National Guideline Alliance

Version 1.0

Eating disorders: recognition and treatment of eating disorders

Appendix R - Network (Mixed Treatment Comparison) Meta-Analytic Methods Used in the Economic Analysis of Treatments for People with Eating Disorders

NICE Guideline

Methods, evidence and recommendations

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Appendix R: Network (Mixed Treatment Comparison) Meta-Analytic Methods

R.1 Clinical data considered in the network meta-analyses

Clinical data (that is, full remission at the end of treatment) were synthesised using network meta-analytic techniques for the economic models on:

1. psychological, pharmacological, and combination treatments (psychological and pharmacological) for people with BN;
2. psychological (mainly individual) interventions for people with BED;
3. psychological (group) interventions for people with BED.

Psychological individual and group interventions for people with BED could not be analysed in a single network, since there was no common treatment between the 2 networks.

All data were derived from trials included in the relevant guideline systematic reviews.

R.1.1 Interventions for people with BN

Inspection of the relevant data included in the review indicated that 20 RCTs with 1,456 participants provided direct or indirect evidence on full remission associated with the 12 treatment options (that is, waitlist, CBT-ED individual, IPT individual, self-help with support, BT individual, self-help with no support, CBT-ED group, fluoxetine, relaxation, CBT-ED individual plus fluoxetine, BT group, and supportive psychotherapy).

Definitions of 'full remission', in all BN trials, varied. However, only studies that defined full remission as cessation of BN-related symptoms over and above 2 weeks were included. If it was unclear how 'full remission' was defined, the study was reviewed by the GC sub-group and a decision was made whether to include or exclude the study on an individual basis.

The following studies were excluded due to other reasons:

- Pope 1983 comparing imipramine and placebo: in this study imipramine was connected to the rest of the network via a placebo arm with zero events, which exaggerated its relative effect. Following the discussion with the GC it was decided to remove this study from the analysis.
- Mitchell 1990 comparing imipramine and CBT general group: treatments were not connected to the rest of the network.
- Schmidt 2004 comparing fluoxetine and placebo: treatments were not connected to the rest of the network.
- Olmsted 1991 comparing psychoeducation and CBT general individual: treatments were not connected to the rest of the network.
- Walsh 1997: all desipramine arms were excluded since this treatment is not available in the UK.
- Burton 2006 comparing nutritional intervention with waitlist: the GC expressed the view that this nutritional intervention was unlikely to be recommended; also, it was not connected to the rest of the network.
- Mitchell 1990 comparing four types of CBT-ED group removed following inconsistency checks (see Appendix Q).

Also, all treatment as usual (TAU) arms in the data set were excluded since TAU across studies vary and it is not meaningful.

Definitions of ‘full remission’ in all included studies are detailed in Table 1.

The rate of full remission in each arm of a trial was estimated as the number of people in the arm who achieved full remission to treatment, divided by the total number of participants in this arm. It must be noted that a number of trials included in the guideline systematic review reported full remission data, but the definition of full remission did not meet the inclusion criteria; therefore these studies were not considered in the respective network meta-analysis.

Table 1: Definitions of 'full remission' for people with BN in included studies

Study	Definition of full remission
Treasure 1994	No binge eating, vomiting, other weight control behaviours
Banasiak 2005	Resolution of all compensatory behaviours (purging, dietary restriction and excessive exercise) and bingeing over past 28 days
Palmer 2002	No bingeing or purging (likely to be per month)
Sanchez-Ortiz 2011	Did not meet DSM-IV diagnosis for eating disorder
Lee 1986	100% decrease in binge frequency
Leitenberg 1988	Stopped vomiting in the last 3 weeks
Fairburn 2009	Cessation of all eating disorder forms of behaviour present at baseline
Ghaderi 2006	No objective binge eating over past 28 days
Wilson 1991	Abstinence from binge eating over past 28 days
Agras 2000	No binge eating or purging over past 28 days
Fairburn 2015	Cessation of all eating disorder forms of behaviour present at baseline
Fairburn 1993	Cessation of bulimic episodes
Mitchell 2008	Abstinence of binge eating and purging over past 28 days
Cooper 1995	No bulimic episodes over past 28 days
Goldbloom 1997	No binge eating or vomiting episodes over past 28 days
Jacobi 2002	Abstinence of bingeing over past 28 days
Walsh 1997	Abstinence of binging and vomiting over past 28 days
Bailer 2004	No bingeing, vomiting or laxative use in the preceding month
Bulik 1998	No bingeing or purging over the prior fortnight
Wagner 2013b	No BN symptoms as defined by DSM

Table 2: RCTs reporting data on full remission for people with BN considered in the network meta-analysis

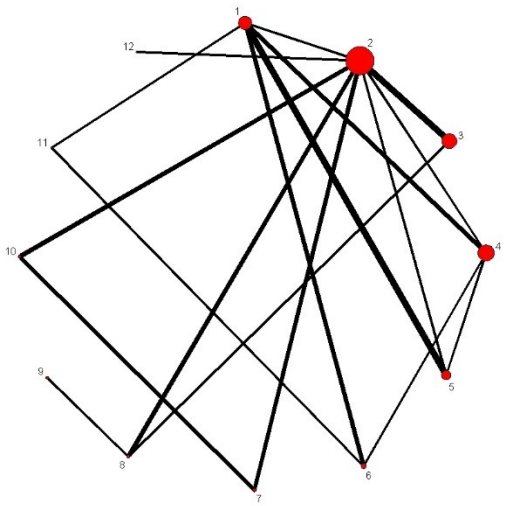
Study	Wait list 1	CBT-ED individual 2	IPT individual 3	Self-help with support 4	Self-help no support 5	CBT-ED group 6	Fluoxetine 7	BT individual 8	Relaxation 9	CBT-ED individual plus fluoxetine 10	BT group 11	Supportive psychotherapy 12
Treasure 1994	2/27	5/28			9/55							
Banasiak 2005	6/54			14/55								
Palmer 2002	0/31			4/28 and 3/30 *	2/32							
Sanchez-Ortiz 2011	1/38				7/38							
Lee 1986	1/15					4/15						
Leitenberg 1988	0/12					1/12					4/13 and 4/13 *	
Fairburn 2009		26/53 and 29/50*										
Ghaderi 2006		22/24 and18/26*										
Wilson 1991		7/11 and 7/11*										
Thomson-Brenner 2016		11/25 and 10/25*										

Study	Wait list 1	CBT-ED individual 2	IPT individual 3	Self-help with support 4	Self-help no support 5	CBT-ED group 6	Fluoxetine 7	BT individual 8	Relaxation 9	CBT-ED individual plus fluoxetine 10	BT group 11	Supportive psychotherapy 12
Agras 2000		35/110	8/110									
Fairburn 2015		22/65	7/65									
Fairburn 1993		9/25	11/25					5/25				
Mitchell 2008		19/66		17/62								
Cooper 1995		7/15						6/16				
Goldbloom 1997		6/24					2/29			3/23		
Jacobi 2002		5/19					2/18			3/16		
Walsh 1997		3/25										2/22
Bailer 2004				1/40		3/41						
Bulik 1998								24/37 and 15/35*	18/39			
Wagner 2013b					12/83 and 11/72*							

1 (*) These are the RCTs categorised by the GC as comparing the same type of intervention

The evidence network constructed from data on full remission for people with BN is presented in Figure 1.

Figure 1: Evidence network of data on full remission for people with BN considered in the network meta-analysis.



Code	Intervention name	Total N
1	WL	177
2	CBT-ED-ind	377
3	IPT	200
4	SH [support]	215
5	SH [no support]	125
6	CBT-ED-gr	68
7	Fluoxetine	47
8	BT-ind	41
9	Relaxation	39
10	CBT-ED ind + fluoxetine	39
11	BT-gr	26
12	Supportive psychotherapy	22

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R.1.2 Network meta-analyses of data on data on full remission – full random effects models – base case

R.1.2.1 Model description

Both random and fixed effects models were run. However, random effects model provided better fit for the data. The random effects model was constructed to estimate the relative effects of each treatment compared to the reference treatment, using data from the 20 RCTs reporting data on full remission summarised in **Error! Reference source not found.**. In the model, the data for each trial j comprised a binomial likelihood:

$$r_{jk} \sim \text{Bin}\,(p_{jk}, n_{jk})$$

where p_{jk} is the probability of the event of interest (that is, full remission) in trial *j* under treatment *k*, r_{jk} is the number of people experiencing the event in trial j under treatment *k*, and n_{jk} is the total number of people at risk of the event in trial *j* under treatment *k*.

Since the parameters of interest, p_{jk}, are probabilities and therefore can only take values between 0 and 1, a transformation (link function) is used that maps these probabilities into a continuous measure between plus infinity and minus infinity. Since this was a Binomial likelihood the logit link function was used. The probabilities of success p_{jk} were modelled on the logit scale as:

$$\text{logit}(p_{jk}) = \mu_j + \delta_{j,1k} I_{\{k \neq 1\}}$$

where

$$I_{\{u\}} = \begin{cases} 1 & \text{if } u \text{ is true} \\ 0 & \text{otherwise} \end{cases}$$

In this set up, μ_i are trial-specific baselines, representing the log-odds of the outcome associated with the waitlist (that is, treatment indexed 1), $\delta_{j,12}$ are the trial-specific log-odds ratios of success (that is, full remission) on the treatment group (2) compared to waitlist (1). This can be expressed as:

$$\text{logit}(p_{j1}) = \mu_j$$

$$\text{logit}(p_{j2}) = \mu_j + \delta_{j,12}$$

where, for a random effects model the trial-specific log-odds ratios come from a common distribution:

$$\delta_{i,12} \sim N(d_{12}, \sigma^2)$$

Generally in the dataset many trials were very small and several had 0 cells (that is, 0 events). These trials with 0 events contributed to a model misfit. As a result, in trials with 0 events 1 was added to the denominator and 0.5 to the numerator to each trial arm (Palmer 2002 and Leitenberg 1988).

R.1.2.2 Baseline selection

The GC reviewed all the trials that used waitlist in the dataset. Since the baseline remission should be as specific as possible to the population of interest and the UK setting the GC judged that it would be more appropriate to obtain the baseline rate of remission associated with the waitlist from a naturalistic study. The GC reviewed available naturalistic studies and decided to use the baseline rate of remission (that is, the natural recovery rate) reported in

the cohort study conducted in the UK by Fairburn and colleagues (2000). The study reported natural recovery rates in untreated population of people with BN. The rate was used to inform the baseline rate of remission associated with the waitlist in BN model.

Using data from Fairburn and colleagues (2000) a fixed effects baseline model (binomial likelihood with logit link) was run. And, then, assuming normality of the posterior distribution of the baseline effect, the posterior summaries (the mean and uncertainty) were obtained and inserted into the relative effect code. The WinBUGS code for the fixed effects baseline model is provided in Table 3.

Table 3: WinBUGS code for a baseline model

```
model{
for(i in 1:ns){
   r[i] ~ dbin(p[i],n[i])                                  # binomial likelihood
   logit(p[i]) <- m                                        # log-odds of response
rhat[i] <- p[i] * n[i]                                     # expected value of numerators
dev[i] <- 2 * (r[i] * (log(r[i])-log(rhat[i]))             # deviance contribution
           +  (n[i]-r[i]) * (log(n[i]-r[i]) - log(n[i]-rhat[i])))
}
totresdev <- sum(dev[])                                    # total residual deviance
m ~ dnorm(0,.0001)                                         # vague prior for mean
logit(R) <- m                                              # posterior probability of response
}
}
```

R.1.2.3 The estimation of the absolute probability of remission

In the BN model the absolute probability of remission p_{jk} of each treatment *k* was estimated based on the treatment effect relative to waitlist added to the absolute probability of remission associated with waitlist. The output of the model used in the economic analysis was the probability of remission for each intervention at the end of treatment (that is, 16 weeks).

R.1.2.4 Approach to the analysis

Analysis was undertaken following Bayesian statistics principles and conducted using Markov chain Monte Carlo simulation techniques implemented in WinBUGS 1.4 (Lunn et al., 2000; Spiegelhalter et al., 2001). In each model the first 70,000 iterations were discarded, and 70,000 further iterations were run. The model was thinned so that every 7th simulation was retained. Consequently, 10,000 posterior simulations were recorded.

The WinBUGS code used to estimate the end of treatment probability of remission is provided in Table 4.

The goodness of fit of the models was tested by comparing the posterior mean of the summed deviance contributions (totresdev) to the number of data points.

Table 4: WinBUGS code used to estimate the probability of remission at the end of treatment of all treatment options

```
model{
for(i in 1:ns){
  w[i,1] <- 0                                                  # adjustment for multi-arm trials is zero for control arm

  delta[i,1] <- 0                                              # treatment effect is zero for control arm
  mu[i] ~ dnorm(0,.0001)                                       # vague priors for all trial baselines
  for (k in 1:na[i]) {
    r[i,k] ~ dbin(p[i,k],n[i,k])                               # binomial likelihood
    logit(p[i,k]) <- mu[i] + delta[i,k]                        # model for linear predictor
     rhat[i,k] <- p[i,k] * n[i,k]                              # expected value of the numerators
     dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))    # deviance contribution
         + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
}
resdev[i] <- sum(dev[i,1:na[i]])                               # summed residual deviance contribution for this trial

for (k in 2:na[i]) {
  delta[i,k] ~ dnorm(md[i,k],taud[i,k])                        # trial-specific LOR distributions
  md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]                   # mean of LOR distributions (with multi-arm correction)
  taud[i,k] <- tau *2*(k-1)/k                                  # precision of LOR distributions (with multi-arm correction)
  w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])               # adjustment for multi-arm RCTs
  sw[i,k] <- sum(w[i,1:k-1])/(k-1)                             # cumulative adjustment for multi-arm trials
   }
}
totresdev <- sum(resdev[])                                     # total residual deviance
d[1]<- 0                                                       # treatment effect is zero for reference treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.0001)}                      # vague priors for treatment effects
sd ~ dunif(0,2)
tau <- pow(sd,-2)

# pairwise ORs and LORs for all possible pair-wise
comparisons
for (c in 1:(nt-1)) {  for (k in (c+1):nt) {
     or[c,k] <- exp(d[k] - d[c])
     lor[c,k] <- (d[k]-d[c])
      }
}

# ranking
for (k in 1:nt) {
  rk[k] <- nt+1-rank(d[],k)                                    # assumes events are “good”
  best[k] <- equals(rk[k],1)                                   # calculate probability that treat k is best
for (h in 1:nt) {prob[h,k] <-equals(rk[k],h) }
}

# absolute effects
A ~ dnorm(meanA,precA)
for (k in 1:nt) { logit(T[k]) <- A + d[k] }                    # based on baseline model for treatment (A) (waitlist)

}
}
```

R.1.2.5 Results

The totresdev of the model was 49.37 (which is good, given that the model has 51 data points).

Summary statistics for all the treatment options for people with BN are provided in Table 5. Results are reported as mean values with 95% credible intervals, which are analogous to confidence intervals in frequentist statistics.

According to the NMA, BT group has the highest probability of remission, however it has very wide credible intervals and the pooled N across all the studies is very small (N=26). BT group is followed by BT-ED individual, CBT general, CBT-ED group, CBT-ED individual, self-help with support, self-help with no support, CBT-ED individual plus fluoxetine, BT individual, IPT, relaxation, fluoxetine, and waitlist.

The GC considered the results, and expressed the view that to inform a recommendation the pooled N for an intervention across all the studies should be 150 or above, any intervention with pooled N less than 30 should not be considered at all, and anything in between could potentially inform a research recommendation.

Table 5: Summary statistics of WinBUGS model (full remission) for people with BN

Node	mean	Sd	MC error	2.50%	median	97.50%	start	sample
T[1]	0.10	0.04	0.00	0.05	0.10	0.19	20001	20000
T[2]	0.32	0.15	0.00	0.09	0.30	0.66	20001	20000
T[3]	0.16	0.11	0.00	0.03	0.13	0.45	20001	20000
T[4]	0.32	0.13	0.00	0.11	0.30	0.61	20001	20000
T[5]	0.30	0.14	0.00	0.09	0.28	0.61	20001	20000
T[6]	0.48	0.21	0.00	0.12	0.47	0.88	20001	20000
T[7]	0.13	0.12	0.00	0.01	0.10	0.46	20001	20000
T[8]	0.16	0.12	0.00	0.02	0.12	0.48	20001	20000
T[9]	0.13	0.12	0.00	0.01	0.09	0.47	20001	20000
T[10]	0.22	0.16	0.00	0.03	0.18	0.62	20001	20000
T[11]	0.72	0.21	0.00	0.24	0.77	0.98	20001	20000
T[12]	0.29	0.22	0.00	0.02	0.23	0.81	20001	20000
d[2]	1.38	0.63	0.01	0.16	1.37	2.66	20001	20000
d[3]	0.29	0.74	0.01	-1.11	0.27	1.83	20001	20000
d[4]	1.37	0.51	0.00	0.40	1.36	2.42	20001	20000
d[5]	1.27	0.57	0.01	0.20	1.26	2.41	20001	20000
d[6]	2.13	0.92	0.01	0.45	2.08	4.05	20001	20000
d[7]	-0.02	0.98	0.01	-1.98	-0.02	1.89	20001	20000
d[8]	0.27	0.85	0.01	-1.41	0.26	1.97	20001	20000
d[9]	-0.06	1.02	0.01	-2.07	-0.08	1.99	20001	20000
d[10]	0.70	0.92	0.01	-1.11	0.69	2.54	20001	20000
d[11]	3.48	1.28	0.01	1.20	3.39	6.24	20001	20000
d[12]	0.97	1.33	0.01	-1.74	0.98	3.50	20001	20000
or[1,2]	4.88	3.71	0.03	1.17	3.93	14.24	20001	20000
or[1,3]	1.79	1.80	0.02	0.33	1.32	6.25	20001	20000
or[1,4]	4.51	2.69	0.02	1.49	3.88	11.25	20001	20000
or[1,5]	4.21	2.89	0.02	1.22	3.52	11.16	20001	20000
or[1,6]	13.41	22.00	0.19	1.57	8.02	57.64	20001	20000
or[1,7]	1.60	2.33	0.02	0.14	0.98	6.58	20001	20000
or[1,8]	1.90	2.24	0.02	0.25	1.30	7.19	20001	20000
or[1,9]	1.64	3.22	0.03	0.13	0.92	7.32	20001	20000
or[1,10]	3.12	4.30	0.04	0.33	2.00	12.73	20001	20000
or[1,11]	89.28	377.20	3.07	3.31	29.69	513.10	20001	20000
or[1,12]	6.25	13.49	0.10	0.18	2.67	33.16	20001	20000
sd	0.42	0.23	0.00	0.03	0.40	0.92	20001	20000
totresdev	49.37	9.50	0.08	32.40	48.81	69.50	20001	20000

T – absolute probability of remission; d – relative effect to wait list; or – odds ratios; totresdev – total residual deviance; sd – standard deviation

R.1.2.6 Conclusions

According to the base case analysis, CBT-ED individual results in the highest probability of remission for people with BN when treatments with a pooled N less than 150 are excluded. Self-help with support is the second best treatment.

The inconsistency checks did not identify any significant inconsistency in the direct and indirect evidence included in the NMA. This strengthens the conclusions from the base case analysis.

The bias adjustment sensitivity analysis suggested that bias due to small study effects may be exaggerating the treatment effects in this network. However, as the bias coefficient included 0 in all scenarios and there was no reduction in heterogeneity as a result of the bias adjustment, no strong conclusions about the presence of bias can be made.

For a report on the inconsistency checks and the bias adjustment analyses see Appendix Q.

R.1.3 Interventions for people with BED

R.1.3.1 Psychological (mainly individual) interventions for people with BED

Inspection of the relevant data included in the review indicated that 8 RCTs with 712 participants provided direct or indirect evidence on full remission associated with the 6 treatment options (that is, waitlist, self-help ED specific with support, self-help ED specific with no support, IPT general individual, behavioural weight loss individual [BWLT], and BT group).

R.1.3.2 Psychological (group) interventions for people with BED

Inspection of the relevant data included in the review indicated that only 4 RCTs with 404 participants provided direct or indirect evidence on full remission associated with the 5 treatment options (that is, waitlist, CBT-ED group, IPT-ED group, CBT-ED group plus group diet [gBWLT], and CT group).

Definitions of ‘full remission’, in BED trials also varied. However, again, only studies that defined full remission as cessation of the BED-related symptoms over and above 2 weeks were included. Studies that were excluded for other reasons included Grilo 2005 which was classified by the GC as comparing the same treatment (self-help ED). This treatment classification assumes that the effect of each of the options compared to each of the others is 0 as they are the same intervention. The data suggested however that the two interventions have very different effectiveness in terms of remission rates and this was translated as high heterogeneity in the BED (mainly individual) interventions model. Also, as the study did not contribute to the estimates of the relative effects of self-help ED compared to any of the other treatments it was removed following consultation with the GC. For the same reasons Hilbert 2004 comparing CBT-ED group was removed from the BED group analysis. Safer 2010 comparing DBT group and waitlist was also excluded from the BED group analysis since it was not connected to the rest of the network. All TAU arms in the data set were again omitted.

Definitions of ‘full remission’ in all included studies are detailed in Table 6.

Table 6: Definitions of 'full remission' for people with BED in included studies

Study	Definition of full remission
BED (mainly individual treatment) studies	
Carrard 2011	Abstinence of bingeing over past 28 days
Masson 2013	Abstinence of bingeing over past 28 days
Carter 1988	Ceased bingeing over past 28 days
Alfonsson 2015	Ceased bingeing over past 28 days
Cassin 2008	No longer met the DSM-IV frequency criteria for BED (2 or more binges/week)
Loeb 2000	Ceased bingeing over past 28 days
Ghaderi 2003	Abstinence of bingeing over past 28 days
Wilson 2010	No longer met the DSM-IV frequency criteria for BED
BED (group treatment) studies	
Munsch 2007	No bingeing over past 28 days
Grilo 2011	No bingeing over past 28 days
Nauta 2000	No bingeing over past 28 days
Wilfley 2002	No bingeing over past 28 days

The rate of full remission was estimated in the same way as outlined for BN (section R.1.2.3).

Data on 'full remission' for people with BED that were considered in mainly individual interventions and group therapies NMAs are provided in Table 7 and Table 8, respectively.

Table 7: RCTs reporting data on full remission for people with BED (mainly individual therapies) considered in the network meta-analysis

Study	Waitlist 1	Self-help ED individual (support) 2	Self-help ED individual (no support) 3	IPT general individual 4	Behavioural weight loss (individual) 5	BT group 6
Carrard 2011	3/37	13/37				
Masson 2013	1/30	12/30				
Carter 1988	2/25	17/34	15/35			
Alfonsson 2015	10/50					10/50
Cassin 2008		47/54	31/54			
Loeb 2000		10/20	6/20			
Ghaderi 2003		3/15	4/16			
Wilson 2010		54/66		65/75	52/64	

Table 8: RCTs reporting data on full remission for people with BED (group therapies) considered in the network meta-analysis

Study	Group behavioural weight loss 1	CBT-ED group 2	IPT-ED group 3	CBT-ED group plus group diet (gBWLT) 4	CT group 5
Munsch 2007	7/36	22/44			
Grilo 2011	17/45	20/45		17/35	
Nauta 2000	7/16				14/21
Wilfley 2002		64/81	59/81		

The evidence networks constructed from data on full remission for people with BED receiving mainly individual interventions and group interventions, are presented in Figure 2 and Figure 3, respectively.

Figure 2: Evidence network of data on full remission for people with BED (mainly individual therapies) considered in the network meta-analysis.

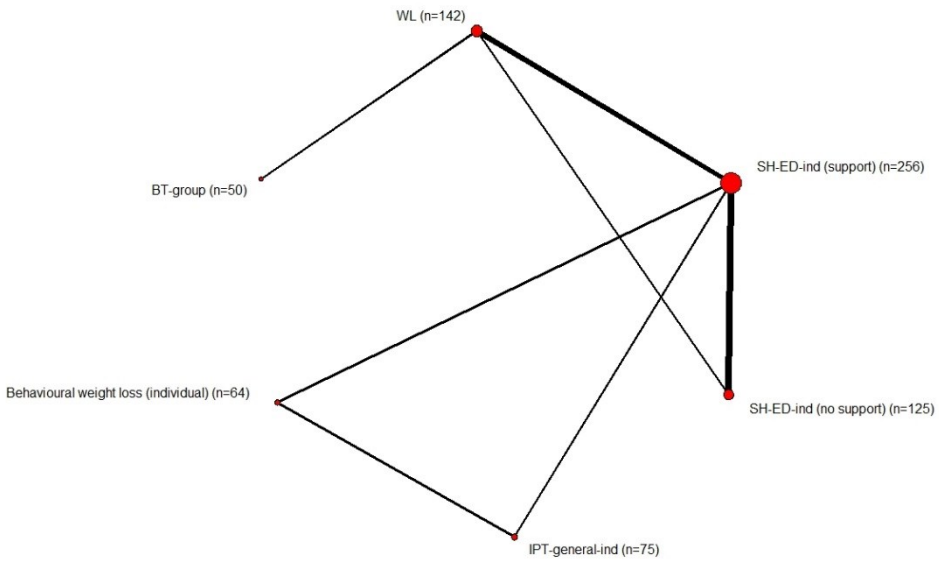
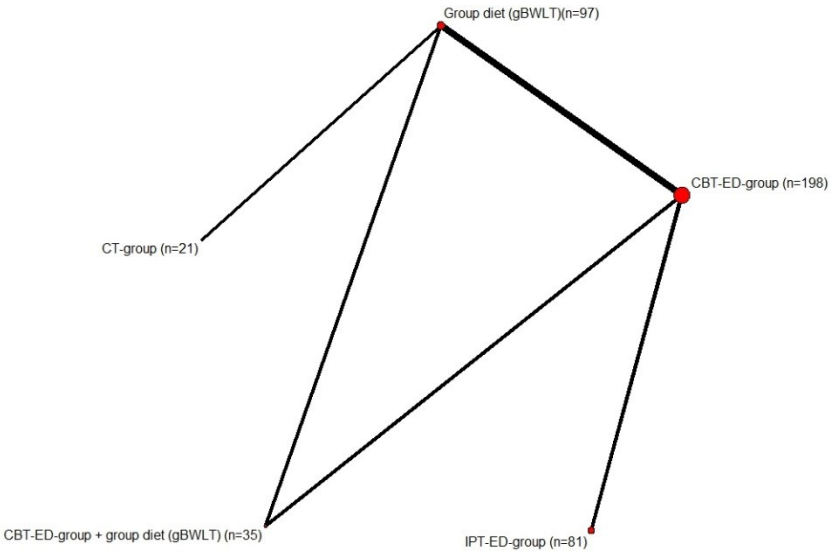


Figure 3: Evidence network of data on full remission for people with BED (group therapies) considered in the network meta-analysis.



R.1.4 Network meta-analyses of data on data on full remission – fixed effects model

R.1.4.1 Model description

Both random and fixed effects models were run. However, fixed effects model provided better fit for the data. As a result, 2 fixed effects models were constructed to estimate the relative effect between k interventions, using data from the 8 RCTs reporting data on full remission for people with BED (mainly individual therapies) and 4 RCTs for people with BED (group therapies) summarised in Table 7 and Table 8, respectively. In the model, the data for each trial j comprised a binomial likelihood:

$$r_{jk} \sim \text{Bin}\ (p_{jk}, n_{jk})$$

where p_{jk} is the probability of the event of interest (that is, full remission) in trial *j* under treatment *k*, r_{jk} is the number of people experiencing the event in trial j under treatment *k*, and n_{jk} is the total number of people at risk of the event in trial *j* under treatment *k*.

Since the parameters of interest, p_{jk}, are probabilities and therefore can only take values between 0 and 1, a transformation (link function) was used that mapped these probabilities into a continuous measure between plus infinity and minus infinity. Also, since this was a Binomial likelihood the logit link function was used. The probabilities of success p_{jk} were modelled on the logit scale as:

$$\text{logit}(p_{ik}) = \mu_i + d_{12} \text{ x } I_{\{k \neq 1\}}$$

where

$$I_{\{u\}} = \begin{cases} 1 & \text{if } u \text{ is true} \\ 0 & \text{otherwise} \end{cases}$$

In the fixed effects model the between-trial heterogeneity σ^2 was set to 0 which was equivalent to assuming homogeneity of the underlying true treatment effects.

R.1.4.21 Baseline selection

The GC reviewed all the trials that used waitlist in the BED (mainly individual) dataset and decided to use the baseline rate of remission (that is, the natural recovery rate) for people with BED reported in the cohort study conducted in the UK by Fairburn and colleagues (2000). The study reported natural recovery rates in an untreated population for BED. This rate was used to inform the baseline rate of remission associated with the waitlist in BED (mainly individual therapies) model.

Since the baseline treatment in the BED (group therapies) relative effects model was gBWLT, the rate of recovery reported in Fairburn and colleagues (2000) for people with BED was judged by the GC to be not appropriate. The GC reviewed all the trials that used the baseline treatment (that is, gBWLT) in the relative effects model and judged that only 1 trial (Grilo 2011) could be considered as representative of the absolute rate of remission associated with gBWLT that would be applicable to the UK setting.

Using data from Fairburn and colleagues (2000) for BED (mainly individual therapies) and the data from Grilo and colleagues (2011) for BED (group therapies) two fixed effects baseline models (binomial likelihood with logit link) were run. And, then, assuming normality of the posterior distribution of the baseline effect, the posterior summaries (the mean and uncertainty) were obtained and inserted into the relevant relative effect code. The WinBUGS code for the fixed effects baseline model is provided in Table 3.

R.1.4.22 The estimation of the absolute probability of remission

In BED (mainly individual treatments) models the absolute probability of remission p_{jk} of each treatment *k* was estimated based on the treatment effect relative to waitlist added to the absolute probability of remission associated with a waitlist. Similarly, in the BED (group treatments) model the absolute probability of remission p_{jk} of each treatment *k* was estimated based on the treatment effect relative to gBWLT added to a the absolute probability of remission associated with gBWLT. The output of the models used in the economic analysis was the probability of remission for each intervention at the end of treatment (that is, 16 weeks).

R.1.4.23 Approach to the analysis

Analysis was undertaken following Bayesian statistics principles as outlined in section R.1.2.4. The goodness of fit of the models was tested using the total residual deviance (totresdev).

The WinBUGS code used to estimate the end of treatment probability of remission is provided in Table 9.

R.1.4.25 Results

The totresdev of the model for BED (mainly individual therapies) was 19.95 (which is acceptable, given that the model has 17 data points) and the totresdev of model for BED (group therapies) was 11.13 (which is acceptable, given that the model has 8 data points)

Summary statistics for all the treatment options for people with BED (mainly individual therapies) and group therapies are provided in Table 10 and Table 11, respectively. Results are reported as mean values with 95% credible intervals, which are analogous to confidence intervals in frequentist statistics.

According to the NMA (mainly individual therapies), the IPT general individual has the highest end of treatment probability of remission, however it has very wide credible intervals

and the pooled N across all the studies for it is small (N=75). The IPT general individual is followed by BWLT, self-help ED individual with support, self-help individual with no support, BT group, and waitlist.

According to the NMA (group therapies), CT group has the highest end of treatment probability of remission, however the pooled N across all the studies for it is very small (N=21). CT group is followed by CBT-ED group, CBT-ED group plus group diet, IPT-ED group, and gBWLT.

Table 9: WinBUGS code used to estimate the probability of remission at the end of treatment of all treatment options for people with BED – fixed effects model

```
model{
for(i in 1:ns){
  mu[i] ~ dnorm(0,.0001)                                  # vague priors for all trial baselines
  for (k in 1:na[i]) {
    r[i,k] ~ dbin(p[i,k],n[i,k])                          # binomial likelihood
    logit(p[i,k]) <- mu[i] + d[t[i,k]]-d[t[i,1]]          # model for linear predictor
    rhat[i,k] <- p[i,k] * n[i,k]                          # expected value of the numerators
    dev[i,k] <- 2 * (r[i,k] * (log(r[i,k])-log(rhat[i,k]))   # Deviance contribution
        + (n[i,k]-r[i,k]) * (log(n[i,k]-r[i,k]) - log(n[i,k]-rhat[i,k])))
  }
  resdev[i] <- sum(dev[i,1:na[i]])                        # summed residual deviance contribution for
                                                          this trial
}
totresdev <- sum(resdev[])                                # Total Residual Deviance
d[1]<- 0                                                  # treatment effect is zero for reference
                                                          treatment
for (k in 2:nt)  { d[k] ~ dnorm(0,.0001) }                # vague priors for treatment effects

# pairwise ORs and LORs for all possible pair-wise
comparisons
for (c in 1:(nt-1)) {  for (k in (c+1):nt) {
       or[c,k] <- exp(d[k] - d[c])
       lor[c,k] <- (d[k]-d[c])
      }
}

# ranking
for (k in 1:nt) {
   rk[k] <- nt+1-rank(d[],k)                              # assumes events are “good”
   best[k] <- equals(rk[k],1)                             # calculate probability that treat k is best
}

# Absolute effects
A ~ dnorm(meanA,precA)                                    #  both based on baseline fixed effects model
                                                          for WL (BED mainly individual therapies) or
                                                          gBWLT (BED group therapies) arms
for (k in 1:nt) { logit(T[k]) <- A + d[k] }
}
}
```

Table 10: Summary statistics of WinBUGS model (full remission) for people with BED (mainly individual therapies)

Node	Mean	SD	MC error	2.50%	Median	97.5%	Start	Sample
T[1]	0.20	0.07	0.00	0.09	0.19	0.36	20001	20000
T[2]	0.73	0.12	0.00	0.46	0.75	0.92	20001	20000
T[3]	0.56	0.15	0.00	0.26	0.56	0.84	20001	20000
T[4]	0.78	0.13	0.00	0.48	0.81	0.96	20001	20000
T[5]	0.72	0.15	0.00	0.38	0.74	0.93	20001	20000
T[6]	0.21	0.11	0.00	0.06	0.19	0.47	20001	20000
d[2]	2.51	0.48	0.00	1.63	2.49	3.51	20001	20000
d[3]	1.69	0.53	0.01	0.70	1.68	2.77	20001	20000
d[4]	2.89	0.68	0.01	1.59	2.88	4.24	20001	20000
d[5]	2.47	0.66	0.01	1.20	2.46	3.80	20001	20000
d[6]	0.00	0.51	0.00	-1.00	0.00	1.01	20001	20000
or[1,2]	13.88	7.65	0.07	5.12	12.01	33.59	20001	20000
or[1,3]	6.27	3.81	0.03	2.01	5.34	15.98	20001	20000
or[1,4]	22.68	18.41	0.15	4.91	17.82	69.53	20001	20000
or[1,5]	14.79	11.37	0.09	3.32	11.74	44.67	20001	20000
or[1,6]	1.14	0.63	0.01	0.37	1.00	2.75	20001	20000
totresdev	19.95	5.19	0.04	11.76	19.30	31.73	20001	20000

T – absolute probability of remission; d – relative effect to wait list; or – odds ratios; totresdev – total residual deviance; sd – standard deviation

Table 11: Summary statistics of WinBUGS model (full remission) for people with BED (group therapies)

Node	mean	Sd	MC error	2.50%	median	97.50%	start	sample
T[1]	0.27	0.07	0.00	0.16	0.27	0.41	20001	20000
T[2]	0.45	0.11	0.00	0.24	0.44	0.67	20001	20000
T[3]	0.37	0.13	0.00	0.15	0.36	0.65	20001	20000
T[4]	0.43	0.13	0.00	0.20	0.43	0.69	20001	20000
T[5]	0.50	0.17	0.00	0.18	0.49	0.82	20001	20000
d[2]	0.79	0.33	0.00	0.15	0.78	1.43	20001	20000
d[3]	0.44	0.50	0.00	-0.54	0.43	1.41	20001	20000
d[4]	0.72	0.45	0.00	-0.15	0.72	1.60	20001	20000
d[5]	1.00	0.71	0.01	-0.35	0.99	2.41	20001	20000
or[1,2]	2.31	0.78	0.01	1.16	2.19	4.19	20001	20000
or[1,3]	1.76	0.94	0.01	0.58	1.54	4.11	20001	20000
or[1,4]	2.26	1.08	0.01	0.86	2.04	4.95	20001	20000
or[1,5]	3.51	2.89	0.02	0.70	2.68	11.17	20001	20000

Node	mean	Sd	MC error	2.50%	median	97.50%	start	sample
totresdev	11.13	4.08	0.03	5.17	10.47	20.97	20001	20000

T – absolute probability of remission; d – relative effect to wait list; or – odds ratios; totresdev – total residual deviance; sd – standard deviation

R.1.4.63 Conclusions

According to the analysis, self-help ED individual and CBT-ED group result in the highest end of treatment probability of remission for people with BED. It was not possible to compare these two treatments in 1 analysis.

R.21 References

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