow-up scores for all interventions. Equations (2) and (3) were then applied to obtain the required transition probabilities for each intervention. Simulation was used to capture the uncertainty in the estimated mean BDI scores which was then propagated through to the transition probabilities, and it was these simulated values that were used in the probabilistic sensitivity analysis.

Appendix 2: Remission and response probabilities for TAU

We used results from the IPCRESS RCT to inform TAU in the short-term treatment model, as representative of a UK population relevant to our decision population.2 The control arm is described as wait-list, however our collaborators felt that it in fact represented current UK practice, and would be better described as treatment as usual (TAU). Furthermore, we had access to the IPD from IPCRESS, which allowed us to check our approximation method.

Table A1 shows mean and standard deviation for BDI at baseline in each arm, and across arms. Baseline BDI is balanced across arms, and we therefore assume a mean BDI of 33.175 with SD=8.805 in our TAU reference population. In our network meta-analysis we assumed a correlation between baseline and follow-up scores of 0.65, based on studies in our systematic review that provided summaries at baseline, follow-up, and also gave change from baseline summaries (and hence allowed a correlation to be estimated) 1. Table A1 shows that in IPCRESS the correlation between baseline and 4-month (end of treatment) follow-up BDI scores was lower than this in both the TAU and CBT arms (with correlations of 0.56 and 0.40 resp.). We chose to use the higher value of 0.65 to be consistent with the network meta-analysis. The mean change from baseline on TAU was -11.27 with standard error 1.16. We assume the SD for BDI scores at follow-up is 12.859, based on the SD for BDI across both arms of IPCRESS at end of treatment (4-months follow-up).

**Table A1: Summary statistics from the IPCRESS RCT at baseline, and end of treatment (4 months follow-up).**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Baseline** | |  | **End of treatment (4 months Follow-up)** | | **Change from baseline** | |
|  | mean BDI | SD BDI | Correlation baseline and 4month BDI scores | mean BDI | SD BDI | mean change from baseline | SE (change from baseline) |
| TAU arm | 33.527 | 9.270 | 0.562 | 22.253 | 13.466 | -11.274 | 1.16 |
| CBT arm | 32.826 | 8.336 | 0.401 | 14.509 | 11.204 | -21.92 | 0.973 |
| Pooled | 33.175 | 8.805 |  | 18.063 | 12.859 |  |  |

Based on the figures reported in IPCRESS we can estimate the remission and response probabilities under a Normal approximation (Appendix 1), giving the results shown in Table A2, for various assumed values for the correlation between baseline and 4-month follow-up. In IPCRESS, remission probabilities were higher than response probabilities, and both response and remission probabilities were higher on the CBT arm compared with the TAU arm Table A2. The Normal approximation slightly under-estimates the probability of remission, although the estimates are fairly close and well within the confidence limits. Similarly, the Normal approximation underestimates the response probabilities, most notably for the TAU arm, but the approximation is still within the confidence bounds. Although the approximation is not perfect, we considered it to be sufficiently accurate to use it to obtain estimates of response and remission probabilities based on population characteristics from IPCRESS (see Table A2 legend) and the estimates of mean difference in change from baseline on the BDI scale, obtained from our network meta-analysis (Appendix 3).

**Table A2: Comparison of response and remission probabilities estimated directly from IPCRESS data, and those obtained by the Normal approximation method assuming: baseline mean BDI = 33.175 with sd=8.805, mean change from baseline as found in IPCRESS, and follow-up sd in BDI of 12.859. Remission is assumed to be defined as BDI <10. Approximations to response probabilities are presented for correlations between baseline and follow-up measures of 0.5, 0.6, and 0.65.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **IPCRESS** | **Normal approximation to p(response)** | | | **IPCRESS** | **Normal approximation to p(remission)** |
|  | **p(response) (95%CI)** | **Cor=0.5** | **Cor=0.6** | **Cor=0.65** | **p(remission)**  **(95% CI)** |
| **TAU arm** | 0.37  (0.27, 0.47) | 0.3216 | 0.3137 | 0.3093 | 0.21  (0.13, 0.30) | 0.181 |
| **CBT arm** | 0.60  (0.51, 0.69) | 0.5770 | 0.5809 | 0.5832 | 0.38  (0.29, 0.46) | 0.344 |

Appendix 3: Relative effects on the BDI scale

The RCTs identified in the systematic review form a network of intervention comparisons, including CBT interventions, TAU, wait list, no treatment and placebo 1. We conducted a network meta-analysis (NMA) which is a method to simultaneously estimate intervention effects respecting the randomisation in the RCTs 3. Lopez-Lopez report results from an NMA on the standardised mean difference (SMD) scale because different measures of depression are used in different studies 1. The economic model however is based on the BDI depression scale, and so we require estimates of intervention effects on the BDI scale.

Not all studies report the BDI outcome, however all studies report at least one depression measure, and many studies report multiple outcomes. Figure A1 shows a network of outcomes plot, which indicates which outcomes are measured together in the same study (indicated with a connecting line). This gives us the opportunity to estimate mapping coefficients between intervention effects on different depression scales, so that all studies can be combined in a single analysis to estimate intervention effects on the BDI scale (regardless as to whether they included BDI as an outcome) 4. Lopez-Lopez 1 found some weak evidence on the SMD scale that intensity of intervention may be an effect modifier for F2F CBT but not for MM CBT, where intensity is defined as:



We therefore explored the inclusion of intensity as a covariate in the NMA model on the BDI scale. Due to limited data, we were unable to assess whether intensity was associated with intervention effect for Hybrid CBT. However, since Hybrid CBT involved therapist contact, after discussion with our project team we made the assumption that the interaction with intensity for Hybrid was equal to that for F2F CBT (but the main intervention effects were assumed to differ between F2F and Hybrid CBT). Table A3 presents parameter estimates from this model (on the BDI scale) along with estimates of the mapping coefficients. We found that results from the mapping approach were similar to those obtained using a standardised mean difference scale, but had the advantage that the resulting estimates were on an interpretable depression scale where thresholds for remission were available. The relative effects from Table A3 were combined with information on TAU (see Appendix 2) to obtain a distribution of absolute scores on the BDI for each intervention at follow-up for a given baseline distribution of BDI scores. These were then used to construct predicted probabilities of response and remission required in the economic model based on a bivariate Normal assumption (equations (2) and (3) in Appendix 1). The resulting transition probabilities are summarised in Table A4 which shows the mean and 95% CrIs from the PSA samples.

**Table A3:** Posterior summaries (posterior mean and 95% credible interval) for mean difference in change from baseline to end of treatment on BDI scale, and estimated mappings between intervention effects on the different depression scales. Abbreviations: BDI: Beck Depression Inventory (any version); BSI: Brief Symptom Inventory; CES-D: Center for Epidemiologic Studies Depression Scale (CES-D); HAM-D: Hamilton Depression Scale; MADRS: Montgomery Asberg Depression Rating Scale; MMPI-depression: Minnesota Multiphasic Personality Inventory (depression subscale); PHQ-8 and PHQ-9: Patient’s Health Questionnaire (8-item and 9-item versions, respectively).

|  |  |
| --- | --- |
| **Posterior mean difference in change from baseline to end of treatment on BDI (95% CrI)** | **Main Effects for F2F, Hybrid, MM**  **Interaction with intensity (F2F, Hybrid)** |
| F2F CBT | -5.535 (-10.42, -0.707) |
| Hybrid | -5.018 (-10.81, 0.608) |
| MM | -4.304 (-9.565, 0.835) |
| Interaction with intensity (F2F and Hybrid) | -0.496 (-0.922, -0.063) |
| Between studies sd | 5.70 (4.61, 7.07) |
| No. studies for NMA with interaction with intensity | 54 |
| **Mappings** |  |
| Mapping BSI->BDI | 0.902 (0.684,1.141) |
| Mapping CES-D->BDI | 1.053 (0.955,1.163) |
| Mapping HAM-D->BDI | 0.926 (0.5451,1.618) |
| Mapping MADRS->BDI | 2.564 (0.159,15.75) |
| Mapping MMPI->BDI | 0.223 (0.076,0.548) |
| Mapping PHQ8->BDI | 1.169 (0.800,1.57) |
| Mapping PHQ9->BDI | 0.902 (0.684,1.141) |

**Figure A1: a network plot showing where outcomes scales have been measured in the same rct (indicated by lines). based on 70 studies. abbreviations: bdi: beck depression inventory (any version); bsi: brief symptom inventory; ces-d: center for epidemiologic studies**



**Table A4: Estimated response and remission probabilities at the end of treatment**

|  |  |  |  |
| --- | --- | --- | --- |
| **Interventions** | **Probability of response & remission (95% CI)** | **Probability of response but no remission (95% CI)** | **Probability of no response & no remission (95% CI)** |
| TAU | 0.18 (0.14,0.23) | 0.13 (0.10, 0.16) | 0.69 (0.60, 0.76) |
| F2F CBT 6 sessions 30mins | 0.3438 (0.2154,0.4891) | 0.2048 (0.153,0.2335) | 0.4514 (0.2771,0.6316) |
| F2F CBT 8 sessions 30mins | 0.3521 (0.2258,0.4937) | 0.2075 (0.1589,0.2336) | 0.4405 (0.2724,0.6153) |
| F2F CBT 10 sessions 30mins | 0.3604 (0.2362,0.4988) | 0.21 (0.1645,0.2337) | 0.4295 (0.2673,0.5993) |
| F2F CBT 12 sessions 30mins | 0.3689 (0.2463,0.5044) | 0.2125 (0.1697,0.2338) | 0.4187 (0.2616,0.584) |
| F2F CBT 14 sessions 30mins | 0.3774 (0.2562,0.5105) | 0.2148 (0.1747,0.2338) | 0.4078 (0.2557,0.5691) |
| F2F CBT 16 sessions 30mins | 0.386 (0.2658,0.5165) | 0.2169 (0.1793,0.2339) | 0.397 (0.2498,0.5549) |
| F2F CBT 6 sessions 60mins | 0.3689 (0.2463,0.5044) | 0.2125 (0.1697,0.2338) | 0.4187 (0.2616,0.584) |
| F2F CBT 8 sessions 60mins | 0.386 (0.2658,0.5165) | 0.2169 (0.1793,0.2339) | 0.397 (0.2498,0.5549) |
| F2F CBT 10 sessions 60mins | 0.4035 (0.2854,0.5297) | 0.2208 (0.188,0.2339) | 0.3757 (0.2371,0.5266) |
| F2F CBT 12 sessions 60mins | 0.4212 (0.3038,0.5453) | 0.224 (0.1956,0.234) | 0.3548 (0.2225,0.5006) |
| F2F CBT 14 sessions 60mins | 0.4391 (0.3207,0.5624) | 0.2265 (0.2019,0.234) | 0.3344 (0.2072,0.4774) |
| F2F CBT 16 sessions 60mins | 0.4572 (0.3364,0.5813) | 0.2283 (0.2072,0.234) | 0.3145 (0.1907,0.4563) |
| Hybrid CBT 6 sessions 30mins | 0.3308 (0.182,0.5082) | 0.1984 (0.1327,0.2336) | 0.4708 (0.2579,0.6853) |
| Hybrid CBT 8 sessions 30mins | 0.3389 (0.1889,0.5166) | 0.201 (0.1371,0.2337) | 0.46 (0.2497,0.674) |
| Hybrid CBT 10 sessions 30mins | 0.3472 (0.1958,0.5251) | 0.2036 (0.1414,0.2338) | 0.4493 (0.2415,0.6628) |
| Hybrid CBT 12 sessions 30mins | 0.3555 (0.2023,0.5334) | 0.2059 (0.1453,0.2338) | 0.4385 (0.2336,0.6523) |
| Hybrid CBT 14 sessions 30mins | 0.3639 (0.2089,0.5425) | 0.2082 (0.1493,0.2339) | 0.4279 (0.2251,0.6418) |
| Hybrid CBT 16 sessions 30mins | 0.3724 (0.2155,0.5524) | 0.2103 (0.153,0.2339) | 0.4172 (0.2161,0.6315) |
| Hybrid CBT 6 sessions 60mins | 0.3555 (0.2023,0.5334) | 0.2059 (0.1453,0.2338) | 0.4385 (0.2336,0.6523) |
| Hybrid CBT 8 sessions 60mins | 0.3724 (0.2155,0.5524) | 0.2103 (0.153,0.2339) | 0.4172 (0.2161,0.6315) |
| Hybrid CBT 10 sessions 60mins | 0.3897 (0.2281,0.5719) | 0.2141 (0.1601,0.2339) | 0.3963 (0.1988,0.6118) |
| Hybrid CBT 12 sessions 60mins | 0.4071 (0.24,0.5921) | 0.2172 (0.1665,0.2339) | 0.3757 (0.1817,0.5935) |
| Hybrid CBT 14 sessions 60mins | 0.4247 (0.251,0.6139) | 0.2197 (0.172,0.234) | 0.3556 (0.1641,0.577) |
| Hybrid CBT 16 sessions 60mins | 0.4425 (0.2613,0.6364) | 0.2215 (0.1765,0.234) | 0.336 (0.1468,0.5616) |
| MM CBT | 0.29 (0.16, 0.45) | 0.18 (0.12, 0.23) | 0.53 (0.32, 0.73) |

Appendix 4: Treatment costs

**Table A5: Unit cost of other materials used in the process of delivery of CBTs (2016/17 price)**

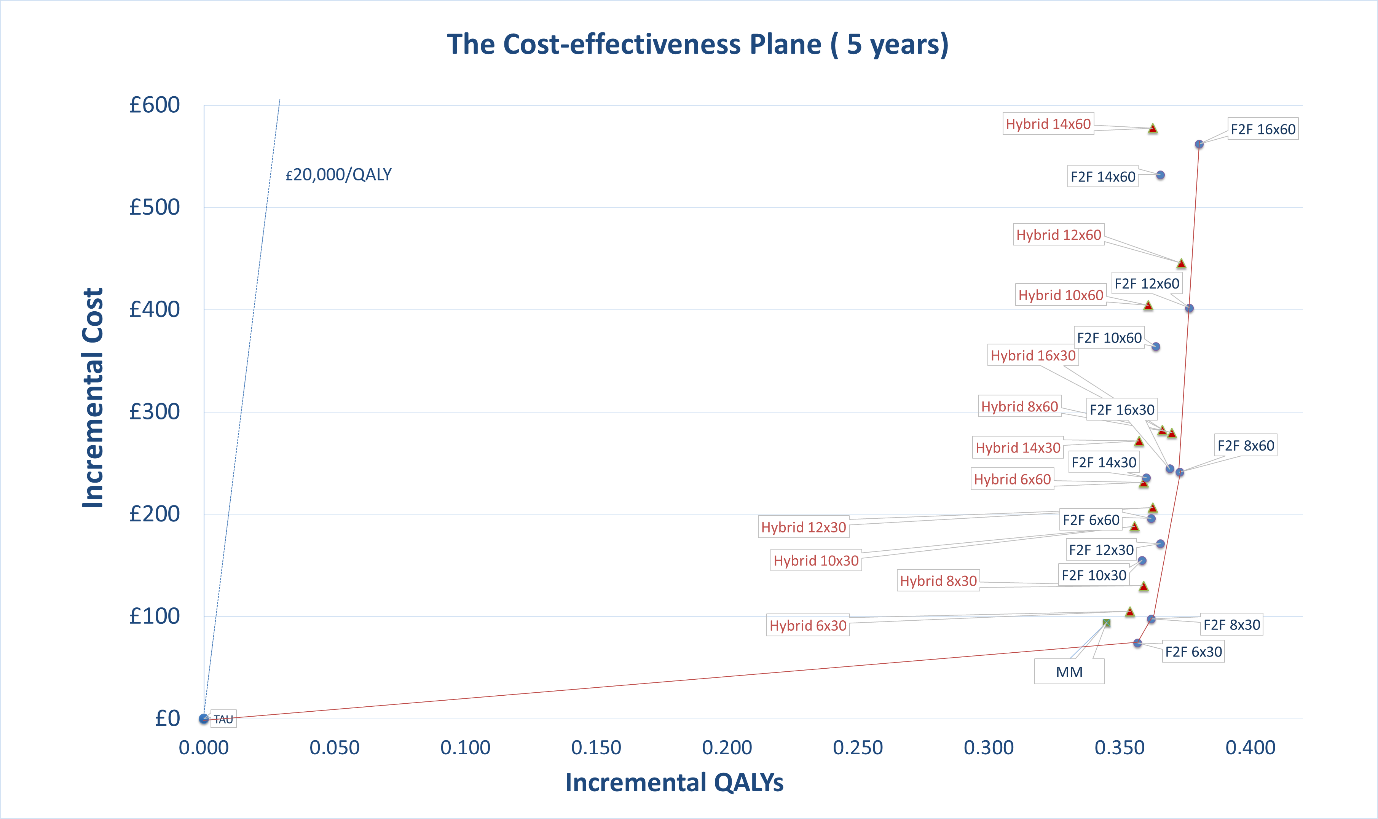
|  |  |  |
| --- | --- | --- |
| Item/Service | Unit cost | Sources |
| Book | £15 / book | Estimated from market price of similar products |
| CD | £10 / CD |
| DVD | £20 / DVD |
| Online CBT/Smartphone app | £50 / subscription | License fee of Beating the Blues 5 |
| Telephone | £0.12 / minute | BT market price personal landline cost 6 |
| Videoconference | £0.18 / minute | BT market price of data and Skype data usage per minute 6,7 |

Appendix 5: Markov Model Parameters and results

**Table A6: Markov Model Parameters (after the end of treatment)**

|  |  |  |
| --- | --- | --- |
| **Probability of remission (monthly)** | Value (95% CI) | Source |
| Remission within 6 months after the end of treatment (TAU) | 2.03% (1.22%, 3.15%) | 8 |
| Relative risk of any CBT compared with TAU (within 6 months) | 2.17 (1.30, 3.63) | 8 |
| Remission from month 7 to 5-year after the end of treatment (TAU) | 0.38% (0.19%, 0.69%) | 8 |
| Relative risk of any CBT compared with TAU (7-month to 5-year) | 1.42 (0.68, 2.98) | 8 |
| **Probability of relapse (monthly)** |  | 8 |
| Relapse within 6 months (TAU) | 8.90% (4.47%, 15.72%) | 8 |
| Relative risk of any CBT compared with TAU (within 6 months) | 0.53 (0.27, 1.02) | 8 |
| Relapse from month 7 to 5-year after the end of treatment (TAU) | 2.54% (1.20%, 4.70%) | 8 |
| Relative risk of any CBT compared with TAU (7-month to 5-year) | 0.96 (0.61, 1.50) | 8 |
| **Mortality (monthly)** |  | 8 |
| Male (Age-standardised mortality rates 2016) | 0.09% | 9 |
| Female (Age-standardised mortality rates 2016) | 0.07% | 9 |
| Female percentage | 65.10%  (58.90%, 70.94%) | 10 |
| Relative risk of depression compared with remission | 1.52 (1.45, 1.59) | 11 |
| Monthly age-standardised mortality (Remission) | 0.08% |  |
| Monthly age-standardised mortality (Depression) | 0.12% |  |
| **Costs** |  |  |
| Monthly cost (Depression in TAU group) | £66.73 (SE £13.07) | 8 |
| Monthly cost (Remission in TAU group) | £41.32 (SE £12.29) | 8 |
| Monthly cost (Depression in any CBT group) | £78.88 (SE £20.12) | 8 |
| Monthly cost (Remission in any CBT group) | £21.77 (SE £5.25) | 8 |
| **QALY** |  |  |
| Monthly QALY gained (Depression in TAU group) | 0.058 (SE 0.002) |  |
| Monthly QALY gained (Remission in TAU group) | 0.077 (SE 0.001) | 8,12 |
| Monthly QALY gained (Depression in any CBT group) | 0.064 (SE 0.002) | 8,12 |
| Monthly QALY gained (Remission in any CBT group) | 0.076 (SE 0.002) | 8,12 |
| **Yearly discount rate** |  |  |
| Cost discount rate | 3.5% | 13 |
| QALY discount rate | 3.5% | 13 |
| **Willingness-to-pay thresholds** | £20,000-£30,000/QALY | 13 |

Figure A2 The Cost-effectiveness Plane with TAU as comparator (5 years)



Appendix 6: Results of sensitivity analysis

**Table A7:** **Results of sensitivity analysis using RR of mortality =1, 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 | £3,360 | 3.533 | - |  | £67,299 | £102,629 |
| **F2F 6x30** | **£3,431** | **3.886** | **£201/QALY** | **£201/QALY** | £74,284 | £113,142 |
| MM | £3,451 | 3.875 | £269/QALY | Dominated | £74,045 | £112,794 |
| **F2F 8x30** | **£3,454** | **3.891** | **£263/QALY** | **£4,713/QALY** | £74,359 | £113,266 |
| Hybrid 6x30 | £3,462 | 3.883 | £292/QALY | Dominated | £74,202 | £113,034 |
| Hybrid 8x30 | £3,486 | 3.888 | £357/QALY | Dominated | £74,273 | £113,153 |
| F2F 10x30 | £3,511 | 3.887 | £428/QALY | Dominated | £74,236 | £113,110 |
| F2F 12x30 | £3,527 | 3.894 | £464/QALY | Extended Dominated | £74,351 | £113,290 |
| Hybrid 10x30 | £3,545 | 3.885 | £527/QALY | Dominated | £74,150 | £112,997 |
| F2F 6x60 | £3,552 | 3.891 | £538/QALY | Dominated | £74,261 | £113,167 |
| Hybrid 12x30 | £3,562 | 3.891 | £566/QALY | Dominated | £74,262 | £113,175 |
| Hybrid 6x60 | £3,588 | 3.888 | £642/QALY | Dominated | £74,172 | £113,051 |
| F2F 14x30 | £3,592 | 3.889 | £653/QALY | Dominated | £74,187 | £113,077 |
| **F2F 8x60** | **£3,597** | **3.901** | **£644/QALY** | **£14,166/QALY** | **£74,418** | **£113,425** |
| F2F 16x30 | £3,600 | 3.897 | £660/QALY | Dominated | £74,346 | £113,319 |
| Hybrid 14x30 | £3,628 | 3.886 | £760/QALY | Dominated | £74,100 | £112,964 |
| Hybrid 8x60 | £3,635 | 3.898 | £755/QALY | Dominated | £74,324 | £113,303 |
| Hybrid 16x30 | £3,638 | 3.895 | £770/QALY | Dominated | £74,254 | £113,200 |
| F2F 10x60 | £3,720 | 3.892 | £1003/QALY | Dominated | £74,125 | £113,048 |
| F2F 12x60 | £3,757 | 3.904 | £1070/QALY | Extended Dominated | £74,327 | £113,368 |
| Hybrid 10x60 | £3,761 | 3.890 | £1124/QALY | Dominated | £74,032 | £112,928 |
| Hybrid 12x60 | £3,801 | 3.901 | £1197/QALY | Dominated | £74,226 | £113,239 |
| F2F 14x60 | £3,888 | 3.894 | £1463/QALY | Dominated | £73,991 | £112,930 |
| **F2F 16x60** | **£3,917** | **3.908** | **£1487/QALY** | **£46,396/QALY** | £74,236 | £113,312 |
| Hybrid 14x60 | £3,934 | 3.891 | £1602/QALY | Dominated | £73,891 | £112,804 |
| Hybrid 16x60 | £3,966 | 3.905 | £1631/QALY | Dominated | £74,129 | £113,176 |

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