National Institute for Health and Care Excellence

Consultation draft

Depression in adults: treatment and management

Appendix N1: Network meta-analysis - detailed methods and results

NICE Guideline <…>

Appendices

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1 Appendix N1: Network meta-analysis of treatments for people with a new episode of depression: detailed methods and results

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1.1 Introduction

The purpose of this analysis was to estimate the comparative effectiveness of various interventions for treating depression in populations with less severe and more severe populations. In total 366 studies were included in these analyses comparing 98 interventions and combinations of interventions.

The outcomes analysed were discontinuation for any reason, discontinuation due to side effects, remission, response and standardised mean difference (SMD). The SMD measure of effect was used to combine evidence from studies reporting efficacy in terms of a continuous measurement on various depression scales.

The studies and data used for every outcome analysed in the NMA are provided in Appendix N3 of the full guideline.

1.2 Methods

1.2.1 Network meta-analysis

In order to take all trial information into consideration network meta-analyses (NMA) were conducted. NMA is a generalisation of standard pairwise meta-analysis for A versus B trials, to data structures that include, for example, A versus B, B versus C, and A versus C trials (Dias et al. 2004, Lu and Ades 2004, Caldwell et al. 2005). A basic assumption of NMA methods is that direct and indirect evidence estimate the same parameter, that is, the relative effect between A and B measured directly from an A versus B trial, is the same as the relative effect between A and B estimated indirectly from A versus C and B versus C trials. NMA techniques strengthen inference concerning the relative effect of two treatments by including both direct and indirect comparisons between treatments, and, at the same time, allow simultaneous inference on all treatments inference on all treatments while respecting randomisation (Lu and Ades 2004, Caldwell et al. 2004).

Simultaneous inference on the relative effects of all treatments is possible whenever treatments are part of a single ‘network of evidence’, that is, every treatment is linked to at least one of the other treatments under assessment. The correlation between the random effects of multi-arm trials (i.e. those with more than 2 arms) in the network is taken into account in the analysis (Dias et al. 2004). In a NMA we assume that intervention A is similar (in dose, administration etc.) when it appears in the A *v* B and A *v* C studies and also that every patient included the network could have been assigned to any of the interventions (Caldwell et al. 2005) - a concept called ‘joint randomisability’ (Salanti 2012).

A Bayesian framework is used to estimate all parameters, using Markov chain Monte Carlo simulation methods implemented in WinBUGS 1.4.3. Convergence was assessed using the Brooks-Gelman-Rubin diagnostic (Brooks and Gelman 1998) and was satisfactory by 60,000 simulations for all outcomes (Gelman and Rubin 1992). A further simulation sample of at

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least 50,000 iterations post-convergence was obtained on which all reported results were based. Sample WinBUGS code is provided at the end of this document, in Appendix 1: WinBUGS codes.

For binary data, studies with zero or 100% events in all arms were excluded from the analysis because these studies provide no evidence on relative effects (Dias et al. 2011). For studies with zero or 100% events in one arm only, we planned to analyse the data without continuity corrections where computationally possible. Where this was not possible, we used a continuity correction where we added 0.5 to both the number of events and the number of non-events, which has shown to perform well when there is an approximate 1:1 randomisation ratio across intervention arms (Sweeting et al. 2004).

1.2.21 Reporting of Results

Network diagrams are presented for each population and outcome. The edges (lines) connecting each pair of interventions represent a direct comparison.

Relative intervention effects are reported in the *'or relative to pill placebo'* or *'SMD relative to pill placebo'* worksheets of the Excel files in Appendix N3 as posterior median odds ratios (ORs) or standardised mean differences (SMDs) and 95% Credible Intervals (CrIs) compared to Pill placebo. We noted which intervention (and classes) increased or decreased the odds, or had a lower or higher SMD, compared to Pill placebo (Placebo) when the 95% CrIs corresponding to their effect excluded zero. The full list of log ORs and SMDs for each intervention and class compared to every other are reported in the *'Direct lors'* or *'Direct SMDs'* worksheets of the Excel files in Appendix N3.

We also report posterior mean rank of each class (and 95% CrIs), with the convention that the lower the rank the better the class. The posterior median rank of each intervention can be found in the *'Ranks'* worksheet of the Excel files in Appendix N3. Only interventions and classes of interest were included in the calculations of the rankings. The interventions that were deemed not of interest by the guideline committee and therefore excluded from the rankings were

- Behavioural activation (BA) + TAU
- CBT individual (under 15 sessions) + TAU
- CBT individual (over 15 sessions) + TAU
- CBT individual (under 15 sessions) + enhanced TAU
- Third-wave cognitive therapy individual + TAU
- Coping with Depression course (group) + TAU
- CBT group (under 15 sessions) + TAU
- CBT group (under 15 sessions) + enhanced TAU
- CBT group (over 15 sessions) + TAU
- Third-wave cognitive therapy group + TAU
- Problem solving individual + TAU
- Problem solving individual + enhanced TAU
- Non-directive counselling + TAU
- Psychodynamic counselling + TAU
- Interpersonal therapy (IPT) + TAU
- Interpersonal therapy (IPT) group + TAU
- Psychoeducational group programme + TAU
- Cognitive bibliotherapy + TAU
- Computerised-CBT (CCBT) + TAU

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- Computerised-CBT (CCBT) + enhanced TAU
- Cognitive bibliotherapy with support + TAU
- Computerised-CBT (CCBT) with support + TAU
- Cognitive bias modification with support + TAU
- Short-term psychodynamic psychotherapy individual + TAU
- CBT individual (under 15 sessions) + Pill placebo
- CBT individual (over 15 sessions) + Pill placebo
- Interpersonal psychotherapy (IPT) + Pill placebo
- Supportive psychotherapy + Pill placebo
- Any SSRI
- Any SSRI + Enhanced TAU
- Imipramine
- Any TCA
- Any AD
- Exercise + TAU
- Yoga + TAU
- Enhanced TAU
- No treatment
- Attention placebo + TAU

Note that the above active interventions were not of interest per se, as they were not candidates for recommendation or they were variations of a control within the same class. However, each of them contributed to its respective class effect and its inclusion allowed a wider range of evidence to be considered. For example, 'any SSRI' was not of interest as an intervention, as at the intervention level we were interested in the effects of specific SSRIs. However, it does contribute to the SSRI class effect, which was of interest at the class level. Similarly, active interventions added onto TAU were not of interest per se, as the candidates for recommendation were the active interventions alone; however, active interventions plus TAU were included in the respective class of the active intervention and contributed to the class effect.

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The classes that were deemed not of interest by the guideline committee and therefore excluded from the rankings were

- Combined (psych + placebo)
- Any AD

1.2.3 Class models

Classes of treatments are groups of interventions which are thought to have similar effects. Class models were used so that strength could be borrowed across treatments in the same class and to reconnect disconnected networks. For all outcomes, random class effect models were used which assume that the effects of treatments in a class are distributed around a common class mean with a within-class variance. In this way treatment effects are shrunk towards a class mean and can borrow strength from other elements of the class.

For treatments belonging to classes consisting of more than two treatments the pooled relative treatment effects were assumed to be exchangeable within class:

$$d_{1,k} \sim N\left(m_{D_k}, \tau^2{}_{D_k}\right)$$

where D_k indicates the class to which treatment k belongs.

For treatments belonging to a class with one or two treatments in a particular analysis, the relative treatment effects were assumed to come from a normal distribution with a class mean and variance being borrowed from another similar class in the model, where possible. The following rules applied where classes had only one or two treatments but variance could be shared with another class with more than 1 treatment. The following variance sharing rules were used when necessary:

- CBT/CT (individual) borrowed variance from Behavioural therapies (individual)
- Behavioural therapies (individual) borrowed variance from CBT/CT
- Behavioural, cognitive, or CBT groups borrowed variance from CBT/CT
- Counselling borrowed variance from CBT/CT
- Interpersonal psychotherapy (IPT) borrowed variance from CBT/CT
- Psychoeducational interventions borrowed variance from CBT/CT
- Problem solving borrowed variance from CBT/CT
- Self-help borrowed variance from CBT/CT
- Self-help with support borrowed variance from CBT/CT
- Long-term psychodynamic psychotherapies borrowed variance from CBT/CT
- Combined (CBT/CT individual + AD) borrowed variance from CBT/CT
- Combined (psych + placebo) borrowed variance from CBT/CT
- Short-term psychodynamic psychotherapies borrowed variance from Counselling
- Combined (Behavioural, cognitive, or CBT groups + AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (Counselling + AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (IPT +AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (Problem solving + AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (Self-help + AD/CBT) borrowed variance from Combined (CBT/CT + AD).
- Combined (Short-term psychodynamic psychotherapies + AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (Long-term psychodynamic psychotherapies + AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (Exercise + AD/CBT) borrowed variance from Combined (CBT/CT + AD)
- TCA borrowed variance from SSRI
- Exercise borrowed variance from Self-help with support or if this was not possible, from CBT/CT.

In addition, the following rules always applied:

- Attention placebo, no treatment and TAU share a class variance
- Any AD always has variance equal to the sum of the variance of SSRIs and TCAs, where

$$\tau^2_{AnyAD} = \tau^2_{SSRI} + \tau^2_{TCA}$$

These assumptions were based on expert opinion from the guideline committee.

For treatments not believed to belong to a class in clinical practice (mirtazapine), the relative treatment effects were given non-informative priors $d_{1,k} \sim N(0,100^2)$.

The within-class mean treatment effects were given vague priors $m_j \sim N(0,100^2)$ and the within-class variability had priors $\tau^2 \sim$ Half-normal$(0,0.19^2)$ chosen to express the prior belief that 95% of trials will give odds ratios within a factor of 1.5 from the estimated median odds ratio. This prior distribution was necessary due to the small number of interventions in each

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class, although it still covers a wide range of possible odds ratios within a class. This prior distribution was also used for the SMD and has a similar interpretation.

For treatments not believed to belong to a class (mirtazapine), the within-class mean treatment effect was equal to the individual treatment effect, with no added variability.

Intervention effects are reported for both individual treatments and classes of treatments.

We compared the fit of the random class effect models to that of fixed class effect models which assume that all treatments in a class have the same relative effect. In most cases the models had a very similar fit suggesting that the interventions had been grouped well into classes with small within-class variability.

1.2.40 Inconsistency checks

Consistency between the different sources of indirect and direct evidence was explored statistically by comparing the fit of a model assuming consistency with a model which allowed for inconsistency (also known as an unrelated mean effect model). Goodness of fit was measured using the posterior mean of the residual deviance, which is a measure of the magnitude of the difference between the observed data and their model predictions (Spiegelhalter et al. 2002). Smaller values are preferred, and in a well-fitting model the posterior mean residual deviance should be close to the number of data points (Spiegelhalter et al. 2002). We also report the deviance information criterion (DIC) which penalises model fit with model complexity (Spiegelhalter et al. 2002). Finally, we report the between studies standard deviation (heterogeneity parameter) to assess the degree of statistical heterogeneity. If the inconsistency model had the smallest posterior mean residual deviance or heterogeneity then this indicated potential inconsistency in the data. In comparing models, differences of ≥5 points for posterior mean residual deviance and DIC were considered meaningful (Spiegelhalter et al. 2002), with lower values being favoured. It should be noted that the inconsistency model did not assume any class relation between interventions.

Comparisons between the relative effects of all pairs of interventions obtained from the consistency (NMA) model and those obtained from the inconsistency (pairwise) model (which does not take into account the indirect evidence in the estimation of effects) for each outcome are provided in Appendix N3.

1.2.50 SMD analysis: methods

We wished to include as many trials and information as possible in each analysis even when data were reported in different ways. This meant transforming the data in some cases. For the SMD analysis we wanted to conduct a NMA on the mean difference in change from baseline (CFB) (for which standard methods are available) (Dias et al. 2011). The data required for each arm of each study are the mean CFB, the standard deviation in CFB and the total number of individuals in that arm (or the standard error of the mean change from baseline).

However, some studies did not report these data, and instead reported:

1) the baseline and follow-up means, standard deviations and number of individuals, for each arm of the study;
2) the number of individuals responding to treatment in each arm of each study, out of the total number of individuals, defined as those improving by more than a certain percentage from baseline.

Studies reporting outcomes a) or b) above also provide information on the mean change from baseline, through the relationship between the underlying continuous scale and the measurements that can be derived from it.

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For our analysis, if CFB data were available in a study we used that data. If that study did not report CFB but reported baseline and follow-up data we used the baseline and follow up data and transformed it to CFB. If a study reported neither CFB nor baseline and follow up data but did report response, we used the response data and transformed it to CFB.

This analysis was carried out on all patients randomised. If a study did not report appropriate data on all patients randomised (e.g. if it reported completers' data instead) it was not included in this analysis.

1.2.5.18 Notation

To transform the data we assumed that n_{ik} individuals are randomised to each arm k (k>1) of study i=1,…,M, on which the following outcomes are recorded for individual j=1,…,n_{ik}:

x_{jik} - the score at baseline for individual j in arm k of trial i, on a given continuous scale;

y_{jik} - the score at follow-up for individual j in arm k of trial i, on a given continuous scale;

c_{jik} - the change from baseline for individual j in arm k of trial i, on a given continuous scale, where $c_{jik} = y_{jik} - x_{jik}$;

R_{jik} - response status at follow-up for individual j in arm k of trial i, defined as **at least a q_i% reduction** of the follow-up measurement on a given continuous scale, compared to baseline, i.e.

$$R_{jik} = \begin{cases} 1 & \text{if } y_{jik} - x_{jik} \le -q_i x_{jik} \\ 0 & \text{otherwise} \end{cases} \quad (1)$$

Note that different studies may have used a different cut-off q (although they would be expected to be the same for all arms of a study), and these are therefore indexed by study.

1.2.5.21 Reported outcomes

Studies may report all or some of the following observed outcomes

$m_{X,ik}$ - the observed mean at baseline in arm k of trial i, on a given continuous scale;

$sd_{X,ik}$ - the observed standard deviation at baseline in arm k of trial i, on a given continuous scale;

$m_{Y,ik}$ - the observed mean at follow-up in arm k of trial i, on a given continuous scale;

$sd_{Y,ik}$ - the observed standard deviation at follow-up in arm k of trial i, on a given continuous scale;

$m_{C,ik}$ - the observed mean change from baseline in arm k of trial i, on a given continuous scale;

$sd_{C,ik}$ - the observed standard deviation in change from baseline in arm k of trial i, on a given continuous scale;

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ρ_{ik} - the observed correlation between baseline and follow-up scores measured on the same individual in arm *k* of trial *i*. (Although this is rarely reported directly, it can be calculated when the means and standard deviations at baseline, follow-up and from the CFB are provided);

$r_{resp,ik}$ - the number of individuals achieving response in arm *k* of trial *i*, with response defined in equation (1).

1.2.5.37 Relationship between different outcomes

We assume that for each patient the baseline and follow-up measurements are sampled from a bivariate Normal distribution. Thus for all patients in arm *k* of trial *i*, we assume that their baseline, X_{ik}, and follow-up measurements Y_{ik}, are independent and identically distributed as

$$\begin{pmatrix} X_{ik} \\ Y_{ik} \end{pmatrix} \sim \mathrm{N}_2\left(\begin{pmatrix} \mu_{X,ik} \\ \mu_{Y,ik} \end{pmatrix}, \begin{pmatrix} \sigma^2_{X,ik} & \rho_{ik}\sigma_{X,ik}\sigma_{Y,ik} \\ \rho_{ik}\sigma_{X,ik}\sigma_{Y,ik} & \sigma^2_{Y,ik} \end{pmatrix}\right) \quad (2)$$

with $\mu_{X,ik}$ and $\mu_{Y,ik}$ representing the means and $\sigma^2_{X,ik}$ and $\sigma^2_{Y,ik}$ the variances at baseline and follow-up for individuals in arm *k* of trial *i*, respectively, and ρ_{ik} being the within arm and study correlation between baseline and follow-up measurements on the same individuals.

We define the mean change from baseline in arm *k* of trial *i* as $\theta_{ik} = \mu_{Y,ik} - \mu_{X,ik}$ as the parameter of interest.

1.2.5.49 NMA model for continuous outcomes

With continuous outcome data, meta-analysis is usually based on the sample means with standard errors assumed known. Here we are interested in modelling the mean changes from baseline, which are assumed to be approximately normally distributed, with likelihood

$$m_{C,ik} \sim N\left(\theta_{ik}, se^2_{C,ik}\right)$$

The parameter of interest is the mean, θ_{ik}, of this distribution. For a random effects model we write

$$\theta_{ik} = \gamma_i + \delta_{ik} \quad (3)$$

where γ_i are the trial-specific effects of the treatment in arm 1 of trial *i*, treated as unrelated nuisance parameters, and the δ_{ik} are the trial-specific treatment effects of the treatment in arm *k* relative to the treatment in arm 1 in that trial, where $\delta_{i1} = 0$. The trial-specific random effects δ_{ik}, represent the mean differences between the change from baseline for the treatment in arm *k* and the treatment in arm 1 of trial *i* and, in a random effects model,

$$\delta_{ik} \sim \mathrm{Normal}(d_{t_{i1},t_{ik}}, \sigma^2) \quad (4)$$

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where σ^2 denotes the between-study heterogeneity, assumed common to all treatment comparisons and $d_{t_{i1}t_{ik}} = d_{1,t_{ik}} - d_{1,t_{i1}}$ are the pooled mean differences, defined by the consistency equations ($d_{11} = 0$). The fixed effect model is obtained by replacing equation (3) with $\theta_{ik} = \gamma_i + d_{1,t_{ik}} - d_{1,t_{i1}}$. Where studies with more than 2 arms are present, a correlation is induced in the trial specific effects δ_{ik} so equation (4) is replaced by a multivariate normal distribution with correlation equal to 0.5 (Higgins and Whitehead 1996, Dias et al. 2011).

1.2.5.5 Likelihood and link functions for studies reporting other outcomes

1.2.5.5.1 Studies reporting mean and variance at follow-up

From the joint bivariate normal distribution in equation (2) we know that

$$(Y_{ik} - X_{ik}) \sim N\left(\theta_{ik}, \sigma^2_{X,ik} + \sigma^2_{Y,ik} - 2\rho_{ik}\sigma_{X,ik}\sigma_{Y,ik}\right) \quad (5)$$

Therefore, studies not reporting change from baseline but reporting the mean and variance at baseline and follow-up also provide information on the parameter of interest θ_{ik}, the mean change from baseline.

For these studies we can calculate the mean change from baseline as $m_{C,ik} = m_{Y,ik} - m_{X,ik}$. Using equation (5), the likelihood can be written as

$$m_{C,ik} \sim N\left(\theta_{ik}, se^2_{X,ik} + se^2_{Y,ik} - 2\rho_{ik}se_{X,ik}se_{Y,ik}\right)$$

Provided the standard errors at baseline and follow up can be obtained and that we have information on the within-study correlation, the remaining model is given in equations (3) and (4) can be used to pool the mean differences in change from baseline.

1.2.5.5.2 Studies reporting number of responders

Using equation (1), the probability of response for individuals in arm *k* of trial *i* is defined as

$$R_{ik} = \Pr(Y_{ik} - X_{ik} \leq -qX_{ik}) \quad (6)$$

Conditioning on the baseline value X_{ik} we have

$$Y_{ik} \mid X_{ik} \sim N\left(\mu_{X,ik}(1-\rho_{ik}) + \theta_{ik} + \rho_{ik}X_{jik}, (1-\rho^2_{ik})\sigma^2_{X,ik}\right) \quad (7)$$

thus,

$$\begin{aligned} R_{ik} \mid X_{ik} &= \Pr_{Y|X}\left(Y_{ik} < (1-q)X_{ik}\right) \\ &= \Phi\left(aX_{ik} + b\right) \end{aligned} \quad (8)$$

with

$$a = \frac{1-q-\rho_{ik}}{\sigma_{X,ik}\sqrt{1-\rho^2_{ik}}}, \quad b = -\frac{\mu_{X,ik}(1-\rho_{ik}) + \theta_{ik}}{\sigma_{X,ik}\sqrt{1-\rho^2_{ik}}}$$

Therefore the unconditional probability of response in arm *k* of trial *i* is

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$$R_{ik} = E_{X_{ik}}\left[\Phi\left(aX_{ik}+b\right)\right] \quad (9)$$

It can be shown that

$$E_X\left[\Phi\left(aX+b\right)\right] = \Phi\left(\frac{aE(X)+b}{\sqrt{1+a^2Var(X)}}\right) \quad (10)$$

thus the probability of response for individuals in arm *k* of trial *i* can be written as

$$R_{ik} = \Phi\left(\frac{-(q\mu_{X,ik}+\theta_{ik})}{\sigma_{X,ik}\sqrt{1+(1-q)(1-q-2\rho_{ik})}}\right) \quad (11)$$

Therefore, studies not reporting the change from baseline or follow-up measures, but providing information on the probability of response, also provide information on the parameter of interest, the mean change from baseline θ_{ik}.

These studies have a binomial likelihood

$$r_{resp,ik} \sim \text{Binomial}(R_{ik}, n_{ik})$$

Provided the baseline mean and standard deviation for each study are reported and that we also have information on the correlation between baseline and follow-up scores in each arm of each study, we can replace these as if they are known into equation (11) and then use equations (3) and (4), as before.

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1.2.5.6 Prior distributions and computation

In this case non-informative prior distributions are chosen for the pooled treatment effects, relative to treatment 1, d_{1k}, k=2,…,nt , where nt is the number of treatments in the network

$$d_{1k} \sim \text{Normal}(0, 100^2) \quad (12)$$

and a Uniform prior between 0 and 5 is chosen for the between-study heterogeneity, which is thought to be sufficiently wide to capture the variability in difference in mean change from baseline across trials making the same comparisons.

An informative prior distribution for the within class standard deviation is given as detailed in section 1.2.3.

1.2.5.7 Analysis on the SMD scale

In this case, studies also used different underlying continuous scales on which they report the means or the number of responders. As the methods noted above are study and arm specific, they apply regardless of which scale was used in that trial, although care needs to be taken to ensure that the pre-specified cut-offs *q* and *h* are appropriate for the scale used in a particular study.

Pooling of the difference in means across different scales is not appropriate. A common approach is to use the SMD, where the mean difference is divided by a standardising constant, which can be the population standard deviation for each scale (if known), or its estimate, s_i, often obtained by pooling the estimated standard deviations across all arms of the study (Cooper et al. 2009). The standardising constant can be adjusted in different ways

(Cooper et al. 2009). We will illustrate the model using Cohen's d[16], but the analysis using another standardising constant can be done following the same principles.

The SMD for arm *k* of study *i* compared to arm 1 of study i, λ_{ik}, is given as

$$\lambda_{ik} = \frac{m_{ik} - m_{i1}}{s_i} \quad (13)$$

where s_i in a two arm study is given as

$$s_i = \sqrt{\frac{(n_{i1}-1)sd^2_{i1} + (n_{i2}-1)sd^2_{i2}}{n_{i1}+n_{i2}-2}} \quad (14)$$

and in a three arm study is given as

$$s_i = \sqrt{\frac{(n_{i1}-1)sd^2_{i1} + (n_{i2}-1)sd^2_{i2} + (n_{i3}-1)sd^2_{i3}}{n_{i1}+n_{i2}+n_{i3}-3}} \quad (15)$$

The likelihood for each study reporting the various outcomes are as before, but the parameter of interest is now the SMD λ_{ik}. Thus the model is defined as

$$\lambda_{ik} = \gamma_i + \delta_{ik} \quad (16)$$

This model is linked to the mean change from baseline through the following relationship

$$\theta_{ik} = \lambda_{ik} s_i \quad (17)$$

Prior distributions can be defined as before.

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1.2.6 Response analysis: methods

The economic model is driven by the probabilities of response on each treatment which are informed both by studies reporting response and studies reporting continuous measures. Again we wanted to include as much data as possible in the analysis. For studies not reporting response we transformed the continuous data first to the SMD scale and then to response. The data required for each arm of each study are the number of individuals responding to treatment in each arm of each study, out of the total number of individuals, defined as those improving by more than a certain percentage from baseline;

However, some studies did not report these data, and instead reported:

a) the mean CFB, the standard deviation in CFB and the total number of individuals in that arm (or the standard error of the mean change from baseline).
b) the baseline and follow-up means, standard deviations and number of individuals, for each arm of the study.

Studies reporting outcomes a) or b) above also provide information on probability of response through the relationship between the underlying continuous scale and the measurements that can be derived from it.

For this analysis, if response data were available in a study we used that data. If that study did not report response but reported CFB we used the CFB data and transformed it to response. If a study reported neither response nor CFB but did report baseline and follow up data, we used the baseline and follow up data and transformed it to response.

We first hoped to transform the continuous data to response using the same method as that for transforming the response to continuous data given in equation (11). Due to limitations with the WinBUGS software however we were unable to do so and instead used a different method of converting SMD to log-odds ratio (LOR) of response recommended by the Cochrane collaboration (Higgins and Green 2011).

1.2.6.16 Notation

For trials reporting response the following model was used:

$$r_{ik} \sim \text{Binomial}(p_{ik}, n_{ik})$$

where r_{jk} is the number of individuals achieving response in arm k of trial j, n_{jk} is the total number of individuals in arm k of trial j, and p_{jk} is the probability of response in arm k of trial j. These probabilities are modelled on the log-odds scale as:

$$\text{logit}(p_{ik}) = \alpha_i + \eta_{ik}$$

where η_{ik} represents the relative treatment effect of the treatment in arm k compared with the treatment in arm 1 in trial i, on the log-odds ratio (LOR) scale and $\eta_{i1} = 0$. Thus $\eta_{ik} > 0$ favours the treatment in arm k and $\eta_{ik} < 0$ favours the treatment in arm 1.

The LOR of response can be related to a notional SMD for response using the formula (Chinn 2000):

$$LOR_{\text{Re}sponse} = -\frac{\pi}{\sqrt{3}} SMD_{\text{Re}sponse} \qquad (18)$$

noting the change in sign to retain the interpretation of a positive LOR favouring treatment k.

The LOR was obtained by transforming the treatment effect from the SMD scale using equation (18). So, the treatment effect on response is informed by the treatment effect in studies on the pooled scale of symptoms as:

$$\eta_{ik} = \left(-\frac{\pi}{\sqrt{3}} \delta_{ik} \right)$$

Standard NMA random and fixed effects model can used to pool η, as described in section 1.2.5.4. Prior distributions can also be defined as before.

Sample WinBUGS codes for both the SMD and response analyses are provided at the end of this document, in Appendix 1.

1.2.7 Information on within-study correlation and standard deviation at follow-up

To apply the methods described in sections 1.2.5.5.1 and 1.2.5.5.2 we needed information on a) the correlation between baseline and follow-up scores and b) the relationship between standard deviations (SDs) at baseline and follow up.

For a) we identified 7 studies in our dataset that provided information on mean and SD at baseline, mean and SD at follow-up and the mean and SD of change from baseline (Appendix 2 at the end of this document). The correlations calculated from these studies ranged from -0.67 to 0.92, which meant that no meaningful summary of this correlation could be used.

We also identified various data sources (included in Appendix 2) for correlations relating to psychological and pharmacological treatments but the evidence was inconclusive and often

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based on limited numbers of patients. We decided to assume a correlation of 0.5 and vary this in sensitivity analysis as described in section 1.4.

For b) we plotted the SDs at baseline and follow-up from every study that reported both by type of intervention and population (Figure 1 and Figure 2). The black line on these plots is the regression line and the red line is the line of equality where y=x. The regression equation is also shown. We assumed equality of the SD at baseline and follow-up as this was reasonably supported by the data in Figure 1 and Figure 2. In a sensitivity analysis, the regression equations in Figure 1 and Figure 2 were used to obtain the SD at follow-up from the reported SD at baseline.

Figure 1: Plot of SDs at baseline and follow-up – Population with more severe depression

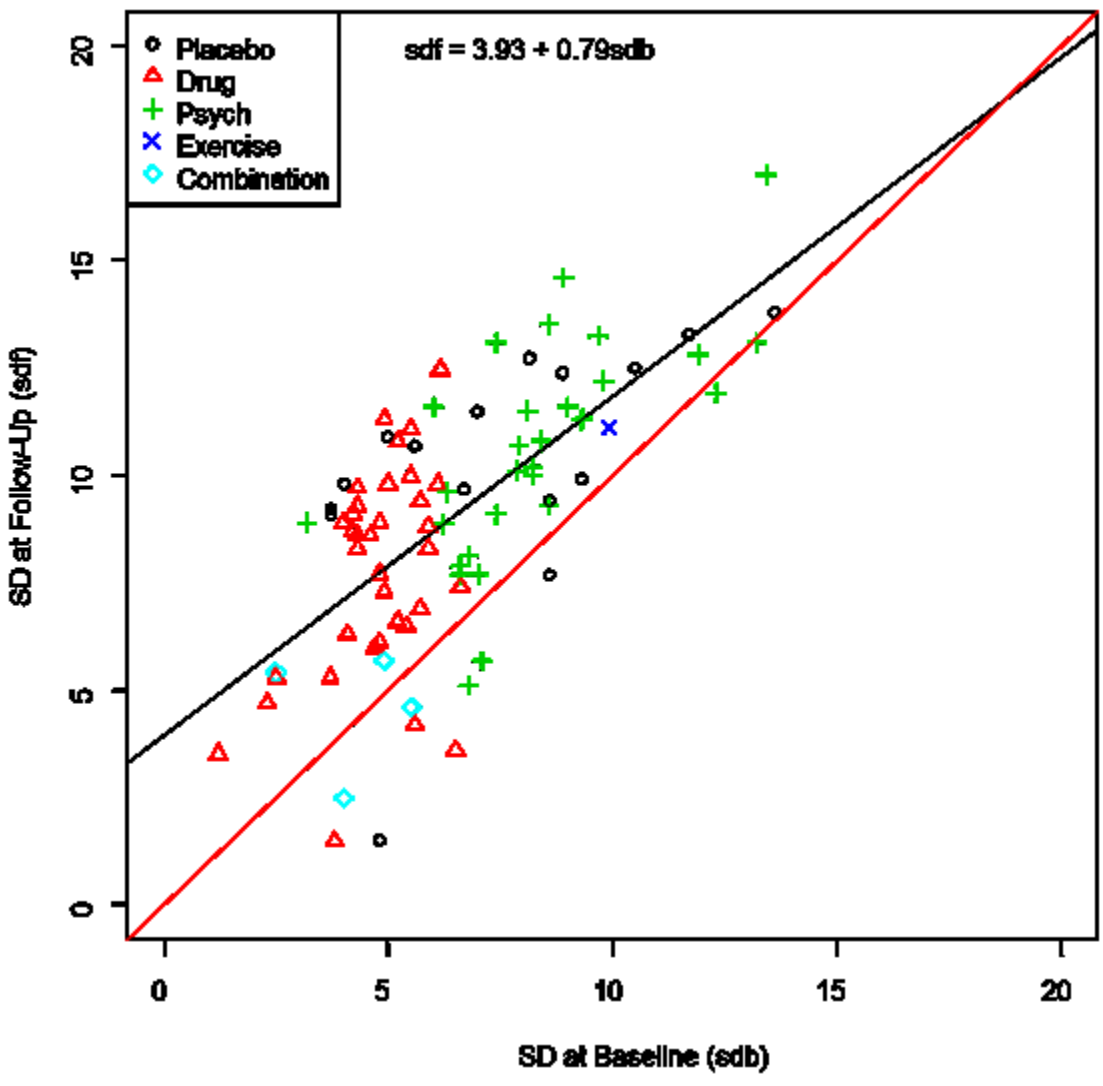

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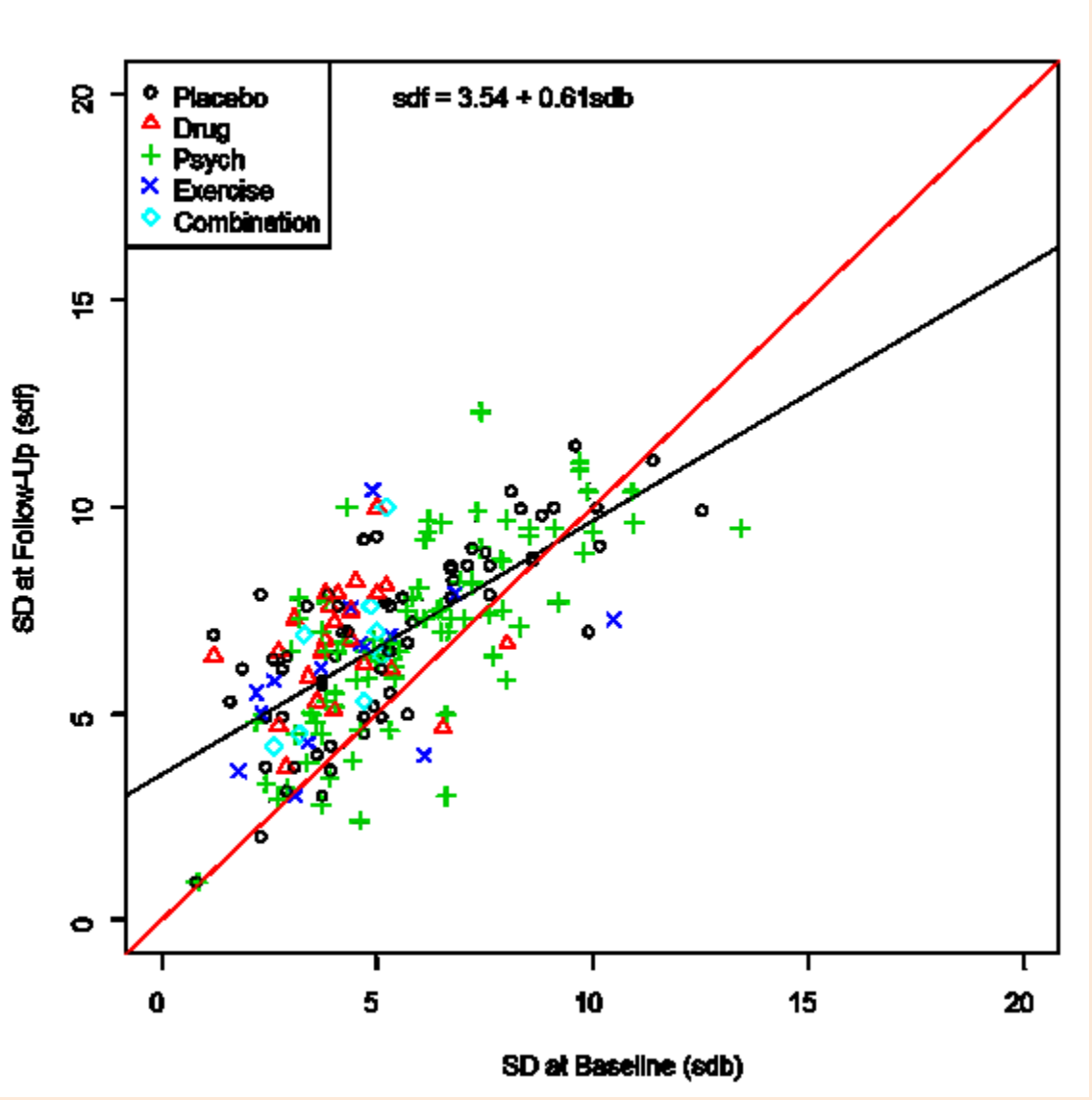
Figure 2: Plot of SDs at baseline and follow up – population with less severe depression



1.2.84 Empirical checks

Some studies reported change from baseline as well as response, remission or both. We therefore checked agreement between the observed change from baseline and that obtained through the inverse of the transformations in equation (11), using the observed probabilities of response, calculated as the number of events out of the total number of individuals randomised (ITT analysis). The results for each population are plotted in Figure 3 and Figure 4 below. The black line is the line of equality. From these we were satisfied that the calculated figures provided a good estimation of the observed data.

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Figure 3: CFB estimated from responders v reported CFB – Less severe depression

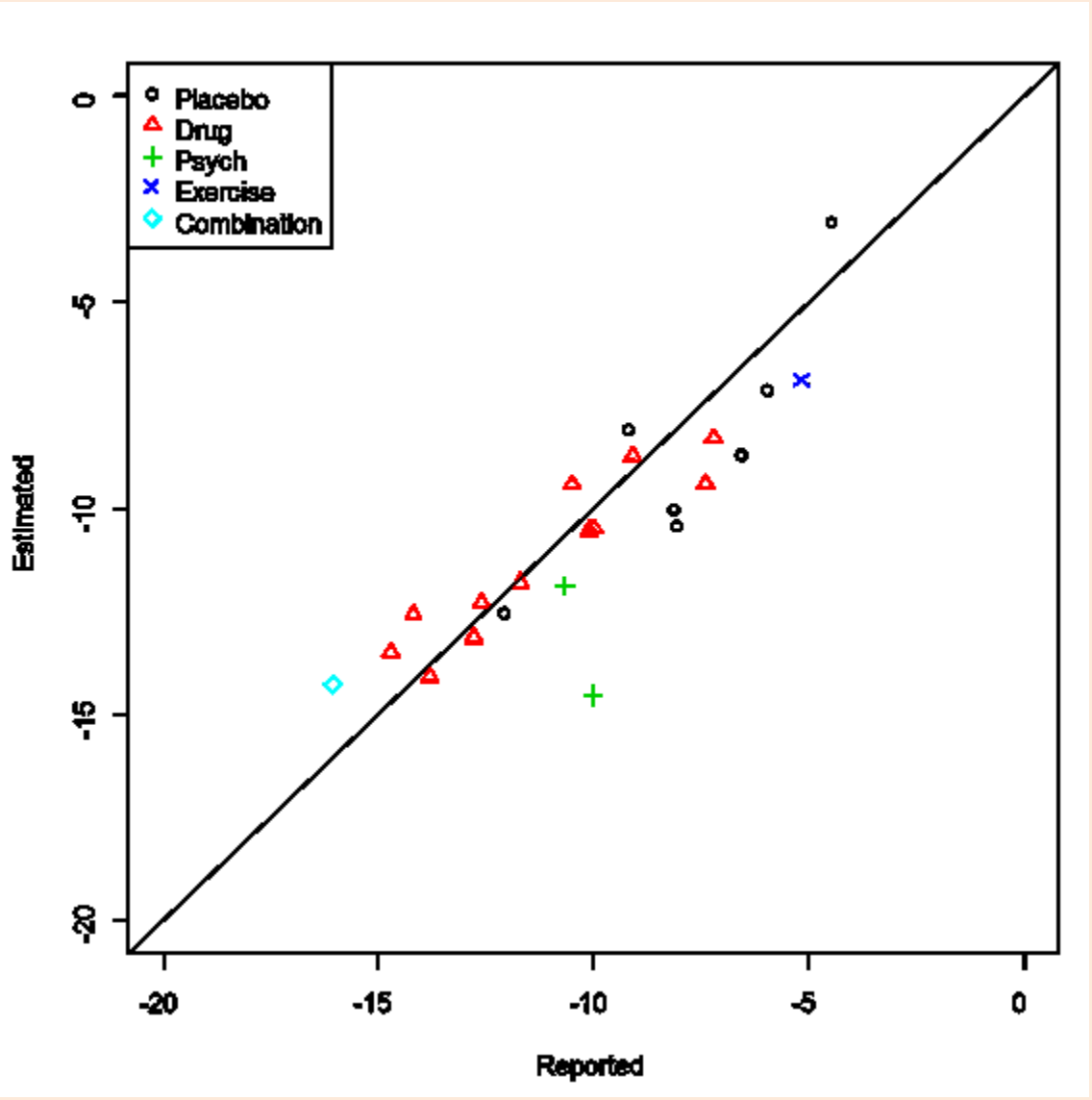
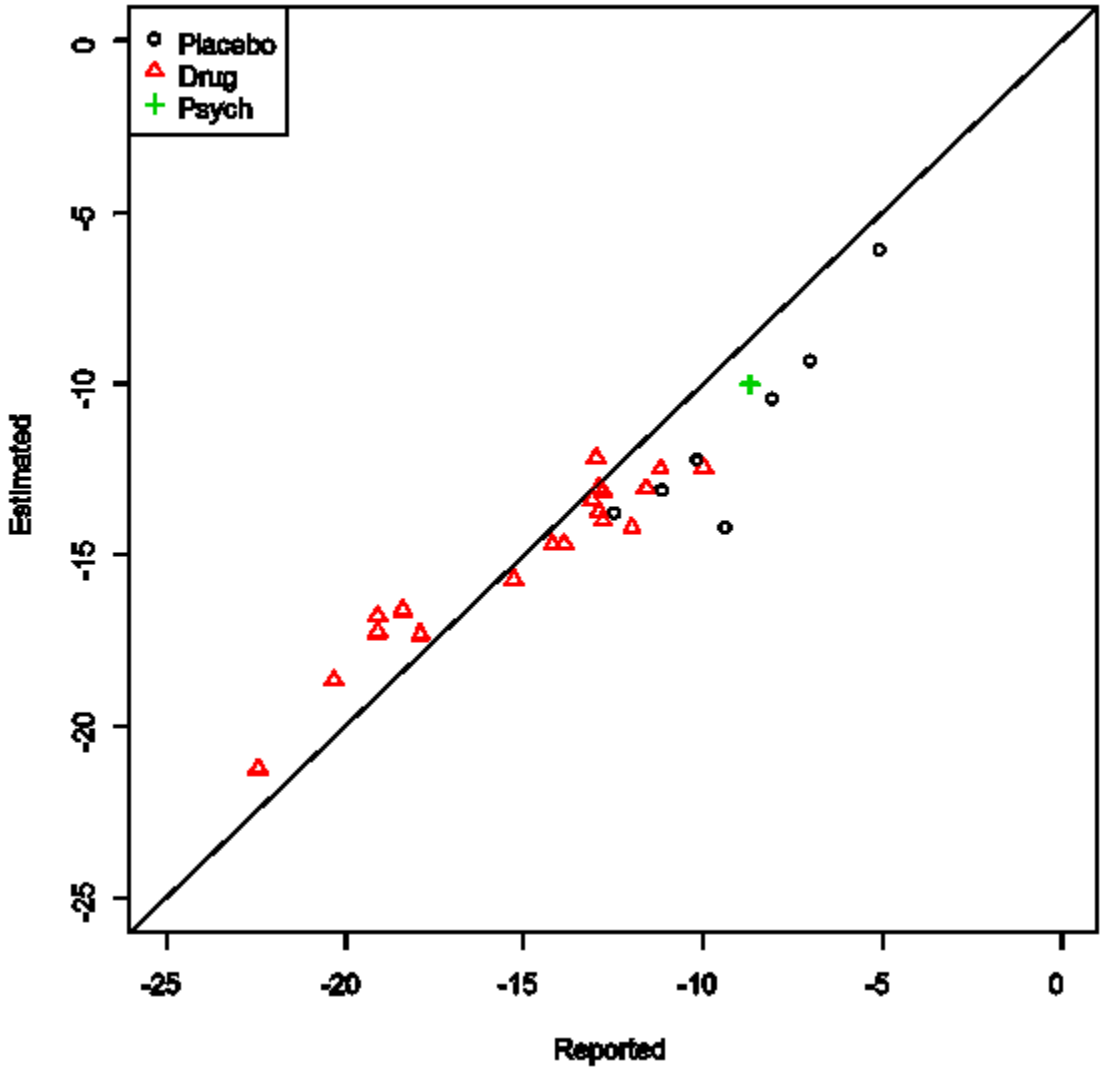


Figure 4: CFB estimated from responders v reported CFB – More severe depression



We also considered transforming the remission data to CFB using the following equation where;

L_{jik} - remission status at follow-up for individual *j* in arm *k* of trial *i*, defined as having follow-up measurement below pre-defined threshold h_i on a given continuous scale, i.e.

$$L_{jik} = \begin{cases} 1 & \text{if } y_{jik} \le h_i \\ 0 & \text{otherwise} \end{cases} \quad (19)$$

Using equation (19), the probability of remission for individuals in arm *k* of trial *i* is defined as

$$L_{ik} = \Pr(Y_{ik} \le h) = \Phi\left(\frac{h - \theta_{ik} - \mu_{X,ik}}{\sigma_{Y,ik}}\right) \quad (20)$$

Therefore, studies providing information on the probability of remission, also provide information on the parameter of interest, the mean change from baseline θ_{ik}.

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We again checked agreement between the observed change from baseline and that obtained through the inverse of the transformations in equation (20), using the observed probabilities of remission. However there were not enough data to check agreement, particularly for the population with more severe depression (Figure 5 and Figure 6), so we decided not to include this transformation in the analysis.

Figure 5: CFB estimated from remitters v reported CFB – Less severe depression

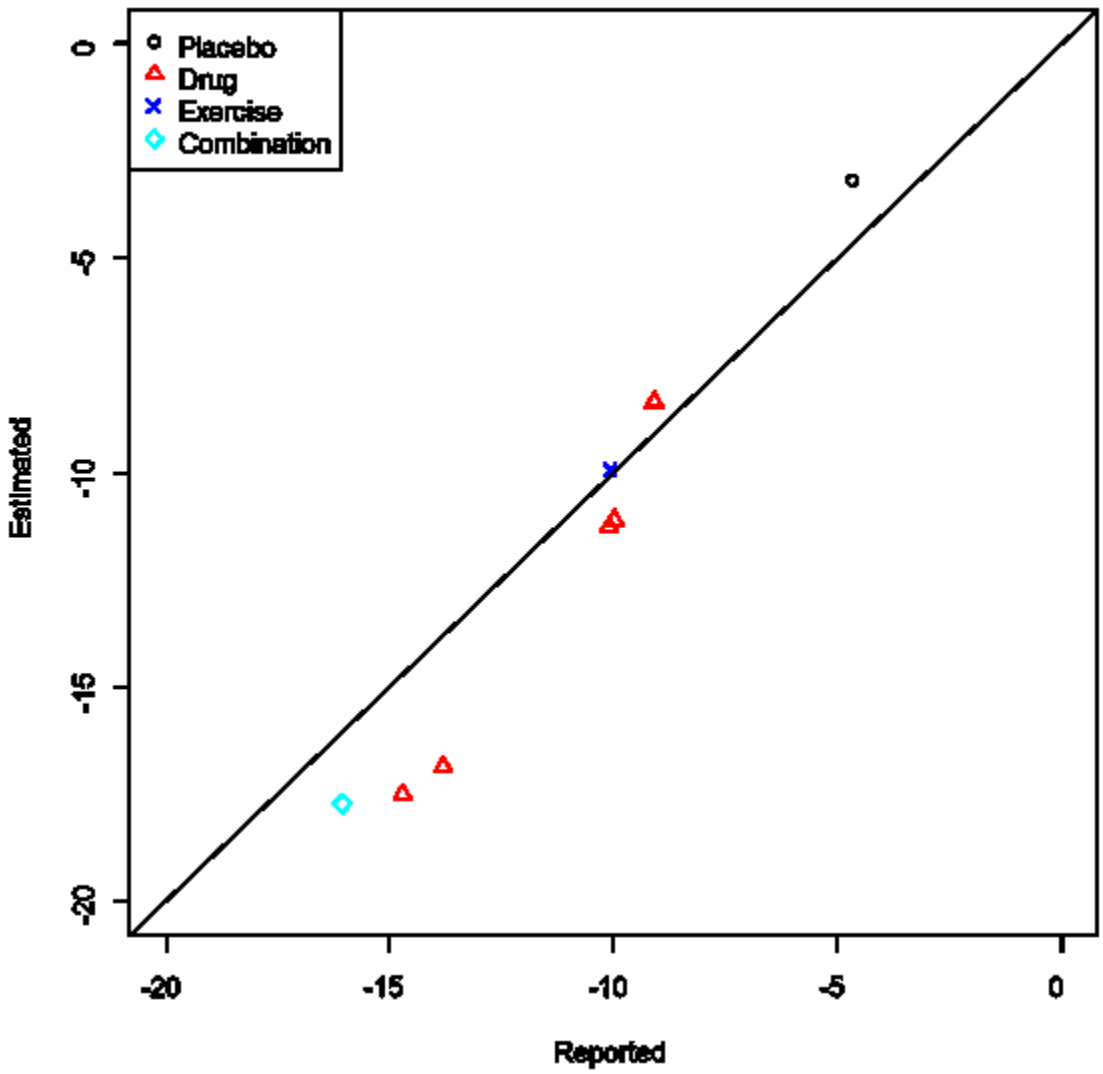
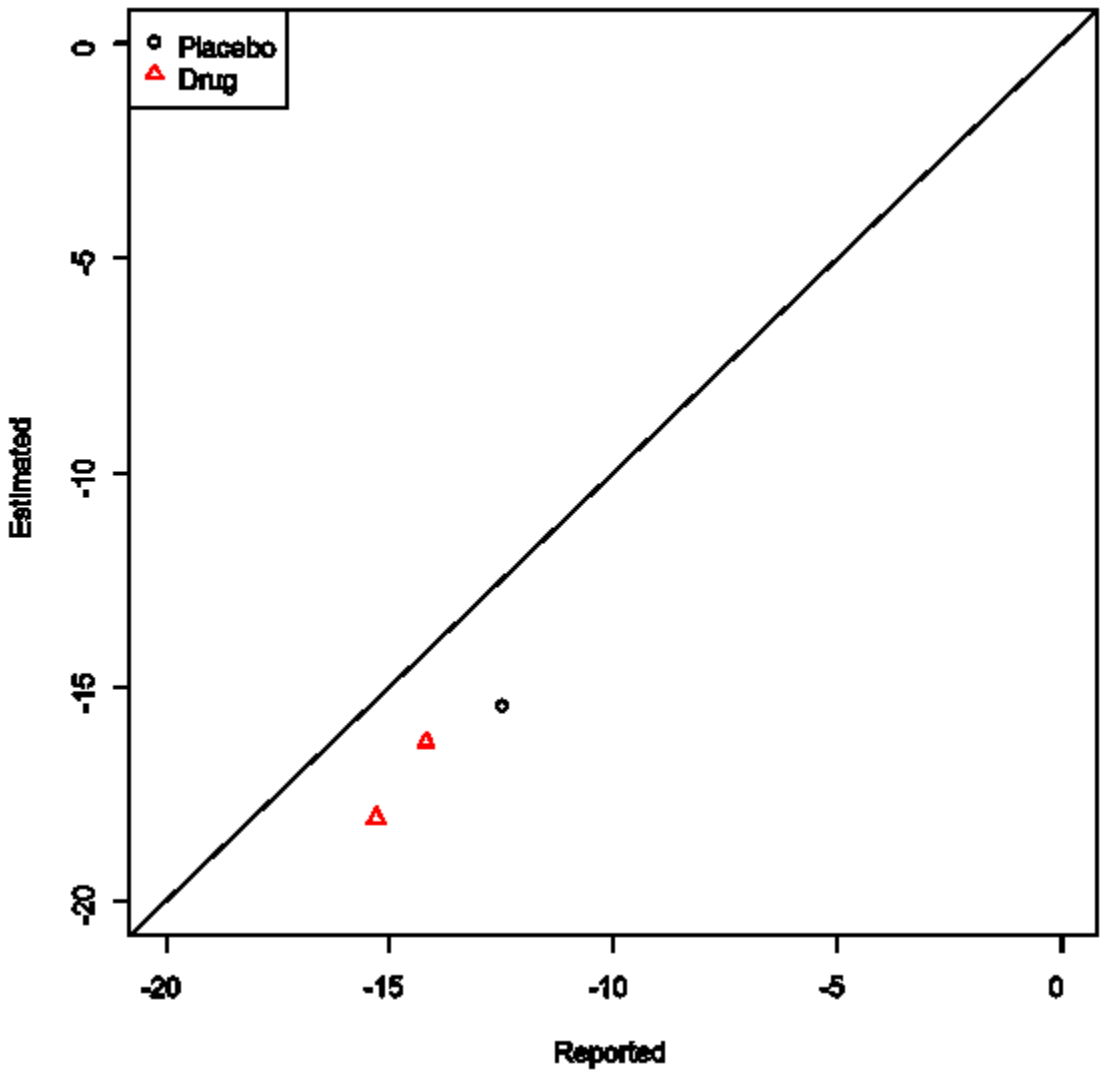


Figure 6: CFB estimated from remitters v reported CFB – More severe depression



1.3 Results

1.3.1 Population: less severe depression

1.3.1.1 Outcome: discontinuation for any reason – less severe depression

This analysis was conducted using the NMA code given by Dias et al for binomial data (Dias et al. 2013, Dias et al. 2011) with the denominator being the total number of patients randomised. After excluding trials with zero events in all arms, 199 trials of 92 interventions and 27 classes were included for this outcome (Table 1, Figure 7, Figure 8). A continuity correction was applied to data in 16 studies containing at least one zero cell to stabilise the results.

Lower posterior mean residual deviance and DIC values in the NMA random effects consistency model, as well as minimal improvement in the prediction of data in individual studies by the inconsistency model, suggested that there was no evidence of inconsistency (Table 29; Figure 9). The between-study heterogeneity slightly decreased in the inconsistency model, which may be partly explained by the between-study heterogeneity contributed by Richards 2015 and Furukawa 2012 (Table 29). Reported results are therefore

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based on the random-effects NMA model, assuming consistency. Moderate between trials heterogeneity was observed relative to the size of the intervention effect estimates,($\tau = 0.49$ (95% CrI 0.40 to 0.60)).

Table 1: Interventions, classes and number of patients randomised (N) included in discontinuation for any reason analysis – less severe depression

	Intervention	N	Class		N
1	Pill placebo	3028	**Pill placebo**	1	3028
2	Waitlist	1216	**No treatment**	2	1552
3	No treatment	336		2	
4	Attention placebo	421	**Attention placebo**	3	532
5	Attention placebo + TAU	111		3	
6	TAU	3205	**TAU**	4	3451
7	Enhanced TAU	246		4	
8	Exercise	831	**Exercise**	5	1174
9	Exercise + TAU	328		5	
10	Yoga + TAU	15		5	
11	Any TCA	273	**TCAs**	6	2084
12	Amitriptyline	668		6	
13	Imipramine	889		6	
14	Lofepramine	254		6	
15	Any SSRI	419	**SSRIs**	7	4981
16	Any SSRI + Enhanced TAU	112		7	
17	Citalopram	725		7	
18	Escitalopram	969		7	
19	Fluoxetine	1124		7	
20	Sertraline	1632		7	
21	Any AD	817	**Any AD***	8	817
22	Mirtazapine	45	**Mirtazapine**	9	45
23	Short-term psychodynamic psychotherapy individual	361	**Short-term psychodynamic psychotherapies***	10	385
24	Short-term psychodynamic psychotherapy group	24		10	
25	Cognitive bias modification with support + TAU	40	**Self-help with support**	11	1961
26	Cognitive bibliotherapy with support	373		11	
27	Cognitive bibliotherapy with support + TAU	27		11	
28	Computerised behavioural activation with support	80		11	
29	Computerised psychodynamic therapy with support	46		11	
30	Computerised third-wave cognitive therapy with support	19		11	
31	Computerised-CBT (CCBT) with support	658		11	

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	Intervention	N	Class		N
32	Computerised-CBT (CCBT) with support + TAU	649		11	
33	Tailored computerised-CBT (CCBT) with support	69		11	
34	Behavioural bibliotherapy	23	**Self-help without support**	12	3232
35	Cognitive bibliotherapy	501		12	
36	Cognitive bibliotherapy + TAU	182		12	
37	Computerised cognitive bias modification	60		12	
38	Computerised mindfulness intervention	41		12	
39	Computerised-CBT (CCBT)	1200		12	
40	Computerised-CBT (CCBT) + TAU	424		12	
41	Online positive psychological intervention	143		12	
42	Psychoeducational website	484		12	
43	Tailored computerised psychoeducation and self-help strategies	174		12	
44	Lifestyle factors discussion	178	**Psychoeducational interventions**	13	653
45	Psychoeducational group programme	124		13	
46	Psychoeducational group programme + TAU	351		13	
47	Interpersonal psychotherapy (IPT)	693	**Interpersonal psychotherapy (IPT)***	14	726
48	Interpersonal psychotherapy (IPT) + TAU	33		14	
49	Emotion-focused therapy (EFT)	60	**Counselling**	15	943
50	Interpersonal counselling	286		15	
51	Non-directive counselling	161		15	
52	Non-directive counselling + TAU	302		15	
53	Psychodynamic counselling + TAU	73		15	
54	Relational client-centered therapy	17		15	
55	Wheel of wellness counselling	44		15	
56	Problem solving group	20	**Problem solving**	16	391
57	Problem solving individual	197		16	
58	Problem solving individual + TAU	90		16	
59	Problem solving individual + enhanced TAU	84		16	
60	Behavioural activation (BA)	109	**Behavioural therapies (individual)**	17	162

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	Intervention	N	Class		N
61	Behavioural activation (BA) + TAU	23		17	
62	Behavioural therapy (Lewinsohn 1976)	15		17	
63	Coping with Depression course (individual)	15		17	
64	CBT individual (under 15 sessions)	370	**Cognitive and cognitive behavioural therapies (individual)**	18	1983
65	CBT individual (under 15 sessions) + TAU	151		18	
66	CBT individual (over 15 sessions)	1201		18	
67	CBT individual (over 15 sessions) + TAU	15		18	
68	Rational emotive behaviour therapy (REBT) individual	57		18	
69	Third-wave cognitive therapy individual	159		18	
70	Third-wave cognitive therapy individual + TAU	30		18	
71	CBT group (under 15 sessions)	153	**Behavioural, cognitive, or CBT groups**	19	731
72	CBT group (under 15 sessions) + TAU	105		19	
73	CBT group (over 15 sessions)	47		19	
74	Coping with Depression course (group)	131		19	
75	Coping with Depression course (group) + TAU	137		19	
76	Rational emotive behaviour therapy (REBT) group	15		19	
77	Third-wave cognitive therapy group	125		19	
78	Third-wave cognitive therapy group + TAU	18		19	
79	CBT individual (over 15 sessions) + any AD	25	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	20	108
80	CBT individual (over 15 sessions) + any TCA	58		20	
81	CBT individual (over 15 sessions) + imipramine	25		20	
82	CBT group (under 15 sessions) + imipramine	34	**Combined (Behavioural, cognitive, or CBT groups + AD)***	21	34
83	Problem solving individual + any SSRI	35	**Combined (Problem solving + AD)***	22	35
84	Supportive psychotherapy + any SSRI	39	**Combined (Counselling + AD)***	23	39
85	Interpersonal psychotherapy (IPT) + any AD	65	**Combined (IPT + AD)***	24	78

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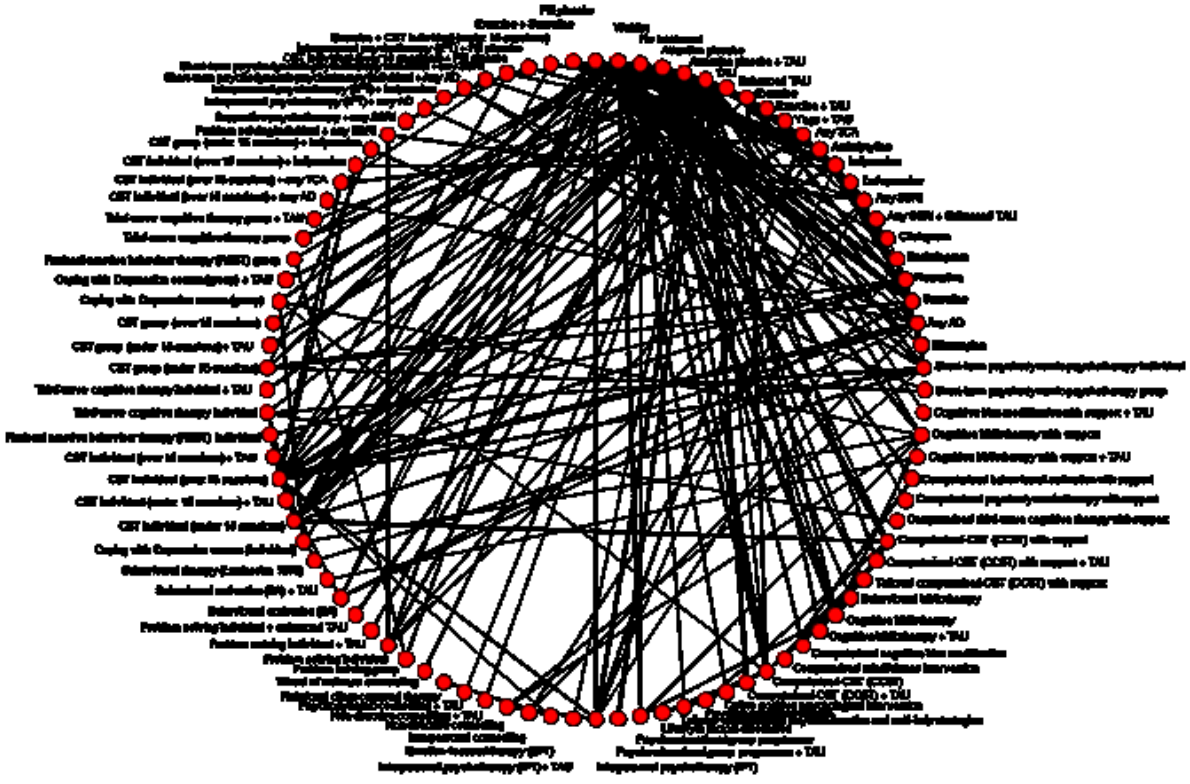
	Intervention	N	Class		N
86	Interpersonal psychotherapy (IPT) + imipramine	13		24	
87	Short-term psychodynamic psychotherapy individual + Any AD	271	**Combined (Short-term psychodynamic psychotherapies + AD)***	25	335
88	Short-term psychodynamic psychotherapy individual + any SSRI	64		25	
89	CBT individual (over 15 sessions) + Pill placebo	17	**Combined (psych + placebo)***	26	60
90	Interpersonal psychotherapy (IPT) + Pill placebo	43		26	
91	Exercise + CBT individual (under 15 sessions)	21	**Combined (Exercise + AD/CBT)***	27	210
92	Exercise + Sertraline	189		27	
*Variance borrowed from another class as described in section 1.2.3					

Figure 7: Network diagram of interventions. Discontinuation for any reason – less severe depression



Note: Without the use of a class model Cognitive bibliotherapy with support + TAU and Behavioural activation (BA) + TAU would be disconnected from the rest of the network.

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Figure 8: Network diagram of classes. Discontinuation for any reason – less severe depression.

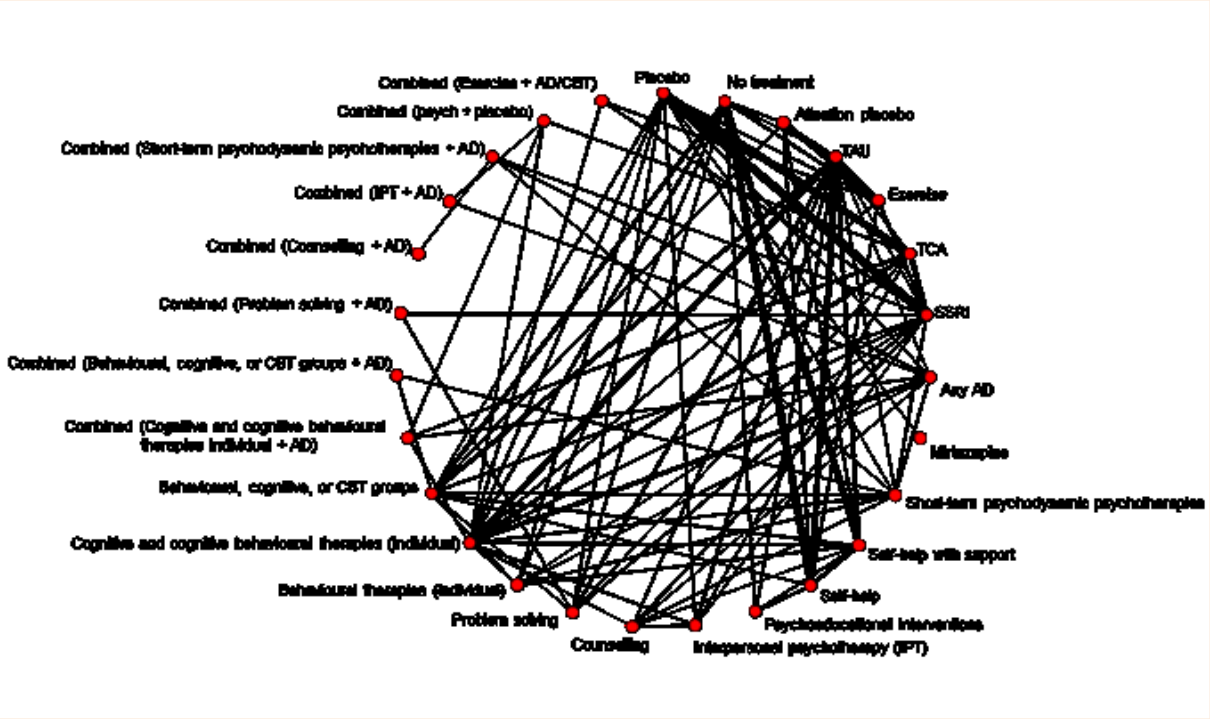

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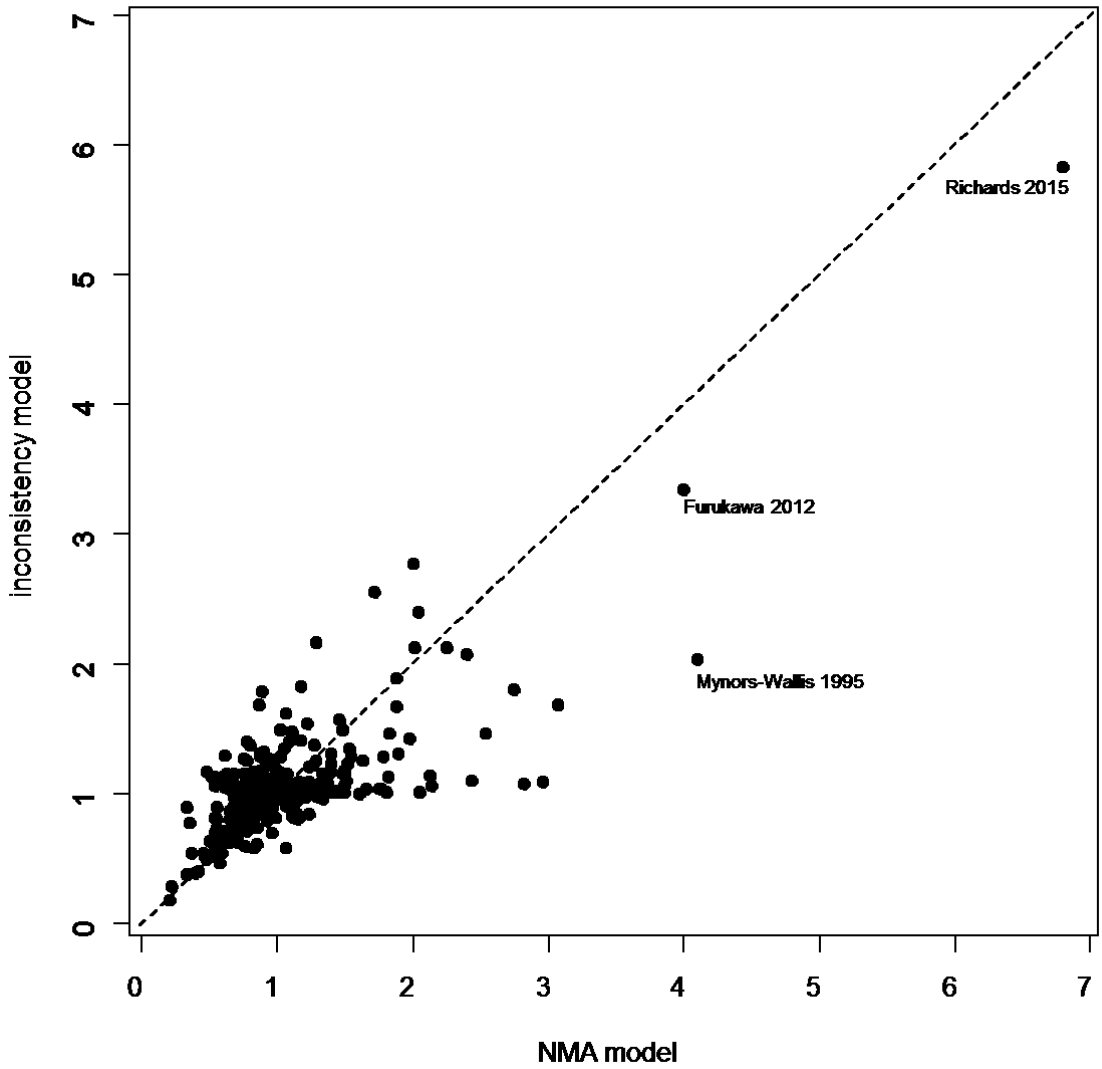
Figure 9: Deviance plot. Discontinuation for any reason – less severe depression.



There is evidence of Waitlist, CBT group (under 15 sessions) + TAU, and CBT individual (over 15 sessions) + Pill placebo having a decreased odds of discontinuation compared to Pill placebo (Figure 49). There is no evidence of any intervention having an increased odds of discontinuation compared to Pill placebo, nor is there evidence of any classes of interventions having a decreased or increased odds of discontinuation compared to Pill placebo (Figure 49 and Figure 50).

The highest ranked class is Combined (Problem solving + AD) with a posterior median rank of 3rd (95% CrI 1st to 24th). One of the highest ranked interventions (Problem solving individual + SSRI) is the only intervention belonging to this class. The lowest ranked class is Combined (Behavioural, cognitive, or CBT groups + AD) at 25th (95% CrI 4th to 25th). The lowest ranked intervention, CBT group (under 15 sessions) + imipramine, is the only intervention belonging to this class. We note however the wide credible intervals in the ranks, reflecting the uncertainty in which class or treatment is best. Rankings of classes are shown in Table 2; rankings of interventions are shown in the respective excel file in Appendix N3, *"Ranks"* worksheet.

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Table 2: Posterior median rank and 95% credible intervals by class. Discontinuation for any reason – less severe depression.

Class	Posterior median rank	95% CrI
Combined (Problem solving + AD)	3	(1, 24)
Mirtazapine	4	(1, 24)
Psychoeducational interventions	5	(1, 18)
No treatment	6	(1, 18)
Behavioural therapies (individual)	8	(1, 23)
Interpersonal psychotherapy (IPT)	9	(2, 21)
Problem solving	9	(2, 22)
Cognitive and cognitive behavioural therapies (individual)	9	(3, 17)
Combined (psych + placebo)	9	(1, 23)
Behavioural, cognitive, or CBT groups	10	(2, 20)
TAU	11	(3, 22)
Counselling	11	(3, 22)
Combined (IPT + AD)	11	(1, 25)
Exercise	12	(2, 23)
SSRIs	14	(6, 21)
Short-term psychodynamic psychotherapies	15	(3, 24)
Combined (Counselling + AD)	15	(1, 25)
Pill placebo	17	(11, 22)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	17	(3, 25)
Attention placebo	19	(5, 25)
Self-help without support	19	(10, 24)
TCAs	20	(12, 24)
Self-help with support	21	(11, 25)
Combined (Short-term psychodynamic psychotherapies + AD)	23	(6, 25)
Combined (Behavioural, cognitive, or CBT groups + AD)	25	(4, 25)

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1.3.1.23 Outcome: discontinuation due to side effects (SE) – less severe depression

This analysis was also conducted using the NMA code given by Dias et al for binomial data (Dias et al. 2013, Dias et al. 2011). As the economic model required an estimate of the relative effects (odds ratios) for discontinuation due to SE conditional on discontinuing, this analysis involved using the number of patients who discontinued for any reason as the denominator and the number who discontinued due to SE as the numerator. This was required as discontinuation and discontinuation due to SE are inter-related in the model with probabilities which must sum to 1.

After excluding trials which did not report both discontinuation and discontinuation due to SE as well as trials with zero events in all arms, and 2 trials due to the network being disconnected (Schramm 2007/Zobel 2011, Weissman 1992), 32 trials of 19 interventions and 13 classes were included for this outcome (

Table 3, Figure 10, Figure 11). A continuity correction was applied to data containing at least one zero cell to stabilise the results.

Lower between trials heterogeneity and DIC values in the random effects model assuming consistency, as well as minimal improvement in the prediction of data in individual studies by the inconsistency model, suggested that there was no evidence of inconsistency (Table 30;

Figure 12). Reported results are therefore based on the random-effects NMA model, assuming consistency. Moderate to high between trials heterogeneity was found relative to the size of the intervention effect estimates (τ =0.56 (95% 0.06 CrI 1.12)), meaning that the results should be interpreted with caution.

Table 3: Interventions, classes and number of patients randomised (N) included in discontinuation due to SE analysis – less severe depression.

	Intervention	N	Class		N
1	Pill placebo	631	Pill placebo	1	631
2	Exercise	15	Exercise	2	15
3	Amitriptyline	201	TCAs	3	383
4	Imipramine	179		3	
5	Lofepramine	3		3	
6	Any SSRI	10	SSRIs	4	704
7	Citalopram	45		4	
8	Escitalopram	101		4	
9	Fluoxetine	231		4	
10	Sertraline	317		4	
11	Mirtazapine	18	Mirtazapine	5	18
12	Short-term psychodynamic psychotherapy individual	5	Short-term psychodynamic psychotherapies*	6	5
13	Problem solving individual	25	Problem solving*	7	25
14	CBT individual (over 15 sessions)	10	Cognitive and cognitive behavioural therapies (individual)	8	10
15	CBT group (under 15 sessions)	28	Behavioural, cognitive, or CBT groups*	9	28
16	CBT individual (over 15 sessions) + imipramine	10	Combined (Cognitive and cognitive behavioural therapies individual + AD)	10	10
17	Problem solving individual + any SSRI	7	Combined (Problem solving + AD)*	11	7
18	Short-term psychodynamic psychotherapy individual + any SSRI	4	Combined (Short-term psychodynamic psychotherapies + AD)*	12	4
19	Exercise + Sertraline	12	Combined (Exercise + AD/CBT)*	13	12

*Variance borrowed from another class as described in section 1.2.3

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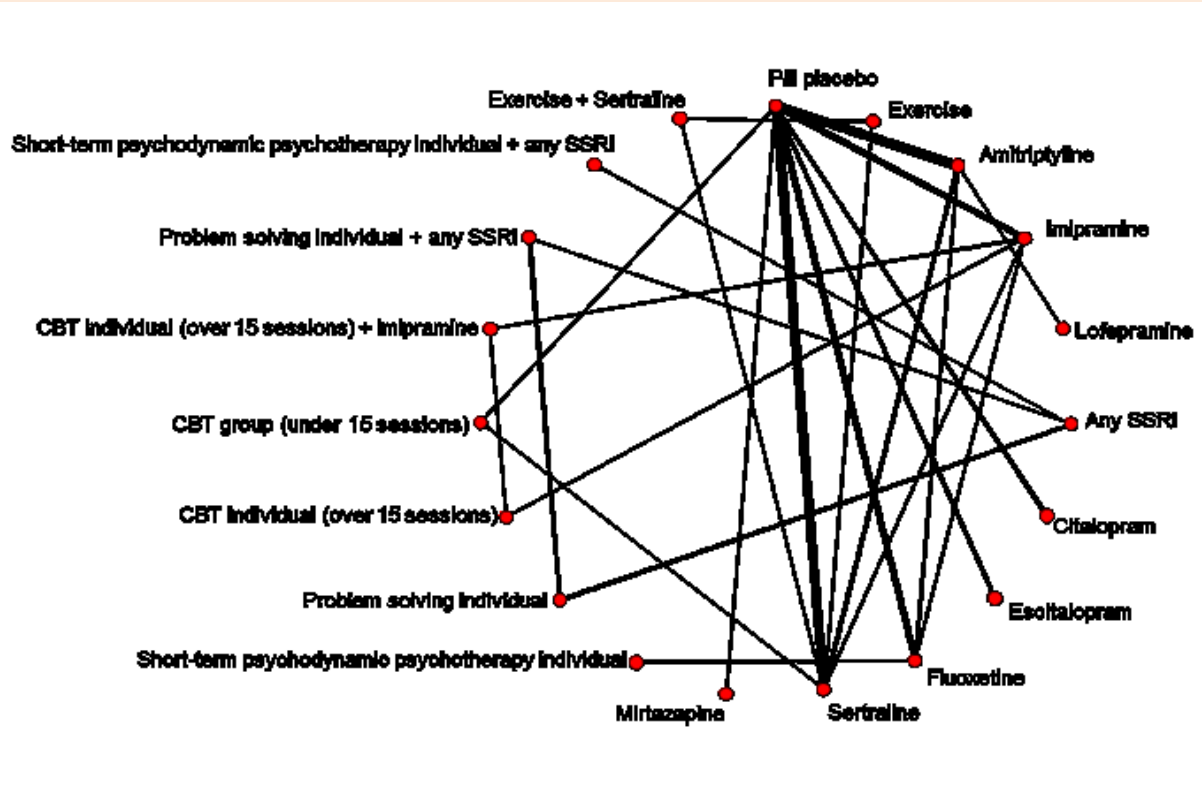
Figure 10: Network diagram of interventions. Discontinuation due to SE – less severe depression.



Note: Without the use of a class network Any SSRI, Problem solving individual, Problem solving individual + any SSRI, and Short-term psychodynamic psychotherapy individual + any SSRI would be disconnected from the rest of the network and would have to be excluded from the analysis.

Figure 11: Network diagram of classes. Discontinuation due to SE – less severe depression.

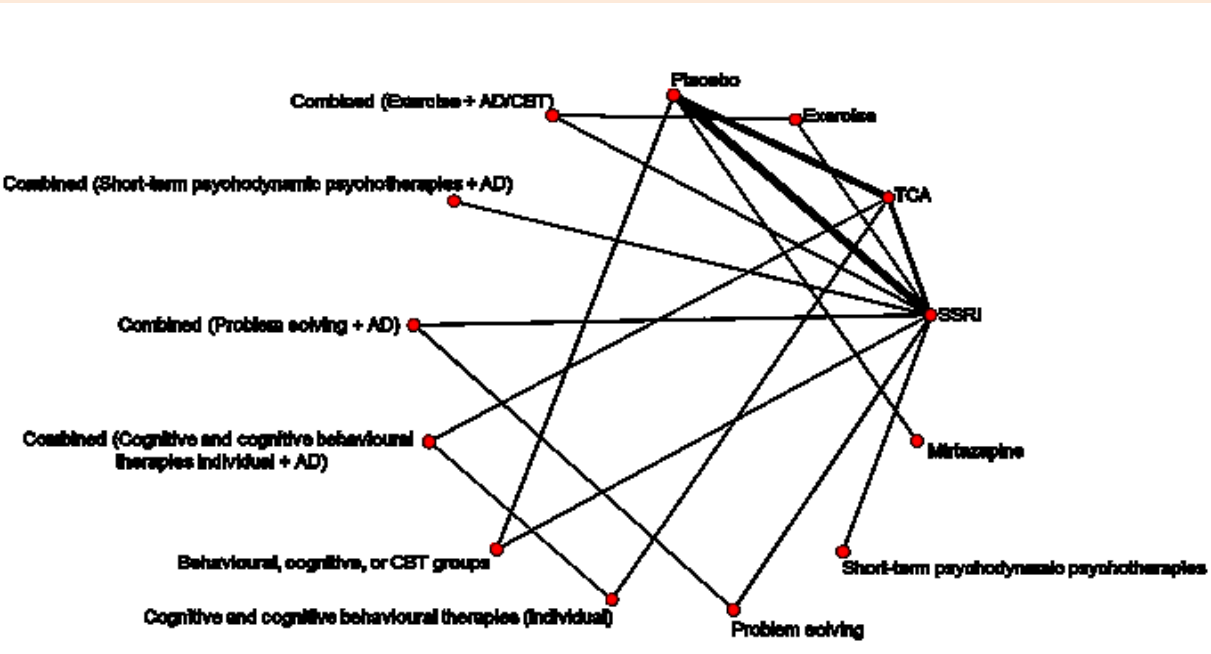


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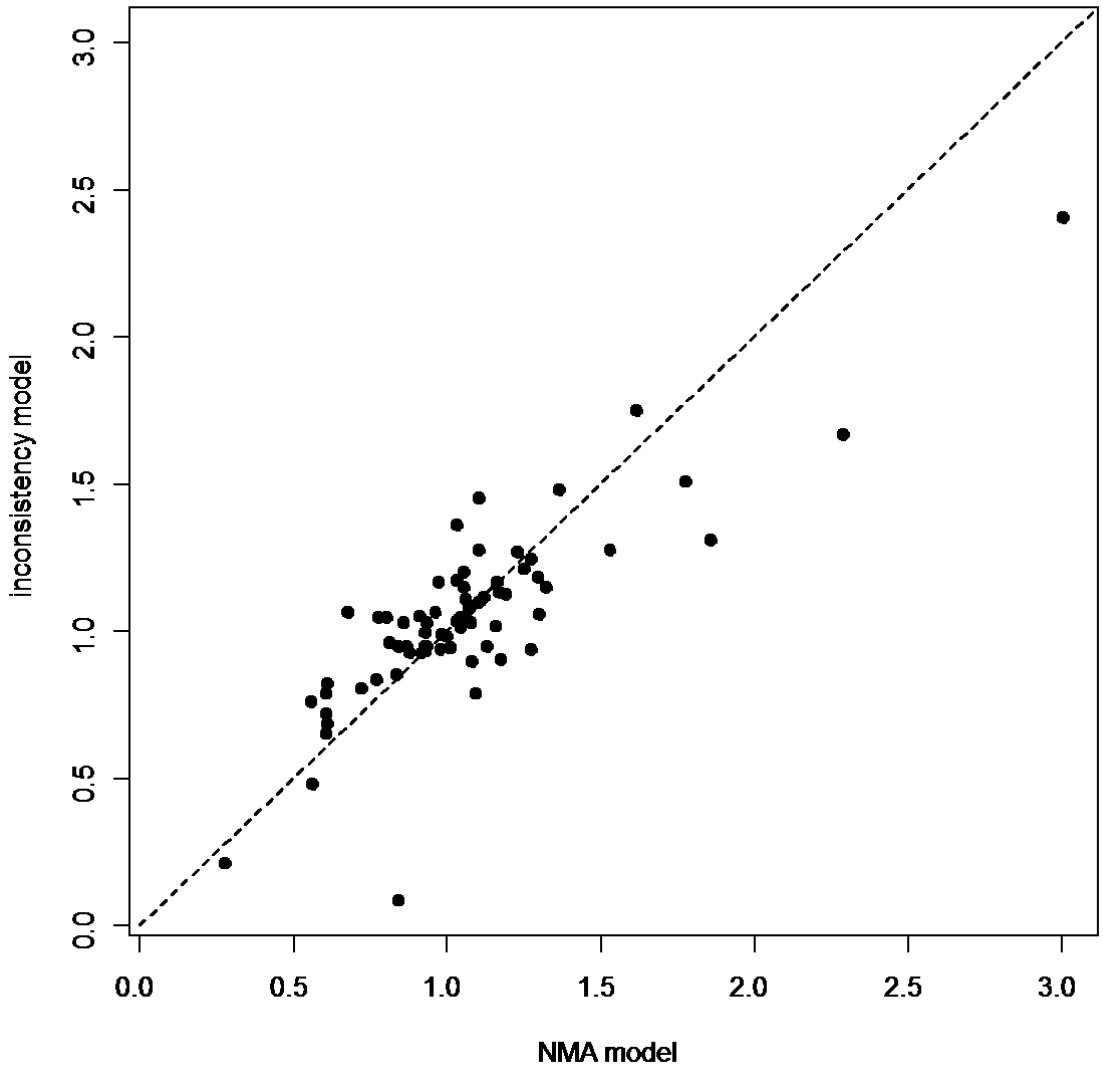
Figure 12: Deviance plot. Discontinuation due to SE – less severe depression.



There is evidence of exercise having a decreased odds of discontinuation due to SE compared to pill placebo and evidence of amitriptyline, imipramine, lofepramine, fluoxetine, and sertraline having an increased odds of discontinuation due to SE (Figure 51**Error! Reference source not found.**). Exercise was the only class for which there was evidence of having a decreased odds of discontinuation due to SE compared to pill placebo, while TCAs and SSRIs both have an increased odds of discontinuation due to SE (Figure 52**Error! Reference source not found.**).

The highest ranked class is Exercise with a posterior median rank of 1 (95% CrI 1st to 3rd). This was also the highest ranked intervention at 1st (95% CrI 1st to 5th). The lowest ranked interventions were Short-term psychodynamic psychotherapy individual at 15th (95% CrI 4th to 17th), Problem solving individual + any SSRI at 15th (95% CrI 5th to 17th), and Amitriptyline at 15th (95% CrI 13th to 17th). The lowest ranked classes are short-term psychodynamic psychotherapies at 12th (95 CrI 4th to 13th) and Combined (Problem solving + AD) at 12th (95% CrI 5th to 13th). Rankings of classes are shown in Table 4; rankings of interventions are shown in the respective excel file in Appendix N3, “Ranks” worksheet.

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Table 4: Posterior median rank and 95% credible intervals by class. Discontinuation due to SE – less severe depression.

Class	Posterior median rank	95% CrI
Exercise	1	(1, 5)
Problem solving	3	(1, 9)
Behavioural, cognitive, or CBT groups	4	(1, 9)
Pill placebo	6	(3, 8)
Cognitive and cognitive behavioural therapies (individual)	6	(1, 13)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	6	(1, 13)
Combined (Short-term psychodynamic psychotherapies + AD)	6	(1, 13)
Combined (Exercise + AD/CBT)	7	(2, 12)
SSRIs	8	(6, 11)
Mirtazapine	10	(4, 13)
TCAs	11	(8, 13)
Short-term psychodynamic psychotherapies	12	(4, 13)
Combined (Problem solving + AD)	12	(5, 13)

1.3.1.33 Outcome: remission in completers – less severe depression

This remission analysis was carried out only in those who completed treatment. After excluding trials which did not report remission in completers and trials with zero events in all arms, 70 trials of 61 interventions and 26 classes were included for this outcome (Table 5, Figure 13, Figure 14). We initially observed a spike in the posterior distribution of the between-study standard deviation, suggesting there was little evidence contributing to the between study heterogeneity. Consequently, we gave the between-study variance an informative prior distribution, log-Normal(-2.34, 1.72) (Lu and Ades 2004), in this model. This was selected from a list of predictive distributions for between-study heterogeneity that are typical of mental health indicators and we selected the distribution with the largest variance (Turner et al. 2015).

The inconsistency model only notably improved in the prediction of data in individual studies with zero cells, and lower posterior mean residual deviance and DIC values in the NMA random effects consistency model, suggesting there was no evidence of inconsistency (Figure 15; Table 31). Reported results are therefore based on the random-effects NMA model, assuming consistency. Moderate to low between trials heterogeneity was observed relative to the size of the intervention effect estimates ($\tau = 0.21$ (95% CrI 0.06 to 0.42)).

Table 5: Interventions, classes and number of patients (N) included in remission in completers analysis – less severe depression.

	Intervention	N	Class		N
1	Pill placebo	574	**Pill placebo**	1	574
2	Waitlist	118	**No treatment**	2	290
3	No treatment	172		2	
4	Attention placebo	94	**Attention placebo**	3	115
5	Attention placebo + TAU	21		3	
6	TAU	931	**TAU**	4	1098
7	Enhanced TAU	167		4	
8	Exercise	263	**Exercise**	5	282
9	Exercise + TAU	19		5	
10	Any TCA	168	**TCAs**	6	399

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	Intervention	N	Class		N
11	Amitriptyline	51		6	
12	Imipramine	97		6	
13	Lofepramine	83		6	
14	Any SSRI	288	**SSRIs**	7	2049
15	Any SSRI + Enhanced TAU	96		7	
16	Citalopram	102		7	
17	Escitalopram	691		7	
18	Fluoxetine	457		7	
19	Sertraline	415		7	
20	Any AD	425	**Any AD***	8	425
21	Short-term psychodynamic psychotherapy individual	165	**Short-term psychodynamic psychotherapies***	9	185
22	Short-term psychodynamic psychotherapy group	20		9	
23	Computerised behavioural activation with support	40	**Self-help with support**	10	580
24	Computerised psychodynamic therapy with support	42		10	
25	Computerised-CBT (CCBT) with support	115		10	
26	Computerised-CBT (CCBT) with support + TAU	347		10	
27	Tailored computerised-CBT (CCBT) with support	36		10	
28	Cognitive bibliotherapy	189	**Self-help without support**	11	671
29	Cognitive bibliotherapy + TAU	68		11	
30	Computerised-CBT (CCBT)	162		11	
31	Computerised-CBT (CCBT) + TAU	136		11	
32	Tailored computerised psychoeducation and self-help strategies	116		11	
33	Psychoeducational group programme + TAU	93	**Psychoeducational interventions***	12	93
34	Interpersonal psychotherapy (IPT)	269	**Interpersonal psychotherapy (IPT)***	13	269
35	Emotion-focused therapy (EFT)	15	**Counselling**	14	319
36	Interpersonal counselling	185		14	
37	Non-directive counselling	39		14	
38	Psychodynamic counselling + TAU	65		14	
39	Relational client-centered therapy	15		14	
40	Problem solving individual	85	**Problem solving***	15	157
41	Problem solving individual + enhanced TAU	72		15	
42	Behavioural activation (BA)	96	**Behavioural therapies (individual)***	16	106

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	Intervention	N	Class		N
43	Behavioural therapy (Lewinsohn 1976)	10		16	
44	CBT individual (under 15 sessions)	218	**Cognitive and cognitive behavioural therapies (individual)**	17	598
45	CBT individual (over 15 sessions)	233		17	
46	CBT individual (over 15 sessions) + TAU	10		17	
47	Rational emotive behaviour therapy (REBT) individual	52		17	
48	Third-wave cognitive therapy individual	85		17	
49	CBT group (under 15 sessions)	59	**Behavioural, cognitive, or CBT groups**	18	216
50	CBT group (under 15 sessions) + TAU	96		18	
51	Coping with Depression course (group) + TAU	61		18	
52	CBT individual (over 15 sessions) + any TCA	18	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	19	34
53	CBT individual (over 15 sessions) + imipramine	16		19	
54	CBT group (under 15 sessions) + imipramine	23	**Combined (Behavioural, cognitive, or CBT groups + AD)***	20	23
55	Problem solving individual + any SSRI	29	**Combined (Problem solving + AD)***	21	29
56	Supportive psychotherapy + any SSRI	16	**Combined (Counselling + AD)***	22	16
57	Interpersonal psychotherapy (IPT) + any AD	53	**Combined (IPT + AD)***	23	53
58	Short-term psychodynamic psychotherapy individual + Any AD	102	**Combined (Short-term psychodynamic psychotherapies + AD)***	24	141
59	Short-term psychodynamic psychotherapy individual + any SSRI	39		24	
60	CBT individual (over 15 sessions) + Pill placebo	17	**Combined (psych + placebo)***	25	17
61	Exercise + Sertraline	88	**Combined (Exercise + AD/CBT)***	26	88

*Variance borrowed from another class as described in section 1.2.3

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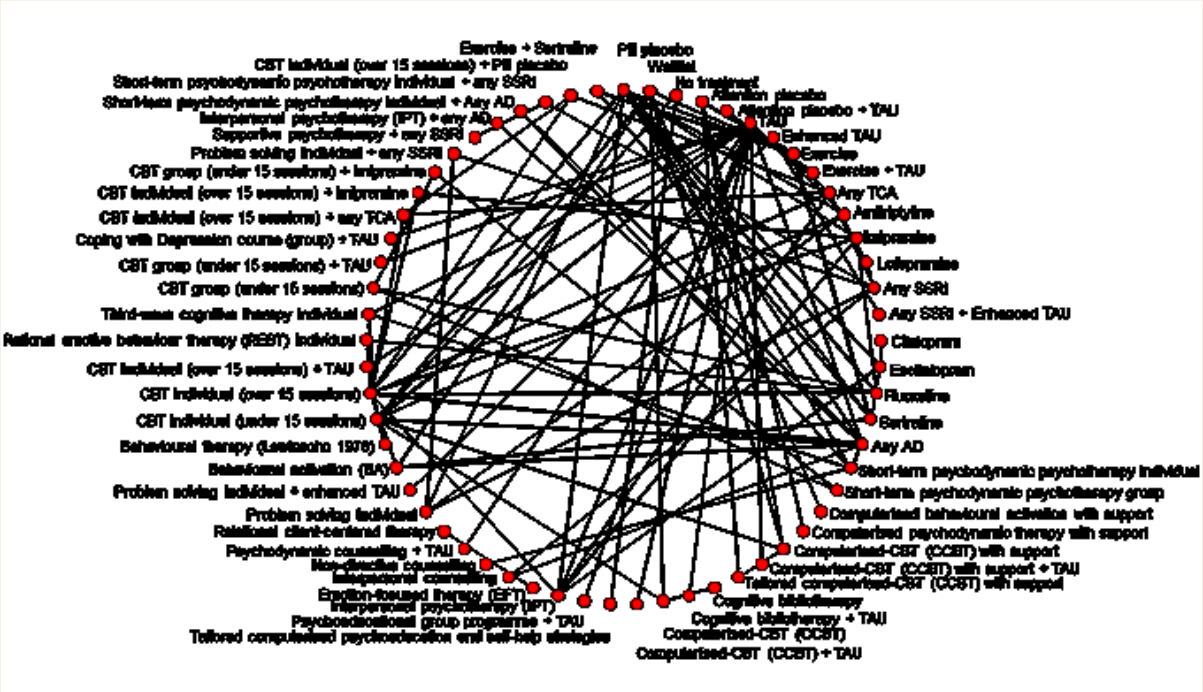
Figure 13: Network diagram of all studies included in analysis by intervention. Remission in completers – less severe depression.



Note: Without the use of a class network Attention placebo + TAU, Enhanced TAU, Exercise + TAU, Any SSRI + Enhanced TAU, Emotion-focused therapy (EFT), Relational client-centered therapy, and Problem solving individual + enhanced TAU would be disconnected from the rest of the network and would have to be excluded from the analysis.

Figure 14: Network diagram of all studies included in analysis by class. Remission in completers – less severe depression.

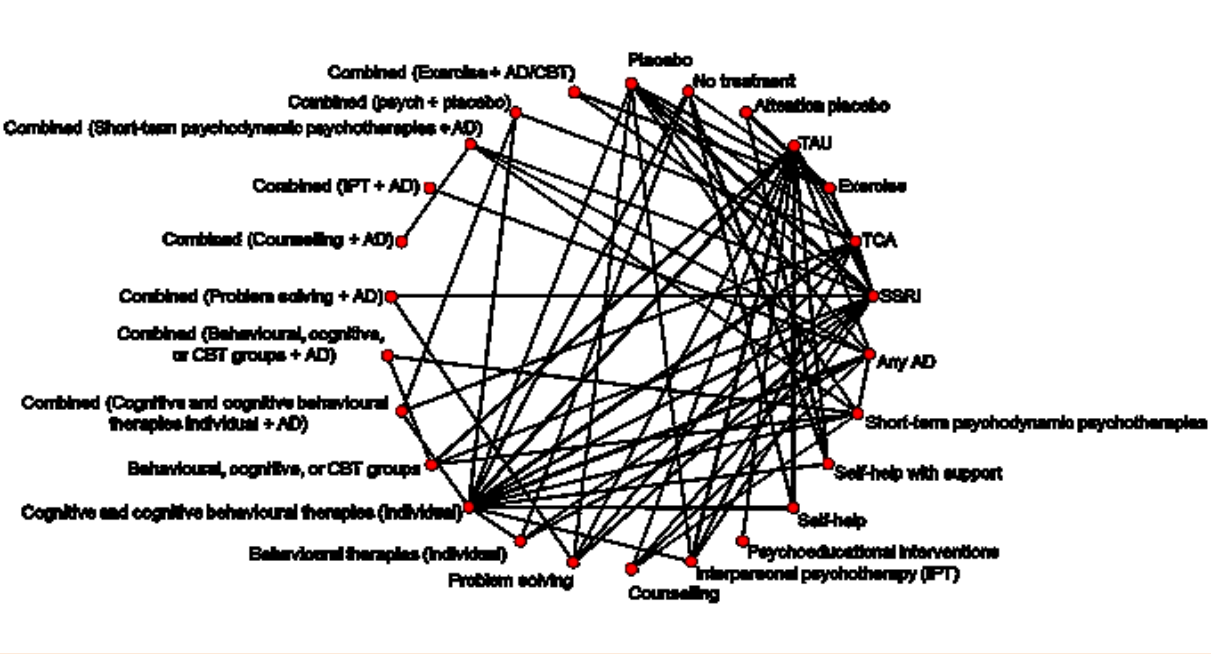


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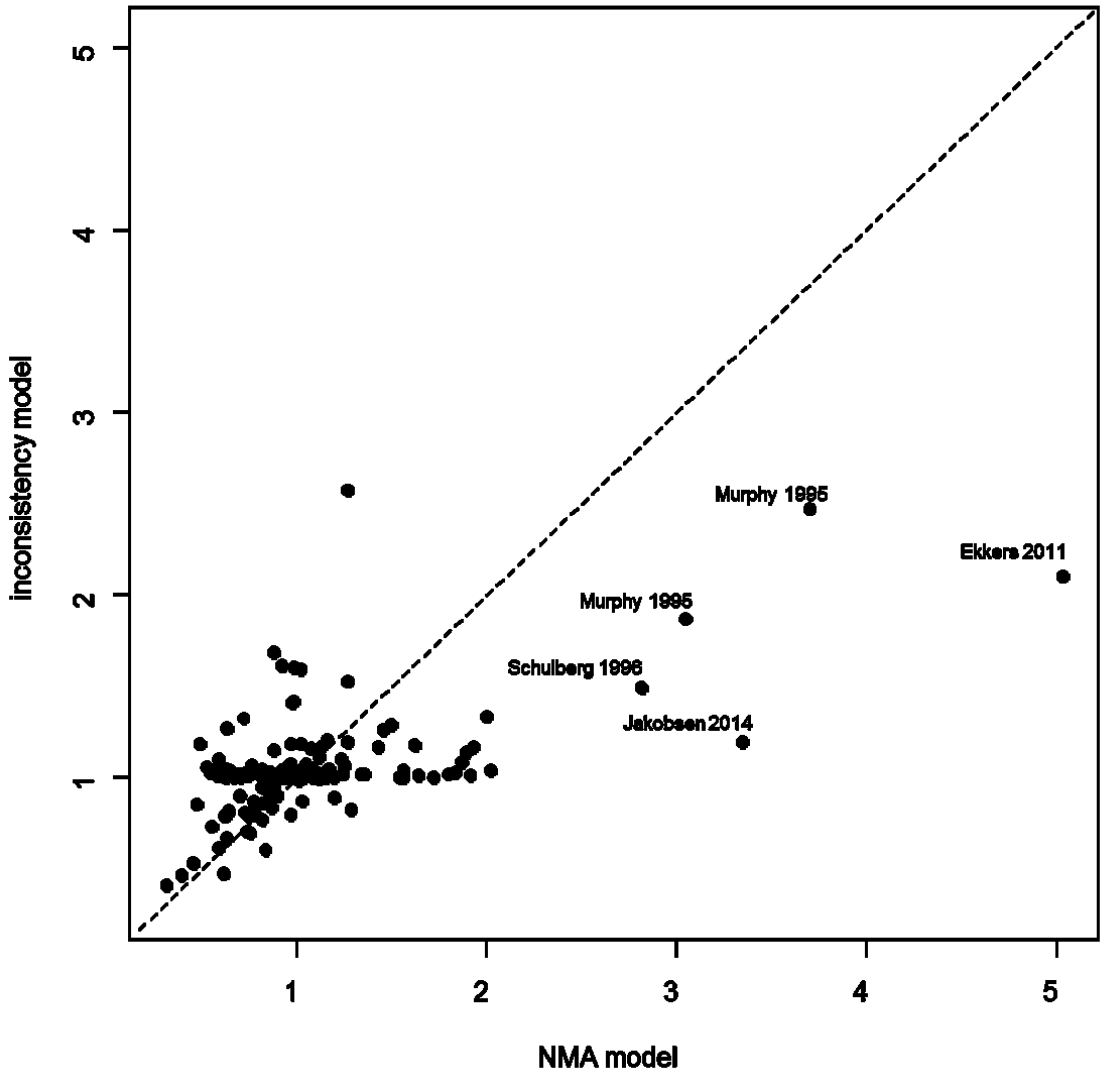
Figure 15: Deviance plot. Remission in completers – less severe depression.



The interventions for which there is evidence of an increased odds of remission in completers compared to Pill placebo are Imipramine, Any SSRI + Enhanced TAU, Escitalopram, Fluoxetine, Sertraline, any AD, Computerised-CBT (CCBT) + TAU, Interpersonal psychotherapy (IPT), Interpersonal counselling, Behavioural activation (BA), CBT individual (over 15 sessions), Third-wave cognitive therapy individual, CBT group (under 15 sessions), CBT group (under 15 sessions) + TAU, Coping with Depression course (group) + TAU, CBT individual (over 15 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, CBT group (under 15 sessions) + imipramine, Supportive psychotherapy + any SSRI, Interpersonal psychotherapy (IPT) + any AD, Short-term psychodynamic psychotherapy individual + Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, and CBT individual (over 15 sessions) + Pill placebo (Figure 53). There is evidence that Waitlist, No treatment, Attention placebo, and Attention placebo + TAU have a decreased odds of remission in completers compared with pill placebo. The classes for which evidence suggests an increased odds of remission in completers compared to Pill placebo are SSRIs, Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual), Behavioural, cognitive, or CBT groups, Combined (Cognitive and cognitive behavioural therapies individual + AD), Combined (Behavioural, cognitive, or CBT groups + AD), Combined (Counselling + AD), Combined (IPT + AD), Combined (Short-term psychodynamic psychotherapies + AD), and Combined (psych

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+ placebo) (Figure 54). There is evidence of No treatment and Attention placebo having a decreased odds of remission in completers compared to Pill placebo.

Combined (Counselling + AD) is the highest ranked class at 1st (95% CrI 1st to 11th). The lowest ranked class is Attention placebo at 24th (95% CrI 21st to 24th). The highest ranked intervention is Supportive psychotherapy + any SSRI with a posterior median rank of 1st (95% CrI 1st to 18th). The lowest ranked intervention is Attention placebo at 42nd (95% CrI 38th to 42nd). Rankings of classes are shown in Table 6; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 6: Posterior median rank and 95% credible intervals by class. Remission in completers – less severe depression.

Class	Posterior median rank	95% CrI
Combined (Counselling + AD)	1	(1, 11)
Combined (Behavioural, cognitive, or CBT groups + AD)	3	(1, 13)
Combined (Short-term psychodynamic psychotherapies + AD)	3	(1, 7)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	4	(1, 13)
Combined (IPT + AD)	5	(1, 16)
Behavioural therapies (individual)	6	(2, 16)
Behavioural, cognitive, or CBT groups	6	(2, 13)
Interpersonal psychotherapy (IPT)	10	(4, 19)
Cognitive and cognitive behavioural therapies (individual)	10	(6, 16)
SSRIs	11	(7, 16)
Psychoeducational interventions	11	(3, 21)
TCAs	12	(7, 19)
Counselling	12	(5, 20)
Exercise	15	(6, 22)
Self-help without support	15	(7, 22)
Combined (Exercise + AD/CBT)	15	(6, 22)
Self-help with support	17	(8, 22)
Pill placebo	18	(14, 22)
Combined (Problem solving + AD)	18	(5, 23)
TAU	19	(12, 22)
Problem solving	19	(10, 22)
Short-term psychodynamic psychotherapies	20	(10, 23)
No treatment	23	(21, 24)
Attention placebo	24	(21, 24)

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1.3.1.41 Outcome: remission in those randomised – less severe depression

An additional analysis was carried out on all trials reporting remission with the number randomised to treatment as the denominator. After excluding trials with zero events in all arms, 69 trials of 60 interventions and 26 classes were included for this outcome (Table 7, Figure 16 and Figure 17). We initially observed a spike in the posterior distribution of the between-study standard deviation, which suggested there was little evidence contributing to the between study heterogeneity. Consequently, we gave the between-study variance an informative prior, log-Normal(-2.34, 1.72) (Lu and Ades 2004), in this model. This was selected from a list of predictive distributions for between-study heterogeneity that are typical

of mental health indicators and we selected the distribution with the largest variance (Turner et al. 2015).

The inconsistency model only notably improved in the prediction of data in individual studies with zero cells, and the DIC favoured the random effects consistency model (Figure 18; Table 32). The between study heterogeneity slightly decreased in the inconsistency model, however overall there is no evidence of inconsistency (Table 32).

Reported results are based on the random-effects NMA model, assuming consistency. Note the model fit is poor and thus results should be interpreted with caution (Table 32). Small between trials heterogeneity was found relative to the size of the intervention effect estimates ($\tau = 0.20$ (95% CrI 0.05 to 0.40)).

Table 7: Interventions, classes and number of patients (N) included in remission in those randomised analysis – less severe depression

	Intervention	N	Class		N
1	Pill placebo	806	**Pill placebo**	1	806
2	Waitlist	128	**No treatment**	2	349
3	No treatment	221		2	
4	Attention placebo	101	**Attention placebo**	3	127
5	Attention placebo + TAU	26		3	
6	TAU	1160	**TAU**	4	1355
7	Enhanced TAU	195		4	
8	Exercise	303	**Exercise***	5	329
9	Exercise + TAU	26		5	
10	Any TCA	240	**TCAs**	6	588
11	Amitriptyline	62		6	
12	Imipramine	181		6	
13	Lofepramine	105		6	
14	Any SSRI	419	**SSRIs**	7	2716
15	Any SSRI + Enhanced TAU	112		7	
16	Citalopram	120		7	
17	Escitalopram	953		7	
18	Fluoxetine	581		7	
19	Sertraline	531		7	
20	Any AD	571	**Any AD***	8	571
21	Short-term psychodynamic psychotherapy individual	213	**Short-term psychodynamic psychotherapies***	9	237
22	Short-term psychodynamic psychotherapy group	24		9	
23	Computerised behavioural activation with support	40	**Self-help with support**	10	717
24	Computerised psychodynamic therapy with support	46		10	
25	Computerised-CBT (CCBT) with support	140		10	
26	Computerised-CBT (CCBT) with support + TAU	452		10	
27	Tailored computerised-CBT (CCBT) with support	39		10	
28	Cognitive bibliotherapy	204	**Self-help without support**	11	872

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	Intervention	N	Class		N
29	Cognitive bibliotherapy + TAU	86		11	
30	Computerised-CBT (CCBT)	214		11	
31	Computerised-CBT (CCBT) + TAU	194		11	
32	Tailored computerised psychoeducation and self-help strategies	174		11	
33	Psychoeducational group programme + TAU	119	**Psychoeducational interventions***	12	119
34	Interpersonal psychotherapy (IPT)	385	**Interpersonal psychotherapy (IPT)***	13	385
35	Emotion-focused therapy (EFT)	17	**Counselling**	14	448
36	Interpersonal counselling	286		14	
37	Non-directive counselling	55		14	
38	Psychodynamic counselling + TAU	73		14	
39	Relational client-centered therapy	17		14	
40	Problem solving individual	110	**Problem solving***	15	194
41	Problem solving individual + enhanced TAU	84		15	
42	Behavioural activation (BA)	109	**Behavioural therapies (individual)***	16	109
43	CBT individual (under 15 sessions)	248	**Cognitive and cognitive behavioural therapies (individual)**	17	751
44	CBT individual (over 15 sessions)	314		17	
45	CBT individual (over 15 sessions) + TAU	15		17	
46	Rational emotive behaviour therapy (REBT) individual	57		17	
47	Third-wave cognitive therapy individual	117		17	
48	CBT group (under 15 sessions)	65	**Behavioural, cognitive, or CBT groups**	18	238
49	CBT group (under 15 sessions) + TAU	105		18	
50	Coping with Depression course (group) + TAU	68		18	
51	CBT individual (over 15 sessions) + any TCA	22	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	19	47
52	CBT individual (over 15 sessions) + imipramine	25		19	
53	CBT group (under 15 sessions) + imipramine	34	**Combined (Behavioural, cognitive, or CBT groups + AD)***	20	34
54	Problem solving individual + any SSRI	35	**Combined (Problem solving + AD)***	21	35

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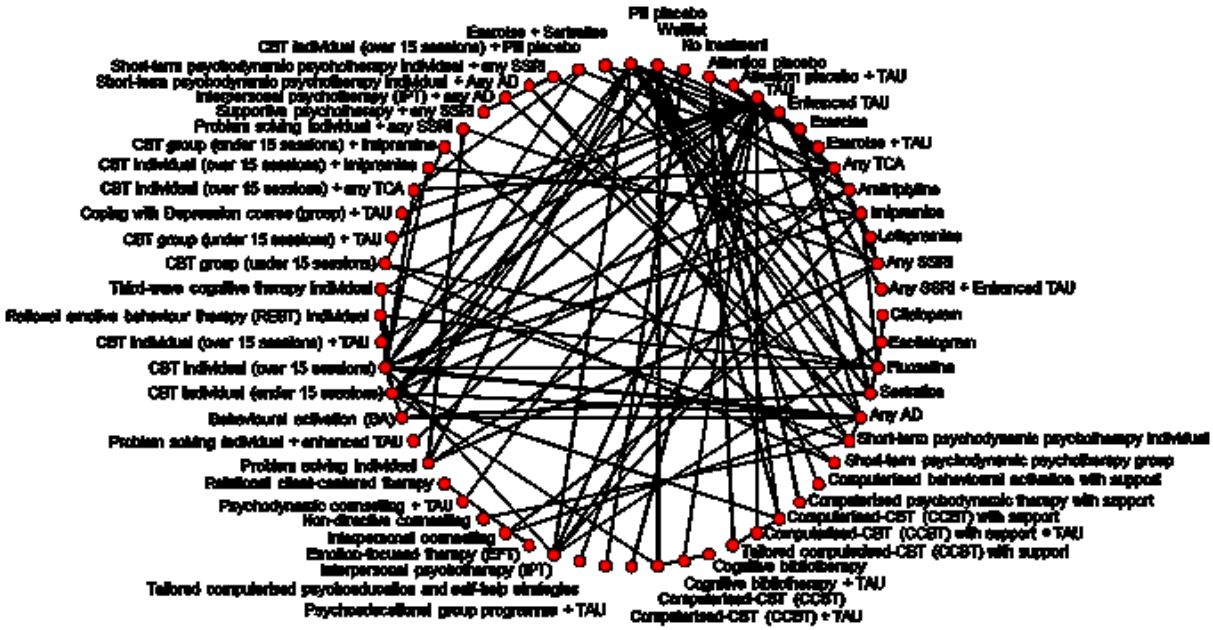
	Intervention	N	Class		N
55	Supportive psychotherapy + any SSRI	20	**Combined (Counselling + AD)***	22	20
56	Interpersonal psychotherapy (IPT) + any AD	65	**Combined (IPT + AD)***	23	65
57	Short-term psychodynamic psychotherapy individual + Any AD	168	**Combined (Short-term psychodynamic psychotherapies + AD)***	24	216
58	Short-term psychodynamic psychotherapy individual + any SSRI	48		24	
59	CBT individual (over 15 sessions) + Pill placebo	17	**Combined (psych + placebo)***	25	17
60	Exercise + Sertraline	110	**Combined (Exercise + AD/CBT)***	26	110
*Variance borrowed from another class as described in section 1.2.3					

Figure 16: Network diagram of all studies included in analysis by intervention. Remission in those randomised – less severe depression.



Note: Without the use of a class network Attention placebo + TAU, Enhanced TAU, Exercise + TAU, Any SSRI + Enhanced TAU, Emotion-focused therapy (EFT), Relational client-centered therapy, and Problem solving individual + enhanced TAU would be disconnected from the rest of the network and would have to be excluded from the analysis.

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Figure 17: Network diagram of all studies included in analysis by class. Remission in those randomised – less severe depression.

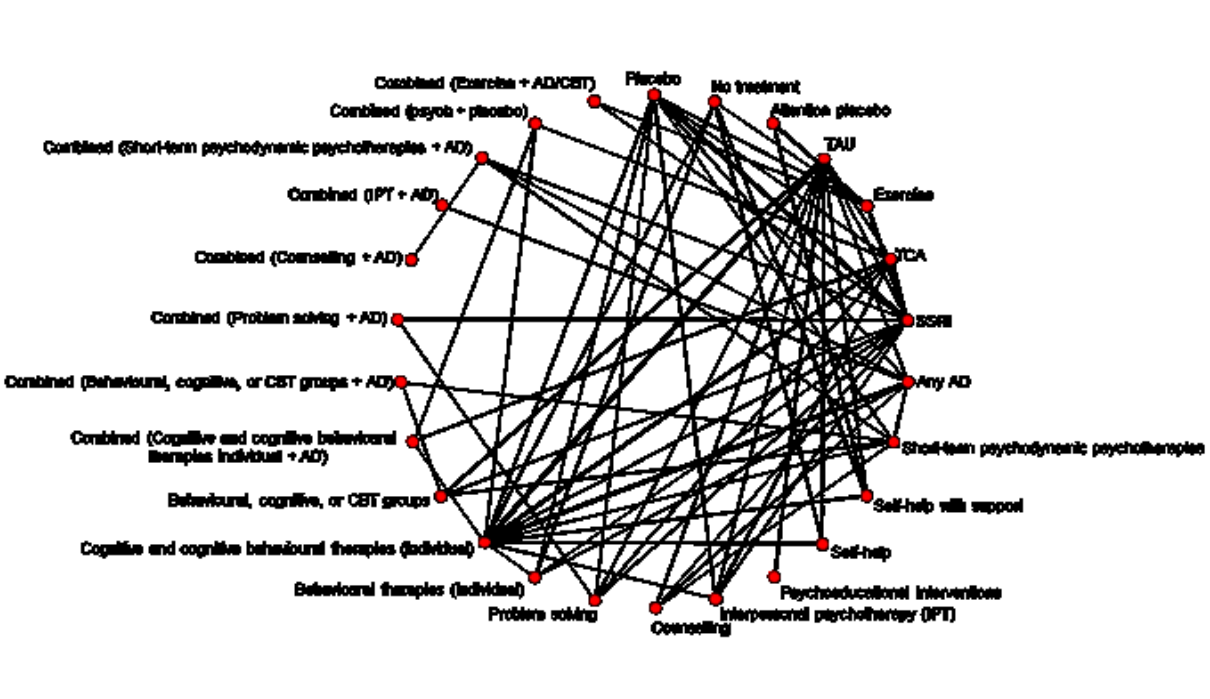
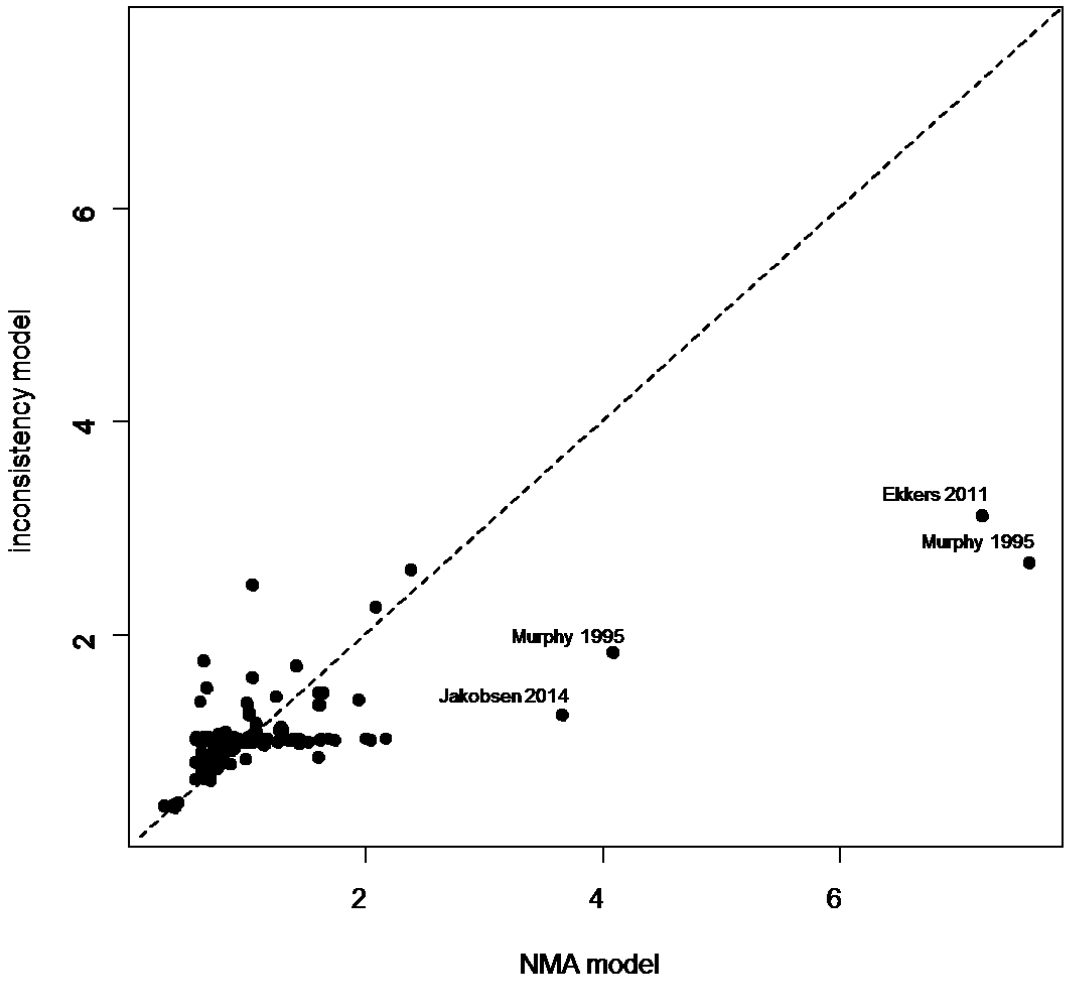


Figure 18: Deviance plot. Remission in those randomised – less severe depression.



The interventions for which there is evidence of an increased odds of remission in those randomised compared to Pill placebo are Imipramine, Any SSRI, Any SSRI + Enhanced TAU, Citalopram, Escitalopram, Fluoxetine, Sertraline, Any AD, Psychoeducational group programme + TAU, Interpersonal psychotherapy (IPT), Interpersonal counselling, Behavioural activation (BA), CBT individual (under 15 sessions), CBT individual (over 15 sessions), CBT individual (over 15 sessions) + TAU, Rational emotive behaviour therapy (REBT) individual, Third-wave cognitive therapy individual, CBT group (under 15 sessions), CBT group (under 15 sessions) + TAU, Coping with Depression course (group) + TAU, CBT individual (over 15 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, CBT group (under 15 sessions) + imipramine, Supportive psychotherapy + any SSRI, Interpersonal psychotherapy (IPT) + any AD, Short-term psychodynamic psychotherapy individual + Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, and CBT individual (over 15 sessions) + Pill placebo (Figure 55). Waitlist and Attention placebo are the only interventions with evidence of a decreased odds of remission in those randomised compared to Pill placebo. The classes for which there is evidence of an increased odds of remission in those randomised compared to Pill placebo are SSRI, Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual), Behavioural, cognitive, or CBT groups, Combined (Cognitive and cognitive behavioural therapies individual + AD), Combined (Behavioural, cognitive, or CBT groups + AD), Combined (Counselling + AD), Combined (Short-term psychodynamic psychotherapies +

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AD), and Combined (psych + placebo) (Figure 56). Attention placebo is the only class for which there is evidence of a decreased odds of remission in those randomised compared to Pill placebo.

Combined (Counselling + AD) is the highest ranked class at 1st (95% CrI 1st to 17th). The highest ranked intervention, Supportive psychotherapy + any SSRI (1st, 95% CrI 1st to 28th), belongs to this class. The lowest ranked class and intervention are both Attention placebo. Rankings of classes are shown in Table 8; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 8: Posterior median rank and 95% credible intervals by class. Remission in those randomised – less severe depression.

Class	Posterior median rank	95% CrI
Combined (Counselling + AD)	1	(1, 17)
Behavioural therapies (individual)	4	(1, 11)
Combined (Behavioural, cognitive, or CBT groups + AD)	4	(1, 19)
Combined (Short-term psychodynamic psychotherapies + AD)	4	(1, 12)
Behavioural, cognitive, or CBT groups	5	(1, 11)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	5	(1, 14)
Combined (IPT + AD)	6	(1, 19)
Psychoeducational interventions	8	(2, 20)
Cognitive and cognitive behavioural therapies (individual)	10	(5, 16)
Interpersonal psychotherapy (IPT)	11	(4, 20)
SSRIs	12	(7, 17)
Counselling	12	(6, 21)
Combined (Problem solving + AD)	13	(3, 23)
TCAs	15	(9, 20)
Self-help with support	16	(8, 22)
Self-help without support	16	(7, 22)
Combined (Exercise + AD/CBT)	16	(5, 23)
Exercise	17	(7, 23)
TAU	18	(10, 23)
Problem solving	18	(8, 23)
Short-term psychodynamic psychotherapies	19	(8, 23)
Pill placebo	20	(16, 22)
No treatment	23	(19, 24)
Attention placebo	24	(21, 24)

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1.3.1.51 Outcome: response in completers – less severe depression

As mentioned in the methods section, this analysis included trials reporting three types of data:

1. Number of individuals responding to treatment in each arm of each study, out of the total number of individuals, defined as those improving by more than a certain percentage from baseline
2. Mean change from baseline (CFB), the standard deviation in CFB and the total number of individuals in that arm

3. Baseline and follow-up means, standard deviations, and number of individuals, for each arm of the study.

The response analysis was first carried out only in those who completed treatment. After excluding trials with zero events in all arms, 51 trials reported response. Out of the remaining studies, 10 reported change from baseline in completers (but not response) and 46 reported baseline and final scores in completers (but not response or change from baseline) . This meant that 107 trials of 75 interventions and 26 classes were included in the analysis for this outcome (Table 9, Figure 19, Figure 20).

No meaningful differences were observed in posterior mean residual deviance or between study heterogeneity, and there was minimal improvement in the prediction of data in individual studies by the inconsistency model, suggesting that there was no evidence of inconsistency (Table 33, Figure 21). Reported results are therefore based on the random-effects NMA model, assuming consistency. Moderate between trials heterogeneity was found relative to the size of the intervention effect estimates (τ =0.45 (95% CrI 0.29 to 0.61)).

Table 9: Interventions, classes and number of patients (N) included in response in completers analysis – less severe depression.

	Intervention	N	Class		N
1	Pill placebo	1632	**Pill placebo**	1	1632
2	Waitlist	431	**No treatment**	2	650
3	No treatment	219		2	
4	Attention placebo	91	**Attention placebo**	3	134
5	Attention placebo + TAU	43		3	
6	TAU	735	**TAU**	4	937
7	Enhanced TAU	202		4	
8	Exercise	210	**Exercise***	5	331
9	Exercise + TAU	121		5	
10	Any TCA	23	**TCAs**	6	829
11	Amitriptyline	349		6	
12	Imipramine	368		6	
13	Lofepramine	89		6	
14	Any SSRI	57	**SSRIs**	7	3022
15	Any SSRI + Enhanced TAU	96		7	
16	Citalopram	609		7	
17	Escitalopram	583		7	
18	Fluoxetine	695		7	
19	Sertraline	982		7	
20	Any AD	349	**Any AD***	8	349
21	Mirtazapine	27	**Mirtazapine**	9	27
22	Short-term psychodynamic psychotherapy individual	135	**Short-term psychodynamic psychotherapies***	10	157
23	Short-term psychodynamic psychotherapy group	22		10	
24	Cognitive bibliotherapy with support	58	**Self-help with support**	11	221
25	Cognitive bibliotherapy with support + TAU	20		11	
26	Computerised-CBT (CCBT) with support	31		11	

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	Intervention	N	Class		N
27	Computerised-CBT (CCBT) with support + TAU	112		11	
28	Behavioural bibliotherapy	19	**Self-help without support**	12	1045
29	Cognitive bibliotherapy	85		12	
30	Cognitive bibliotherapy + TAU	94		12	
31	Computerised cognitive bias modification	36		12	
32	Computerised-CBT (CCBT)	292		12	
33	Computerised-CBT (CCBT) + TAU	172		12	
34	Online positive psychological intervention	95		12	
35	Psychoeducational website	136		12	
36	Tailored computerised psychoeducation and self-help strategies	116		12	
37	Lifestyle factors discussion	157	**Psychoeducational interventions**	13	209
38	Psychoeducational group programme	40		13	
39	Psychoeducational group programme + TAU	12		13	
40	Interpersonal psychotherapy (IPT)	188	**Interpersonal psychotherapy (IPT)***	14	212
41	Interpersonal psychotherapy (IPT) + TAU	24		14	
42	Emotion-focused therapy (EFT)	48	**Counselling**	15	135
43	Interpersonal counselling	42		15	
44	Non-directive counselling	30		15	
45	Relational client-centered therapy	15		15	
46	Problem solving group	15	**Problem solving**	16	244
47	Problem solving individual	86		16	
48	Problem solving individual + TAU	71		16	
49	Problem solving individual + enhanced TAU	72		16	
50	Behavioural activation (BA)	81	**Behavioural therapies (individual)**	17	133
51	Behavioural activation (BA) + TAU	19		17	
52	Behavioural therapy (Lewinsohn 1976)	20		17	
53	Coping with Depression course (individual)	13		17	
54	CBT individual (under 15 sessions)	198	**Cognitive and cognitive behavioural therapies (individual)**	18	731
55	CBT individual (over 15 sessions)	515		18	
56	Third-wave cognitive therapy individual	18		18	
57	CBT group (under 15 sessions)	52	**Behavioural, cognitive, or CBT groups**	19	305

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	Intervention	N	Class		N
58	CBT group (under 15 sessions) + TAU	48		19	
59	CBT group (over 15 sessions)	53		19	
60	Coping with Depression course (group)	25		19	
61	Coping with Depression course (group) + TAU	113		19	
62	Rational emotive behaviour therapy (REBT) group	14		19	
63	CBT individual (over 15 sessions) + any AD	21	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	20	55
64	CBT individual (over 15 sessions) + any TCA	18		20	
65	CBT individual (over 15 sessions) + imipramine	16		20	
66	Problem solving individual + any SSRI	29	**Combined (Problem solving + AD)***	21	29
67	Supportive psychotherapy + any SSRI	34	**Combined (Counselling + AD)***	22	34
68	Interpersonal psychotherapy (IPT) + any AD	53	**Combined (IPT + AD)***	23	60
69	Interpersonal psychotherapy (IPT) + imipramine	7		23	
70	Short-term psychodynamic psychotherapy individual + Any AD	214	**Combined (Short-term psychodynamic psychotherapies + AD)***	24	267
71	Short-term psychodynamic psychotherapy individual + any SSRI	53		24	
72	CBT individual (over 15 sessions) + Pill placebo	17	**Combined (psych + placebo)***	25	46
73	Interpersonal psychotherapy (IPT) + Pill placebo	29		25	
74	Exercise + CBT individual (under 15 sessions)	18	**Combined (Exercise + AD/CBT)***	26	62
75	Exercise + Sertraline	44		26	

*Variance borrowed from another class as described in section 1.2.3

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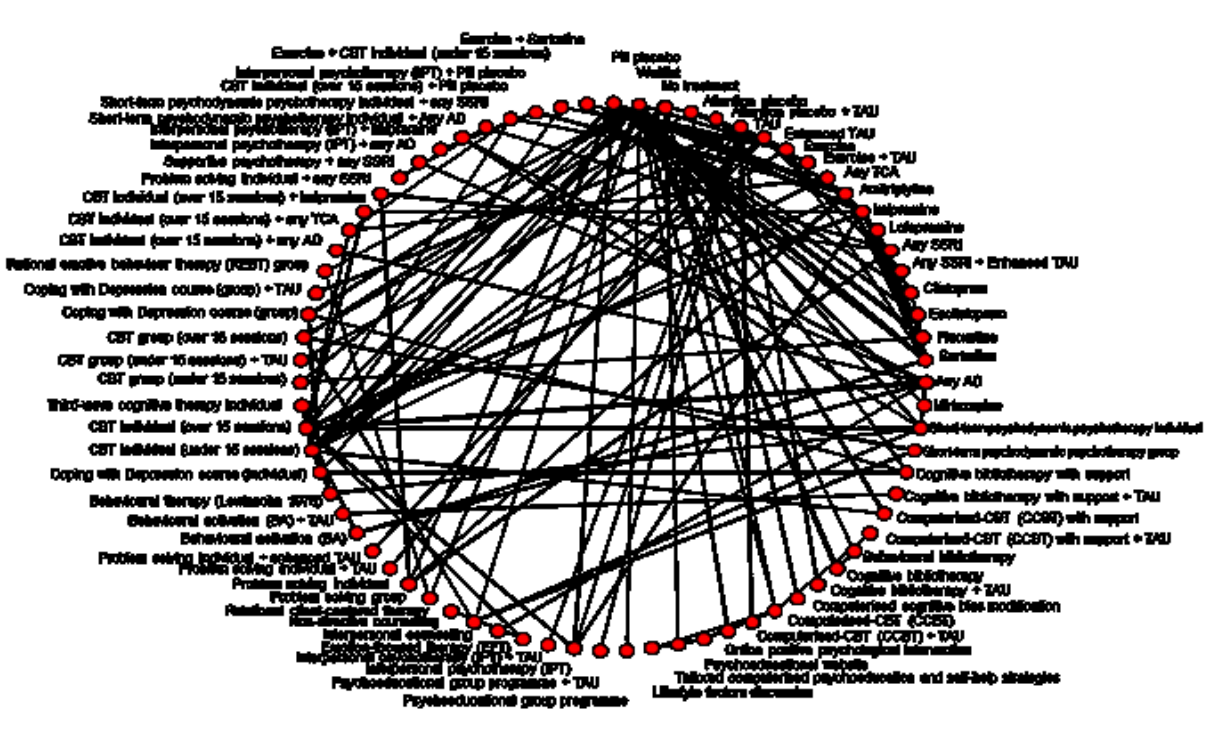
Figure 19: Network diagram of all studies included in analysis by intervention. Response in completers – less severe depression.



Note: Note: Without the use of a class network Cognitive bibliotherapy with support + TAU and Behavioural activation (BA) + TAU would be disconnected from the rest of the network and would have to be excluded from the analysis.

Figure 20: Network diagram of all studies included in analysis by class. Response in completers – less severe depression.

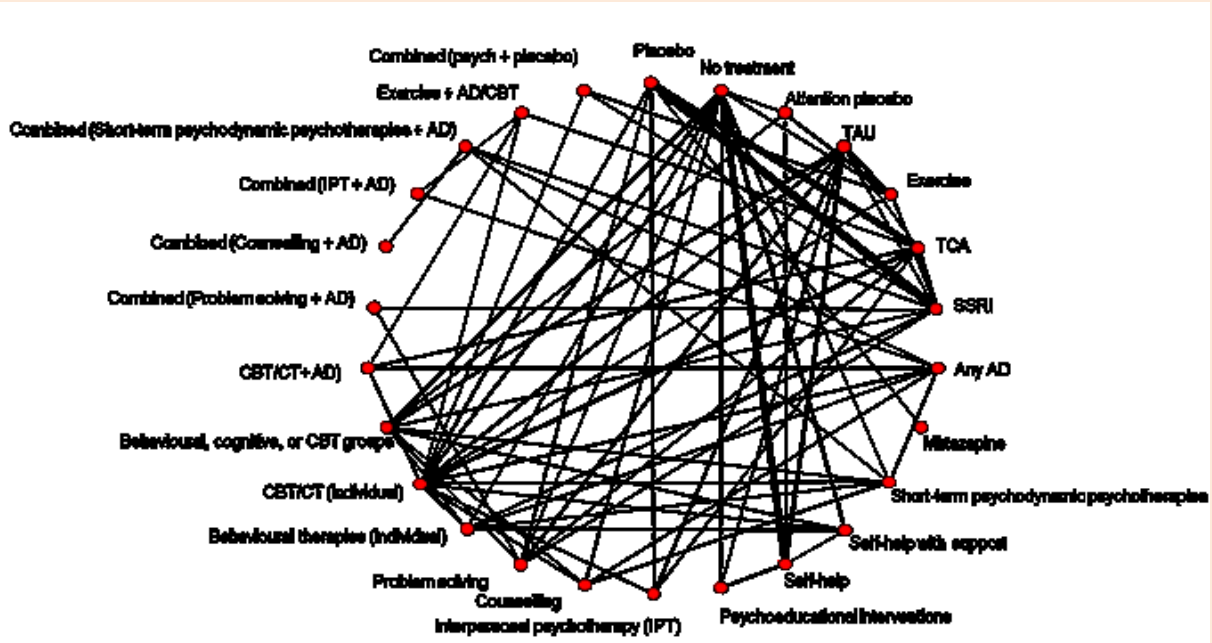


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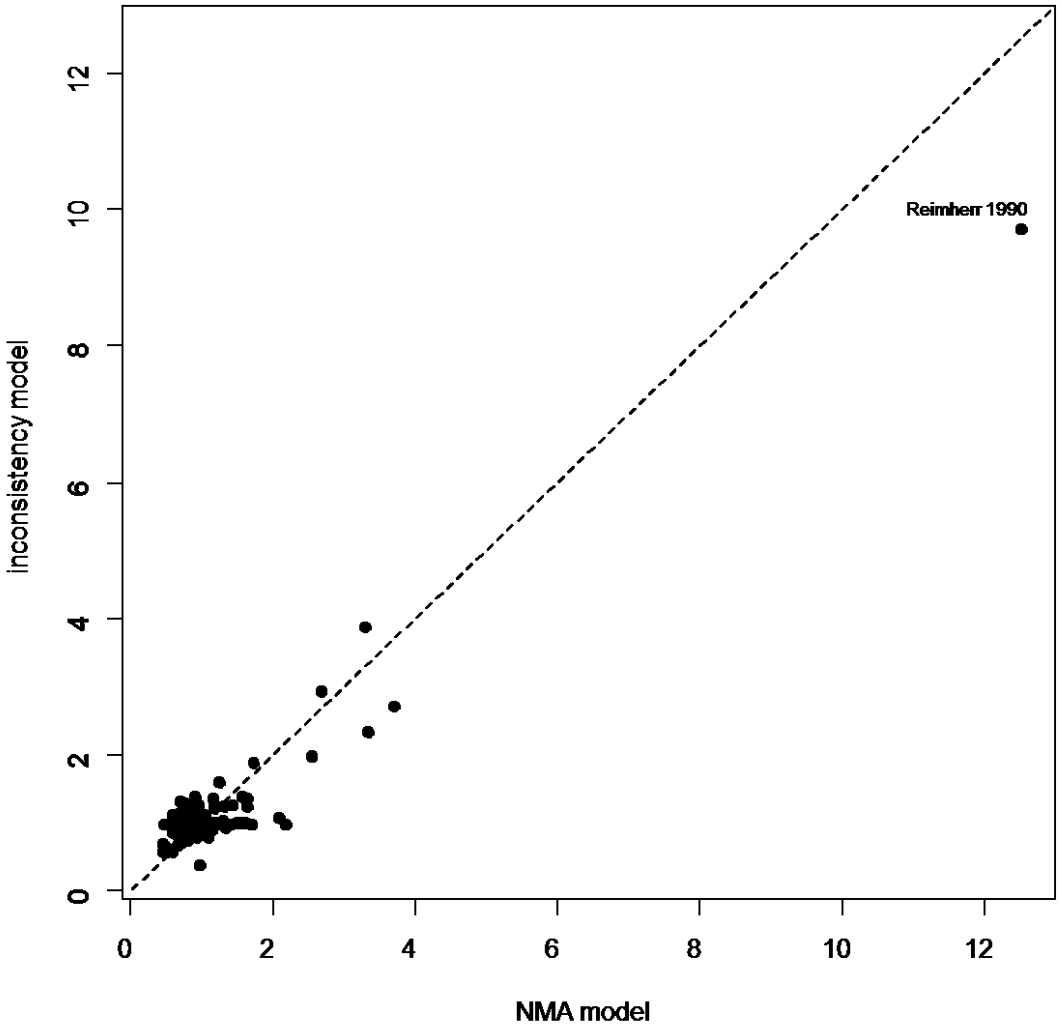
Figure 21



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There is evidence of an increased odds of response in completers compared to Pill placebo for Exercise, Exercise + TAU, Any TCA, Amitriptyline, Imipramine, Lofepramine, Any SSRI, Any SSRI + Enhanced TAU, Citalopram, Escitalopram, Fluoxetine, Sertraline, Any AD, Cognitive bibliotherapy with support + TAU, Computerised-CBT (CCBT) with support, Behavioural bibliotherapy, Cognitive bibliotherapy, Cognitive bibliotherapy + TAU, Computerised cognitive bias modification, Computerised-CBT (CCBT) + TAU, Problem solving individual, Behavioural activation (BA), Behavioural activation (BA) + TAU, Behavioural therapy (Lewinsohn 1976), Coping with Depression course (individual), CBT individual (under 15 sessions), CBT individual (over 15 sessions), Third-wave cognitive therapy individual, CBT group (under 15 sessions), CBT group (under 15 sessions) + TAU, CBT group (over 15 sessions), Coping with Depression course (group), Coping with Depression course (group) + TAU, Rational emotive behaviour therapy (REBT) group, CBT individual (over 15 sessions) + any AD, CBT individual (over 15 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, Interpersonal psychotherapy (IPT) + any AD, Interpersonal psychotherapy (IPT) + imipramine, Short-term psychodynamic psychotherapy individual + Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, CBT individual (over 15 sessions) + Pill placebo, and Interpersonal psychotherapy (IPT) + Pill placebo (Figure 57). There is evidence of a reduction in the odds of response in completers compared to Pill placebo for Waitlist.

The classes for which there is evidence of an increased odds of response in completers compared to Pill placebo are Exercise, TCA, SSRI, any AD, Self-help with support, Self-help,

Behavioural Therapies (Individual), Cognitive and cognitive behavioural therapies (individual), Behavioural, cognitive, or CBT groups, Combined (Cognitive and cognitive behavioural therapies individual + AD), Combined (IPT + AD), Combined (Short-term psychodynamic psychotherapies + AD), and Combined (psych + placebo) (Figure 58). There is no evidence of any classes having a decreased odds of response compared to Pill placebo.

Combined (IPT + AD) is the highest ranked class at 2nd (95% CrI 1st to 17th). The highest ranked interventions are CBT individual (over 15 sessions) + any AD with a posterior median rank of 4th (95% CrI 1st to 26th) and Interpersonal psychotherapy (IPT) + any AD with a posterior median rank of 4th (95% CrI 1st to 35th). The lowest ranked intervention is Waitlist at 53rd (95% CrI 52nd to 53rd). The lowest ranked active intervention is Lifestyle factors discussion at 48th (95% CrI 25th to 52nd). The lowest ranked active class is Psychoeducational Interventions at 19th (95% CrI 7th to 24th). Rankings of classes are shown in Table 10; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 10: Posterior median rank and 95% credible intervals by class. Response in Completers – less severe depression.

Class	Posterior median rank	95% CrI
Combined (IPT + AD)	2	(1, 17)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	3	(1, 12)
Combined (Counselling + AD)	4	(1, 23)
Behavioural therapies (individual)	5	(1, 15)
Combined (Short-term psychodynamic psychotherapies + AD)	5	(1, 18)
Mirtazapine	8	(1, 23)
Cognitive and cognitive behavioural therapies (individual)	8	(3, 17)
Behavioural, cognitive, or CBT groups	9	(3, 17)
TCAs	10	(4, 18)
Exercise	11	(3, 20)
Self-help with support	11	(3, 21)
Self-help without support	11	(4, 18)
SSRIs	12	(5, 18)
Short-term psychodynamic psychotherapies	14	(4, 22)
Counselling	14	(4, 22)
Interpersonal psychotherapy (IPT)	15	(5, 22)
Combined (Problem solving + AD)	15	(2, 24)
Problem solving	17	(8, 22)
Combined (Exercise + AD/CBT)	18	(5, 24)
Attention placebo	19	(7, 24)
Psychoeducational interventions	19	(7, 24)
TAU	20	(11, 24)
Pill placebo	22	(18, 24)
No treatment	24	(20, 24)

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1.3.1.68 Outcome: response in those randomised – less severe depression

The response analysis was also carried out in all patients randomised, including those who discontinued treatment. After excluding trials with zero events in all arms, 53 trials reported response. Out of the remaining studies 11 reported change from baseline (but not response)

and 65 reported baseline and final scores (but not response or change from baseline). This meant that 129 trials of 67 interventions and 26 classes were included in the analysis for this outcome (Table 11, Figure 22 and Figure 23).

No evidence of inconsistency was identified with the NMA model having a lower posterior mean residual deviance and DIC (Table 34). Reported results are therefore based on the random-effects NMA model, assuming consistency. However, note the inconsistency model better predicted the data in Miller 1989b, which was the only study comparing TAU and CBT individual (over 15 sessions) +TAU (Figure 24). Moderate between trials heterogeneity was found relative to the size of the intervention effect estimates (τ =0.37 (95% CrI 0.27 to 0.49).

Table 11: Interventions, classes and number of patients (N) included in response in those randomised analysis – less severe depression.

	Intervention	N	Class		N
1	Pill placebo	2510	**Pill placebo**	1	2510
2	Waitlist	974	**No treatment**	2	1205
3	No treatment	231		2	
4	Attention placebo	265	**Attention placebo**	3	352
5	Attention placebo + TAU	87		3	
6	TAU	1340	**TAU**	4	1586
7	Enhanced TAU	246		4	
8	Exercise	749	**Exercise**	5	986
9	Exercise + TAU	213		5	
10	Internet-delivered therapist-guided physical activity	24		5	
11	Any TCA	57	**TCAs**	6	1261
12	Amitriptyline	437		6	
13	Imipramine	674		6	
14	Lofepramine	93		6	
15	Any SSRI	30	**SSRIs**	7	4406
16	Any SSRI + Enhanced TAU	112		7	
17	Citalopram	725		7	
18	Escitalopram	873		7	
19	Fluoxetine	1110		7	
20	Sertraline	1556		8	
21	Any AD	633	**Any AD***	8	633
22	Mirtazapine	45	**Mirtazapine**	9	45
23	Short-term psychodynamic psychotherapy individual	171	**Short-term psychodynamic psychotherapies***	10	171
24	Cognitive bibliotherapy with support	252	**Self-help with support**	11	698
25	Computerised behavioural activation with support	80		11	
26	Computerised psychodymic therapy with support	46		11	
27	Computerised-CBT (CCBT) with support	268		11	

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	Intervention	N	Class		N
28	Computerised-CBT (CCBT) with support + TAU	52		11	
29	Cognitive bibliotherapy	509	**Self-help without support**	12	1933
30	Cognitive bibliotherapy + TAU	86		12	
31	Computerised mindfulness intervention	41		12	
32	Computerised-CBT (CCBT)	815		12	
33	Online positive psychological intervention	143		12	
34	Psychoeducational website	165		12	
35	Tailored computerised psychoeducation and self-help strategies	174		12	
36	Lifestyle factors discussion	178	**Psychoeducational interventions**	13	411
37	Psychoeducational group programme	114		13	
38	Psychoeducational group programme + TAU	119		13	
39	Interpersonal psychotherapy (IPT)	427	**Interpersonal psychotherapy (IPT)***	14	427
40	Interpersonal counselling	43	**Counselling**	15	239
41	Non-directive counselling	152		15	
42	Wheel of wellness counselling	44		15	
43	Problem solving individual + enhanced TAU	84	**Problem solving***	16	84
44	Behavioural activation	123	**Behavioural therapies (individual)***	17	123
45	CBT individual (under 15 sessions)	144	**Cognitive and cognitive behavioural therapies (individual)**	18	1457
46	CBT individual (under 15 sessions) + TAU	127		18	
47	CBT individual (over 15 sessions)	994		18	
48	CBT individual (over 15 sessions) + TAU	15		18	
49	Rational emotive behaviour therapy (REBT) individual	57		18	
50	Third-wave cognitive therapy individual	90		18	
51	Third-wave cognitive therapy individual + TAU	30		18	
52	CBT group (under 15 sessions)	94	**Behavioural, cognitive, or CBT groups**	19	441
53	CBT group (under 15 sessions) + TAU	105		19	
54	Coping with Depression course (group)	99		19	
55	Third-wave cognitive therapy group	125		19	
56	Third-wave cognitive therapy group + TAU	18		19	

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	Intervention	N	Class		N
57	CBT individual (over 15 sessions) + any TCA	58	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	20	83
58	CBT individual (over 15 sessions) + imipramine	25		20	
59	Supportive psychotherapy + any SSRI	39	**Combined (Counselling + AD)***	21	39
60	Interpersonal psychotherapy (IPT) + any AD	65	**Combined (IPT + AD)***	22	78
61	Interpersonal psychotherapy (IPT) + imipramine	13		22	
62	Short-term psychodynamic psychotherapy individual + Any AD	83	**Combined (Short-term psychodynamic psychotherapies + AD)***	23	147
63	Short-term psychodynamic psychotherapy individual + any SSRI	64		23	
64	CBT individual (over 15 sessions) + Pill placebo	17	**Combined (psych + placebo)***	24	29
65	Interpersonal psychotherapy (IPT) + Pill placebo	12		24	
66	Exercise + Sertraline	79	**Combined (Exercise + AD/CBT)***	25	79
67	Cognitive bibliotherapy + escitalopram	79	**Combined (Self-help + AD)***	26	79

*Variance borrowed from another class as described in section 1.2.3

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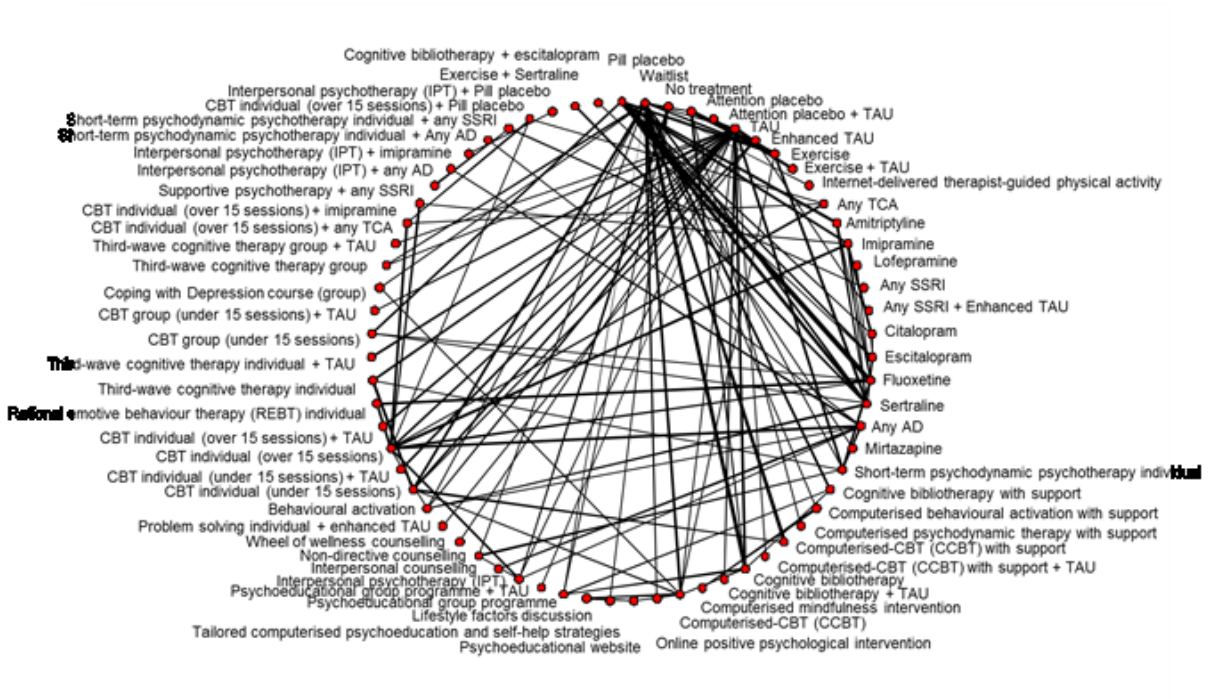
Figure 22: Network diagram of all studies included in analysis by intervention. Response in those randomised – less severe depression.



Note: Without the use of a class network Any SSRI, Supportive psychotherapy + any SSRI, Interpersonal psychotherapy (IPT) + imipramine, Short-term psychodynamic psychotherapy individual + any SSRI, and Interpersonal psychotherapy (IPT) + Pill placebo would be disconnected from the rest of the network and would have to be excluded from the analysis.

Figure 23: Network diagram of all studies included in analysis by class. Response in those randomised – less severe depression.

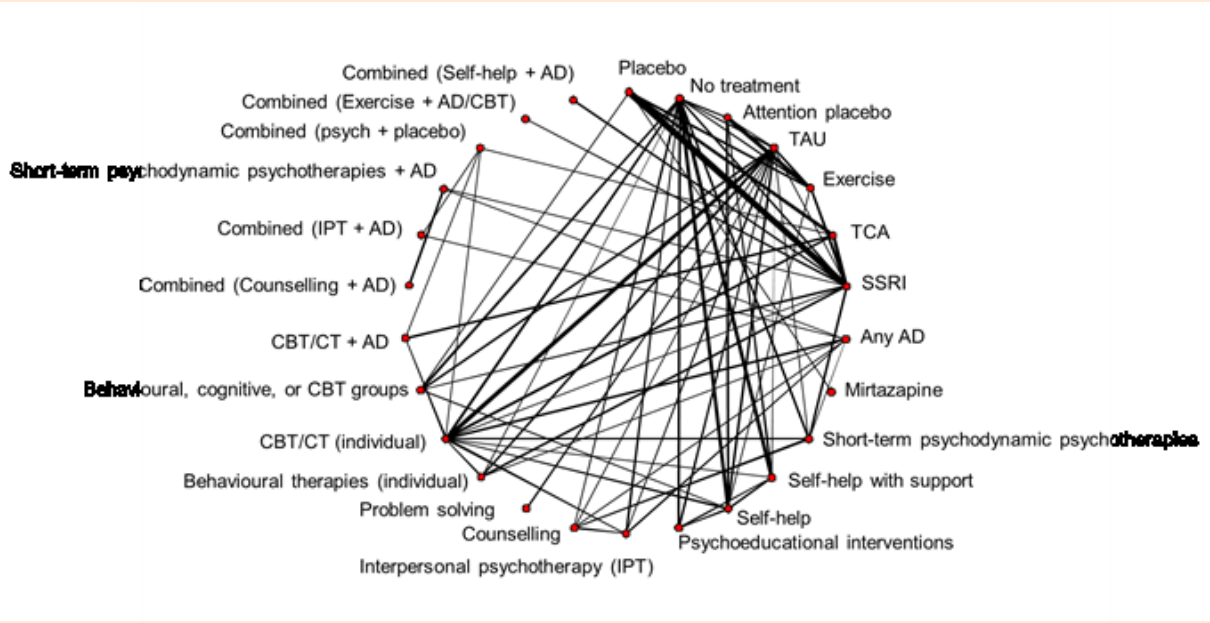


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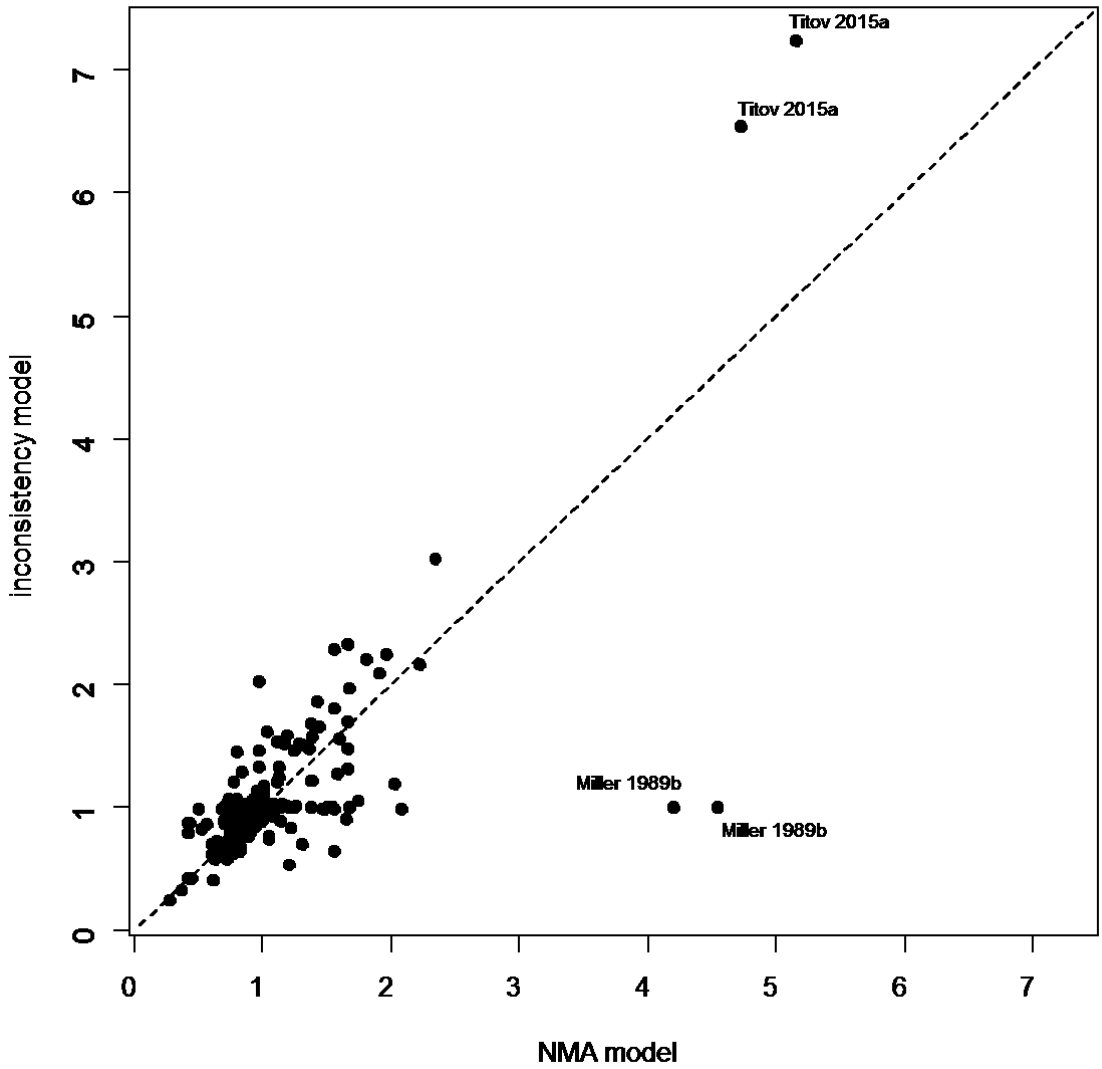
Figure 24: Deviance plot. Response in those randomised – less severe depression.



There is evidence of an increased odds of response in those randomised compared to Pill placebo for Exercise, Amitriptyline, Imipramine, any SSRI, Citalopram, Escitalopram, Fluoxetine, Sertraline, any AD, Mirtazapine, Computerised psychodynamic therapy with support, Computerised-CBT (CCBT) with support, Behavioural activation, CBT individual (under 15 sessions), CBT individual (under 15 sessions) + TAU, CBT individual (over 15 sessions), Rational emotive behaviour therapy (REBT) individual, Third-wave cognitive therapy individual, Third-wave cognitive therapy individual + TAU, CBT individual (over 15 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, Supportive psychotherapy + any SSRI, Interpersonal psychotherapy (IPT) + any AD, Interpersonal psychotherapy (IPT) + imipramine, Short-term psychodynamic psychotherapy individual + Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, CBT individual (over 15 sessions) + Pill placebo, Interpersonal psychotherapy (IPT) + Pill Placebo, and Exercise + Sertraline (Figure 59). Waitlist and No treatment were the only interventions for which there was evidence of a reduction in odds of response in those randomised compared to Pill placebo. The classes for which there is an increased odds of response in those randomised compared to Pill placebo are TCAs, SSRIs, any AD, Mirtazapine, Self-help with support, Behavioural Therapies (individual), Cognitive and cognitive behavioural therapies (individual), Combined (Cognitive and cognitive behavioural therapies individual + AD), Combined (Counselling + AD), Combined (IPT + AD), Combined (Short-term psychodynamic psychotherapies + AD), Combined (psych + placebo), and Combined (Exercise + AD/CBT)

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(Figure 60). No treatment is the only class for which there is evidence of a decreased odds of response in those randomised compared to Pill placebo.

Combined (Exercise + AD/CBT) is the highest ranked class at 2nd (95% CrI 1st to 9th). The highest ranked intervention is Exercise + Sertraline with a posterior median rank of 3rd (95% CrI 1st to 13th). The lowest ranked intervention is Waitlist at 47th (95% CrI 46th to 47th). The lowest ranked active intervention is tailored computerised psychoeducation and self-help strategies at 44th (95% CrI 31st to 47th). The lowest ranked active class is Problem solving at 22nd (95% CrI 10th to 24th). Rankings of classes are shown in Table 12; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 12: Posterior median rank and 95% credible intervals by class. Response in those randomised – less severe depression.

Class	Posterior median rank	95% CrI
Combined (Exercise + AD/CBT)	2	(1, 9)
Combined (IPT + AD)	3	(1, 10)
Behavioural therapies (individual)	4	(1, 10)
Combined (Counselling + AD)	4	(1, 18)
Combined (Short-term psychodynamic psychotherapies + AD)	5	(1, 12)
Mirtazapine	6	(1, 19)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	6	(2, 14)
Cognitive and cognitive behavioural therapies (individual)	9	(5, 15)
Self-help with support	10	(5, 16)
SSRIs	12	(8, 17)
Short-term psychodynamic psychotherapies	12	(4, 21)
TCAs	13	(7, 18)
Counselling	13	(6, 20)
Combined (Self-help + AD)	13	(3, 23)
Exercise	15	(8, 21)
Interpersonal psychotherapy (IPT)	15	(6, 23)
Behavioural, cognitive, or CBT groups	15	(8, 20)
Self-help without support	18	(13, 22)
Psychoeducational interventions	18	(10, 22)
Pill placebo	19	(15, 22)
TAU	21	(15, 23)
Attention placebo	22	(16, 24)
Problem solving	22	(10, 24)
No treatment	24	(22, 24)

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1.3.1.12 Outcome: SMD – less severe depression

As mentioned in the methods section, this analysis also included trials reporting three types of data:

1) Mean change from baseline (CFB), the standard deviation in CFB and the total number of individuals in that arm
2) Baseline and follow-up means, standard deviations, and number of individuals, for each arm of the study

3) Number of individuals responding to treatment in each arm of each study, out of the total number of individuals, defined as those improving by more than a certain percentage from baseline.

This analysis was carried out on all patients randomised. After excluding trials with zero events in all arms, 22 trials reported CFB. Out of the remaining studies 74 reported baseline and follow-up scores (but not CFB) and 13 reported response (but not CFB or baseline and follow-up). This meant that 109 trials of 61 interventions and 25 classes were included in the analysis for this outcome (Table 13, Figure 25 and Figure 26).

Lower DIC values in the NMA random effects consistency model and no meaningful difference in the posterior mean residual deviance and between-study heterogeneity suggested that there was no evidence of inconsistency (Table 35). Reported results are therefore based on the random-effects NMA model, assuming consistency. However, note the inconsistency model better predicted the data in Miller 1989b, which was the only study comparing TAU and CBT individual (over 15 sessions) + TAU (Figure 27). In addition, the model fit of the consistency model is poor and thus results should be interpreted with caution (Table 35).

Relative to the size of the intervention effect estimates, moderate to low between trial heterogeneity was observed for this outcome (τ =0.23 (95% CrI 0.17 to 0.30))

Table 13: Interventions, classes and number of patients (N) included in SMD analysis – less severe depression.

	Intervention	N	Class		N
1	Pill placebo	1645	Pill placebo	1	1645
2	Waitlist	974	No treatment	2	1205
3	No treatment	231		2	
4	Attention placebo	250	Attention placebo	3	294
5	Attention placebo + TAU	44		3	
6	TAU	1228	TAU	4	1366
7	Enhanced TAU	138		4	
8	Exercise	708	Exercise	5	794
9	Exercise + TAU	62		5	
10	Internet-delivered therapist-guided physical activity	24		5	
11	Any TCA	57	TCAs	6	840
12	Amitriptyline	306		6	
13	Imipramine	384		6	
14	Lofepramine	93		6	
15	Citalopram	247	SSRIs	7	3110
16	Escitalopram	873		7	
17	Fluoxetine	739		7	
18	Sertraline	1251		7	
19	Any AD	502	Any AD*	8	502
20	Short-term psychodynamic psychotherapy individual	171	Short-term psychodynamic psychotherapies*	9	171
21	Cognitive bibliotherapy with support	252	Self-help with support	10	698
22	Computerised behavioural activation with support	80		10	

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	Intervention	N	Class		N
23	Computerised psychodynamic therapy with support	46		10	
24	Computerised-CBT (CCBT) with support	268		10	
25	Computerised-CBT (CCBT) with support + TAU	52		10	
26	Cognitive bibliotherapy	509	Self-help without support	11	1933
27	Cognitive bibliotherapy + TAU	86		11	
28	Computerised mindfulness intervention	41		11	
29	Computerised-CBT (CCBT)	815		11	
30	Online positive psychological intervention	143		11	
31	Psychoeducational website	165		11	
32	Tailored computerised psychoeducation and self-help strategies	174		11	
33	Lifestyle factors discussion	178	Psychoeducational interventions	12	421
34	Psychoeducational group programme	114		12	
35	Psychoeducational group programme + TAU	119		12	
36	Interpersonal psychotherapy (IPT)	427	Interpersonal psychotherapy (IPT)*	13	427
37	Non-directive counselling	152	Counselling*	14	196
38	Wheel of wellness counselling	44		14	
39	Problem solving individual + enhanced TAU	84	Problem solving*	15	84
40	Behavioural activation (BA)	123	Behavioural therapies (individual)*	16	123
41	CBT individual (under 15 sessions)	144	Cognitive and cognitive behavioural therapies (individual)	17	1440
42	CBT individual (under 15 sessions) + TAU	127		17	
43	CBT individual (over 15 sessions)	977		17	
44	CBT individual (over 15 sessions) + TAU	15		17	
45	Rational emotive behaviour therapy (REBT) individual	57		17	
46	Third-wave cognitive therapy individual	90		17	
47	Third-wave cognitive therapy individual + TAU	30		17	
48	CBT group (under 15 sessions)	94	Behavioural, cognitive, or CBT groups	18	441
49	CBT group (under 15 sessions) + TAU	105		18	

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	Intervention	N	Class		N
50	Coping with Depression course (group)	99		18	
51	Third-wave cognitive therapy group	125		18	
52	Third-wave cognitive therapy group + TAU	18		18	
53	CBT individual (over 15 sessions) + any TCA	58	Combined (Cognitive and cognitive behavioural therapies individual + AD)	19	83
54	CBT individual (over 15 sessions) + imipramine	25		19	
55	Supportive psychotherapy + any SSRI	19	Combined (Counselling + AD)*	20	19
56	Interpersonal psychotherapy (IPT) + any AD	65	Combined (IPT + AD)*	21	65
57	Short-term psychodynamic psychotherapy individual + Any AD	83	Combined (Short-term psychodynamic psychotherapies + AD)*	22	99
58	Short-term psychodynamic psychotherapy individual + any SSRI	16		22	
59	CBT individual (over 15 sessions) + Pill placebo	17	Combined (psych + placebo)*	23	17
60	Exercise + Sertraline	79	Combined (Exercise + AD/CBT)*	24	79
61	Cognitive bibliotherapy + escitalopram	79	Combined (Self-help + AD)*	25	79

*Variance borrowed from another class as described in section 1.2.3

1

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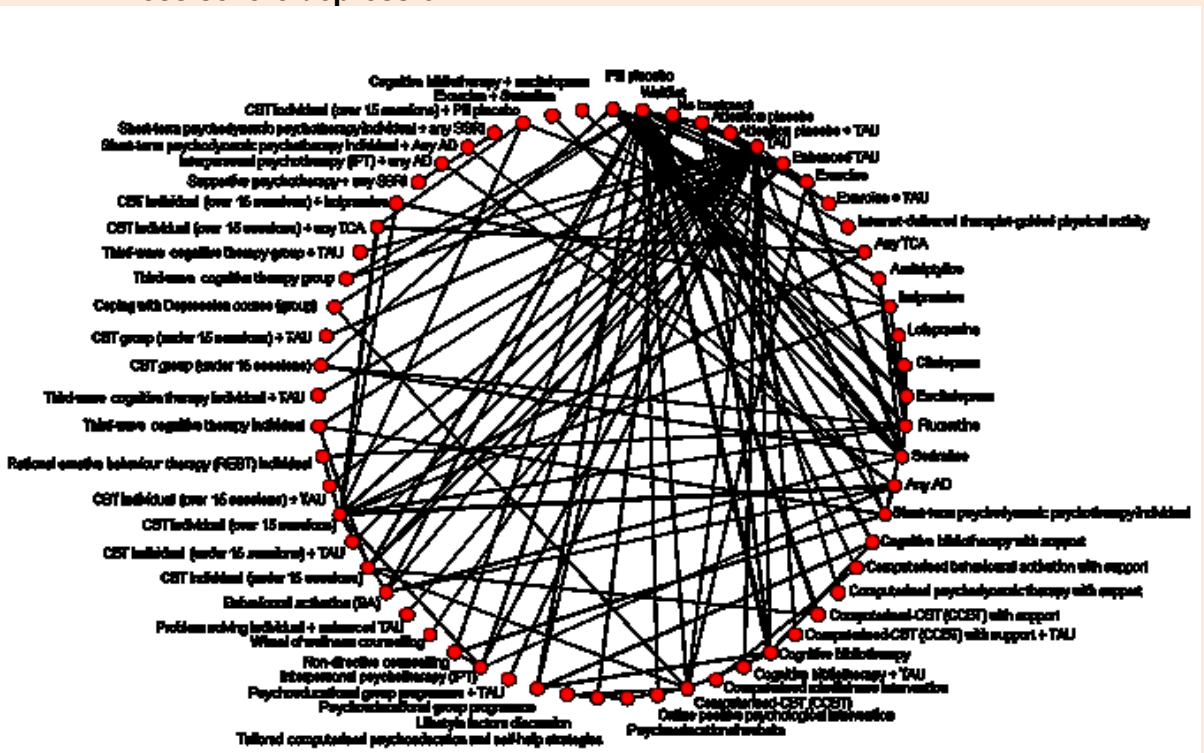
Figure 25: Network diagram of all studies included in analysis by intervention. SMD – less severe depression.



Note: Without the use of a class network Attention placebo + TAU, Exercise + TAU, Supportive psychotherapy + any SSRI, and Short-term psychodynamic psychotherapy individual + any SSRI would be disconnected from the rest of the network and would have to be excluded from the analysis.

Figure 26: Network diagram of all studies included in analysis by class. SMD – less severe depression.

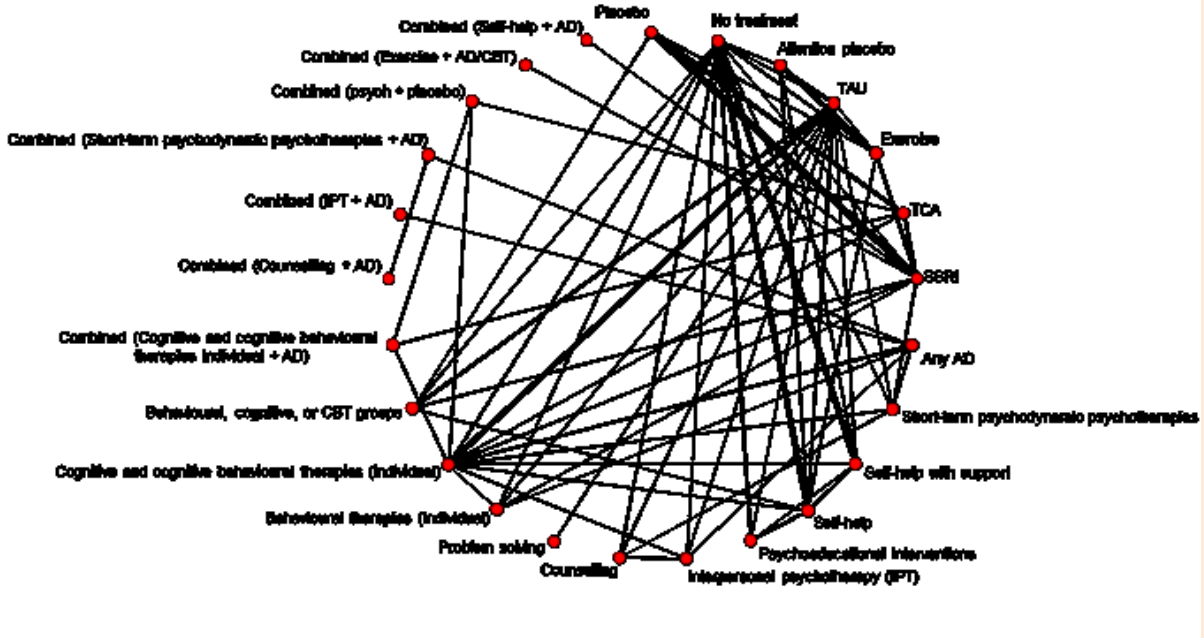
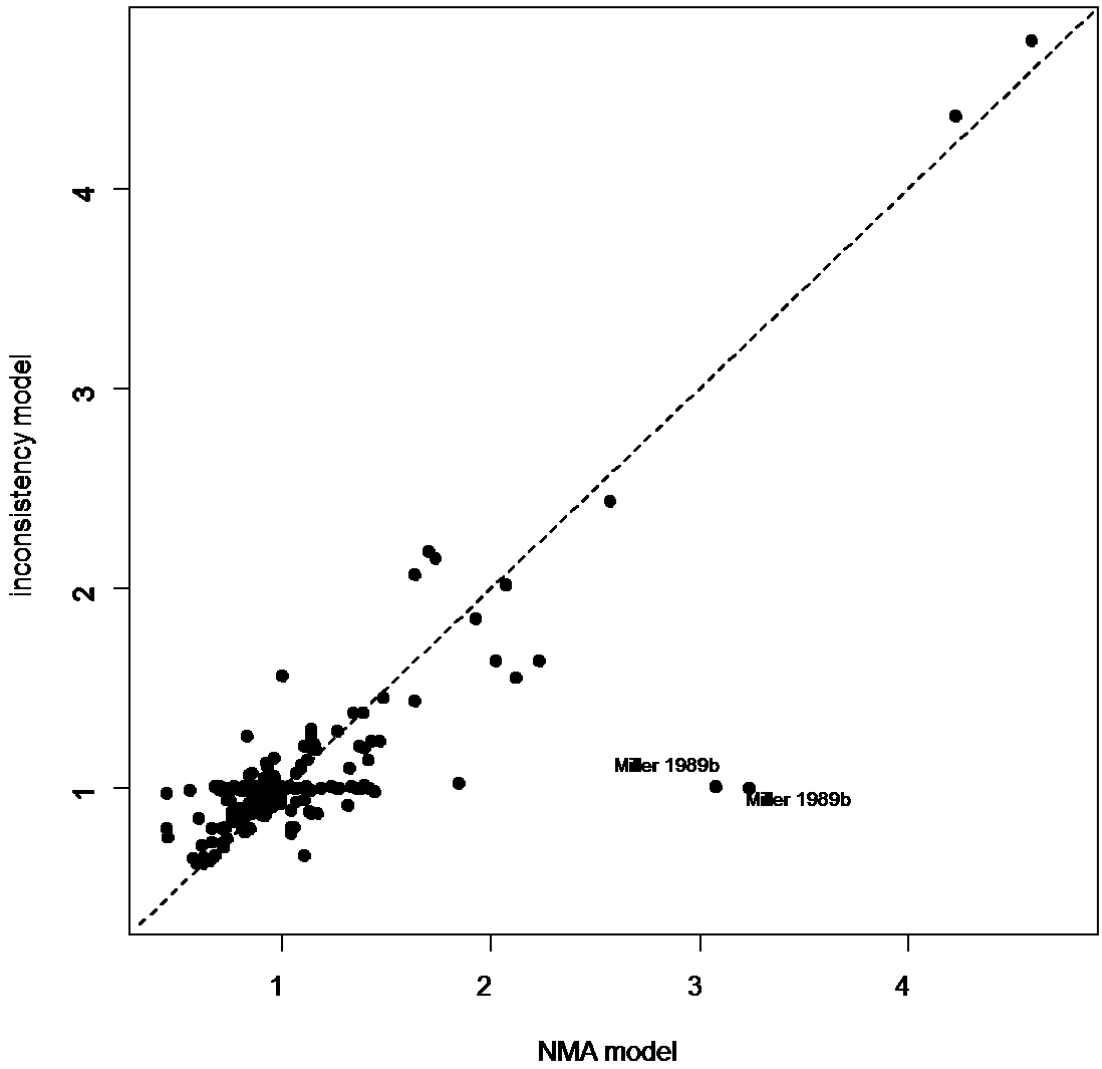


Figure 27: Deviance plot. SMD – less severe depression.



There is evidence suggesting that Amitriptyline, Imipramine, Lofepramine, Fluoxetine, Sertraline, Any AD, Computerised psychodynamic therapy with support, Computerised-CBT (CCBT) with support, Behavioural activation (BA), CBT individual (under 15 sessions), CBT individual (under 15 sessions) + TAU, CBT individual (over 15 sessions), Rational emotive behaviour therapy (REBT) individual, Third-wave cognitive therapy individual, Third-wave cognitive therapy individual + TAU, CBT individual (over 15 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, Interpersonal psychotherapy (IPT) + any AD, Short-term psychodynamic psychotherapy individual + Any AD, CBT individual (over 15 sessions) + Pill placebo, and Exercise + Sertraline have a lower standardized mean difference in depression compared to Pill placebo whereas Waitlist, No treatment, and TAU have a higher standardized mean difference compared to Pill placebo (Figure 61). The classes for which there is evidence suggesting a lower standardized mean difference in depression compared to Pill placebo are TCA, Cognitive and cognitive behavioural therapies (individual), Combined (Cognitive and cognitive behavioural therapies individual + AD), Combined (IPT + AD), Combined (Short-term psychodynamic psychotherapies + AD), Combined (psych + placebo), and Combined (Exercise + AD/CBT) (Figure 62). The only class for which there is evidence of a higher standardized mean difference compared to Pill placebo is No treatment.

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Combined (IPT + AD) is the highest ranked class at 2nd (95% CrI 1st to 8th) along with Combined (Counselling +AD) at 2nd (95% CrI 1st to 20th). The highest ranked interventions are Interpersonal psychotherapy (IPT) + any AD with a posterior median rank of 2nd (95% CrI 1st to 7th) and Supportive psychotherapy + any SSRI with a posterior median rank of 2nd (95% CrI 1st to 39th). The lowest ranked intervention is Waitlist at 44th (95% CrI 42nd to 44th). The lowest ranked active intervention is Tailored computerised psychoeducation and self-help strategies at 41st (95% CrI 26th to 44th). The lowest ranked active class is Problem solving at 22nd (95% CrI 11th to 23rd). Rankings of classes are shown in Table 14; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 14: Posterior median rank and 95% credible intervals by class. SMD – less severe depression.

Class	Posterior median rank	95% CrI
Combined (Counselling + AD)	2	(1, 20)
Combined (IPT + AD)	2	(1, 8)
Combined (Short-term psychodynamic psychotherapies + AD)	3	(1, 14)
Combined (Exercise + AD/CBT)	4	(1, 15)
Behavioural therapies (individual)	5	(1, 17)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	6	(2, 15)
Cognitive and cognitive behavioural therapies (individual)	8	(4, 15)
Self-help with support	9	(4, 16)
TCAs	10	(5, 17)
Short-term psychodynamic psychotherapies	11	(3, 21)
Exercise	12	(5, 20)
SSRIs	12	(7, 18)
Combined (Self-help + AD)	13	(3, 22)
Interpersonal psychotherapy (IPT)	14	(4, 22)
Behavioural, cognitive, or CBT groups	14	(8, 20)
Counselling	15	(5, 21)
Psychoeducational interventions	16	(8, 21)
Pill placebo	17	(13, 20)
Self-help without support	17	(10, 21)
Attention placebo	19	(9, 22)
TAU	21	(15, 23)
No treatment	22	(19, 23)
Problem solving	22	(11, 23)

Update 2018

1.3.22 Population: more severe depression

1.3.2.13 Outcome: discontinuation for any reason – more severe depression

After excluding trials with zero events in all arms, and one trial (Chaudry 1998) that delayed convergence, 125 trials of 53 interventions and 23 classes were included for this outcome (Table 15, Figure 28 and Figure 29). Note that Chaudry 1998 provided the direct evidence on CBT individual (under 15 sessions) + Pill placebo. This intervention was only connected to the network at a class level and the comparator that connected this intervention to the network had zero events. This delayed convergence and the results on CBT individual (under 15 sessions) + Pill placebo were very uncertain, even after applying a continuity correction.

Lower DIC values in the NMA random effects consistency model and no meaningful differences were found in the posterior mean residual deviance and between-study heterogeneity (Table 36). The inconsistency model only notably improved in the prediction of data in individual studies with zero cells (Figure 30). Therefore, there is no evidence of inconsistency and reported results are therefore based on the random-effects NMA model, assuming consistency. Moderate between trials heterogeneity was observed relative to the size of the intervention effect estimates (τ =0.46 (95% CrI 0.36 to 0.59)).

Table 15: Interventions, classes and number of patients (N) included in discontinuation for any reason analysis – more severe depression.

	Intervention	N	Class		N
1	Pill placebo	4210	**Pill placebo**	1	4210
2	Waitlist	350	**No treatment**	2	350
3	Attention placebo	87	**Attention placebo**	3	154
4	Attention placebo + TAU	67		3	
5	TAU	1275	**TAU**	4	1375
6	Enhanced TAU	100		4	
7	Exercise	53	**Exercise**	5	118
8	Exercise + TAU	45		5	
9	Yoga + TAU	20		5	
10	Any TCA	71	**TCAs**	6	3253
11	Amitriptyline	1757		6	
12	Imipramine	1300		6	
13	Lofepramine	125		6	
14	Citalopram	1789	**SSRIs**	7	6388
15	Escitalopram	1782		7	
16	Fluoxetine	2125		7	
17	Sertraline	692		7	
18	Any AD	51	**Any AD***	8	51
19	Mirtazapine	832	**Mirtazapine**	9	832
20	Short-term psychodynamic psychotherapy individual + TAU	44	**Short-term psychodynamic psychotherapies***	10	44
21	Long-term psychodynamic psychotherapy individual	90	**Long-term psychodynamic psychotherapies***	11	90
22	Cognitive bibliotherapy with support + TAU	141	**Self-help with support**	12	215
23	Computerised-CBT (CCBT) with support	25		12	
24	Computerised-problem solving therapy with support	49		12	
25	Cognitive bibliotherapy + TAU	50	**Self-help without support**	13	1040
26	Computerised cognitive bias modification	76		13	
27	Computerised-CBT (CCBT)	356		13	
28	Computerised-CBT (CCBT) + TAU	438		13	
29	Computerised-CBT (CCBT) + enhanced TAU	32		13	

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	Intervention	N	Class		N
30	Computerised-problem solving therapy	88		13	
31	Psychoeducational group programme	228	**Psychoeducational interventions***	14	228
32	Interpersonal psychotherapy (IPT)	95	**Interpersonal psychotherapy (IPT)***	15	95
33	Counselling (any type)	52	**Counselling**	16	157
34	Emotion-focused therapy (EFT)	19		16	
35	Non-directive counselling	67		16	
36	Relational client-centered therapy	19		16	
37	Problem solving group	30	**Problem solving***	17	30
38	Behavioural activation (BA)	172	**Behavioural therapies (individual)***	18	193
39	Behavioural activation (BA) + TAU	21		18	
40	CBT individual (under 15 sessions)	157	**Cognitive and cognitive behavioural therapies (individual) [CBT/CT]**	19	628
41	CBT individual (under 15 sessions) + TAU	219		19	
42	CBT individual (under 15 sessions) + enhanced TAU	35		19	
43	CBT individual (over 15 sessions)	206		19	
44	Third-wave cognitive therapy individual	11		19	
45	CBT group (under 15 sessions)	80	**Behavioural, cognitive, or CBT groups**	20	188
46	CBT group (over 15 sessions) + TAU	47		20	
47	Coping with Depression course (group)	31		20	
48	Third-wave cognitive therapy group	30		20	
49	CBT individual (under 15 sessions) + escitalopram	52	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	21	127
50	CBT individual (over 15 sessions) + amitriptyline	15		21	
51	CBT individual (over 15 sessions) + any SSRI	60		21	
52	Short-term psychodynamic psychotherapy individual + any TCA	47	**Combined (Short-term psychodynamic psychotherapies + AD)***	22	47
53	Long-term psychodynamic psychotherapy individual + fluoxetine	91	**Combined (Long-term psychodynamic psychotherapies + AD)***	23	91

*Variance borrowed from another class as described in section 1.2.3

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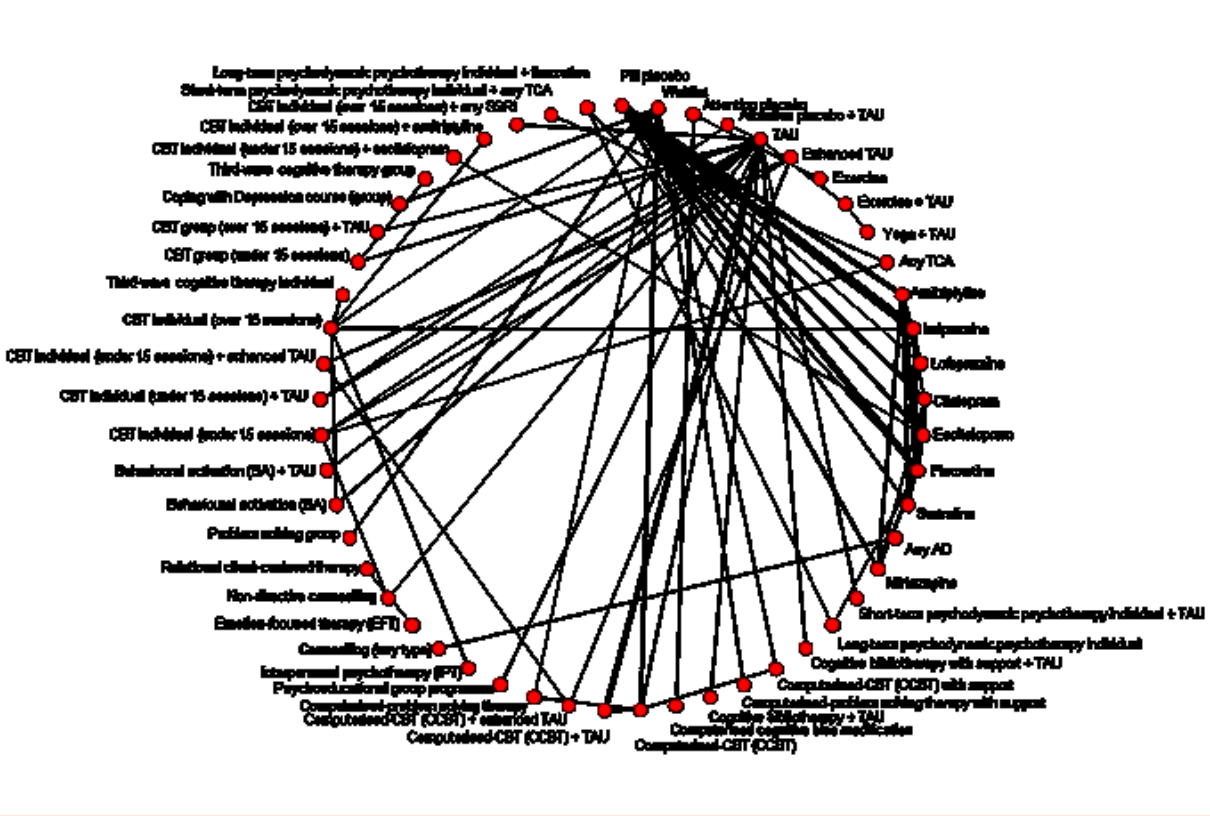
Figure 28: Network diagram of all studies included in analysis by intervention. Discontinuation for any reason – more severe depression.



Note: Without the use of a class network Attention placebo, Exercise, Any AD, Computerised cognitive bias modification, Counselling (any type), Emotion-focused therapy (EFT), and Relational client-centered therapy would be disconnected from the rest of the network and would have to be excluded from the analysis.

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Figure 29: Network diagram of all studies included in analysis by class. Discontinuation for any reason – more severe depression.

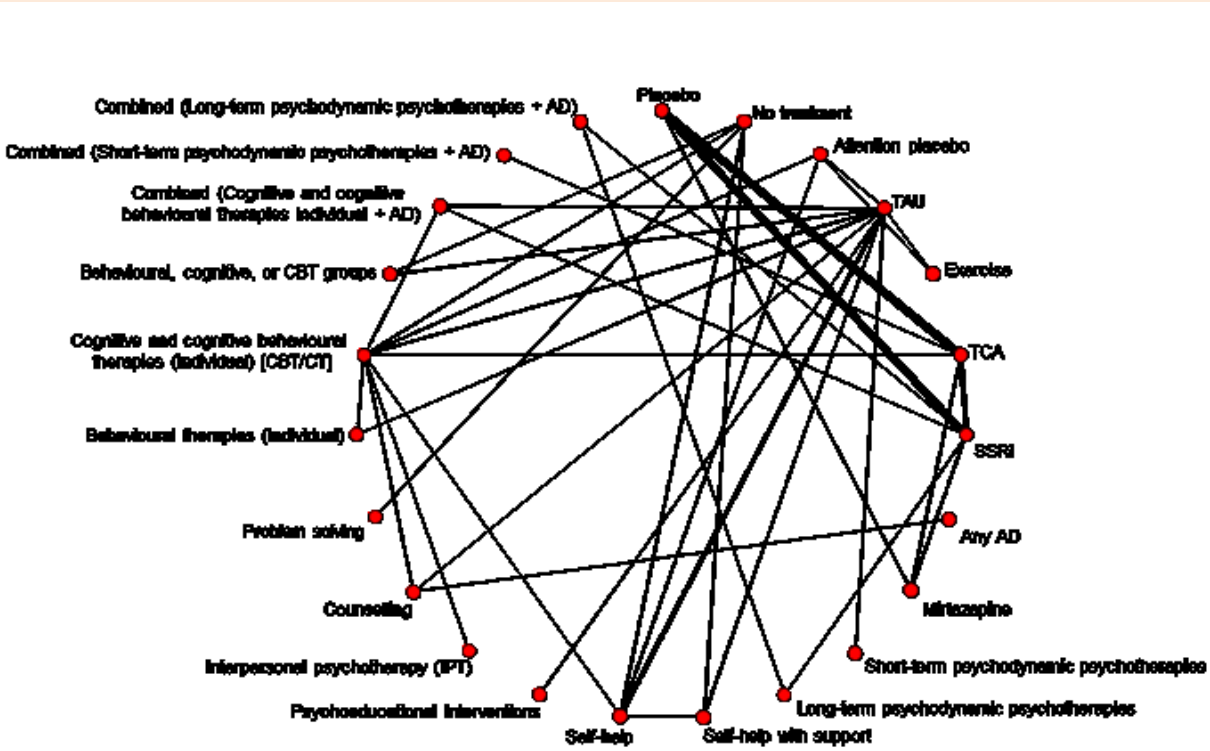

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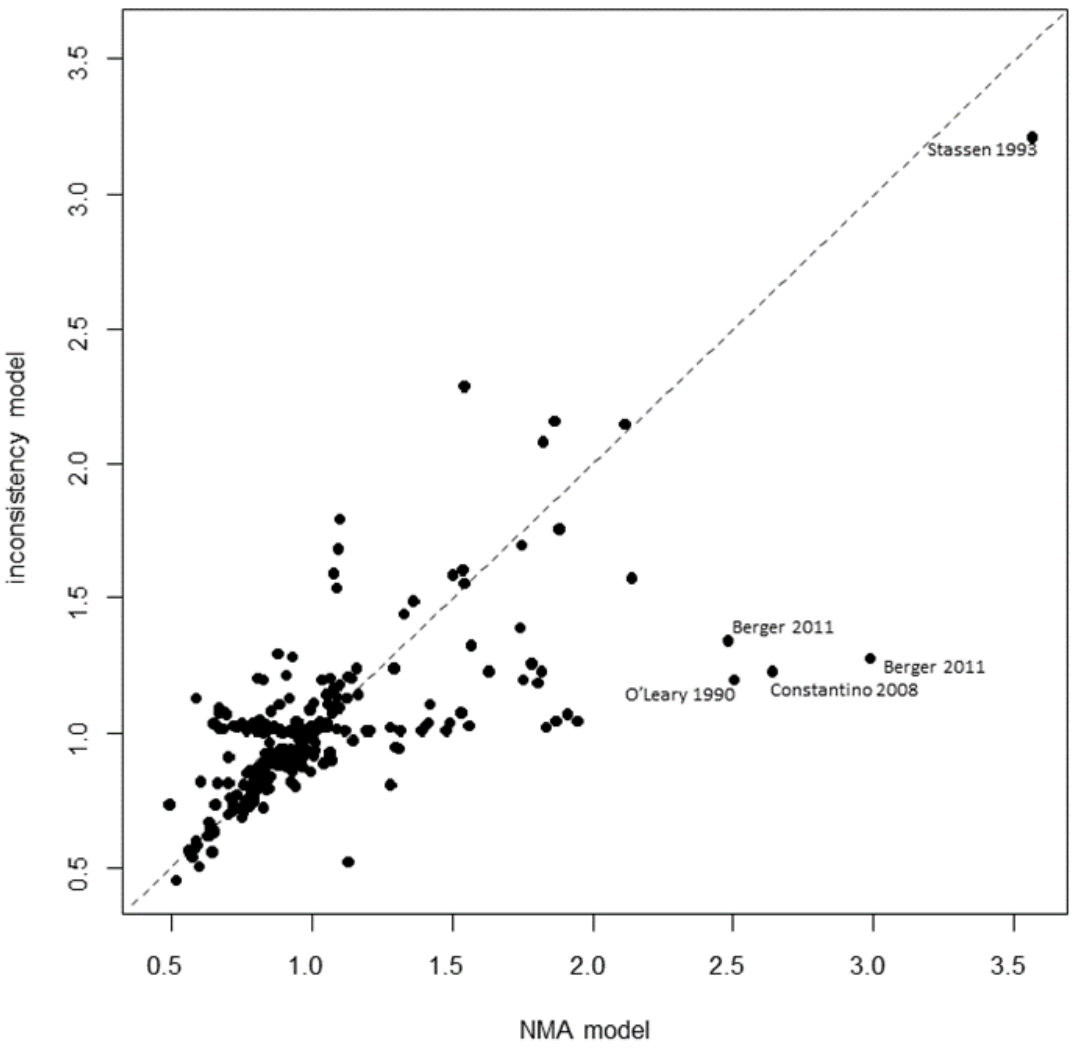
Figure 30: Deviance plot. Discontinuation for any reason – more severe depression.



There is no evidence to suggest any interventions or classes have a decreased odds of discontinuation for any reason compared to Pill placebo (Figure 63 and Figure 64). There is only evidence suggesting Psychoeducational group programme and its class, Psychoeducational interventions, have an increased odds in discontinuation for any reason compared to Pill placebo.

Problem solving is the highest ranked class at 1st (95% CrI 1st to 20th). The highest ranked intervention, Problem solving group, belongs to this class with a posterior median rank of 2nd (95% CrI 1st to 34th). The lowest ranked intervention is Psychoeducational group programme at 37th (95% CrI 35th to 37th). Its corresponding class, Psychoeducational interventions, ranked the lowest at 22nd (95% CrI 20th to 22nd). Rankings of classes are shown in Table 16; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 16: Posterior median rank and 95% credible intervals by class. Discontinuation for any reason – more severe depression.

Class	Posterior median rank	95% CrI
Problem solving	1	(1, 20)
Exercise	4	(1, 20)

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Class	Posterior median rank	95% CrI
No treatment	5	(1, 16)
Interpersonal psychotherapy (IPT)	5	(1, 19)
Self-help with support	6	(1, 17)
Counselling	6	(1, 20)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	7	(2, 15)
TAU	9	(3, 18)
Behavioural, cognitive, or CBT groups	11	(3, 20)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	11	(3, 19)
Behavioural therapies (individual)	12	(3, 21)
Attention placebo	13	(3, 21)
Mirtazapine	13	(3, 19)
TCAs	14	(4, 19)
Short-term psychodynamic psychotherapies	14	(2, 21)
Self-help without support	14	(7, 20)
SSRIs	15	(5, 19)
Pill placebo	16	(7, 20)
Long-term psychodynamic psychotherapies	16	(2, 21)
Combined (Short-term psychodynamic psychotherapies + AD)	18	(2, 22)
Combined (Long-term psychodynamic psychotherapies + AD)	20	(7, 22)
Psychoeducational interventions	22	(20, 22)

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1.3.2.21 Outcome: discontinuation due to SE – more severe depression

After excluding trials with zero events in all arms and those which did not report both discontinuation and discontinuation due to SE, 53 trials of 14 interventions and 6 classes were included for this outcome (Table 17, Figure 31 and Figure 32). A continuity correction was applied to data containing at least one zero cell to stabilize the results.

There was no evidence of inconsistency with higher posterior mean residual deviance and DIC values in the inconsistency model, and minimal improvement was observed in the prediction of data in individual studies by the inconsistency model (Table 37; Figure 33). Reported results are therefore based on the random-effects NMA model, assuming consistency. Relative to the size of the intervention effect estimates, high between trial heterogeneity was observed for this outcome $(\tau = 0.78\ (95\%\ \text{CrI}\ 0.41\ \text{to}\ 1.21))$.

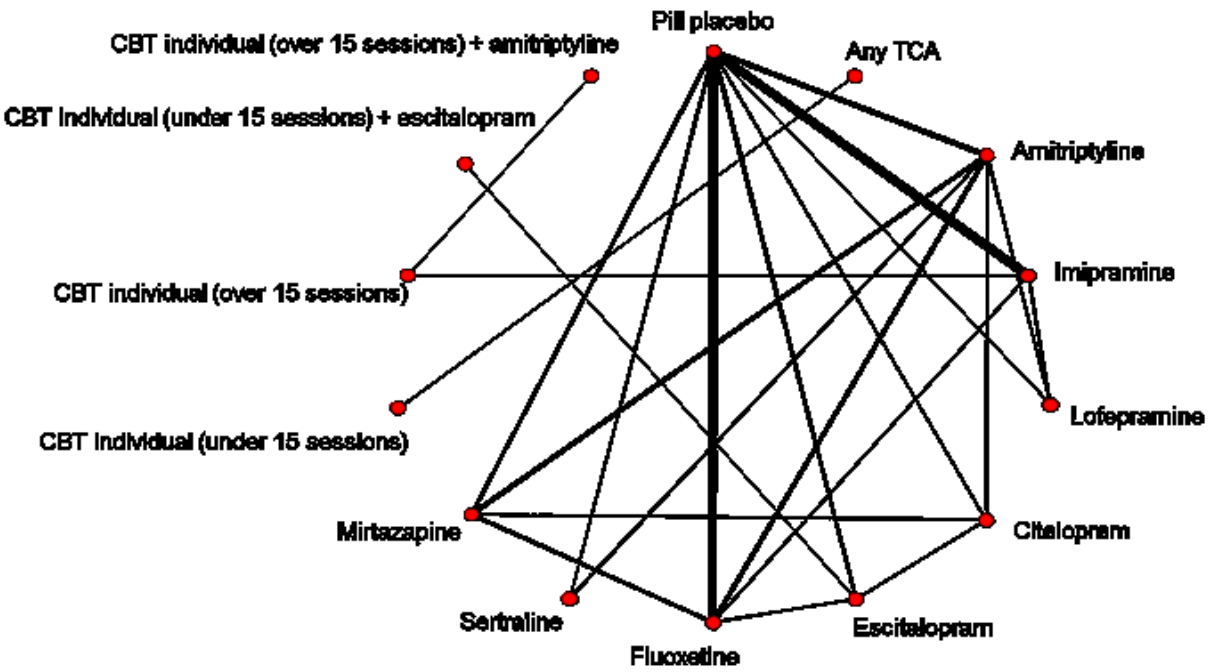
Table 17: Interventions, classes and number of patients (N) included in discontinuation due to SE analysis – more severe depression.

	Intervention	N	Class		N
1	Pill placebo	913	Pill placebo	1	913
2	Any TCA	3	TCAs	2	670
3	Amitriptyline	301		2	
4	Imipramine	337		2	
5	Lofepramine	29		2	
6	Citalopram	150	SSRIs	3	691
7	Escitalopram	108		3	
8	Fluoxetine	389		3	

	Intervention	N	Class		N
9	Sertraline	44		3	
10	Mirtazapine	134	Mirtazapine	4	134
11	CBT individual (under 15 sessions)	2	Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	5	8
12	CBT individual (over 15 sessions)	6		5	
13	CBT individual (under 15 sessions) + escitalopram	12	Combined (Cognitive and cognitive behavioural therapies individual + AD)*	6	16
14	CBT individual (over 15 sessions) + amitriptyline	4		6	

*Variance borrowed from another class as described in section 1.2.3

Figure 31: Network diagram of every study included in analysis by intervention. Discontinuation due to SE – more severe depression.



Note: Without the use of a class network Any TCA and CBT individual (under 15 sessions) would be disconnected from the rest of the network and would have to be excluded from the analysis.

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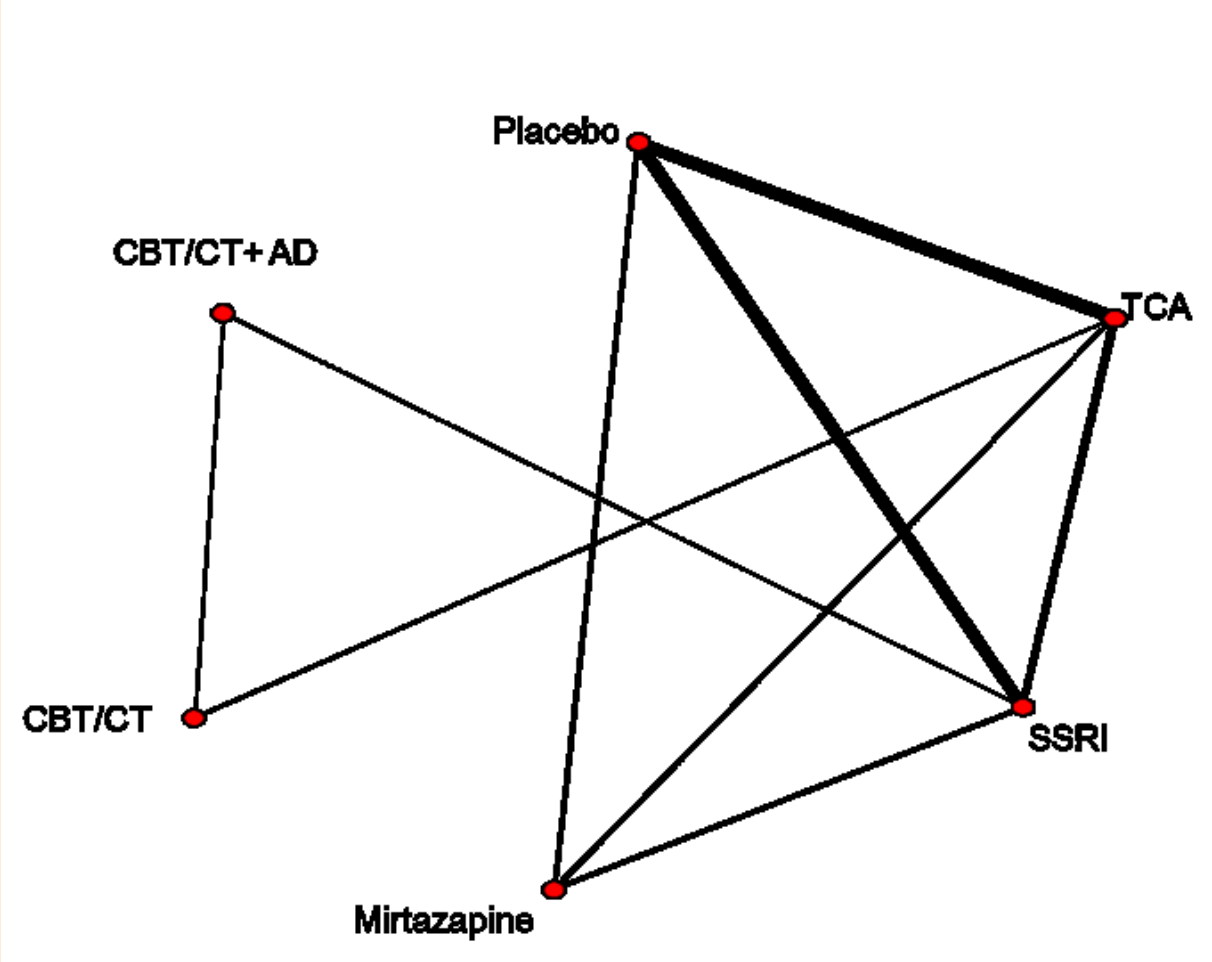
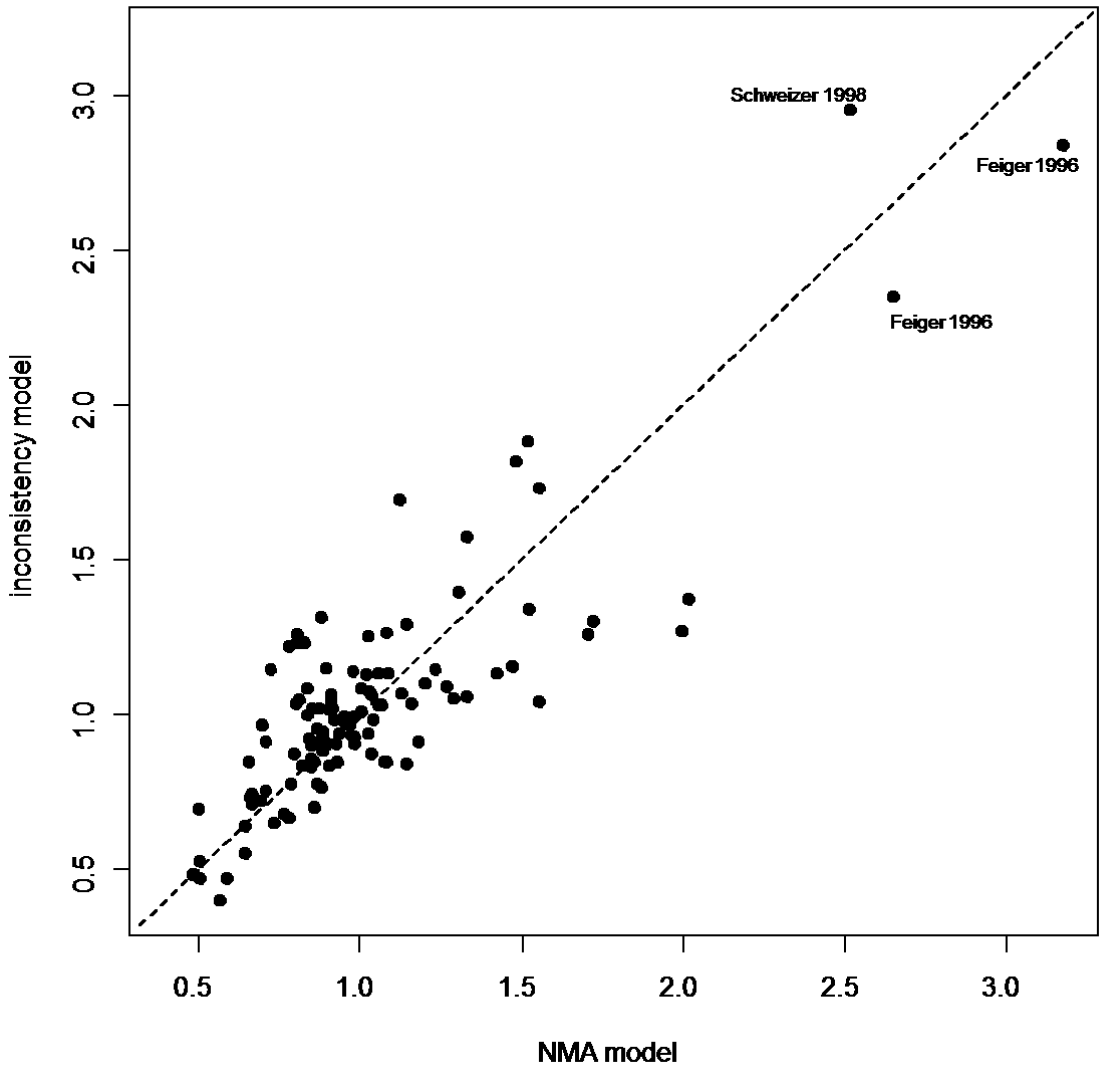
Figure 32: Network diagram of every study included in analysis by class. Discontinuation due to SE – more severe depression.



Update 2018

Figure 33: Deviance plot. Discontinuation due to SE – more severe depression.



There is evidence suggesting that Any TCA, Amitriptyline, Imipramine, Lofepramine, Citalopram, Escitalopram, Fluoxetine, Sertraline, and Mirtazapine have an increased odds of discontinuation due to SE compared to Pill placebo, while no interventions or classes have a decreased odds (Figure 65 and Figure 66). The classes for which there is evidence of having an increased odds in discontinuation due to SE are Mirtazapine, TCA, and SSRI (Figure 66).

Cognitive and cognitive behavioural therapies (individual) [CBT/CT] is the highest ranked class at 1st (95% CrI 1st to 5th). The highest ranked intervention is CBT individual (under 15 sessions) at 2nd (95% CrI 1st to 9th). The lowest ranked intervention is Mirtazapine with a posterior median rank of 10th (95% CrI 5th to 12th). Mirtazapine is also the lowest ranked class. Rankings of classes are shown in Table 18; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 18: Posterior median rank and 95% credible intervals by class. Discontinuation due to SE – more severe depression.

Class	Posterior median rank	95% CrI
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	1	(1, 5)

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Class	Posterior median rank	95% CrI
Pill placebo	2	(1, 3)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	3	(1, 6)
SSRIs	4	(2, 6)
TCAs	5	(3, 6)
Mirtazapine	5	(3, 6)

1.3.2.31 Outcome: remission in completers – more severe depression

After excluding trials with zero events in all arms, and one trial due to the network being disconnected (Goldman 2006), 34 trials of 28 interventions and 18 classes remained to be included in the analysis for this outcome (Table 19, Figure 34 and Figure 35).

The NMA model had lower posterior mean residual deviance and between study heterogeneity suggesting that there was no evidence of inconsistency (Table 38). Reported results are therefore based on the random-effects NMA model, assuming consistency. Note, however, the inconsistency model better predicted the data in Yevtunshenko 2007 (Figure 36). Relative to the size of the intervention effect estimates, high between trial heterogeneity was observed for this outcome (τ =0.64 (95% CrI 0.42 to 0.99)).

Table 19: Interventions, classes and number of patients (N) included in remission in completers analysis – more severe depression.

	Intervention	N	Class		N
1	Pill placebo	899	Pill placebo	1	899
2	Waitlist	101	No treatment	2	101
3	TAU	310	TAU	3	310
4	Exercise + TAU	23	Exercise*	4	23
5	Any TCA	39	TCAs	5	620
6	Amitriptyline	196		5	
7	Imipramine	385		5	
8	Citalopram	648	SSRIs	6	2548
9	Escitalopram	830		6	
10	Fluoxetine	956		6	
11	Sertraline	114		6	
12	Mirtazapine	186	Mirtazapine	7	186
13	Short-term psychodynamic psychotherapy individual + TAU	33	Short-term psychodynamic psychotherapies	8	33
14	Long-term psychodynamic psychotherapy individual	73	Long-term psychodynamic psychotherapies*	9	73
15	Computerised-problem solving therapy with support	26	Self-help with support*	10	26
16	Computerised-CBT (CCBT)	146	Self-help without support	11	293
17	Computerised-CBT (CCBT) + TAU	96		11	
18	Computerised-problem solving therapy	51		11	
19	Interpersonal psychotherapy (IPT)	62	Interpersonal psychotherapy (IPT)*	12	62

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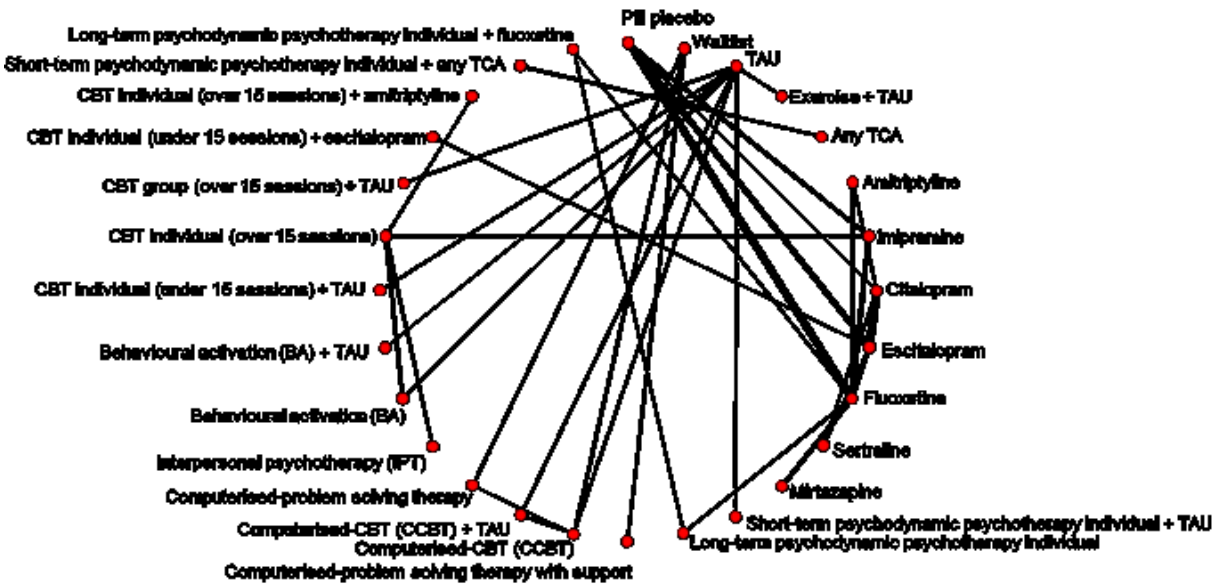
	Intervention	N	Class		N
20	Behavioural activation (BA)	66	Behavioural therapies (individual)*	13	82
21	Behavioural activation (BA) + TAU	16		13	
22	CBT individual (under 15 sessions) + TAU	113	Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	14	250
23	CBT individual (over 15 sessions)	137		14	
24	CBT group (over 15 sessions) + TAU	42	Behavioural, cognitive, or CBT groups*	15	42
25	CBT individual (under 15 sessions) + escitalopram	40	Combined (Cognitive and cognitive behavioural therapies individual + AD)*	16	51
26	CBT individual (over 15 sessions) + amitriptyline	11		16	
27	Short-term psychodynamic psychotherapy individual + any TCA	35	Combined (Short-term psychodynamic psychotherapies + AD)*	17	35
28	Long-term psychodynamic psychotherapy individual + fluoxetine	62	Combined (Long-term psychodynamic psychotherapies + AD)*	18	62
*Variance borrowed from another class as described in section 1.2.3					

Figure 34: Network diagram of every study included in analysis by intervention. Remission in completers – more severe depression.



Note: Without the use of a class network Any TCA and Short-term psychodynamic psychotherapy individual + any TCA would be disconnected from the rest of the network and would have to be excluded from the analysis.

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Figure 35: Network diagram of every study included in analysis by class. Remission in completers – more severe depression.

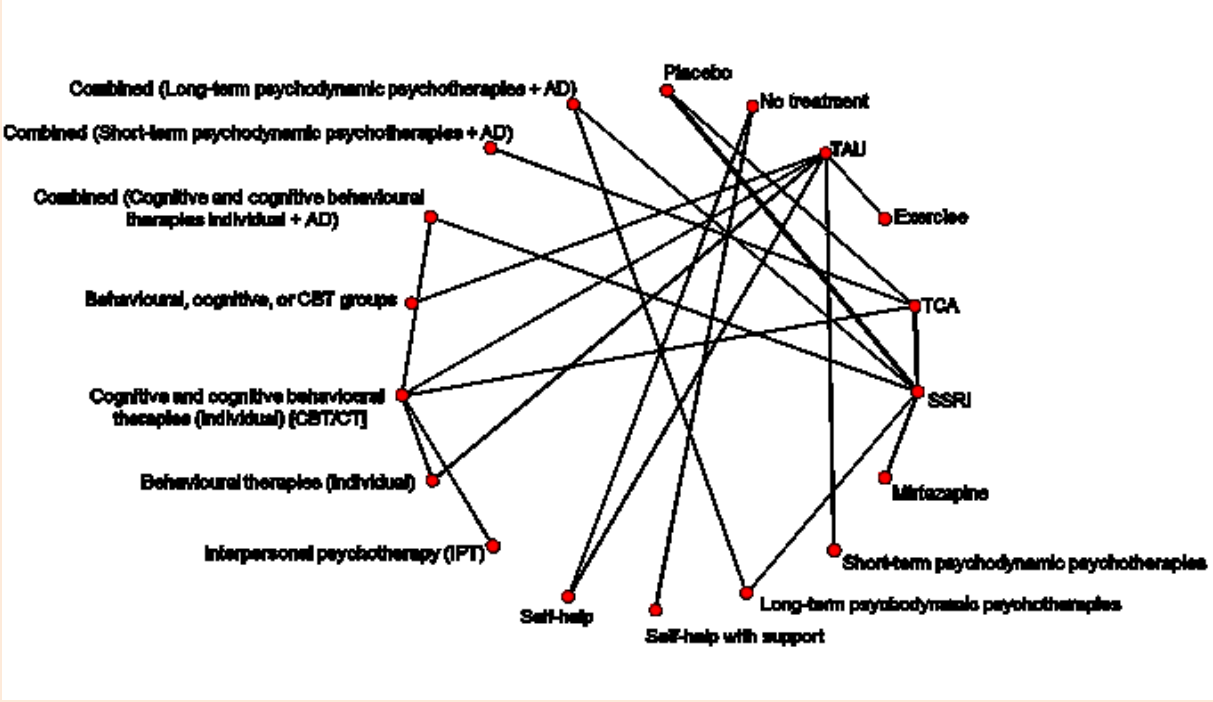

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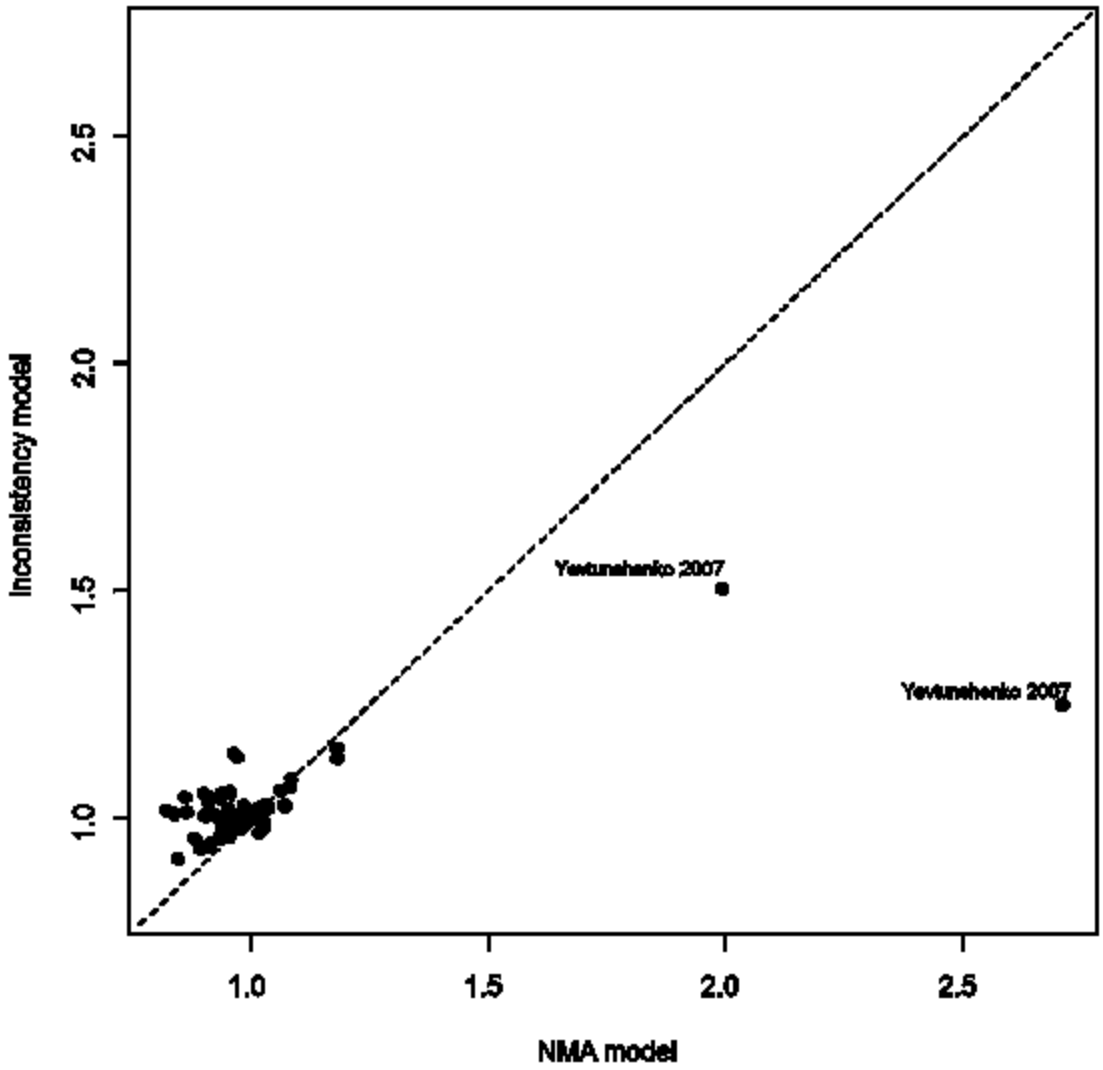
Figure 36: Deviance plot. Remission in completers – more severe depression.



There is evidence suggesting the interventions with an increased odds of remission in completers compared to Pill placebo are Long-term psychodynamic psychotherapy individual, Computerised-problem solving therapy with support, Interpersonal psychotherapy (IPT), Behavioural activation (BA), Behavioural activation (BA) + TAU, CBT individual (under 15 sessions) + TAU, CBT individual (over 15 sessions), and Long-term psychodynamic psychotherapy individual + fluoxetine, while there is no evidence to suggest any intervention has a decreased odds of remission in completers compared to Pill placebo (Figure 67). The classes for which there is evidence of an increased odds of remission in completers compared to Pill placebo are Long-term psychodynamic psychotherapies, Self-help with support, Interpersonal psychotherapy (IPT), Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual) [CBT/CT], and Combined (Long-term psychodynamic psychotherapies + AD) (Figure 68). There is no evidence of any class having a decreased odds of remission in completers compared to Pill placebo.

Self-help with support and Combined (Long-term psychodynamic psychotherapies + AD) are the highest ranked classes at 2nd (95% CrI 1st to 13th) and 2nd (95% CrI 1st to 9th), respectively. The highest ranked intervention is Long-term psychodynamic psychotherapy individual + fluoxetine with a posterior median rank of 1st (95% CrI 1st to 7th). The lowest ranked interventions are Citalopram and Pill Placebo. The lowest ranked active classes are Mirtazapine at 16th (95% CrI 9th to 18th) and SSRI at 16th (95% CrI 10th to 18th). Rankings of

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classes are shown in Table 20; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 20: Posterior median rank and 95% credible intervals by class. Remission in completers – more severe depression.

Class	Posterior median rank	95% CrI
Self-help with support	2	(1, 13)
Combined (Long-term psychodynamic psychotherapies + AD)	2	(1, 9)
Long-term psychodynamic psychotherapies	3	(1, 12)
Behavioural therapies (individual)	6	(2, 12)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	6	(3, 11)
Short-term psychodynamic psychotherapies	7	(1, 18)
Interpersonal psychotherapy (IPT)	7	(2, 14)
Exercise	8	(2, 17)
Behavioural, cognitive, or CBT groups	8	(2, 17)
Combined (Short-term psychodynamic psychotherapies + AD)	9	(2, 17)
Self-help without support	10	(4, 17)
TAU	11	(6, 17)
No treatment	13	(5, 18)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	13	(6, 18)
TCAs	14	(8, 18)
SSRIs	16	(10, 18)
Mirtazapine	16	(9, 18)
Pill placebo	17	(12, 18)

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1.3.2.45 Outcome: remission in those randomised – more severe depression

After excluding trials with zero events in all arms, and one trial due to the network being disconnected (Goldman 2006), 34 trials of 28 interventions and 18 classes remained to be included in the analysis for this outcome (Table 21, Figure 37 and Figure 38).

No meaningful differences were observed in posterior mean residual deviance or DIC, and between-study heterogeneity increased in the inconsistency model, suggesting that there was no evidence of inconsistency (Table 39). Reported results are therefore based on the random-effects NMA model, assuming consistency. Note, however, the inconsistency model better predicted the data in Yevtunshenko 2007 (Figure 1). This study compared Citalopram and Escitalopram and the estimated relative treatment effect was much stronger compared to studies making the same comparison. Thus this study contributes to the moderate to high between trial heterogeneity observed for this outcome (τ=0.62 (95% CrI 0.41 to 0.95)).

Table 21: Interventions, classes and number of patients (N) included in remission in those randomised analysis – more severe depression.

	Intervention	N	Class		N
1	Pill placebo	1185	**Pill placebo**	1	1185
2	Waitlist	134	**No treatment**	2	134
3	TAU	391	**TAU**	3	391
4	Exercise + TAU	25	**Exercise***	4	25
5	Any TCA	48	**TCAs**	5	858

	Intervention	N	Class		N
6	Amitriptyline	279		5	
7	Imipramine	531		5	
8	Citalopram	736	**SSRIs**	6	3025
9	Escitalopram	975		6	
10	Fluoxetine	1180		6	
11	Sertraline	134		6	
12	Mirtazapine	213	**Mirtazapine**	7	213
13	Short-term psychodynamic psychotherapy individual + TAU	44	**Short-term psychodynamic psychotherapies***	8	44
14	Long-term psychodynamic psychotherapy individual	90	**Long-term psychodynamic psychotherapies***	9	90
15	Computerised-problem solving therapy with support	49	**Self-help with support***	10	49
16	Computerised-CBT (CCBT)	188	**Self-help without support**	11	376
17	Computerised-CBT (CCBT) + TAU	100		11	
18	Computerised-problem solving therapy	88		11	
19	Interpersonal psychotherapy (IPT)	75	**Interpersonal psychotherapy (IPT)***	12	75
20	Behavioural activation (BA)	79	**Behavioural therapies (individual)***	13	100
21	Behavioural activation (BA) + TAU	21		13	
22	CBT individual (under 15 sessions) + TAU	149	**Cognitive and cognitive behavioural therapies (individual) [CBT/CT]**	14	312
23	CBT individual (over 15 sessions)	163		14	
24	CBT group (over 15 sessions) + TAU	47	**Behavioural, cognitive, or CBT groups***	15	47
25	CBT individual (under 15 sessions) + escitalopram	52	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	16	67
26	CBT individual (over 15 sessions) + amitriptyline	15		16	
27	Short-term psychodynamic psychotherapy individual + any TCA	47	**Combined (Short-term psychodynamic psychotherapies + AD)***	17	47
28	Long-term psychodynamic psychotherapy individual + fluoxetine	91	**Combined (Long-term psychodynamic psychotherapies + AD)***	18	91

*Variance borrowed from another class as described in section 1.2.3

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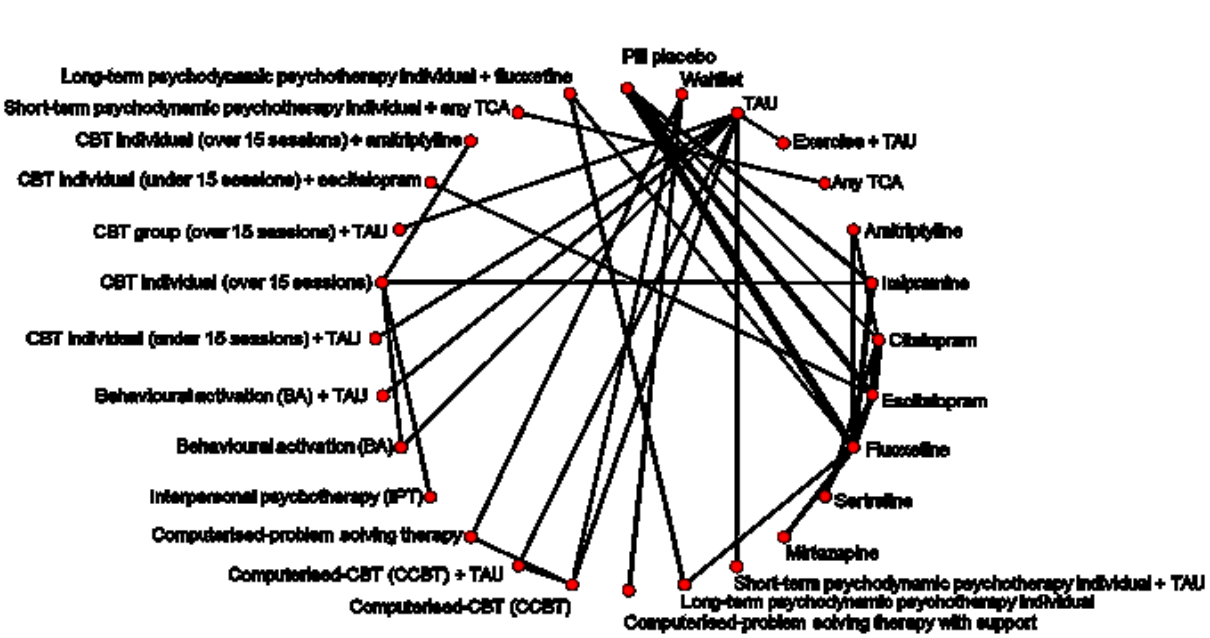
Figure 37: Network diagram of every study included in analysis by intervention. Remission in those randomised – more severe depression.



Note: Without the use of a class network Any TCA and Short-term psychodynamic psychotherapy individual + any TCA would be disconnected from the rest of the network and would have to be excluded from the analysis.

Figure 38: Network diagram of every study included in analysis by class. Remission in those randomised – more severe depression.

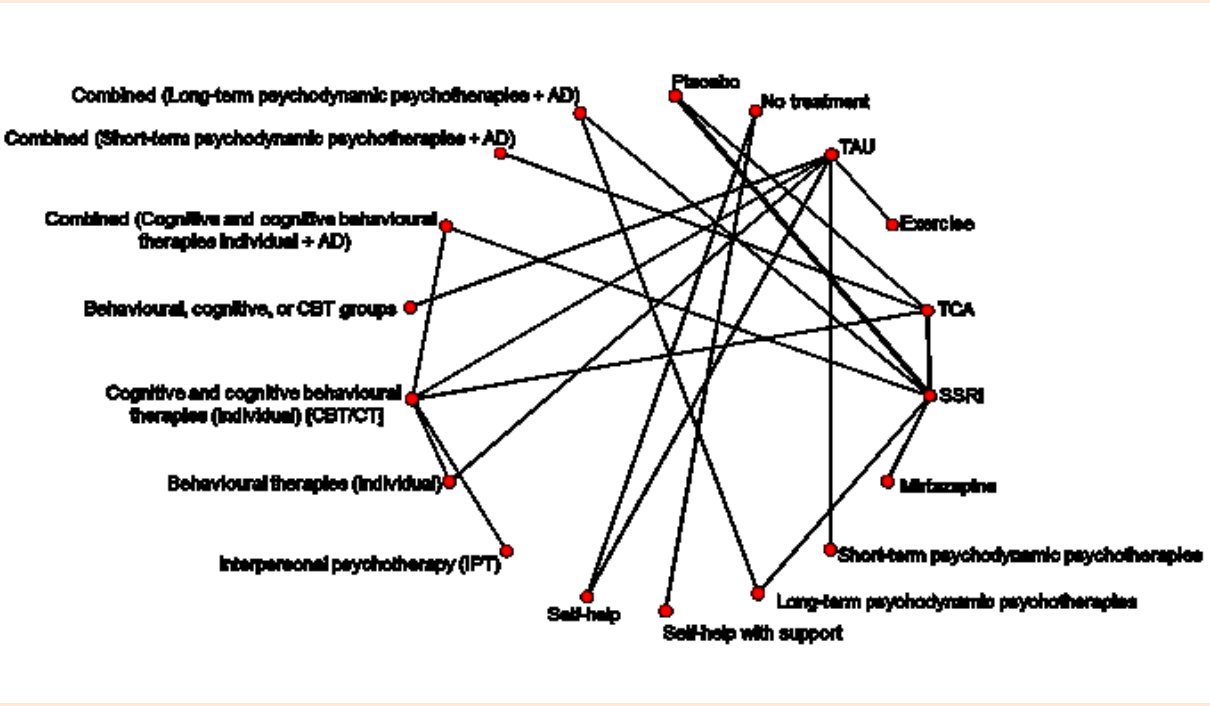


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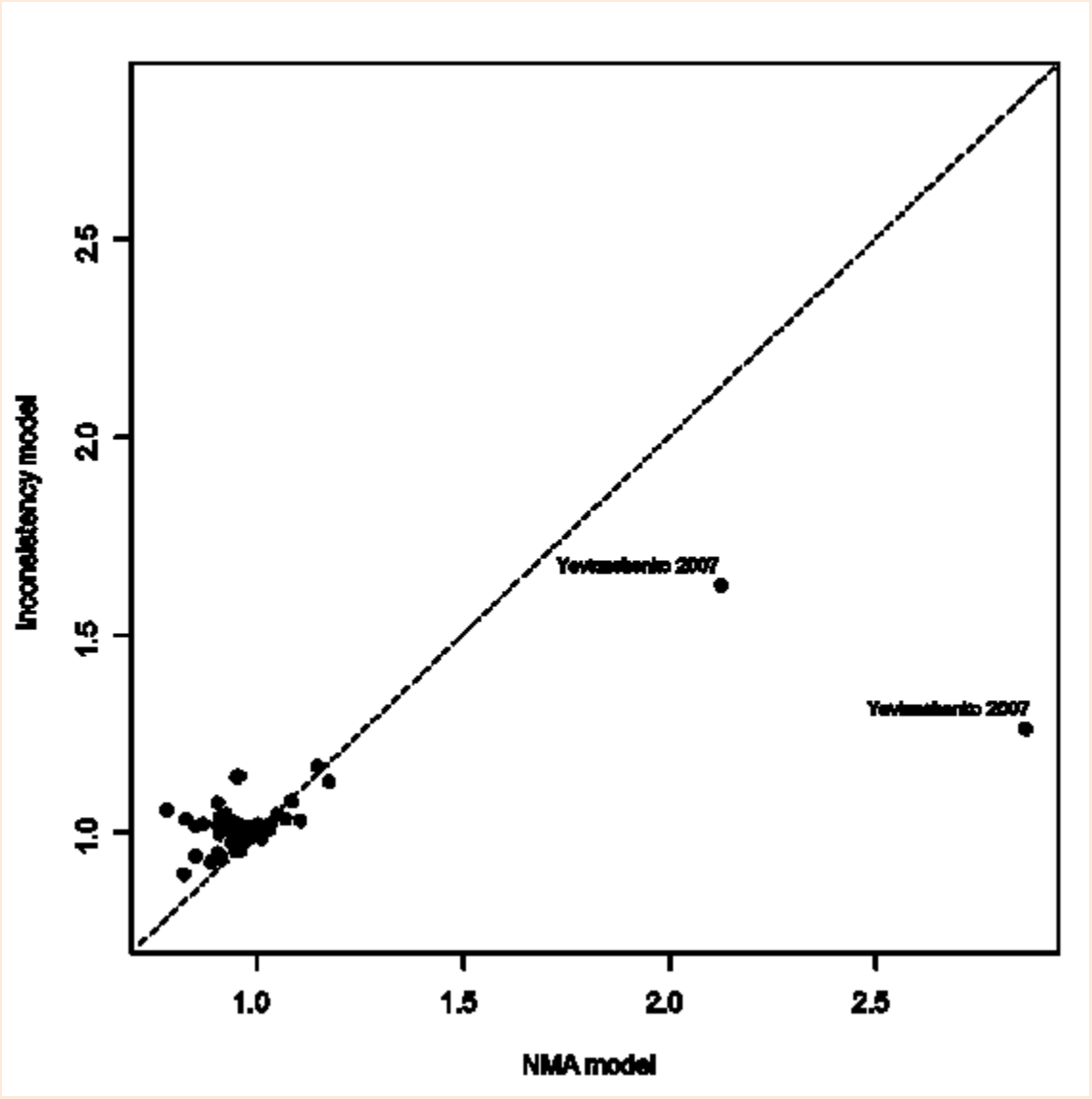
Figure 39: Deviance plot. Remission in those randomised – more severe depression.



There is evidence suggesting Long-term psychodynamic psychotherapy individual, Computerised-problem solving therapy with support, Interpersonal psychotherapy (IPT), Behavioural activation (BA), Behavioural activation (BA) + TAU, CBT individual (under 15 sessions) + TAU, CBT individual (over 15 sessions), and Long-term psychodynamic psychotherapy individual + fluoxetine have an increased the odds of remission in those randomised compared to Pill placebo (Figure 69). However, there is no evidence to suggest any intervention or class have a decreased odds of remission in those randomised compared to Pill placebo (Figure 69 and Figure 70). The classes for which evidence suggests there is an increased odds of remission in those randomised compared to Pill placebo are Long-term psychodynamic psychotherapies, Self-help with support, Interpersonal psychotherapy (IPT), Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual) [CBT/CT], and Combined (Long-term psychodynamic psychotherapies + AD) (Figure 70).

Self-help with support was the highest ranked class at 1st (95% CrI 1st to 11th). The highest ranked intervention, Computerised-problem solving therapy with support, belonged to this class with a posterior median rank of 1st (95% CrI 1st to 10th). The lowest ranked intervention is Citalopram, with a posterior median rank of 18th (95 CrI 12th to 20th). The lowest ranked active class is Mirtazapine at 16th (95% CrI 8th to 18th). Rankings of classes are shown in Table 22; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

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Table 22: Posterior median rank and 95% credible intervals. Remission in those randomised – more severe depression.

Class	Posterior median rank	95% CrI
Self-help with support	1	(1, 11)
Long-term psychodynamic psychotherapies	5	(1, 13)
Interpersonal psychotherapy (IPT)	5	(1, 13)
Behavioural therapies (individual)	5	(2, 12)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	5	(2, 10)
Short-term psychodynamic psychotherapies	6	(1, 18)
Exercise	7	(1, 17)
Behavioural, cognitive, or CBT groups	7	(1, 17)
Combined (Long-term psychodynamic psychotherapies + AD)	7	(1, 14)
Self-help without support	9	(3, 17)
No treatment	11	(3, 18)
TAU	11	(5, 17)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	13	(6, 18)
Combined (Short-term psychodynamic psychotherapies + AD)	13	(3, 18)
TCAs	15	(9, 18)
SSRIs	15	(10, 18)
Pill placebo	16	(11, 18)
Mirtazapine	16	(8, 18)

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1.3.2.53 Outcome: response in completers – more severe depression

After excluding trials with zero events in all arms, 57 trials reported response. Out of the remaining studies, 7 reported change from baseline in completers (but not response) and 24 reported baseline and final scores in completers (but not response or change from baseline). This meant that 88 trials of 44 interventions and 22 classes were included in the analysis for this outcome (Table 23, Figure 40 and Figure 41 **Error! Reference source not found.**).

No meaningful differences were observed in posterior mean residual deviance or between study heterogeneity suggesting that there was no evidence of inconsistency (Table 40). Reported results are therefore based on the random-effects NMA model, assuming consistency. Note, however, the inconsistency model better predicted the data in Fabre 1992, which compares Pill Placebo and Imipramine (Figure 42).

Relative to the size of the intervention effect estimates, high between trial heterogeneity was observed for this outcome $(\tau = 0.81\ (95\%\ \text{CrI}\ 0.65\ \text{to}\ 0.99))$.

Table 23: Interventions, classes and number of patients (N) included in response in completers analysis.

	Intervention	N	Class		N
1	Pill placebo	2495	**Pill placebo**	1	2495
2	Waitlist	11	**No treatment**	2	22
3	No treatment	11		2	
4	Attention placebo + TAU	58	**Attention placebo**	3	58
5	TAU	505	**TAU**	4	526
6	Enhanced TAU	21		4	

	Intervention	N	Class		N
7	Exercise	38	**Exercise**	5	95
8	Exercise + TAU	39		5	
9	Yoga + TAU	18		5	
10	Any TCA	60	**TCAs**	6	1917
11	Amitriptyline	945		6	
12	Imipramine	815		6	
13	Lofepramine	97		6	
14	Citalopram	918	**SSRIs**	7	4050
15	Escitalopram	1330		7	
16	Fluoxetine	1247		7	
17	Sertraline	555		7	
18	Any AD	73	**Any AD***	8	73
19	Mirtazapine	396	**Mirtazapine**	9	396
20	Short-term psychodynamic psychotherapy individual + TAU	33	**Short-term psychodynamic psychotherapies***	10	33
21	Cognitive bibliotherapy with support + TAU	101	**Self-help with support***	11	101
22	Cognitive bibliotherapy + TAU	38	**Self-help without support**	12	252
23	Computerised-CBT (CCBT)	95		12	
24	Computerised-CBT (CCBT) + TAU	96		12	
25	Computerised-CBT (CCBT) + enhanced TAU	23		12	
26	Interpersonal psychotherapy (IPT)	34	**Interpersonal psychotherapy (IPT)***	13	34
27	Counselling (any type)	39	**Counselling***	14	101
28	Non-directive counselling	62		14	
29	Problem solving group	28	**Problem Solving***	15	28
30	Behavioural activation (BA)	66	**Behavioural therapies (individual)***	16	82
31	Behavioural activation (BA) + TAU	16		16	
32	CBT individual (under 15 sessions)	78	**Cognitive and cognitive behavioural therapies (individual) [CBT/CT]**	17	264
33	CBT individual (under 15 sessions) + TAU	64		17	
34	CBT individual (under 15 sessions) + enhanced TAU	23		17	
35	CBT individual (over 15 sessions)	88		17	
36	Third-wave cognitive therapy individual	11		17	
37	CBT group (under 15 sessions)	77	**Behavioural, cognitive, or CBT groups***	18	96
38	Third-wave cognitive therapy group	19		18	

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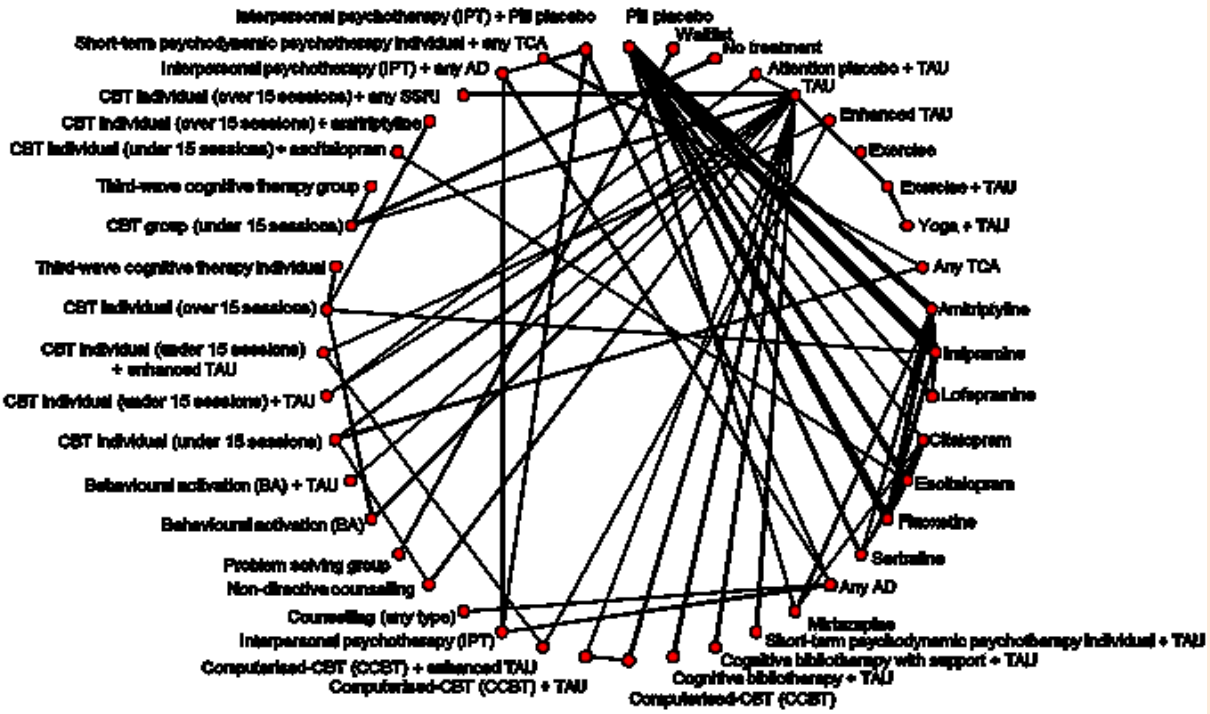
	Intervention	N	Class		N
39	CBT individual (under 15 sessions) + escitalopram	40	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	19	94
40	CBT individual (over 15 sessions) + amitriptyline	11		19	
41	CBT individual (over 15 sessions) + any SSRI	43		19	
42	Interpersonal psychotherapy (IPT) + any AD	32	**Combined (IPT + AD)***	20	32
43	Short-term psychodynamic psychotherapy individual + any TCA	35	**Combined (Short-term psychodynamic psychotherapies + AD)***	21	35
44	Interpersonal psychotherapy (IPT) + Pill placebo	34	**Combined (psych + placebo)***	22	34

*Variance borrowed from another class as described in section 1.2.3

Figure 40: Network diagram of every study included in analysis by intervention. Response in completers – more severe depression.



Note: Without the use of a class network Waitlist, Enhanced TAU, Exercise, Any AD, Computerised-CBT (CCBT) + enhanced TAU, Interpersonal psychotherapy (IPT), Counselling (any type), Problem solving group, CBT individual (under 15 sessions) + enhanced TAU, Interpersonal psychotherapy (IPT) + any AD, and Interpersonal psychotherapy (IPT) + Pill placebo would be disconnected from the rest of the network and would have to be excluded from the analysis.

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Figure 41: Network diagram of every study included in analysis by class. Response in completers – more severe depression.

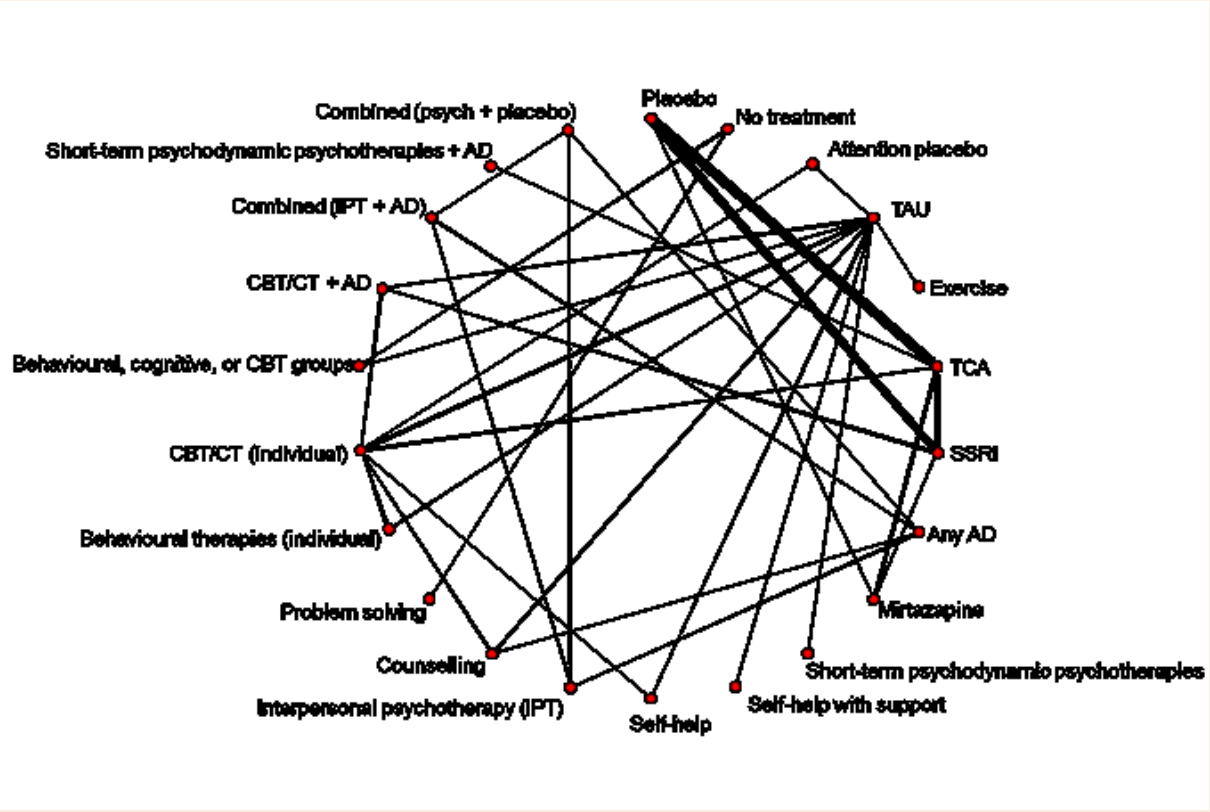

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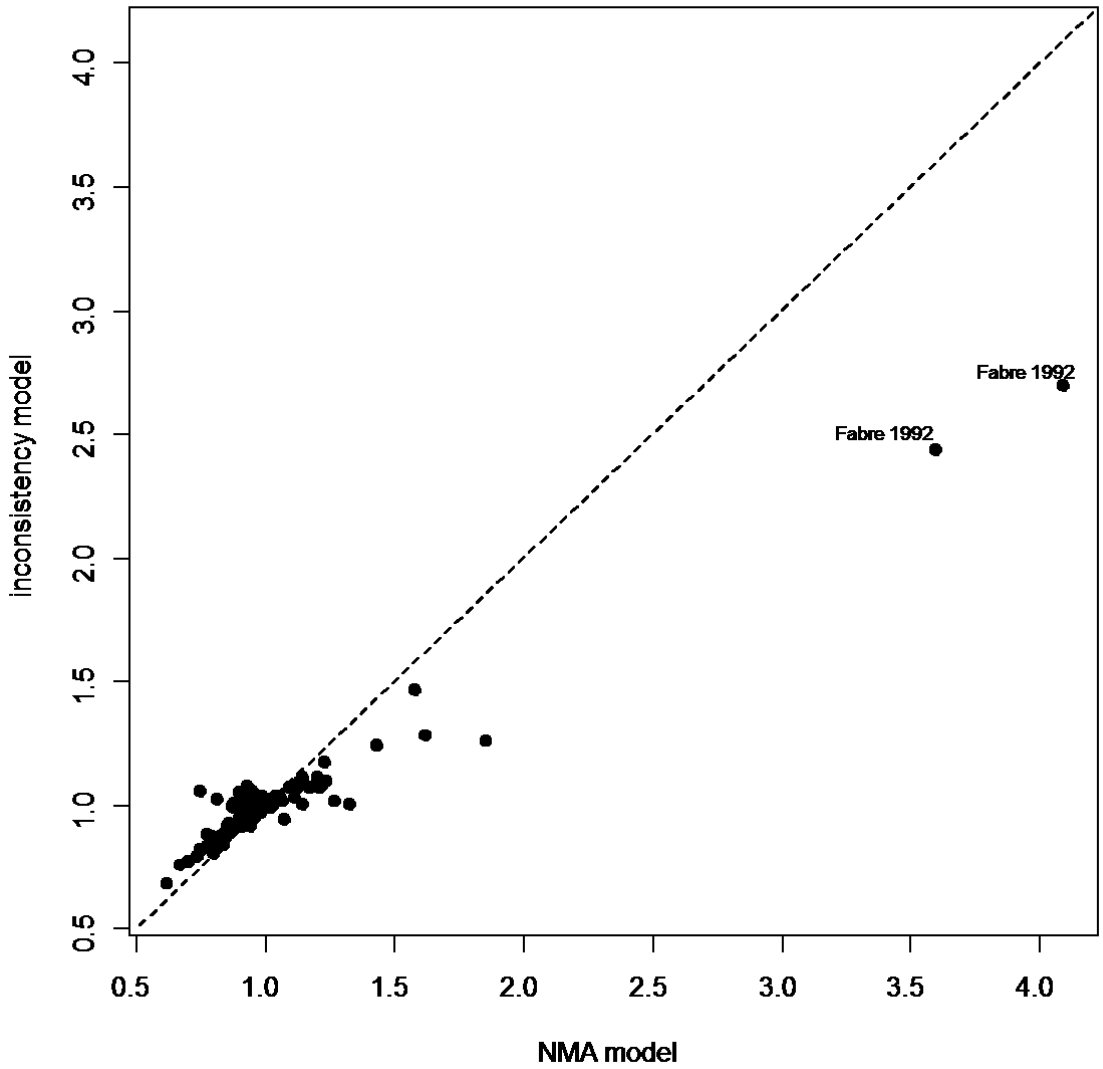
Figure 42: Deviance plot. Response in completers – more severe depression.



There is evidence suggesting the interventions with an increased odds of response in completers compared to Pill placebo are Waitlist, No treatment, Exercise + TAU, Any TCA, Amitriptyline, Imipramine, Lofepramine, Citalopram, Escitalopram, Fluoxetine, Sertraline, Mirtazapine, Problem solving group, Behavioural activation (BA), Behavioural activation (BA) + TAU, CBT individual (under 15 sessions), CBT individual (under 15 sessions) + TAU, CBT individual (under 15 sessions) + enhanced TAU, CBT individual (over 15 sessions), Third-wave cognitive therapy individual, CBT group (under 15 sessions), Third-wave cognitive therapy group, CBT individual (under 15 sessions) + escitalopram, CBT individual (over 15 sessions) + amitriptyline, and CBT individual (over 15 sessions) + any SSRI (Figure 71). There is no evidence to suggest any intervention or class have a decreased odds of response in completers compared to Pill placebo (Figure 71 and Figure 72).

The classes for which there is evidence of an increased odds of response in completers compared to Pill placebo are No treatment, Exercise, TCA, SSRI, Mirtazapine, Problem solving, Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual) [CBT/CT], Behavioural, cognitive, or CBT groups, and Combined (Cognitive and cognitive behavioural therapies individual + AD) (Figure 72).

Problem solving is the highest ranked class at 1st (95% CrI 1st to 2nd). The highest ranked interventions are Problem solving group (1st, 95% CrI 1st to 3rd) and CBT group (under 15

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sessions) (2nd, 95% CrI 1st to 3rd). The lowest ranked intervention is Pill placebo. The lowest ranked active intervention is Citalopram at 24th (95% CrIs 16th to 26th). The lowest ranked active class is SSRI at 17th (95% CrI 10th to 19th). Rankings of classes are shown in Table 24; rankings of interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Table 24: Posterior median rank and 95% credible intervals by class. Response in completers – more severe depression.

Class	Posterior median rank	95% CrI
Problem solving	1	(1, 2)
Behavioural, cognitive, or CBT groups	2	(1, 3)
No treatment	3	(2, 5)
Exercise	6	(3, 18)
Combined (IPT + AD)	6	(3, 19)
Interpersonal psychotherapy (IPT)	7	(4, 20)
Behavioural therapies (individual)	7	(4, 15)
Short-term psychodynamic psychotherapies	9	(4, 19)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	9	(5, 13)
Self-help with support	11	(4, 20)
Counselling	11	(5, 19)
Combined (Short-term psychodynamic psychotherapies + AD)	11	(4, 20)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	12	(5, 19)
TCAs	13	(6, 17)
Mirtazapine	14	(7, 19)
Attention placebo	15	(6, 20)
TAU	16	(11, 20)
Self-help without support	16	(9, 20)
SSRIs	17	(10, 19)
Pill placebo	20	(15, 20)

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1.3.2.68 Outcome: response in those randomised – more severe depression

After excluding trials with zero events in all arms, 57 trials reported response. Out of the remaining studies, 3 reported change from baseline in completers (but not response) and 25 reported baseline and final scores in completers (but not response or change from baseline). This meant that 85 trials of 41 interventions and 18 classes were included in the analysis for this outcome (Table 25, Figure 43 and Figure 44).

Lower posterior mean residual deviance and between study heterogeneity in the inconsistency model suggested evidence of inconsistency (Table 41). The inconsistency model notably predicted the data in a few studies much better than the consistency model, further adding evidence of inconsistency (Figure 45).

Reported results are based on the random-effects NMA model, assuming consistency but should be interpreted with caution due to the identification of potential inconsistency. Relative to the size of the intervention effect estimates, moderate between trial heterogeneity was observed for this outcome $\left(\tau = 0.49\ (95\%\ \text{CrI}\ 0.37\ \text{to}\ 0.62)\right)$.

Table 25: Interventions, classes and number of patients (N) included in response in those randomised analysis – more severe depression.

	Intervention	N	Class		N
1	Pill placebo	3316	**Pill placebo**	1	3316
2	Waitlist	128	**No treatment**	2	141
3	No treatment	13		2	
4	Attention placebo	13	**Attention placebo**	3	80
5	Attention placebo + TAU	67		3	
6	TAU	689	**TAU**	4	759
7	Enhanced TAU	70		4	
8	Exercise	10	**Exercise***	5	35
9	Exercise + TAU	25		5	
10	Amitriptyline	1119	**TCAs**	6	1915
11	Imipramine	750		6	
12	Lofepramine	46		6	
13	Citalopram	1254	**SSRIs**	7	5488
14	Escitalopram	1869		7	
15	Fluoxetine	1724		7	
16	Sertraline	641		7	
17	Any AD	13	**Any AD***	8	13
18	Mirtazapine	592	**Mirtazapine**	9	592
19	Short-term psychodymic psychotherapy individual + TAU	44	**Short-term psychodynamic psychotherapies***	10	44
20	Cognitive bibliotherapy with support + TAU	141	**Self-help with support**	11	166
21	Computerised-CBT (CCBT) with support	25		11	
22	Cognitive bibliotherapy + TAU	50	**Self-help without support**	12	576
23	Computerised cognitive bias modification	26		12	
24	Computerised-CBT (CCBT)	113		12	
25	Computerised-CBT (CCBT) + TAU	299		12	
26	Computerised-problem solving therapy	88		12	
27	Interpersonal psychotherapy (IPT)	95	**Interpersonal psychotherapy (IPT)***	13	95
28	Emotion-focused therapy (EFT)	19	**Counselling**	14	120
29	Non-directive counselling	82		14	
30	Relational client-centered therapy	19		14	
31	Behavioural activation (BA)	182	**Behavioural therapies (individual)***	15	203
32	Behavioural activation (BA) + TAU	21		15	

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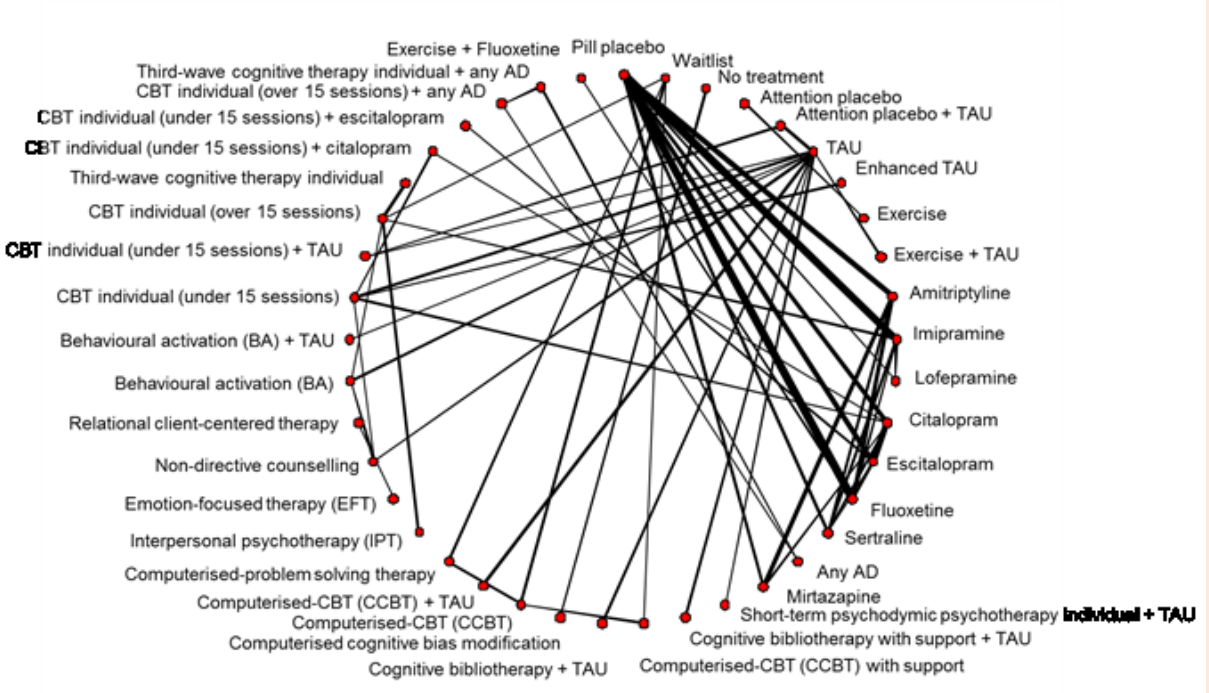
	Intervention	N	Class		N
33	CBT individual (under 15 sessions)	174	**Cognitive and cognitive behavioural therapies (individual) [CBT/CT]**	16	446
34	CBT individual (under 15 sessions) + TAU	70		16	
35	CBT individual (over 15 sessions)	191		16	
36	Third-wave cognitive therapy individual	11		16	
37	CBT individual (under 15 sessions) + citalopram	40	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	18	112
38	CBT individual (under 15 sessions) + escitalopram	52		18	
39	CBT individual (over 15 sessions) + any AD	10		18	
40	Third-wave cognitive therapy individual + any AD	10			
41	Exercise + Fluoxetine	41	**Combined (Exercise + AD/CBT)***	19	41

*Variance borrowed from another class as described in section 1.2.3

Figure 43: Network diagram of every study included in analysis by intervention. Response in those randomised – more severe depression.



Note: Without the use of a class network No treatment, Attention placebo, Exercise, Any AD, Computerised cognitive bias modification, Emotion-focused therapy (EFT), Relational client-centered therapy, CBT individual (over 15 sessions) + any AD, and Third-wave cognitive therapy individual + any AD would be disconnected from the rest of the network and would have to be excluded from the analysis.

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Figure 44: Network diagram of every study included in analysis by class. Response in those randomised – more severe depression.

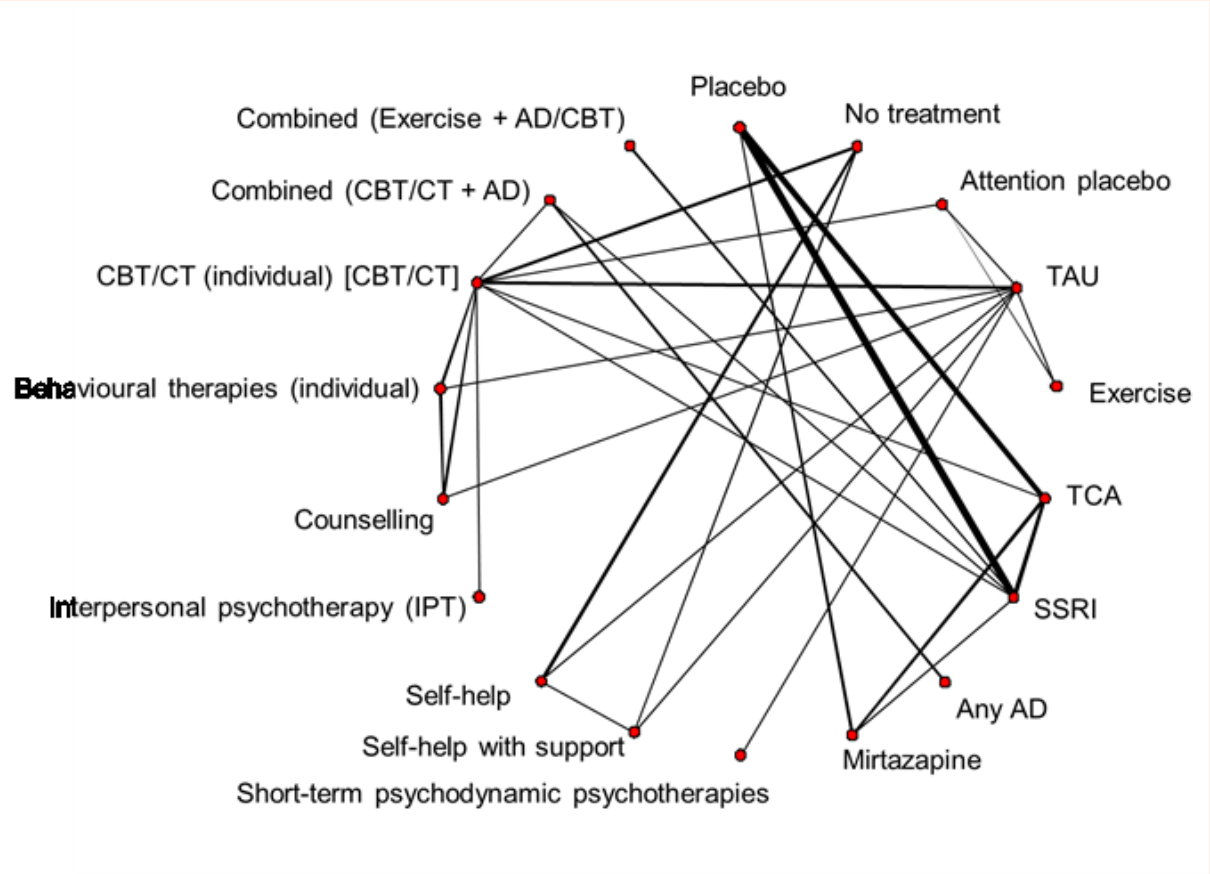
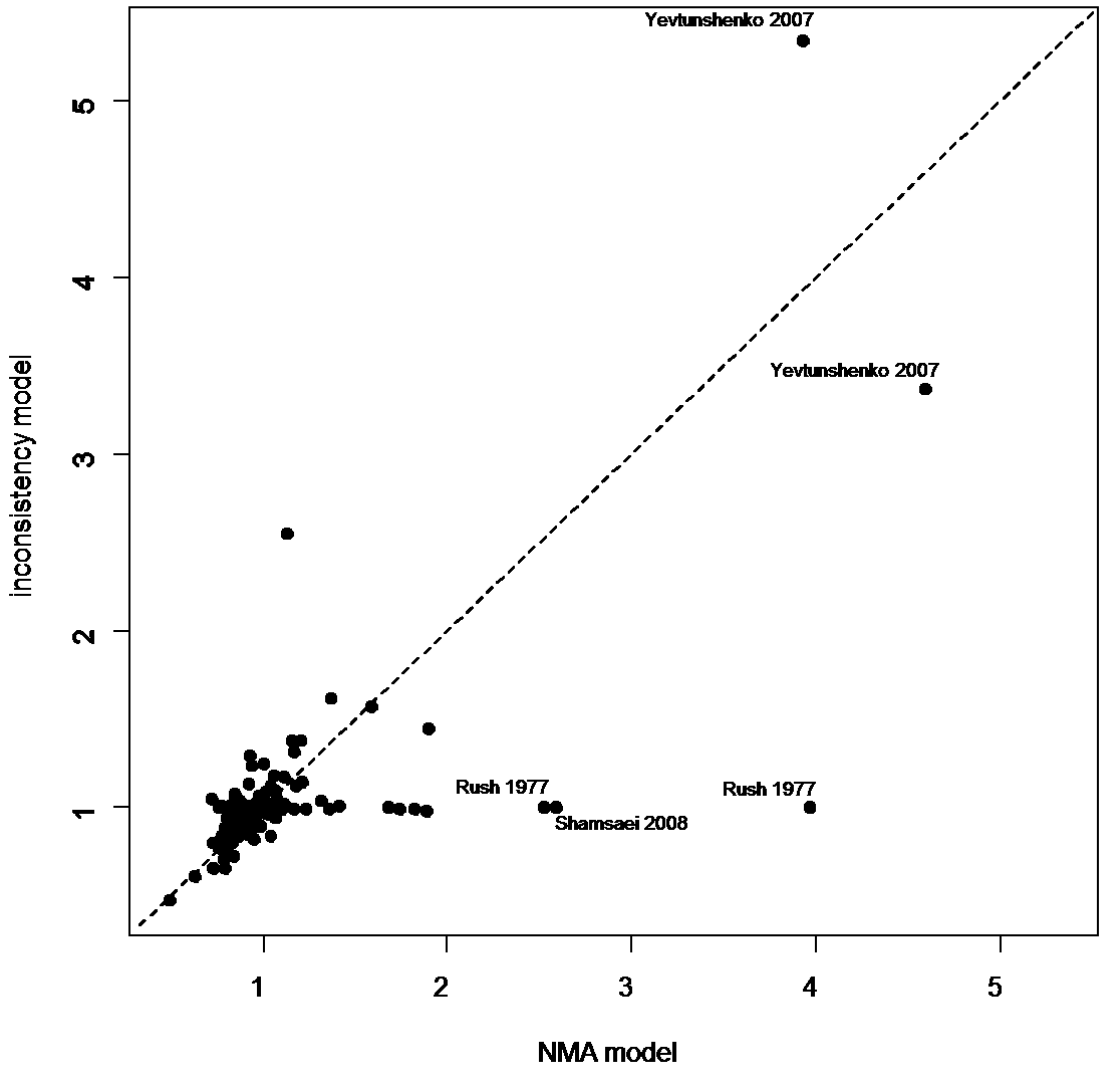


Figure 45: Deviance plot. Response in those randomised – more severe depression.



Interventions for which evidence suggests an increased odds of response in those randomised compared to Pill placebo are Amitriptyline, Imipramine, Lofepramine, Citalopram, Escitalopram, Fluoxetine, Sertraline, Mirtazapine, CBT individual (under 15 sessions) + citalopram, Third-wave cognitive therapy individual + any AD, and Exercise + Fluoxetine (Figure 73). There is evidence suggesting any AD is the only intervention and class with a decreased odds in response in those randomised compared to Pill placebo. The classes for which there is evidence of an increased odds of response in those randomised compared to Pill placebo are Mirtazapine, TCA, SSRI, Combined (Cognitive and cognitive behavioural therapies individual + AD), and Combined (Exercise + AD/CBT) (Figure 74).

Combined (Exercise +AD/CBT) is the highest ranked class at 1st (95% CrI 1st to 1st). The highest ranked intervention is Third-wave cognitive therapy individual + any AD with a posterior median rank of 3rd (95% CrI 1st to 16th). The lowest ranked intervention is Waitlist at 27th (95% CrI 21st to 28th), while the lowest ranked active intervention is Relational client-centered therapy. The lowest ranked active class is Counselling at 13th (95% CrI 5th to 17th). Rankings of classes are shown in Table 26; rankings of interventions are shown in the respective excel file in Appendix N3, “Ranks” worksheet.

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Table 26: Posterior median rank and 95% credible intervals by class. Response in those randomised – more severe depression.

Class	Posterior median rank	95% CrI
Combined (Exercise + AD/CBT)	1	(1, 1)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	3	(2, 11)
TCAs	4	(2, 10)
Mirtazapine	5	(2, 11)
SSRIs	6	(3, 12)
Behavioural therapies (individual)	6	(2, 12)
Interpersonal psychotherapy (IPT)	7	(2, 15)
Exercise	9	(2, 16)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	9	(3, 13)
Pill placebo	10	(6, 16)
Short-term psychodynamic psychotherapies	10	(2, 17)
Self-help with support	12	(4, 17)
Self-help without support	13	(8, 16)
Counselling	13	(5, 17)
Attention placebo	15	(7, 17)
TAU	15	(11, 17)
No treatment	16	(12, 17)

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1.3.2.73 Outcome: SMD – more severe depression

This analysis was carried out on all patients randomised. After excluding trials with zero events in all arms, 12 trials reported CFB. Out of the remaining studies 34 reported baseline and follow-up scores (but not CFB) and 15 reported response (but not CFB or baseline and follow-up). This meant that 61 trials of 40 interventions and 18 classes were included in the analysis for this outcome (Table 27, Figure 46 and Figure 47).

Although there were no meaningful differences in DIC and between-study heterogeneity, the lower posterior mean residual deviance in the inconsistency model suggests evidence of inconsistency (Table 42). The inconsistency model notably predicted the data in a few studies much better than the consistency model, further adding evidence of inconsistency (Figure 48). Reported results are based on the random-effects NMA model, assuming consistency, however they must be interpreted with caution.

Relative to the size of the intervention effect estimates, small between trial heterogeneity was observed for this outcome $(\tau = 0.17\ (95\%\ \text{CrI}\ 0.10\ \text{to}\ 0.26))$.

Table 27: Interventions, classes and number of patients (N) included in SMD analysis

	Intervention	N	Class		N
1	Pill placebo	1888	**Pill placebo**	1	1888
2	Waitlist	128	**No treatment**	2	141
3	No treatment	13		2	
4	Attention placebo	13	**Attention placebo**	3	80
5	Attention placebo + TAU	67		3	
6	TAU	689	**TAU**	4	759
7	Enhanced TAU	70		4	

	Intervention	N	Class		N
8	Exercise	10	**Exercise***	5	35
9	Exercise + TAU	25		5	
10	Amitriptyline	460	**TCAs**	6	803
11	Imipramine	297		6	
12	Lofepramine	46		6	
13	Citalopram	1034	**SSRIs**	7	4279
14	Escitalopram	1706		7	
15	Fluoxetine	1212		7	
16	Sertraline	327		7	
17	Any AD	13	**Any AD***	8	13
18	Mirtazapine	272	**Mirtazapine**	9	272
19	Short-term psychodynamic psychotherapy individual + TAU	44	**Short-term psychodynamic psychotherapies***	10	44
20	Cognitive bibliotherapy with support + TAU	141	**Self-help with support**	11	166
21	Computerised-CBT (CCBT) with support	25		11	
22	Cognitive bibliotherapy + TAU	50	**Self-help without support**	12	576
23	Computerised cognitive bias modification	26		12	
24	Computerised-CBT (CCBT)	113		12	
25	Computerised-CBT (CCBT) + TAU	299		12	
26	Computerised-problem solving therapy	88		12	
27	Interpersonal psychotherapy (IPT)	95	**Interpersonal psychotherapy (IPT)***	13	95
28	Emotion-focused therapy (EFT)	19	**Counselling**	14	120
29	Non-directive counselling	82		14	
30	Relational client-centered therapy	19		14	
31	Behavioural activation (BA)	182	**Behavioural therapies (individual)***	15	203
32	Behavioural activation (BA) + TAU	21		15	
33	CBT individual (under 15 sessions)	174	**Cognitive and cognitive behavioural therapies (individual) [CBT/CT]**	16	446
34	CBT individual (under 15 sessions) + TAU	70		16	
35	CBT individual (over 15 sessions)	191		16	
36	Third-wave cognitive therapy individual	11		16	
37	CBT individual (under 15 sessions) + citalopram	40	**Combined (Cognitive and cognitive behavioural therapies individual + AD)**	17	60

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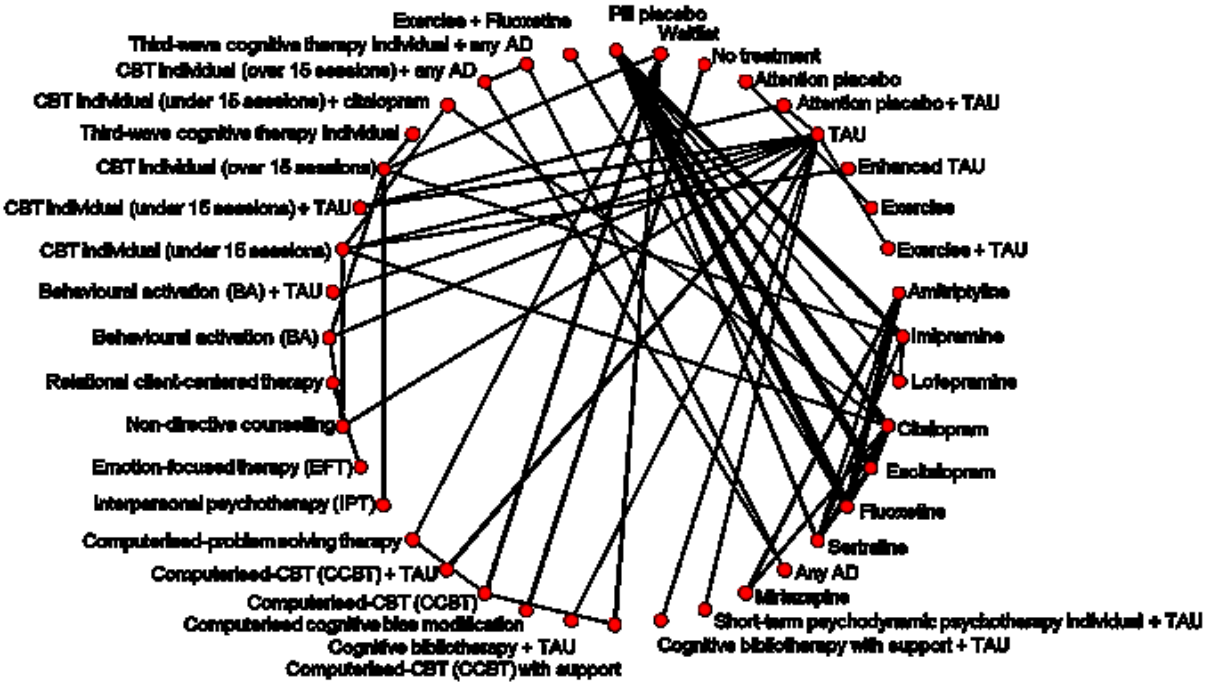
	Intervention	N	Class		N
38	CBT individual (over 15 sessions) + any AD	10		17	
39	Third-wave cognitive therapy individual + any AD	10		17	
40	Exercise + Fluoxetine	41	**Combined (Exercise + AD/CBT)***	18	41

*Variance borrowed from another class as described in section 1.2.3

Figure 46: Network diagram of every study included in analysis by intervention. SMD – more severe depression.



Note: Without the use of a class network No treatment, Attention placebo, Exercise, Any AD, Computerised cognitive bias modification, Emotion-focused therapy (EFT), Relational client-centered therapy, CBT individual (over 15 sessions) + any AD, and Third-wave cognitive therapy individual + any AD would be disconnected from the rest of the network and would have to be excluded from the analysis.

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Figure 47: Network diagram of every study included in analysis by class. SMD – more severe depression.

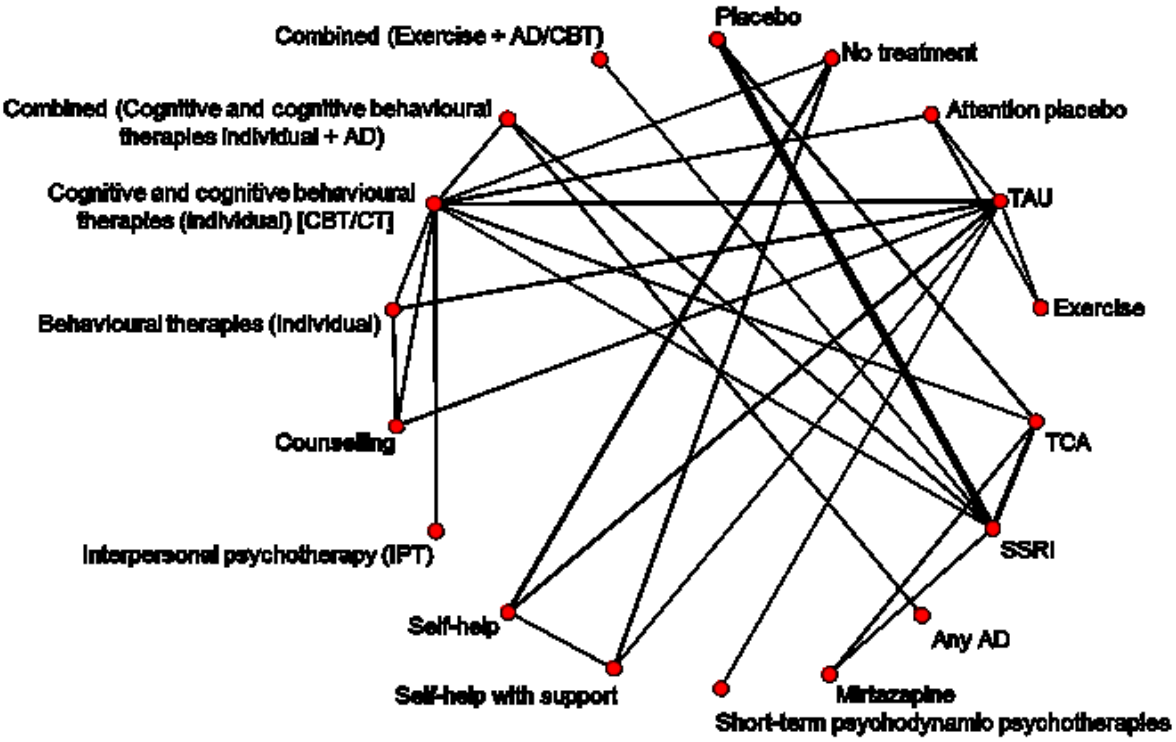

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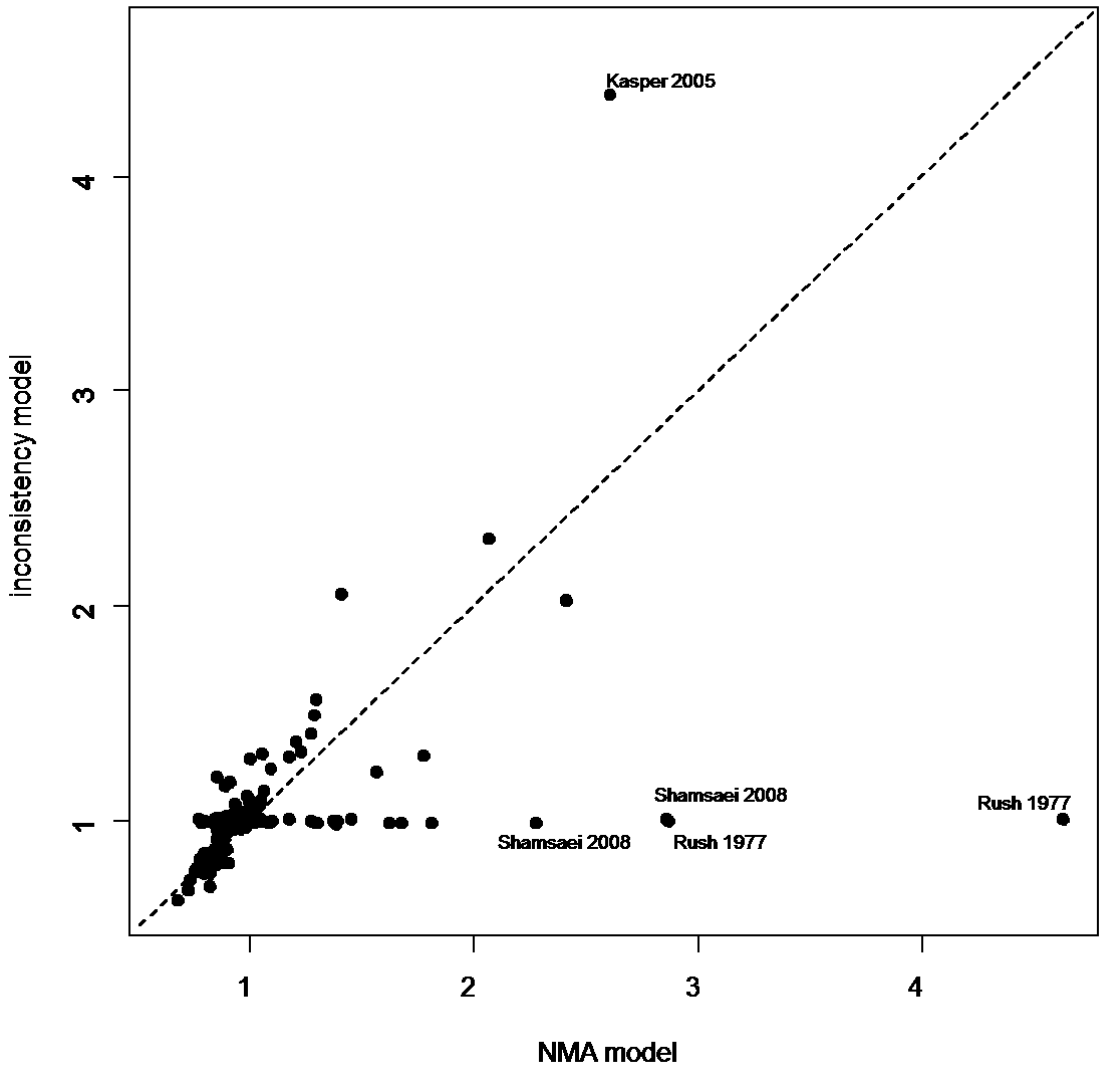
Figure 48: Deviance plot. SMD – more severe depression.



There is evidence that Amitriptyline, Imipramine, Lofepramine, Citalopram, Escitalopram, Fluoxetine, Sertraline, CBT individual (under 15 sessions) + citalopram, and Exercise + Fluoxetine have a lower standardized mean difference in depression compared to Pill placebo (Figure 75). TAU is the only intervention for which there is evidence suggesting a higher standardized mean difference. SSRI and Combined (Exercise + AD/CBT) were the only classes with evidence suggesting a lower standardized mean difference in depression compared to Pill placebo (Figure 76). There is no evidence to suggest any class has a higher standardized mean difference.

Combined (Exercise + AD/CBT) is the highest ranked class at 1st (95% CrI 1st to 3rd). The highest ranked intervention, Exercise + Fluoxetine, belongs to this class with a posterior median rank of 1st (95% CrI 1st to 3rd). The lowest ranked interventions are Attention placebo, Waitlist and TAU with posterior median ranks of 26th (95% CrI 13th to 28th), 26th (95% CrI 20th to 28th), and 26th (95% CrI 22nd to 28th), respectively. The lowest ranked active intervention is Relational client-centered therapy, with a posterior median rank of 24th (95% CrI 8th to 28th). The lowest ranked active class is Counselling at 13th (95% CrI 4th to 17th). Rankings of classes are shown in Table 28; rankings of interventions are shown in the respective excel file in Appendix N3, “Ranks” worksheet.

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Table 28: Posterior median rank and 95% credible intervals by class. SMD – more severe depression.

Class	Posterior median rank	95% CrI
Combined (Exercise + AD/CBT)	1	(1, 3)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	3	(1, 13)
TCAs	4	(2, 11)
Interpersonal psychotherapy (IPT)	4	(1, 15)
Behavioural therapies (individual)	5	(2, 14)
SSRIs	6	(3, 11)
Mirtazapine	7	(3, 13)
Cognitive and cognitive behavioural therapies (individual) (CBT/CT)	8	(3, 13)
Pill placebo	9	(6, 15)
Short-term psychodynamic psychotherapies	10	(2, 17)
Self-help with support	10	(3, 16)
Exercise	12	(3, 17)
Self-help without support	13	(7, 16)
Counselling	13	(4, 17)
Attention placebo	15	(8, 17)
TAU	15	(10, 17)
No treatment	16	(9, 17)

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1.43 Assumptions and limitations

- We assumed that our methods for converting baseline and final and response data to CFB would give reliable estimates of CFB. These equations are based on a mathematical relationship with the assumption of normality of the underlying continuous data. As mentioned in the methods section we checked these assumptions by looking at the observed data for studies reporting all outcomes. It is not possible to know if this agreement also applies to the other studies.
- Similarly we assumed that the method we used to convert SMD to response gave reliable estimates of response. This method is well known and recommended by the Cochrane Collaboration, although it may not always perform well (Meister et al. 2015.).
- The observed correlation between baseline and follow-up was assumed to be 0.5. This value was used following convention, as we failed to find consistency in estimates of these correlations for any scale in the literature. We tested this assumption in a sensitivity analysis using a correlation of 0.3 for Response in completers, Response in those randomised, and SMD in both populations. Overall the results were similar to the original analyses although for most outcomes the uncertainty slightly decreased. For response in completers in the moderate/severe population, the uncertainty slightly decreased for some relative effects, and slightly increased for other relative effects, although overall, the results were similar to the original analysis.
- For the SMD analysis we needed to make an assumption about the relationship between the standard deviation at baseline and standard deviation at follow-up. From looking at the data we had, we assumed that these were equal. This was also tested in sensitivity analysis using the regression equation to transform the baseline standard deviation. Overall, there was a slight reduction in uncertainty, but results were very similar to the original analysis.

- We assumed the existence of class effects and modelled the data in this way. We tested this by running fixed class effect models and noted their comparability to random class effect models. We therefore conclude that there is evidence of agreement of relative treatment effects across elements of the same class.
- As we had several classes with only 1 or 2 interventions we needed to make some assumptions about the variance of those classes. The assumptions we made are highlighted in the report. These were informed by clinical opinion from members of the guideline committee.

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1.66 Appendix 1: WinBUGS codes

1.6.17 Sample WinBUGS code – SMD analysis

```
# Normal likelihood, identity link: SMD with arm-based means
# Random effects model for multi-arm trials
model{                                  # *** PROGRAM STARTS
for(i in 1:ns){                         #   LOOP THROUGH STUDIES
  w[i,1] <- 0   # adjustment for multi-arm trials is zero for control arm
  delta[i,1] <- 0                       # treatment effect is zero for control
arm
  mu[i] ~ dnorm(0,.0001)                # vague priors for all trial baselines
 }
# (1) CFB DATA
for(i in 1:nsCFB){
  # calculate pooled.sd and adjustment for SMD
  df[i] <- sum(nCFB[i,1:naCFB[i]]) - naCFB[i] # denominator for pooled.var
  Pooled.var[i] <- sum(nvar[i,1:naCFB[i]])/df[i]
      # pooled sd for study i, for SMD
  Pooled.sd[i] <- sqrt(Pooled.var[i])
#  H[i] <- 1 - 3/(4*df[i]-1)           # use Hedges' g
  H[i] <- 1                             # use Cohen's d (ie no adjustment)
  for (k in 1:naCFB[i]){
    se[i,k] <- sdCFB[i,k]/sqrt(nCFB[i,k])
```

Update 2018

```
    var[i,k] <- pow(se[i,k],2)       # calcultate variances
    prec[i,k] <- 1/var[i,k]          # set precisions
    y[i,k] ~ dnorm(phi[i,k], prec[i,k]) # normal likelihood
    phi[i,k] <- theta[i,k] * (Pooled.sd[i]/H[i]) # theta is stand mean
    theta[i,k] <- mu[i] + delta[i,k] # model for linear predictor, delta is
SMD
    dev[i,k] <- (y[i,k]-phi[i,k])*(y[i,k]-phi[i,k])*prec[i,k]
    nvar[i,k] <- (nCFB[i,k]-1) * pow(sdCFB[i,k],2) # for pooled.sd
   }
  # summed residual deviance contribution for this trial
  resdev[i] <- sum(dev[i,1:naCFB[i]])
 }
# (2) BASELINE + FOLLOW-UP DATA (no CFB)
for(i in 1:nsBF){                    #   LOOP THROUGH STUDIES
  # calculate pooled.sd and adjustment for SMD
  df[i+nsCFB] <- sum(n[i,1:na[i]]) - na[i] # denominator for pooled.var
  Pooled.var[i+nsCFB] <- sum(nvarBF[i,1:na[i]])/df[i+nsCFB]
      # pooled sd for study i, for SMD
  Pooled.sd[i+nsCFB] <- sqrt(Pooled.var[i+nsCFB])
#  H[i] <- 1 - 3/(4*df[i]-1)           # use Hedges' g
  H[i+nsCFB] <- 1                    # use Cohen's d (ie no adjustment)
  for (k in 1:na[i]){
    yBF[i,k] <- yF[i,k] - yB[i,k]     # calculate mean CFB
    seF[i,k] <- sdF[i,k]/sqrt(n[i,k]) # se at followup
    seB[i,k] <- sdB[i,k]/sqrt(n[i,k]) # se at baseline
    # variance of mean CFB, assuming correlation corr[i]
    var[i+nsCFB,k] <- pow(seF[i,k],2)+ pow(seB[i,k],2)
-2*(seF[i,k]*seB[i,k]*corr[i])
    prec[i+nsCFB,k] <- 1/var[i+nsCFB,k] # set CFB precisions
    yBF[i,k] ~ dnorm(phi[i+nsCFB,k], prec[i+nsCFB,k]) # normal likelihood
    # theta is standardised mean
    phi[i+nsCFB,k] <- theta[i+nsCFB,k] * (Pooled.sd[i+nsCFB]/H[i+nsCFB])
    # model for linear predictor, delta is SMD
    theta[i+nsCFB,k] <- mu[i+nsCFB] + delta[i+nsCFB,k]
    # residual deviance contribution
```

Update 2018

```
    dev[i+nsCFB,k] <- (yBF[i,k]-phi[i+nsCFB,k]) * (yBF[i,k]-phi[i+nsCFB,k])
* prec[i+nsCFB,k]
    # variance of CFB, assuming correlation corrBF[i] (var is sd squared)
    varBF[i,k] <- pow(sdF[i,k],2) + pow(sdB[i,k],2)
- 2*(sdF[i,k]*sdB[i,k]*corr[i])
    nvarBF[i,k] <- (n[i,k]-1) * varBF[i,k] # for pooled.sd
   }
  # summed residual deviance contribution for this trial
  resdev[i+nsCFB] <- sum(dev[i+nsCFB,1:na[i]])
 }
# (3) RESPONSE DATA (no CFB or BL+follow-up)
for(i in 1:nsR){                    #   LOOP THROUGH STUDIES
  # calculate pooled.sd and adjustment for SMD
  df[i+nsCFB+nsBF] <- sum(nR[i,1:naR[i]]) - naR[i] # denominator for
pooled.var
  Pooled.var[i+nsCFB+nsBF] <- sum(nvarR[i,1:naR[i]])/df[i+nsCFB+nsBF]
      # pooled sd for study i, for SMD
      Pooled.sd[i+nsCFB+nsBF] <- sqrt(Pooled.var[i+nsCFB+nsBF])
#  H[i] <- 1 - 3/(4*df[i]-1)          # use Hedges' g
  H[i+nsCFB+nsBF] <- 1               # use Cohen's d (ie no adjustment)
  for (k in 1:naR[i]){
    r[i,k] ~ dbin(R[i,k], nR[i,k])    # binomial likelihood
    R[i,k] <- phi.adj[i,k]
    x[i,k] <- -(q[i]*yBR[i,k]+ phi[i+nsCFB+nsBF,k])/(sdBR[i,k] *
sqrt(1+(1-q[i])*(1-q[i]-2*corrR[i])))
    # adjust link function phi(x) for extreme values that can give
numerical
    # errors when x< -5, phi(x)=0, when x> 5, phi(x)=1
    phi.adj[i,k] <- (step(5+x[i,k]) * step(x[i,k]-5)
           + step(5-x[i,k])* step(x[i,k]+5) * phi(x[i,k]))*(1-
equals(x[i,k],5))
           + equals(x[i,k],5)    # correct for x=5
    # theta is standardised mean
    phi[i+nsCFB+nsBF,k] <- theta[i+nsCFB+nsBF,k]
                * (Pooled.sd[i+nsCFB+nsBF]/H[i+nsCFB+nsBF])
    # model for linear predictor, delta is SMD
    theta[i+nsCFB+nsBF,k] <- mu[i+nsCFB+nsBF] + delta[i+nsCFB+nsBF,k]
    # residual deviance contribution
```

Update 2018

```
    rhat[i,k] <- R[i,k] * nR[i,k]
    dev[i+nsCFB+nsBF,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))
         + (nR[i,k]-r[i,k]) * (log(nR[i,k]-r[i,k]) - log(nR[i,k]-
rhat[i,k])))
# Sensitivity analysis
#    sdR[i,k] <-  3.54 + sdBR[i,k] * 0.61  # sd for response
    sdR[i,k] <-  sdBR[i,k]          # sd for response
    nvarR[i,k] <- (nR[i,k]-1) * pow(sdR[i,k],2) # for pooled.sd
   }
  # summed residual deviance contribution for this trial
  resdev[i+nsCFB+nsBF] <- sum(dev[i+nsCFB+nsBF,1:naR[i]])
 }
#
# RE MODEL (CFB data)
for(i in 1:nsCFB){                    # LOOP THROUGH STUDIES WITH CFB DATA
  for (k in 2:naCFB[i]){              # LOOP THROUGH ARMS
    # trial-specific RE distributions
    delta[i,k] ~ dnorm(md[i,k], taud[i,k])
    md[i,k] <- d[tCFB[i,k]] - d[tCFB[i,1]] + sw[i,k]
    # precision of RE distributions (with multi-arm trial correction)
    taud[i,k] <- tau *2*(k-1)/k
    #adjustment, multi-arm RCTs
    w[i,k] <- delta[i,k] - d[tCFB[i,k]] + d[tCFB[i,1]]
    # cumulative adjustment for multi-arm trials
    sw[i,k] <-sum(w[i,1:k-1])/(k-1)
   }
 }
# RE MODEL (BL and F-up data)
for(i in 1:nsBF){                     # LOOP THROUGH STUDIES WITH BL+FUP
DATA
  for (k in 2:na[i]){                 # LOOP THROUGH ARMS
    # trial-specific RE distributions
    delta[i+nsCFB,k] ~ dnorm(md[i+nsCFB,k], taud[i+nsCFB,k])
    md[i+nsCFB,k] <- d[t[i,k]] - d[t[i,1]] + sw[i+nsCFB,k]
    # precision of RE distributions (with multi-arm trial correction)
    taud[i+nsCFB,k] <- tau *2*(k-1)/k
```

Update 2018

```
    #adjustment, multi-arm RCTs
    w[i+nsCFB,k] <- delta[i+nsCFB,k] - d[t[i,k]] + d[t[i,1]]
    # cumulative adjustment for multi-arm trials
    sw[i+nsCFB,k] <-sum(w[i+nsCFB,1:k-1])/(k-1)
   }
 }
# RE MODEL (Response data)
for(i in 1:nsR){                    # LOOP THROUGH STUDIES WITH RESPONSE
DATA
  for (k in 2:naR[i]){              # LOOP THROUGH ARMS
    # trial-specific RE distributions
    delta[i+nsCFB+nsBF,k] ~ dnorm(md[i+nsCFB+nsBF,k], taud[i+nsCFB+nsBF,k])
    md[i+nsCFB+nsBF,k] <- d[tR[i,k]] - d[tR[i,1]] + sw[i+nsCFB+nsBF,k]
    # precision of RE distributions (with multi-arm trial correction)
    taud[i+nsCFB+nsBF,k] <- tau *2*(k-1)/k
    #adjustment, multi-arm RCTs
    w[i+nsCFB+nsBF,k] <- delta[i+nsCFB+nsBF,k] - d[tR[i,k]] + d[tR[i,1]]
    # cumulative adjustment for multi-arm trials
    sw[i+nsCFB+nsBF,k] <-sum(w[i+nsCFB+nsBF,1:k-1])/(k-1)
  }
 }
#
totresdev <- sum(resdev[])              # Total Residual Deviance (all
data)
# Partial Residual Deviance
totresdev.p[1] <- sum(resdev[1:nsCFB])                    # CFB data
totresdev.p[2] <- sum(resdev[nsCFB+1:nsCFB+nsBF])         # BL + Fup data
totresdev.p[3] <- sum(resdev[nsCFB+nsBF+1:nsCFB+nsBF+nsR]) # Response data
#
# Priors and model assumptions (classes)
d[1]<-0                        # treatment effect is zero for control arm
      # treatments borrowing variance
      # Variance from 'No treatment'
      for(k in 4:7){ d[k] ~ dnorm(m[D[k]], prec2[2]) }
      # Any AD, variance from SSRIs & TCAS
```

Update 2018

```
      d[19] ~ dnorm(m[D[19]], prec2[8])    # prec2[8]=precision of any AD class
      z <- (1/prec2[7]) + (1/prec2[6])          # sum of SSRI & TCA variances
      prec2[8] <- 1/z
      # Variance from CBT/CT
      d[20] ~ dnorm(m[D[20]], prec2[17]) # through counselling
      for(k in 36:40) { d[k] ~ dnorm(m[D[k]], prec2[17]) }
      d[59] ~ dnorm(m[D[59]], prec2[17])
      # Variance from CBT + AD
      for(k in 55:58){ d[k] ~ dnorm(m[D[k]], prec2[19]) }
      for(k in 60:61){ d[k] ~ dnorm(m[D[k]], prec2[19]) }

      # treatment effects from Class
      # No treatment
      for (k in 2:3){  d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
      # Exercise, TCA, SSRI
      for(k in 8:18){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
      # Self-help with support, Self-help, Psychoeducational interventions
      for(k in 21:35){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
      # CBT/CT; Behavioural, cognitive, or CBT groups
      for(k in 41:52){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
      # CBT + AD
  for(k in 53:54) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
#
m[1] <- 0
#
# priors for mean class effect
for (k in 2:nc){ m[k] ~ dnorm(0, .0001) }
# priors for within-class variability
for (k in 2:7){
  sd2[k] ~ dnorm(0,tau2)I(0,)      # prior for class variance
  prec2[k] <- pow(sd2[k], -1)      # class precision
 }
for (k in 9:nc){
  sd2[k] ~ dnorm(0,tau2)I(0,)      # prior for class variance
```

Update 2018

```
  prec2[k] <- pow(sd2[k], -1)      # class precision
 }
#
tau2 <- pow(0.19,-2)
sdev ~ dunif(0,5)                    # vague prior for between-trial SD
tau <- pow(sdev,-2)                  # between-trial precision
# all pairwise differences
for (c in 1:(nt-1)) {
      for (k in (c+1):nt)  { diff[c,k] <- d[k] - d[c] }
      }
#
# pairwise SMDs for all possible class comparisons
for (c in 1:(nt-1)){
  for (k in (c+1):nc)  { diffClass[c,k] <- (m[k]-m[c]) }
 }
#
# rank treatments
for(k in 1:2){ dR[k] <- d[k] }
for(k in 3:3){ dR[k] <- d[k+1] }
for(k in 4:4){ dR[k] <- d[k+2] }
for(k in 5:5){ dR[k] <- d[k+3] }
for(k in 6:6){ dR[k] <- d[k+4] }
for(k in 7:7){ dR[k] <- d[k+5] }
for(k in 8:12){ dR[k] <- d[k+6] }
for(k in 13:17){ dR[k] <- d[k+7] }
for(k in 18:18){ dR[k] <- d[k+8] }
for(k in 19:25){ dR[k] <- d[k+9] }
for(k in 26:28){ dR[k] <- d[k+10] }
for(k in 29:30){ dR[k] <- d[k+11] }
for(k in 31:31){ dR[k] <- d[k+12] }
for(k in 32:33){ dR[k] <- d[k+13] }
for(k in 34:34){ dR[k] <- d[k+14] }
for(k in 35:36){ dR[k] <- d[k+15] }
for(k in 37:42){ dR[k] <- d[k+16] }
for(k in 43:44){ dR[k] <- d[k+17] }
```

Update 2018

```
#
for (k in 1:nt)  {
  rk[k]  <- rank(d[],k)          # lower values are "good"
  best[k]  <- equals(rk[k],1)    # Smallest is best (i.e. rank 1)
  # prob treat k is h-th best, prob[1,k]=best[k]
  for (h in 1:nt) { prob[h,k] <- equals(rk[k],h) }
 }
for (k in 1:ntR){
#  rk2[k] <- ntR+1-rank(dR[],k)     # lower values are "bad"
  rk2[k] <- rank(dR[],k)             # lower values are "good"
  best2[k]  <- equals(rk2[k],1)  # Smallest is best (i.e. rank 1)
  # prob treat k is h-th best, prob[1,k]=best[k]
  for (h in 1:ntR) { prob2[h,k] <- equals(rk2[k],h) }
 }
# rank classes
for(k in 1:7){ mR[k] <- m[k]  }
for(k in 8:21){ mR[k] <- m[k+1]  }
for(k in 22:23){ mR[k] <- m[k+2]  }
for (k in 1:nc){
  rkClass[k] <- rank(m[],k)     # lower values are "good"
  bestClass[k] <- equals(rkClass[k],1) # Smallest is best (i.e. rank 1)
  # prob class k is h-th best, prob[1,k]=best[k]
  for (h in 1:nc){ probClass[h,k] <- equals(rkClass[k],h) }
 }
for (k in 1:ncR)  {
  rkClass2[k]  <- rank(mR[],k)  # lower values are "good"
  bestClass2[k]  <- equals(rkClass2[k],1)    # Smallest is best (i.e. rank
1)
  # prob class k is h-th best, prob[1,k]=best[k]
  for (h in 1:ncR) { probClass2[h,k] <- equals(rkClass2[k],h) }
 }
}                                  # *** PROGRAM ENDS
```

1.6.23 Sample WinBUGS code – Response analysis

```
# Random effects model for multi-arm trials
model{                             # *** PROGRAM STARTS
```

Update 2018

```
for(i in 1:ns){                    #   LOOP THROUGH ALL STUDIES
  w[i,1] <- 0   # adjustment for multi-arm trials is zero for control arm
  # RESPONSE DATA
  delta[i,1] <- 0                  # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
  # CONTINUOUS DATA
  deltaX[i,1] <- 0                 # treatment effect is zero for control arm
  muX[i] ~ dnorm(0,.0001)          # vague priors for all trial baselines
 }
#
# RESPONSE DATA
for(i in 1:nsR){                   # LOOP THROUGH STUDIES WITH RESPONSE DATA
  for (k in 1:naR[i]){             # LOOP THROUGH ARMS
    r[i,k] ~ dbin(p[i,k],nR[i,k])  # binomial likelihood
    logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor
    rhat[i,k] <- p[i,k] * nR[i,k]  # expected value of the numerators
    #Deviance contribution
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))
          +  (nR[i,k]-r[i,k]) * (log(nR[i,k]-r[i,k]) - log(nR[i,k]-rhat[i,k])))
   }
  # Summed residual deviance contribution for this trial
  resdev[i] <- sum(dev[i,1:naR[i]])
 }
#
# (1) CFB DATA
for(i in 1:nsCFB){                 # LOOP THROUGH STUDIES WITH CFB DATA
  # calculate pooled.sd and adjustment for SMD
  df[i] <- sum(nCFB[i,1:naCFB[i]]) - naCFB[i] # denominator for pooled.var
  Pooled.var[i] <- sum(nvar[i,1:naCFB[i]])/df[i]
  Pooled.sd[i] <- sqrt(Pooled.var[i]) # pooled sd for study i, for SMD
  # H[i] <- 1 - 3/(4*df[i]-1)       # use Hedges' g
  H[i] <- 1                        # use Cohen's d (ie no adjustment)
  for (k in 1:naCFB[i]){           # LOOP THROUGH ARMS
```

Update 2018

```
    se[i,k] <- sdCFB[i,k]/sqrt(nCFB[i,k]) # calculate st error of CFB
    var[i,k] <- pow(se[i,k],2)      # calcultate variances of CFB
    prec[i,k] <- 1/var[i,k]         # set precisions of CFB
    y[i,k] ~ dnorm(phi[i,k], prec[i,k]) # normal likelihood
    phi[i,k] <- theta[i,k] * (Pooled.sd[i]/H[i]) # theta is stand mean
    # model for linear predictor, deltaX is SMD
    theta[i,k] <- muX[i] + deltaX[i,k]
    dev[i+nsR,k] <- (y[i,k]-phi[i,k])*(y[i,k]-phi[i,k])*prec[i,k]
    nvar[i,k] <- (nCFB[i,k]-1) * pow(sdCFB[i,k],2) # for pooled.sd
   }
  # summed residual deviance contribution for this trial
  resdev[i+nsR] <- sum(dev[i+nsR,1:naCFB[i]])
 }
# (2) BASELINE + FOLLOW-UP DATA (no CFB)
for(i in 1:nsBF){                  # LOOP THROUGH STUDIES WITH BL + F-UP
DATA
  # calculate pooled.sd and adjustment for SMD
  df[i+nsCFB] <- sum(n[i,1:na[i]]) - na[i] # denominator for pooled.var
  Pooled.var[i+nsCFB] <- sum(nvarBF[i,1:na[i]])/df[i+nsCFB]
  Pooled.sd[i+nsCFB] <- sqrt(Pooled.var[i+nsCFB])# pooled sd for study
i,for SMD   # H[i+nsCFB] <- 1 - 3/(4*df[i]-1) # use Hedges' g
  H[i+nsCFB] <- 1                   # use Cohen's d (ie no adjustment)
  for (k in 1:na[i]){               # LOOP THROUGH ARMS
    yBF[i,k] <- yF[i,k] - yB[i,k]   # calculate mean CFB
    seF[i,k] <- sdF[i,k]/sqrt(n[i,k]) # se at followup
    seB[i,k] <- sdB[i,k]/sqrt(n[i,k]) # se at baseline
    # variance of mean CFB, assuming correlation corr[i]
    var[i+nsCFB,k] <- pow(seF[i,k],2)+ pow(seB[i,k],2)
-2*(seF[i,k]*seB[i,k]*corrBF[i])
    prec[i+nsCFB,k] <- 1/var[i+nsCFB,k] # set CFB precisions
    yBF[i,k] ~ dnorm(phi[i+nsCFB,k], prec[i+nsCFB,k]) # normal likelihood
    # theta is standardised mean
    phi[i+nsCFB,k] <- theta[i+nsCFB,k] * (Pooled.sd[i+nsCFB]/H[i+nsCFB])
    # model for linear predictor, deltaX is SMD
    theta[i+nsCFB,k] <- muX[i+nsCFB] + deltaX[i+nsCFB,k]
    # residual deviance contribution
```

Update 2018

```
    dev[i+nsR+nsCFB,k] <- (yBF[i,k]-phi[i+nsCFB,k]) * (yBF[i,k]-
phi[i+nsCFB,k])                              * prec[i+nsCFB,k]
    # variance of CFB, assuming correlation corrBF[i] (var is sd squared)
    varBF[i,k] <- pow(sdF[i,k],2) + pow(sdB[i,k],2)
                - 2*(sdF[i,k]*sdB[i,k]*corrBF[i])
    nvarBF[i,k] <- (n[i,k]-1) * varBF[i,k] # for pooled.sd
   }
  # summed residual deviance contribution for this trial
  resdev[i+nsR+nsCFB] <- sum(dev[i+nsR+nsCFB,1:na[i]])
 }
#
# RE MODEL (Response data)
for(i in 1:nsR){                  # LOOP THROUGH STUDIES WITH RESPONSE
DATA
  for (k in 2:naR[i]){            # LOOP THROUGH ARMS
    delta[i,k] ~ dnorm(md[i,k], taud[i,k]) # trial-specific LOR
distributions
    # mean of LOR distributions (with multi-arm trial correction)
    md[i,k] <-  d[tR[i,k]] - d[tR[i,1]] + sw[i,k]
    # precision of LOR distributions (with multi-arm trial correction)
    taud[i,k] <- tau *2*(k-1)/k
    # adjustment for multi-arm RCTs
    w[i,k] <- (delta[i,k] - d[tR[i,k]] + d[tR[i,1]])
    # cumulative adjustment for multi-arm trials
    sw[i,k] <- sum(w[i,1:k-1])/(k-1)
   }
 }
# RE MODEL (CFB data)
for(i in 1:nsCFB){                # LOOP THROUGH STUDIES WITH CFB DATA
  for (k in 2:naCFB[i]){          # LOOP THROUGH ARMS
    # convert SMD to LOR
    deltaX[i,k] <- delta[i+nsR,k]*((sqrt(3))/-3.1416)
    # trial-specific RE distributions
    delta[i+nsR,k] ~ dnorm(md[i+nsR,k], taud[i+nsR,k])
    md[i+nsR,k] <- d[tCFB[i,k]] - d[tCFB[i,1]] + sw[i+nsR,k]
    # precision of RE distributions (with multi-arm trial correction)
```

Update 2018

```
    taud[i+nsR,k] <- tau *2*(k-1)/k
    # adjustment, multi-arm RCTs
    w[i+nsR,k] <- delta[i+nsR,k] - d[tCFB[i,k]] + d[tCFB[i,1]]
    # cumulative adjustment for multi-arm trials
    sw[i+nsR,k] <-sum(w[i+nsR,1:k-1])/(k-1)
   }
 }
# RE MODEL (BL and F-up data)
for(i in 1:nsBF){                  # LOOP THROUGH STUDIES WITH BL + F-UP
DATA
  for (k in 2:na[i]){              # LOOP THROUGH ARMS
    # convert SMD to LOR
    deltaX[i+nsCFB,k] <- delta[i+nsR+nsCFB,k]*((sqrt(3))/-3.1416)
    # trial-specific RE distributions
    delta[i+nsCFB+nsR,k] ~ dnorm(md[i+nsCFB+nsR,k], taud[i+nsCFB+nsR,k])
    md[i+nsCFB+nsR,k] <- d[t[i,k]] - d[t[i,1]] + sw[i+nsCFB+nsR,k]
    # precision of RE distributions (with multi-arm trial correction)
    taud[i+nsCFB+nsR,k] <- tau *2*(k-1)/k
    #adjustment, multi-arm RCTs
    w[i+nsCFB+nsR,k] <- delta[i+nsR+nsCFB,k] - d[t[i,k]] + d[t[i,1]]
    # cumulative adjustment for multi-arm trials
    sw[i+nsCFB+nsR,k] <-sum(w[i+nsCFB+nsR,1:k-1])/(k-1)
   }
 }
#
# Calculate residual deviance
totresdev <- sum(resdev[])             # Total Residual Deviance (all data)
totresdev.p[1] <- sum(resdev[1:nsR])  # Response data
totresdev.p[2] <- sum(resdev[nsR+1:nsR+nsCFB]) # CFB data
totresdev.p[3] <- sum(resdev[nsR+nsCFB+1:nsCFB+nsBF+nsR]) # BL + FL data
d[1] <- 0                    # treatment effect is zero for reference
treatment
m[1] <- 0                    # treatment effect is zero for reference class
#
# Priors and model assumptions (classes)
# treatment effects from Class
```

Update 2018

```
for (k in 2:3){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
for (k in 10:19){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
for (k in 24:39){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
for (k in 42:65){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }

# variance from no treatment
for (k in 4:7){ d[k] ~ dnorm(m[D[k]], prec2[D[2]]) }
# variance from self-help with support
for (k in 8:9){ d[k] ~ dnorm(m[D[k]], prec2[D[11]]) }
# sum of variances from SSRI/TCAs
d[20] ~ dnorm(m[D[20]], prec2[8])
x <- (1/prec2[6]) + (1/prec2[7])
prec2[8] <- 1/x
# variance from counselling
for (k in 22:23){ d[k] ~ dnorm(m[D[k]], prec2[D[15]]) }
# variance from CBT/CT
for (k in 40:41){ d[k] ~ dnorm(m[D[k]], prec2[D[18]]) }
for (k in 72:73){ d[k] ~ dnorm(m[D[k]], prec2[D[18]]) }
# variance from CBT/CT + AD
for (k in 66:71){ d[k] ~ dnorm(m[D[k]], prec2[D[20]]) }
for (k in 74:75){ d[k] ~ dnorm(m[D[k]], prec2[D[20]]) }

# no class treatments [mirtazapine]
d[21] ~ dnorm(0, .0001)          # vague prior for treatment effects
m[9] <- d[21]                    # class effect = treat effect

for (k in 2:8){ m[k] ~ dnorm(0, .0001) }
for (k in 10:nc){ m[k] ~ dnorm(0, .0001) }
# priors for class precision
tau2 <- pow(0.19,-2)
for (k in 1:7){
  sd2[k] ~ dnorm(0,tau2)I(0,)    # informative prior for within-class st dev
  prec2[k] <- pow(sd2[k], -1) # within-class precision
 }
for (k in 9:nc){
```

Update 2018

```
  sd2[k] ~ dnorm(0,tau2)I(0,)    # informative prior for within-class st dev
  prec2[k] <- pow(sd2[k], -1) # within-class precision
}
#
sdev ~ dunif(0,5)               # vague prior for between-trial SD
tau <- pow(sdev,-2)             # between-trial precision
# pairwise ORs and LORs for all possible pair-wise comparisons
for (c in 1:(nt-1)){
  for (k in (c+1):nt){
    or[c,k] <- exp(d[k] - d[c])
    lor[c,k] <- (d[k]-d[c])
   }
 }

#
# pairwise differences for classes
for (c in 1:(nc-1)){
  for (k in (c+1):nc){
    diffClass[c,k] <- m[k] - m[c]
    orClass[c,k] <- exp(m[k] - m[c])
   }
 }
#
# rank treatments
for(k in 1:2){  dR[k] <- d[k] }
dR[3] <- d[4]
dR[4] <- d[6]
dR[5] <- d[8]
dR[6] <- d[11]
dR[7] <- d[13]
dR[8] <- d[16]
dR[9] <- d[17]
dR[10] <- d[18]
dR[11] <- d[19]
dR[12] <- d[21]
```

Update 2018

```
dR[13] <- d[22]
dR[14] <- d[23]
dR[15] <- d[24]
dR[16] <- d[26]
dR[17] <- d[28]
dR[18] <- d[29]
dR[19] <- d[31]
dR[20] <- d[32]
dR[21] <- d[34]
dR[22] <- d[35]
dR[23] <- d[36]
dR[24] <- d[37]
dR[25] <- d[38]
dR[26] <- d[40]
dR[27] <- d[42]
dR[28] <- d[43]
dR[29] <- d[44]
dR[30] <- d[45]
dR[31] <- d[46]
dR[32] <- d[47]
dR[33] <- d[50]
dR[34] <- d[52]
dR[35] <- d[53]
dR[36] <- d[54]
dR[37] <- d[55]
dR[38] <- d[56]
dR[39] <- d[57]
dR[40] <- d[59]
dR[41] <- d[60]
dR[42] <- d[62]
dR[43] <- d[63]
dR[44] <- d[64]
dR[45] <- d[65]
dR[46] <- d[66]
dR[47] <- d[67]
```

```
dR[48] <- d[68]
dR[49] <- d[69]
dR[50] <- d[70]
dR[51] <- d[71]
dR[52] <- d[74]
dR[53] <- d[75]
#
for (k in 1:nt){
  rk[k] <- nt+1-rank(d[],k)       # assumes events are "good"
#  rk[k] <- rank(d[],k)          # assumes events are "bad"
  best[k]  <- equals(rk[k],1)    # Smallest is best (i.e. rank 1)
  # prob treat k is h-th best, prob[1,k]=best[k]
  for (h in 1:nt) { prob[h,k] <- equals(rk[k],h) }
 }
for (k in 1:ntR){
  rk2[k] <- ntR+1-rank(dR[],k)       # assumes events are "good"
#  rk2[k] <- rank(dR[],k)            # assumes events are "bad"
  best2[k]  <- equals(rk2[k],1)  # Smallest is best (i.e. rank 1)
  # prob treat k is h-th best, prob[1,k]=best[k]
  for (h in 1:ntR) { prob2[h,k] <- equals(rk2[k],h) }
 }
#
# rank classes
for(k in 1:7){ mR[k] <- m[k] }
for(k in 8:23){ mR[k] <- m[k+1] }
mR[24] <- m[26]
for (k in 1:nc){
  rkClass[k] <- nc+1-rank(m[],k)    # assumes events are "good"
  bestClass[k] <- equals(rkClass[k],1) # Smallest is best (i.e. rank 1)
  # prob class k is h-th best, prob[1,k]=best[k]
  for (h in 1:nc){ probClass[h,k] <- equals(rkClass[k],h) }
 }
for (k in 1:ncR)  {
  rkClass2[k]  <- ncR+1-rank(mR[],k)
  bestClass2[k]  <- equals(rkClass2[k],1)    # Smallest is best (i.e. rank
1)
```

Update 2018

```
  # prob class k is h-th best, prob[1,k]=best[k]
  for (h in 1:ncR) { probClass2[h,k] <- equals(rkClass2[k],h) }
 }
}                                    # *** PROGRAM ENDS
```

1.71 Appendix 2: Correlations

1.7.12 Data from trials

Study	Intervention	Scale	Number of items	Mean baseline completers	SD baseline completers	Mean endpoint completers	SD endpoint completers	Mean change completers	SD change completers	N_Compl	Correlation
Beasley 1991b	Fluoxetine	HAMD	17	27.1	5.1	15.2	9.7	-11.8	9.7	233	0.26
	Imipramine	HAMD	17	27.7	5.4	16.3	9.8	-11.4	9.7	233	0.29
	Pill placebo	HAMD	17	27.4	5.6	20.1	9.2	-7.3	9.0	222	0.34
Callaghan 2011	Exercise	BDI-ii	21	26.5	10.7	18.1	13	-8.5	9.8	19	0.67
	Exercise	BDI	21	30.5	12	29.6	13.9	-0.9	6.6	19	0.88
Kendrick 2009	Any SSRI + Enhanced TAU	HAMD	17	15.45	2.09	8.73	5.2	-6.8	4.9	96	0.34
	Enhanced TAU	HAMD	17	15.7	2.5	11.2	5.8	-4.5	5.3	90	0.41
Legrand 2014	Exercise	BDI-II	21	21.7	6.8	12.8	4.4	-8.9	6.7	15	0.35
	Waitlist	BDI-II	21	19.3	9.3	19.7	8.2	0.4	3.7	12	0.92
McClelland 1979	Amitriptyline	HAMD	17	19.5	4.5	8.4	4.4	-11.1	5.5	20	0.24
	Lofepramine	HAMD	17	19.5	4.3	7.2	5.1	-12.3	6.1	21	0.17
Zu 2014	CBT individual (over 15 sessions) + any SSRI	HAMD	17	25.1	6.0	5.7	6.9	-19.4	7.6	43	0.31
	TAU	HAMD	17	21.6	5.1	6.2	6.6	-15.3	9.1	16	-0.20
Schramm 2007/Zobel 2011	Interpersonal psychotherapy (IPT) + any AD	HAMD	17	24.8	5.3	7.5	5.2	-17.4	7.6	53	-0.05
	Any AD	HAMD	17	21.6	3.9	10.6	7.5	-11.1	7.6	52	0.23
Spring 1992	Amitriptyline	HAMD	21	25.2	2.8	8.5	5.3	-16.7	6	10	0.00

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Study	Intervention	Scale	Number of items	Mean baseline completers	SD baseline completers	Mean endpoint completers	SD endpoint completers	Mean change completers	SD change completers	N_Compl	Correlation
	Pill placebo	HAMD	21	24.8	4.5	13.1	9.8	-11.7	9	15	0.40
Andersson 2005	Computerised-CBT (CCBT)	MADRS	9	20.1	5.7	12.7	8.3	-5.5	8.1	36	0.37
	Waitlist	MADRS	9	21.6	7.2	19.0	7.6	-2.6	9.1	49	0.25
Liu 2009	Cognitive bibliotherapy	BDI-II	21	28.9	9.7	18.8	10.0	-10.1	8.1	21	0.66
	Waitlist	BDI-II	21	24.9	7.5	20.9	8.5	-4.0	9.8	19	0.25
Schneider 2003	Sertraline	HAMD	17	21.4	2.7	13.0	6.2	-8.4	6.1	284	0.25
	Pill placebo	HAMD	17	21.2	2.5	14.5	6.2	-6.8	6.2	311	0.20
Lam 2013	CBT individual (under 15 sessions) + escitalopram	MADRS	10	28.2	5.1	12.5	9.1	-15.7	8.8	48	0.34
	Escitalopram	MADRS	10	27.1	4.9	12.8	8.4	-14.3	8.3	51	0.31

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Study	Intervention	Scale	Number of items	Mean baseline ITT	SD baseline ITT	Mean endpoint ITT	SD endpoint ITT	Mean change ITT	SD change ITT	N_Rand	Correlation
Bagby 2008	CBT individual (over 15 sessions)	HAMD	21	18.9	3.5	6.6	5.0	-12.22	5.72	146	0.13
	Any AD	HAMD	21	18.4	4.0	5.06	5.10	-13.38	6.03	129	0.14
Brenes 2007	Exercise	HAMD	17	12.7	3.4	7.8	4.3	-4.9	6.6	14	-0.46
	Sertraline	HAMD	17	13.7	2.7	7.4	4.7	-6.3	3.9	11	0.56

Study	Intervention	Scale	Number of items	Mean baseline ITT	SD baseline ITT	Mean endpoint ITT	SD endpoint ITT	Mean change ITT	SD change ITT	N_Rand	Correlation
	Waitlist	HAMD	17	9.5	3.7	10.9	5.8	1.5	5.3	12	0.45
Cassano 1996	Imipramine	MADRS	10	31.4	4.8	18.4	12.0	-12.9	10.4	64	0.51
	Pill placebo	MADRS	10	31.0	3.8	22.3	11.5	-8.7	11.5	59	0.17
Colonna 2005	Escitalopram	MADRS	10	29.5	4.3	8.4	8.6	-21.3	8.7	175	0.22
	Citalopram	MADRS	10	30.2	4.7	9.7	6.0	-20.5	9.8	182	-0.67
Forest Laboratories 2000	Escitalopram	MADRS	10	28.7	4.3	15.9	9.7	-12.9	10.0	129	0.15
	Citalopram	MADRS	10	25.0	5.5	15.3	11.1	-13.0	9.8	128	0.46
	Pill placebo	MADRS	10	28.8	5.0	17.5	10.9	-11.2	10.4	129	0.33
Jordan 2014	Third-wave cognitive therapy individual	MADRS	10	23.6	7.4	13.6	12.3	-10.0	11.6	23	0.40
	CBT individual (under 15 sessions)	MADRS	10	21.6	7.3	10.9	9.9	-10.7	11.7	25	0.08
Lepola 2003	Escitalopram	MADRS	10	29.0	4.3	13.7	8.3	-15.3	8.4	155	0.24
	Citalopram	MADRS	10	29.2	4.2	15.0	8.7	-14.2	8.9	160	0.19
	Pill placebo	MADRS	10	28.7	4.0	16.2	9.8	-12.5	9.5	154	0.28
Ou 2011	Escitalopram	HAMD	17	23.0	4.0	8.6	7.2	-14.7	8.2	120	0.01
	Citalopram	HAMD	17	22.9	4.4	9.1	7.5	-13.8	7.5	120	0.29

Update 2018

Study	Intervention	Scale	Number of items	Mean baseline ITT	SD baseline ITT	Mean endpoint ITT	SD endpoint ITT	Mean change ITT	SD change ITT	N_Rand	Correlation
Versiani 1999a	Fluoxetine	HAMD	21	28.4	4.8	10.5	8.9	-17.9	7.4	77	0.56
	Amitriptyline	HAMD	21	27.8	4.8	8.7	7.7	-19.1	8.1	80	0.23
Schramm 2007/Zobel 2011	Interpersonal psychotherapy (IPT) + any AD	HAMD	17	25.1	5.1	8.9	6.4	-16.1	8.0	65	0.05
	Any AD	HAMD	17	21.9	4.1	11.8	7.9	-10.1	7.8	65	0.30
Ho 2014	Exercise + TAU	MADRS	10	19.23	10.48	9.15	7.27	-10.08	9.41	26	0.49
	Attention placebo + TAU	MADRS	10	18.77	10.14	14.08	9.04	-4.69	7.33	26	0.71
Liu 2009	Cognitive bibliotherapy	BDI-II	21	27.7	9.1	18.2	9.5	-9.6	8.4	27	0.59
	Waitlist	BDI-II	21	23.4	7.6	20.9	8.6	-2.5	10.0	25	0.24
Schneider 2003	Sertraline	HAMD	17	21.4	2.7	14.0	6.5	-7.4	6.3	371	0.28
	Pill placebo	HAMD	17	21.4	2.6	14.8	6.3	-6.6	6.4	376	0.17
Tollefson 1994	Fluoxetine	HAMD	17	21.6	3.9	11.6	7.6	-10.0	6.7	62	0.47
	Imipramine	HAMD	17	21.3	3.8	12.2	7.9	-9.1	8.0	62	0.21

Update 2018

1.7.21 IAPT psych

			PHQ-9 Baseline		PHQ-9 Endpoint		Correlation	
Intervention	PHQ range	n	mean	sd	mean	sd	r	p
High Intensity (Only receiving HI treatment during episode of care)	PHQ: 5 - 17	2814	11.48	3.56	7.65	5.60	0.3405	<0.001
	PHQ: 5 - 9 (GAD <=9)	561	7.03	1.33	5.17	4.54	0.1143	0.0067
	PHQ: 10 - 17	1906	13.51	2.27	8.70	5.77	0.2364	<0.001
	PHQ: 10+	3817	17.70	4.88	11.72	7.31	0.4743	<0.001

			PHQ-9 Baseline		PHQ-9 Endpoint		Correlation	
Intervention	**PHQ range**	**n**	**mean**	**sd**	**mean**	**sd**	**r**	**p**
	PHQ: 18+	1911	21.87	2.75	14.72	7.45	0.2727	<0.001
Low Intensity (Only receiving LI treatment during episode of care)	PHQ: 5 - 17	5329	11.36	3.60	7.66	5.19	0.3922	<0.001
	PHQ: 5 - 9 (GAD <=9)	1117	6.92	1.38	5.11	3.73	0.2151	<0.001
	PHQ: 10 - 17	3535	13.49	2.24	8.86	5.39	0.2358	<0.001
	PHQ: 10+	5872	16.50	4.37	10.89	6.53	0.4486	<0.001
	PHQ: 18+	2337	21.05	2.47	13.94	6.90	0.2791	<0.001
Cognitive Behavioural Therapy	PHQ: 5 - 17	2758	11.52	3.58	7.50	5.64	0.3455	<0.001
	PHQ: 5 - 9 (GAD <=9)	506	7.03	1.29	4.92	4.35	0.1093	0.0139
	PHQ: 10 - 17	1862	13.57	2.28	8.58	5.82	0.2396	<0.001
	PHQ: 10+	3772	17.74	4.82	11.35	7.31	0.4454	<0.001
	PHQ: 18+	1910	21.80	2.72	14.06	7.59	0.2721	<0.001
Guided Self-Help	PHQ: 5 - 17	3164	11.18	3.64	7.22	5.06	0.3903	<0.001
	PHQ: 5 - 9 (GAD <=9)	663	6.86	1.38	4.84	3.51	0.2566	<0.001
	PHQ: 10 - 17	2033	13.45	2.26	8.46	5.31	0.2239	<0.001
	PHQ: 10+	3175	16.13	4.26	10.25	6.40	0.4243	<0.001
	PHQ: 18+	1142	20.91	2.39	13.43	6.91	0.2193	<0.001
Pure Self-Help	PHQ: 5 - 17	44	10.18	3.99	7.00	4.77	0.209	0.1734
	PHQ: 5 - 9 (GAD <=9)	15	6.73	1.39	6.87	5.49	0.4172	0.1218
	PHQ: 10 - 17	23	13.48	2.41	7.48	4.35	0.1204	0.5843
	PHQ: 10+	30	14.90	3.46	9.23	5.47	0.5739	<0.001
	PHQ: 18+	7	19.57	1.81	15.00	4.97	0.759	0.0478
Either Self-Help	PHQ: 5 - 17	3202	11.16	3.65	7.22	5.05	0.3875	<0.001
	PHQ: 5 - 9 (GAD <=9)	676	6.86	1.38	4.88	3.57	0.2582	<0.001
	PHQ: 10 - 17	2053	13.45	2.26	8.45	5.30	0.2236	<0.001
	PHQ: 10+	3200	16.12	4.25	10.23	6.39	0.4253	<0.001
	PHQ: 18+	1147	20.90	2.39	13.43	6.90	0.22	<0.001
Behavioural activation	PHQ: 5 - 17	119	12.39	3.63	9.27	5.73	0.5059	<0.001
	PHQ: 5 - 9 (GAD <=9)	22	6.59	1.14	4.91	3.32	0.1531	0.4964

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			PHQ-9 Baseline		PHQ-9 Endpoint		Correlation	
Intervention	**PHQ range**	**n**	**mean**	**sd**	**mean**	**sd**	**r**	**p**
	PHQ: 10 - 17	94	13.88	2.38	10.44	5.70	0.3571	<0.001
	PHQ: 10+	236	18.50	4.52	13.34	6.81	0.4715	<0.001
	PHQ: 18+	142	21.55	2.60	15.26	6.82	0.3472	<0.001
cCBT	PHQ: 5 - 17	157	11.35	3.82	6.83	4.97	0.4583	<0.001
	PHQ: 5 - 9 (GAD <=9)	34	6.53	1.42	3.97	2.69	-0.3052	0.0792
	PHQ: 10 - 17	103	13.68	2.30	8.33	5.25	0.2748	0.005
	PHQ: 10+	145	15.64	3.86	9.17	5.92	0.3369	<0.001
	PHQ: 18+	42	20.45	2.43	11.24	6.97	0.2656	0.0891
Counselling	PHQ: 5 - 17	316	11.31	3.45	7.86	5.66	0.392	<0.001
	PHQ: 5 - 9 (GAD <=9)	76	7.14	1.34	5.16	4.03	0.2052	0.0754
	PHQ: 10 - 17	214	13.26	2.23	9.10	5.95	0.2658	<0.001
	PHQ: 10+	382	16.85	4.76	11.58	7.02	0.4696	<0.001
	PHQ: 18+	168	21.42	2.78	14.73	7.03	0.2766	<0.001

Notes

- LI and HI criteria = recorded as receiving only this step of care during treatment episode
- Method for designating interventions: a case is allocated to an intervention in this analysis IF they had at least 2 sessions of that intervention recorded AND no more than 2 sessions of any other intervention.
- Counselling, behavioural activation and cCBT: might be quite varied in nature at delivery. Counselling seems to be delivered across LI and HI, but also a lot of step-ups.
- For low severity group GAD<=9 was included as well so wasn't just an anxiety group, but anxiety was not considered in other bands.
- Low intensity: self help, self help with suport, psychoeducational interventions; include exercise too. All other psych interventions: high intensity.

Update 2018

1.7.31 PHQ9

		PHQ-9 T1		PHQ-9 T2		Correlation	
Sample (criteria)	**n**	**mean**	**sd**	**mean**	**sd**	**r**	**p**
Caseness PHQ (>=10)	13405	17.11	4.62	11.56	6.91	0.455	<0.001
Caseness PHQ (>=10)	5872	16.5	4.37	10.89	6.53	0.4486	<0.001
+ Low intensity received							
Caseness PHQ (>=10)	3817	17.7	4.88	11.72	7.31	0.4743	<0.0
+ High intensity received							

1.7.42 STAR*D COMED drugs

		PHQ-9 T1		PHQ-9 T2		Correlation	
Sample (criteria)	**n**	**mean**	**sd**	**mean**	**sd**	**r**	**p**
Caseness PHQ (>=10)	13405	17.11	4.62	11.56	6.91	0.455	<0.001
Caseness PHQ (>=10) + Low intensity received	5872	16.5	4.37	10.89	6.53	0.4486	<0.001
Caseness PHQ (>=10) + High intensity received	3817	17.7	4.88	11.72	7.31	0.4743	<0.0

Update 2018

3

Study	Intervention	Severity	number of participants	Correlation (baseline and endpoint)
STAR-D	Citalopram	All participants	3593	r = 0.3765 (p<0.001)
		QIDS <=16	2109	r = 0.2546 (p<0.001)
		QIDS >=17	1484	r = 0.2077 (p<0.001)
CO-MED	Escit + Plb	All participants	196	r = 0.2544 (p<0.001)
		QIDS <=16	124	r = 0.157 (p=0.0816)
		QIDS >=17	72	r = 0.0295 (p=0.8058)
CO-MED	Escit + Bupro	All participants	190	r = 0.2887 (p<0.001)
		QIDS <=16	107	r = 0.232 (p=0.0162)
		QIDS >=17	83	r = 0.1903 (p=0.0849)
CO-MED	Venla + Mirtz	All participants	191	r = 0.2595 (p<0.001)

Study	Intervention	Severity	number of participants	Correlation (baseline and endpoint)
		QIDS <=16	102	r = 0.2116 (p=0.0328)
		QIDS >=17	89	r = -0.077 (p=0.4728)

1.7.51 AHEAD

			HADs-D Baseline		HADs-D Endpoint		Correlation	
Intervention	PHQ range	n	mean	sd	mean	sd	r	p
SSRIs	HAD-D: 8+	60	11.65	2.77	6.05	4.74	0.2737	0.0343
	HAD-D: 8 - 15	56	11.27	2.45	6.16	4.86	0.3756	0.0043
	HAD-D: 16+	4	17.00	0.82	4.50	2.08	0.3922	0.6078
TCAs	HAD-D: 8+	46	11.85	3.04	6.24	4.51	0.1016	0.5016
	HAD-D: 8 - 15	41	11.17	2.44	6.12	4.31	0.0454	0.7778
	HAD-D: 16+	5	17.40	1.14	7.20	6.38	0.4674	0.4273
Lofepramine (is a TCA)	HAD-D: 8+	54	11.54	2.58	6.52	4.59	0.107	0.4414
	HAD-D: 8 - 15	49	10.94	1.81	6.35	4.58	0.0328	0.8227
	HAD-D: 16+	5	17.40	1.14	8.20	4.87	-0.018	0.9771

Update 2018

1.8 Appendix 3: NMA model fit statistics

1.8.1 Population: less severe depression

Table 29: Outcome: discontinuation for any reason – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.49 (0.40, 0.60)	458.4	458	2480.53
RE – inconsistency	0.45 (0.31, 0.61)	471.1	458	2547.31
RE – random class effect: bias adjustment	0.44 (0.34, 0.55)	444.8	458	2478.43

Table 30: Outcome: discontinuation due to SE – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.56 (0.06, 1.12)	77.23	73	339.013
RE – inconsistency	0.60 (0.10, 1.25)	76.5	73	342.5

Table 31: Outcome: remission in completers – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.21 (0.06, 0.42)	176.4	169	938.944
RE – inconsistency	0.18 (0.04, 0.48)	177.7	169	979.202

Table 32: Outcome: remission in those randomised – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.20 (0.05, 0.40)	184.8	167	974.658
RE – inconsistency	0.16 (0.04, 0.45)	176.2	167	1003.58

Table 33: Outcome: response in completers – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.45 (0.29, 0.61)	258.2	248	1194.94
RE – inconsistency	0.49 (0.27, 0.74)	260.9	248	1231.56
RE – random class effect: bias adjustment	0.22 (0.01, 0.45)	253.7	248	1183.52

Table 34: Outcome: response in those randomised – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.37 (0.27, 0.49)	305.4	297	1382.66
RE – inconsistency	0.26 (0.02, 0.44)	313.2	297	1410.97

Table 35: Outcome: SMD – less severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.23 (0.17, 0.30)	263.2	254	984.225
RE – inconsistency	0.23 (0.14, 0.33)	263.6	254	1005.37
RE – random class effect: bias adjustment	0.20 (0.13, 0.28)	256.7	254	981.305

Update 2018

1.8.21 Population: more severe depression

Table 36: Outcome: discontinuation for any reason – more severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.46 (0.36, 0.59)	274.4	272	1541.2
RE – inconsistency	0.42 (0.30, 0.56)	272.2	272	1559.61
RE – random class effect: bias adjustment	0.44 (0.33, 0.57)	267.4	272	1541.13

Table 37: Outcome: discontinuation due to side effects – more severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.78 (0.41, 1.21)	114	111	510.13
RE – inconsistency	0.80 (0.31, 1.34)	115.8	111	514.67

Table 38: Outcome: remission in completers – more severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.64 (0.42, 0.99)	75.58	75	462.31
RE – inconsistency	0.81 (0.47, 1.50)	76.62	75	467.57

Table 39: Outcome: remission in those randomised – more severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.62 (0.41, 0.95)	75.6	77	480.094
RE – inconsistency	0.75 (0.43, 1.43)	76.5	77	484.881

Table 40: Outcome: response in completers – more severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.81 (0.65, 0.99)	191	192	1050.16
RE – inconsistency	0.95 (0.75, 1.20)	191.9	192	1016.02
RE – random class effect: bias adjustment	0.77 (0.59, 0.96)	192	192	1052.01

Table 41: Outcome: response in those randomised – more severe depression

Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.49 (0.37, 0.62)	194.1	191	1092.36
RE – inconsistency	0.44 (0.32, 0.59)	190.6	191	1096.95

Table 42: Outcome: SMD – more severe depression

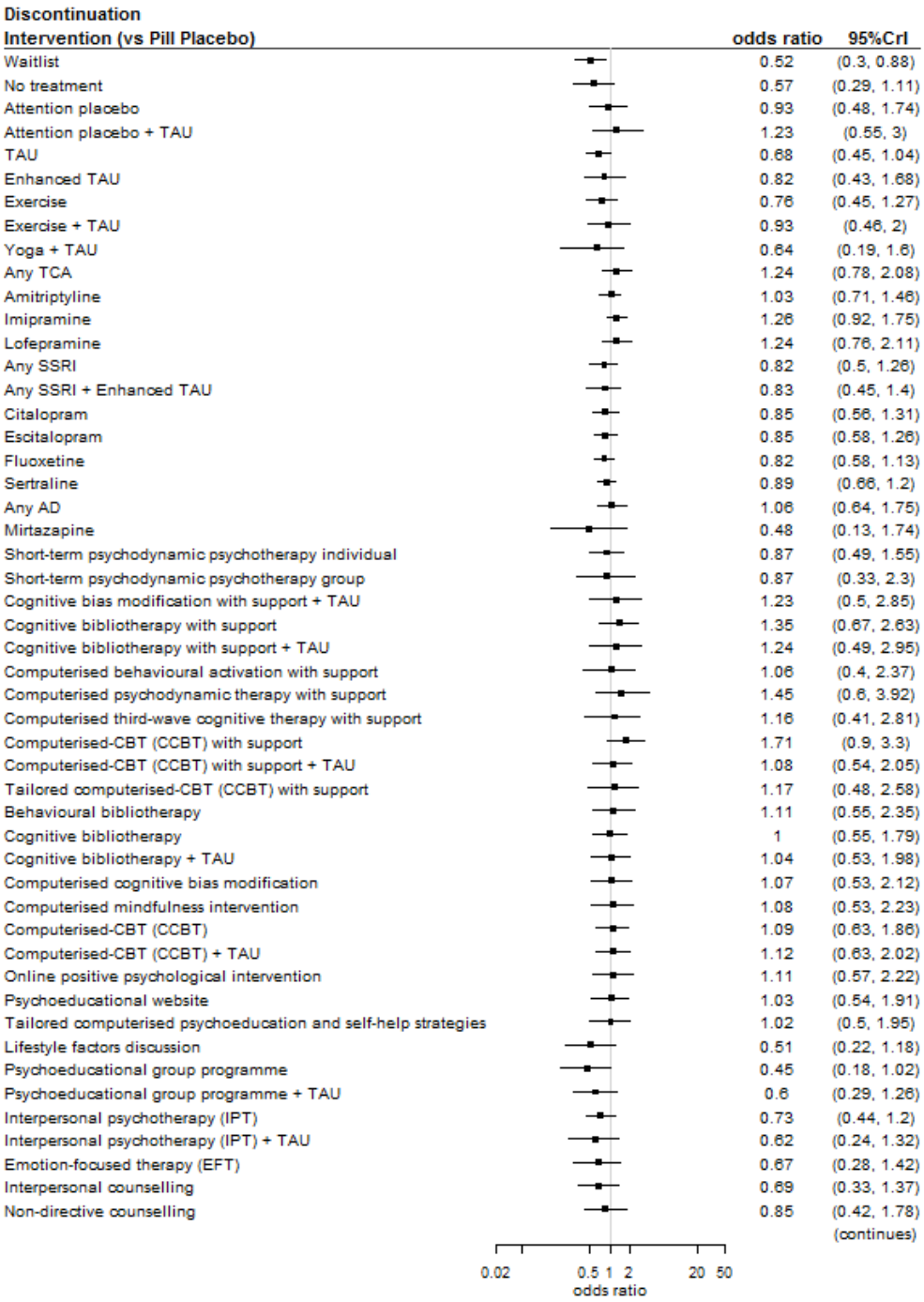
Model	SD	Totresdev	Datapoints	DIC
RE – random class effect	0.17 (0.10, 0.26)	147.1	137	636.488
RE – inconsistency	0.14 (0.05, 0.23)	141.3	137	636.728
RE – random class effect: bias adjustment	0.10 (0.01, 0.20)	139.2	137	631.209

1.99 Forest plots

1.9.10 Appendix 4: Forest plots – Population with less severe depression

Update 2018

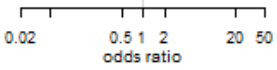
Figure 49: Odds ratio and 95% credible intervals for every intervention compared to pill placebo. Discontinuation for any reason – less severe depression.



Update 2018

Discontinuation

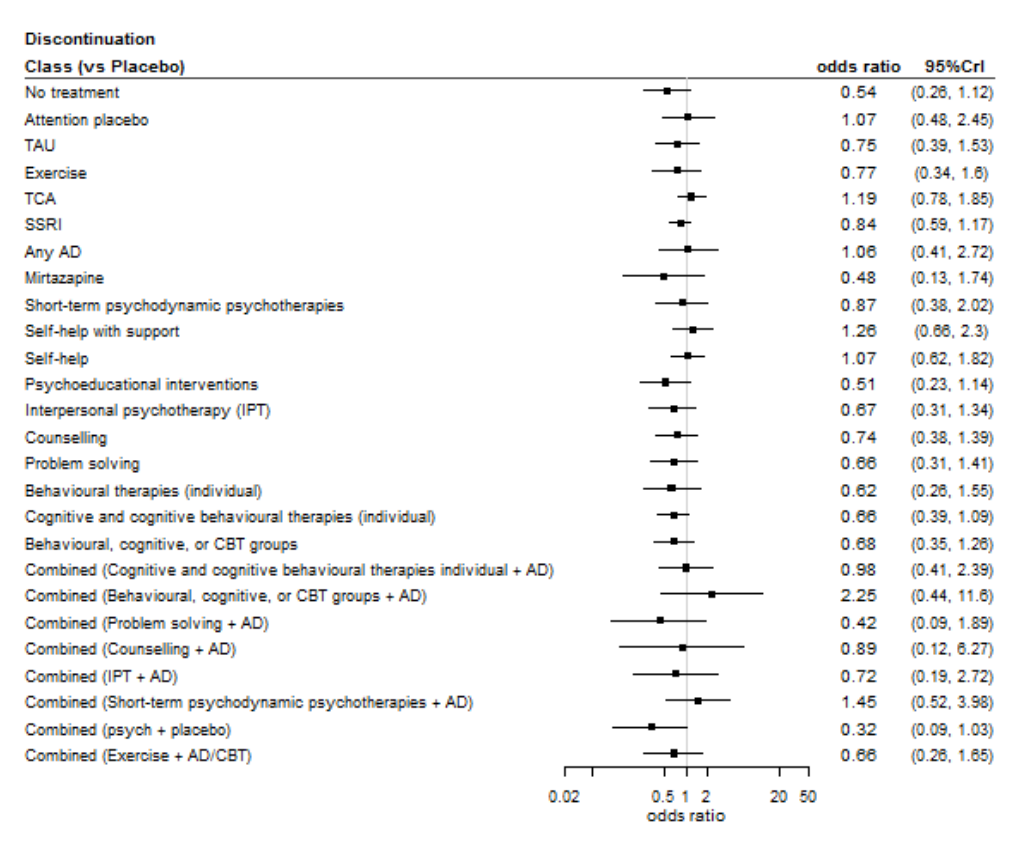
Intervention (vs Pill Placebo)	odds ratio	95%CrI
		(continued)
Non-directive counselling + TAU	0.82	(0.38, 1.82)
Psychodynamic counselling + TAU	0.75	(0.32, 1.69)
Relational client-centered therapy	0.73	(0.28, 1.78)
Wheel of wellness counselling	0.69	(0.26, 1.6)
Problem solving group	0.7	(0.29, 1.86)
Problem solving individual	0.64	(0.33, 1.25)
Problem solving individual + TAU	0.59	(0.24, 1.33)
Problem solving individual + enhanced TAU	0.72	(0.3, 1.86)
Behavioural activation (BA)	0.49	(0.22, 1.08)
Behavioural activation (BA) + TAU	0.63	(0.22, 1.91)
Behavioural therapy (Lewinsohn 1976)	0.75	(0.27, 2.48)
Coping with Depression course (individual)	0.63	(0.21, 1.96)
CBT individual (under 15 sessions)	0.7	(0.42, 1.17)
CBT individual (under 15 sessions) + TAU	0.73	(0.4, 1.51)
CBT individual (over 15 sessions)	0.66	(0.43, 1)
CBT individual (over 15 sessions) + TAU	0.64	(0.29, 1.3)
Rational emotive behaviour therapy (REBT) individual	0.64	(0.3, 1.25)
Third-wave cognitive therapy individual	0.61	(0.32, 1.09)
Third-wave cognitive therapy individual + TAU	0.63	(0.29, 1.27)
CBT group (under 15 sessions)	0.83	(0.43, 1.63)
CBT group (under 15 sessions) + TAU	0.41	(0.14, 0.98)
CBT group (over 15 sessions)	0.7	(0.29, 1.63)
Coping with Depression course (group)	0.72	(0.33, 1.55)
Coping with Depression course (group) + TAU	0.95	(0.43, 2.35)
Rational emotive behaviour therapy (REBT) group	0.55	(0.18, 1.36)
Third-wave cognitive therapy group	0.84	(0.37, 2.07)
Third-wave cognitive therapy group + TAU	0.61	(0.22, 1.5)
CBT individual (over 15 sessions) + any AD	1.05	(0.39, 3.07)
CBT individual (over 15 sessions) + any TCA	0.96	(0.42, 2.19)
CBT individual (over 15 sessions) + imipramine	0.94	(0.38, 2.32)
CBT group (under 15 sessions) + imipramine	2.24	(0.52, 9.89)
Problem solving individual + any SSRI	0.42	(0.1, 1.62)
Supportive psychotherapy + any SSRI	0.89	(0.14, 5.54)
Interpersonal psychotherapy (IPT) + any AD	0.77	(0.22, 2.62)
Interpersonal psychotherapy (IPT) + imipramine	0.69	(0.17, 2.69)
Short-term psychodynamic psychotherapy individual + Any AD	1.46	(0.62, 3.46)
Short-term psychodynamic psychotherapy individual + any SSRI	1.43	(0.48, 4.29)
CBT individual (over 15 sessions) + Pill placebo	0.3	(0.08, 0.97)
Interpersonal psychotherapy (IPT) + Pill placebo	0.35	(0.11, 1.07)
Exercise + CBT individual (under 15 sessions)	0.63	(0.22, 1.67)
Exercise + Sertraline	0.7	(0.34, 1.47)



1

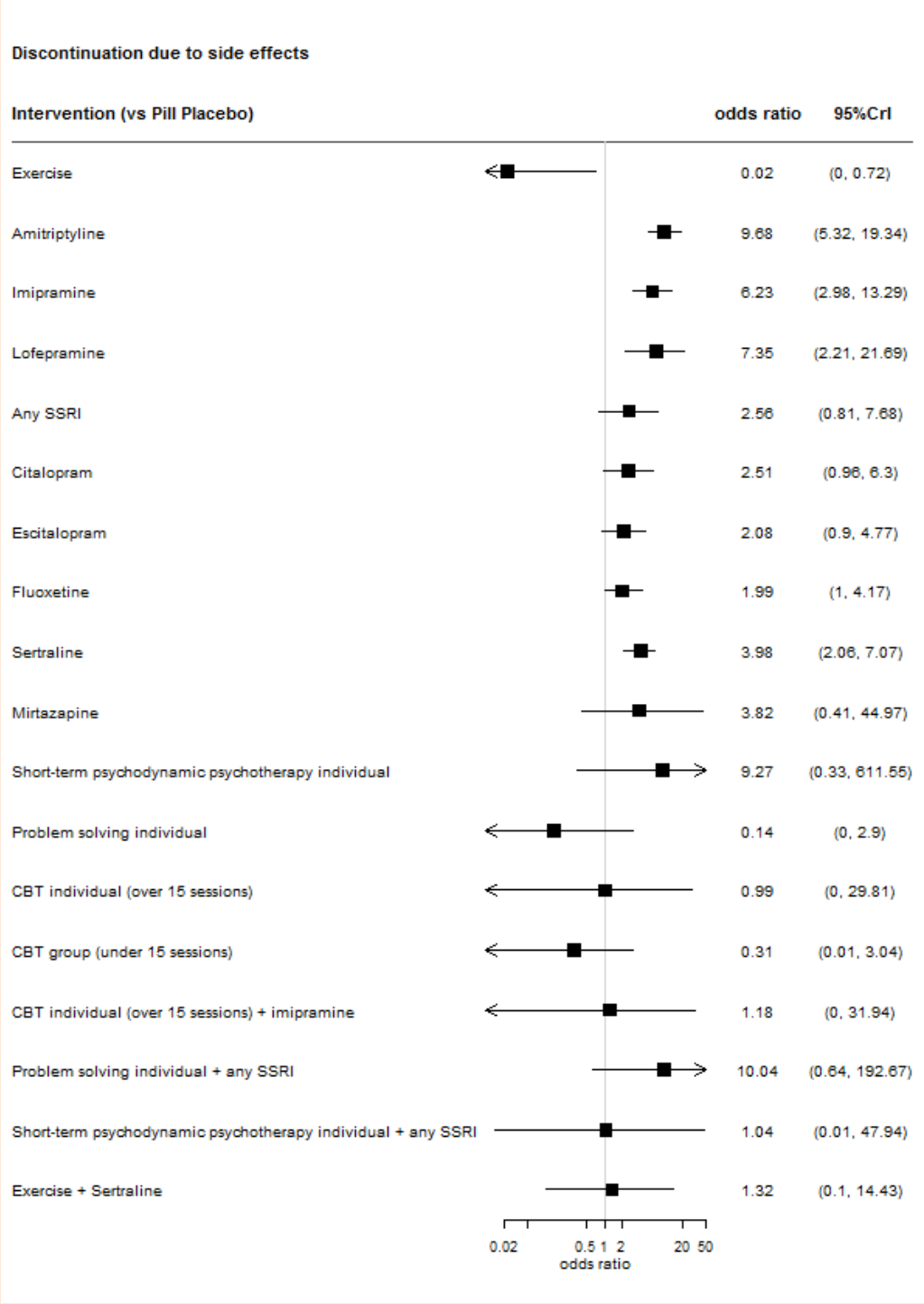
Update 2018

Figure 50: Odds ratios and 95% credible intervals for every class compared to pill placebo. Discontinuation for any reason – less severe depression.



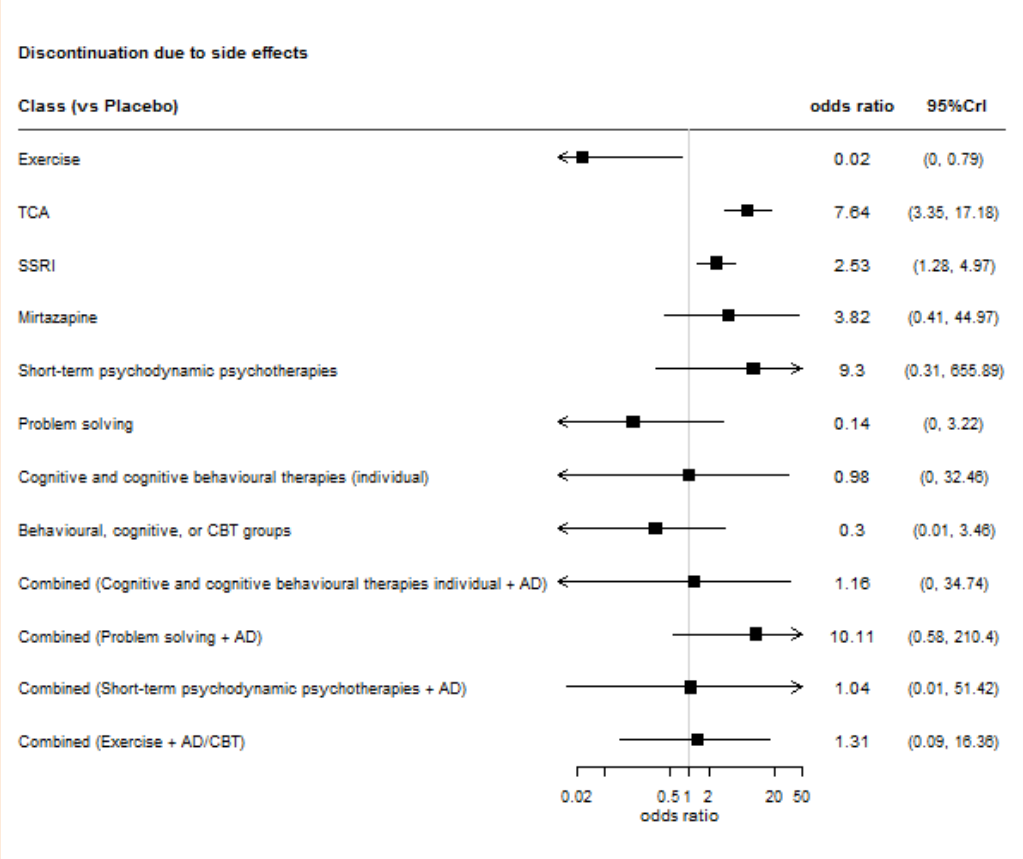
Update 2018

Figure 51: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Discontinuation due to SE – less severe depression.



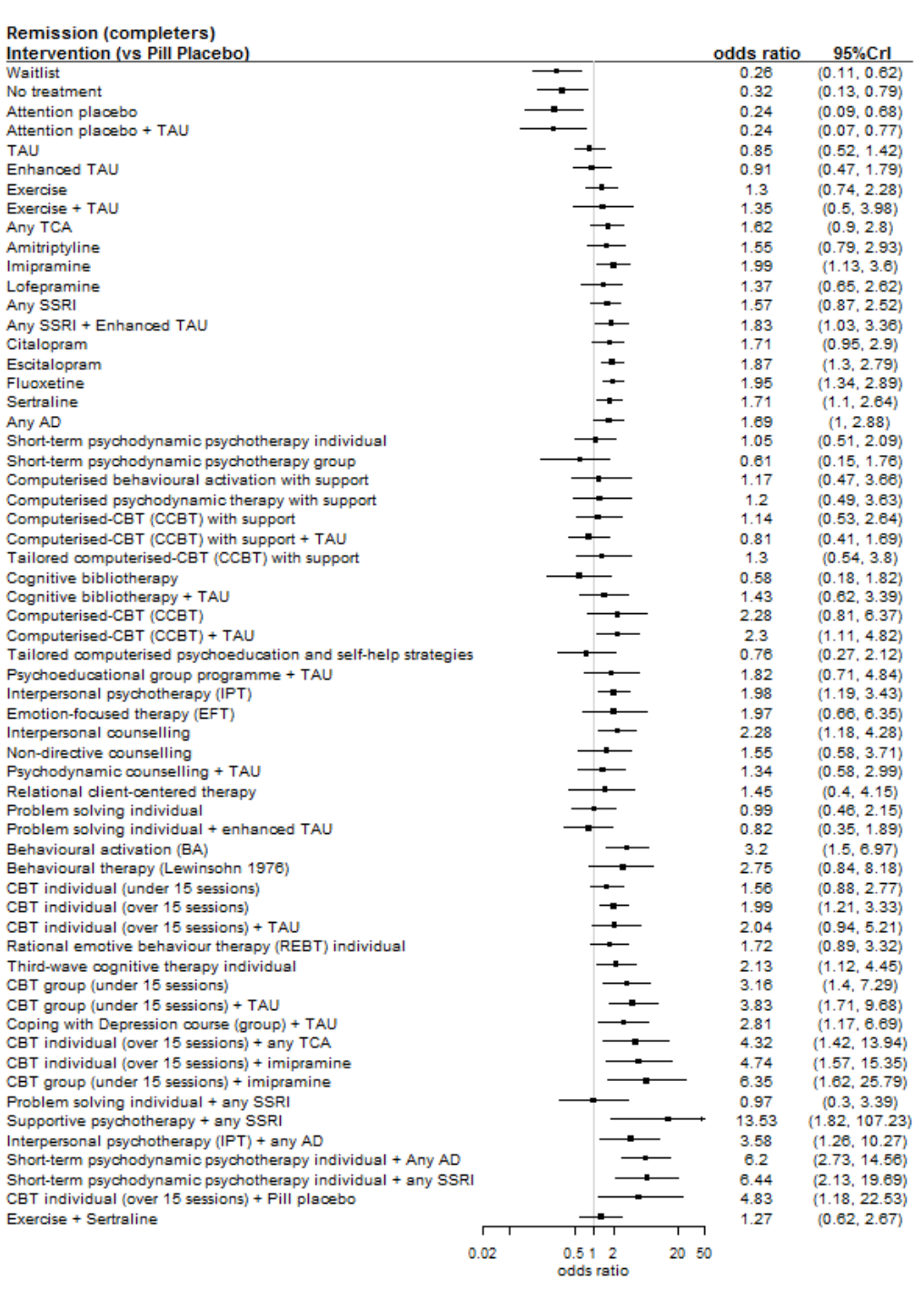
Update 2018

Figure 52: Odds ratios and 95% credible intervals for every class compared to pill placebo. Discontinuation due to SE – less severe depression.



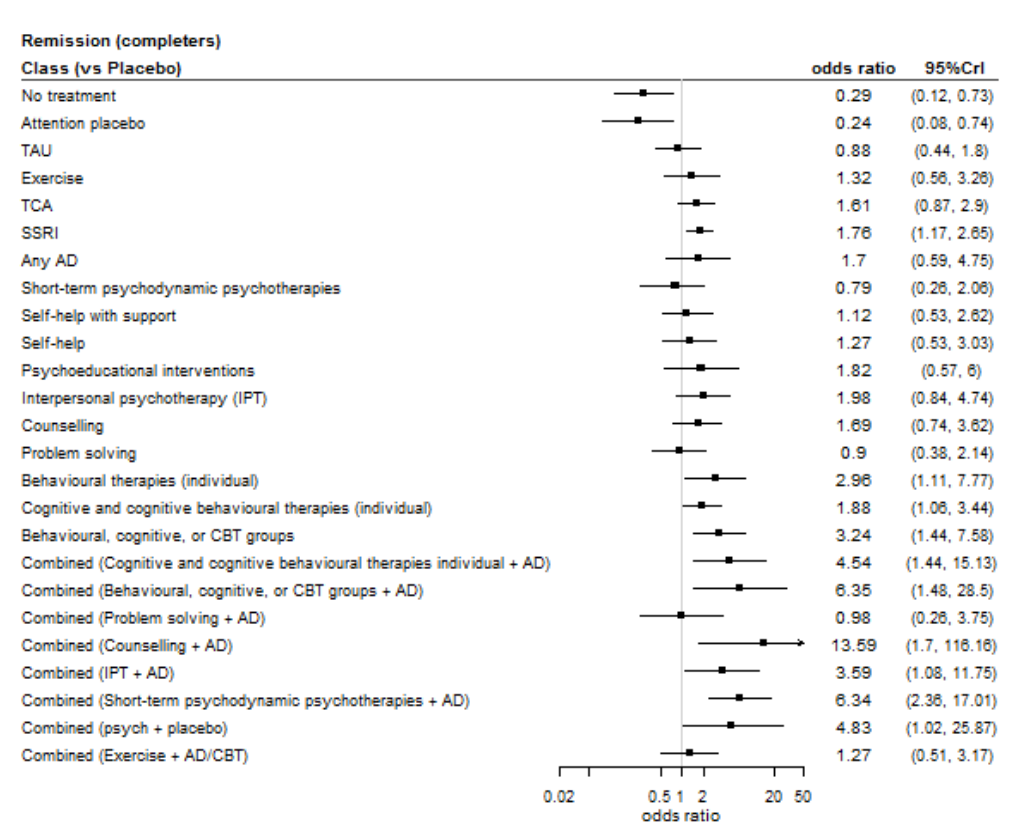
Update 2018

Figure 53: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Remission in completers – less severe depression.



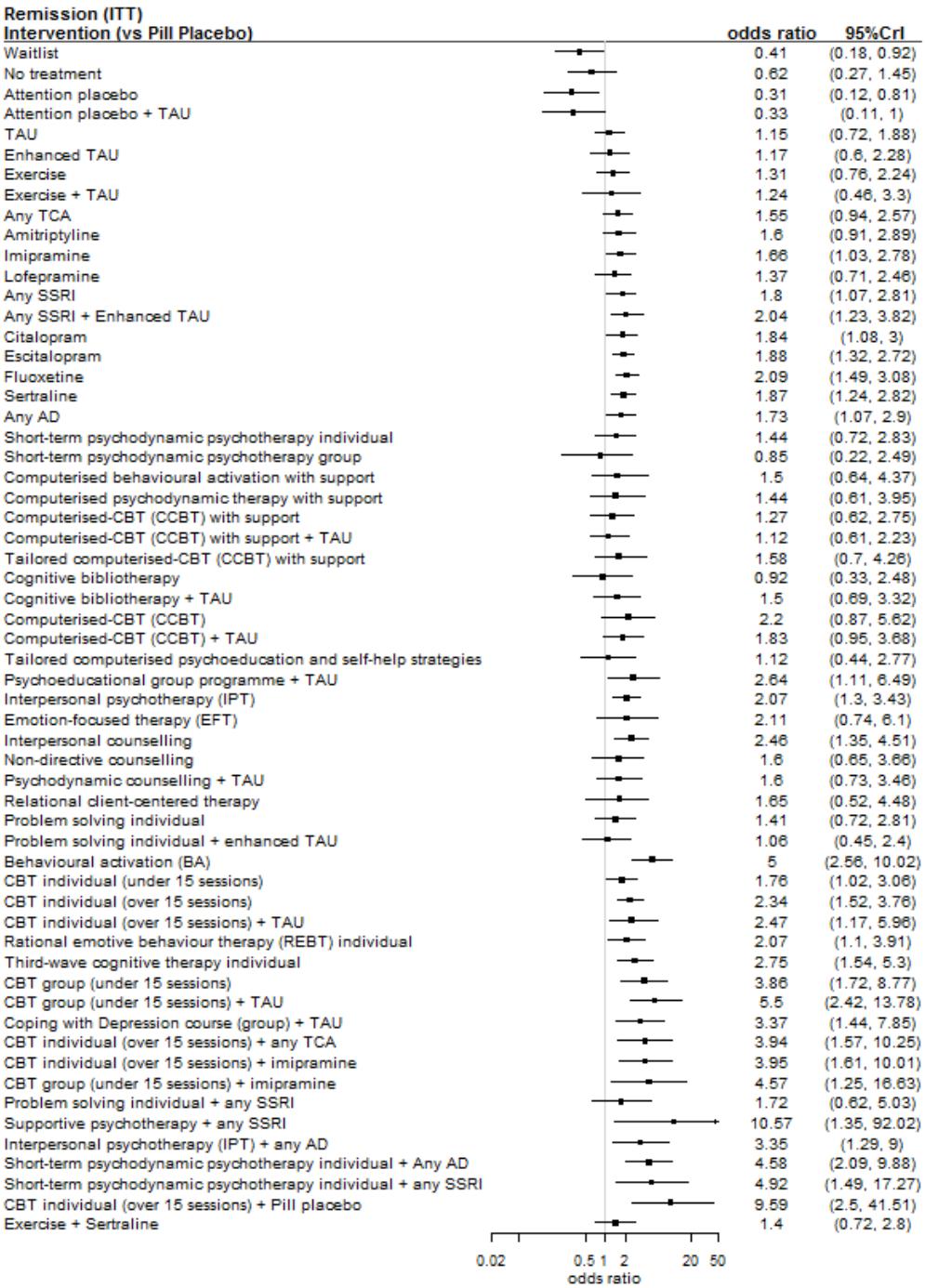
Update 2018

Figure 54: Odds ratios and 95% credible intervals for every class compared to pill placebo. Remission in completers – less severe depression.



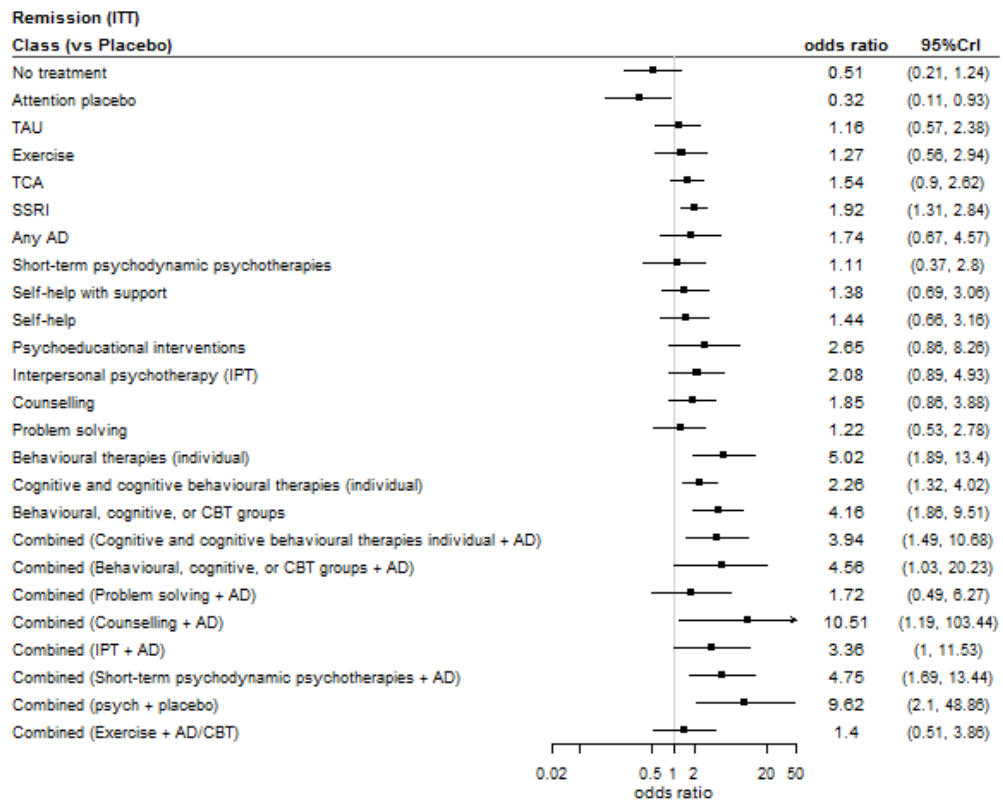
Update 2018

Figure 55: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Remission in those randomised – less severe depression.



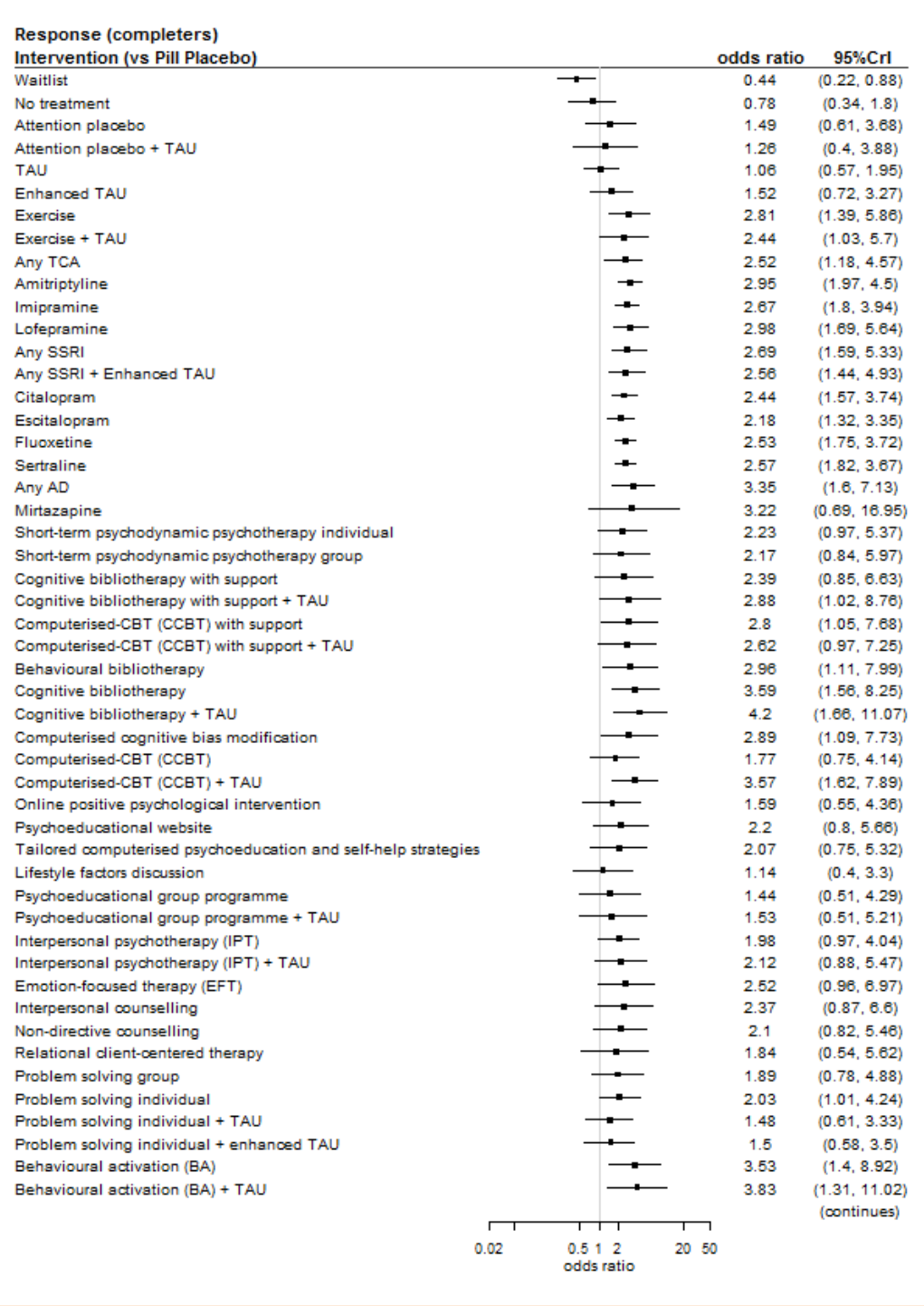
Update 2018

Figure 56: Odds ratios and 95% credible intervals for every class compared to pill placebo. Remission in those randomised – less severe depression.



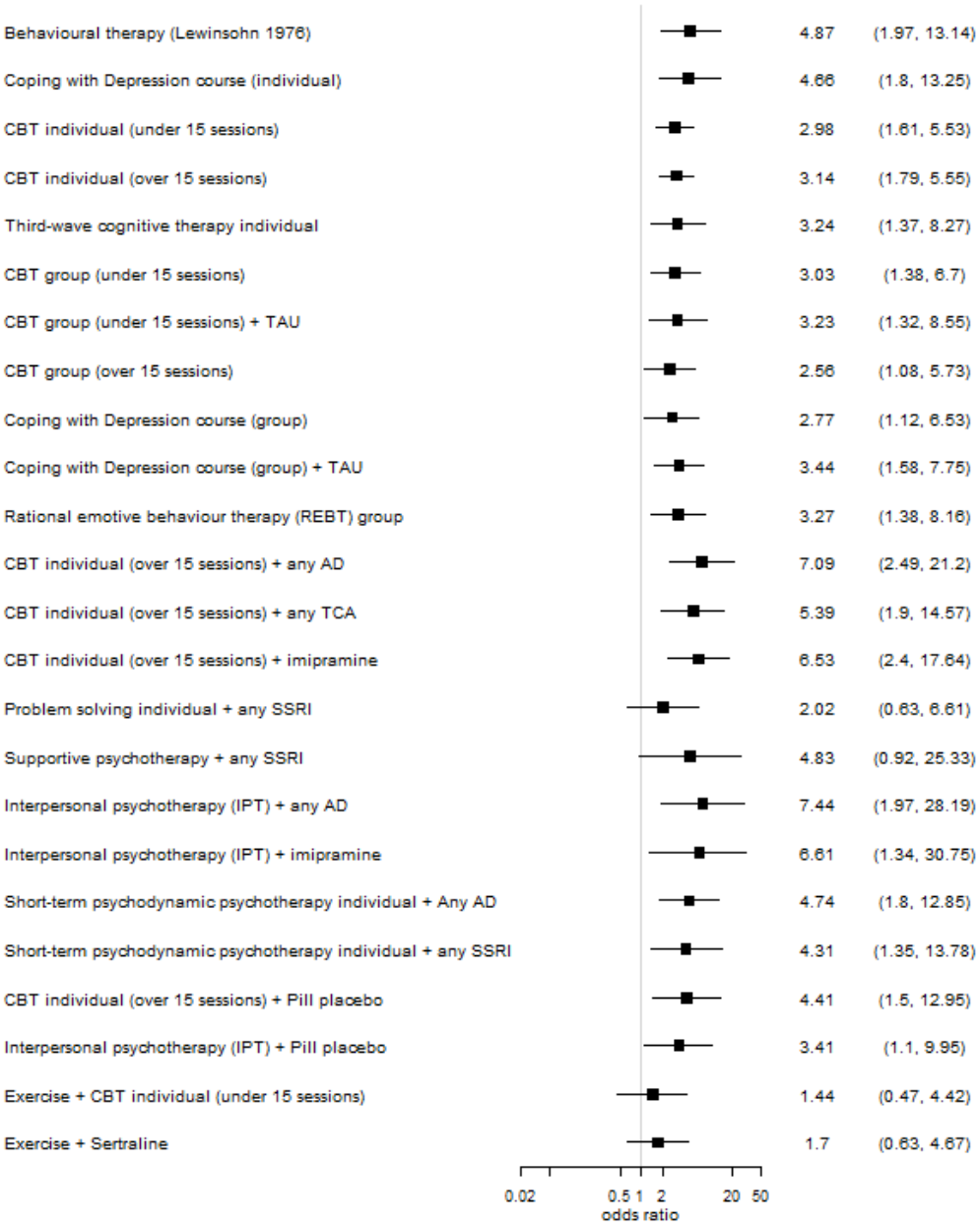
Update 2018

Figure 57: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Response in completers – less severe depression.



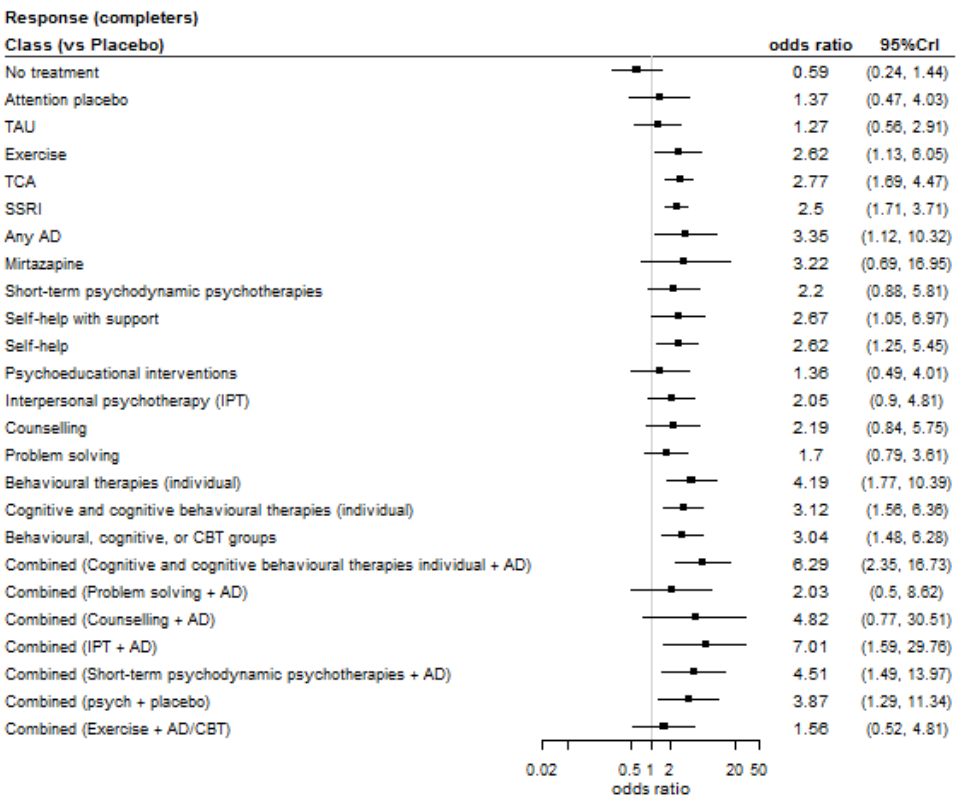
Update 2018

Response (completers)



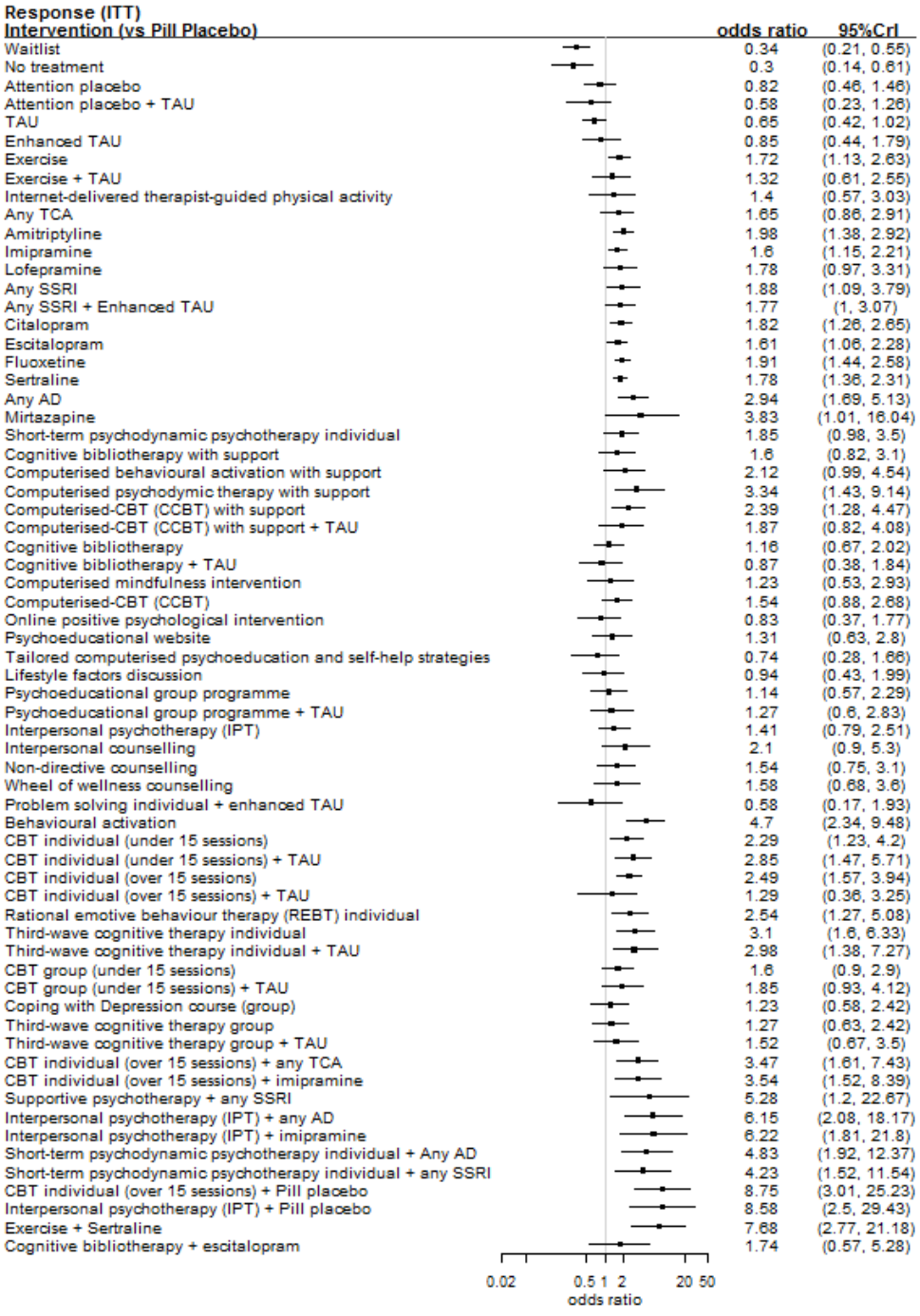
Update 2018

Figure 58: Odds ratios and 95% credible intervals for every class compared to pill placebo. Response in completers – less severe depression.



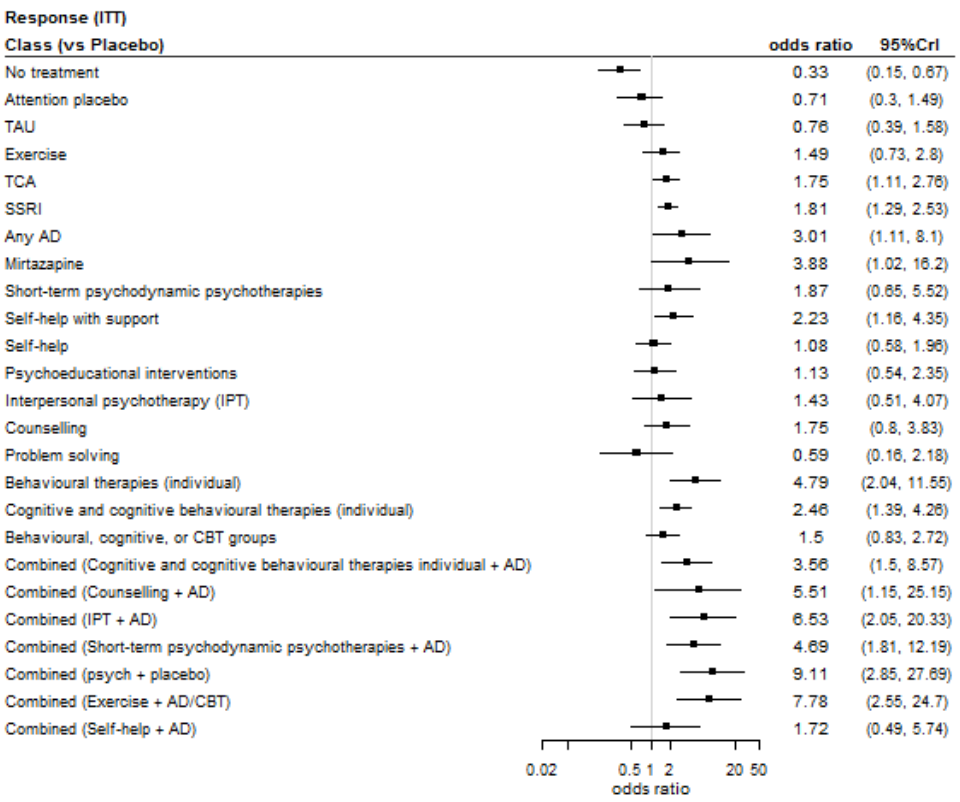
Update 2018

Figure 59: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Response in those randomised – less severe depression.



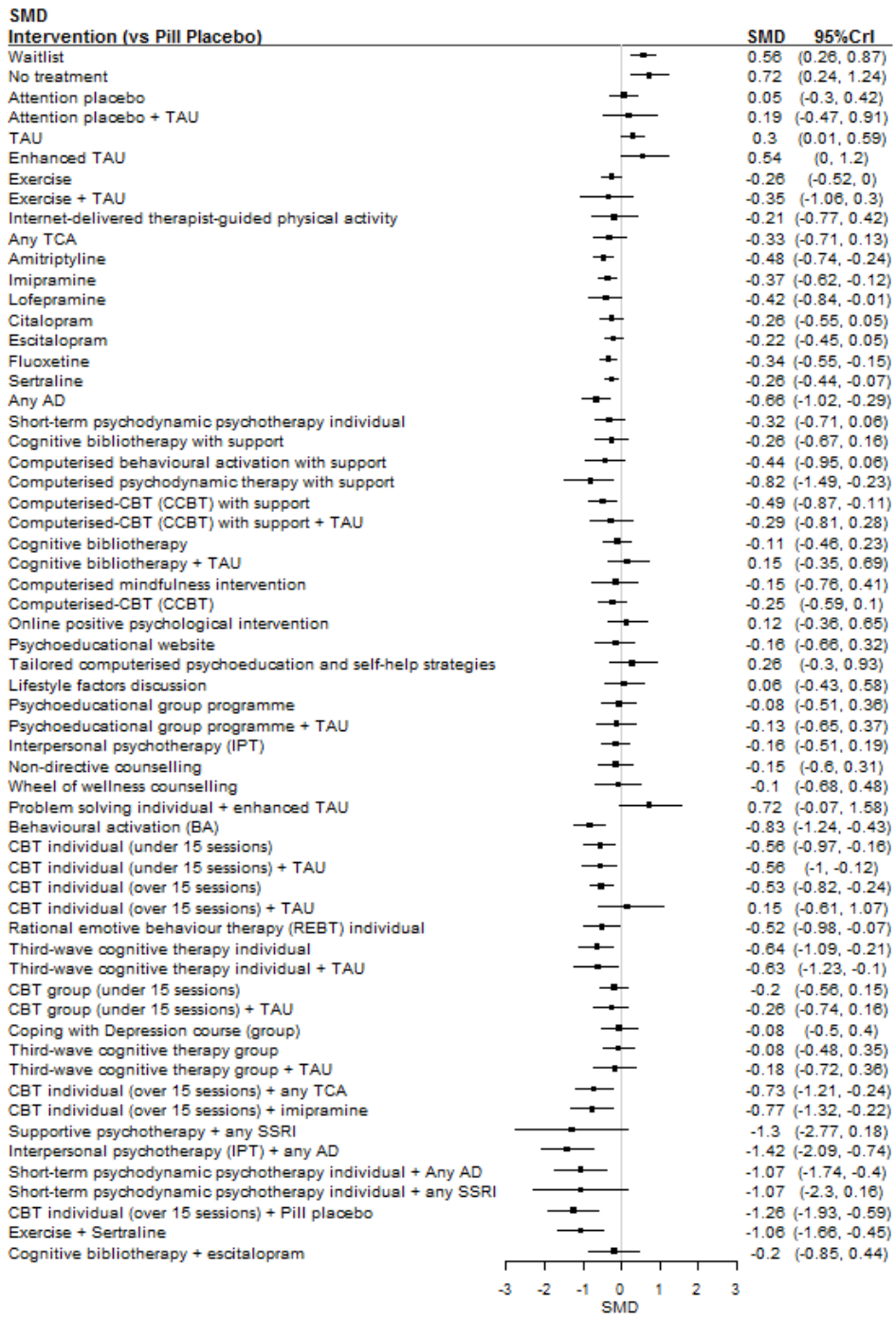
Update 2018

Figure 60: Odds ratios and 95% credible intervals for every class compared to pill placebo. Response in those randomised – less severe depression.



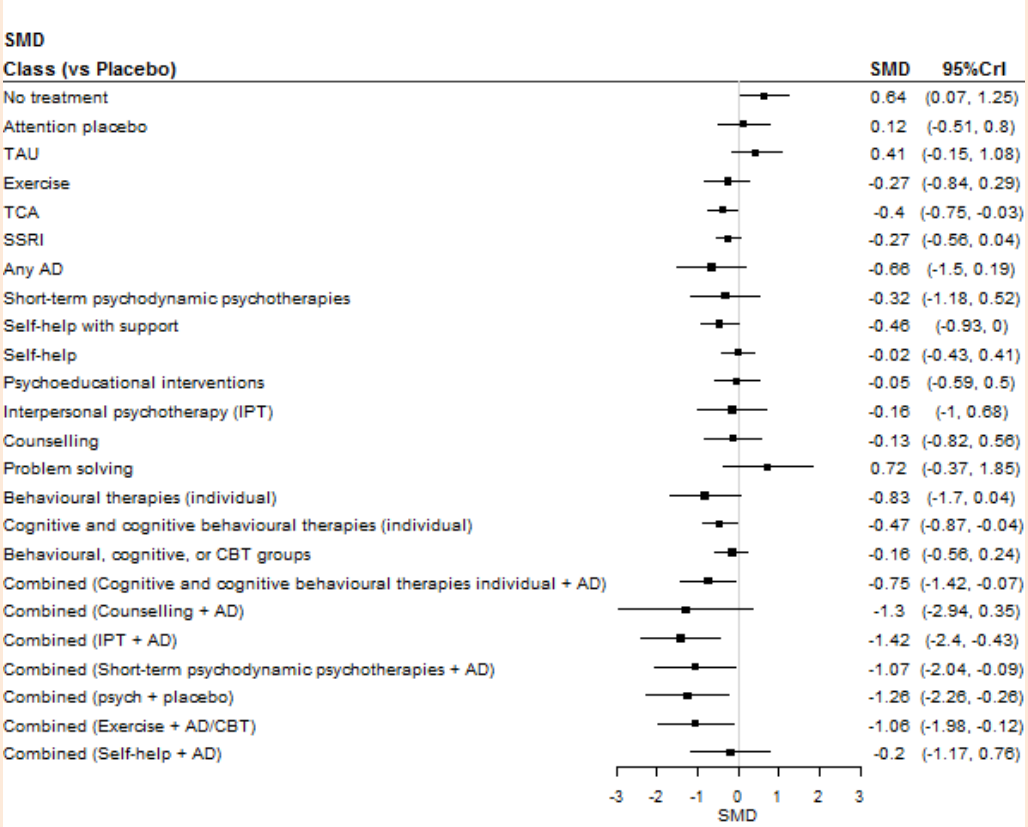
Update 2018

Figure 61: SMD and 95% credible intervals for every intervention compared to pill placebo. SMD – less severe depression.



Update 2018

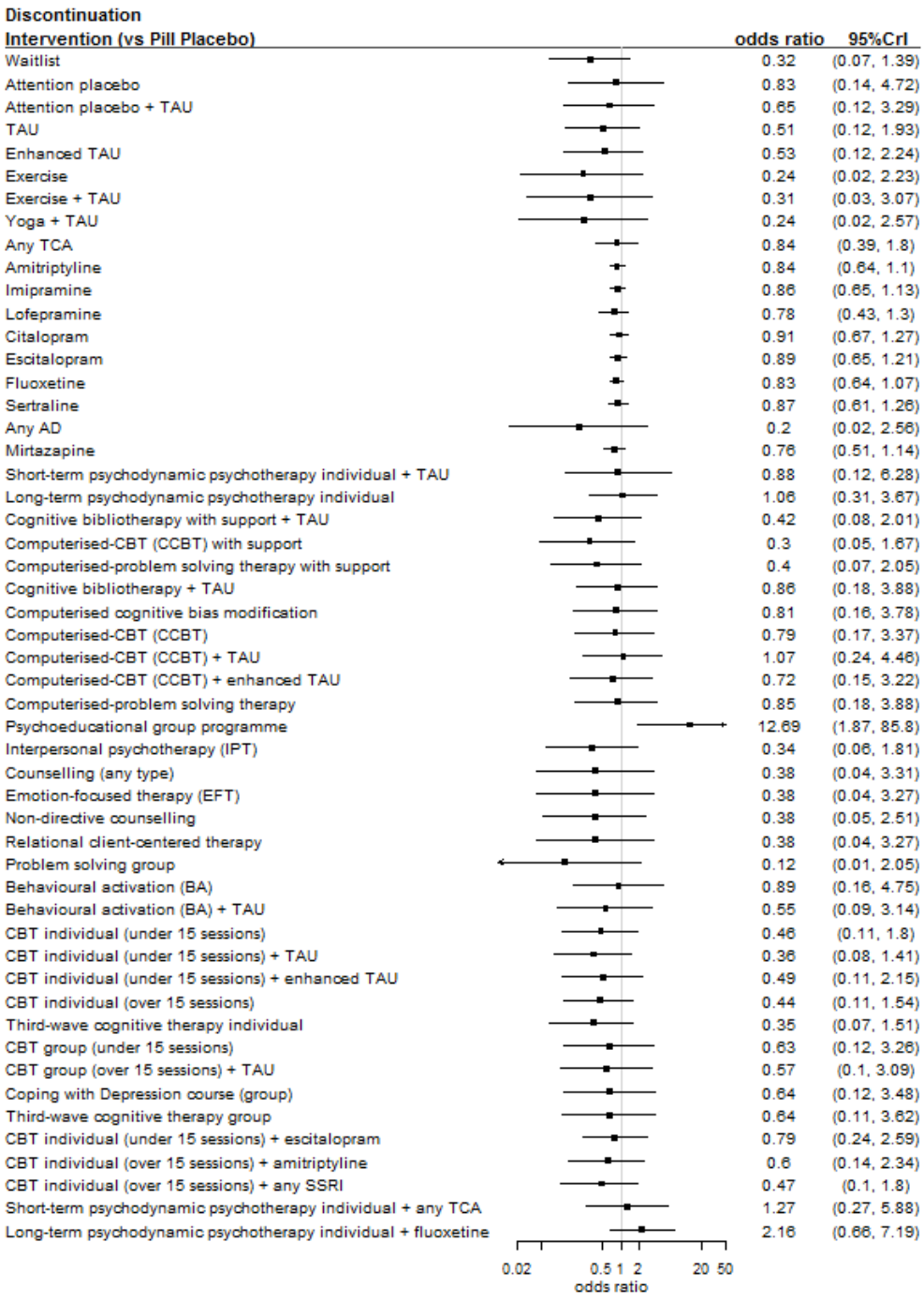
Figure 62: MD and 95% credible intervals for every class compared to pill placebo. SMD – less severe depression.



Update 2018

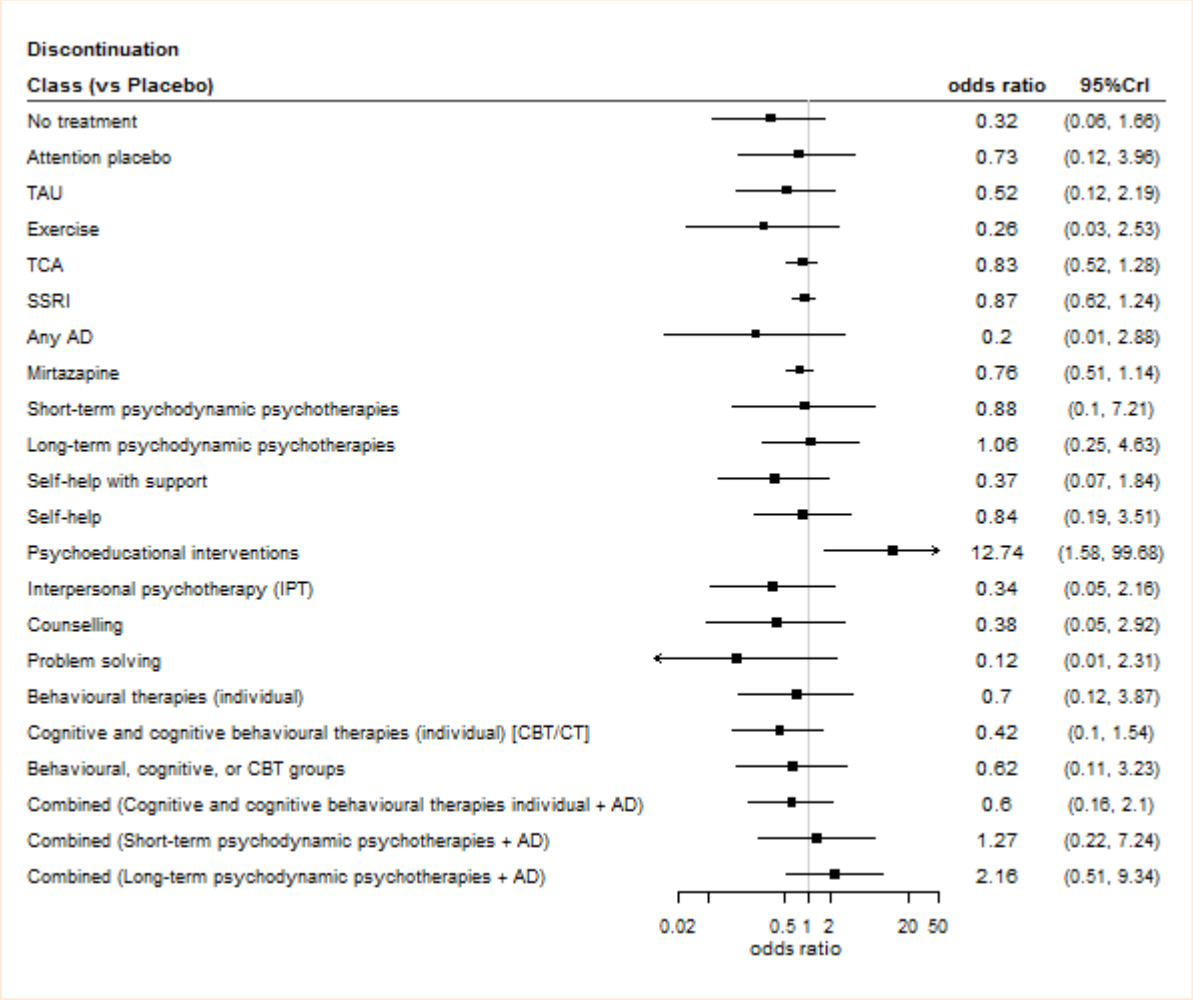
1.9.21 Appendix 5 - Population: more severe depression

Figure 63: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Discontinuation for anfor any reason – more severe depression.



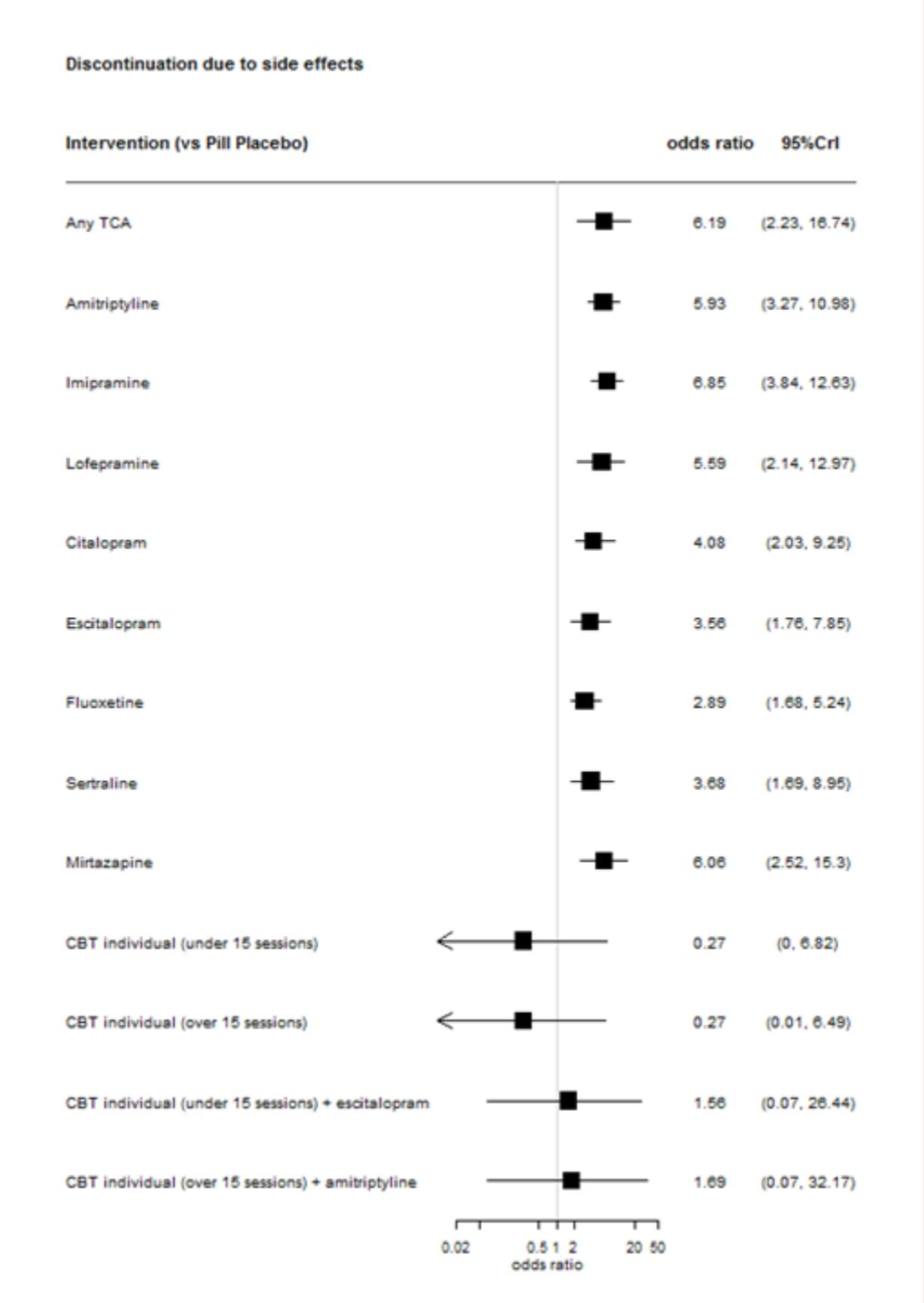
Update 2018

Figure 64: Odds ratios and 95% credible intervals for every class compared to pill placebo. Discontinuation for any reason – more severe depression.



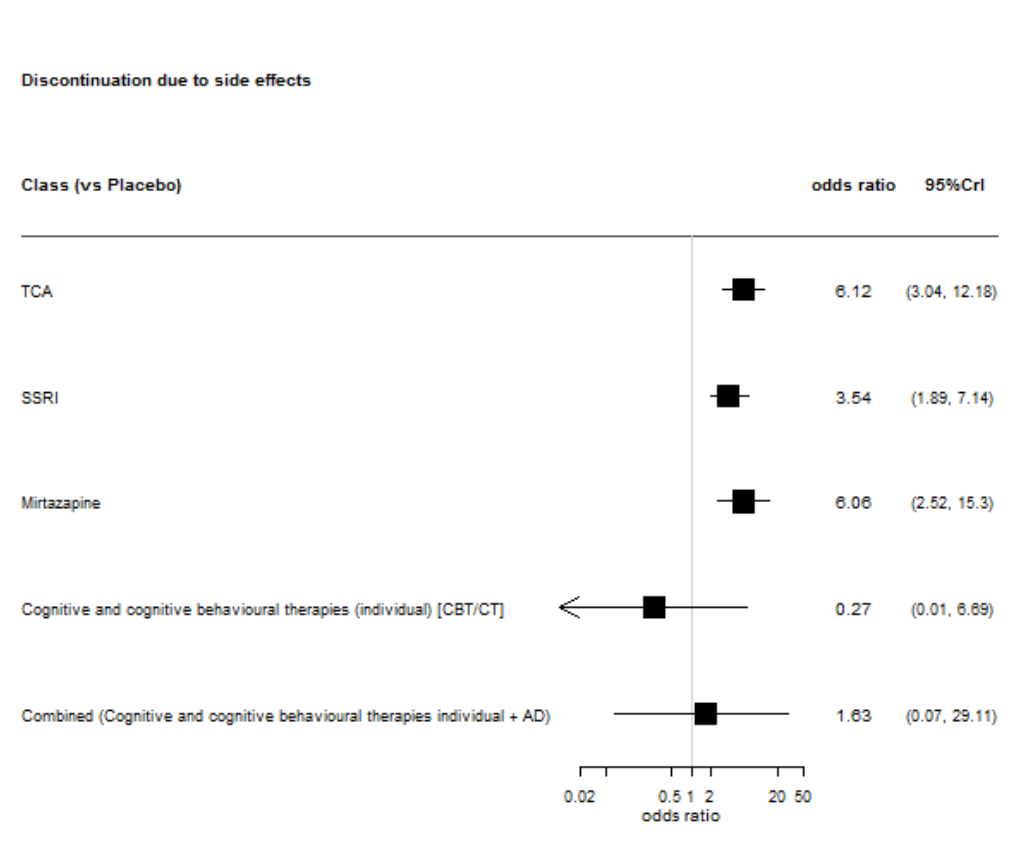
Update 2018

Figure 65: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Discontinuation due to side effects – more severe depression.



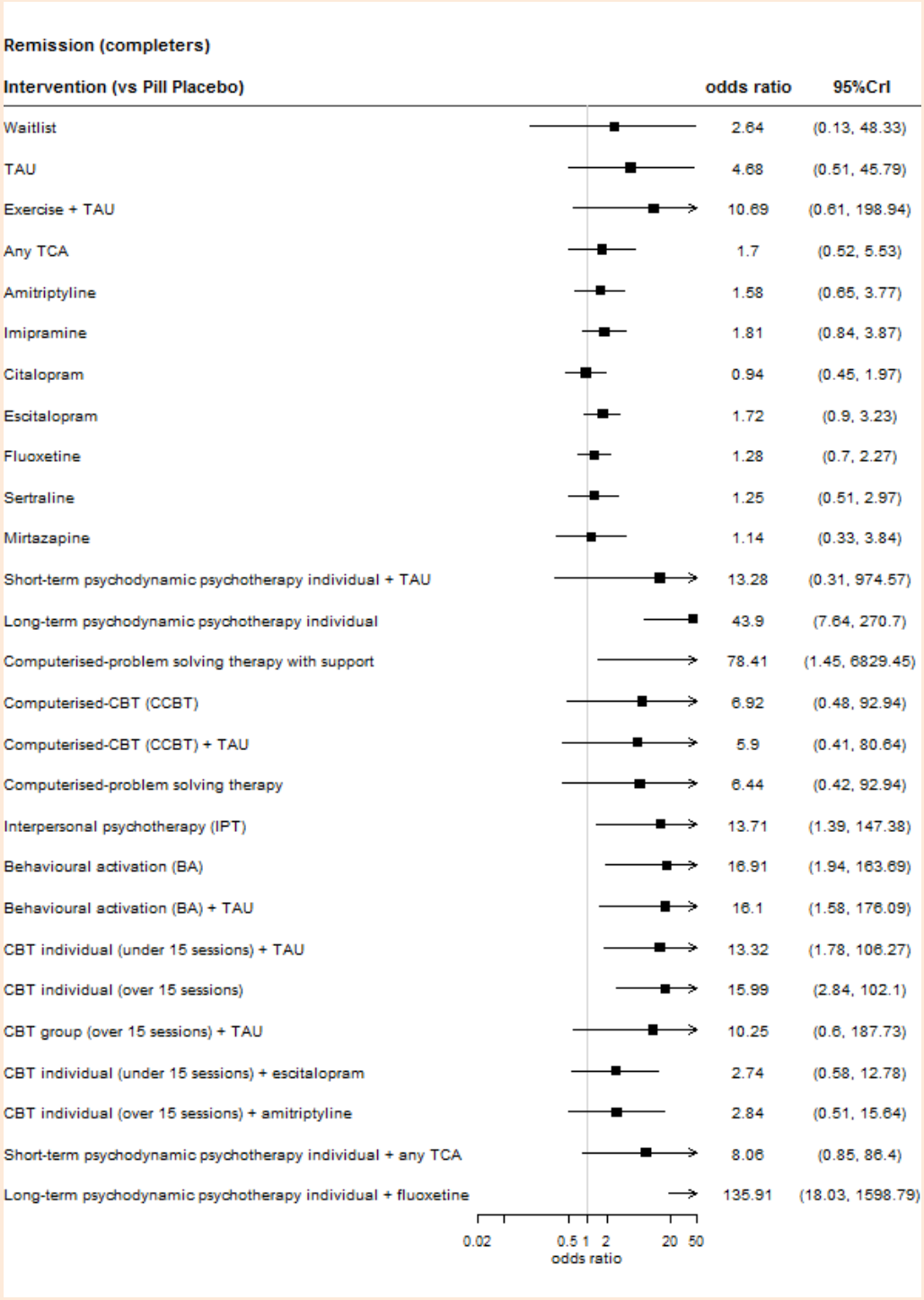
Update 2018

Figure 66: Odds ratios and 95% credible intervals for every class compared to pill placebo. Discontinuation due to side effects – more severe depression.



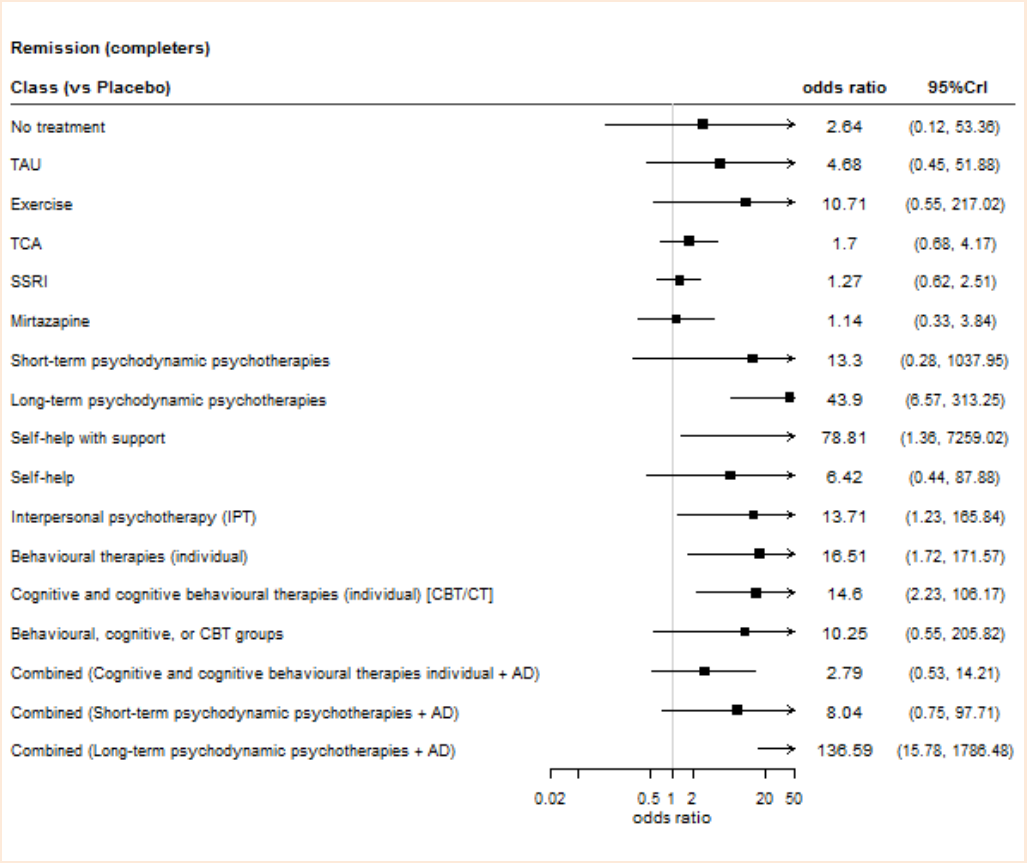
Update 2018

Figure 67: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Remission in completers – more severe depression.



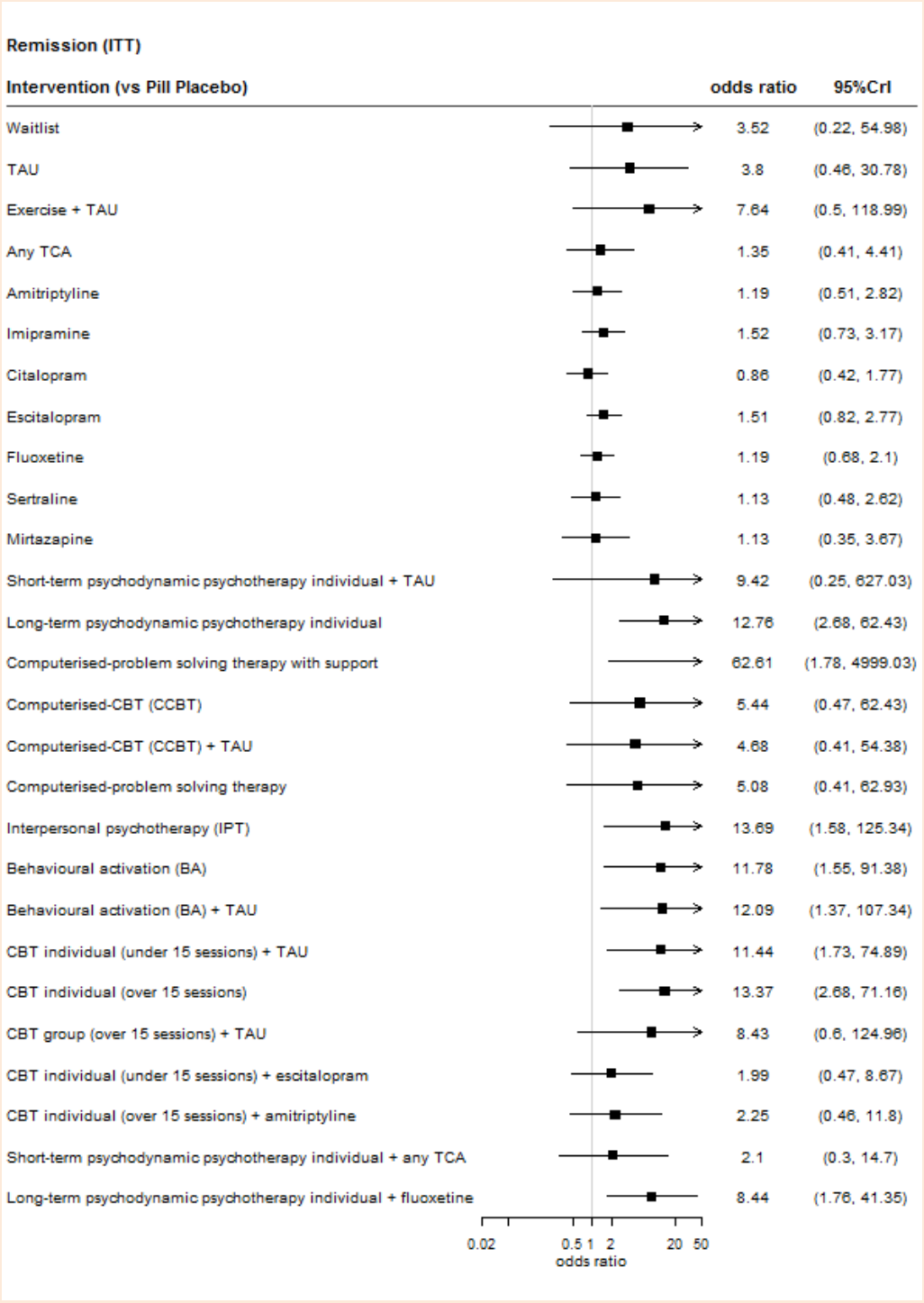
Update 2018

Figure 68: Odds ratios and 95% credible intervals for every class compared to pill placebo. Remission in completers – more severe depression.



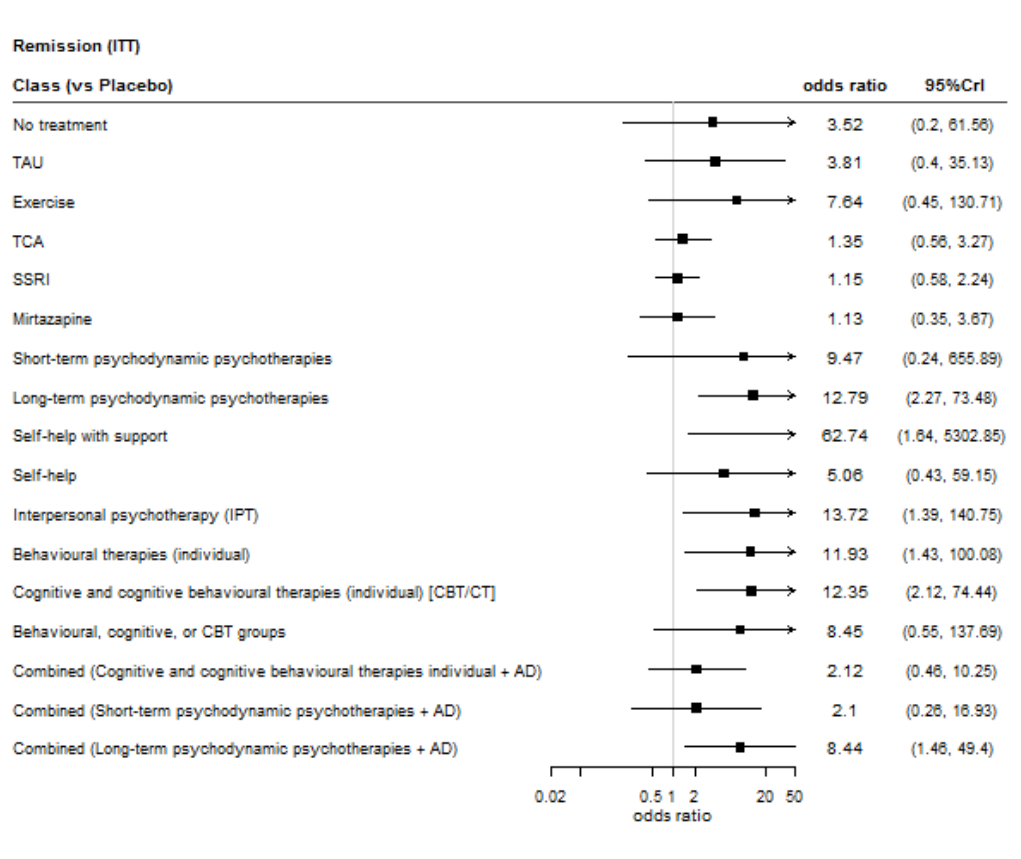
Update 2018

Figure 69: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Remission in those randomised – more severe depression.



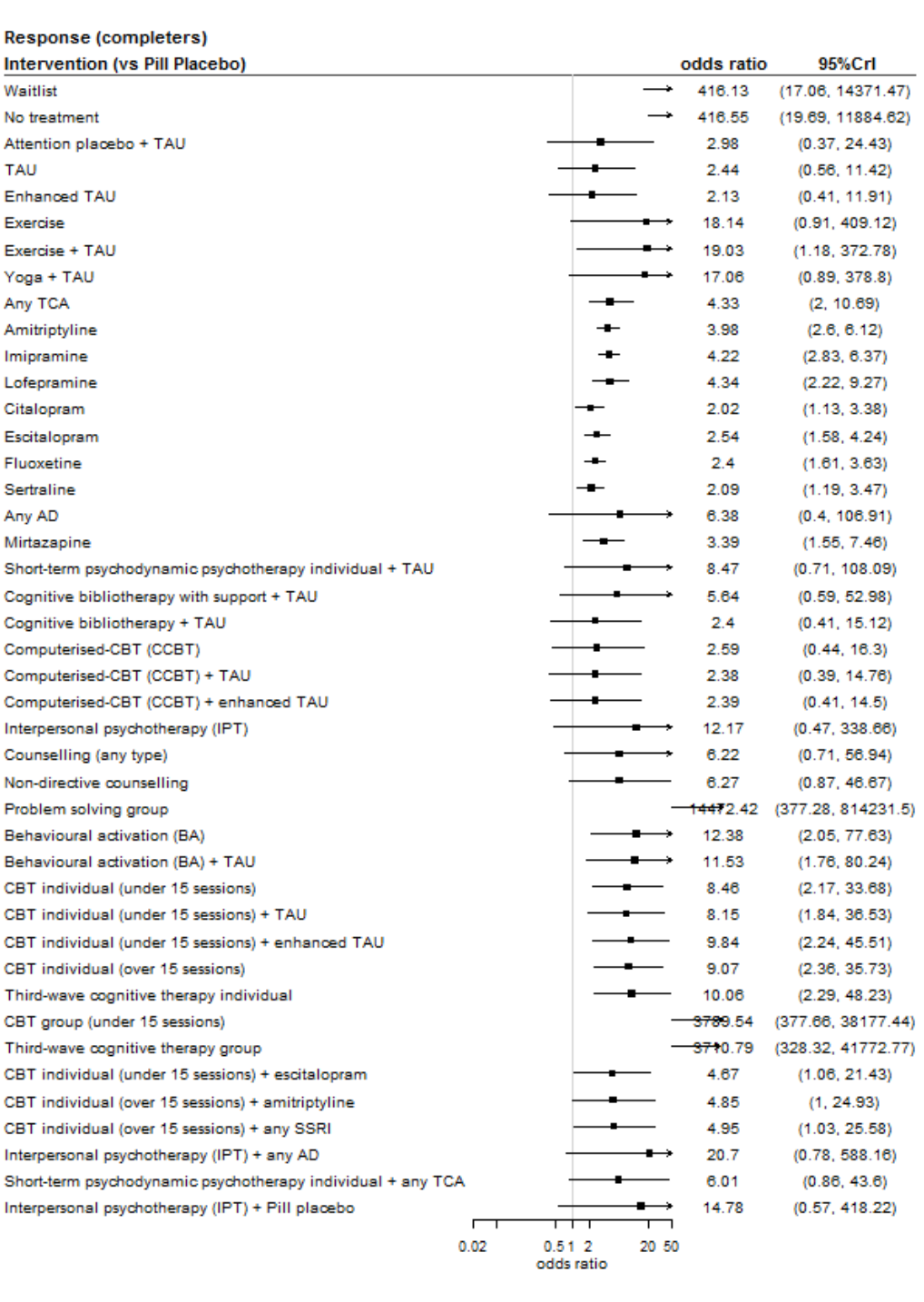
Update 2018

Figure 70: Odds ratios and 95% credible intervals for every class compared to pill placebo. Remission in those randomised – more severe depression.



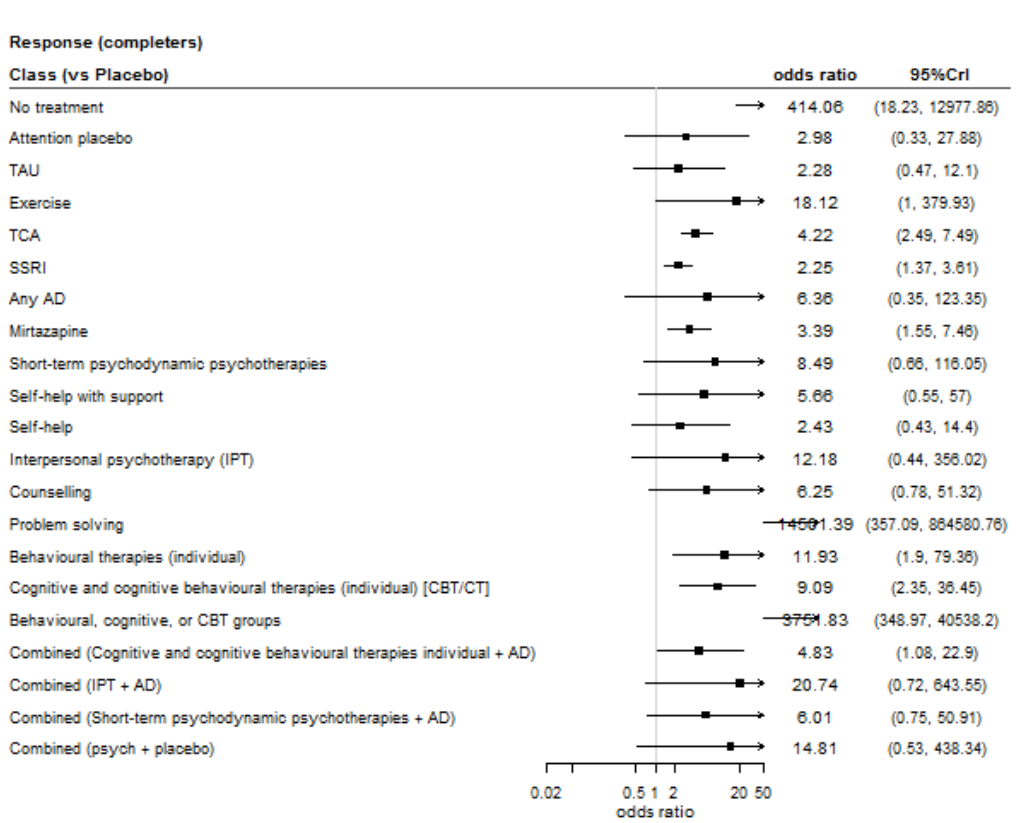
Update 2018

Figure 71: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Response in completers – more severe depression.



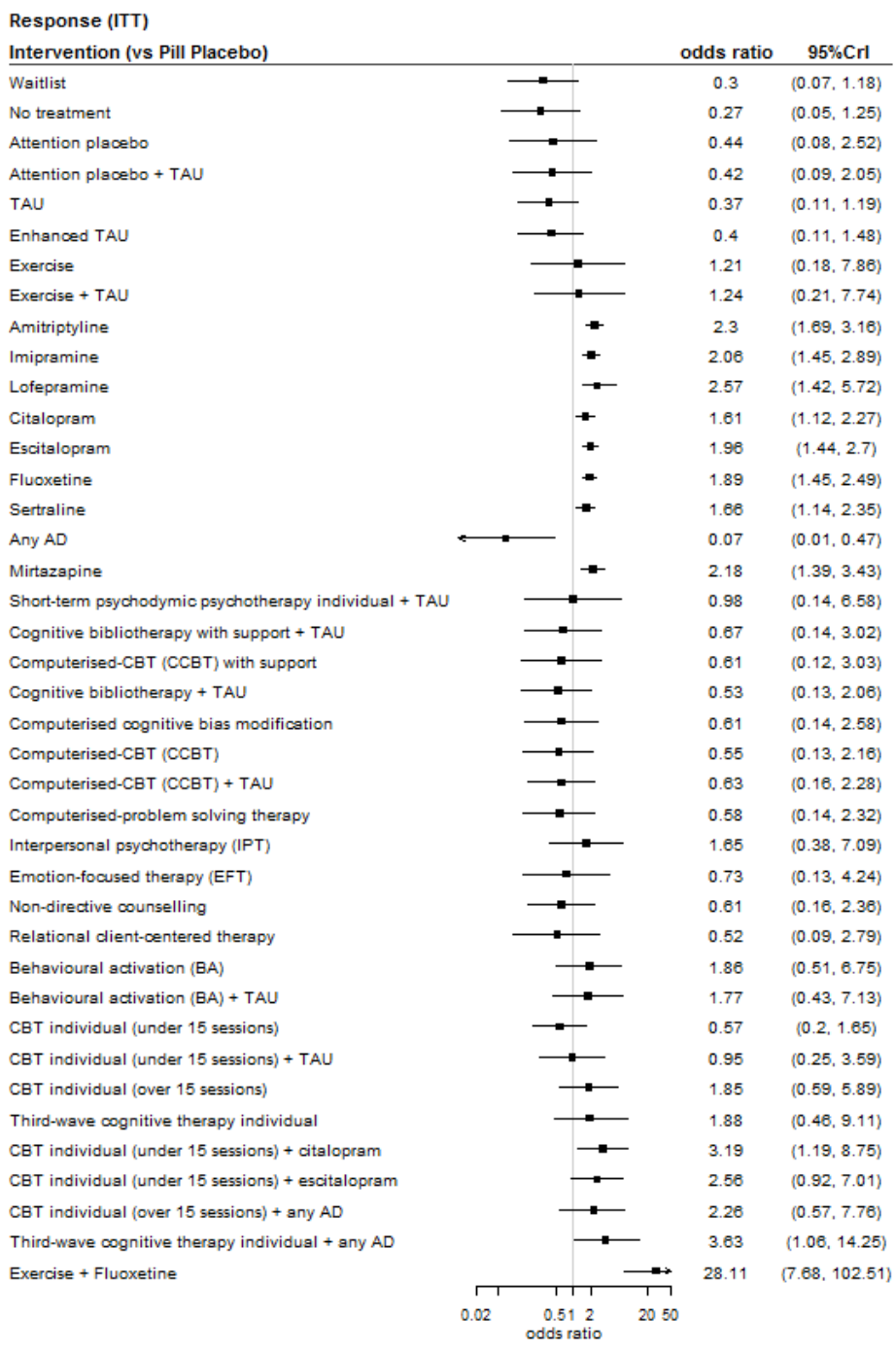
Update 2018

Figure 72: Odds ratios and 95% credible intervals for every class compared to pill placebo. Response in completers – more severe depression.



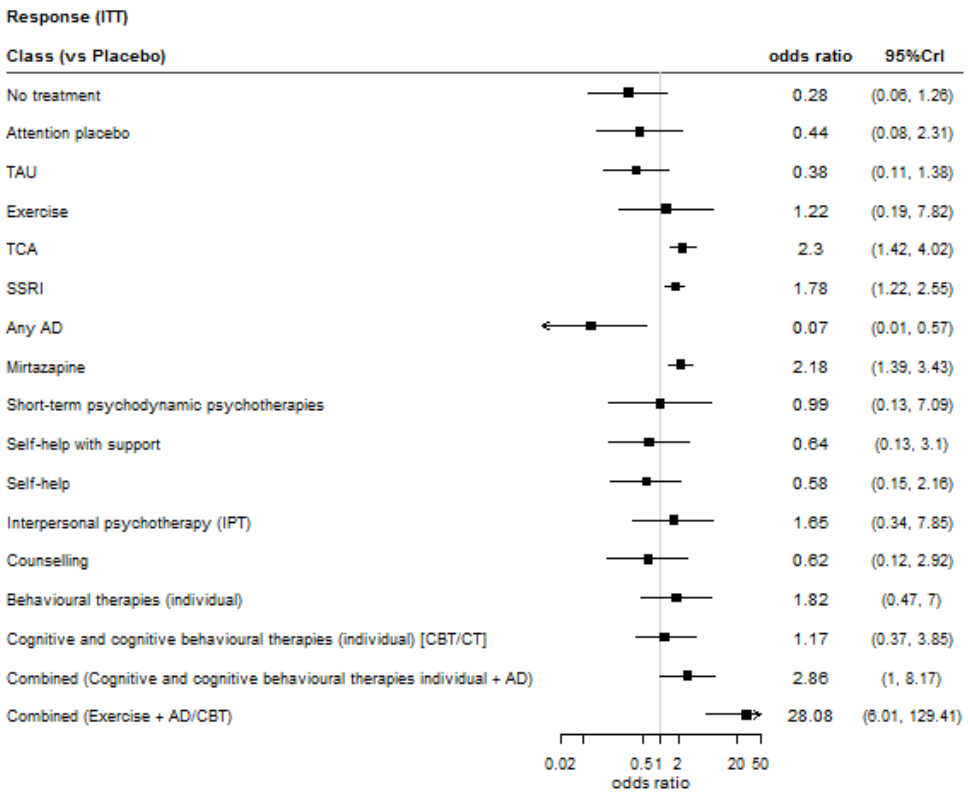
Update 2018

Figure 73: Odds ratios and 95% credible intervals for every intervention compared to pill placebo. Response in those randomised – more severe depression.



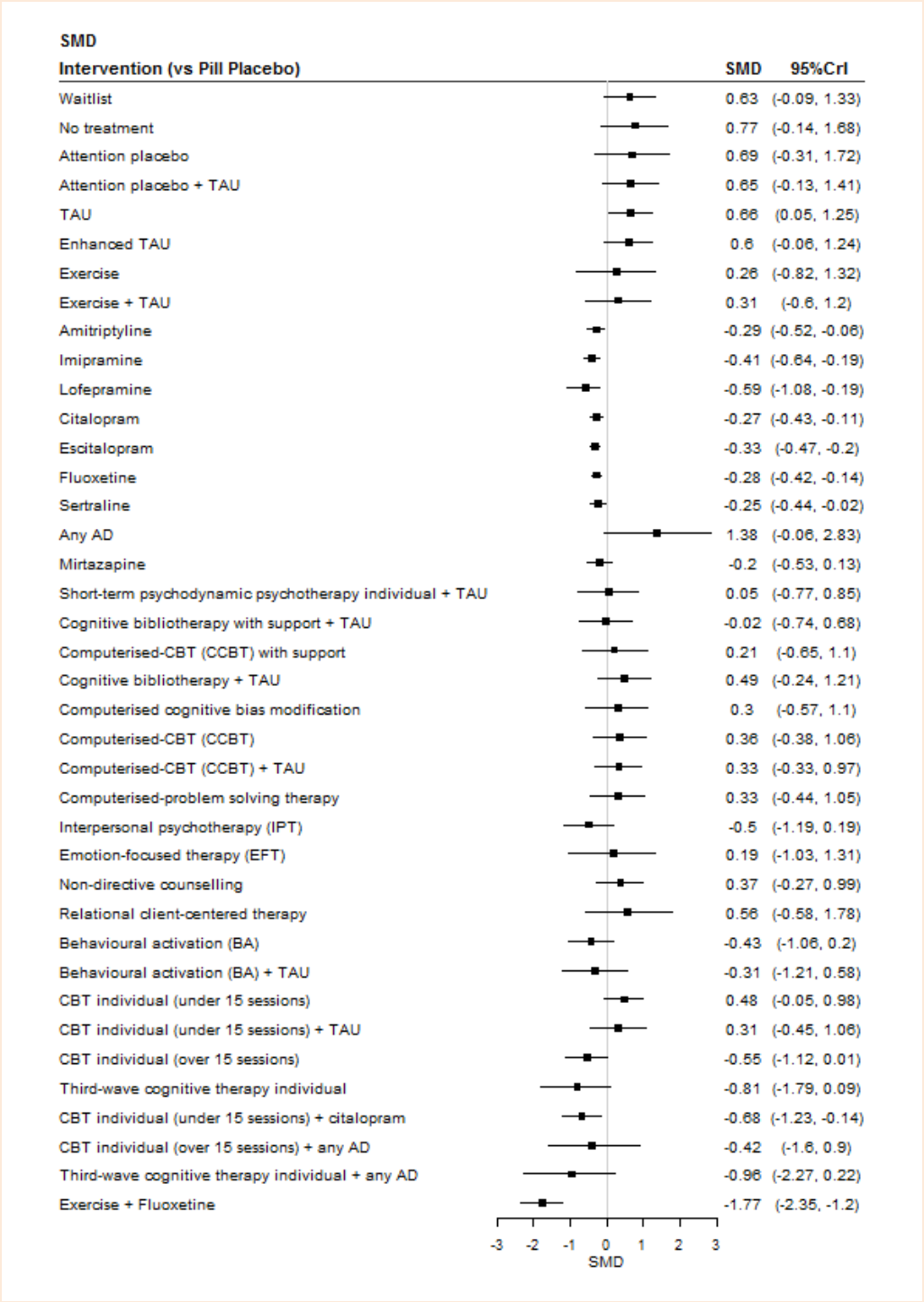
Update 2018

Figure 74: Odds ratios and 95% credible intervals for every class compared to pill placebo. Response in those randomised – more severe depression.



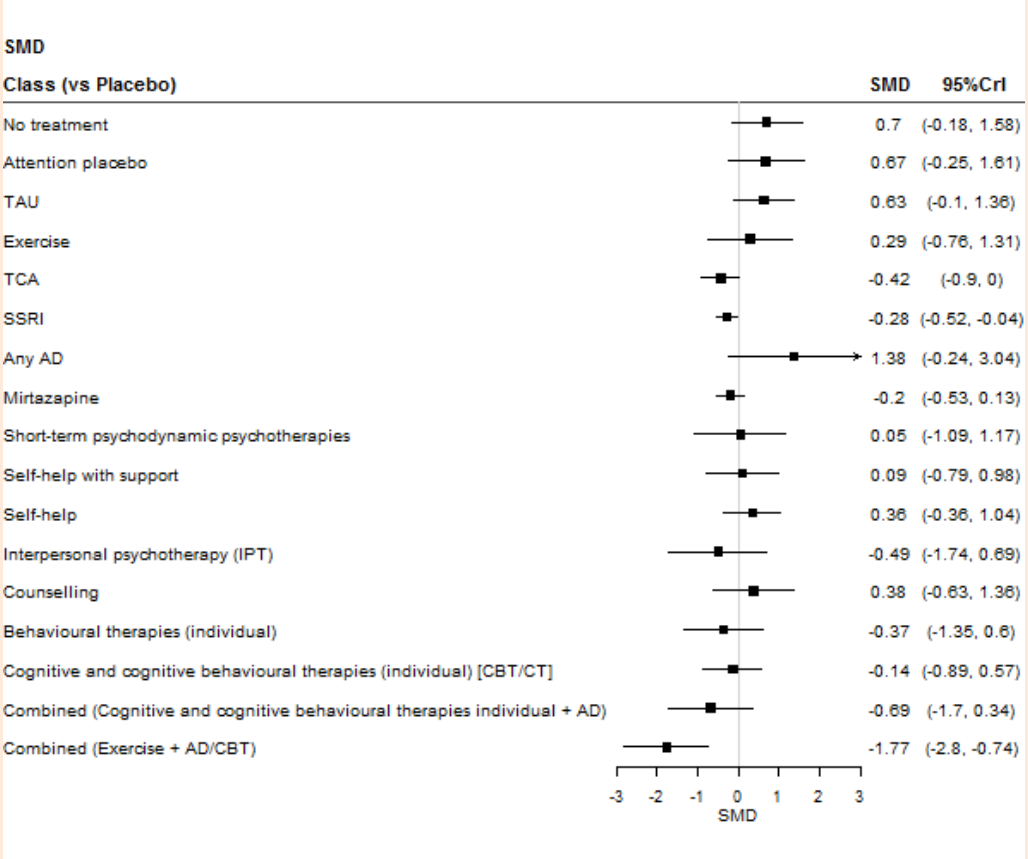
Update 2018

Figure 75: SMD and 95% credible intervals for every intervention compared to pill placebo. SMD – more severe depression.



Update 2018

Figure 76: SMD and 95% credible intervals for every class compared to pill placebo. SMD – more severe depression.



Update 2018