# National Institute for Health and Care Excellence

Consultation draft

## Depression in adults: treatment and management

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

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Consultation draft

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

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### **1**<sub>1</sub> Appendix N1: Network meta-analysis of treatments for people with a new episode 2

#### of depression: detailed methods and 3 results 4

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### 1.17 Introduction

8 The purpose of this analysis was to estimate the comparative effectiveness of various

9 interventions for treating depression in populations with less severe and more severe

- 10 populations. In total 366 studies were included in these analyses comparing 98 interventions 11 and combinations of interventions.
- 12 The outcomes analysed were discontinuation for any reason, discontinuation due to side

13 effects, remission, response and standardised mean difference (SMD). The SMD measure of 14 effect was used to combine evidence from studies reporting efficacy in terms of a continuous

- 15 measurement on various depression scales.
- 16 The studies and data used for every outcome analysed in the NMA are provided in Appendix 17 N3 of the full guideline.

### 1.28 Methods

### 1.2.19 Network meta-analysis

20 In order to take all trial information into consideration network meta-analyses (NMA) were

21 conducted. NMA is a generalisation of standard pairwise meta-analysis for A versus B trials,

22 to data structures that include, for example, A versus B, B versus C, and A versus C trials 23 (Dias et al. 2004, Lu and Ades 2004, Caldwell et al. 2005). A basic assumption of NMA

24 methods is that direct and indirect evidence estimate the same parameter, that is, the relative

25 effect between A and B measured directly from an A versus B trial, is the same as the

26 relative effect between A and B estimated indirectly from A versus C and B versus C trials.

27 NMA techniques strengthen inference concerning the relative effect of two treatments by

28 including both direct and indirect comparisons between treatments, and, at the same time,

29 allow simultaneous inference on all treatments inference on all treatments while respecting

30 randomisation (Lu and Ades 2004, Caldwell et al. 2004).

31 Simultaneous inference on the relative effects of all treatments is possible whenever 32 treatments are part of a single 'network of evidence', that is, every treatment is linked to at 33 least one of the other treatments under assessment. The correlation between the random 34 effects of multi-arm trials (i.e. those with more than 2 arms) in the network is taken into 35 account in the analysis (Dias et al. 2004). In a NMA we assume that intervention A is similar 36 (in dose, administration etc.) when it appears in the A v B and A v C studies and also that 37 every patient included the network could have been assigned to any of the interventions 38 (Caldwell et al. 2005) - a concept called 'joint randomisability' (Salanti 2012).

39 A Bayesian framework is used to estimate all parameters, using Markov chain Monte Carlo 40 simulation methods implemented in WinBUGS 1.4.3. Convergence was assessed using the

41 Brooks-Gelman-Rubin diagnostic (Brooks and Gelman 1998) and was satisfactory by 60,000

- 1 least 50,000 iterations post-convergence was obtained on which all reported results were
- 2 based. Sample WinBUGS code is provided at the end of this document, in Appendix 1:
- 3 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

12 Network diagrams are presented for each population and outcome. The edges (lines)13 connecting each pair of interventions represent a direct comparison.

14 Relative intervention effects are reported in the 'or relative to pill placebo' or 'SMD relative to

15 *pill placebo'* worksheets of the Excel files in Appendix N3 as posterior median odds ratios

16 (ORs) or standardised mean differences (SMDs) and 95% Credible Intervals (CrIs)

17 compared to Pill placebo. We noted which intervention (and classes) increased or decreased

18 the odds, or had a lower or higher SMD, compared to Pill placebo (Placebo) when the 95%

19 Crls corresponding to their effect excluded zero. The full list of log ORs and SMDs for each

20 intervention and class compared to every other are reported in the 'Direct lors' or 'Direct

21 *SMDs'* worksheets of the Excel files in Appendix N3.

We also report posterior mean rank of each class (and 95% Crls), 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

- 28 Behavioural activation (BA) + TAU
- 29 CBT individual (under 15 sessions) + TAU
- 30 CBT individual (over 15 sessions) + TAU
- 31 CBT individual (under 15 sessions) + enhanced TAU
- 32 Third-wave cognitive therapy individual + TAU
- 33 Coping with Depression course (group) + TAU
- CBT group (under 15 sessions) + TAU
- 35 CBT group (under 15 sessions) + enhanced TAU
- 36 CBT group (over 15 sessions) + TAU
- Third-wave cognitive therapy group + TAU
- 38 Problem solving individual + TAU
- Problem solving individual + enhanced TAU
- 40 Non-directive counselling + TAU
- 41 Psychodynamic counselling + TAU
- 42 Interpersonal therapy (IPT) + TAU
- 43 Interpersonal therapy (IPT) group + TAU
- 44 Psychoeducational group programme + TAU
- 45 Cognitive bibliotherapy + TAU
- 46 Computerised-CBT (CCBT) + TAU

- 1 Computerised-CBT (CCBT) + enhanced TAU
- 2 Cognitive bibliotherapy with support + TAU
- 3 Computerised-CBT (CCBT) with support + TAU
- 4 Cognitive bias modification with support + TAU
- 5 Short-term psychodynamic psychotherapy individual + TAU
- 6 CBT individual (under 15 sessions) + Pill placebo
- 7 CBT individual (over 15 sessions) + Pill placebo
- 8 Interpersonal psychotherapy (IPT) + Pill placebo
- 9 Supportive psychotherapy + Pill placebo
- 10 Any SSRI
- 11 Any SSRI + Enhanced TAU
- 12 Imipramine
- 13 Any TCA
- 14 Any AD
- 15 Exercise + TAU
- 16 Yoga + TAU
- 17 Enhanced TAU
- 18 No treatment
- 19 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.

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

- 32 Combined (psych + placebo)
- 33 Any AD

### 1.2.34 Class models

35 Classes of treatments are groups of interventions which are thought to have similar effects.
36 Class models were used so that strength could be borrowed across treatments in the same
37 class and to reconnect disconnected networks. For all outcomes, random class effect models
38 were used which assume that the effects of treatments in a class are distributed around a
39 common class mean with a within-class variance. In this way treatment effects are shrunk
40 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:

- $43 \qquad d_{1,k} \sim N\left(m_{D_k}, \tau_{D_k}^2\right)$
- 44 where  $D_k$  indicates the class to which treatment k belongs.

- 1 For treatments belonging to a class with one or two treatments in a particular analysis, the
- 2 relative treatment effects were assumed to come from a normal distribution with a class
- 3 mean and variance being borrowed from another similar class in the model, where possible.
  4 The following rules applied where classes had only one or two treatments but variance could
- 5 be shared with another class with more than 1 treatment. The following variance sharing
- 6 rules were used when necessary:
- 7 CBT/CT (individual) borrowed variance from Behavioural therapies (individual)
- 8 Behavioural therapies (individual) borrowed variance from CBT/CT
- 9 Behavioural, cognitive, or CBT groups borrowed variance from CBT/CT
- 10 Counselling borrowed variance from CBT/CT
- 11 Interpersonal psychotherapy (IPT) borrowed variance from CBT/CT
- 12 Psychoeducational interventions borrowed variance from CBT/CT
- 13 Problem solving borrowed variance from CBT/CT
- 14 Self-help borrowed variance from CBT/CT
- 15 Self-help with support borrowed variance from CBT/CT
- 16 Long-term psychodynamic psychotherapies borrowed variance from CBT/CT
- 17 Combined (CBT/CT individual + AD) borrowed variance from CBT/CT
- 18 Combined (psych + placebo) borrowed variance from CBT/CT
- 19 Short-term psychodynamic psychotherapies borrowed variance from Counselling
- Combined (Behavioural, cognitive, or CBT groups + AD) borrowed variance from
   Combined (CBT/CT + AD)
- 22 Combined (Counselling + AD) borrowed variance from Combined (CBT/CT + AD)
- 23 Combined (IPT +AD) borrowed variance from Combined (CBT/CT + AD)
- Combined (Problem solving + AD) borrowed variance from Combined (CBT/CT + AD)
- 25 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)
- 30 Combined (Exercise + AD/CBT) borrowed variance from Combined (CBT/CT + AD)
- 31 TCA borrowed variance from SSRI
- Exercise borrowed variance from Self-help with support or if this was not possible, from CBT/CT.
- 34 In addition, the following rules always applied:
- 35 Attention placebo, no treatment and TAU share a class variance
- 36 Any AD always has variance equal to the sum of the variance of SSRIs and TCAs, where

$$\tau_{AnyAD}^2 = \tau_{SSRI}^2 + \tau_{TCA}^2$$

- 38 These assumptions were based on expert opinion from the guideline committee.
- 39 For treatments not believed to belong to a class in clinical practice (mirtazapine), the relative 40 treatment effects were given non-informative priors  $d_{1,k} \sim N(0,100^2)$ .
- 41 The within-class mean treatment effects were given vague priors  $m_j \sim N(0, 100^2)$  and the
- 42 within-class variability had priors  $\tau^2 \sim$  Half-normal(0,0.19<sup>2</sup>) chosen to express the prior belief
- 43 that 95% of trials will give odds ratios within a factor of 1.5 from the estimated median odds
- 44 ratio. This prior distribution was necessary due to the small number of interventions in each

1 class, although it still covers a wide range of possible odds ratios within a class. This prior 2 distribution was also used for the SMD and has a similar interpretation.

3 For treatments not believed to belong to a class (mirtazapine), the within-class mean 4 treatment effect was equal to the individual treatment effect, with no added variability.

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

6 We compared the fit of the random class effect models to that of fixed class effect models

7 which assume that all treatments in a class have the same relative effect. In most cases the

8 models had a very similar fit suggesting that the interventions had been grouped well into

9 classes with small within-class variability.

### **1.2.4**0 Inconsistency checks

11 Consistency between the different sources of indirect and direct evidence was explored

12 statistically by comparing the fit of a model assuming consistency with a model which

13 allowed for inconsistency (also known as an unrelated mean effect model). Goodness of fit

14 was measured using the posterior mean of the residual deviance, which is a measure of the

15 magnitude of the difference between the observed data and their model predictions

- 16 (Spiegelhalter et al. 2002). Smaller values are preferred, and in a well-fitting model the
- 17 posterior mean residual deviance should be close to the number of data points (Spiegelhalter
- 18 et al. 2002). We also report the deviance information criterion (DIC) which penalises model fit 19 with model complexity (Spiegelhalter et al. 2002). Finally, we report the between studies

20 standard deviation (heterogeneity parameter) to assess the degree of statistical

21 heterogeneity. If the inconsistency model had the smallest posterior mean residual deviance

22 or heterogeneity then this indicated potential inconsistency in the data. In comparing models,

23 differences of ≥5 points for posterior mean residual deviance and DIC were considered

24 meaningful (Spiegelhalter et al. 2002), with lower values being favoured. It should be noted

25 that the inconsistency model did not assume any class relation between interventions.

26 Comparisons between the relative effects of all pairs of interventions obtained from the

27 consistency (NMA) model and those obtained from the inconsistency (pairwise) model (which

28 does not take into account the indirect evidence in the estimation of effects) for each

29 outcome are provided in Appendix N3.

### 1.2.50 SMD analysis: methods

31 We wished to include as many trials and information as possible in each analysis even when 32 data were reported in different ways. This meant transforming the data in some cases. For

33 the SMD analysis we wanted to conduct a NMA on the mean difference in change from

34 baseline (CFB) (for which standard methods are available) (Dias et al. 2011). The data

35 required for each arm of each study are the mean CFB, the standard deviation in CFB and

36 the total number of individuals in that arm (or the standard error of the mean change from

37 baseline).

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

- 39 1) the baseline and follow-up means, standard deviations and number of individuals, for 40 each arm of the study;
- 41 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 42
- 43 from baseline.

44 Studies reporting outcomes a) or b) above also provide information on the mean change

45 from baseline, through the relationship between the underlying continuous scale and the

46 measurements that can be derived from it.

- 1 For our analysis, if CFB data were available in a study we used that data. If that study did not
- 2 report CFB but reported baseline and follow-up data we used the baseline and follow up data
- 3 and transformed it to CFB. If a study reported neither CFB nor baseline and follow up data
- 4 but did report response, we used the response data and transformed it to CFB.
- 5 This analysis was carried out on all patients randomised. If a study did not report appropriate
- 6 data on all patients randomised (e.g. if it reported completers' data instead) it was not
- 7 included in this analysis.

### 1.2.5.18 Notation

- 9 To transform the data we assumed that  $n_{ik}$  individuals are randomised to each arm k (k>1) of 10 study i=1,...,M, on which the following outcomes are recorded for individual  $j=1,...,n_{ik}$ :
- 11  $x_{jik}$  the score at baseline for individual *j* in arm *k* of trial *i*, on a given continuous scale;
- 12  $\mathcal{Y}_{jik}$  the score at follow-up for individual *j* in arm *k* of trial *i*, on a given continuous scale;
- 13  $C_{jik}$  the change from baseline for individual *j* in arm *k* of trial *i*, on a given continuous scale,
- 14 where  $c_{jik} = y_{jik} x_{jik}$ ;

15  $R_{jik}$  - response status at follow-up for individual *j* in arm *k* of trial *i*, defined as **at least a**  $q_i$ % 16 **reduction** of the follow-up measurement on a given continuous scale, compared to baseline, 17 i.e.

19 Note that different studies may have used a different cut-off q (although they would be 20 expected to be the same for all arms of a study), and these are therefore indexed by study.

(1)

### 1.2.5.21 Reported outcomes

22 Studies may report all or some of the following observed outcomes

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

- 23  $m_{X,ik}$  the observed mean at baseline in arm *k* of trial *i*, on a given continuous scale;
- 24  $sd_{x,ik}$  the observed standard deviation at baseline in arm *k* of trial *i*, on a given continuous scale;
- 26  $m_{Y,ik}$  the observed mean at follow-up in arm *k* of trial *i*, on a given continuous scale;
- 27  $sd_{Y,ik}$  the observed standard deviation at follow-up in arm *k* of trial *i*, on a given continuous scale;
- 29  $m_{C,ik}$  the observed mean change from baseline in arm *k* of trial *i*, on a given continuous 30 scale;
- 31  $sd_{C,ik}$  the observed standard deviation in change from baseline in arm *k* of trial *i*, on a 32 given continuous scale;

1  $\rho_{ik}$  - the observed correlation between baseline and follow-up scores measured on the

2 same individual in arm k of trial i. (Although this is rarely reported directly, it can be

3 calculated when the means and standard deviations at baseline, follow-up and from the CFB 4 are provided);

5  $r_{resp,ik}$  - the number of individuals achieving response in arm *k* of trial *i*, with response defined 6 in equation (1).

### 1.2.5.37 Relationship between different outcomes

8 We assume that for each patient the baseline and follow-up measurements are sampled 9 from a bivariate Normal distribution. Thus for all patients in arm *k* of trial *i*, we assume that

10 their baseline,  $X_{ik}$ , and follow-up measurements  $Y_{ik}$ , are independent and identically 11 distributed as

12

13 
$$\begin{pmatrix} X_{ik} \\ Y_{ik} \end{pmatrix} \sim N_2 \begin{pmatrix} \mu_{X,ik} \\ \mu_{Y,ik} \end{pmatrix}, \begin{pmatrix} \sigma_{X,ik}^2 & \rho_{ik}\sigma_{X,ik}\sigma_{Y,ik} \\ \rho_{ik}\sigma_{X,ik}\sigma_{Y,ik} & \sigma_{Y,ik}^2 \end{pmatrix}$$
 (2)

14 with  $\mu_{X,ik}$  and  $\mu_{Y,ik}$  representing the means and  $\sigma_{X,ik}^2$  and  $\sigma_{Y,ik}^2$  the variances at baseline 15 and follow-up for individuals in arm *k* of trial *i*, respectively, and  $\rho_{ik}$  being the within arm and

16 study correlation between baseline and follow-up measurements on the same individuals.

17 We define the mean change from baseline in arm *k* of trial *i* as  $\theta_{ik} = \mu_{Y,ik} - \mu_{X,ik}$  as the 18 parameter of interest.

### 1.2.5.49 NMA model for continuous outcomes

20 With continuous outcome data, meta-analysis is usually based on the sample means with 21 standard errors assumed known. Here we are interested in modelling the mean changes

22 from baseline, which are assumed to be approximately normally distributed, with likelihood

$$m_{C,ik} \sim N(\theta_{ik}, se_{C,ik}^2)$$

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

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

27 where  $\gamma_i$  are the trial-specific effects of the treatment in arm 1 of trial *i*, treated as unrelated 28 nuisance parameters, and the  $\delta_{ik}$  are the trial-specific treatment effects of the treatment in 29 arm *k* relative to the treatment in arm 1 in that trial, where  $\delta_{i1} = 0$ . The trial-specific random 30 effects  $\delta_{ik}$ , represent the mean differences between the change from baseline for the 31 treatment in arm *k* and the treatment in arm 1 of trial *i* and, in a random effects model,  $\delta_{ik} = Normal(d_{ik} - \sigma^2)$ 

32 
$$\delta_{ik} \sim \operatorname{Normal}(d_{t_{i1},t_{ik}},\sigma^2)$$
 (4)

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

### **1.2.5.57** Likelihood and link functions for studies reporting other outcomes

### 1.2.5.5.18 Studies reporting mean and variance at follow-up

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

10 
$$(Y_{ik} - X_{ik}) \sim N(\theta_{ik}, \sigma_{X,ik}^2 + \sigma_{Y,ik}^2 - 2\rho_{ik}\sigma_{X,ik}\sigma_{Y,ik})$$
(5)

- 11 Therefore, studies not reporting change from baseline but reporting the mean and variance
- 12 at baseline and follow-up also provide information on the parameter of interest  $\theta_{ik}$ , the mean 13 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

16 
$$m_{C,ik} \sim N\left(\theta_{ik}, se_{X,ik}^2 + se_{Y,ik}^2 - 2\rho_{ik}se_{X,ik}se_{Y,ik}\right)$$

17 Provided the standard errors at baseline and follow up can be obtained and that we have

18 information on the within-study correlation, the remaining model is given in equations (3) and

19 (4) can be used to pool the mean differences in change from baseline.

### **1.2.5.5.20** Studies reporting number of responders

- 21 Using equation (1), the probability of response for individuals in arm *k* of trial *i* is defined as
- 22

24

26

$$R_{ik} = \Pr(Y_{ik} - X_{ik} \le -qX_{ik}) \tag{6}$$

23 Conditioning on the baseline value  $X_{ik}$  we have

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

25 thus,

$$R_{ik} | X_{ik} = \Pr_{Y|X} (Y_{ik} < (1-q)X_{ik}) = \Phi (aX_{ik} + b)$$
(8)

27 with

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

28

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

1

$$R_{ik} = E_{X_{ik}} \left\lfloor \Phi \left( a X_{ik} + b \right) \right\rfloor \tag{9}$$

2 It can be shown that

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

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

5

6

3

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

7 Therefore, studies not reporting the change from baseline or follow-up measures, but8 providing information on the probability of response, also provide information on the

9 parameter of interest, the mean change from baseline  $\theta_{ik}$  .

10 These studies have a binomial likelihood

11 
$$r_{resp,ik} \sim \text{Binomial}(R_{ik}, n_{ik})$$

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

15 equations (3) and (4), as before.

### **1.2.5.6**6 **Prior distributions and computation**

17 In this case non-informative prior distributions are chosen for the pooled treatment effects, 18 relative to treatment 1,  $d_{1k}$ , k=2,...,nt, where *nt* is the number of treatments in the network

19 
$$d_{1k} \sim \text{Normal}(0, 100^2)$$
 (12)

20 and a Uniform prior between 0 and 5 is chosen for the between-study heterogeneity, which is

21 thought to be sufficiently wide to capture the variability in difference in mean change from

22 baseline across trials making the same comparisons.

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

### 1.2.5.25 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.

31 Pooling of the difference in means across different scales is not appropriate. A common

32 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<sub>i</sub>*, often obtained by pooling the estimated standard deviations across all arms of
- 35 the study (Cooper et al. 2009). The standardising constant can be adjusted in different ways

1 (Cooper et al. 2009). We will illustrate the model using Cohen's d<sup>16</sup>, but the analysis using
2 another standardising constant can be done following the same principles.

3 The SMD for arm *k* of study *i* compared to arm 1 of study i,  $\lambda_{ik}$ , is given as

(13)

$$\lambda_{ik} = \frac{m_{ik} - m_{i1}}{s_i}$$

4

6

8

5 where  $s_i$  in a two arm study is given as

$$s_{i} = \sqrt{\frac{(n_{i1} - 1)sd_{i1}^{2} + (n_{i2} - 1)sd_{i2}^{2}}{n_{i1} + n_{i2} - 2}}$$
(14)

7 and in a three arm study is given as

$$s_{i} = \sqrt{\frac{(n_{i1} - 1)sd_{i1}^{2} + (n_{i2} - 1)sd_{i2}^{2} + (n_{i3} - 1)sd_{i3}^{2}}{n_{i1} + n_{i2} + n_{i3} - 3}}$$
(15)

9 The likelihood for each study reporting the various outcomes are as before, but the

10 parameter of interest is now the SMD  $\lambda_{ik}$ . Thus the model is defined as

11 
$$\lambda_{ik} = \gamma_i + \delta_{ik}$$
 (16)

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

$$\theta_{ik} = \lambda_{ik} s_i$$

14 Prior distributions can be defined as before.

(17)

### 1.2.65 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 thatarm (or the standard error of the mean change from baseline).
- b) the baseline and follow-up means, standard deviations and number of individuals, foreach arm of the study.

28 Studies reporting outcomes a) or b) above also provide information on probability of 29 response through the relationship between the underlying continuous scale and the 30 measurements that can be derived from it.

31 For this analysis, if response data were available in a study we used that data. If that study

32 did not report response but reported CFB we used the CFB data and transformed it to

33 response. If a study reported neither response nor CFB but did report baseline and follow up

34 data, we used the baseline and follow up data and transformed it to response.

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

### 1.2.6.16 Notation

7 For trials reporting response the following model was used:

8

12

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

9 where  $r_{jk}$  is the number of individuals achieving response in arm k of trial j,  $n_{jk}$  is the total

10 number of individuals in arm k of trial j, and  $p_{jk}$  is the probability of response in arm k of trial j. 11 These probabilities are modelled on the log-odds scale as:

These probabilities are modelled on the log-odds scale as.

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

13 where  $\eta_{ik}$  represents the relative treatment effect of the treatment in arm *k* compared with the 14 treatment in arm 1 in trial *i*, on the log-odds ratio (LOR) scale and  $\eta_{i1} = 0$ . Thus  $\eta_{ik} > 0$  favours 15 the treatment in arm k and  $\eta_{ik} < 0$  favours the treatment in arm 1.

16 The LOR of response can be related to a notional SMD for response using the formula 17 (Chinn 2000):

18

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

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

- 20 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:

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

23

24 Standard NMA random and fixed effects model can used to pool  $\eta$ , as described in section 25 1.2.5.4. Prior distributions can also be defined as before.

26 Sample WinBUGS codes for both the SMD and response analyses are provided at the end27 of this document, in Appendix 1.

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

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

32 For a) we identified 7 studies in our dataset that provided information on mean and SD at

33 baseline, mean and SD at follow-up and the mean and SD of change from baseline

34 (Appendix 2 at the end of this document). The correlations calculated from these studies

35 ranged from -0.67 to 0.92, which meant that no meaningful summary of this correlation could

36 be used.

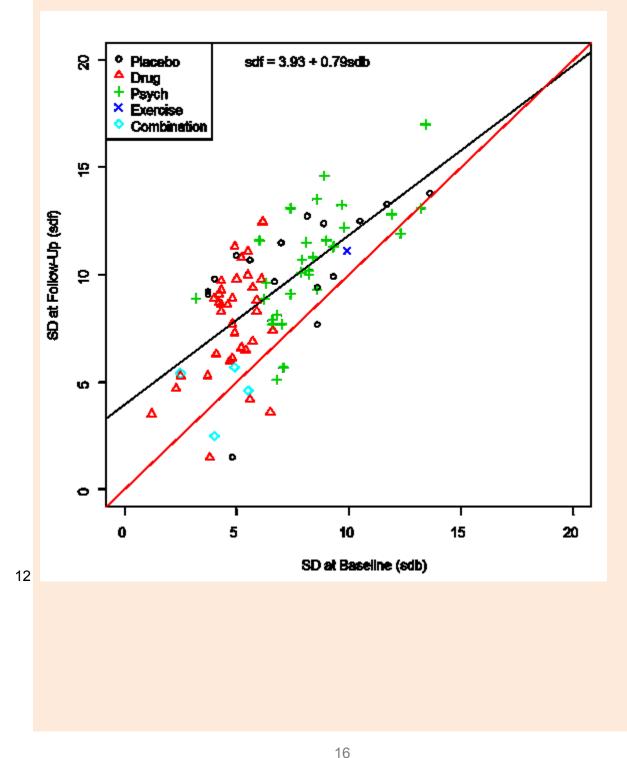
37 We also identified various data sources (included in Appendix 2) for correlations relating to

38 psychological and pharmacological treatments but the evidence was inconclusive and often

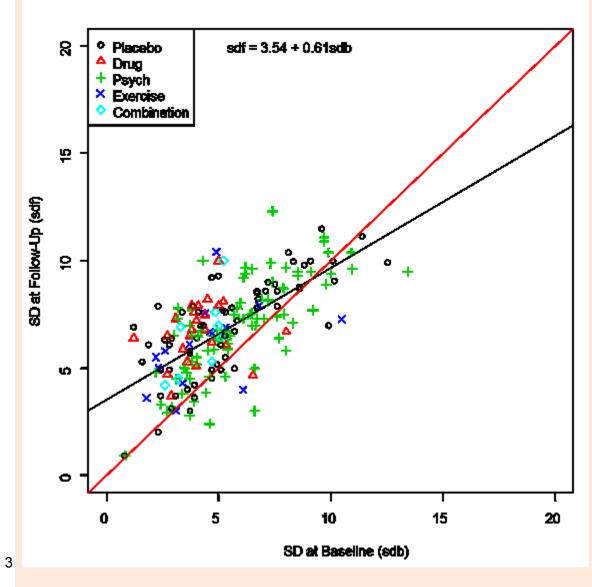
1 based on limited numbers of patients. We decided to assume a correlation of 0.5 and vary2 this in sensitivity analysis as described in section 1.4.

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



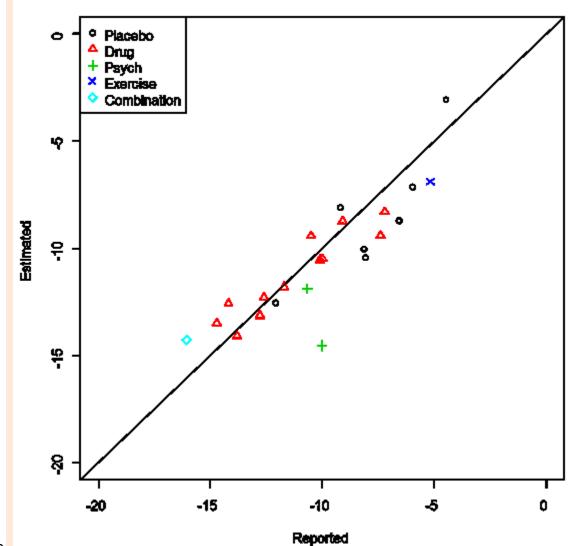
### Figure 2: Plot of SDs at baseline and follow up – population with less severe depression



### 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.

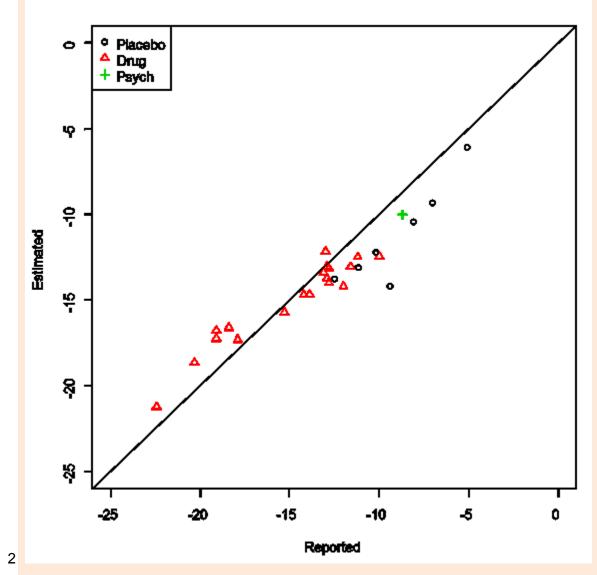
### 1 Figure 3: CFB estimated from responders v reported CFB – Less severe depression



2

Update 2018

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



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

5  $L_{jik}$  - remission status at follow-up for individual *j* in arm *k* of trial *i*, defined as having follow-6 up measurement below pre-defined threshold  $h_i$  on a given continuous scale, i.e.

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

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

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

9

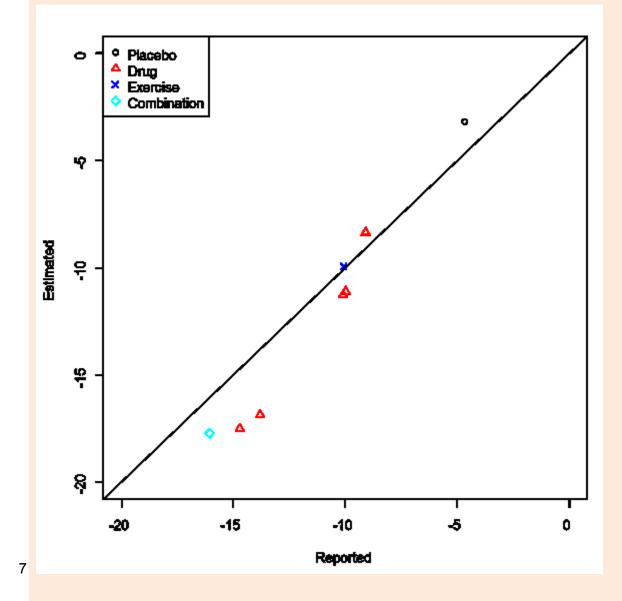
7

10 Therefore, studies providing information on the probability of remission, also provide

11 information on the parameter of interest, the mean change from baseline  $\theta_{ik}$ .

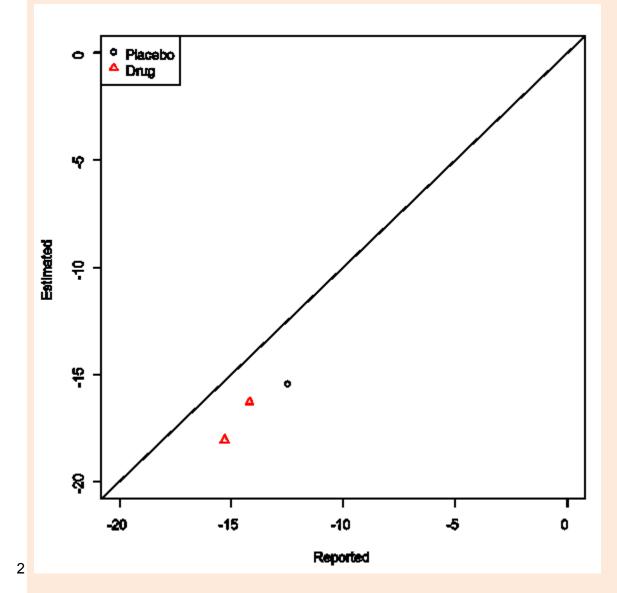
- 1 We again checked agreement between the observed change from baseline and that
- 2 obtained through the inverse of the transformations in equation (20), using the observed
- 3 probabilities of remission. However there were not enough data to check agreement,
- 4 particularly for the population with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

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



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- 20

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



### 1.33 Results

### 1.3.14 Population: less severe depression

### **1.3.1.15** Outcome: discontinuation for any reason – less severe depression

6 This analysis was conducted using the NMA code given by Dias et al for binomial data (Dias 7 et al. 2013, Dias et al. 2011) with the denominator being the total number of patients 8 randomised. After excluding trials with zero events in all arms, 199 trials of 92 interventions 9 and 27 classes were included for this outcome (Table 1, Figure 7, Figure 8). A continuity 10 correction was applied to data in 16 studies containing at least one zero cell to stabilise the 11 results. 12 Lower posterior mean residual deviance and DIC values in the NMA random effects 13 consistency model, as well as minimal improvement in the prediction of data in individual 14 studies by the inconsistency model, suggested that there was no evidence of inconsistency 15 (Table 29; Figure 9). The between-study heterogeneity slightly decreased in the

- 16 inconsistency model, which may be partly explained by the between-study heterogeneity
- 17 contributed by Richards 2015 and Furukawa 2012 (Table 29). Reported results are therefore

1 based on the random-effects NMA model, assuming consistency. Moderate between trials

2 heterogeneity was observed relative to the size of the intervention effect estimates, ( $\tau = 2.0.40$  (0.5% ( $\tau = 0.40$  to 0.00)

**3** 0.49 (95% CrI 0.40 to 0.60)).

### 4 Table 1: Interventions, classes and number of patients randomised (N) included in 5 discontinuation for any reason analysis – less severe depression

	Intervention	N	Talysis – less severe depressio		Ν
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	

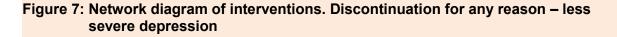
	Intervention	Ν	Class		Ν
32	Computerised-CBT (CCBT) with support + TAU	649		11	
33	Tailored computerised-CBT (CCBT) with support	69		11	
34	Behavioural bibliotherapy	23	Self-help without support	12	3232
35	Cognitive bibliotherapy	501		12	
36	Cognitive bibliotherapy + TAU	182		12	
37	Computerised cognitive 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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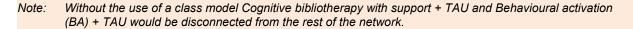
	Intervention	Ν	Class		Ν
61	Behavioural activation (BA) + TAU	23		17	
62	Behavioural therapy (Lewinsohn 1976)	15		17	
63	Coping with Depression course (individual)	15		17	
64	CBT individual (under 15 sessions)	370	Cognitive and cognitive behavioural therapies (individual)	18	1983
65	CBT individual (under 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

	Intervention	Ν	Class		Ν
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



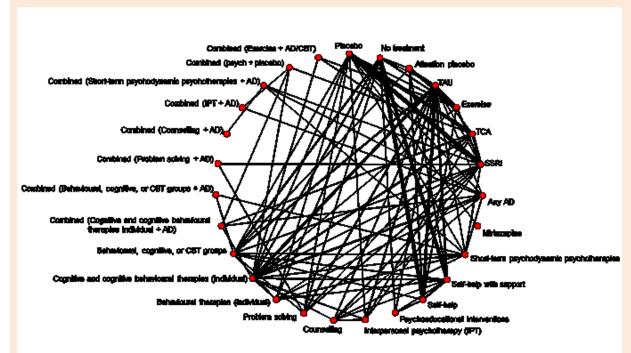




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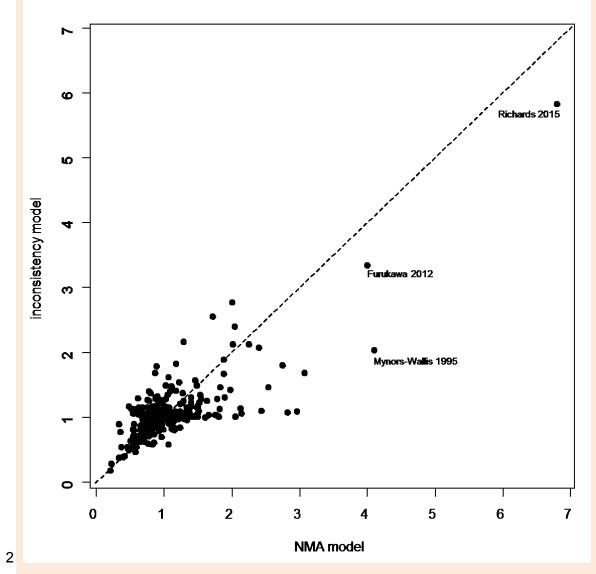
### 1 Figure 8: Network diagram of classes. Discontinuation for any reason – less severe 2 depression.



3

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



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

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

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

for any reason – less severe depression.	Posterior median	
Class	rank	95% Crl
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)

### **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.

11 After excluding trials which did not report both discontinuation and discontinuation due to SE

12 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
14 13 classes were included for this outcome (

15 Table 3, Figure 10, Figure 11). A continuity correction was applied to data containing at least16 one zero cell to stabilise the results.

17 Lower between trials heterogeneity and DIC values in the random effects model assuming

18 consistency, as well as minimal improvement in the prediction of data in individual studies by

19 the inconsistency model, suggested that there was no evidence of inconsistency (Table 30;

28

1 Figure 12). Reported results are therefore based on the random-effects NMA model,

2 assuming consistency. Moderate to high between trials heterogeneity was found relative to 3 the size of the intervention effect estimates ( $\tau = 0.56$  (95% 0.06 Crl 1.12)), meaning that the

4 results should be interpreted with caution.

### 5 Table 3: Interventions, classes and number of patients randomised (N) included in 6 discontinuation due to SE analysis – less severe depression.

7

	Intervention	Ν	Class		Ν
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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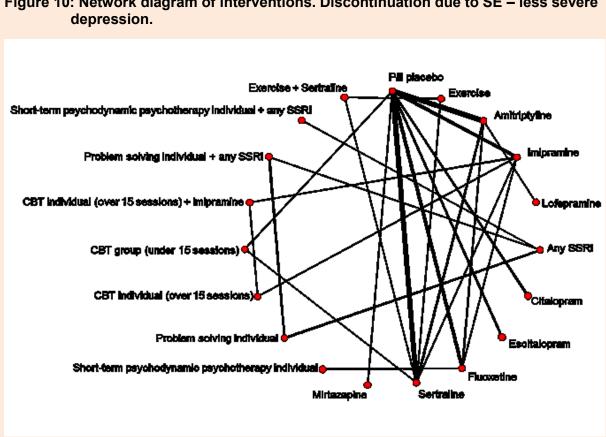
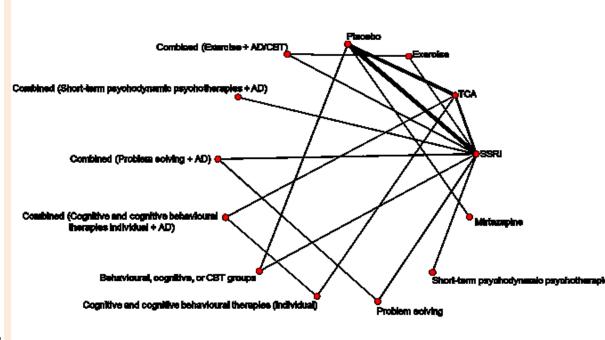


Figure 10: Network diagram of interventions. Discontinuation due to SE - less severe

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.

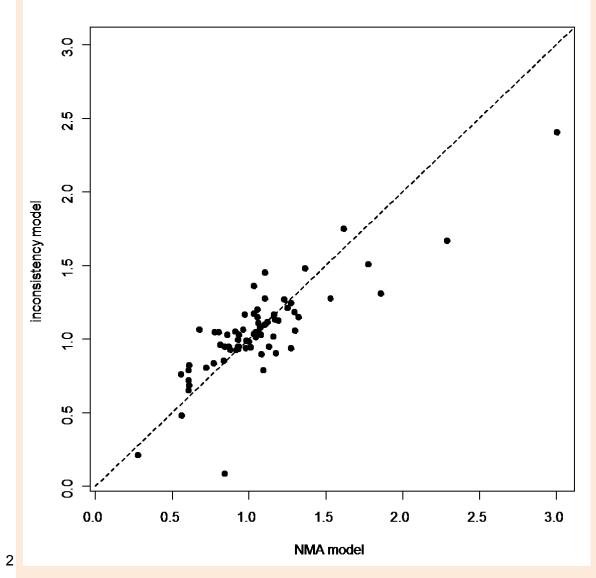
#### 1 Figure 11: Network diagram of classes. Discontinuation due to SE – less severe 2 depression.



Update 2018

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



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

10 The highest ranked class is Exercise with a posterior median rank of 1 (95% Crl 1<sup>st</sup> to 3<sup>rd</sup>). 11 This was also the highest ranked intervention at 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 5<sup>th</sup>). The lowest ranked 12 interventions were Short-term psychodynamic psychotherapy individual at 15<sup>th</sup> (95% Crl 4<sup>th</sup> 13 to 17<sup>th</sup>), Problem solving individual + any SSRI at 15<sup>th</sup> (95% Crl 5<sup>th</sup> to 17<sup>th</sup>), and Amitriptyline 14 at 15<sup>th</sup> (95% Crl 13<sup>th</sup> to 17<sup>th</sup>). The lowest ranked classes are short-term psychodynamic 15 psychotherapies at 12<sup>th</sup> (95 Crl 4<sup>th</sup> to 13<sup>th</sup>) and Combined (Problem solving + AD) at 12<sup>th</sup> 16 (95% Crl 5<sup>th</sup> to 13<sup>th</sup>). Rankings of classes are shown in Table 4; rankings of interventions are 17 shown in the respective excel file in Appendix N3, "Ranks" worksheet.

Update 2018

#### 1 Table 4: Posterior median rank and 95% credible intervals by class. Discontinuation 2 due to SE – less severe depression.

Class	Posterior median rank	95% Crl					
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)					

### **1.3.1.3**3 **Outcome: remission in completers – less severe depression**

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

15 with zero cells, and lower posterior mean residual deviance and DIC values in the NMA

16 random effects consistency model, suggesting there was no evidence of inconsistency17 (Figure 15; Table 31). Reported results are therefore based on the random-effects NMA

18 model, assuming consistency. Moderate to low between trials heterogeneity was observed

19 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.

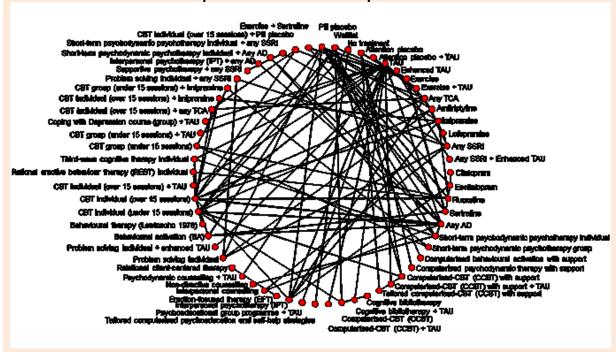
		Intervention	Ν	Class		Ν			
1		Pill placebo	574	Pill placebo	1	574			
2	2	Waitlist	118	No treatment	2	290			
3	3	No treatment	172		2				
4	ŀ	Attention placebo	94	Attention placebo	3	115			
5	5	Attention placebo + TAU	21		3				
6	6	TAU	931	TAU	4	1098			
7	,	Enhanced TAU	167		4				
8	3	Exercise	263	Exercise	5	282			
9	)	Exercise + TAU	19		5				
1	0	Any TCA	168	TCAs	6	399			

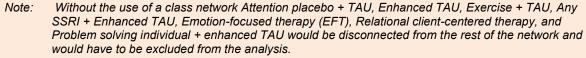
32

	Intervention	Ν	Class		Ν
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

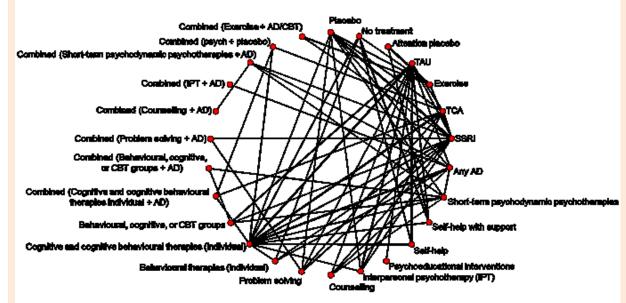
	Intervention	Ν	Class		Ν
43	Behavioural therapy (Lewinsohn 1976)	10		16	
44	CBT individual (under 15 sessions)	218	Cognitive and cognitive behavioural therapies (individual)	17	598
45	CBT individual (over 15 sessions)	233		17	
46	CBT individual (over 15 sessions) + TAU	10		17	
47	Rational emotive behaviour 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
*Vai	riance borrowed from another clas	ss as des	cribed in section 1.2.3		

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

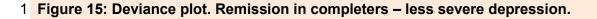


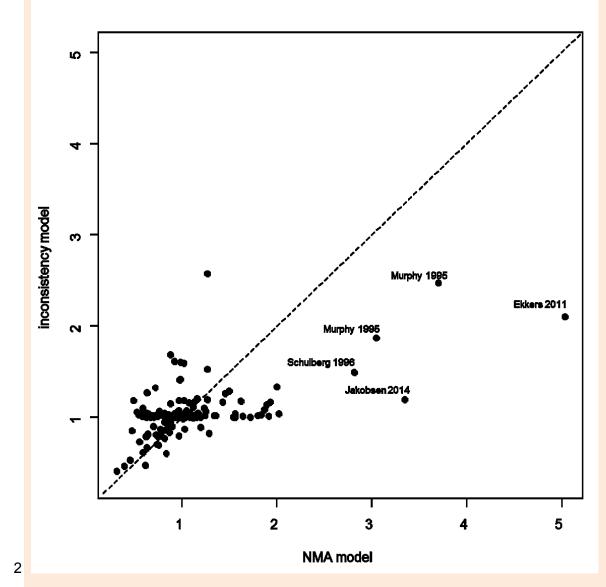


### Figure 14: Network diagram of all studies included in analysis by class. Remission in completers – less severe depression.



3





3 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, 4 5 Escitalopram, Fluoxetine, Sertraline, any AD, Computerised-CBT (CCBT) + TAU, 6 Interpersonal psychotherapy (IPT), Interpersonal counselling, Behavioural activation (BA), 7 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 8 9 (group) + TAU, CBT individual (over 15 sessions) + any TCA, CBT individual (over 15 10 sessions) + imipramine, CBT group (under 15 sessions) + imipramine, Supportive 11 psychotherapy + any SSRI, Interpersonal psychotherapy (IPT) + any AD, Short-term 12 psychodynamic psychotherapy individual + Any AD, Short-term psychodynamic 13 psychotherapy individual + any SSRI, and CBT individual (over 15 sessions) + Pill placebo 14 (Figure 53). There is evidence that Waitlist, No treatment, Attention placebo, and Attention 15 placebo + TAU have a decreased odds of remission in completers compared with pill 16 placebo. The classes for which evidence suggests an increased odds of remission in 17 completers compared to Pill placebo are SSRIs, Behavioural therapies (individual), Cognitive 18 and cognitive behavioural therapies (individual), Behavioural, cognitive, or CBT groups, 19 Combined (Cognitive and cognitive behavioural therapies individual + AD), Combined 20 (Behavioural, cognitive, or CBT groups + AD), Combined (Counselling + AD), Combined (IPT 21 + AD), Combined (Short-term psychodynamic psychotherapies + AD), and Combined (psych

1 + placebo) (Figure 54). There is evidence of No treatment and Attention placebo having a2 decreased odds of remission in completers compared to Pill placebo.

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

### 9 Table 6: Posterior median rank and 95% credible intervals by class. Remission in 10 completers – less severe depression.

Class	Posterior median rank	95% Crl
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)

#### 1.3.1.41 Outcome: remission in those randomised – less severe depression

12 An additional analysis was carried out on all trials reporting remission with the number

13 randomised to treatment as the denominator. After excluding trials with zero events in all

14 arms, 69 trials of 60 interventions and 26 classes were included for this outcome (Table 7,

15 Figure 16 and Figure 17). We initially observed a spike in the posterior distribution of the

16 between-study standard deviation, which suggested there was little evidence contributing to

17 the between study heterogeneity. Consequently, we gave the between-study variance an

- 18 informative prior, log-Normal(-2.34, 1.72) (Lu and Ades 2004), in this model. This was
- 19 selected from a list of predictive distributions for between-study heterogeneity that are typical

1 of mental health indicators and we selected the distribution with the largest variance (Turner 2 et al. 2015).

3 The inconsistency model only notably improved in the prediction of data in individual studies

4 with zero cells, and the DIC favoured the random effects consistency model (Figure 18;

5 Table 32). The between study heterogeneity slightly decreased in the inconsistency model,

6 however overall there is no evidence of inconsistency (Table 32).

7 Reported results are based on the random-effects NMA model, assuming consistency. Note

8 the model fit is poor and thus results should be interpreted with caution (Table 32). Small

9 between trials heterogeneity was found relative to the size of the intervention effect estimates

10  $(\tau = 0.20 (95\% \text{ CrI } 0.05 \text{ to } 0.40)).$ 

### 11 Table 7: Interventions, classes and number of patients (N) included in remission in 12 those randomised analysis – less severe depression

	Intervention	Ν	Class		Ν
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

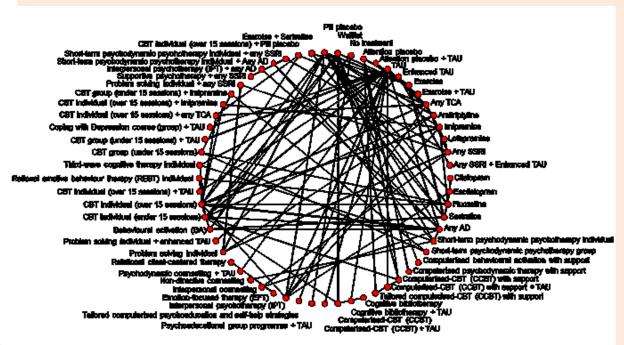
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	Intervention	Ν	Class		Ν
29	Cognitive bibliotherapy + TAU	86		11	
30	Computerised-CBT (CCBT)	214		11	
31	Computerised-CBT (CCBT) + TAU	194		11	
32	Tailored computerised psychoeducation and self-help strategies	174		11	
33	Psychoeducational group programme + 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

	Intervention	Ν	Class		Ν
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.

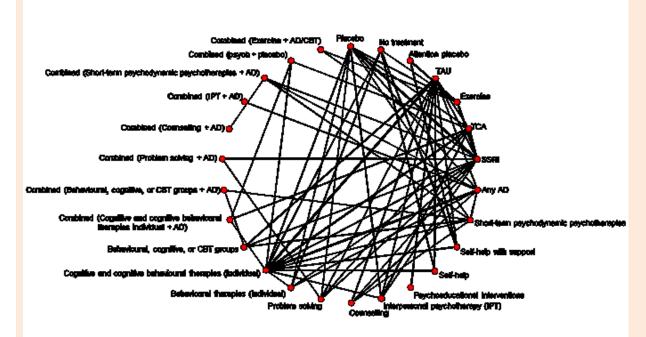


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4 Note: Without the use of a class network Attention placebo + TAU, Enhanced TAU, Exercise + TAU, Any SSRI +
5 Enhanced TAU, Emotion-focused therapy (EFT), Relational client-centered therapy, and Problem solving
6 individual + enhanced TAU would be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

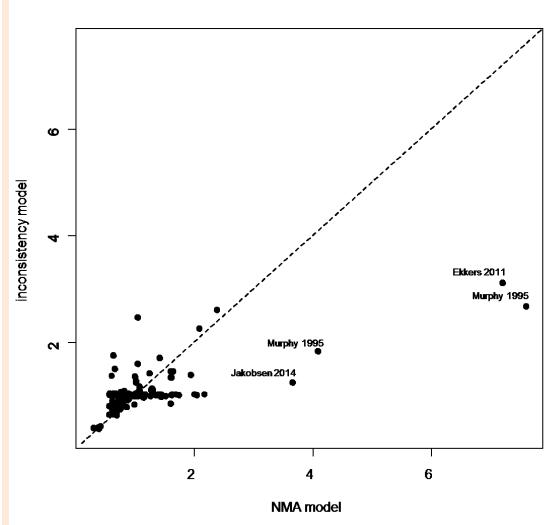
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### Figure 17: Network diagram of all studies included in analysis by class. Remission in those randomised – less severe depression.



3

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



2

3 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 4 5 TAU, Citalopram, Escitalopram, Fluoxetine, Sertraline, Any AD, Psychoeducational group 6 programme + TAU, Interpersonal psychotherapy (IPT), Interpersonal counselling, Behavioural activation (BA), CBT individual (under 15 sessions), CBT individual (over 15 7 8 sessions), CBT individual (over 15 sessions) + TAU, Rational emotive behaviour therapy 9 (REBT) individual, Third-wave cognitive therapy individual, CBT group (under 15 sessions), 10 CBT group (under 15 sessions) + TAU, Coping with Depression course (group) + TAU, CBT 11 individual (over 15 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, 12 CBT group (under 15 sessions) + imipramine, Supportive psychotherapy + any SSRI, 13 Interpersonal psychotherapy (IPT) + any AD, Short-term psychodynamic psychotherapy 14 individual + Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, and 15 CBT individual (over 15 sessions) + Pill placebo (Figure 55). Waitlist and Attention placebo 16 are the only interventions with evidence of a decreased odds of remission in those 17 randomised compared to Pill placebo. The classes for which there is evidence of an 18 increased odds of remission in those randomised compared to Pill placebo are SSRI, 19 Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual), 20 Behavioural, cognitive, or CBT groups, Combined (Cognitive and cognitive behavioural 21 therapies individual + AD), Combined (Behavioural, cognitive, or CBT groups + AD), 22 Combined (Counselling + AD), Combined (Short-term psychodynamic psychotherapies +

1 AD), and Combined (psych + placebo) (Figure 56). Attention placebo is the only class for

2 which there is evidence of a decreased odds of remission in those randomised compared to
3 Pill placebo.

Combined (Counselling + AD) is the highest ranked class at 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 17<sup>th</sup>). The
highest ranked intervention, Supportive psychotherapy + any SSRI (1<sup>st</sup>, 95% Crl 1<sup>st</sup> to 28<sup>th</sup>),
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

8 respective excel file in Appendix N3, "Ranks" worksheet.

#### 9 Table 8: Posterior median rank and 95% credible intervals by class. Remission in 10 those randomised – less severe depression.

Class	Posterior median rank	95% Crl
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)

### **1.3.1.51** Outcome: response in completers – less severe depression

12 As mentioned in the methods section, this analysis included trials reporting three types of 13 data:

- 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
- Mean change from baseline (CFB), the standard deviation in CFB and the total number of individuals in that arm

### 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).

9 No meaningful differences were observed in posterior mean residual deviance or between 10 study heterogeneity, and there was minimal improvement in the prediction of data in 11 individual studies by the inconsistency model, suggesting that there was no evidence of 12 inconsistency (Table 33, Figure 21). Reported results are therefore based on the random-13 effects NMA model, assuming consistency. Moderate between trials heterogeneity was found 14 relative to the size of the intervention effect estimates ( $\tau = 0.45$  (95% Crl 0.29 to 0.61)).

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

	Intervention	Ν	Class		Ν
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	

44

	Intervention	Ν	Class		Ν
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

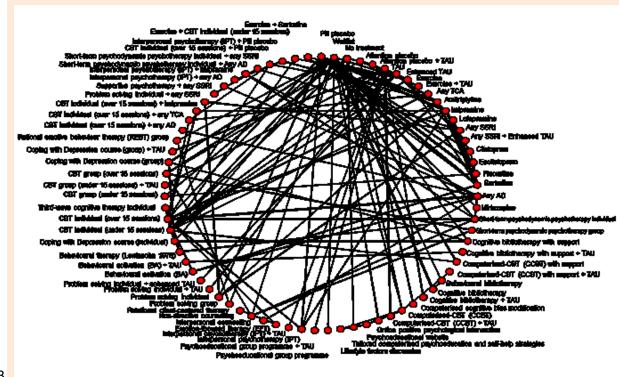
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	Intervention	Ν	Class		Ν
58	CBT group (under 15 sessions) + TAU	48		19	
59	CBT group (over 15 sessions)	53		19	
60	Coping with Depression course (group)	25		19	
61	Coping with Depression course (group) + TAU	113		19	
62	Rational emotive behaviour therapy (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

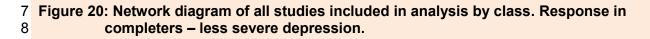
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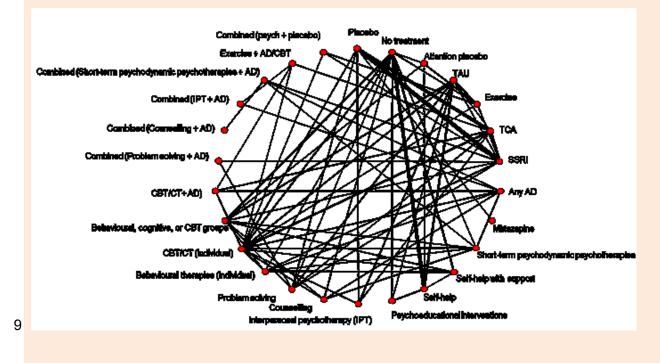
### Figure 19: Network diagram of all studies included in analysis by intervention. Response in completers – less severe depression.



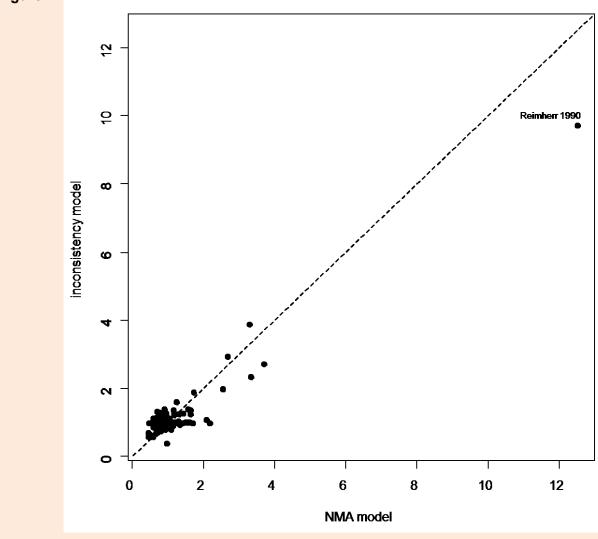
3

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









2

3 There is evidence of an increased odds of response in completers compared to Pill placebo 4 for Exercise, Exercise + TAU, Any TCA, Amitriptyline, Imipramine, Lofepramine, Any SSRI, 5 Any SSRI + Enhanced TAU, Citalopram, Escitalopram, Fluoxetine, Sertraline, Any AD, 6 Cognitive bibliotherapy with support + TAU, Computerised-CBT (CCBT) with support, Behavioural bibliotherapy, Cognitive bibliotherapy, Cognitive bibliotherapy + TAU, 7 8 Computerised cognitive bias modification, Computerised-CBT (CCBT) + TAU, Problem 9 solving individual, Behavioural activation (BA), Behavioural activation (BA) + TAU, 10 Behavioural therapy (Lewinsohn 1976), Coping with Depression course (individual), CBT 11 individual (under 15 sessions), CBT individual (over 15 sessions), Third-wave cognitive 12 therapy individual, CBT group (under 15 sessions), CBT group (under 15 sessions) + TAU, 13 CBT group (over 15 sessions), Coping with Depression course (group), Coping with 14 Depression course (group) + TAU, Rational emotive behaviour therapy (REBT) group, CBT 15 individual (over 15 sessions) + any AD, CBT individual (over 15 sessions) + any TCA, CBT 16 individual (over 15 sessions) + imipramine, Interpersonal psychotherapy (IPT) + any AD, 17 Interpersonal psychotherapy (IPT) + imipramine, Short-term psychodynamic psychotherapy 18 individual + Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, CBT 19 individual (over 15 sessions) + Pill placebo, and Interpersonal psychotherapy (IPT) + Pill 20 placebo (Figure 57). There is evidence of a reduction in the odds of response in completers 21 compared to Pill placebo for Waitlist.

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

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1 Behavioural Therapies (Individual), Cognitive and cognitive behavioural therapies

2 (individual), Behavioural, cognitive, or CBT groups, Combined (Cognitive and cognitive

3 behavioural therapies individual + AD), Combined (IPT + AD), Combined (Short-term

4 psychodynamic psychotherapies + AD), and Combined (psych + placebo) (Figure 58). There
5 is no evidence of any classes having a decreased odds of response compared to Pill

5 is no evidence 6 placebo.

7 Combined (IPT + AD) is the highest ranked class at  $2^{nd}$  (95% Crl 1<sup>st</sup> to 17<sup>th</sup>). The highest 8 ranked interventions are CBT individual (over 15 sessions) + any AD with a posterior median

9 rank of 4<sup>th</sup> (95% Crl 1<sup>st</sup> to 26<sup>th</sup>) and Interpersonal psychotherapy (IPT) + any AD with a

posterior median rank of 4<sup>th</sup> (95% Crl 1<sup>st</sup> to 35<sup>th</sup>). The lowest ranked intervention is Waitlist at
 53<sup>rd</sup> (95% Crl 52<sup>nd</sup> to 53<sup>rd</sup>). The lowest ranked active intervention is Lifestyle factors

12 discussion at  $48^{\text{th}}$  (95% Crl 25<sup>th</sup> to 52<sup>nd</sup>). The lowest ranked active intervention is Ellestric

13 Psychoeducational Interventions at 19<sup>th</sup> (95% Crl 7<sup>th</sup> to 24<sup>th</sup>). Rankings of classes are shown

14 in Table 10; rankings of interventions are shown in the respective excel file in Appendix N3,

15 "Ranks" worksheet.

### 16 **Table 10: Posterior median rank and 95% credible intervals by class. Response in**

#### 17 Completers – less severe depression.

Class	Posterior median rank	95% Crl
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)

### **1.3.1.68** Outcome: response in those randomised – less severe depression

19 The response analysis was also carried out in all patients randomised, including those who

20 discontinued treatment. After excluding trials with zero events in all arms, 53 trials reported

21 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

9 found relative to the size of the intervention effect estimates ( $\tau$  =0.37 (95% CrI 0.27 to 0.49).

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

	Intervention	Ν	Class		Ν
1	Pill placebo	251 0	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	134 0	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	111 0		7	
20	Sertraline	155 6		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	

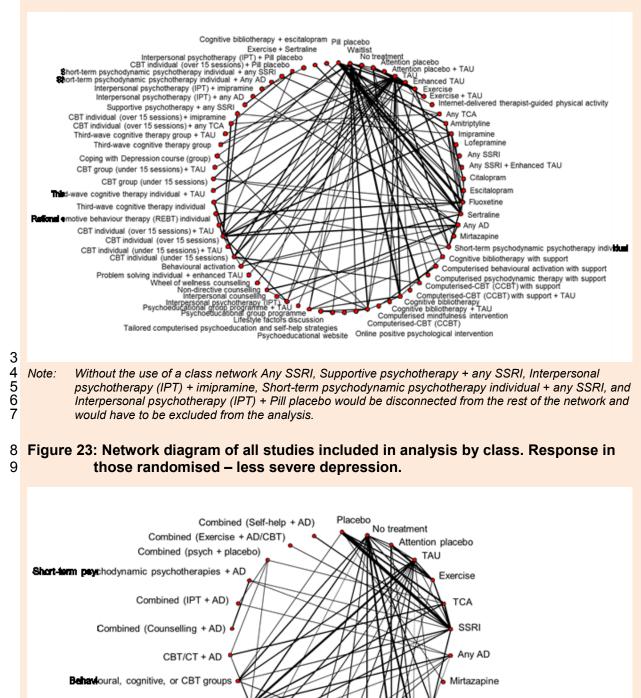
# Depression in adults: treatment and management Network meta-analysis – detailed methods and results

	Intervention	Ν	Class		Ν
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	

	Intervention	Ν	Class		Ν
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

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



10

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CBT/CT (individual)

Problem solving

Counselling

Interpersonal psychotherapy (IPT)

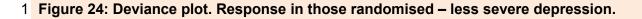
Behavioural therapies (individual)

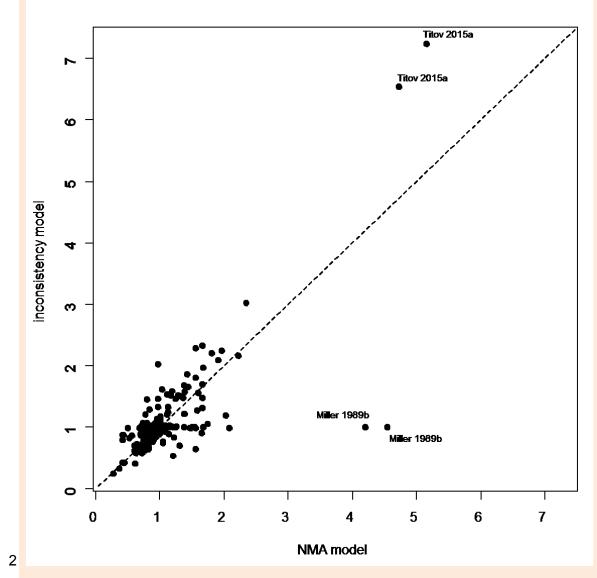
Short-term psychodynamic psychomerapies

Self-help with support

Self-help

Psychoeducational interventions





3 There is evidence of an increased odds of response in those randomised compared to Pill placebo for Exercise, Amitriptyline, Imipramine, any SSRI, Citalopram, Escitalopram, 4 Fluoxetine, Sertraline, any AD, Mirtazapine, Computerised psychodynamic therapy with 5 6 support, Computerised-CBT (CCBT) with support, Behavioural activation, CBT individual 7 (under 15 sessions), CBT individual (under 15 sessions) + TAU, CBT individual (over 15 8 sessions), Rational emotive behaviour therapy (REBT) individual, Third-wave cognitive 9 therapy individual, Third-wave cognitive therapy individual + TAU, CBT individual (over 15 10 sessions) + any TCA, CBT individual (over 15 sessions) + imipramine, Supportive 11 psychotherapy + any SSRI, Interpersonal psychotherapy (IPT) + any AD, Interpersonal 12 psychotherapy (IPT) + imipramine, Short-term psychodynamic psychotherapy individual + 13 Any AD, Short-term psychodynamic psychotherapy individual + any SSRI, CBT individual 14 (over 15 sessions) + Pill placebo, Interpersonal psychotherapy (IPT) + Pill Placebo, and 15 Exercise + Sertraline (Figure 59). Waitlist and No treatment were the only interventions for 16 which there was evidence of a reduction in odds of response in those randomised compared 17 to Pill placebo. The classes for which there is an increased odds of response in those 18 randomised compared to Pill placebo are TCAs, SSRIs, any AD, Mirtazapine, Self-help with 19 support, Behavioural Therapies (individual), Cognitive and cognitive behavioural therapies 20 (individual), Combined (Cognitive and cognitive behavioural therapies individual + AD), 21 Combined (Counselling + AD), Combined (IPT + AD), Combined (Short-term psychodynamic 22 psychotherapies + AD), Combined (psych + placebo), and Combined (Exercise + AD/CBT)

54

1 (Figure 60). No treatment is the only class for which there is evidence of a decreased odds of 2 response in those randomised compared to Pill placebo.

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

#### 10 Table 12: Posterior median rank and 95% credible intervals by class. Response in 11 those randomised – less severe depression.

	Posterior	
Class	median rank	95% Crl
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)

#### 1.3.1.72 Outcome: SMD – less severe depression

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

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

1 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).

9 Lower DIC values in the NMA random effects consistency model and no meaningful

10 difference in the posterior mean residual deviance and between-study heterogeneity

11 suggested that there was no evidence of inconsistency (Table 35). Reported results are

12 therefore based on the random-effects NMA model, assuming consistency. However, note

13 the inconsistency model better predicted the data in Miller 1989b, which was the only study

14 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).

17 Relative to the size of the intervention effect estimates, moderate to low between trial

18 heterogeneity was observed for this outcome ( $\tau$  =0.23 (95% CrI 0.17 to 0.30))

### 19 Table 13: Interventions, classes and number of patients (N) included in SMD analysis – 20 less severe depression.

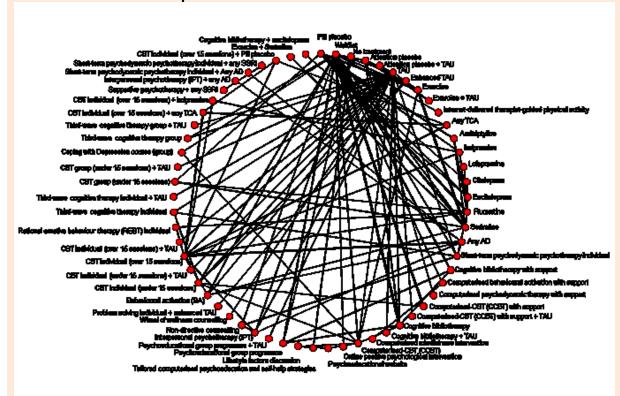
	Intervention	Ν	Class		Ν
1	Pill placebo	1645	Pill placebo	1	1645
2	Waitlist	974	No treatment	2	1205
3	No treatment	231		2	
4	Attention placebo	250	Attention placebo	3	294
5	Attention placebo + TAU	44		3	
6	TAU	1228	TAU	4	1366
7	Enhanced TAU	138		4	
8	Exercise	708	Exercise	5	794
9	Exercise + TAU	62		5	
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	

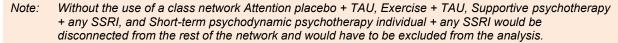
	Intervention	Ν	Class		Ν
23	Computerised psychodynamic therapy with support	46		10	
24	Computerised-CBT (CCBT) with support	268		10	
25	Computerised-CBT (CCBT) with support + TAU	52		10	
26	Cognitive bibliotherapy	509	Self-help without support	11	1933
27	Cognitive bibliotherapy + TAU	86		11	
28	Computerised 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	

	Intervention	Ν	Class		Ν
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

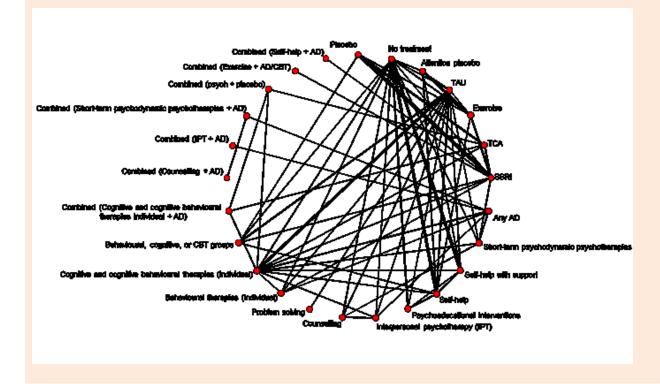
\*Variance borrowed from another class as described in section 1.2.3

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



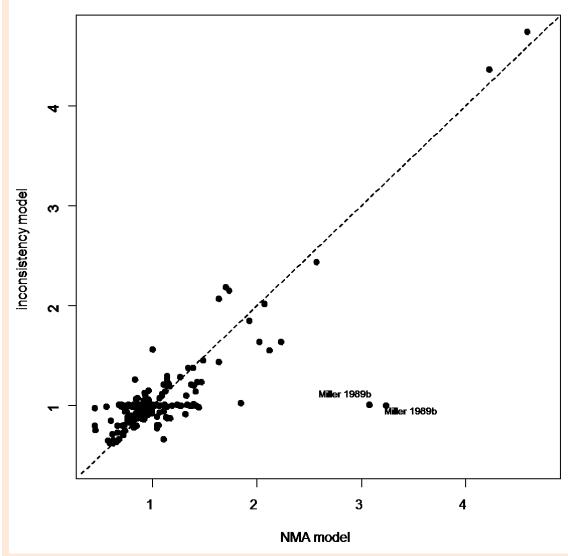


### Figure 26: Network diagram of all studies included in analysis by class. SMD – less severe depression.



1

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



3

4 There is evidence suggesting that Amitriptyline, Imipramine, Lofepramine, Fluoxetine, 5 Sertraline, Any AD, Computerised psychodynamic therapy with support, Computerised-CBT 6 (CCBT) with support, Behavioural activation (BA), CBT individual (under 15 sessions), CBT 7 individual (under 15 sessions) + TAU, CBT individual (over 15 sessions), Rational emotive 8 behaviour therapy (REBT) individual, Third-wave cognitive therapy individual, Third-wave 9 cognitive therapy individual + TAU, CBT individual (over 15 sessions) + any TCA, CBT 10 individual (over 15 sessions) + imipramine, Interpersonal psychotherapy (IPT) + any AD, 11 Short-term psychodynamic psychotherapy individual + Any AD, CBT individual (over 15 12 sessions) + Pill placebo, and Exercise + Sertraline have a lower standardized mean 13 difference in depression compared to Pill placebo whereas Waitlist, No treatment, and TAU 14 have a higher standardized mean difference compared to Pill placebo (Figure 61). The 15 classes for which there is evidence suggesting a lower standardized mean difference in 16 depression compared to Pill placebo are TCA, Cognitive and cognitive behavioural therapies 17 (individual), Combined (Cognitive and cognitive behavioural therapies individual + AD), 18 Combined (IPT + AD), Combined (Short-term psychodynamic psychotherapies + AD), 19 Combined (psych + placebo), and Combined (Exercise + AD/CBT) (Figure 62). The only 20 class for which there is evidence of a higher standardized mean difference compared to Pill

21 placebo is No treatment.

1 Combined (IPT + AD) is the highest ranked class at 2<sup>nd</sup> (95% CrI 1<sup>st</sup> to 8<sup>th</sup>) along with

Combined (Counselling +AD) at 2<sup>nd</sup> (95% Crl 1<sup>st</sup> to 20<sup>th</sup>). The highest ranked interventions
 are Interpersonal psychotherapy (IPT) + any AD with a posterior median rank of 2<sup>nd</sup> (95% Crl

4  $1^{\text{st}}$  to  $7^{\text{th}}$ ) and Supportive psychotherapy + any SSRI with a posterior median rank of  $2^{\text{nd}}$  (95%)

5 Crl 1<sup>st</sup> to 39<sup>th</sup>). The lowest ranked intervention is Waitlist at 44<sup>th</sup> (95% Crl 42<sup>nd</sup> to 44<sup>th</sup>). The

6 lowest ranked active intervention is Tailored computerised psychoeducation and self-help

7 strategies at 41<sup>st</sup> (95% CrI 26<sup>th</sup> to 44<sup>th</sup>). The lowest ranked active class is Problem solving at

8 22<sup>nd</sup> (95% CrI 11<sup>th</sup> to 23<sup>rd</sup>). Rankings of classes are shown in Table 14; rankings of

9 interventions are shown in the respective excel file in Appendix N3, "Ranks" worksheet.

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

11 severe depression.

Class	Posterior median rank	95% Crl
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)

### 1.3.22 Population: more severe depression

### **1.3.2.1**<sup>3</sup> 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. 1 Lower DIC values in the NMA random effects consistency model and no meaningful

2 differences were found in the posterior mean residual deviance and between-study

3 heterogeneity (Table 36). The inconsistency model only notably improved in the prediction of

4 data in individual studies with zero cells (Figure 30). Therefore, there is no evidence of

5 inconsistency and reported results are therefore based on the random-effects NMA model,

6 assuming consistency. Moderate between trials heterogeneity was observed relative to the

7 size of the intervention effect estimates ( $\tau$  =0.46 (95% Crl 0.36 to 0.59)).

### 8 Table 15: Interventions, classes and number of patients (N) included in

9 discontinuation for any reason analysis – more severe depression.

	Intervention	N	Class		Ν
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	

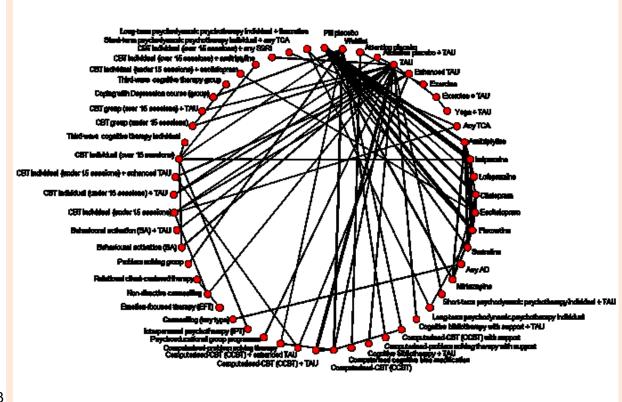
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	Intervention	Ν	Class		Ν
30	Computerised-problem solving therapy	88		13	
31	Psychoeducational group programme	228	Psychoeducational interventions*	14	228
32	Interpersonal psychotherapy (IPT)	95	Interpersonal psychotherapy (IPT)*	15	95
33	Counselling (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



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

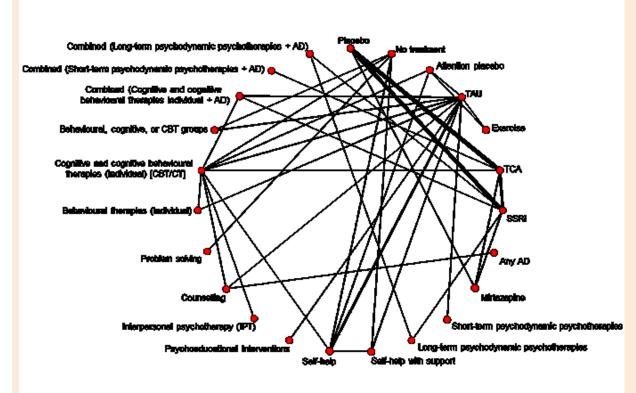


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4 Note: Without the use of a class network Attention placebo, Exercise, Any AD, Computerised cognitive bias

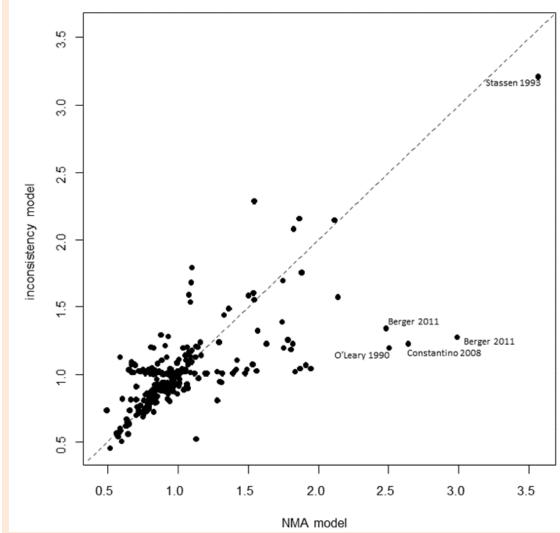
5 modification, Counselling (any type), Emotion-focused therapy (EFT), and Relational client-centered therapy 6 would be disconnected from the rest of the network and would have to be excluded from the analysis.

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



3

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



2

3 There is no evidence to suggest any interventions or classes have a decreased odds of
4 discontinuation for any reason compared to Pill placebo (Figure 63 and Figure 64). There is

5 only evidence suggesting Psychoeducational group programme and its class,

6 Psychoeducational interventions, have an increased odds in discontinuation for any reason7 compared to Pill placebo.

Problem solving is the highest ranked class at 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 20<sup>th</sup>). The highest ranked
intervention, Problem solving group, belongs to this class with a posterior median rank of 2<sup>nd</sup>
(95% Crl 1<sup>st</sup> to 34<sup>th</sup>). The lowest ranked intervention is Psychoeducational group programme
at 37<sup>th</sup> (95% Crl 35<sup>th</sup> to 37<sup>th</sup>). Its corresponding class, Psychoeducational interventions,
ranked the lowest at 22<sup>nd</sup> (95% Crl 20<sup>th</sup> to 22<sup>nd</sup>). 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% Crl
Problem solving	1	(1, 20)
Exercise	4	(1, 20)

Class	Posterior median rank	95% Crl
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)

### **1.3.2.21** Outcome: discontinuation due to SE – more severe depression

- 2 After excluding trials with zero events in all arms and those which did not report both
- 3 discontinuation and discontinuation due to SE, 53 trials of 14 interventions and 6 classes
- 4 were included for this outcome (Table 17, Figure 31 and Figure 32). A continuity correction
- 5 was applied to data containing at least one zero cell to stabilize the results.
- 6 There was no evidence of inconsistency with higher posterior mean residual deviance and
- 7 DIC values in the inconsistency model, and minimal improvement was observed in the
- 8 prediction of data in individual studies by the inconsistency model (Table 37; Figure 33).
- 9 Reported results are therefore based on the random-effects NMA model, assuming
- 10 consistency. Relative to the size of the intervention effect estimates, high between trial
- 11 heterogeneity was observed for this outcome ( $\tau = 0.78 (95\% \text{ CrI } 0.41 \text{ to } 1.21)$ ).

### 12 Table 17: Interventions, classes and number of patients (N) included in

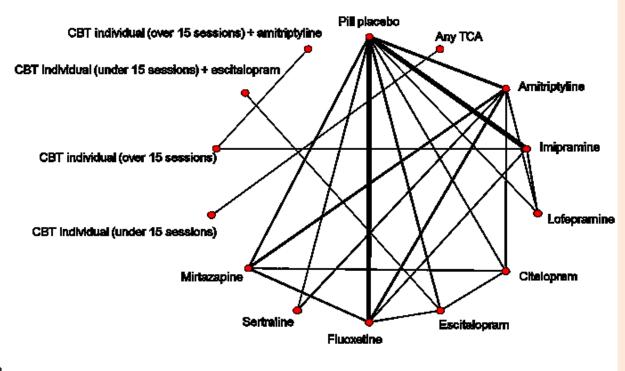
#### 13 discontinuation due to SE analysis – more severe depression.

	Intervention	Ν	Class		Ν
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	Ν	Class		Ν
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.



3

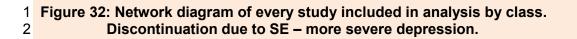
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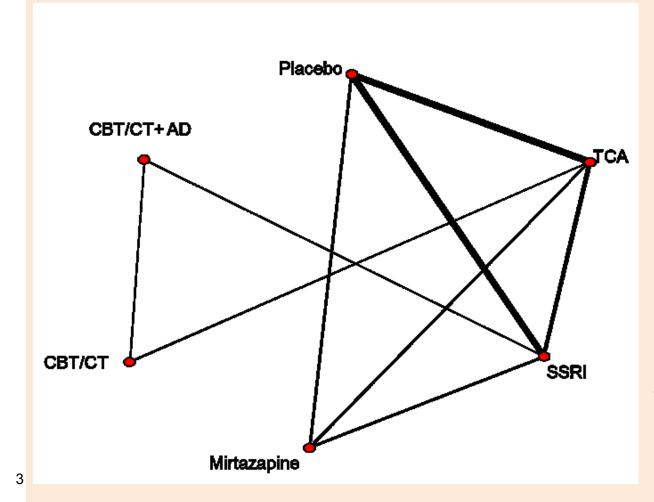
5 Note: Without the use of a class network Any TCA and CBT individual (under 15 sessions)

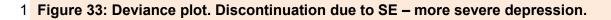
6 would be disconnected from the rest of the network and would have to be excluded from the 7 analysis.

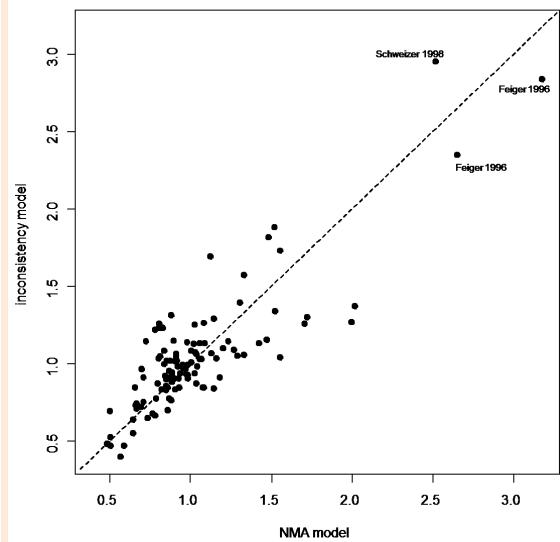
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2

3 There is evidence suggesting that Any TCA, Amitriptyline, Imipramine, Lofepramine,

4 Citalopram, Escitalopram, Fluoxetine, Sertraline, and Mirtazapine have an increased odds of 5 discontinuation due to SE compared to Pill placebo, while no interventions or classes have a 6 decreased odds (Figure 65 and Figure 66). The classes for which there is evidence of having

7 an increased odds in discontinuation due to SE are Mirtazapine, TCA, and SSRI (Figure 66).

8 Cognitive and cognitive behavioural therapies (individual) [CBT/CT] is the highest ranked 9 class at 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 5<sup>th</sup>). The highest ranked intervention is CBT individual (under 15 10 sessions) at 2<sup>nd</sup> (95% Crl 1<sup>st</sup> to 9<sup>th</sup>). The lowest ranked intervention is Mirtazapine with a 11 posterior median rank of 10<sup>th</sup> (95% Crl 5<sup>th</sup> to 12<sup>th</sup>). Mirtazapine is also the lowest ranked 12 class. Rankings of classes are shown in Table 18; rankings of interventions are shown in the 13 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% Crl
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	1	(1, 5)

Class	Posterior median rank	95% Crl
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

2 After excluding trials with zero events in all arms, and one trial due to the network being 3 disconnected (Goldman 2006), 34 trials of 28 interventions and 18 classes remained to be

4 included in the analysis for this outcome (Table 19, Figure 34 and Figure 35).

5 The NMA model had lower posterior mean residual deviance and between study

6 heterogeneity suggesting that there was no evidence of inconsistency (Table 38). Reported

7 results are therefore based on the random-effects NMA model, assuming consistency. Note,

8 however, the inconsistency model better predicted the data in Yevtunshenko 2007 (Figure

9 36). Relative to the size of the intervention effect estimates, high between trial heterogeneity

10 was observed for this outcome ( $\tau = 0.64$  (95% Crl 0.42 to 0.99)).

### 11 Table 19: Interventions, classes and number of patients (N) included in remission in

12

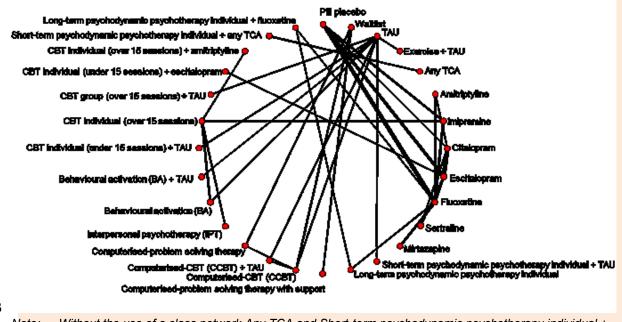
### completers analysis - more severe depression.

	Intervention	Ν	Class		Ν
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	254 8
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
	()				

	Intervention	Ν	Class		Ν		
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							

#### 1 Figure 34: Network diagram of every study included in analysis by intervention. 2 Remission in completers - more severe depression.



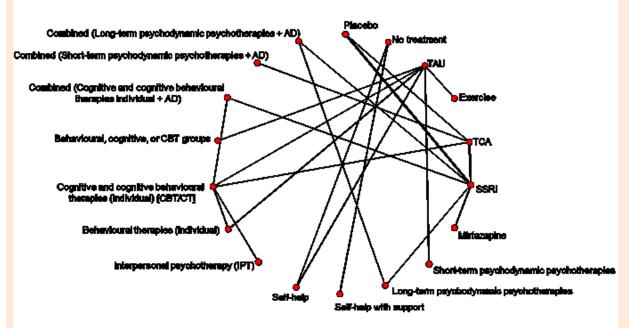


Without the use of a class network Any TCA and Short-term psychodynamic psychotherapy individual + Note: any TCA would be disconnected from the rest of the network and would have to be excluded from the analysis.

7

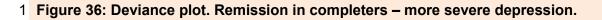
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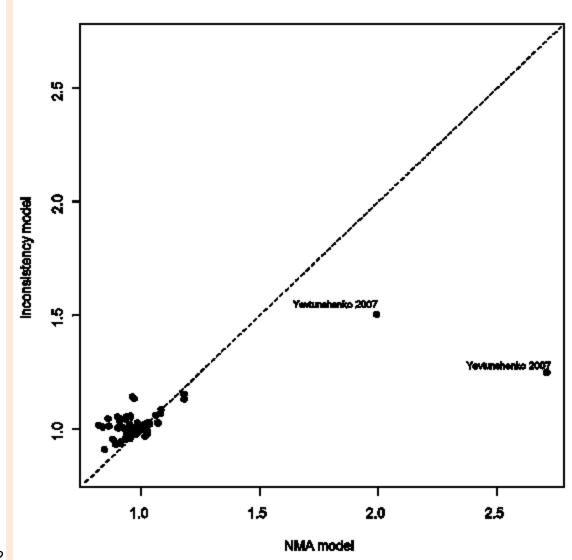
### Figure 35: Network diagram of every study included in analysis by class. Remission in completers – more severe depression.



3

Update 2018





Update 2018

2

3 There is evidence suggesting the interventions with an increased odds of remission in 4 completers compared to Pill placebo are Long-term psychodynamic psychotherapy individual, Computerised-problem solving therapy with support, Interpersonal psychotherapy 5 6 (IPT), Behavioural activation (BA), Behavioural activation (BA) + TAU, CBT individual (under 7 15 sessions) + TAU, CBT individual (over 15 sessions), and Long-term psychodynamic 8 psychotherapy individual + fluoxetine, while there is no evidence to suggest any intervention 9 has a decreased odds of remission in completers compared to Pill placebo (Figure 67). The 10 classes for which there is evidence of an increased odds of remission in completers 11 compared to Pill placebo are Long-term psychodynamic psychotherapies, Self-help with 12 support, Interpersonal psychotherapy (IPT), Behavioural therapies (individual), Cognitive and 13 cognitive behavioural therapies (individual) [CBT/CT], and Combined (Long-term 14 psychodynamic psychotherapies + AD) (Figure 68). There is no evidence of any class having 15 a decreased odds of remission in completers compared to Pill placebo. 16 Self-help with support and Combined (Long-term psychodynamic psychotherapies + AD) are 17 the highest ranked classes at 2nd (95% Crl 1st to 13th) and 2nd (95% Crl 1st to 9th),

18 respectively. The highest ranked intervention is Long-term psychodynamic psychotherapy

- 19 individual + fluoxetine with a posterior median rank of 1st (95% Crl 1st to 7th). The lowest
- 20 ranked interventions are Citalopram and Pill Placebo. The lowest ranked active classes are
- 21 Mirtazapine at 16<sup>th</sup> (95% Crl 9<sup>th</sup> to 18<sup>th</sup>) and SSRI at 16<sup>th</sup> (95% Crl 10<sup>th</sup> to 18<sup>th</sup>). Rankings of

1 classes are shown in Table 20; rankings of interventions are shown in the respective excel

2 file in Appendix N3, "Ranks" worksheet.

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

	Posterior	
Class	median rank	95% Crl
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)

### **1.3.2.45** Outcome: remission in those randomised – more severe depression

6 After excluding trials with zero events in all arms, and one trial due to the network being

- 7 disconnected (Goldman 2006), 34 trials of 28 interventions and 18 classes remained to be
- 8 included in the analysis for this outcome (Table 21, Figure 37 and Figure 38).

9 No meaningful differences were observed in posterior mean residual deviance or DIC, and 10 between-study heterogeneity increased in the inconsistency model, suggesting that there

11 was no evidence of inconsistency (Table 39). Reported results are therefore based on the

12 random-effects NMA model, assuming consistency. Note, however, the inconsistency model

13 better predicted the data in Yevtunshenko 2007 (Figure 1). This study compared Citalopram

- 14 and Escitalopram and the estimated relative treatment effect was much stronger compared
- 15 to studies making the same comparison. Thus this study contributes to the moderate to high
- 16 between trial heterogeneity observed for this outcome ( $\tau$ =0.62 (95% CrI 0.41 to 0.95)).

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

	Intervention	Ν	Class		Ν	
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	

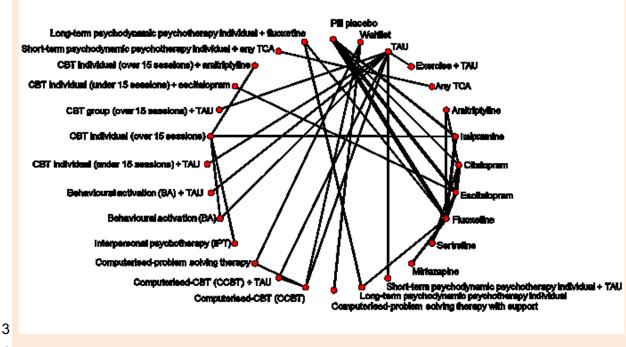
	Intervention	Ν	Class		Ν
6	Amitriptyline	279		5	
7	Imipramine	531		5	
8	Citalopram	736	SSRIs	6	3025
9	Escitalopram	975		6	
10	Fluoxetine	1180		6	
11	Sertraline	134		6	
12	Mirtazapine	213	Mirtazapine	7	213
13	Short-term psychodynamic psychotherapy individual + TAU	44	Short-term psychodynamic psychotherapies*	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*	1 0	49
16	Computerised-CBT (CCBT)	188	Self-help without support	1 1	376
17	Computerised-CBT (CCBT) + TAU	100		1 1	
18	Computerised-problem solving therapy	88		1 1	
19	Interpersonal psychotherapy (IPT)	75	Interpersonal psychotherapy (IPT)*	1 2	75
20	Behavioural activation (BA)	79	Behavioural therapies (individual)*	1 3	100
21	Behavioural activation (BA) + TAU	21		1 3	
22	CBT individual (under 15 sessions) + TAU	149	Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	1 4	312
23	CBT individual (over 15 sessions)	163		1 4	
24	CBT group (over 15 sessions) + TAU	47	Behavioural, cognitive, or CBT groups*	1 5	47
25	CBT individual (under 15 sessions) + escitalopram	52	Combined (Cognitive and cognitive behavioural therapies individual + AD)	1 6	67
26	CBT individual (over 15 sessions) + amitriptyline	15		1 6	
27	Short-term psychodynamic psychotherapy individual + any TCA	47	Combined (Short-term psychodynamic psychotherapies + AD)*	1 7	47
28	Long-term psychodynamic psychotherapy individual + fluoxetine	91	Combined (Long-term psychodynamic psychotherapies + AD)*	1 8	91

\*Variance borrowed from another class as described in section 1.2.3

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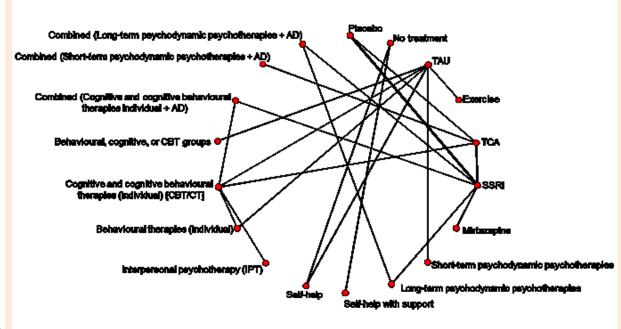
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# Figure 37: Network diagram of every study included in analysis by intervention. Remission in those randomised – more severe depression.



4 Note: Without the use of a class network Any TCA and Short-term psychodynamic psychotherapy individual + any
 5 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.

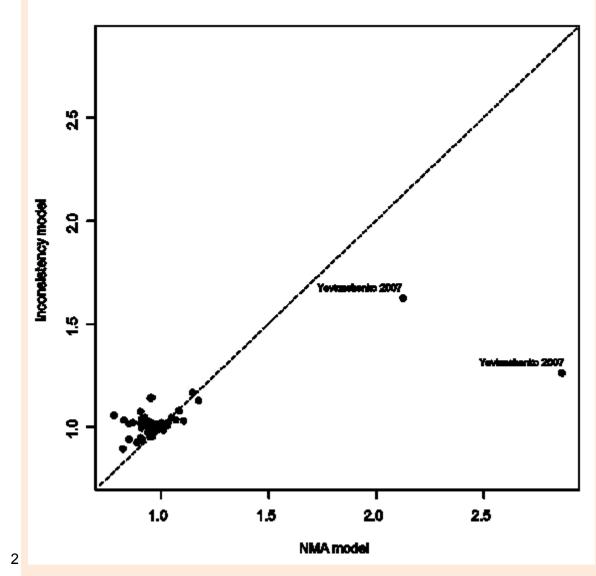


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### **1** Figure 39: Deviance plot. Remission in those randomised – more severe depression.



3 There is evidence suggesting Long-term psychodynamic psychotherapy individual,

4 Computerised-problem solving therapy with support, Interpersonal psychotherapy (IPT),
5 Behavioural activation (BA), Behavioural activation (BA) + TAU, CBT individual (under 15)

6 sessions) + TAU, CBT individual (over 15 sessions), and Long-term psychodynamic

7 psychotherapy individual + fluoxetine have an increased the odds of remission in those

8 randomised compared to Pill placebo (Figure 69). However, there is no evidence to suggest

- 9 any intervention or class have a decreased odds of remission in those randomised compared 10 to Pill placebo (Figure 69 and Figure 70). The classes for which evidence suggests there is
- 11 an increased odds of remission in those randomised compared to Pill placebo are Long-term

12 psychodynamic psychotherapies, Self-help with support, Interpersonal psychotherapy (IPT),

13 Behavioural therapies (individual), Cognitive and cognitive behavioural therapies (individual)

14 [CBT/CT], and Combined (Long-term psychodynamic psychotherapies + AD) (Figure 70).

15 Self-help with support was the highest ranked class at 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 11<sup>th</sup>). The highest 16 ranked intervention, Computerised-problem solving therapy with support, belonged to this 17 class with a posterior median rank of 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 10<sup>th</sup>). The lowest ranked intervention 18 is Citalopram, with a posterior median rank of 18<sup>th</sup> (95 Crl 12<sup>th</sup> to 20<sup>th</sup>). The lowest ranked 19 active class is Mirtazapine at 16<sup>th</sup> (95% Crl 8<sup>th</sup> to 18<sup>th</sup>). Rankings of classes are shown in 20 Table 22; rankings of interventions are shown in the respective excel file in Appendix N3, 21 "Panke" workshoot.

21 "Ranks" worksheet.

#### 1 Table 22: Posterior median rank and 95% credible intervals. Remission in those 2 randomised – more severe depression.

Class	Posterior median rank	95% Crl
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)

#### **1.3.2.53** Outcome: response in completers – more severe depression

4 After excluding trials with zero events in all arms, 57 trials reported response. Out of the

5 remaining studies, 7 reported change from baseline in completers (but not response) and 24

6 reported baseline and final scores in completers (but not response or change from baseline).

7 This meant that 88 trials of 44 interventions and 22 classes were included in the analysis for

8 this outcome (Table 23, Figure 40 and Figure 41 Error! Reference source not found.).

9 No meaningful differences were observed in posterior mean residual deviance or between

10 study heterogeneity suggesting that there was no evidence of inconsistency (Table 40).

11 Reported results are therefore based on the random-effects NMA model, assuming

12 consistency. Note, however, the inconsistency model better predicted the data in Fabre

13 1992, which compares Pill Placebo and Imipramine (Figure 42).

14 Relative to the size of the intervention effect estimates, high between trial heterogeneity was 15 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.

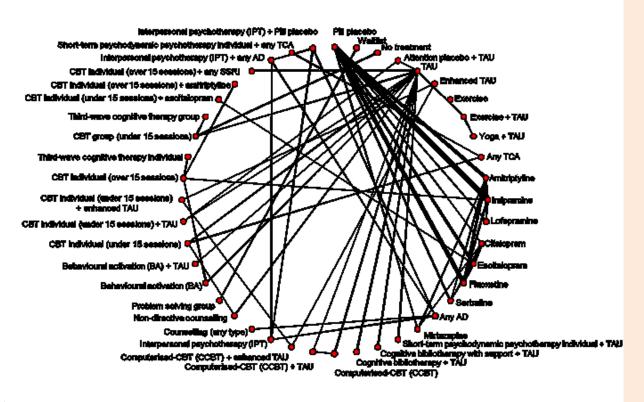
	Intervention	Ν	Class		Ν
1	Pill placebo	2495	Pill placebo	1	2495
2	Waitlist	11	No treatment	2	22
3	No treatment	11		2	
4	Attention placebo + TAU	58	Attention placebo	3	58
5	TAU	505	TAU	4	526
6	Enhanced TAU	21		4	

	Intervention	N	Class		Ν
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	

	Intervention	Ν	Class		Ν
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.



3

4 Note: Without the use of a class network Waitlist, Enhanced TAU, Exercise, Any AD, Computerised-CBT (CCBT)

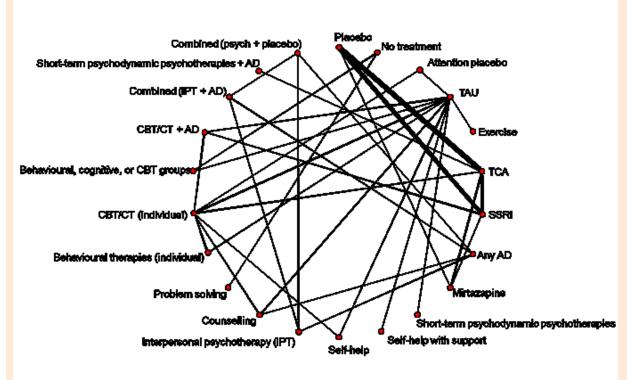
5 + enhanced TAU, Interpersonal psychotherapy (IPT), Counselling (any type), Problem solving group, CBT 6 individual (under 15 sessions) + enhanced TAU, Interpersonal psychotherapy (IPT) + any AD, and Interpersonal

7 psychotherapy (IPT) + Pill placebo would be disconnected from the rest of the network and would have to be

8 excluded from the analysis.

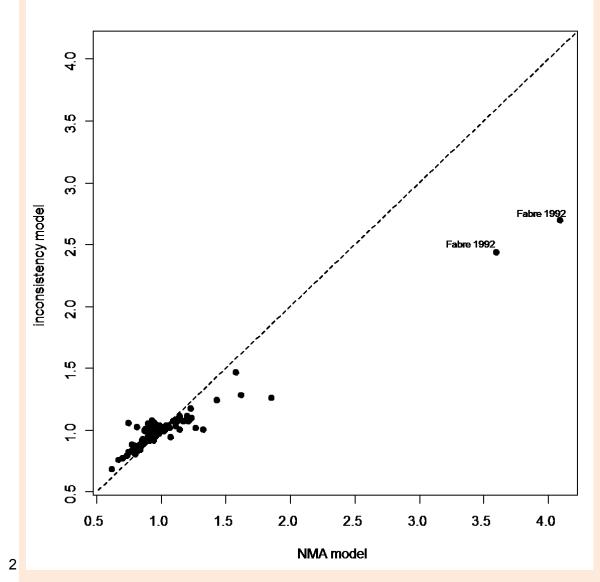
01

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



3

#### 1 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), Thirdwave 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 1<sup>st</sup> (95% Crl 1<sup>st</sup> to 2<sup>nd</sup>). The highest ranked
 interventions are Problem solving group (1<sup>st</sup>, 95% Crl 1<sup>st</sup> to 3<sup>rd</sup>) and CBT group (under 15

83

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

5 worksheet.

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

	Posterior	
Class	median rank	95% Crl
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)

### 1.3.2.68 Outcome: response in those randomised – more severe depression

9 After excluding trials with zero events in all arms, 57 trials reported response. Out of the

10 remaining studies, 3 reported change from baseline in completers (but not response) and 25

11 reported baseline and final scores in completers (but not response or change from baseline).

12 This meant that 85 trials of 41 interventions and 18 classes were included in the analysis for

13 this outcome (Table 25, Figure 43 and Figure 44).

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

17 further adding evidence of inconsistency (Figure 45).

18 Reported results are based on the random-effects NMA model, assuming consistency but

19 should be interpreted with caution due to the identification of potential inconsistency. Relative

- 20 to the size of the intervention effect estimates, moderate between trial heterogeneity was
- 21 observed for this outcome ( $\tau = 0.49 (95\% \text{ CrI } 0.37 \text{ to } 0.62)$ ).

#### 1 Table 25: Interventions, classes and number of patients (N) included in response in 2 those randomised analysis – more severe depression.

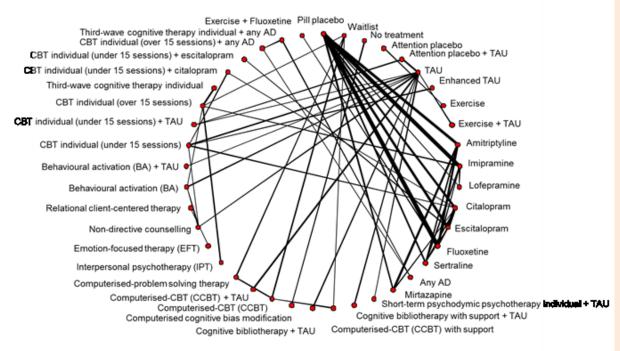
	Intervention	N	more severe depression.		Ν
4					
1	Pill placebo	3316	Pill placebo	1	3316
2	Waitlist	128	No treatment	2	141
3	No treatment	13		2	
4	Attention placebo	13	Attention placebo	3	80
5	Attention placebo + TAU	67		3	
6	TAU	689	TAU	4	759
7	Enhanced TAU	70		4	
8	Exercise	10	Exercise*	5	35
9	Exercise + 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	

85

	Intervention	Ν	Class		Ν
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.

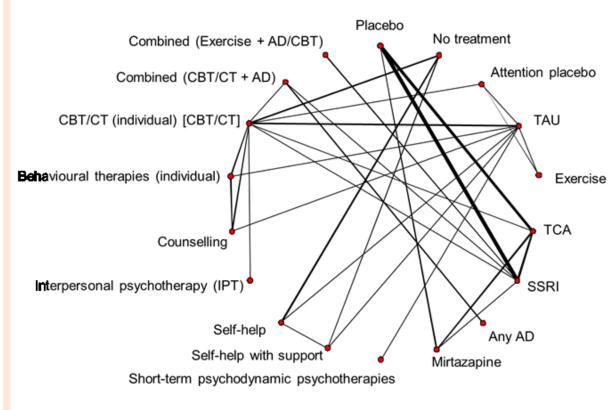


3

4 Note: Without the use of a class network No treatment, Attention placebo, Exercise, Any AD, Computerised

5 cognitive bias modification, Emotion-focused therapy (EFT), Relational client-centered therapy, CBT individual
6 (over 15 sessions) + any AD, and Third-wave cognitive therapy individual + any AD would be disconnected from
7 the rest of the network and would have to be excluded from the analysis.

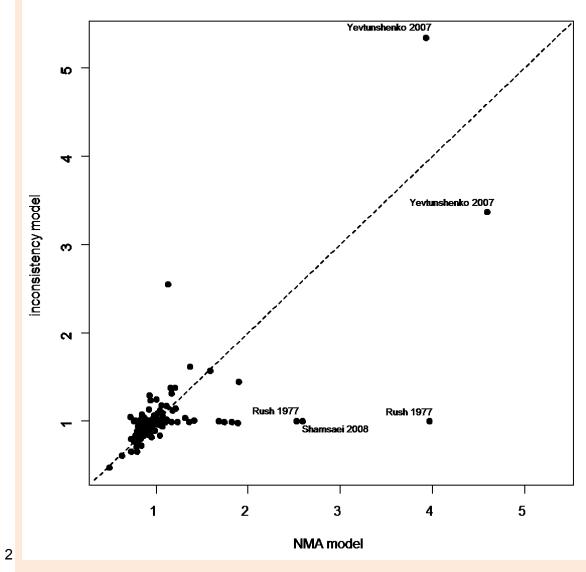
# Figure 44: Network diagram of every study included in analysis by class. Response in those randomised – more severe depression.



3

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



3 Interventions for which evidence suggests an increased odds of response in those

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

11 therapies individual + AD), and Combined (Exercise + AD/CBT) (Figure 74).

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

#### 1 Table 26: Posterior median rank and 95% credible intervals by class. Response in 2 those randomised – more severe depression.

Class	Posterior median rank	95% Crl
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)

### **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

8 analysis for this outcome (Table 27, Figure 46 and Figure 47).

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

14 consistency, however they must be interpreted with caution.

15 Relative to the size of the intervention effect estimates, small between trial heterogeneity was 16 observed for this outcome ( $\tau = 0.17 (95\% \text{ CrI } 0.10 \text{ to } 0.26)$ ).

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

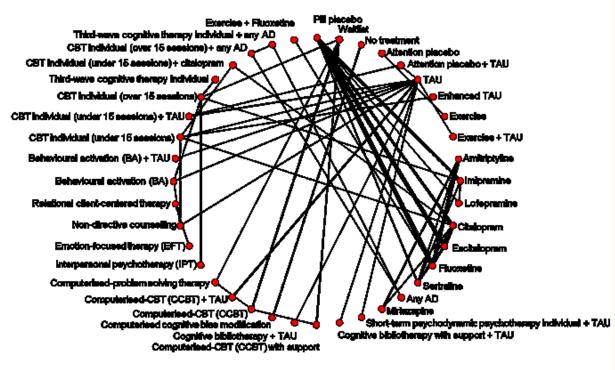
	Intervention	Ν	Class		Ν
1	Pill placebo	1888	Pill placebo	1	1888
2	Waitlist	128	No treatment	2	141
3	No treatment	13		2	
4	Attention placebo	13	Attention placebo	3	80
5	Attention placebo + TAU	67		3	
6	TAU	689	TAU	4	759
7	Enhanced TAU	70		4	

	Intervention	Ν	Class		Ν
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

	Intervention	Ν	Class		Ν
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.



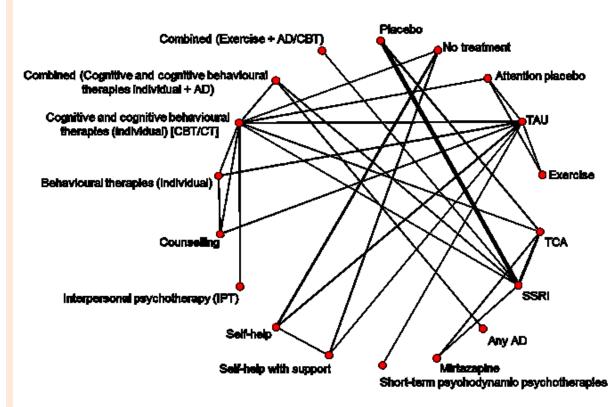
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4 Note: Without the use of a class network No treatment, Attention placebo, Exercise, Any AD, Computerised

- 5 cognitive bias modification, Emotion-focused therapy (EFT), Relational client-centered therapy, CBT individual
- 6 (over 15 sessions) + any AD, and Third-wave cognitive therapy individual + any AD would be disconnected from 7 the rest of the petwork and would have to be excluded from the analysis
- 7 the rest of the network and would have to be excluded from the analysis.

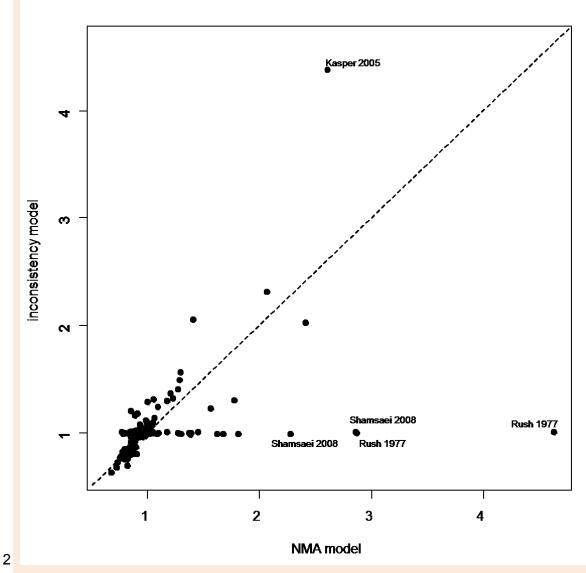
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# Figure 47: Network diagram of every study included in analysis by class. SMD – more severe depression.



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

#### 1 Table 28: Posterior median rank and 95% credible intervals by class. SMD – more 2 severe depression.

Class	Posterior median rank	95% Crl
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)

### **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.).

13 • The observed correlation between baseline and follow-up was assumed to be 0.5. This 14 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 15 analysis using a correlation of 0.3 for Response in completers, Response in those 16 randomised, and SMD in both populations. Overall the results were similar to the original 17 analyses although for most outcomes the uncertainty slightly decreased. For response in 18 19 completers in the moderate/severe population, the uncertainty slightly decreased for some 20 relative effects, and slightly increased for other relative effects, although overall, the 21 results were similar to the original analysis. 22 • 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 sensitivityanalysis using the regression equation to transform the baseline standard deviation.
- 26 Overall, there was a slight reduction in uncertainty, but results were very similar to the
- 27 original analysis.

- 1 We assumed the existence of class effects and modelled the data in this way. We tested
- 2 this by running fixed class effect models and noted their comparability to random class
- 3 effect models. We therefore conclude that there is evidence of agreement of relative
- 4 treatment effects across elements of the same class.
- 5 As we had several classes with only 1 or 2 interventions we needed to make some
- 6 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.

### 1.59 References

10 Brooks S, Gelman A. Alternative methods for monitoring convergence of iterative

11 simulations. Journal of Computatinal and Graphical Statistics 1998;7:434-55

12 Caldwell DM, Ades AE, Higgins JPT. Simultaneous comparison of multiple treatments:13 combining direct and indirect evidence. BMJ. 2005; 331: 897-900

14 Chinn S. A simple method for converting an odds ratio to effect size for use in metaanalysis.15 Statistics in Medicine. 2000;19: 3127–31

16 Cohen J. Statistical power analysis for the behavioral sciences. Academic Press, New York,17 1969

18 Cooper H., Hedges LV, Valentine JC. 2009. The Handbook of Research Synthesis and19 Meta-analysis, New York, Russel Sage Foundation

Dias S, Ades A, Sutton A, Welton N. Evidence synthesis for decision making 2: a generalized
linear modeling framework for pairwise and network meta-analysis of randomized controlled
trials. Medical Decision Making 2013; 33:607-17.

Dias S, Welton N, Sutton A, Ades A. A generalised linear modelling framework for pairwise
and network meta-analysis of randomised controlled trials NICE Decision Support Unit
Evidence Synthesis Technical Support Document 2 2011; August 2011

Gelman A, Rubin D. Inferences from iterative simulation using multiple sequences. Statistical
 Science 1992;7: 457-72.

- 28 Higgins JPT, and Green S (editors). Cochrane Handbook for Systematic Reviews of
- Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011.
   Available from www.cochrane-handbook.org
- 31 Higgins JPT, and Whitehead A. 1996. Borrowing strength from external trials in a meta-
- 32 analysis.Statist.Med.,15: 2733-2749.Doi:10.1002/(Sici)1097-
- 33 0258(19961230)15:24<2733::Aid-Sim562>3.0.Co;2-0
- 34 Lewinsohn PM, Biglan A, Zeiss AM. 1976. Behavioral treatment of depression. In P.O.
- 35 Davidson (Ed.), The behavioral management of anxiety, depression and pain.
- 36 Brunner/Mazel, New York

37 Lu G, Ades A. Combination of direct and indirect evidence in mixed treatment comparisons.38 Stat Med. 2004 2004;23: 3105-3124.

39 Lunn D, Jackson C, Best N, Thomas A, Spiegelhalter D. The BUGS book. Boca Raton, FL:40 CRC Press; 2013.

41 Lunn DJ, Thomas A, Best N, Spiegelhalter D. WinBUGS -- a Bayesian modelling framework:

42 concepts, structure, and extensibility. Statistics and Computing. 2000;10: 325-337.

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- 1 Meister R., Von Wolff A. Kriston L. 2015. Odds ratios of treatment response were well
- 2 approximated from continuous rating scale scores for meta-analysis. Journal of Clinical
  3 Epidemiology, 68, 740-751

4 Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta5 analysis: many names, many benefits, many concerns for the next generation evidence
6 synthesis tool. Research Synthesis Methods 2012;3(2):http://dx.doi.org/10.1002/jrsm.37.

- 7 Spiegelhalter DJ, Best,NG, Carlin BP and van der Linde A. Bayesian measures of model
  8 complexity and fit. Journal of the Royal Statistical Society 2002;B,64:583-616
- 9 Sweeting M, Sutton A, Lambert P. What to add to nothing? Use and avoidance of continuity 10 corrections in meta-analysis of sparse data. Statistics in Medicine 2004; 23(9):1351-75.
- 11 Turner RM, Jackson D, Wei Y, Thompson SG, Higgins JPT. Predictive distributions for
- 12 between-study heterogeneity and simple methods for their application in Bayesian meta-13 analysis. Statistics in Medicine 2015; 34:984-998.
- Welton N, Sutton A, Cooper N, Abrams K, Ades A. 2012 Evidence synthesis for decisionmaking in healthcare: Wiley

### 1.66 Appendix 1: WinBUGS codes

### 1.6.17 Sample WinBUGS code – SMD analysis

```
18 # Normal likelihood, identity link: SMD with arm-based means
19 # Random effects model for multi-arm trials
20 model{
                                         # *** PROGRAM STARTS
21 for(i in 1:ns) {
                                         # LOOP THROUGH STUDIES
22
     w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
23
     delta[i,1] <- 0
                                         # treatment effect is zero for control
24 arm
25
    mu[i] ~ dnorm(0,.0001)
                                        # vague priors for all trial baselines
26
   }
27 # (1) CFB DATA
28 for(i in 1:nsCFB) {
29
     # calculate pooled.sd and adjustment for SMD
30
     df[i] <- sum(nCFB[i,1:naCFB[i]]) - naCFB[i] # denominator for pooled.var</pre>
31
     Pooled.var[i] <- sum(nvar[i,1:naCFB[i]])/df[i]</pre>
32
         # pooled sd for study i, for SMD
33
     Pooled.sd[i] <- sqrt(Pooled.var[i])</pre>
34 # H[i] <- 1 - 3/(4*df[i]-1) # use Hedges' g
35
     H[i] <- 1
                                        # use Cohen's d (ie no adjustment)
36
     for (k in 1:naCFB[i]) {
37
       se[i,k] <- sdCFB[i,k]/sqrt(nCFB[i,k])</pre>
```

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```
1
       var[i,k] <- pow(se[i,k],2)</pre>
                                         # calcultate variances
 2
       prec[i,k] <- 1/var[i,k]
                                         # set precisions
 3
       y[i,k] ~ dnorm(phi[i,k], prec[i,k]) # normal likelihood
 4
       phi[i,k] <- theta[i,k] * (Pooled.sd[i]/H[i]) # theta is stand mean</pre>
 5
       theta[i,k] <- mu[i] + delta[i,k] # model for linear predictor, delta is
 6
  SMD
 7
       dev[i,k] <- (y[i,k]-phi[i,k])*(y[i,k]-phi[i,k])*prec[i,k]</pre>
 8
       nvar[i,k] <- (nCFB[i,k]-1) * pow(sdCFB[i,k],2) # for pooled.sd</pre>
 9
      }
10
     # summed residual deviance contribution for this trial
11
     resdev[i] <- sum(dev[i,1:naCFB[i]])</pre>
12
    }
13 # (2) BASELINE + FOLLOW-UP DATA (no CFB)
14 for(i in 1:nsBF) {
                                           # LOOP THROUGH STUDIES
15
     # calculate pooled.sd and adjustment for SMD
16
     df[i+nsCFB] <- sum(n[i,1:na[i]]) - na[i] # denominator for pooled.var
17
     Pooled.var[i+nsCFB] <- sum(nvarBF[i,1:na[i]])/df[i+nsCFB]</pre>
18
         # pooled sd for study i, for SMD
19
     Pooled.sd[i+nsCFB] <- sqrt(Pooled.var[i+nsCFB])</pre>
20 # H[i] <- 1 - 3/(4*df[i]-1) # use Hedges' g
21
     H[i+nsCFB] <- 1
                                          # use Cohen's d (ie no adjustment)
22
     for (k in 1:na[i]) {
23
       yBF[i,k] <- yF[i,k] - yB[i,k] # calculate mean CFB</pre>
24
       seF[i,k] <- sdF[i,k]/sqrt(n[i,k]) # se at followup</pre>
25
       seB[i,k] <- sdB[i,k]/sqrt(n[i,k]) # se at baseline</pre>
26
       # variance of mean CFB, assuming correlation corr[i]
27
       var[i+nsCFB,k] <- pow(seF[i,k],2)+ pow(seB[i,k],2)</pre>
28 -2*(seF[i,k]*seB[i,k]*corr[i])
29
       prec[i+nsCFB,k] <- 1/var[i+nsCFB,k] # set CFB precisions</pre>
30
       yBF[i,k] ~ dnorm(phi[i+nsCFB,k], prec[i+nsCFB,k]) # normal likelihood
31
       # theta is standardised mean
32
       phi[i+nsCFB,k] <- theta[i+nsCFB,k] * (Pooled.sd[i+nsCFB]/H[i+nsCFB])</pre>
33
       # model for linear predictor, delta is SMD
34
       theta[i+nsCFB,k] <- mu[i+nsCFB] + delta[i+nsCFB,k]</pre>
35
       # residual deviance contribution
```

```
1
       dev[i+nsCFB,k] <- (yBF[i,k]-phi[i+nsCFB,k]) * (yBF[i,k]-phi[i+nsCFB,k])</pre>
 2
  * prec[i+nsCFB,k]
 3
       # variance of CFB, assuming correlation corrBF[i] (var is sd squared)
 4
       varBF[i,k] \leq pow(sdF[i,k],2) + pow(sdB[i,k],2)
 5
  - 2*(sdF[i,k]*sdB[i,k]*corr[i])
 6
       nvarBF[i,k] <- (n[i,k]-1) * varBF[i,k] # for pooled.sd</pre>
 7
      }
 8
     # summed residual deviance contribution for this trial
 9
     resdev[i+nsCFB] <- sum(dev[i+nsCFB,1:na[i]])</pre>
10
11 # (3) RESPONSE DATA (no CFB or BL+follow-up)
                                              LOOP THROUGH STUDIES
12 for(i in 1:nsR) {
                                           #
13
     # calculate pooled.sd and adjustment for SMD
14
     df[i+nsCFB+nsBF] <- sum(nR[i,1:naR[i]]) - naR[i] # denominator for</pre>
15 pooled.var
16
     Pooled.var[i+nsCFB+nsBF] <- sum(nvarR[i,1:naR[i]])/df[i+nsCFB+nsBF]</pre>
17
         # pooled sd for study i, for SMD
18
         Pooled.sd[i+nsCFB+nsBF] <- sqrt(Pooled.var[i+nsCFB+nsBF])</pre>
19 #
     H[i] < -1 - 3/(4*df[i]-1)
                                           # use Hedges' g
20
     H[i+nsCFB+nsBF] <- 1
                                          # use Cohen's d (ie no adjustment)
21
     for (k in 1:naR[i]) {
22
       r[i,k] ~ dbin(R[i,k], nR[i,k]) # binomial likelihood
23
       R[i,k] <- phi.adj[i,k]</pre>
24
       x[i,k] <- -(q[i]*yBR[i,k]+ phi[i+nsCFB+nsBF,k])/(sdBR[i,k] *</pre>
25 sqrt(1+(1-q[i])*(1-q[i]-2*corrR[i])))
26
       # adjust link function phi(x) for extreme values that can give
27 numerical
28
       # errors when x < -5, phi(x)=0, when x > 5, phi(x)=1
29
       phi.adj[i,k] <- (step(5+x[i,k]) * step(x[i,k]-5)</pre>
30
               + step(5-x[i,k])* step(x[i,k]+5) * phi(x[i,k]))*(1-
31 equals(x[i,k],5))
32
               + equals(x[i,k],5) # correct for x=5
33
       # theta is standardised mean
34
       phi[i+nsCFB+nsBF,k] <- theta[i+nsCFB+nsBF,k]</pre>
35
                     * (Pooled.sd[i+nsCFB+nsBF]/H[i+nsCFB+nsBF])
36
       # model for linear predictor, delta is SMD
37
       theta[i+nsCFB+nsBF,k] <- mu[i+nsCFB+nsBF] + delta[i+nsCFB+nsBF,k]</pre>
38
       # residual deviance contribution
```

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```
1
       rhat[i,k] <- R[i,k] * nR[i,k]</pre>
 2
       dev[i+nsCFB+nsBF,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))</pre>
 3
            + (nR[i,k]-r[i,k]) * (log(nR[i,k]-r[i,k]) - log(nR[i,k]-
 4 rhat[i,k]))
 5 # Sensitivity analysis
 6 #
        sdR[i,k] <- 3.54 + sdBR[i,k] * 0.61 # sd for response</pre>
 7
       sdR[i,k] <- sdBR[i,k]</pre>
                                  # sd for response
 8
       nvarR[i,k] <- (nR[i,k]-1) * pow(sdR[i,k],2) # for pooled.sd</pre>
 9
      }
10
     # summed residual deviance contribution for this trial
11
     resdev[i+nsCFB+nsBF] <- sum(dev[i+nsCFB+nsBF,1:naR[i]])</pre>
12
    }
13 #
14 # RE MODEL (CFB data)
15 for(i in 1:nsCFB) {
                                            # LOOP THROUGH STUDIES WITH CFB DATA
16
     for (k in 2:naCFB[i]) {
                                            # LOOP THROUGH ARMS
17
       # trial-specific RE distributions
18
       delta[i,k] ~ dnorm(md[i,k], taud[i,k])
19
       md[i,k] <- d[tCFB[i,k]] - d[tCFB[i,1]] + sw[i,k]</pre>
20
       # precision of RE distributions (with multi-arm trial correction)
21
       taud[i,k] <- tau *2*(k-1)/k
22
       #adjustment, multi-arm RCTs
23
       w[i,k] <- delta[i,k] - d[tCFB[i,k]] + d[tCFB[i,1]]</pre>
24
       # cumulative adjustment for multi-arm trials
25
       sw[i,k] <-sum(w[i,1:k-1])/(k-1)</pre>
26
      }
27
    }
28 # RE MODEL (BL and F-up data)
29 for(i in 1:nsBF) {
                                            # LOOP THROUGH STUDIES WITH BL+FUP
30 DATA
31
                                            # LOOP THROUGH ARMS
     for (k in 2:na[i]) {
32
       # trial-specific RE distributions
33
       delta[i+nsCFB,k] ~ dnorm(md[i+nsCFB,k], taud[i+nsCFB,k])
34
       md[i+nsCFB,k] <- d[t[i,k]] - d[t[i,1]] + sw[i+nsCFB,k]</pre>
35
       # precision of RE distributions (with multi-arm trial correction)
36
       taud[i+nsCFB,k] <- tau *2*(k-1)/k</pre>
```

```
1
       #adjustment, multi-arm RCTs
 2
       w[i+nsCFB,k] <- delta[i+nsCFB,k] - d[t[i,k]] + d[t[i,1]]</pre>
 3
       # cumulative adjustment for multi-arm trials
 4
       sw[i+nsCFB,k] <-sum(w[i+nsCFB,1:k-1])/(k-1)</pre>
 5
      }
 6
    }
 7 # RE MODEL (Response data)
 8 for(i in 1:nsR) {
                                           # LOOP THROUGH STUDIES WITH RESPONSE
 9 DATA
10
                                           # LOOP THROUGH ARMS
     for (k in 2:naR[i]) {
11
       # trial-specific RE distributions
12
       delta[i+nsCFB+nsBF,k] ~ dnorm(md[i+nsCFB+nsBF,k], taud[i+nsCFB+nsBF,k])
13
       md[i+nsCFB+nsBF,k] <- d[tR[i,k]] - d[tR[i,1]] + sw[i+nsCFB+nsBF,k]</pre>
14
       # precision of RE distributions (with multi-arm trial correction)
15
       taud[i+nsCFB+nsBF,k] < - tau *2*(k-1)/k
16
       #adjustment, multi-arm RCTs
17
       w[i+nsCFB+nsBF,k] <- delta[i+nsCFB+nsBF,k] - d[tR[i,k]] + d[tR[i,1]]</pre>
18
       # cumulative adjustment for multi-arm trials
19
       sw[i+nsCFB+nsBF,k] <-sum(w[i+nsCFB+nsBF,1:k-1])/(k-1)</pre>
20
     }
21
    }
22 #
23 totresdev <- sum(resdev[])
                                            # Total Residual Deviance (all
24 data)
25 # Partial Residual Deviance
26 totresdev.p[1] <- sum(resdev[1:nsCFB])</pre>
                                                                 # CFB data
27 totresdev.p[2] <- sum(resdev[nsCFB+1:nsCFB+nsBF])
                                                                 # BL + Fup data
28 totresdev.p[3] <- sum(resdev[nsCFB+nsBF+1:nsCFB+nsBF+nsR]) # Response data</pre>
29 #
30 # Priors and model assumptions (classes)
31 d[1]<-0
                                    # treatment effect is zero for control arm
32
         # treatments borrowing variance
33
         # Variance from 'No treatment'
34
         for(k in 4:7) { d[k] ~ dnorm(m[D[k]], prec2[2]) }
35
         # Any AD, variance from SSRIs & TCAS
```

Update 2018

```
1
         d[19] ~ dnorm(m[D[19]], prec2[8])
                                              # prec2[8]=precision of any AD
 2 class
 3
         z <- (1/prec2[7]) + (1/prec2[6])
                                                   # sum of SSRI & TCA
 4
  variances
 5
         prec2[8] <- 1/z
 6
         # Variance from CBT/CT
 7
         d[20] ~ dnorm(m[D[20]], prec2[17]) # through counselling
 8
         for(k in 36:40) { d[k] ~ dnorm(m[D[k]], prec2[17]) }
 9
         d[59] ~ dnorm(m[D[59]], prec2[17])
10
         # Variance from CBT + AD
11
         for(k in 55:58){ d[k] ~ dnorm(m[D[k]], prec2[19]) }
12
         for(k in 60:61){ d[k] ~ dnorm(m[D[k]], prec2[19]) }
13
14
         # treatment effects from Class
15
         # No treatment
16
         for (k in 2:3) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
17
         # Exercise, TCA, SSRI
18
         for(k in 8:18){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
19
         # Self-help with support, Self-help, Psychoeducational interventions
20
         for(k in 21:35) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
21
         # CBT/CT; Behavioural, cognitive, or CBT groups
22
         for(k in 41:52){ d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
23
         \# CBT + AD
24
     for(k in 53:54) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
25 #
26 m[1] < -0
27 #
28 # priors for mean class effect
29 for (k in 2:nc) { m[k] ~ dnorm(0, .0001) }
30 # priors for within-class variability
31 for (k in 2:7) {
32
     sd2[k] ~ dnorm(0,tau2)I(0,)
                                      # prior for class variance
33
     prec2[k] <- pow(sd2[k], -1)</pre>
                                      # class precision
34
    }
35 for (k in 9:nc) {
36
     sd2[k] \sim dnorm(0,tau2)I(0,)
                                       # prior for class variance
```

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```
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```

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

```
1 #
    2 for (k in 1:nt) {
    3
        rk[k] <- rank(d[],k)  # lower values are "good"</pre>
    4
        best[k] <- equals(rk[k],1) # Smallest is best (i.e. rank 1)</pre>
    5
         # prob treat k is h-th best, prob[1,k]=best[k]
    6
        for (h in 1:nt) { prob[h,k] <- equals(rk[k],h) }</pre>
    7
        1
    8 for (k in 1:ntR) {
    9 # rk2[k] <- ntR+1-rank(dR[],k) # lower values are "bad"</pre>
   10
                                             # lower values are "good"
        rk2[k] <- rank(dR[],k)
   11
        best2[k] <- equals(rk2[k],1) # Smallest is best (i.e. rank 1)</pre>
   12
         # prob treat k is h-th best, prob[1,k]=best[k]
   13
        for (h in 1:ntR) { prob2[h,k] \leq equals(rk2[k],h) }
   14
       }
   15 # rank classes
   16 for(k in 1:7) { mR[k] <- m[k] }
   17 for(k in 8:21) { mR[k] <- m[k+1] }
   18 for(k in 22:23) { mR[k] <- m[k+2] }
   19 for (k in 1:nc) {
   20
        rkClass[k] <- rank(m[],k)  # lower values are "good"</pre>
   21
        bestClass[k] <- equals(rkClass[k],1) # Smallest is best (i.e. rank 1)</pre>
   22
         # prob class k is h-th best, prob[1,k]=best[k]
   23
        for (h in 1:nc) { probClass[h,k] <- equals(rkClass[k],h) }</pre>
   24
        }
   25 for (k in 1:ncR) {
   26
         rkClass2[k] <- rank(mR[],k) # lower values are "good"</pre>
   27
        bestClass2[k] <- equals(rkClass2[k],1)  # Smallest is best (i.e. rank</pre>
   28 1)
   29
         # prob class k is h-th best, prob[1,k]=best[k]
   30
       for (h in 1:ncR) { probClass2[h,k] <- equals(rkClass2[k],h) }</pre>
   31
        }
   32 }
                                             # *** PROGRAM ENDS
1.6.2<sup>3</sup> Sample WinBUGS code – Response analysis
   34 # Random effects model for multi-arm trials
   35 model{
                                            # *** PROGRAM STARTS
```

Update 2018

```
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```

```
# LOOP THROUGH ALL STUDIES
 1 for(i in 1:ns) {
 2
     w[i,1] <- 0 # adjustment for multi-arm trials is zero for control arm
 3
     # RESPONSE DATA
 4
     delta[i,1] <- 0
                                       # treatment effect is zero for control
 5 arm
 6
     mu[i] ~ dnorm(0,.0001)
                                      # vague priors for all trial baselines
 7
    # CONTINUOUS DATA
 8
    deltaX[i,1] <- 0
                                       # treatment effect is zero for control
 9 arm
10
   muX[i] ~ dnorm(0,.0001)
                                      # vague priors for all trial baselines
11 }
12 #
13 # RESPONSE DATA
14 for(i in 1:nsR) {
                                      # LOOP THROUGH STUDIES WITH RESPONSE
15 DATA
16
     for (k in 1:naR[i]) {
                                      # LOOP THROUGH ARMS
17
       r[i,k] ~ dbin(p[i,k],nR[i,k]) # binomial likelihood
18
       logit(p[i,k]) <- mu[i] + delta[i,k] # model for linear predictor</pre>
19
       rhat[i,k] <- p[i,k] * nR[i,k] # expected value of the numerators</pre>
20
       #Deviance contribution
21
       dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))</pre>
22
             + (nR[i,k]-r[i,k]) * (log(nR[i,k]-r[i,k]) - log(nR[i,k]-
23 rhat[i,k]))
24
      }
25
     # Summed residual deviance contribution for this trial
26
     resdev[i] <- sum(dev[i,1:naR[i]])</pre>
27
    }
28 #
29 # (1) CFB DATA
30 for(i in 1:nsCFB) {
                                      # LOOP THROUGH STUDIES WITH CFB DATA
31
     # calculate pooled.sd and adjustment for SMD
32
     df[i] <- sum(nCFB[i,1:naCFB[i]]) - naCFB[i] # denominator for pooled.var</pre>
33
     Pooled.var[i] <- sum(nvar[i,1:naCFB[i]])/df[i]</pre>
34
     Pooled.sd[i] <- sqrt(Pooled.var[i]) # pooled sd for study i, for SMD</pre>
35
     # H[i] <- 1 - 3/(4*df[i]-1)
                                       # use Hedges' g
36
     H[i] <- 1
                                       # use Cohen's d (ie no adjustment)
37
     for (k in 1:naCFB[i]) {
                                       # LOOP THROUGH ARMS
```

Update 2018

```
1
       se[i,k] <- sdCFB[i,k]/sqrt(nCFB[i,k]) # calculate st error of CFB</pre>
 2
       var[i,k] <- pow(se[i,k],2)</pre>
                                         # calcultate variances of CFB
 3
       prec[i,k] <- 1/var[i,k]</pre>
                                         # set precisions of CFB
 4
       y[i,k] ~ dnorm(phi[i,k], prec[i,k]) # normal likelihood
 5
       phi[i,k] <- theta[i,k] * (Pooled.sd[i]/H[i]) # theta is stand mean</pre>
 6
       # model for linear predictor, deltaX is SMD
 7
       theta[i,k] <- muX[i] + deltaX[i,k]</pre>
 8
       dev[i+nsR,k] <- (y[i,k]-phi[i,k])*(y[i,k]-phi[i,k])*prec[i,k]</pre>
 9
       nvar[i,k] <- (nCFB[i,k]-1) * pow(sdCFB[i,k],2) # for pooled.sd</pre>
10
      }
11
     # summed residual deviance contribution for this trial
12
     resdev[i+nsR] <- sum(dev[i+nsR,1:naCFB[i]])</pre>
13
    }
14 # (2) BASELINE + FOLLOW-UP DATA (no CFB)
15 for(i in 1:nsBF) {
                                         # LOOP THROUGH STUDIES WITH BL + F-UP
16 DATA
17
     # calculate pooled.sd and adjustment for SMD
18
     df[i+nsCFB] <- sum(n[i,1:na[i]]) - na[i] # denominator for pooled.var
19
     Pooled.var[i+nsCFB] <- sum(nvarBF[i,1:na[i]])/df[i+nsCFB]</pre>
20
     Pooled.sd[i+nsCFB] <- sqrt(Pooled.var[i+nsCFB])# pooled sd for study</pre>
21 i,for SMD  # H[i+nsCFB] <- 1 - 3/(4*df[i]-1) # use Hedges' g</pre>
22
     H[i+nsCFB] <- 1
                                          # use Cohen's d (ie no adjustment)
23
     for (k in 1:na[i]) {
                                          # LOOP THROUGH ARMS
24
       yBF[i,k] <- yF[i,k] - yB[i,k] # calculate mean CFB</pre>
25
       seF[i,k] <- sdF[i,k]/sqrt(n[i,k]) # se at followup</pre>
26
       seB[i,k] <- sdB[i,k]/sqrt(n[i,k]) # se at baseline</pre>
27
       # variance of mean CFB, assuming correlation corr[i]
28
       var[i+nsCFB,k] <- pow(seF[i,k],2)+ pow(seB[i,k],2)</pre>
29 -2*(seF[i,k]*seB[i,k]*corrBF[i])
30
       prec[i+nsCFB,k] <- 1/var[i+nsCFB,k] # set CFB precisions</pre>
31
       yBF[i,k] ~ dnorm(phi[i+nsCFB,k], prec[i+nsCFB,k]) # normal likelihood
32
       # theta is standardised mean
33
       phi[i+nsCFB,k] <- theta[i+nsCFB,k] * (Pooled.sd[i+nsCFB]/H[i+nsCFB])</pre>
34
       # model for linear predictor, deltaX is SMD
35
       theta[i+nsCFB,k] <- muX[i+nsCFB] + deltaX[i+nsCFB,k]</pre>
36
       # residual deviance contribution
```

```
1
       dev[i+nsR+nsCFB,k] <- (yBF[i,k]-phi[i+nsCFB,k]) * (yBF[i,k]-</pre>
 2 phi[i+nsCFB,k])
                                                 * prec[i+nsCFB,k]
 3
       # variance of CFB, assuming correlation corrBF[i] (var is sd squared)
 4
       varBF[i,k] \le pow(sdF[i,k],2) + pow(sdB[i,k],2)
 5
                    - 2*(sdF[i,k]*sdB[i,k]*corrBF[i])
 6
       nvarBF[i,k] <- (n[i,k]-1) * varBF[i,k] # for pooled.sd</pre>
 7
      }
 8
     # summed residual deviance contribution for this trial
9
     resdev[i+nsR+nsCFB] <- sum(dev[i+nsR+nsCFB,1:na[i]])</pre>
10
    }
11 #
12 # RE MODEL (Response data)
13 for(i in 1:nsR) {
                                        # LOOP THROUGH STUDIES WITH RESPONSE
14 DATA
15
     for (k in 2:naR[i]) {
                                       # LOOP THROUGH ARMS
16
       delta[i,k] ~ dnorm(md[i,k], taud[i,k]) # trial-specific LOR
17 distributions
18
       # mean of LOR distributions (with multi-arm trial correction)
19
       md[i,k] <- d[tR[i,k]] - d[tR[i,1]] + sw[i,k]</pre>
20
       # precision of LOR distributions (with multi-arm trial correction)
21
       taud[i,k] <- tau *2*(k-1)/k
22
       # adjustment for multi-arm RCTs
23
       w[i,k] <- (delta[i,k] - d[tR[i,k]] + d[tR[i,1]])</pre>
24
       # cumulative adjustment for multi-arm trials
25
       sw[i,k] <- sum(w[i,1:k-1])/(k-1)</pre>
26
      }
27
    }
28 # RE MODEL (CFB data)
29 for(i in 1:nsCFB) {
                                        # LOOP THROUGH STUDIES WITH CFB DATA
30
     for (k in 2:naCFB[i]) {
                                        # LOOP THROUGH ARMS
31
       # convert SMD to LOR
32
       deltaX[i,k] <- delta[i+nsR,k]*((sqrt(3))/-3.1416)</pre>
33
       # trial-specific RE distributions
34
       delta[i+nsR,k] ~ dnorm(md[i+nsR,k], taud[i+nsR,k])
35
       md[i+nsR,k] <- d[tCFB[i,k]] - d[tCFB[i,1]] + sw[i+nsR,k]</pre>
       # precision of RE distributions (with multi-arm trial correction)
36
```

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```
1
       taud[i+nsR,k] <- tau *2*(k-1)/k</pre>
 2
       # adjustment, multi-arm RCTs
 3
       w[i+nsR,k] <- delta[i+nsR,k] - d[tCFB[i,k]] + d[tCFB[i,1]]</pre>
 4
       # cumulative adjustment for multi-arm trials
 5
       sw[i+nsR,k] <-sum(w[i+nsR,1:k-1])/(k-1)</pre>
 6
      }
 7
    }
 8 # RE MODEL (BL and F-up data)
                                        # LOOP THROUGH STUDIES WITH BL + F-UP
9 for(i in 1:nsBF) {
10 DATA
11
                                       # LOOP THROUGH ARMS
     for (k in 2:na[i]) {
12
       # convert SMD to LOR
13
       deltaX[i+nsCFB,k] <- delta[i+nsR+nsCFB,k]*((sqrt(3))/-3.1416)</pre>
14
       # trial-specific RE distributions
15
       delta[i+nsCFB+nsR,k] ~ dnorm(md[i+nsCFB+nsR,k], taud[i+nsCFB+nsR,k])
16
       md[i+nsCFB+nsR,k] <- d[t[i,k]] - d[t[i,1]] + sw[i+nsCFB+nsR,k]</pre>
17
       # precision of RE distributions (with multi-arm trial correction)
18
       taud[i+nsCFB+nsR,k] <- tau *2*(k-1)/k</pre>
19
       #adjustment, multi-arm RCTs
20
       w[i+nsCFB+nsR,k] <- delta[i+nsR+nsCFB,k] - d[t[i,k]] + d[t[i,1]]</pre>
21
       # cumulative adjustment for multi-arm trials
22
       sw[i+nsCFB+nsR,k] <-sum(w[i+nsCFB+nsR,1:k-1])/(k-1)</pre>
23
      1
24
    }
25 #
26 # Calculate residual deviance
27 totresdev <- sum(resdev[])</pre>
                                           # Total Residual Deviance (all data)
28 totresdev.p[1] <- sum(resdev[1:nsR]) # Response data</pre>
29 totresdev.p[2] <- sum(resdev[nsR+1:nsR+nsCFB]) # CFB data
30 totresdev.p[3] <- sum(resdev[nsR+nsCFB+1:nsCFB+nsBF+nsR]) # BL + FL data
31 d[1] <- 0
                                  # treatment effect is zero for reference
32 treatment
33 m[1] <- 0
                                  # treatment effect is zero for reference class
34 #
35 # Priors and model assumptions (classes)
36 # treatment effects from Class
```

```
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```

```
1 for (k in 2:3) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
 2 for (k in 10:19) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
 3 for (k in 24:39) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
 4 for (k in 42:65) { d[k] ~ dnorm(m[D[k]], prec2[D[k]]) }
 5
 6 # variance from no treatment
 7 for (k in 4:7) { d[k] ~ dnorm(m[D[k]], prec2[D[2]]) }
 8 # variance from self-help with support
 9 for (k in 8:9){ d[k] ~ dnorm(m[D[k]], prec2[D[11]]) }
10 # sum of variances from SSRI/TCAs
11 d[20] ~ dnorm(m[D[20]], prec2[8])
12 x <- (1/prec2[6]) + (1/prec2[7])
13 prec2[8] <- 1/x
14 # variance from counselling
15 for (k in 22:23) { d[k] ~ dnorm(m[D[k]], prec2[D[15]]) }
16 # variance from CBT/CT
17 for (k in 40:41) { d[k] ~ dnorm(m[D[k]], prec2[D[18]]) }
18 for (k in 72:73) { d[k] ~ dnorm(m[D[k]], prec2[D[18]]) }
19 # variance from CBT/CT + AD
20 for (k in 66:71) { d[k] ~ dnorm(m[D[k]], prec2[D[20]]) }
21 for (k in 74:75) { d[k] ~ dnorm(m[D[k]], prec2[D[20]]) }
22
23 # no class treatments [mirtazapine]
24 d[21] ~ dnorm(0, .0001)  # vague prior for treatment effects
25 m[9] <- d[21]
                                   # class effect = treat effect
26
27 for (k in 2:8) { m[k] ~ dnorm(0, .0001) }
28 for (k in 10:nc) { m[k] ~ dnorm(0, .0001) }
29 # priors for class precision
30 tau2 <- pow(0.19, -2)
31 for (k in 1:7) {
32
     sd2[k] ~ dnorm(0,tau2)I(0,) # informative prior for within-class st dev
33
     prec2[k] <- pow(sd2[k], -1) # within-class precision</pre>
34
   }
35 for (k in 9:nc) {
```

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```
1
   sd2[k] ~ dnorm(0,tau2)I(0,) # informative prior for within-class st dev
 2
    prec2[k] <- pow(sd2[k], -1) # within-class precision</pre>
 3 }
 4 #
 5 sdev ~ dunif(0,5)
                                    # vague prior for between-trial SD
 6 tau <- pow(sdev,-2)
                                    # between-trial precision
 7 # pairwise ORs and LORs for all possible pair-wise comparisons
 8 for (c in 1:(nt-1)) {
 9
     for (k in (c+1):nt) {
10
       or[c,k] \leq exp(d[k] - d[c])
11
      lor[c,k] <- (d[k]-d[c])
12
      }
13
    }
14
15 #
16 # pairwise differences for classes
17 for (c in 1: (nc-1)) {
18
     for (k in (c+1):nc) {
19
       diffClass[c,k] <- m[k] - m[c]</pre>
20
       orClass[c,k] <- exp(m[k] - m[c])</pre>
21
      }
22
    }
23 #
24 # rank treatments
25 for(k in 1:2) { dR[k] <- d[k] }
26 dR[3] <- d[4]
27 dR[4] <- d[6]
28 dR[5] <- d[8]
29 dR[6] <- d[11]
30 dR[7] <- d[13]
31 dR[8] <- d[16]
32 dR[9] <- d[17]
33 dR[10] <- d[18]
34 dR[11] <- d[19]
35 dR[12] <- d[21]
```

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

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```
1 dR[48] <- d[68]
 2 dR[49] < - d[69]
 3 \, dR[50] < - d[70]
 4 dR[51] <- d[71]
 5 dR[52] <- d[74]
 6 dR[53] <- d[75]
 7 #
 8 for (k in 1:nt) {
 9
    rk[k] <- nt+1-rank(d[],k)  # assumes events are "good"</pre>
10 # rk[k] <- rank(d[],k)
                                     # assumes events are "bad"
11
     best[k] <- equals(rk[k],1)</pre>
                                    # Smallest is best (i.e. rank 1)
12
     # prob treat k is h-th best, prob[1,k]=best[k]
13
     for (h in 1:nt) { prob[h,k] <- equals(rk[k],h) }</pre>
14
    1
15 for (k in 1:ntR) {
16
     rk2[k] <- ntR+1-rank(dR[],k)
                                        # assumes events are "good"
17 # rk2[k] <- rank(dR[],k)
                                         # assumes events are "bad"
18
     best2[k] <- equals(rk2[k],1) # Smallest is best (i.e. rank 1)</pre>
19
     # prob treat k is h-th best, prob[1,k]=best[k]
20
     for (h in 1:ntR) { prob2[h,k] \leq equals(rk2[k],h) }
21
    }
22 #
23 # rank classes
24 for(k in 1:7) { mR[k] <- m[k] }
25 for(k in 8:23) { mR[k] <- m[k+1] }
26 mR[24] <- m[26]
27 for (k in 1:nc) {
28
     rkClass[k] <- nc+1-rank(m[],k)  # assumes events are "good"</pre>
29
     bestClass[k] <- equals(rkClass[k],1) # Smallest is best (i.e. rank 1)</pre>
30
     # prob class k is h-th best, prob[1,k]=best[k]
31
     for (h in 1:nc) { probClass[h,k] <- equals(rkClass[k],h) }</pre>
32
    }
33 for (k in 1:ncR) {
34
    rkClass2[k] <- ncR+1-rank(mR[],k)</pre>
     bestClass2[k] <- equals(rkClass2[k],1)  # Smallest is best (i.e. rank</pre>
35
36 1)
```

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```
1 # prob class k is h-th best, prob[1,k]=best[k]
2 for (h in 1:ncR) { probClass2[h,k] <- equals(rkClass2[k],h) }
3 }
4 } # *** PROGRAM ENDS
5
```

### **1.71** Appendix 2: Correlations

#### 1.7.12 Data from trials

Study	Intervention	Scale	Numbe r of items	Mean baseline completers	SD baseline completer s	Mean endpoint completers	SD endpoint completer s	Mean change completers	SD change completer s	N_ Co mpl	Corr elati on	
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	Ę
Kendrick 2009	Any SSRI + Enhanced TAU	HAMD	17	15.45	2.09	8.73	5.2	-6.8	4.9	96	0.34	Update
	Enhanced TAU	HAMD	17	15.7	2.5	11.2	5.8	-4.5	5.3	90	0.41	2018
Legrand 2014	Exercise	BDI-II	21	21.7	6.8	12.8	4.4	-8.9	6.7	15	0.35	8
	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	

Study	Intervention	Scale	Numbe r of items	Mean baseline completers	SD baseline completer s	Mean endpoint completers	SD endpoint completer s	Mean change completers	SD change completer s	N_ Co mpl	Corr elati on
	Pill placebo	HAMD	21	24.8	4.5	13.1	9.8	-11.7	9	15	0.40
Andersson 2005	Computerised-CBT (CCBT)	MADR S	9	20.1	5.7	12.7	8.3	-5.5	8.1	36	0.37
	Waitlist	MADR S	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	MADR S	10	28.2	5.1	12.5	9.1	-15.7	8.8	48	0.34
	Escitalopram	MADR S	10	27.1	4.9	12.8	8.4	-14.3	8.3	51	0.31

1

Study	Intervention	Scale	Nu mb er of ite ms	Mean baseline ITT	SD baseline ITT	Mean endpoint ITT	SD endpoint ITT	Mean change ITT	SD change ITT	N_ Ran d	Corr elati on
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	Nu mb er of ite ms	Mean baseline ITT	SD baseline ITT	Mean endpoint ITT	SD endpoint ITT	Mean change ITT	SD change ITT	N_ Ran d	Corr elati on	
	Waitlist	HAMD	17	9.5	3.7	10.9	5.8	1.5	5.3	12	0.45	Ī.
Cassano 1996	Imipramine	MADR S	10	31.4	4.8	18.4	12.0	-12.9	10.4	64	0.51	
	Pill placebo	MADR S	10	31.0	3.8	22.3	11.5	-8.7	11.5	59	0.17	
Colonna 2005	Escitalopram	MADR S	10	29.5	4.3	8.4	8.6	-21.3	8.7	175	0.22	
	Citalopram	MADR S	10	30.2	4.7	9.7	6.0	-20.5	9.8	182	-0.67	
Forest Laboratorie s 2000	Escitalopram	MADR S	10	28.7	4.3	15.9	9.7	-12.9	10.0	129	0.15	
	Citalopram	MADR S	10	25.0	5.5	15.3	11.1	-13.0	9.8	128	0.46	
	Pill placebo	MADR S	10	28.8	5.0	17.5	10.9	-11.2	10.4	129	0.33	
Jordan 2014	Third-wave cognitive therapy individual	MADR S	10	23.6	7.4	13.6	12.3	-10.0	11.6	23	0.40	
	CBT individual (under 15 sessions)	MADR S	10	21.6	7.3	10.9	9.9	-10.7	11.7	25	0.08	
Lepola 2003	Escitalopram	MADR S	10	29.0	4.3	13.7	8.3	-15.3	8.4	155	0.24	
	Citalopram	MADR S	10	29.2	4.2	15.0	8.7	-14.2	8.9	160	0.19	
	Pill placebo	MADR S	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	

Study	Intervention	Scale	Nu mb er of ite ms	Mean baseline ITT	SD baseline ITT	Mean endpoint ITT	SD endpoint ITT	Mean change ITT	SD change ITT	N_ Ran d	Corr elati on
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	MADR S	10	19.23	10.48	9.15	7.27	-10.08	9.41	26	0.49
	Attention placebo + TAU	MADR S	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

### 1.7.21 IAPT psych

		PHQ-9 Base	line	PHQ-9 Endpoint		Correlation	l	
Intervention	PHQ range	n	mean	sd	mean	sd	r	р
High Intensity (Only receiving HI	PHQ: 5 - 17	2814	11.48	3.56	7.65	5.60	0.3405	<0.001
treatment during episode of care)	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 Ba	aseline	PHQ-9 Er	ndpoint	Correlation	
Intervention	PHQ range	n	mean	sd	mean	sd	r	р
	PHQ: 18+	1911	21.87	2.75	14.72	7.45	0.2727	<0.00
Low Intensity (Only receiving LI	PHQ: 5 - 17	5329	11.36	3.60	7.66	5.19	0.3922	<0.00
treatment during episode of care)	PHQ: 5 - 9 (GAD <=9)	1117	6.92	1.38	5.11	3.73	0.2151	< 0.00
	PHQ: 10 - 17	3535	13.49	2.24	8.86	5.39	0.2358	< 0.00
	PHQ: 10+	5872	16.50	4.37	10.89	6.53	0.4486	< 0.00
	PHQ: 18+	2337	21.05	2.47	13.94	6.90	0.2791	< 0.00
Cognitive Behavioural Therapy	PHQ: 5 - 17	2758	11.52	3.58	7.50	5.64	0.3455	<0.00
	PHQ: 5 - 9 (GAD <=9)	506	7.03	1.29	4.92	4.35	0.1093	0.013
	PHQ: 10 - 17	1862	13.57	2.28	8.58	5.82	0.2396	<0.00
	PHQ: 10+	3772	17.74	4.82	11.35	7.31	0.4454	<0.00
	PHQ: 18+	1910	21.80	2.72	14.06	7.59	0.2721	<0.00
Guided Self-Help	PHQ: 5 - 17	3164	11.18	3.64	7.22	5.06	0.3903	<0.00
	PHQ: 5 - 9 (GAD <=9)	663	6.86	1.38	4.84	3.51	0.2566	<0.00
	PHQ: 10 - 17	2033	13.45	2.26	8.46	5.31	0.2239	<0.00
	PHQ: 10+	3175	16.13	4.26	10.25	6.40	0.4243	<0.00
	PHQ: 18+	1142	20.91	2.39	13.43	6.91	0.2193	<0.00
Pure Self-Help	PHQ: 5 - 17	44	10.18	3.99	7.00	4.77	0.209	0.173
	PHQ: 5 - 9 (GAD <=9)	15	6.73	1.39	6.87	5.49	0.4172	0.121
	PHQ: 10 - 17	23	13.48	2.41	7.48	4.35	0.1204	0.584
	PHQ: 10+	30	14.90	3.46	9.23	5.47	0.5739	<0.00
	PHQ: 18+	7	19.57	1.81	15.00	4.97	0.759	0.047
Either Self-Help	PHQ: 5 - 17	3202	11.16	3.65	7.22	5.05	0.3875	<0.00
	PHQ: 5 - 9 (GAD <=9)	676	6.86	1.38	4.88	3.57	0.2582	<0.00
	PHQ: 10 - 17	2053	13.45	2.26	8.45	5.30	0.2236	<0.00
	PHQ: 10+	3200	16.12	4.25	10.23	6.39	0.4253	<0.00
	PHQ: 18+	1147	20.90	2.39	13.43	6.90	0.22	<0.00
Behavioural activation	PHQ: 5 - 17	119	12.39	3.63	9.27	5.73	0.5059	<0.00
	PHQ: 5 - 9 (GAD <=9)	22	6.59	1.14	4.91	3.32	0.1531	0.4964

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

			PHQ-9 Ba	aseline	PHQ-9 Er	ndpoint	Correlatio	on
Intervention	PHQ range	n	mean	sd	mean	sd	r	р
	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.

### 1.7.31 PHQ9

		PHQ-9 T1	PHQ-9 T1 PHQ-9 T2			Correlation	on	
Sample (criteria)	n	mean	sd	mean	sd	r	р	
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	р
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

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	ntervention Severity		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 Ba	HADs-D Baseline		e HADs-D Endpoint		Correlation	
Intervention	PHQ range	n	mean	sd	mean	sd	r	р	
SSRIs	HAD-D: 8+	60	11.65	2.77	6.05	4.74	0.2737	0.0343	puare
	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	

### **1.81** Appendix 3: NMA model fit statistics

#### 1.8.12 Population: less severe depression

#### 3 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

#### 4 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

#### 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

#### 6 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

#### 7 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

#### 8 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

#### 9 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

#### 1.8.21 Population: more severe depression

#### 2 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

#### 3 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

4 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

#### 5 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

#### 6 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

#### 7 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

#### 8 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

#### 1 Figure 49: Odds ratio and 95% credible intervals for every intervention compared to 2 pill placebo. Discontinuation for any reason – less severe depression.

ntervention (vs Pill Placebo)		odds ratio	95%Crl
Naitlist		0.52	(0.3, 0.88
No treatment		0.57	(0.29, 1.11
Attention placebo		0.93	(0.48, 1.74
Attention placebo + TAU		1.23	(0.55, 3)
TAU		0.68	(0.45, 1.04
Enhanced TAU		0.82	(0.43, 1.68
Exercise		0.76	(0.45, 1.27
Exercise + TAU	_ <b>_</b>	0.93	(0.46, 2)
roga + TAU		0.64	(0.19, 1.6
Any TCA		1.24	(0.78, 2.08
Amitriptyline	+ + + + + + + + + + + +	1.03	(0.71, 1.46
mipramine	-	1.26	(0.92, 1.75
ofepramine		1.24	(0.76, 2.11
Any SSRI		0.82	(0.5, 1.26)
Any SSRI + Enhanced TAU		0.83	(0.45, 1.4
Citalopram		0.85	(0.56, 1.31
Escitalopram		0.85	(0.58, 1.26
Fluoxetine		0.82	(0.58, 1.13
Sertraline	-	0.89	(0.66, 1.2
Any AD	-	1.06	(0.64, 1.75
Mirtazapine		0.48	(0.13, 1.74
Short-term psychodynamic psychotherapy individual		0.87	(0.49, 1.55
Short-term psychodynamic psychotherapy group		0.87	(0.33, 2.3
Cognitive bias modification with support + TAU		1.23	(0.5, 2.85
Cognitive bibliotherapy with support		1.35	(0.67, 2.63
Cognitive bibliotherapy with support + TAU		1.24	(0.49, 2.95
Computerised behavioural activation with support		1.06	(0.4, 2.37
Computerised psychodynamic therapy with support		1.45	(0.6, 3.92
Computerised third-wave cognitive therapy with support	<b>_</b>	1.16	(0.41, 2.81
Computerised-CBT (CCBT) with support		1.71	(0.9, 3.3)
Computerised-CBT (CCBT) with support + TAU		1.08	(0.54, 2.05
Tailored computerised-CBT (CCBT) with support		1.17	(0.48, 2.58
Behavioural bibliotherapy		1.11	(0.55, 2.35
Cognitive bibliotherapy	-	1	(0.55, 1.79
Cognitive bibliotherapy + TAU		1.04	(0.53, 1.98
Computerised cognitive bias modification		1.07	(0.53, 2.12
Computerised mindfulness intervention	_	1.08	(0.53, 2.23
Computerised-CBT (CCBT)		1.09	(0.63, 1.86
Computerised-CBT (CCBT) + TAU		1.12	(0.63, 2.02
Online positive psychological intervention	_	1.11	(0.57, 2.22
Psychoeducational website		1.03	(0.54, 1.91
Failored computerised psychoeducation and self-help strategies	_	1.02	(0.5, 1.95
ifestyle factors discussion		0.51	(0.22, 1.18
Psychoeducational group programme		0.45	(0.18, 1.02
Psychoeducational group programme + TAU		0.6	(0.29, 1.26
nterpersonal psychotherapy (IPT)		0.73	(0.44, 1.2
nterpersonal psychotherapy (IPT) + TAU		0.62	(0.24, 1.32
Emotion-focused therapy (EFT)		0.67	(0.28, 1.42
nterpersonal counselling		0.69	(0.33, 1.3)
Non-directive counselling		0.85	(0.42, 1.78
		0.00	(continues
г	- T T T	T - T	
0.0	2 0.5 1 2	20 50	

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Discontinuation			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
		oudo rado	(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	_ <b>-</b> -	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)	_ <b>_</b>	0.75	(0.27, 2.48)
Coping with Depression course (individual)	_ <b>-</b>	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)	<b></b>	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)
0.02	0.512 205	0	
	odds ratio		

1

#### 1 Figure 50: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Discontinuation for any reason – less severe depression.

Class (vs Placebo)			odd	ls ratio	95%Crl
No treatment			(	).54	(0.26, 1.12)
Attention placebo		-		1.07	(0.48, 2.45)
TAU			(	0.75	(0.39, 1.53)
Exercise			(	).77	(0.34, 1.6)
TCA		-		1.19	(0.78, 1.85)
SSRI			(	0.84	(0.59, 1.17)
Any AD		_ <b>_</b>		1.06	(0.41, 2.72)
Mirtazapine	_		(	0.48	(0.13, 1.74)
Short-term psychodynamic psychotherapies			(	0.87	(0.38, 2.02)
Self-help with support				1.26	(0.66, 2.3)
Self-help				1.07	(0.62, 1.82)
Psychoeducational interventions			(	0.51	(0.23, 1.14)
Interpersonal psychotherapy (IPT)			(	0.67	(0.31, 1.34)
Counselling			(	0.74	(0.38, 1.39)
Problem solving			(	0.66	(0.31, 1.41)
Behavioural therapies (individual)			(	0.62	(0.26, 1.55)
Cognitive and cognitive behavioural therapies (individual)			(	0.66	(0.39, 1.09)
Behavioural, cognitive, or CBT groups			(	86.0	(0.35, 1.26)
Combined (Cognitive and cognitive behavioural therapies individual -	+ AD)		(	0.98	(0.41, 2.39)
Combined (Behavioural, cognitive, or CBT groups + AD)			- :	2.25	(0.44, 11.6)
Combined (Problem solving + AD)			(	).42	(0.09, 1.89)
Combined (Counselling + AD)			(	0.89	(0.12, 6.27)
Combined (IPT + AD)	-		(	).72	(0.19, 2.72)
Combined (Short-term psychodynamic psychotherapies + AD)				1.45	(0.52, 3.98)
Combined (psych + placebo)			(	0.32	(0.09, 1.03)
Combined (Exercise + AD/CBT)			(	0.66	(0.26, 1.65)
		054.0			
	0.02	0.5 1 2 odds ratio	20 50		

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#### 1 Figure 51: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Discontinuation due to SE – less severe depression.

Intervention (vs Pill Placebo)			odds ratio	95%Crl
Exercise	<∎		0.02	(0, 0.72)
Amitriptyline		-#-	9.68	(5.32, 19.34)
Imipramine			6.23	(2.98, 13.29)
Lofepramine			7.35	(2.21, 21.69)
Any SSRI	-		2.58	(0.81, 7.68)
Citalopram			2.51	(0.96, 6.3)
Escitalopram			2.08	(0.9, 4.77)
Fluoxetine			1.99	(1, 4.17)
Sertraline			3.98	(2.06, 7.07)
Mirtazapine	_		3.82	(0.41, 44.97)
Short-term psychodynamic psychotherapy individual		_∎>	9.27	(0.33, 611.55)
Problem solving individual	←∎		0.14	(0, 2.9)
CBT individual (over 15 sessions)	I		0.99	(0, 29.81)
CBT group (under 15 sessions)	← ∎		0.31	(0.01, 3.04)
CBT individual (over 15 sessions) + imipramine	<		1.18	(0, 31.94)
Problem solving individual + any SSRI	-	∎→	10.04	(0.64, 192.67)
Short-term psychodynamic psychotherapy individual + any SSRI			1.04	(0.01, 47.94)
Exercise + Sertraline	0.02 0.5 1 odds r			(0.1, 14.43)

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

Discontinuation due to side effects			
Class (vs Placebo)		odds ratio	95%Crl
Exercise	<∎	0.02	(0, 0.79)
TCA		7.64	(3.35, 17.18)
SSRI		2.53	(1.28, 4.97)
Mirtazapine		- 3.82	(0.41, 44.97)
Short-term psychodynamic psychotherapies		> 9.3	(0.31, 655.89)
Problem solving	< <b>─■</b> ──	0.14	(0, 3.22)
Cognitive and cognitive behavioural therapies (individual)	<	0.98	(0, 32.46)
Behavioural, cognitive, or CBT groups	<	0.3	(0.01, 3.46)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	<	1.16	(0, 34.74)
Combined (Problem solving + AD)		→ 10.11	(0.58, 210.4)
Combined (Short-term psychodynamic psychotherapies + AD)		→ 1.04	(0.01, 51.42)
Combined (Exercise + AD/CBT)	0.02 0.51 2 20	1.31 50	(0.09, 16.36)
	odds ratio		

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#### 1 Figure 53: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Remission in completers – less severe depression.

Remission (completers)			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist	_ <b>-</b>	0.26	(0.11, 0.62)
No treatment	<b>e</b>	0.32	(0.13, 0.79)
Attention placebo	<b>e</b>	0.24	(0.09, 0.68)
Attention placebo + TAU	<b>_</b>	0.24	(0.07, 0.77)
TAU		0.85	(0.52, 1.42)
Enhanced TAU		0.91	(0.47, 1.79)
Exercise		1.3	(0.74, 2.28)
Exercise + TAU		1.35	(0.5, 3.98)
Any TCA	_ <b>_</b> _	1.62	(0.9, 2.8)
Amitriptyline		1.55	(0.79, 2.93)
Imipramine	_ <b></b>	1.99	(1.13, 3.6)
Lofepramine		1.37	(0.65, 2.62)
Any SSRI		1.57	(0.87, 2.52)
Any SSRI + Enhanced TAU		1.83	(1.03, 3.36)
Citalopram		1.71	(0.95, 2.9)
Escitalopram		1.87	(1.3, 2.79)
Fluoxetine		1.95	(1.34, 2.89)
Sertraline		1.71	(1.1, 2.64)
Any AD		1.69	(1, 2.88)
Short-term psychodynamic psychotherapy individual		1.05	(0.51, 2.09)
Short-term psychodynamic psychotherapy group		0.61	(0.15, 1.76)
Computerised behavioural activation with support		1.17	(0.47, 3.66)
Computerised behavioural activation with support		1.2	(0.49, 3.63)
Computerised psychodynamic merapy with support Computerised-CBT (CCBT) with support		1.14	(0.53, 2.64)
		0.81	(0.41, 1.69)
Computerised-CBT (CCBT) with support + TAU Tailored computerised-CBT (CCBT) with support		1.3	(0.54, 3.8)
		0.58	(0.18, 1.82)
Cognitive bibliotherapy Cognitive bibliotherapy + TAU		1.43	(0.62, 3.39)
Computerised-CBT (CCBT)		2.28	(0.81, 6.37)
Computerised-CBT (CCBT) + TAU		2.3	(1.11, 4.82)
Tailored computerised psychoeducation and self-help strategi		0.76	(0.27, 2.12)
Psychoeducational group programme + TAU		1.82	(0.27, 2.12)
Interpersonal psychotherapy (IPT)		1.98	(1.19, 3.43)
Emotion-focused therapy (EFT)		1.97	(0.66, 6.35)
Interpersonal counselling		2.28	(1.18, 4.28)
Non-directive counselling		1.55	(0.58, 3.71)
Psychodynamic counselling + TAU		1.34	(0.58, 2.99)
Relational client-centered therapy		1.45	(0.4, 4.15)
Problem solving individual		0.99	(0.46, 2.15)
Problem solving individual + enhanced TAU		0.82	(0.35, 1.89)
Behavioural activation (BA)		3.2	(1.5, 6.97)
Behavioural therapy (Lewinsohn 1976)		2.75	(0.84, 8.18)
CBT individual (under 15 sessions)		1.56	(0.88, 2.77)
CBT individual (over 15 sessions)	<b></b>	1.99	(1.21, 3.33)
CBT individual (over 15 sessions) + TAU		2.04	(0.94, 5.21)
Rational emotive behaviour therapy (REBT) individual		1.72	(0.89, 3.32)
Third-wave cognitive therapy individual		2.13	(1.12, 4.45)
CBT group (under 15 sessions)		3.16	(1.4, 7.29)
CBT group (under 15 sessions) + TAU		3.83	(1.71, 9.68)
Coping with Depression course (group) + TAU	<b>_</b> _	2.81	(1.17, 6.69)
CBT individual (over 15 sessions) + any TCA	<b>_</b>	4.32	(1.42, 13.94)
CBT individual (over 15 sessions) + imipramine	<b>_</b>	4.74	(1.57, 15.35)
CBT group (under 15 sessions) + imipranine		6.35	(1.62, 25.79)
Problem solving individual + any SSRI		0.97	(0.3, 3.39)
Supportive psychotherapy + any SSRI	<b>_</b>		(1.82, 107.23)
Interpersonal psychotherapy (IPT) + any AD	<b>e</b>	3.58	(1.26, 10.27)
Short-term psychodynamic psychotherapy individual + Any AD	)	6.2	(2.73, 14.56)
Short-term psychodynamic psychotherapy individual + any SS Short-term psychodynamic psychotherapy individual + any SS		6.44	(2.13, 19.69)
CBT individual (over 15 sessions) + Pill placebo		4.83	(1.18, 22.53)
Exercise + Sertraline		1.27	(0.62, 2.67)
			(2.02, 2.01)
	0.02 0.5 1 2 20 50		
	odds ratio		

3 4

#### 1 Figure 54: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Remission in completers – less severe depression.

Remission (completers)					
Class (vs Placebo)				odds ratio	95%Crl
No treatment		-		0.29	(0.12, 0.73)
Attention placebo		-		0.24	(0.08, 0.74)
TAU		-		0.88	(0.44, 1.8)
Exercise				1.32	(0.56, 3.26)
TCA				1.61	(0.87, 2.9)
SSRI				1.76	(1.17, 2.65)
Any AD				1.7	(0.59, 4.75)
Short-term psychodynamic psychotherapies	_			0.79	(0.26, 2.06)
Self-help with support				1.12	(0.53, 2.62)
Self-help				1.27	(0.53, 3.03)
Psychoeducational interventions				1.82	(0.57, 6)
Interpersonal psychotherapy (IPT)				1.98	(0.84, 4.74)
Counselling		+		1.69	(0.74, 3.62)
Problem solving	-	-		0.9	(0.38, 2.14)
Behavioural therapies (individual)				2.96	(1.11, 7.77)
Cognitive and cognitive behavioural therapies (individual)				1.88	(1.06, 3.44)
Behavioural, cognitive, or CBT groups				3.24	(1.44, 7.58)
Combined (Cognitive and cognitive behavioural therapies individual + A	ND)			4.54	(1.44, 15.13)
Combined (Behavioural, cognitive, or CBT groups + AD)				6.35	(1.48, 28.5)
Combined (Problem solving + AD)	_	-		0.98	(0.26, 3.75)
Combined (Counselling + AD)			• •	13.59	(1.7, 116.16)
Combined (IPT + AD)			_	3.59	(1.08, 11.75)
Combined (Short-term psychodynamic psychotherapies + AD)				6.34	(2.38, 17.01)
Combined (psych + placebo)				4.83	(1.02, 25.87)
Combined (Exercise + AD/CBT)				1.27	(0.51, 3.17)
	0.02 0	.512	20 50		
		lds ratio	20 00		

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#### 1 Figure 55: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Remission in those randomised – less severe depression.

Remission (ITT)			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist		0.41	(0.18, 0.92)
No treatment		0.62	(0.27, 1.45)
Attention placebo	_ <b></b>	0.31	(0.12, 0.81)
Attention placebo + TAU	_ <b>-</b> -	0.33	(0.11, 1)
TAU		1.15	(0.72, 1.88)
Enhanced TAU		1.17	(0.6, 2.28)
Exercise		1.31	(0.76, 2.24)
Exercise + TAU	<b>-</b> _	1.24	(0.46, 3.3)
Any TCA		1.55	(0.94, 2.57)
Amitriptyline		1.6	(0.91, 2.89)
Imipramine		1.66	(1.03, 2.78)
Lofepramine	_ <b>_</b> _	1.37	(0.71, 2.46)
Any SSRI		1.8	(1.07, 2.81)
Any SSRI + Enhanced TAU		2.04	(1.23, 3.82)
Citalopram		1.84	(1.08, 3)
Escitalopram		1.88	(1.32, 2.72)
Fluoxetine		2.09	(1.49, 3.08)
Sertraline		1.87	(1.24, 2.82)
Any AD		1.73	(1.07, 2.9)
Short-term psychodynamic psychotherapy individual	_ <b>_</b> _	1.44	(0.72, 2.83)
Short-term psychodynamic psychotherapy group	<b>-</b>	0.85	(0.22, 2.49)
Computerised behavioural activation with support	<b>_</b>	1.5	(0.64, 4.37)
Computerised psychodynamic therapy with support		1.44	(0.61, 3.95)
Computerised Day Clobynamic merapy with support		1.27	(0.62, 2.75)
Computerised-CBT (CCBT) with support + TAU		1.12	(0.61, 2.23)
Tailored computerised-CBT (CCBT) with support		1.58	(0.7, 4.28)
Cognitive bibliotherapy		0.92	(0.33, 2.48)
Cognitive bibliotherapy + TAU		1.5	(0.69, 3.32)
Computerised-CBT (CCBT)		2.2	(0.87, 5.62)
Computerised-CBT (CCBT) + TAU		1.83	(0.95, 3.68)
Tailored computerised psychoeducation and self-help strategies		1.12	(0.44, 2.77)
Psychoeducational group programme + TAU		2.64	(1.11, 6.49)
Interpersonal psychotherapy (IPT)		2.07	(1.3, 3.43)
Emotion-focused therapy (EFT)		2.11	(0.74, 6.1)
Interpersonal counselling		2.46	(1.35, 4.51)
Non-directive counselling	<b>_</b>	1.6	(0.65, 3.66)
Psychodynamic counselling + TAU		1.6	(0.73, 3.46)
Relational client-centered therapy		1.65	(0.52, 4.48)
Problem solving individual	_ <b></b>	1.41	(0.72, 2.81)
Problem solving individual + enhanced TAU		1.06	(0.45, 2.4)
Behavioural activation (BA)		5	(2.56, 10.02)
CBT individual (under 15 sessions)		1.76	(1.02, 3.06)
CBT individual (over 15 sessions)		2.34	(1.52, 3.76)
CBT individual (over 15 sessions) + TAU	_ <b></b>	2.47	(1.17, 5.96)
Rational emotive behaviour therapy (REBT) individual		2.07	(1.1, 3.91)
Third-wave cognitive therapy individual		2.75	(1.54, 5.3)
CBT group (under 15 sessions)		3.86	(1.72, 8.77)
CBT group (under 15 sessions) + TAU		5.5	(2.42, 13.78)
Coping with Depression course (group) + TAU	_ <b></b>	3.37	(1.44, 7.85)
CBT individual (over 15 sessions) + any TCA	_ <b></b>	3.94	(1.57, 10.25)
CBT individual (over 15 sessions) + impramine	_ <b></b>	3.95	(1.61, 10.01)
CBT group (under 15 sessions) + imipramine	<b>_</b>	4.57	(1.25, 16.63)
Problem solving individual + any SSRI		1.72	(0.62, 5.03)
Supportive psychotherapy + any SSRI	<b>_</b>	10.57	(1.35, 92.02)
Interpersonal psychotherapy (IPT) + any AD	<b>_</b>	3.35	(1.29, 9)
Short-term psychodynamic psychotherapy individual + Any AD	_ <b></b>	4.58	(2.09, 9.88)
Short-term psychodynamic psychotherapy individual + any SSRI		4.92	(1.49, 17.27)
CBT individual (over 15 sessions) + Pill placebo		9.59	(2.5, 41.51)
Exercise + Sertraline		1.4	(0.72, 2.8)
		1	
0	02 0.512 20 5	i0	
	odds ratio		

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#### 1 Figure 56: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Remission in those randomised – less severe depression.

Remission (ITT)			
Class (vs Placebo)		odds ratio	95%Crl
No treatment		0.51	(0.21, 1.24)
Attention placebo		0.32	(0.11, 0.93)
TAU		1.16	(0.57, 2.38)
Exercise		1.27	(0.56, 2.94)
TCA		1.54	(0.9, 2.62)
SSRI		1.92	(1.31, 2.84)
Any AD		1.74	(0.67, 4.57)
Short-term psychodynamic psychotherapies	<b>_</b>	1.11	(0.37, 2.8)
Self-help with support		1.38	(0.69, 3.06)
Self-help		1.44	(0.66, 3.16)
Psychoeducational interventions		2.65	(0.86, 8.26)
Interpersonal psychotherapy (IPT)		2.08	(0.89, 4.93)
Counselling		1.85	(0.86, 3.88)
Problem solving		1.22	(0.53, 2.78)
Behavioural therapies (individual)		5.02	(1.89, 13.4)
Cognitive and cognitive behavioural therapies (individual)		2.26	(1.32, 4.02)
Behavioural, cognitive, or CBT groups	<b></b>	4.16	(1.86, 9.51)
Combined (Cognitive and cognitive behavioural therapies individual + A	AD)	3.94	(1.49, 10.68)
Combined (Behavioural, cognitive, or CBT groups + AD)		4.56	(1.03, 20.23)
Combined (Problem solving + AD)		1.72	(0.49, 6.27)
Combined (Counselling + AD)		10.51	(1.19, 103.44)
Combined (IPT + AD)		3.36	(1, 11.53)
Combined (Short-term psychodynamic psychotherapies + AD)		4.75	(1.69, 13.44)
Combined (psych + placebo)		9.62	(2.1, 48.86)
Combined (Exercise + AD/CBT)		1.4	(0.51, 3.86)
	0.02 0.5 1 2 20 5		
	0.02 0.51 2 20 50 odds ratio	,	

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#### 1 Figure 57: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Response in completers – less severe depression.

Response (completers)			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist		0.44	(0.22, 0.88)
No treatment		0.78	(0.34, 1.8)
Attention placebo		1.49	(0.61, 3.68)
Attention placebo + TAU		1.26	(0.4, 3.88)
TAU		1.06	(0.57, 1.95)
Enhanced TAU		1.52	(0.72, 3.27)
Exercise		2.81	(1.39, 5.86)
Exercise + TAU		2.44	(1.03, 5.7)
Any TCA		2.52	(1.18, 4.57)
Amitriptyline		2.95	(1.97, 4.5)
Imipramine		2.67	(1.8, 3.94)
Lofepramine		2.98	(1.69, 5.64)
Any SSRI		2.69	(1.59, 5.33)
Any SSRI + Enhanced TAU		2.56	(1.44, 4.93)
Citalopram		2.44	(1.57, 3.74)
Escitalopram		2.18	(1.32, 3.35)
Fluoxetine		2.53	(1.75, 3.72)
Sertraline		2.57	(1.82, 3.67)
Any AD		3.35	(1.6, 7.13)
Mirtazapine		3.22	(0.69, 16.95)
Short-term psychodynamic psychotherapy individual		2.23	(0.97, 5.37)
Short-term psychodynamic psychotherapy group		2.17	(0.84, 5.97)
Cognitive bibliotherapy with support		2.39	(0.85, 6.63)
Cognitive bibliotherapy with support + TAU		2.88	(1.02, 8.76)
Computerised-CBT (CCBT) with support		2.8	(1.05, 7.68)
Computerised-CBT (CCBT) with support + TAU		2.62	(0.97, 7.25)
Behavioural bibliotherapy		2.96	(1.11, 7.99)
Cognitive bibliotherapy	_ <b></b>	3.59	(1.56, 8.25)
Cognitive bibliotherapy + TAU	<b></b>	4.2	(1.66, 11.07)
Computerised cognitive bias modification		2.89	(1.09, 7.73)
Computerised-CBT (CCBT)		1.77	(0.75, 4.14)
Computerised-CBT (CCBT) + TAU	_ <b></b>	3.57	(1.62, 7.89)
Online positive psychological intervention		1.59	(0.55, 4.36)
Psychoeducational website		2.2	(0.8, 5.66)
Tailored computerised psychoeducation and self-help strategi	es —	2.07	(0.75, 5.32)
Lifestyle factors discussion		1.14	(0.4, 3.3)
Psychoeducational group programme		1.44	(0.51, 4.29)
Psychoeducational group programme + TAU		1.53	(0.51, 5.21)
Interpersonal psychotherapy (IPT)		1.98	(0.97, 4.04)
Interpersonal psychotherapy (IPT) + TAU		2.12	(0.88, 5.47)
Emotion-focused therapy (EFT)		2.52	(0.96, 6.97)
Interpersonal counselling		2.37	(0.87, 6.6)
Non-directive counselling	<b>_</b>	2.1	(0.82, 5.46)
Relational client-centered therapy	<b>_</b>	1.84	(0.54, 5.62)
Problem solving group		1.89	(0.78, 4.88)
Problem solving individual		2.03	(1.01, 4.24)
Problem solving individual + TAU	<b></b>	1.48	(0.61, 3.33)
Problem solving individual + enhanced TAU		1.5	(0.58, 3.5)
Behavioural activation (BA)	— <b>—</b>	3.53	(1.4, 8.92)
Behavioural activation (BA) + TAU	<b></b>	3.83	(1.31, 11.02)
			(continues)
	0.02 0.5 1 2 20	50	
	odds ratio		

3

#### Response (completers)

Intervention (vs Pill Placebo)		odds ratio	95%Crl
			(continued)
Behavioural therapy (Lewinsohn 1976)		4.87	(1.97, 13.14)
Coping with Depression course (individual)		4.66	(1.8, 13.25)
CBT individual (under 15 sessions)		2.98	(1.61, 5.53)
CBT individual (over 15 sessions)		3.14	(1.79, 5.55)
Third-wave cognitive therapy individual		3.24	(1.37, 8.27)
CBT group (under 15 sessions)		3.03	(1.38, 6.7)
CBT group (under 15 sessions) + TAU		3.23	(1.32, 8.55)
CBT group (over 15 sessions)		2.56	(1.08, 5.73)
Coping with Depression course (group)		2.77	(1.12, 6.53)
Coping with Depression course (group) + TAU		3.44	(1.58, 7.75)
Rational emotive behaviour therapy (REBT) group		3.27	(1.38, 8.16)
CBT individual (over 15 sessions) + any AD		7.09	(2.49, 21.2)
CBT individual (over 15 sessions) + any TCA		5.39	(1.9, 14.57)
CBT individual (over 15 sessions) + imipramine		6.53	(2.4, 17.64)
Problem solving individual + any SSRI		2.02	(0.63, 6.61)
Supportive psychotherapy + any SSRI		4.83	(0.92, 25.33)
Interpersonal psychotherapy (IPT) + any AD		7.44	(1.97, 28.19)
Interpersonal psychotherapy (IPT) + imipramine		6.61	(1.34, 30.75)
Short-term psychodynamic psychotherapy individual + Any AD		4.74	(1.8, 12.85)
Short-term psychodynamic psychotherapy individual + any SSRI		4.31	(1.35, 13.78)
CBT individual (over 15 sessions) + Pill placebo		4.41	(1.5, 12.95)
Interpersonal psychotherapy (IPT) + Pill placebo		3.41	(1.1, 9.95)
Exercise + CBT individual (under 15 sessions)		1.44	(0.47, 4.42)
Exercise + Sertraline		1.7	(0.63, 4.67)
0.02	0.5 1 2 20 5 odds ratio	0	

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#### 1 Figure 58: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Response in completers – less severe depression.

No treatment Attention placebo TAU Exercise TCA SSRI Any AD Mirtazapine Short-term psychodynamic psychotherapies Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Behavioural therapies (individual) Behavioural therapies (individual) Behavioural, cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	odds ratio	95%Crl
TAU Exercise TCA SSRI Any AD Mirtazapine Short-term psychodynamic psychotherapies Self-help with support Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	0.59	(0.24, 1.44)
Exercise     -       TCA     -       SSRI     -       Any AD     -       Mirtazapine     -       Short-term psychodynamic psychotherapies     -       Self-help with support     -       Self-help     -       Psychoeducational interventions     -       Interpersonal psychotherapy (IPT)     -       Counselling     -       Problem solving     -       Behavioural therapies (individual)     -       Cognitive and cognitive behavioural therapies (individual)     -       Behavioural, cognitive, or CBT groups     -       Combined (Cognitive and cognitive behavioural therapies individual + AD)     -       Combined (Counselling + AD)     -       Combined (IPT + AD)     -       Combined (Short-term psychodynamic psychotherapies + AD)     -       Combined (psych + placebo)     -	1.37	(0.47, 4.03)
TCA TCA SSRI Any AD Mirtazapine Short-term psychodynamic psychotherapies Self-help with support Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Behavioural therapies (individual) Behavioural therapies (individual) Cognitive and cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Counselling + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	1.27	(0.56, 2.91)
SSRI Any AD Mirtazapine Short-term psychodynamic psychotherapies Self-help with support Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.62	(1.13, 6.05)
Any AD Mirtazapine Short-term psychodynamic psychotherapies Self-help with support Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Counselling + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.77	(1.69, 4.47)
Mirtazapine Short-term psychodynamic psychotherapies Self-help with support Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Behavioural therapies (individual) Behavioural therapies (individual) Cognitive and cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.5	(1.71, 3.71)
Short-term psychodynamic psychotherapies Self-help with support Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Behavioural therapies (individual) Behavioural, cognitive behavioural therapies (individual) Behavioural, cognitive and cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	3.35	(1.12, 10.32)
Self-help with support Self-help Psychoducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	3.22	(0.69, 16.95)
Self-help Psychoeducational interventions Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Counselling + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.2	(0.88, 5.81)
Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.67	(1.05, 6.97)
Interpersonal psychotherapy (IPT) Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.62	(1.25, 5.45)
Counselling Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	1.36	(0.49, 4.01)
Problem solving Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive behavioural therapies individual + AD) Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.05	(0.9, 4.81)
Behavioural therapies (individual) Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive behavioural therapies (individual) Behavioural, cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.19	(0.84, 5.75)
Cognitive and cognitive behavioural therapies (individual) Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	1.7	(0.79, 3.61)
Behavioural, cognitive, or CBT groups Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	4.19	(1.77, 10.39)
Combined (Cognitive and cognitive behavioural therapies individual + AD) Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	3.12	(1.56, 6.36)
Combined (Problem solving + AD) Combined (Counselling + AD) Combined (IPT + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	3.04	(1.48, 6.28)
Combined (Counselling + AD) Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	6.29	(2.35, 16.73)
Combined (IPT + AD) Combined (Short-term psychodynamic psychotherapies + AD) Combined (psych + placebo)	2.03	(0.5, 8.62)
Combined (Short-term psychodynamic psychotherapies + AD)	4.82	(0.77, 30.51)
Combined (psych + placebo)	7.01	(1.59, 29.76)
	4.51	(1.49, 13.97)
	3.87	(1.29, 11.34)
Combined (Exercise + AD/CBT)	1.58	(0.52, 4.81)

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#### 1 Figure 59: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Response in those randomised – less severe depression.

Response (ITT)			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist		0.34	(0.21, 0.55)
No treatment		0.3	(0.14, 0.61)
Attention placebo		0.82	(0.46, 1.46)
Attention placebo + TAU		0.58	(0.23, 1.26)
TAU		0.65	(0.42, 1.02)
Enhanced TAU		0.85	(0.44, 1.79)
Exercise		1.72	(1.13, 2.63)
Exercise + TAU		1.32	(0.61, 2.55)
Internet-delivered therapist-guided physical activity		1.4	(0.57, 3.03)
Any TCA		1.65	(0.86, 2.91)
Amitriptyline	-	1.98	(1.38, 2.92)
Imipramine		1.6	(1.15, 2.21)
Lofepramine		1.78	(0.97, 3.31)
Any SSRI		1.88	(1.09, 3.79)
Any SSRI + Enhanced TAU		1.77	(1, 3.07)
Citalopram		1.82	(1.26, 2.65)
Escitalopram		1.61	(1.06, 2.28)
Fluoxetine	-	1.91	(1.44, 2.58)
Sertraline	+	1.78	(1.36, 2.31)
Any AD		2.94	(1.69, 5.13)
Mirtazapine		3.83	(1.01, 16.04)
Short-term psychodynamic psychotherapy individual		1.85	(0.98, 3.5)
Cognitive bibliotherapy with support		1.6	(0.82, 3.1)
Computerised behavioural activation with support		2.12	(0.99, 4.54)
Computerised psychodymic therapy with support		3.34	(1.43, 9.14)
Computerised-CBT (CCBT) with support		2.39	(1.28, 4.47)
Computerised-CBT (CCBT) with support + TAU		1.87	(0.82, 4.08)
Cognitive bibliotherapy		1.16	(0.67, 2.02)
Cognitive bibliotherapy + TAU	_	0.87	(0.38, 1.84)
Computerised mindfulness intervention	_ <b>-</b> -	1.23	(0.53, 2.93)
Computerised-CBT (CCBT)		1.54	(0.88, 2.68)
Online positive psychological intervention		0.83	(0.37, 1.77)
Psychoeducational website		1.31	(0.63, 2.8)
Tailored computerised psychoeducation and self-help strategies	┙ ┙ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥ ┥	0.74	(0.28, 1.66)
Lifestyle factors discussion	-	0.94	(0.43, 1.99)
Psychoeducational group programme		1.14	(0.57, 2.29)
Psychoeducational group programme + TAU		1.27	(0.6, 2.83)
Interpersonal psychotherapy (IPT)		1.41	(0.79, 2.51)
Interpersonal counselling		2.1	(0.9, 5.3)
Non-directive counselling		1.54	(0.75, 3.1)
Wheel of wellness counselling		1.58	(0.68, 3.6)
Problem solving individual + enhanced TAU		0.58	(0.17, 1.93)
Behavioural activation		4.7	(2.34, 9.48)
CBT individual (under 15 sessions)		2.29	(1.23, 4.2)
CBT individual (under 15 sessions) + TAU		2.85	(1.47, 5.71)
CBT individual (over 15 sessions)		2.49	(1.57, 3.94)
CBT individual (over 15 sessions) + TAU		1.29	(0.36, 3.25)
Rational emotive behaviour therapy (REBT) individual		2.54	(1.27, 5.08)
Third-wave cognitive therapy individual		3.1	(1.6, 6.33)
Third-wave cognitive therapy individual + TAU		2.98	(1.38, 7.27)
CBT group (under 15 sessions)		1.6	(0.9, 2.9)
CBT group (under 15 sessions) + TAU		1.85	(0.93, 4.12)
Coping with Depression course (group)		1.23	(0.58, 2.42)
Third-wave cognitive therapy group		1.27	(0.63, 2.42)
Third-wave cognitive therapy group + TAU		1.52	(0.67, 3.5)
CBT individual (over 15 sessions) + any TCA		3.47	(1.61, 7.43)
CBT individual (over 15 sessions) + imipramine		3.54	(1.52, 8.39)
Supportive psychotherapy + any SSRI		5.28	(1.2, 22.67)
Interpersonal psychotherapy (IPT) + any AD		6.15	(2.08, 18.17)
Interpersonal psychotherapy (IPT) + imipramine		6.22	(1.81, 21.8)
Short-term psychodynamic psychotherapy individual + Any AD		4.83	(1.92, 12.37)
Short-term psychodynamic psychotherapy individual + any SSRI		4.23	(1.52, 11.54)
CBT individual (over 15 sessions) + Pill placebo		8.75	(3.01, 25.23)
Interpersonal psychotherapy (IPT) + Pill placebo	<b>_</b>	8.58	(2.5, 29.43)
Exercise + Sertraline		7.68	(2.77, 21.18)
Cognitive bibliotherapy + escitalopram	<b>;_;•</b> ,	1.74	(0.57, 5.28)
1			
0.02		)	
	odds ratio		

3 4

#### 1 Figure 60: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Response in those randomised – less severe depression.

Class (vs Placebo)		odds ratio	95%Crl
No treatment		0.33	(0.15, 0.67)
Attention placebo		0.71	(0.3, 1.49)
TAU		0.76	(0.39, 1.58)
Exercise		1.49	(0.73, 2.8)
TCA		1.75	(1.11, 2.76)
SSRI	-#-	1.81	(1.29, 2.53)
Any AD		3.01	(1.11, 8.1)
Mirtazapine		3.88	(1.02, 16.2)
Short-term psychodynamic psychotherapies		1.87	(0.65, 5.52)
Self-help with support		2.23	(1.16, 4.35)
Self-help		1.08	(0.58, 1.96)
Psychoeducational interventions		1.13	(0.54, 2.35)
Interpersonal psychotherapy (IPT)		1.43	(0.51, 4.07)
Counselling		1.75	(0.8, 3.83)
Problem solving		0.59	(0.16, 2.18)
Behavioural therapies (individual)		4.79	(2.04, 11.55)
Cognitive and cognitive behavioural therapies (individual)		2.46	(1.39, 4.26)
Behavioural, cognitive, or CBT groups		1.5	(0.83, 2.72)
Combined (Cognitive and cognitive behavioural therapies individual + AD	)	3.56	(1.5, 8.57)
Combined (Counselling + AD)		5.51	(1.15, 25.15)
Combined (IPT + AD)	<b>_</b>	6.53	(2.05, 20.33)
Combined (Short-term psychodynamic psychotherapies + AD)	_ <b></b>	4.69	(1.81, 12.19)
Combined (psych + placebo)		9.11	(2.85, 27.69)
Combined (Exercise + AD/CBT)		7.78	(2.55, 24.7)
Combined (Self-help + AD)		1.72	(0.49, 5.74)
	0.02 0.512 20	50	
	odds ratio		

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

SMD		
Intervention (vs Pill Placebo)		SMD 95%Crl
Waitlist		0.56 (0.26, 0.87)
No treatment		0.72 (0.24, 1.24)
Attention placebo		0.05 (-0.3, 0.42)
Attention placebo + TAU		0.19 (-0.47, 0.91)
TAU Enhanced TAU		0.3 (0.01, 0.59)
Enhanced TAU		0.54 (0, 1.2)
Exercise Exercise + TAU		-0.26 (-0.52, 0) -0.35 (-1.06, 0.3)
Internet-delivered therapist-guided physical activity		-0.21 (-0.77, 0.42)
Any TCA		-0.33 (-0.71, 0.13)
Amitriptyline		-0.48 (-0.74, -0.24)
Imipramine		-0.37 (-0.62, -0.12)
Lofepramine		-0.42 (-0.84, -0.01)
Citalopram		-0.28 (-0.55, 0.05)
Escitalopram		-0.22 (-0.45, 0.05)
Fluoxetine		-0.34 (-0.55, -0.15)
Sertraline	-	-0.26 (-0.44, -0.07)
Any AD		-0.66 (-1.02, -0.29)
Short-term psychodynamic psychotherapy individual		-0.32 (-0.71, 0.06)
Cognitive bibliotherapy with support	┶┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿┿	-0.26 (-0.67, 0.16)
Computerised behavioural activation with support		-0.44 (-0.95, 0.06)
Computerised psychodynamic therapy with support Computerised-CBT (CCBT) with support		-0.82 (-1.49, -0.23) -0.49 (-0.87, -0.11)
Computerised-CBT (CCBT) with support Computerised-CBT (CCBT) with support + TAU		-0.29 (-0.81, 0.28)
Cognitive bibliotherapy		-0.11 (-0.46, 0.23)
Cognitive bibliotherapy + TAU		0.15 (-0.35, 0.69)
Computerised mindfulness intervention	<b>_</b>	-0.15 (-0.76, 0.41)
Computerised-CBT (CCBT)		-0.25 (-0.59, 0.1)
Online positive psychological intervention		0.12 (-0.36, 0.65)
Psychoeducational website		-0.16 (-0.66, 0.32)
Tailored computerised psychoeducation and self-help strategies		0.26 (-0.3, 0.93)
Lifestyle factors discussion		0.06 (-0.43, 0.58)
Psychoeducational group programme		-0.08 (-0.51, 0.36)
Psychoeducational group programme + TAU		-0.13 (-0.65, 0.37)
Interpersonal psychotherapy (IPT)		-0.16 (-0.51, 0.19)
Non-directive counselling Wheel of wellness counselling		-0.15 (-0.6, 0.31) -0.1 (-0.68, 0.48)
Problem solving individual + enhanced TAU		0.72 (-0.07, 1.58)
Behavioural activation (BA)		-0.83 (-1.24, -0.43)
CBT individual (under 15 sessions)		-0.56 (-0.97, -0.16)
CBT individual (under 15 sessions) + TAU		-0.56 (-1, -0.12)
CBT individual (over 15 sessions)		-0.53 (-0.82, -0.24)
CBT individual (over 15 sessions) + TAU		0.15 (-0.61, 1.07)
Rational emotive behaviour therapy (REBT) individual		-0.52 (-0.98, -0.07)
Third-wave cognitive therapy individual		-0.64 (-1.09, -0.21)
Third-wave cognitive therapy individual + TAU		-0.63 (-1.23, -0.1)
CBT group (under 15 sessions)		-0.2 (-0.56, 0.15)
CBT group (under 15 sessions) + TAU		-0.26 (-0.74, 0.16)
Coping with Depression course (group) Third-wave cognitive therapy group		-0.08 (-0.5, 0.4) -0.08 (-0.48, 0.35)
Third-wave cognitive therapy group + TAU	<b>-</b> _	-0.18 (-0.72, 0.36)
CBT individual (over 15 sessions) + any TCA		-0.73 (-1.21, -0.24)
CBT individual (over 15 sessions) + imipramine	<b></b>	-0.77 (-1.32, -0.22)
Supportive psychotherapy + any SSRI	<b>e</b>	-1.3 (-2.77, 0.18)
Interpersonal psychotherapy (IPT) + any AD	<b></b>	-1.42 (-2.09, -0.74)
Short-term psychodynamic psychotherapy individual + Any AD	_ <b>-</b>	-1.07 (-1.74, -0.4)
Short-term psychodynamic psychotherapy individual + any SSRI		-1.07 (-2.3, 0.16)
CBT individual (over 15 sessions) + Pill placebo		-1.26 (-1.93, -0.59)
Exercise + Sertraline		-1.06 (-1.66, -0.45)
Cognitive bibliotherapy + escitalopram		-0.2 (-0.85, 0.44)
	-3 -2 -1 0 1 2	3
	SMD	

3 4

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

SMD	
Class (vs Placebo)	SMD 95%Crl
No treatment	0.64 (0.07, 1.25)
Attention placebo	0.12 (-0.51, 0.8)
TAU	0.41 (-0.15, 1.08)
Exercise	-0.27 (-0.84, 0.29)
TCA	-0.4 (-0.75, -0.03)
SSRI -	-0.27 (-0.56, 0.04)
Any AD	-0.66 (-1.5, 0.19)
Short-term psychodynamic psychotherapies	-0.32 (-1.18, 0.52)
Self-help with support	-0.46 (-0.93, 0)
Self-help	-0.02 (-0.43, 0.41)
Psychoeducational interventions	-0.05 (-0.59, 0.5)
Interpersonal psychotherapy (IPT)	-0.16 (-1, 0.68)
Counselling	-0.13 (-0.82, 0.56)
Problem solving	0.72 (-0.37, 1.85)
Behavioural therapies (individual)	-0.83 (-1.7, 0.04)
Cognitive and cognitive behavioural therapies (individual)	-0.47 (-0.87, -0.04)
Behavioural, cognitive, or CBT groups	-0.16 (-0.56, 0.24)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	-0.75 (-1.42, -0.07)
Combined (Counselling + AD)	-1.3 (-2.94, 0.35)
Combined (IPT + AD)	-1.42 (-2.4, -0.43)
Combined (Short-term psychodynamic psychotherapies + AD)	-1.07 (-2.04, -0.09)
Combined (psych + placebo)	-1.26 (-2.26, -0.26)
Combined (Exercise + AD/CBT)	-1.06 (-1.98, -0.12)
Combined (Self-help + AD)	-0.2 (-1.17, 0.76)
-3 -2 -1 0 1 2	3
-3 -2 -1 0 1 2 SMD	0

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Update 2018

### **1.9.21** Appendix 5 - Population: more severe depression

### 2 Figure 63: Odds ratios and 95% credible intervals for every intervention compared to 3 pill placebo. Discontinuation for anfor any reason – more severe depression.

Discontinuation			
Intervention (vs Pill Placebo)		odds rati	o 95%Crl
Waitlist		0.32	(0.07, 1.39)
Attention placebo		0.83	(0.14, 4.72)
Attention placebo + TAU		0.65	(0.12, 3.29)
TAU	<b>_</b>	0.51	(0.12, 1.93)
Enhanced TAU		0.53	(0.12, 2.24)
Exercise		0.24	(0.02, 2.23)
Exercise + TAU		0.31	(0.03, 3.07)
Yoga + TAU	<b>_</b>	0.24	(0.02, 2.57)
Any TCA		0.84	(0.39, 1.8)
Amitriptyline	-	0.84	(0.84, 1.1)
Imipramine	-	0.86	(0.65, 1.13)
Lofepramine	_	0.78	(0.43, 1.3)
Citalopram		0.78	
Escitalopram	1	0.89	(0.67, 1.27)
			(0.65, 1.21)
Fluoxetine		0.83	(0.64, 1.07)
Sertraline	_	0.87	(0.61, 1.26)
Any AD		0.2	(0.02, 2.58)
Mirtazapine		0.76	(0.51, 1.14)
Short-term psychodynamic psychotherapy individual + TAU		0.88	(0.12, 6.28)
Long-term psychodynamic psychotherapy individual		1.06	(0.31, 3.67)
Cognitive bibliotherapy with support + TAU		0.42	(0.08, 2.01)
Computerised-CBT (CCBT) with support		0.3	(0.05, 1.67)
Computerised-problem solving therapy with support		0.4	(0.07, 2.05)
Cognitive bibliotherapy + TAU		0.86	(0.18, 3.88)
Computerised cognitive bias modification		0.81	(0.16, 3.78)
Computerised-CBT (CCBT)		0.79	(0.17, 3.37)
Computerised-CBT (CCBT) + TAU		1.07	(0.24, 4.46)
Computerised-CBT (CCBT) + enhanced TAU		0.72	(0.15, 3.22)
Computerised-problem solving therapy		0.85	(0.18, 3.88)
Psychoeducational group programme		12.69	(1.87, 85.8)
Interpersonal psychotherapy (IPT)		0.34	(0.06, 1.81)
Counselling (any type)		0.38	(0.04, 3.31)
Emotion-focused therapy (EFT)		0.38	(0.04, 3.27)
Non-directive counselling		0.38	(0.05, 2.51)
Relational client-centered therapy		0.38	(0.04, 3.27)
Problem solving group	•	0.12	(0.01, 2.05)
Behavioural activation (BA)		0.89	(0.16, 4.75)
Behavioural activation (BA) + TAU		0.55	(0.09, 3.14)
CBT individual (under 15 sessions)		0.46	(0.11, 1.8)
CBT individual (under 15 sessions) + TAU		0.36	(0.08, 1.41)
CBT individual (under 15 sessions) + enhanced TAU		0.49	(0.11, 2.15)
CBT individual (over 15 sessions)		0.44	(0.11, 1.54)
Third-wave cognitive therapy individual		0.35	(0.07, 1.51)
CBT group (under 15 sessions)		0.63	(0.12, 3.26)
CBT group (over 15 sessions) + TAU		0.57	(0.1, 3.09)
Coping with Depression course (group)		0.64	(0.12, 3.48)
Third-wave cognitive therapy group	<b>_</b>	0.64	(0.11, 3.62)
CBT individual (under 15 sessions) + escitalopram		0.79	(0.24, 2.59)
CBT individual (over 15 sessions) + amitriptyline	<b>_</b>	0.6	(0.14, 2.34)
CBT individual (over 15 sessions) + any SSRI	<b>_</b>	0.47	(0.1, 1.8)
Short-term psychodynamic psychotherapy individual + any TCA		1.27	(0.27, 5.88)
Long-term psychodynamic psychotherapy individual + fluoxetine		2.16	(0.66, 7.19)
	0.02 0.51 2 20 5 odds ratio		(

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

Discontinuation			
Class (vs Placebo)		odds ratio	95%Crl
No treatment		0.32	(0.06, 1.66)
Attention placebo		0.73	(0.12, 3.96)
TAU		0.52	(0.12, 2.19)
Exercise	<b>e</b>	0.26	(0.03, 2.53)
TCA		0.83	(0.52, 1.28)
SSRI	-	0.87	(0.62, 1.24)
Any AD		0.2	(0.01, 2.88)
Mirtazapine	-8-	0.76	(0.51, 1.14)
Short-term psychodynamic psychotherapies	<b>_</b>	0.88	(0.1, 7.21)
Long-term psychodynamic psychotherapies		1.06	(0.25, 4.63)
Self-help with support		0.37	(0.07, 1.84)
Self-help		0.84	(0.19, 3.51)
Psychoeducational interventions		→ 12.74	(1.58, 99.68)
Interpersonal psychotherapy (IPT)		0.34	(0.05, 2.16)
Counselling		0.38	(0.05, 2.92)
Problem solving	<	0.12	(0.01, 2.31)
Behavioural therapies (individual)	<b>_</b>	0.7	(0.12, 3.87)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	<b>_</b>	0.42	(0.1, 1.54)
Behavioural, cognitive, or CBT groups		0.62	(0.11, 3.23)
Combined (Cognitive and cognitive behavioural therapies individual + AD)		0.6	(0.16, 2.1)
Combined (Short-term psychodynamic psychotherapies + AD)		1.27	(0.22, 7.24)
Combined (Long-term psychodynamic psychotherapies + AD)		2.16	(0.51, 9.34)
	0.02 0.5 1 2 20 odds ratio	50	

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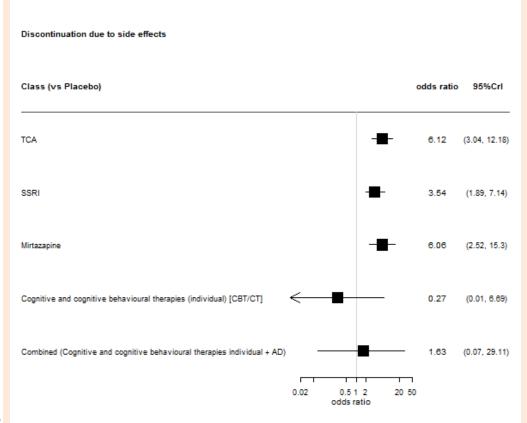
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#### 1 Figure 65: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Discontinuation due to side effects – more severe depression.

Intervention (vs Pill Placebo)				odds ratio	95%Crl
Алу ТСА				6.19	(2.23, 16.74)
Amitriptyline			•	5.93	(3.27, 10.98)
Imipramine			₽	6.85	(3.84, 12.63)
Lofepramine				5.59	(2.14, 12.97)
Citalopram				4.08	(2.03, 9.25)
Escitalopram			-	3.56	(1.76, 7.85)
Fluoxetine			•	2.89	(1.68, 5.24)
Sertraline			-	3.68	(1.69, 8.95)
Mirtazapine				6.06	(2.52, 15.3)
CBT individual (under 15 sessions)	<i>←</i>	•		0.27	(0, 6.82)
CBT individual (over 15 sessions)	<i>←</i>	•		0.27	(0.01, 6.49)
CBT individual (under 15 sessions) + escitalopram	_		•	1.58	(0.07, 26.44)
CBT individual (over 15 sessions) + amitriptyline	_	_	•	1.69	(0.07, 32.17)

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#### 1 Figure 66: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Discontinuation due to side effects – more severe depression.



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#### 1 Figure 67: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Remission in completers – more severe depression.

Remission (completers)

Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist		- 2.64	(0.13, 48.33)
TAU		4.68	(0.51, 45.79)
Exercise + TAU		► 10.69	(0.61, 198.94)
Алу ТСА		1.7	(0.52, 5.53)
Amitriptyline		1.58	(0.65, 3.77)
Imipramine		1.81	(0.84, 3.87)
Citalopram		0.94	(0.45, 1.97)
Escitalopram		1.72	(0.9, 3.23)
Fluoxetine		1.28	(0.7, 2.27)
Sertraline	<b>_</b>	1.25	(0.51, 2.97)
Mirtazapine		1.14	(0.33, 3.84)
Short-term psychodynamic psychotherapy individual + TAU		13.28	(0.31, 974.57)
Long-term psychodynamic psychotherapy individual		43.9	(7.64, 270.7)
Computerised-problem solving therapy with support		▶ 78.41	(1.45, 6829.45)
Computerised-CBT (CCBT)		▶ 6.92	(0.48, 92.94)
Computerised-CBT (CCBT) + TAU		► 5.9	(0.41, 80.64)
Computerised-problem solving therapy		► 6.44	(0.42, 92.94)
Interpersonal psychotherapy (IPT)		• 13.71	(1.39, 147.38)
Behavioural activation (BA)		► 16.91	(1.94, 163.69)
Behavioural activation (BA) + TAU		• 16.1	(1.58, 176.09)
CBT individual (under 15 sessions) + TAU		• 13.32	(1.78, 106.27)
CBT individual (over 15 sessions)		• 15.99	(2.84, 102.1)
CBT group (over 15 sessions) + TAU		• 10.25	(0.6, 187.73)
CBT individual (under 15 sessions) + escitalopram		2.74	(0.58, 12.78)
CBT individual (over 15 sessions) + amitriptyline		2.84	(0.51, 15.64)
Short-term psychodynamic psychotherapy individual + any TCA		× 8.06	(0.85, 86.4)
Long-term psychodynamic psychotherapy individual + fluoxetine		► 135.91	(18.03, 1598.79)
0.02	0.51 2 20 odds ratio		

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#### 1 Figure 68: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Remission in completers – more severe depression.

Remission (completers)					
Class (vs Placebo)			c	odds ratio	95%Crl
No treatment			$\rightarrow$	2.64	(0.12, 53.38)
TAU	-		$\rightarrow$	4.68	(0.45, 51.88)
Exercise	-		<b>→</b>	10.71	(0.55, 217.02)
TCA				1.7	(0.68, 4.17)
SSRI				1.27	(0.62, 2.51)
Mirtazapine	_	-		1.14	(0.33, 3.84)
Short-term psychodynamic psychotherapies			<b>→</b>	13.3	(0.28, 1037.95)
Long-term psychodynamic psychotherapies				43.9	(6.57, 313.25)
Self-help with support			$\rightarrow$	78.81	(1.36, 7259.02)
Self-help	-		<b>→</b>	6.42	(0.44, 87.88)
Interpersonal psychotherapy (IPT)			<b>→</b>	13.71	(1.23, 165.84)
Behavioural therapies (individual)			↦	16.51	(1.72, 171.57)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]			$\mapsto$	14.6	(2.23, 106.17)
Behavioural, cognitive, or CBT groups	-		→	10.25	(0.55, 205.82)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	-			2.79	(0.53, 14.21)
Combined (Short-term psychodynamic psychotherapies + AD)			$\rightarrow$	8.04	(0.75, 97.71)
Combined (Long-term psychodynamic psychotherapies + AD)		· ·	$\rightarrow$	136.59	(15.78, 1786.48)
0.		• •	20 50		

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#### 1 Figure 69: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Remission in those randomised – more severe depression.

Remission (ITT)			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist		3.52	(0.22, 54.98)
TAU		3.8	(0.46, 30.78)
Exercise + TAU	<b>_</b> >	7.64	(0.5, 118.99)
Any TCA		1.35	(0.41, 4.41)
Amitriptyline		1.19	(0.51, 2.82)
Imipramine		1.52	(0.73, 3.17)
Citalopram		0.86	(0.42, 1.77)
Escitalopram		1.51	(0.82, 2.77)
Fluoxetine		1.19	(0.68, 2.1)
Sertraline	<b>_</b>	1.13	(0.48, 2.62)
Mirtszapine		1.13	(0.35, 3.67)
Short-term psychodynamic psychotherapy individual + TAU	<b>_</b> >	9.42	(0.25, 627.03)
Long-term psychodynamic psychotherapy individual		12.76	(2.68, 62.43)
Computerised-problem solving therapy with support		62.61	(1.78, 4999.03)
Computerised-CBT (CCBT)	<b>_</b> • • •	5.44	(0.47, 62.43)
Computerised-CBT (CCBT) + TAU	<b>=</b> >>	4.68	(0.41, 54.38)
Computerised-problem solving therapy	<b>_</b> →	5.08	(0.41, 62.93)
Interpersonal psychotherapy (IPT)	<b>_</b> •	13.69	(1.58, 125.34)
Behavioural activation (BA)	<b>_</b> _>	11.78	(1.55, 91.38)
Behavioural activation (BA) + TAU	<b>∎</b> →	12.09	(1.37, 107.34)
CBT individual (under 15 sessions) + TAU	<b>_</b> _	11.44	(1.73, 74.89)
CBT individual (over 15 sessions)	<b>∎</b> →	13.37	(2.68, 71.16)
CBT group (over 15 sessions) + TAU	<b>∎</b> →	8.43	(0.6, 124.96)
CBT individual (under 15 sessions) + escitalopram		1.99	(0.47, 8.67)
CBT individual (over 15 sessions) + amitriptyline		2.25	(0.46, 11.8)
Short-term psychodynamic psychotherapy individual + any TCA		2.1	(0.3, 14.7)
Long-term psychodynamic psychotherapy individual + fluoxetine		8.44	(1.76, 41.35)
0.02	0.51 2 20 50 odds ratio	0	

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#### 1 Figure 70: Odds ratios and 95% credible intervals for every class compared to pill 2 placebo. Remission in those randomised – more severe depression.

Remission (ITT)				
Class (vs Placebo)			odds ratio	95%Crl
No treatment			→ 3.52	(0.2, 61.56)
TAU		-	3.81	(0.4, 35.13)
Exercise	_		÷ 7.64	(0.45, 130.71)
TCA	-		1.35	(0.58, 3.27)
SSRI	-	-	1.15	(0.58, 2.24)
Mirtazapine		-	1.13	(0.35, 3.67)
Short-term psychodynamic psychotherapies		-	÷ 9.47	(0.24, 655.89)
Long-term psychodynamic psychotherapies			→ 12.79	(2.27, 73.48)
Self-help with support			→ 62.74	(1.64, 5302.85)
Self-help		-	÷ 5.06	(0.43, 59.15)
Interpersonal psychotherapy (IPT)			+ 13.72	(1.39, 140.75)
Behavioural therapies (individual)			→ 11.93	(1.43, 100.08)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]			→ 12.35	(2.12, 74.44)
Behavioural, cognitive, or CBT groups	-	-	÷ 8.45	(0.55, 137.69)
Combined (Cognitive and cognitive behavioural therapies individual + AD)			2.12	(0.48, 10.25)
Combined (Short-term psychodynamic psychotherapies + AD)		-	2.1	(0.26, 16.93)
Combined (Long-term psychodynamic psychotherapies + AD)			8.44	(1.46, 49.4)
г 0.0	0.5	1 2 20 s ratio	50	

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#### 1 Figure 71: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Response in completers – more severe depression.

Response (completers)			
Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist	$\rightarrow$	416.13	(17.06, 14371.47)
No treatment	→	416.55	(19.69, 11884.62)
Attention placebo + TAU -		2.98	(0.37, 24.43)
TAU		2.44	(0.56, 11.42)
Enhanced TAU -		2.13	(0.41, 11.91)
Exercise		18.14	(0.91, 409.12)
Exercise + TAU	<b>-</b> →	19.03	(1.18, 372.78)
Yoga + TAU		17.06	(0.89, 378.8)
Any TCA		4.33	(2, 10.69)
Amitriptyline	-	3.98	(2.6, 6.12)
Imipramine	-	4.22	(2.83, 6.37)
Lofepramine		4.34	(2.22, 9.27)
Citalopram		2.02	(1.13, 3.38)
Escitalopram		2.54	(1.58, 4.24)
Fluoxetine	-	2.4	(1.61, 3.63)
Sertraline		2.09	(1.19, 3.47)
Any AD -	<b>→</b>	6.38	(0.4, 106.91)
Mirtazapine		3.39	(1.55, 7.46)
Short-term psychodynamic psychotherapy individual + TAU	<b>→</b>	8.47	(0.71, 108.09)
Cognitive bibliotherapy with support + TAU	<b></b> • →	5.64	(0.59, 52.98)
Cognitive bibliotherapy + TAU -		2.4	(0.41, 15.12)
Computerised-CBT (CCBT) -		2.59	(0.44, 16.3)
Computerised-CBT (CCBT) + TAU -		2.38	(0.39, 14.76)
Computerised-CBT (CCBT) + enhanced TAU -		2.39	(0.41, 14.5)
Interpersonal psychotherapy (IPT)		12.17	(0.47, 338.66)
Counselling (any type)	<b>→</b>	6.22	(0.71, 56.94)
Non-directive counselling		6.27	(0.87, 46.67)
Problem solving group	-	14472.42	(377.28, 814231.5)
Behavioural activation (BA)	<b></b> →	12.38	(2.05, 77.63)
Behavioural activation (BA) + TAU	<b>-</b> →	11.53	(1.76, 80.24)
CBT individual (under 15 sessions)		8.46	(2.17, 33.68)
CBT individual (under 15 sessions) + TAU		8.15	(1.84, 36.53)
CBT individual (under 15 sessions) + enhanced TAU		9.84	(2.24, 45.51)
CBT individual (over 15 sessions)		9.07	(2.36, 35.73)
Third-wave cognitive therapy individual		10.06	(2.29, 48.23)
CBT group (under 15 sessions)	-	<del>378</del> 9.54	(377.66, 38177.44)
Third-wave cognitive therapy group	-	<del>371</del> 0.79	(328.32, 41772.77)
CBT individual (under 15 sessions) + escitalopram		4.67	(1.06, 21.43)
CBT individual (over 15 sessions) + amitriptyline		4.85	(1, 24.93)
CBT individual (over 15 sessions) + any SSRI		4.95	(1.03, 25.58)
Interpersonal psychotherapy (IPT) + any AD	<b>→</b>	20.7	(0.78, 588.16)
Short-term psychodynamic psychotherapy individual + any TCA		6.01	(0.86, 43.6)
Interpersonal psychotherapy (IPT) + Pill placebo	<b>→</b>	14.78	(0.57, 418.22)
	512 2050	)	
	ls ratio		

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

Response (completers)				
Class (vs Placebo)			odds ratio	95%Crl
No treatment			→ 414.06	(18.23, 12977.86)
Attention placebo			2.98	(0.33, 27.88)
TAU			2.28	(0.47, 12.1)
Exercise			→ 18.12	(1, 379.93)
TCA			4.22	(2.49, 7.49)
SSRI			2.25	(1.37, 3.61)
Any AD			→ 6.36	(0.35, 123.35)
Mirtazapine			3.39	(1.55, 7.46)
Short-term psychodynamic psychotherapies			→ 8.49	(0.66, 116.05)
Self-help with support			→ 5.66	(0.55, 57)
Self-help			2.43	(0.43, 14.4)
Interpersonal psychotherapy (IPT)			→ 12.18	(0.44, 358.02)
Counselling			→ 6.25	(0.78, 51.32)
Problem solving			<del>- 1450</del> 1.39	(357.09, 864580.76)
Behavioural therapies (individual)			→ 11.93	(1.9, 79.36)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]			9.09	(2.35, 38.45)
Behavioural, cognitive, or CBT groups			<del>- 375</del> 1.83	(348.97, 40538.2)
Combined (Cognitive and cognitive behavioural therapies individual +	AD)		4.83	(1.08, 22.9)
Combined (IPT + AD)			→ 20.74	(0.72, 643.55)
Combined (Short-term psychodynamic psychotherapies + AD)			→ 6.01	(0.75, 50.91)
Combined (psych + placebo)			→ 14.81	(0.53, 438.34)
	0.02	0.512 20	50	
	0.02	odds ratio		

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#### 1 Figure 73: Odds ratios and 95% credible intervals for every intervention compared to 2 pill placebo. Response in those randomised – more severe depression.

Intervention (vs Pill Placebo)		odds ratio	95%Crl
Waitlist		0.3	(0.07, 1.18)
No treatment		0.27	(0.05, 1.25)
Attention placebo		0.44	(0.08, 2.52)
Attention placebo + TAU		0.42	(0.09, 2.05)
TAU		0.37	(0.11, 1.19)
Enhanced TAU		0.4	(0.11, 1.48)
Exercise		1.21	(0.18, 7.86)
Exercise + TAU		1.24	(0.21, 7.74)
Amitriptyline	-	2.3	(1.69, 3.16)
mipramine	+	2.06	(1.45, 2.89)
Lofepramine		2.57	(1.42, 5.72)
Ditalopram	+	1.61	(1.12, 2.27)
Escitalopram	+	1.96	(1.44, 2.7)
Fluoxetine	-	1.89	(1.45, 2.49)
Sertraline	-	1.66	(1.14, 2.35)
Any AD		0.07	(0.01, 0.47)
Mirtazapine		2.18	(1.39, 3.43)
Short-term psychodymic psychotherapy individual + TAU	·	0.98	(0.14, 6.58)
Cognitive bibliotherapy with support + TAU		0.67	(0.14, 3.02)
Computerised-CBT (CCBT) with support		0.61	(0.12, 3.03)
Cognitive bibliotherapy + TAU		0.53	(0.13, 2.06)
Computerised cognitive bias modification		0.61	(0.14, 2.58)
Computerised-CBT (CCBT)		0.55	(0.13, 2.16)
Computerised-CBT (CCBT) + TAU		0.63	(0.16, 2.28)
Computerised-problem solving therapy		0.58	(0.14, 2.32)
nterpersonal psychotherapy (IPT)		1.65	(0.38, 7.09)
Emotion-focused therapy (EFT)	<b>_</b>	0.73	(0.13, 4.24)
Non-directive counselling		0.61	(0.16, 2.36)
Relational client-centered therapy		0.52	(0.09, 2.79)
Behavioural activation (BA)		1.86	(0.51, 6.75)
Behavioural activation (BA) + TAU		1.77	(0.43, 7.13)
CBT individual (under 15 sessions)	<b></b>	0.57	(0.2, 1.65)
CBT individual (under 15 sessions) + TAU	_ <b>+</b> _	0.95	(0.25, 3.59)
CBT individual (over 15 sessions)		1.85	(0.59, 5.89)
Third-wave cognitive therapy individual		1.88	(0.46, 9.11)
CBT individual (under 15 sessions) + citalopram		3.19	(1.19, 8.75)
CBT individual (under 15 sessions) + escitalopram		2.56	(0.92, 7.01)
CBT individual (over 15 sessions) + any AD	<b></b>	2.26	(0.57, 7.76)
Third-wave cognitive therapy individual + any AD		3.63	(1.06, 14.25
Exercise + Fluoxetine		28.11	(7.68, 102.51
		0 50	

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

Class (vs Placebo)			odds ratio	95%Crl
No treatment	_		0.28	(0.06, 1.26)
Attention placebo	-		0.44	(0.08, 2.31)
TAU			0.38	(0.11, 1.38)
Exercise			1.22	(0.19, 7.82)
TCA		-	2.3	(1.42, 4.02)
SSRI		-	1.78	(1.22, 2.55)
Any AD	← ■		0.07	(0.01, 0.57)
Mirtazapine		-	2.18	(1.39, 3.43)
Short-term psychodynamic psychotherapies			0.99	(0.13, 7.09)
Self-help with support			0.64	(0.13, 3.1)
Self-help			0.58	(0.15, 2.16)
Interpersonal psychotherapy (IPT)			1.65	(0.34, 7.85)
Counselling			0.62	(0.12, 2.92)
Behavioural therapies (individual)			1.82	(0.47, 7)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]			1.17	(0.37, 3.85)
Combined (Cognitive and cognitive behavioural therapies individual + AD)			2.86	(1, 8.17)
Combined (Exercise + AD/CBT)	0.02	0.51 2	- ■> 28.08 	(6.01, 129.41

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

ntervention (vs Pill Placebo)		SMD 95%Crl
Naitlist		0.63 (-0.09, 1.3
No treatment		0.77 (-0.14, 1.6
Attention placebo		0.69 (-0.31, 1.7)
Attention placebo + TAU		0.65 (-0.13, 1.4
TAU		0.66 (0.05, 1.2
Enhanced TAU		0.6 (-0.06, 1.2
Exercise		0.26 (-0.82, 1.3
Exercise + TAU		0.31 (-0.6, 1.2)
Amitriptyline	-=-	-0.29 (-0.52, -0.0
mipramine	-	-0.41 (-0.64, -0.1
Lofepramine		-0.59 (-1.08, -0.1
Citalopram	+	-0.27 (-0.43, -0.1
Escitalopram	-	-0.33 (-0.47, -0.2
Fluoxetine	-	-0.28 (-0.42, -0.1
Sertraline	-	-0.25 (-0.44, -0.0
Any AD		- 1.38 (-0.06, 2.8
Mirtazapine		-0.2 (-0.53, 0.1
Short-term psychodynamic psychotherapy individual + TAL	, <u> </u>	0.05 (-0.77, 0.8
Cognitive bibliotherapy with support + TAU		-0.02 (-0.74, 0.6
Computerised-CBT (CCBT) with support	<b>e</b>	0.21 (-0.65, 1.1
Cognitive bibliotherapy + TAU		0.49 (-0.24, 1.2
Computerised cognitive bias modification		0.3 (-0.57, 1.1
Computerised-CBT (CCBT)		0.36 (-0.38, 1.0
Computerised-CBT (CCBT) + TAU		0.33 (-0.33, 0.9
Computerised-problem solving therapy		0.33 (-0.44, 1.0
nterpersonal psychotherapy (IPT)		-0.5 (-1.19, 0.1
Emotion-focused therapy (EFT)	<b>e</b>	0.19 (-1.03, 1.3
Non-directive counselling		0.37 (-0.27, 0.9
Relational client-centered therapy		0.56 (-0.58, 1.7
Behavioural activation (BA)		-0.43 (-1.06, 0.2
Behavioural activation (BA) + TAU		-0.31 (-1.21, 0.5
CBT individual (under 15 sessions)		0.48 (-0.05, 0.9
CBT individual (under 15 sessions) + TAU		0.31 (-0.45, 1.0
CBT individual (over 15 sessions)		-0.55 (-1.12, 0.0
Third-wave cognitive therapy individual	<b>-</b> _	-0.81 (-1.79, 0.0
CBT individual (under 15 sessions) + citalopram		-0.68 (-1.23, -0.1
CBT individual (over 15 sessions) + any AD		-0.42 (-1.6, 0.9)
Third-wave cognitive therapy individual + any AD		-0.96 (-2.27, 0.2
Exercise + Fluoxetine	<b></b>	-1.77 (-2.35, -1.2

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

SMD		
Class (vs Placebo)	SMD	95%Crl
No treatment	0.7	(-0.18, 1.58)
Attention placebo	0.67	(-0.25, 1.61)
TAU	0.63	(-0.1, 1.36)
Exercise	0.29	(-0.76, 1.31)
TCA	-0.42	(-0.9, 0)
SSRI -	-0.28	(-0.52, -0.04)
Any AD	→ 1.38	(-0.24, 3.04)
Mirtazapine -	-0.2	(-0.53, 0.13)
Short-term psychodynamic psychotherapies	0.05	(-1.09, 1.17)
Self-help with support	0.09	(-0.79, 0.98)
Self-help	0.36	(-0.36, 1.04)
Interpersonal psychotherapy (IPT)	-0.49	(-1.74, 0.69)
Counselling	0.38	(-0.63, 1.36)
Behavioural therapies (individual)	-0.37	(-1.35, 0.6)
Cognitive and cognitive behavioural therapies (individual) [CBT/CT]	-0.14	(-0.89, 0.57)
Combined (Cognitive and cognitive behavioural therapies individual + AD)	-0.69	(-1.7, 0.34)
Combined (Exercise + AD/CBT)	-1.77	(-2.8, -0.74)
-3 -2 -1 0 1 2 SMD	3	

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