Bulimia nervosa

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ABSTRACT

INTRODUCTION: Up to 1% of young women may have bulimia nervosa, characterised by an intense preoccupation with body weight, uncontrolled binge-eating episodes, and use of extreme measures to counteract the feared effects of overeating. People with bulimia nervosa may be of normal weight, making it difficult to diagnose. After 10 years, about half of people with bulimia nervosa will have recovered fully, one third will have made a partial recovery, and 10% to 20% will still have symptoms. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for bulimia nervosa in adults? What are the effects of discontinuing treatment in people with bulimia nervosa in remission? We searched: Medline, Embase, The Cochrane Library, and other important databases up to January 2010 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 27 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: cognitive behavioural therapy (CBT; alone or plus exposure/response prevention enhancement), cognitive orientation therapy, dialectical behavioural therapy, discontinuing fluoxetine in people with remission, guided self-help cognitive behavioural therapy, hypnobehavioural therapy, interpersonal psychotherapy, mirtazapine, monoamine oxidase inhibitors (MAOIs), motivational enhancement therapy, pharmacotherapy plus psychotherapy, pure or unguided self-help cognitive behavioural therapy, reboxetine, selective serotonin reuptake inhibitors (SSRIs), topiramate, tricyclic antidepressants (TCAs), and venlafaxine.

QUESTIONS

INTERVENTIONS

Key points

- Up to 1% of young women may have bulimia nervosa, characterised by an intense preoccupation with body weight, uncontrolled binge-eating episodes, and use of extreme measures to counteract the feared effects of overeating.

  People with bulimia nervosa may be of normal weight, making it difficult to diagnose.

  Obesity has been associated with both an increased risk of bulimia nervosa and a worse prognosis, as have personality disorders and substance misuse.

  After 10 years, about half of people with bulimia nervosa will have recovered fully, one third will have made a partial recovery, and 10% to 20% will still have symptoms.

- Cognitive behavioural therapy for bulimia nervosa (CBT-BN) may improve clinical problems of bulimia nervosa compared with no treatment, and may be as effective in reducing symptoms as interpersonal psychotherapy at 1 year, or as other psychological treatments, or antidepressants. However, we found no RCTs meeting eligibility criteria comparing the efficacy of interpersonal psychotherapy with waiting list control.

  We don't know whether other psychological therapies such as cognitive orientation therapy, hypnobehavioural therapy, dialectical behavioural therapy, or motivational enhancement therapy are more effective than a waiting list control at improving symptoms, as we found only a few trials.

We found insufficient evidence to support enhancing CBT-BN with exposure and response prevention (ERP).

Pure or unguided self-help CBT is likely to be no more effective than waiting list control at reducing binge eating.

The evidence we found for guided self-help CBT is insufficient to judge this intervention because of high attrition in trials.

- Some antidepressant drugs (fluoxetine, citalopram, desipramine, and imipramine) may improve symptoms in people with bulimia nervosa compared with placebo.

  Monoamine oxidase inhibitors (MAOIs) may increase remission rates compared with placebo, but may not reduce bulimic symptoms or depression scores.

  We don't know whether other antidepressants (topiramate, mirtazapine, reboxetine, or venlafaxine) can improve symptoms or remission in people with bulimia nervosa.

- We don't know whether continuation of antidepressant treatment may maintain a reduction in vomiting frequency compared with withdrawing treatment in people in remission.
- We don't know if combining pharmacotherapy with psychotherapy enhances outcome. Trials that have suggested combinations may enhance outcomes have been limited in power.

DEFINITION

Bulimia nervosa is an intense preoccupation with body weight and shape, with regular episodes of uncontrolled overeating (binge eating) associated with extreme measures to counteract the feared effects of the overeating. If a person also meets the diagnostic criteria for anorexia nervosa, then the diagnosis of anorexia nervosa takes precedence. [1] Bulimia nervosa can be difficult to identify because of extreme secrecy about binge eating and purgative behaviour. Weight may be normal, but there is often a history of anorexia nervosa or of restrictive dieting. Some people alternate between anorexia nervosa and bulimia nervosa. Nearly all cases of bulimia nervosa identified in a national community survey featured an additional psychiatric disorder, and common comorbidities were mood, anxiety, impulse control, and substance-misuse disorders. [2] Some RCTs included people with subthreshold bulimia nervosa, or with a related eating disorder, binge-eating disorder. Where possible, only results relevant to bulimia nervosa are reported in this review.

INCIDENCE/ PREVALENCE

In community-based studies, the prevalence of bulimia nervosa is between 0.5% and 1.0% in young women, with an even social-class distribution. [3] [4] [5] [6] [7] About 90% of people diagnosed with bulimia nervosa are women. The numbers presenting with bulimia nervosa in industrialised countries increased during the decade after its recognition in the late 1970s, although the incidence has plateaued or even fallen since then, with an incidence of new diagnoses at 6.6 per 100,000 in 2000. [8] A "cohort effect", with an increasing incidence, has been reported in community surveys. [2] [3] [9] [10] The prevalence of eating disorders such as bulimia nervosa is lower in non-industrialised populations [11] and varies across ethnic groups. African-American women have a lower rate of restrictive dieting compared with white American women, but they have a similar rate of recurrent binge eating. [12]

AETIOLOGY/ RISK FACTORS

The aetiology of bulimia nervosa is complex, but sociocultural pressures to be thin and the promotion of dieting seem to increase risk. [13] One community-based case-control study compared 102 people with bulimia nervosa versus 204 healthy controls, and found higher rates of obesity, mood disorder, sexual and physical abuse, parental obesity, substance misuse, low self-esteem, perfectionism, disturbed family dynamics, parental weight/shape concern, and early menarche in people with the eating disorder. [14] Heritability is high, ranging from 28% to 83% in one review; [15] although it has been suggested that genotypic variations map onto intermediate phenotypes, such as traits of affective instability and impulsivity, rather than onto a "gross" bulimia nervosa phenotype. [15] [16]

PROGNOSIS

A 10-year follow-up study (50 people with bulimia nervosa from a placebo-controlled trial of mianserin treatment) found that 52% of people receiving placebo had fully recovered, and only 9% continued to experience full symptoms of bulimia nervosa. [17] A larger study (222 people from a trial of antidepressants and structured, intensive group psychotherapy) found that, after a mean follow-up of 11.5 years, 11% still met criteria for bulimia nervosa, whereas 70% were in full or partial remission. [18] Short-term studies found similar results: about 50% of people made a full recovery, 30% made a partial recovery, and 20% continued to be symptomatic. [19] One study (102 women) of the natural course of bulimia nervosa found that 31% continued to have the disorder at 15 months and 15% continued to have the disorder at 5 years. [20] Only 28% received treatment during the follow-up period. A 5-year naturalistic study of 23 people with bulimia nervosa found a 74% remission at 5 years, with a 47% probability of relapse within the 5-year follow-up study in those in remission. [21] There are few consistent predictors of long-term outcome. Good prognosis has been associated with shorter illness duration, a younger age of onset, higher social class, and a family history of alcohol abuse. [17] Poor prognosis has been associated with a history of substance misuse, [22] premorbid and paternal obesity, [23] and, in some studies, a personality disorder. [24] [25] [26] [27]

In an evaluation of the response to cognitive behavioural therapy (CBT), outcome was best predicted by early progress (reduction in purging of >70% by session 6). [28] However, a subsequent systematic review of the outcome literature found no consistent evidence to link early intervention with a better prognosis. [29] A systematic review evaluating the cost effectiveness of treatments and prognostic indicators found only 4 consistent pretreatment predictors of poor outcome for treatment of bulimia nervosa: features of borderline personality disorder, concurrent substance misuse, low motivation for change, and a history of obesity. [30] A consistent post-treatment predictor of a better outcome is an early response to treatment. [31] [32] A more recent systematic review (search date 2009, 3 RCTs, 22 retrospective non-controlled studies) also found features of borderline personality disorder to be associated with treatment withdrawal, but this review included studies of eating disorder (not otherwise specified) and anorexia nervosa as well as bulimia nervosa. [33]

AIMS OF INTERVENTION To reduce symptoms of bulimia nervosa; to improve general psychiatric symptoms; to improve social functioning and quality of life; to minimise the adverse effects of treatment.

OUTCOMES **Symptom improvement** Frequency of binge eating or bingeing, abstinence from binge eating or bingeing, frequency of behaviours to reduce weight and counter the effects of binge eating, severity of extreme weight and shape preoccupation, severity of general psychiatric symptoms, severity of depression, improvement in social and adaptive functioning, remission rates, relapse rates, withdrawal rates, **quality of life**, and **adverse effects**.

METHODS *Clinical Evidence* search and appraisal January 2010. The following databases were used to identify studies for this systematic review: Medline 1966 to January 2010, Embase 1980 to January 2010, and The Cochrane Database of Systematic Reviews 2009, Issue 4 (1966 to date of issue). An additional search within The Cochrane Library was carried out for the Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the contributor for additional assessment, using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language containing >20 individuals of whom >80% were followed up. There was no minimum length of follow-up required to include studies. We included studies described as "open", "open label", or not blinded. We included systematic reviews of RCTs and RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. We also searched for systematic reviews and RCTs on the harms of topiramate for eating disorders. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. To aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 41). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of treatments for bulimia nervosa in adults?

OPTION COGNITIVE BEHAVIOURAL THERAPY FOR BULIMIA NERVOSA

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- Cognitive behavioural therapy for bulimia nervosa (CBT-BN) may improve clinical problems of bulimia nervosa compared with no treatment, and may be as effective in reducing symptoms as interpersonal psychotherapy at 1 year, or as other psychological treatments, or antidepressants.

Benefits and harms

CBT for bulimia nervosa (CBT-BN) versus waiting list control, no treatment, or placebo:

We found one systematic review (search date 2007, see further information on studies). [34] The review identified one RCT [35] using a strict definition of CBT-BN as defined in this *Clinical Evidence* review.

Symptom improvement

Compared with waiting list control, no treatment, or placebo CBT for bulimia nervosa (CBT-BN) may be more effective than waiting list control at 4 months at improving binge-eating remission, bulimic symptoms, and depression (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[34] Systematic review	Women with bulimia nervosa Data from 1 RCT Data presented by systematic review from RCT [35]	**Proportion of people not in remission** 12/22 (55%) with CBT for bulimia nervosa (CBT-BN) 18/19 (95%) with waiting list control	RR 0.58 95% CI 0.39 to 0.86	●○○	CBT-BN
Improvement in bulimic symptoms					
[35] RCT **4-armed trial**	77 women with bulimia nervosa In review [34] The remaining arms evaluated "self-monitoring" only, and CBT plus exposure/response prevention	**Change from baseline in frequency of vomiting over 1 week , 4 months of treatment** –8.3 with CBT-BN –0.2 with waiting list control 41 people in this analysis	P <0.05 Not analysed on an intention-to-treat basis, see further information on studies	○○○	CBT-BN
Depression					
[35] RCT **4-armed trial**	77 women with bulimia nervosa In review [34] The remaining arms evaluated "self-monitoring" only, and CBT plus exposure/response prevention	**Change from baseline in Beck Depression Inventory score , 4 months of treatment** –11.1 with CBT-BN –0.7 with waiting list control 41 people in this analysis	P <0.05 Not analysed on an intention-to-treat basis, see further information on studies	○○○	CBT-BN

Adverse effects

No data from the following reference on this outcome. [35]

CBT-BN versus CBT plus exposure/response prevention:

See option on CBT plus exposure/response prevention therapy, p 6 .

CBT-BN versus pure self-help CBT:

We found no RCTs.

CBT-BN versus guided self-help CBT:

See option on guided self-help CBT, p 11 .

CBT-BN versus cognitive orientation therapy:
See option on cognitive orientation therapy, p 13 .

CBT-BN versus interpersonal psychotherapy:
See option on interpersonal psychotherapy, p 13 .

CBT-BN versus hypnobehavioural therapy:
See option on hypnobehavioural therapy, p 15 .

CBT-BN versus dialectical behavioural therapy:
See option on dialectical behavioural therapy, p 17 .

CBT-BN versus motivational enhancement therapy:
See option on motivational enhancement therapy, p 18 .

CBT-BN versus tricyclic antidepressants (TCAs):
See option on TCAs, p 25 .

CBT-BN versus SSRIs:
See option on SSRIs, p 19 .

CBT-BN versus other pharmacotherapy:
We found no RCTs comparing CBT versus monoamine oxidase inhibitors, mirtazapine, serotonin antagonists, or venlafaxine.

CBT-BN versus pharmacotherapy plus psychotherapy:
See option on pharmacotherapy plus psychotherapy, p 31 .

Further information on studies

[35] A total of 10/77 (13%) people enrolled in the study failed to complete treatment. The review [34] found no significant difference in withdrawal rate between CBT-BN and waiting list control in this RCT, although the confidence intervals were wide, and the trial may have lacked power to detect an important difference (withdrawal rate: 5/22 [23%] with CBT-BN *v* 1/19 [5%] with waiting list; RR 4.32, 95% CI 0.55 to 33.79). Waiting list or delayed-treatment control groups are subject to bias because it is not possible to "blind" someone to their allocation. It is difficult to interpret the clinical importance of the statistically significant changes in depression scores.

[34] The systematic review included RCTs of other binge-eating disorders, although most trials were in people with bulimia nervosa (48 RCTs in total, 31 RCTs solely in people with bulimia nervosa), and it reported data separately for bulimia nervosa. It defined CBT as psychotherapy that uses the techniques and models specified by Wilson and Fairburn, [36] but did not specify therapist expertise, the number of sessions, or their content. Classical CBT-BN specifies 19 individual sessions over 20 weeks, conducted by trained therapists, and consists of specific structure and content. [36] The review performed a meta-analysis of all RCTs using this broader definition of CBT than we examine in this option, and found an increased binge-free remission, improved bulimic symptoms, and improved depression when compared with waiting list control. Effect sizes for CBT were large, but >50% of people were still binge eating at the end of treatment. The quality of these RCTs was variable (e.g., 31/48 [65%] of RCTs were not blinded and sample sizes were often small). Regarding harms, the RCTs did not report details of adverse effects, and the systematic review found no significant difference in completion rates between interventions in people with bulimia nervosa, suggesting no major difference in acceptability (9 RCTs, 331 people, proportion of people who withdrew from treatment for any reason: 41/170 [24%] with CBT *v* 19/161 [12%] with waiting list control: RR 1.89, 95% CI 0.83 to 4.30). However, it could not exclude infrequent serious adverse effects.

Comment:

Further research is needed to evaluate the specific and non-specific effects of CBT and other psychotherapies, to explore individual characteristics (such as readiness to change) that may predict response, and to explore the long-term effects of treatment.

An observational study found that group psychotherapy offered very soon after presentation was sometimes perceived as threatening. [17]

Motivation and compliance factors:
Two observational studies found limited evidence that motivation and compliance factors may influence outcomes. [37] [38] One study [37] performed additional analyses of an RCT that compared CBT-BN versus interpersonal therapy. [39] It found that "stage of change" or psychological motivation and greater readiness to change was not related to non-completion, but was associated with a good outcome in those who completed interpersonal therapy. The second study examined the effects of compliance on outcome in 62 people randomised for 16 weeks to guided self-help or to full CBT. [38] At 6 months' follow-up, but not at the end of treatment, binge-eating abstinence rates were greater in those who had completed two or more of the CBT exercises (P = 0.04; CI not reported).

Studies in mixed populations including bulimia nervosa:
One three-armed RCT (154 people with bulimia nervosa or eating disorder not otherwise specified, 57 people with bulimia nervosa) compared CBT-BN versus waiting list control versus an enhanced "transdiagnostic" CBT-BN. [40] Outcome data were not reported separately for people with bulimia nervosa and the RCT did not meet *Clinical Evidence* inclusion criteria for this review. However, it can be noted that non-completion rates were low in people with bulimia nervosa (8/57 [14%]). The RCT found that both forms of CBT significantly improved outcomes from baseline, in people with either bulimia or eating disorder not otherwise specified, but it found no significant difference from baseline with waiting list control. It found no significant difference in outcomes between the two forms of CBT, supporting both forms of CBT in bulimia nervosa.

Clinical guide:
CBT-BN or derivative CBT for bulimia nervosa is likely to be beneficial. Compliance and engagement in therapy are also likely important outcomes. Most patients who have bulimia nervosa should be offered CBT-BN as first-line therapy.

OPTION CBT PLUS EXPOSURE/RESPONSE PREVENTION THERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We found insufficient evidence to support enhancing CBT for bulimia nervosa (CBT-BN) with exposure and response prevention (ERP).

Benefits and harms

CBT plus exposure/response prevention therapy (CBT-ERP) versus waiting list control:
We found two systematic reviews (search dates 2007 [34] and 2005 [41]), which identified the same RCT. [35]

Symptom improvement

Compared with waiting list control CBT plus exposure/response prevention enhancement may be more effective at 4 months at improving depression scores, but no more effective at improving vomiting frequency (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[35] RCT **4-armed trial**	77 women with bulimia nervosa characterised by purging behaviour In review [34] [41] The remaining arms evaluated CBT for bulimia nervosa (CBT-BN) and self-monitoring of calorific intake and vomiting behaviour	**Change from baseline in frequency of vomiting over 1 week , after 4 months of treatment** –6.4 with CBT plus exposure/response prevention (CBT-ERP) of vomiting –0.2 with waiting list control 36 people in this analysis	Difference reported as not significant P value not reported Not analysed on an intention-to-treat basis, see further information on studies	⟷	Not significant
Depression					
[35] RCT **4-armed trial**	77 women with bulimia nervosa characterised by purging behaviour In review [34] [41] The remaining arms evaluated CBT-BN and self-monitoring of calorific intake and vomiting behaviour	**Change from baseline in Beck Depression Inventory Score** –9.9 with CBT-ERP of vomiting –0.7 with waiting list control 36 people in this analysis	P <0.05 Not analysed on an intention-to-treat basis, see further information on studies	○○○	CBT-ERP

Adverse effects

No data from the following reference on this outcome. [35]

CBT-ERP versus CBT-BN:

We found two systematic reviews (search dates 2007 [34] and 2005 [41]), which identified the same RCT. [35]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) We don't know how effective CBT plus exposure/response prevention enhancement and CBT-BN are, compared with each other, at improving binge-eating remission rates, bulimic symptoms, or depression score at 4 months (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[34] Systematic review	Women with bulimia nervosa Data from 1 RCT Data presented by systematic review from RCT [35]	**Proportion of people not in remission** 12/22 (55%) with CBT for bulimia nervosa (CBT-BN) 12/17 (71%) with CBT plus exposure/response prevention (CBT-ERP)	RR 0.77 95% CI 0.47 to 1.26	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[35] RCT **4-armed trial**	77 women with bulimia nervosa characterised by purging behaviour In review [34] [41] The remaining arms evaluated self-monitoring of calorific intake and vomiting behaviour and waiting list control	**Change from baseline in frequency of vomiting over 1 week , after the 4-month treatment period** –8.3 with CBT-BN –6.4 with CBT-ERP 39 people in this analysis	Significance not assessed Not analysed on an intention-to-treat basis, see further information on studies		
Depression					
[35] RCT **4-armed trial**	77 women with bulimia nervosa characterised by purging behaviour In review [34] [41] The remaining arms evaluated self-monitoring of calorific intake and vomiting behaviour and waiting list control	**Change from baseline in Beck Depression Inventory score** –11.1 with CBT-BN –9.9 with CBT-ERP 39 people in this analysis	Significance not assessed Not analysed on an intention-to-treat basis, see further information on studies		

Adverse effects

No data from the following reference on this outcome. [35]

CBT-ERP versus pharmacotherapy alone or pharmacotherapy plus psychotherapy:
We found no RCTs.

Further information on studies

[35] A total of 10/77 (13%) people enrolled in the study failed to complete treatment. The review [34] found no significant difference in withdrawal rate between CBT-ERP and CBT-BN, although the confidence intervals were wide, and the RCT may have lacked power to detect an important difference (withdrawal rate: 5/22 [23%] with CBT-BN *v* 1/17 [5%] with CBT-ERP; RR 3.86, 95% CI 0.50 to 30.06).

[34] The first systematic review also performed a meta-analysis of RCTs using a broader definition of CBT-BN than we examine in this option, and found no significant difference after 4 months' treatment between CBT-ERP and CBT-BN in binge-free remission, bulimic symptoms, or depression score.

Comment: **Clinical guide:**
CBT-ERP treatment is not commonly used for bulimia nervosa.

OPTION PURE OR UNGUIDED SELF-HELP CBT

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- Pure or unguided self-help CBT is likely to be no more effective than waiting list control at reducing binge eating.

Benefits and harms

Pure or unguided self-help CBT versus waiting list, no treatment, or placebo medication:

We found two systematic reviews (search dates 2007 [34] and 2005 [41]), which identified the same RCT, [42] and we found one additional RCT. [43]

Symptom improvement

Compared with waiting list control, no treatment, or placebo Pure or unguided self-help CBT may be no more effective at improving the proportion of women with a 50% reduction in binge eating or purging at 8 weeks, or at improving remission rates at 16 weeks (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[43] RCT **4-armed trial**	91 women with bulimia nervosa The remaining arms evaluated fluoxetine 60 mg daily alone and fluoxetine plus an unguided self-help CBT manual	**Remission rates , after 16 weeks** 5/22 (24%) with unguided self-help CBT manual plus placebo 2/22 (9%) with placebo alone Data provided upon personal communication with trial author	RR 2.50 95% CI 0.54 to 11.54 RCT may have lacked power to detect clinically important differences between groups	⟷	Not significant
Improvement in bulimia symptoms					
[42] RCT **3-armed trial**	85 women with bulimia nervosa In review [34] [41] The remaining arm evaluated a non-specific manual on self-assertion for women (non-specific self-help) Waiting list group had a significantly higher baseline frequency of purging compared with either of the 2 self-help groups	**Proportion of women achieving a 50% reduction in binge eating or purging , 8 weeks** 15/28 (54%) with specifically modified manual for bulimia nervosa (CBT self-help) 9/29 (31%) with waiting list	P = 0.10 RCT may have lacked power to detect significant differences	⟷	Not significant
[42] RCT **3-armed trial**	85 women with bulimia nervosa In review [34] [41] The remaining arm evaluated a specifically modified manual for bulimia nervosa (CBT self-help) Waiting list group had a significantly higher baseline frequency of purging compared with either of the 2 self-help groups	**Proportion of women achieving a 50% reduction in binge eating or purging , 8 weeks** 14/28 (50%) with non-specific manual on self-assertion for women (non-specific self-help) 9/29 (31%) with waiting list control	P = 0.08 RCT may have lacked power to detect clinically important differences between groups	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [42] [43]

Pure or unguided self-help CBT versus CBT for bulimia nervosa:
We found no RCTs.

Pure or unguided self-help CBT versus guided self-help CBT:
We found no RCTs.

Pure or unguided self-help CBT versus fluoxetine:
We found one RCT. [43]

Symptom improvement

Compared with fluoxetine We don't know how effective unguided self-help CBT and fluoxetine are, compared with each other, at improving remission rates at 16 weeks (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[43] RCT **4-armed trial**	91 women with bulimia nervosa The remaining arms evaluated fluoxetine plus an unguided self-help CBT manual and placebo alone	**Remission rate , after 16 weeks** 5/22 (24%) with placebo plus the unguided self-help CBT manual 4/26 (16%) with fluoxetine 60 mg daily alone Data provided upon personal communication with trial author	RR 1.48 95% CI 0.45 to 4.84 RCT may have lacked power to detect clinically important differences between groups	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [43]

Pure or unguided self-help CBT versus pharmacotherapy plus psychotherapy:
See option on pharmacotherapy plus psychotherapy, p 31 .

Further information on studies

[34] In the systematic review, pure self-help CBT was regarded as synonymous with unguided self-help CBT.

[43] In trials with a drug-treatment arm, people randomised to self-help plus placebo were seen regularly by healthcare professionals, and so results may not generalise to self-help, in which there is no contact with healthcare professionals. The results of this RCT should be regarded with caution.

Comment:

Studies in mixed populations:
Pure or unguided self-help CBT versus waiting list, no treatment, or placebo medication: We identified a systematic review (search date 2004), [44] which found no significant difference in abstinence from binge eating between pure self-help and waiting list in patients with binge-eating disorders (4 RCTs; RR 0.70, 95% CI 0.47 to 1.05). **Pure or unguided self-help CBT versus guided self-help CBT:** A systematic review (search date 2005, 13 RCTs), [45] compared pure or unguided CBT with guided self-help CBT (4 RCTs) in a combination of patients with bulimia nervosa, binge-eating disorders (BED) and eating disorder not otherwise specified (EDNOS). It did not perform a meta-analysis separately for patients with bulimia nervosa. It found no significant difference in abstinence from bingeing and purging, eating disorder symptomatology, proportion of withdrawals, psychiatric and mental-state symptomatology, level of interpersonal functioning, and depression.
Clinical guide:
Pure self-help CBT may be a useful first-step in therapy, particularly where access to CBT-BN is problematic.

OPTION GUIDED SELF-HELP CBT

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- The evidence we found for guided self-help CBT is insufficient to judge this intervention because of high attrition in trials.

Benefits and harms

Guided self-help CBT versus waiting list:

We found one systematic review (search date 2007), [34] which identified no RCTs meeting *Clinical Evidence* inclusion criteria (see comment).

Guided self-help CBT versus CBT for bulimia nervosa (CBT-BN):

We found two RCTs (presented in 3 publications). [38] [46] [47]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) We don't know how effective guided self-help CBT and CBT-BN are, compared with each other, at increasing remission of binge vomiting at 43 weeks, or at improving abstinence from binge eating at the end of treatment or at 1 year (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission/abstinence					
[47] RCT	81 people meeting DSM-IV criteria for bulimia nervosa	**Abstinence from binge eating, at the end of treatment** 7% with guided self-help CBT 12% with CBT for bulimia nervosa (CBT-BN) Absolute numbers not reported	RR 1.05 95% CI 0.91 to 1.22	⟷	Not significant
[47] RCT	81 people meeting DSM-IV criteria for bulimia nervosa	**Abstinence from binge eating, at 1 year** 9% with guided self-help CBT 15% with CBT-BN Absolute numbers not reported	RR 1.05 95% CI 0.74 to 1.12	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[38] [46] RCT	62 people with DSM-III-R bulimia nervosa	**Remission rate of binge vomiting , at 16 weeks** 55% with 16 weekly sessions of CBT-BN 13% with 8 fortnightly sessions of guided self-help CBT Absolute numbers not reported	P value not reported		
[38] [46] RCT	62 people with DSM-III-R bulimia nervosa	**Remission of binge vomiting , mean follow-up of 43 weeks from the end of treatment** 71% with 16 weekly sessions of CBT-BN 61% with 8 fortnightly sessions of guided self-help CBT Absolute numbers not reported	ARR +10% 95% CI –17% to +37%	⟷	Not significant
[48] RCT	62 people with DSM-III-R bulimia nervosa Further report of reference [38] [46]	**Remission , at 4 years** 62% with CBT-BN 67% with guided self-help Absolute numbers not reported	P value not reported		

Adverse effects

No data from the following reference on this outcome. [38] [46] [47]

Guided self-help CBT versus unguided self-help CBT:

See option on pure or unguided self-help CBT, p 9 .

Further information on studies

[47] Abstinence rates in the RCT were lower than those reported in other studies (usually about 40% with CBT-BN). Guided self-help therapy was of similar duration (16 weeks), but it differed from CBT-BN in the number of sessions (8 guided self-help sessions *v* 16 CBT-BN sessions). The therapists were the same for both intervention arms.

Comment:

Guided self-help CBT versus waiting list:

We found two RCTs that did not meet *Clinical Evidence* inclusion criteria for this review but, owing to the paucity of data, we have briefly reported these here. [49] [50]

The first RCT compared 4 treatments in patients with bulimia nervosa (59%), binge-eating disorders (23%), and eating disorder not otherwise specified (EDNOS; 18%): self-help CBT manual with minimal guidance (participants received a brief explanation by a therapist of how to use the supplied self-help manual), self-help CBT manual with face-to-face guidance (participants received 4 guidance sessions over 4 months), self-help CBT manual with telephone guidance (participants received the same guidance as the face-to-face group, delivered over the telephone), and waiting list control. [49] The RCT did not provide a separate analysis in patients with bulimia nervosa. It found no significant difference in the proportion of people who improved (at least 25% improvement on the Eating Disorder Examination global score, the objective binge episode, and self-induced vomiting scores) after 4 months between either of the guidance groups and the waiting list group (25% with

minimal guidance *v* 50% with face-to-face guidance *v* 36% with telephone guidance *v* 19% with waiting list; P values not reported).The RCT may have lacked power to detect clinically important effects.

The second RCT (109 women; 95 women with bulimia nervosa and 14 women with subthreshold bulimia nervosa) [50] had a follow-up rate of <80%. The systematic review [34] extracted data for women with bulimia nervosa only from this RCT, and so we have reported these results from the review. It found that guided self-help significantly improved abstinence rates from binge eating compared with waiting list control at end of treatment (17 weeks) (proportion of people continuing to binge: 27/49 [55%] with guided self-help *v* 41/46 [89%] with waiting list control; RR 0.62, 95% CI 0.47 to 0.81). It also found that guided self-help significantly reduced binge-eating frequency compared with waiting list control at end of treatment (mean bulimic symptom scores: 1.33 with guided self-help *v* 2.7 with waiting list control; SMD –0.99, 95% CI –1.42 to –0.56). However, the attrition rate was high and so the results should be interpreted with caution (17/49 [35%] with guided self-help *v* 12/46 [26%] with waiting list control; RR 1.33, 95% CI 0.72 to 2.47). [34]

Clinical guide:
Guided self-help CBT may be a useful alternative therapy, particularly where access to specialist-administered CBT-BN is problematic.

OPTION COGNITIVE ORIENTATION THERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether cognitive orientation therapy is more effective than a waiting list control at improving symptoms, as we found no trials.

Benefits and harms

Cognitive orientation therapy versus no treatment, placebo, or waiting list:

We found no RCTs of cognitive orientation therapy that met our inclusion criteria.

Cognitive orientation therapy versus CBT, pharmacotherapy, or pharmacotherapy plus psychotherapy:

We found no RCTs.

Further information on studies

Comment: **Clinical guide:**
Cognitive orientation therapy is not known to be a commonly used therapy for bulimia nervosa.

OPTION INTERPERSONAL PSYCHOTHERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- Interpersonal psychotherapy may be as effective as CBT for bulimia nervosa (CBT-BN) in reducing symptoms at 1 year. However, we found no RCTs meeting eligibility criteria comparing the efficacy of interpersonal psychotherapy with waiting list control.

Benefits and harms

Interpersonal psychotherapy (IPT) versus no treatment, placebo, or waiting list:

We found no systematic review or RCTs.

IPT versus CBT for bulimia nervosa (CBT-BN):

We found one systematic review (search date 2002). [30]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) Interpersonal psychotherapy may be less effective at increasing the proportion of people who abstain from binge eating and purging at the end of treatment, but not at 1 year. We don't know how effective interpersonal psychotherapy and CBT-BN are, compared with each other, at reducing the frequency of binge eating at the end of treatment or at 1 year (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[30] Systematic review	262 people with bulimia nervosa 2 RCTs in this analysis	**Frequency of binge eating , at the end of treatment** with CBT for bulimia nervosa (CBT-BN) with interpersonal psychotherapy (IPT; 19 sessions over 20 weeks) Absolute results not reported	SMD –0.24 95% CI –0.48 to +0.01	⟷	Not significant
[30] Systematic review	257 people with bulimia nervosa 2 RCTs in this analysis	**Frequency of binge eating , at follow-up** with CBT-BN with IPT (19 sessions over 20 weeks) Absolute results not reported	SMD –0.04 95% CI –0.29 to +0.20	⟷	Not significant
Abstinence					
[30] Systematic review	295 people 2 RCTs in this analysis	**Abstinence from binge eating , at the end of treatment** with CBT-BN with IPT (19 sessions over 20 weeks) Absolute results not reported	RR 1.29 95% CI 1.15 to 1.49	●○○	CBT-BN
[30] Systematic review	220 people Data from 1 RCT	**Abstinence from purging , at the end of treatment** with CBT-BN with IPT (19 sessions over 20 weeks) Absolute results not reported	RR 1.32 95% CI 1.15 to 1.49	●○○	CBT-BN
[30] Systematic review	295 people 2 RCTs in this analysis	**Abstinence from both binge eating and purging , 1 year** with CBT-BN with IPT (19 sessions over 20 weeks) Absolute results not reported	RR 1.08 95% CI 0.94 to 1.22	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [30]

IPT versus pharmacotherapy or pharmacotherapy plus psychotherapy:
We found no systematic review or RCTs.

Further information on studies

Comment: We found one subsequent systematic review of all treatment modalities in bulimia nervosa (search date 2005). [41] It identified no RCTs with IPT not previously identified, and provided a narrative summary of trials with no meta-analyses, and similar conclusions. It noted high attrition rates and absence of reporting on harms. Another systematic review (search date 2007), [34] reported on the same RCTs as the review; [30] however, it did not pool data specifically for the comparison of IPT versus CBT-BN. It found that the RCTs did not report details of adverse effects. It found no significant difference in completion rates between interventions, suggesting no major difference in acceptability. However, it could not exclude infrequent serious adverse effects.

An observational study found that group psychotherapy offered very soon after presentation was sometimes perceived as threatening. [17]

Clinical guide:
In choosing between CBT-BN and IPT, patient preference and therapist expertise might be taken into consideration — albeit that change seems slower with IPT than with CBT-BN.

OPTION HYPNOBEHAVIOURAL THERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether hypnobehavioural therapy is effective at improving symptoms, as we found few trials.

Benefits and harms

Hypnobehavioural therapy (HBT) versus no treatment, placebo, or waiting list:
We found one systematic review (search date 2005), [41] which identified no RCTs. We found one RCT. [51]

Symptom improvement

Compared with no treatment, placebo, or waiting list control We don't know whether hypnobehavioural therapy is more effective than waiting list control at improving abstinence from bingeing and purging during the week after treatment (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Abstinence					
[51] RCT **3-armed trial**	78 women with bulimia nervosa The remaining arm evaluated CBT for bulimia nervosa (CBT-BN) Treatment groups were not balanced at baseline; see further information on studies	**Abstaining from bingeing , the week after treatment (19 treatment sessions over 18 weeks)** 43% with hypnobehavioural therapy (HBT) 4% with waiting list control Absolute numbers not reported	P value not reported		
[51] RCT **3-armed trial**	78 women with bulimia nervosa The remaining arm evaluated CBT-BN	**Abstaining from purging , the week after treatment (19 treatment sessions over 18 weeks)** 33% with HBT	P value not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	Treatment groups were not balanced at baseline; see further information on studies	4% with waiting list control Absolute numbers not reported			

Adverse effects

No data from the following reference on this outcome. [51]

HBT versus CBT for bulimia nervosa (CBT-BN):

We found one RCT. [51]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) We don't know how effective hypnobehavioural therapy and CBT-BN are, compared with each other, at increasing the proportion of people who abstain from bingeing and purging during the week after treatment (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Abstinence					
[51] RCT **3-armed trial**	78 women with bulimia nervosa The remaining arm evaluated waiting list control Treatment groups were not balanced at baseline; see further information on studies	**AR for abstaining from bingeing , the week after treatment (19 treatment sessions over 18 weeks)** 43% with hypnobehavioural therapy (HBT) 50% with CBT for bulimia nervosa (CBT-BN)	P value not reported		
[51] RCT **3-armed trial**	78 women with bulimia nervosa; see comment below The remaining arm evaluated waiting list control Treatment groups were not balanced at baseline; see further information on studies	**AR for abstaining from purging , the week after treatment (19 treatment sessions over 18 weeks)** 33% with HBT 40% with CBT-BN	P value not reported		

Adverse effects

No data from the following reference on this outcome. [51]

HBT versus pharmacotherapy, or pharmacotherapy plus psychotherapy:
We found no RCTs.

Further information on studies

[51] In the RCT, the three treatment arms were not balanced at baseline. People in the CBT-BN group had had a significantly longer duration of bulimic symptoms before study enrolment compared with people in the HBT group (P <0.05).

Comment: **Clinical guide:**
HBT is not known to be a commonly used therapy for bulimia nervosa.

OPTION DIALECTICAL BEHAVIOURAL THERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether dialectical behavioural therapy is more effective than a waiting list control at improving symptoms, as we found few trials.

Benefits and harms

Dialectical behavioural therapy versus placebo, no treatment, or waiting list:
We found two systematic reviews (search dates 2007 [34] and 2005 [41]), which identified one RCT. [52]

Symptom improvement

Compared with placebo, no treatment, or waiting list control Dialectical behavioural therapy may be more effective at 20 weeks than waiting list control at increasing the cessation of binge eating and purging, and at improving bulimic symptom scores or dietary restraint scores, but not at improving depression scores (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[52] RCT	31 women In review [34] [41]	**Cessation of binge eating or purging , 20 weeks** 4/14 (29%) with dialectical behavioural therapy 0/15 (0%) with waiting list control	P <0.05	○○○	dialectical behavioural therapy
[52] RCT	31 women In review [34] [41]	**Bulimic symptom scores , over 20 weeks** with dialectical behavioural therapy with waiting list control Absolute results not reported	SMD –1.35 95% CI –2.17 to –0.53	○○○	dialectical behavioural therapy
[52] RCT	31 women In review [34] [41]	**Dietary restraint scores , over 20 weeks** with dialectical behavioural therapy with waiting list control Absolute results not reported	SMD –0.80 95% CI –1.56 to –0.04	○○○	dialectical behavioural therapy

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[52] RCT	31 women In review [34] [41]	**Depression scores** with dialectical behavioural therapy with waiting list control Absolute results not reported	SMD –0.33 95% CI –1.07 to +0.40	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [52]

Dialectical behavioural therapy versus CBT for bulimia nervosa (CBT-BN), pharmacotherapy, or pharmacotherapy plus psychotherapy:

We found no systematic review or RCTs.

Further information on studies

[52] The RCT found no significant difference in treatment withdrawal rates between dialectical behavioural therapy and waiting list control (12.5% with dialectical behavioural therapy *v* 7.0% with waiting list; RR 1.88, 95% CI 0.19 to 18.6).

Comment: **Clinical guide:**
In choosing between CBT-BN and dialectical behavioural therapy, patient preference and therapist expertise might be taken into consideration — albeit that evidence for dialectical behavioural therapy is weak.

OPTION MOTIVATIONAL ENHANCEMENT THERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether motivational enhancement therapy is effective, as we found few studies.
- We found no direct information from RCTs about whether motivational enhancement therapy is better than no active treatment.

Benefits and harms

Motivational enhancement therapy versus no treatment, placebo, or waiting list:

We found no systematic review or RCTs.

Motivational enhancement therapy versus CBT for bulimia nervosa (CBT-BN):

We found one RCT. [53]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) We don't know how effective motivational enhancement therapy and CBT-BN are, compared with each other, at achieving a clinically significant reduction in binge frequency at 4 weeks (very low-quality evidence)

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[53] RCT	125 people with bulimia nervosa	**Proportion of people with clinically significant reduction (defined as a reduction in symptom score of at least 1 scale point) in binge frequency , after 4 weeks** 23/43 (53%) with 4 sessions of motivational enhancement therapy 17/25 (68%) with CBT for bulimia nervosa (CBT-BN)	RR 1.3 95% CI 0.9 to 1.9	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [53]

Motivational enhancement therapy versus pharmacotherapy, other psychotherapy, or pharmacotherapy plus psychotherapy:

We found no systematic review or RCTs.

Further information on studies

Comment: **Clinical guide:**
Motivational enhancement therapy is more commonly used for anorexia nervosa than for bulimia nervosa. However, as stage of change has been shown to be a predictor of outcome in bulimia nervosa, clinicians might (despite current weak evidence) use such strategies where patients are at a pre-contemplative stage of change.

OPTION SSRIS

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- Some antidepressant drugs (fluoxetine, citalopram) may improve symptoms in people with bulimia nervosa compared with placebo.

Benefits and harms

SSRIs versus placebo or no treatment:

We found two systematic reviews (search dates 2002 [54] and 2005 [41]) and two subsequent RCTs. [55] [56] The second review provided a narrative summary of 6 RCTs (2 RCTs also included in the first systematic review) with no meta-analysis, see comment for further details. [41]

Symptom improvement

Compared with placebo SSRIs (fluoxetine, citalopram, or sertraline) may be more effective at reducing the proportion of people with binge-eating episodes and purging, but may be no more effective at increasing the proportion of people in remission, or at improving depression (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[54] Systematic review	706 people 3 RCTs in this analysis	**Proportion of people who did not achieve clinical improvement (clinical improvement defined as at least 50% reduction in binge-eating episodes)** with fluoxetine 60 mg daily with placebo Absolute results not reported	RR 0.68 95% CI 0.59 to 0.79	●○○	fluoxetine
[55] RCT	20 women	**Reduction in binge-eating episodes , after 8 weeks' treatment** 65% with citalopram 40 mg daily 12% with placebo Absolute numbers not reported	Difference reported as significant P value not reported The RCT did not report methods of randomisation, allocation concealment, or blinding; neither did it report information on numbers selected for eligibility, withdrawals, or details of statistical analyses	⟷	Not significant
[55] RCT	20 women	**Reduction in purging episodes , after 8 weeks' treatment** 56% with citalopram 40 mg daily 7% with placebo Absolute numbers not reported	Difference reported as significant P value not reported The RCT did not report methods of randomisation, allocation concealment, or blinding; neither did it report information on numbers selected for eligibility, withdrawals, or details of statistical analyses	⟷	Not significant
[56] RCT	20 women	**Reduction in binge-eating episodes , after 12 weeks' treatment** 75% with sertraline 100 mg daily 10% with placebo Absolute numbers not reported	P <0.01 The small size of this RCT and insufficient reporting of statistical analyses makes interpretation problematic	○○○	sertraline
[56] RCT	20 women	**Reduction in purging episodes , after 12 weeks' treatment** 55% with sertraline 100 mg daily 8% with placebo Absolute numbers not reported	P <0.01 The small size of this RCT and insufficient reporting of statistical analyses makes interpretation problematic	○○○	sertraline
Remission					
[54] Systematic review	467 people 3 RCTs in this analysis	**Absolute non-remission rates** 81% with fluoxetine 60 mg daily 89% with placebo Absolute numbers not reported	RR 0.89 95% CI 0.76 to 1.03	⟷	Not significant
Depression					
[54] Systematic review	46 people Data from 1 RCT	**Depression** with fluoxetine 60 mg daily with placebo	SMD –0.44 95% CI –1.03 to +0.14	⟷	Not significant

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[54] Systematic review	706 people 3 RCTs in this analysis	**Treatment withdrawal due to adverse effects** with fluoxetine with placebo Absolute results not reported	RR 1.52 95% CI 0.83 to 2.75	⟷	Not significant
[55] RCT	20 women	**Sedation** 38% with citalopram 5% with placebo Absolute numbers not reported	Significance not reported		
[55] RCT	20 women	**Dry mouth** 24% with citalopram 0% with placebo Absolute results not reported	Significance not reported		
[55] RCT	20 women	**Nausea** 6% with citalopram 0% with placebo Absolute numbers not reported	Significance not reported		
[55] RCT	20 women	**Headache** 3% with citalopram 9% with placebo Absolute numbers not reported	Significance not reported		
[56] RCT	20 women	**Adverse effects** with sertraline with placebo Participants in the sertraline group reported sedation (55%), dry mouth (30%), and mild fatigue (8%), and those in the placebo group reported headache (20%), fatigue (12%), and insomnia (6%)			

No data from the following reference on this outcome. [41]

SSRIs versus CBT for bulimia nervosa (CBT-BN):

We found one systematic review (search date 2001), [57] which identified one RCT, [58] and we found one subsequent RCT. [59]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) We don't know how effective fluoxetine and CBT-BN are, compared with each other, at improving binge-eating remission rates, bulimic symptoms, depression, or self-induced vomiting (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[58] RCT **3-armed trial**	76 people In review [57] The remaining arm evaluated CBT for bulimia nervosa (CBT-BN) plus fluoxetine	**Mean bulimic symptoms , after 16 weeks** with CBT-BN alone with fluoxetine alone Absolute results not reported	SMD +0.29 95% CI –0.29 to +0.88	⟷	Not significant
Remission/abstinence					
[58] RCT **3-armed trial**	76 people In review [57] The remaining arm evaluated CBT-BN plus fluoxetine	**Binge-eating remission rate , after 16 weeks** 13% with CBT-BN alone 13% with fluoxetine alone Absolute numbers not reported	RR 0.99 95% CI 0.80 to 1.24	⟷	Not significant
[59] RCT **3-armed trial**	53 people The remaining arm evaluated CBT-BN plus fluoxetine (18 people)	**Abstinence from binge eating , over the month preceding the end of treatment (4 months)** 5/19 (26%) with group-based CBT-BN 2/16 (12%) with fluoxetine	RR 2.11 95% CI 0.47 to 9.43	⟷	Not significant
[59] RCT **3-armed trial**	53 people The remaining arm evaluated CBT-BN plus fluoxetine (18 people)	**Abstinence from self-induced vomiting , over the month preceding the end of treatment (4 months)** 7/19 (37%) with group-based CBT-BN 1/16 (6%) with fluoxetine	RR 5.90 95% CI 0.81 to 42.99	⟷	Not significant
Depression					
[58] RCT **3-armed trial**	76 people In review [57] The remaining arm evaluated CBT-BN plus fluoxetine	**Depression , after 16 weeks** with CBT-BN alone with fluoxetine alone Absolute results not reported	SMD +0.10 95% CI –0.47 to +0.67	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [58] [59]

SSRIs versus other antidepressants:

We found no systematic review or RCTs comparing SSRIs versus other classes of antidepressants.

SSRIs versus pharmacotherapy plus psychotherapy:

See option on pharmacotherapy plus psychotherapy, p 31 .

SSRIs versus pure self-help CBT:

See option on pure or unguided self-help CBT, p 9 .

Further information on studies

[54] The review found that fluoxetine 60 mg daily significantly reduced non-completion rates compared with placebo (completion: 3 RCTs, 706 people; 37% with fluoxetine *v* 40% with placebo; RR 0.82, 95% CI 0.68 to 0.99).

[56] The RCT also found that sertraline 100 mg daily reduced weight after 12 weeks' treatment (20 women reduction in weight: 9% with sertraline *v* 4% with placebo; P <0.01). The small size of this RCT and insufficient reporting of statistical analyses makes interpretation problematic.

[58] The RCT found no significant difference in withdrawal rates between fluoxetine and CBT-BN (39% with fluoxetine *v* 33% with CBT-BN; RR 1.17, 95% CI 0.55 to 2.51).

[59] The RCT found no significant difference in withdrawals with fluoxetine compared with CBT-BN (42% with CBT-BN *v* 25% with fluoxetine; RR 1.68, 95% CI 0.62 to 4.57).

Comment:

SSRIs versus placebo or no treatment:
One review found 6 RCTs comparing fluoxetine versus placebo, and provided a narrative summary of the RCTs with no meta-analysis. [41] The review concluded that, in the short term, fluoxetine 60 mg daily reduced core bulimic symptoms of binge eating and purging, and associated psychological features. It noted high attrition rates in the RCTs. We found a further systematic review (search date 2002), [30] which reported on the same trials. It concluded that there was insufficient evidence that SSRIs increased remission rates or reduced depression, but it did not report data for these outcomes.

For an overview of non-remission rates with tricyclic antidepressants, SSRIs, or monoamine oxidase inhibitors compared with placebo, see table 1, p 40 .

Drug safety alerts and general harms of SSRIs:
In December 2005 the MHRA [60] and the FDA released warnings that paroxetine taken by women during the first trimester of pregnancy may be associated with an increased risk of congenital malformations compared with other antidepressants, and advised practitioners to carefully consider the potential harms and benefits when considering prescribing paroxetine. [61] Furthermore, the MHRA issued an alert in 2010 regarding a possible small increased risk of congenital cardiac defects associated with fluoxetine in early pregnancy, similar to that seen with paroxetine. [62] There is limited robust evidence available to examine the link between SSRIs and increased risk of self-harm or suicide in adults when used as a treatment for depression. However, a subsequent meta-analysis of 53 RCTs investigating suicidality risk following fluoxetine treatment for disorders other than major depression (including 9 trials of bulimia nervosa) did not find any increase in risk of suicidality with fluoxetine compared with placebo. [63] Practitioners should be guided by the recommendations and warnings issued by their national drug regulatory authorities with respect to the prescribing of antidepressants, particularly in children and adolescents.

For further information about harms of antidepressants see harms of antidepressants in review on depression in children and adolescents, and harms of antidepressants in review on depression in adults.

Clinical guide:
SSRIs are likely to be most efficacious for bulimia nervosa when prescribed in high dose (e.g., fluoxetine 60 mg/day). We found no consistent predictors of response to treatment.

OPTION MONOAMINE OXIDASE INHIBITORS (MAOIS)

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- Monoamine oxidase inhibitors (MAOIs) may increase remission rates compared with placebo, but may not reduce bulimic symptoms or depression scores.

Benefits and harms

Monoamine oxidase inhibitors (MAOIs) versus placebo or no treatment:

We found one systematic review (search date 2002, 4 RCTs). [54]

Symptom improvement

Compared with placebo Monoamine oxidase inhibitors (MAOIs) may be more effective at increasing remission rates, but may be no more effective at improving bulimic symptoms or depression scores (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[54] Systematic review	138 people 3 RCTs in this analysis	**Improvement in bulimic symptoms** with monoamine oxidase inhibitors (MAOIs; phenelzine, moclobemide, or brofaromine) with placebo Absolute results not reported	SMD +0.22 95% CI –0.94 to +1.37	⟷	Not significant
Remission					
[54] Systematic review	98 people 2 RCTs in this analysis	**Absolute non-remission rates** 76% with MAOIs (phenelzine or isocarboxazid) 94% with placebo Absolute numbers not reported	RR 0.81 95% CI 0.68 to 0.96	●○○	MAOIs (phenelzine or isocarboxazid)
Depression					
[54] Systematic review	156 people 4 RCTs in this analysis	**Depression scores** with MAOIs (phenelzine or isocarboxazid) with placebo Absolute results not reported	SMD –0.14 95% CI –0.50 to +0.22	⟷	Not significant

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[54] Systematic review	175 people with bulimia 3 RCTs in this analysis	**Withdrawal rates caused by adverse effects** 15/88 (17%) with MAOIs 7/87 (8%) with placebo	RR 2.06 95% CI 0.45 to 9.53	⟷	Not significant

MAOIs versus psychotherapy:

We found no RCTs.

MAOIs versus pharmacotherapy plus psychotherapy:

We found no RCTs.

Further information on studies

Comment: For further information about harms of antidepressants see harms of antidepressants in review on depression in children and adolescents, and harms of antidepressants in review on depression in adults.

MAOIs versus placebo or no treatment:
We identified a second systematic review (search date 2002). [30] It reported no data, but reached the same conclusions as the first review. [54]

For an overview of non-remission rates with TCAs, SSRIs, or MAOIs compared with placebo, see table 1, p 40 .

OPTION TRICYCLIC ANTIDEPRESSANTS (TCAS)

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- Some antidepressant drugs (desipramine and imipramine) may improve symptoms in people with bulimia nervosa compared with placebo.

Benefits and harms

Tricyclic antidepressants (TCAs) versus placebo:

We found two systematic reviews (search date 2002 [54] and search date 2005 [41]). The second systematic review [41] found one RCT, which was already included within the first systematic review so we report the first, more comprehensive, review below.

Symptom improvement

Compared with placebo Tricyclic antidepressants (desipramine and imipramine) may be more effective at increasing clinical improvement (defined as a reduction of 50% in binge-eating episodes) and bulimic symptoms at 11 weeks, but may be no more effective at improving remission rates or depressive symptoms (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[54] Systematic review	44 people 2 RCTs in this analysis	**Clinical improvement (at least 50% reduction in binge-eating episodes) , after a mean of 11 weeks' treatment** with tricyclic antidepressants (TCAs) with placebo Absolute results not reported	RR 0.29 95% CI 0.13 to 0.64	●●○	TCAs
[54] Systematic review	121 people 3 RCTs in this analysis	**Bulimic symptoms , after a mean of 11 weeks' treatment** with TCAs with placebo Absolute results not reported	SMD –0.75 95% CI –1.12 to –0.38	○○○	TCAs
Remission					
[54] Systematic review	132 people 3 RCTs in this analysis	**Absolute non-remission rates** 79% with TCAs (desipramine, imipramine) 91% with placebo	RR 0.86 95% CI 0.70 to 1.07	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Depression					
[54] Systematic review	People with bulimia 3 RCTs in this analysis	**Depressive symptoms** with TCAs with placebo Absolute results not reported	Reported as not significant No further data reported	⟷	Not significant

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[64] RCT	74 young women with bulimia nervosa	**Adverse effects** with desipramine with placebo Absolute results not reported The RCT reported a significant increase in reclining and standing pulse rate, lying systolic and diastolic blood pressure, and greater orthostatic effects on blood pressure with desipramine. Cardiovascular changes were well tolerated, and few people withdrew because of these effects			

No data from the following reference on this outcome. [54] [41]

TCAs versus CBT for bulimia nervosa (CBT-BN):

We found one systematic review (search date 2001), [57] which identified two RCTs. [65] [66]

Symptom improvement

Compared with CBT for bulimia nervosa (CBT-BN) Imipramine may be less effective than group-based CBT-BN at increasing binge-eating remission rate at 10 weeks. We don't know how effective desipramine and CBT-BN (16 weekly sessions with 2 follow-up sessions) are, compared with each other, at improving binge-eating remission rates or bulimic symptoms (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[66] RCT **3-armed trial**	71 people In review [57] The remaining arm evaluated CBT for bulimia nervosa (CBT-BN) plus desipramine	**Bulimic symptoms** with desipramine (mean 167 mg/day) with CBT-BN (16 weekly sessions with 2 follow-up sessions) Absolute results not reported	SMD –0.02 95% CI –0.72 to +0.68	⟷	Not significant
[65] RCT **3-armed trial**	171 people In review [57] The remaining arms evaluated	**Mean reduction in number of binges a week** 3.6 with imipramine 200 mg to 300 mg daily	Between group significance assessment not performed		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	imipramine plus CBT-BN and placebo	8.2 with group-based CBT-BN			
Remission					
[57] Systematic review	People with bulimia nervosa Data from 1 RCT Data presented by systematic review from RCT [65]	**Binge-eating non-remission rate** 45/54 (83%) with imipramine 200 mg to 300 mg daily 17/34 (50%) with group-based CBT-BN	RR 1.67 95% CI 1.17 to 2.38	●○○	CBT-BN
[57] Systematic review	People with bulimia nervosa Data from 1 RCT Data presented by systematic review from RCT [66]	**Binge-eating non-remission rate** 7/12 (58%) with desipramine (mean 167 mg/day) 10/23 (43%) with CBT-BN (16 weekly sessions with 2 follow-up sessions)	RR 1.34 95% CI 0.69 to 2.62	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [65] [66]

TCAs versus pharmacotherapy plus psychotherapy:

See option on pharmacotherapy plus psychotherapy, p 31 .

Further information on studies

[54] The systematic review found that treatment withdrawal for any cause was more likely with TCAs than with placebo (6 RCTs [2 of desipramine, 4 of imipramine], 277 people; treatment withdrawal for any cause: 29% with TCAs *v* 14% with placebo; RR 1.93, 95% CI 1.15 to 3.25).

[65] The RCT found no significant difference in withdrawal rate between TCAs and CBT-BN, although confidence intervals were wide, and an effect cannot be ruled out (RR 5.75, 95% CI 0.67 to 49.50).

[66] The RCT found that withdrawal rate was significantly greater with TCAs than with CBT-BN (43% with TCAs *v* 15% with CBT-BN; RR 2.9, 95% CI 1.22 to 6.89).

Comment:

For further information about harms of antidepressants see harms of antidepressants in review on depression in children and adolescents, and harms of antidepressants in review on depression in adults.

Tricyclic antidepressants (TCAs) versus placebo:
We identified a second broad systematic review (search date 2002) [30] It identified the same studies as the review we report above [54] and found similar results.

For an overview of non-remission rates with TCAs, SSRIs, or MAOIs compared with placebo, see table 1, p 40 .

Clinical guide:
While there is evidence for efficacy of TCAs, the higher attrition rates indicate that they are likely to be less acceptable to patients than CBT-BN. In clinical practice they are most often used as adjunctive therapy to psychotherapy. We found no consistent predictors of response to treatment.

OPTION TOPIRAMATE

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether topiramate can improve symptoms or remission in people with bulimia nervosa, because we found few RCTs.

Benefits and harms

Topiramate versus placebo:

We found one systematic review (search date 2008, 5 RCTs, of these 2 RCTs in people with bulimia nervosa, 3 RCTs in people with binge-eating disorder) comparing topiramate with placebo. [67] This review did not report a critical appraisal of RCTs and did not pool data, so we have only reported the RCT in bulimia nervosa that satisfied *Clinical Evidence* inclusion criteria (see comment).

Symptom improvement

Compared with placebo Topiramate may be more effective at reducing the number of binge and/or purge episodes at 10 weeks (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[68] RCT	60 women with bulimia nervosa In review [67]	**Mean number of binge, purge episodes, or both per week , after 10 weeks** 4.6 with topiramate 250 mg daily 7.9 with placebo	Mean difference: –3.3 95% CI –4.3 to –2.1	○○○	topiramate

Quality of life

Compared with placebo Topiramate may be more effective at improving quality-of-life scores (measured by SF-36) at 10 weeks (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[68] RCT	60 women with bulimia nervosa In review [67]	**Quality of life (SF-36 domain scores) , after 10 weeks** with topiramate 250 mg daily with placebo Absolute results not reported	P <0.001 for physical functioning, role-physical, bodily pain, general health perceptions, vitality, social functioning, role-emotional, and mental health domains	○○○	topiramate

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[68] RCT	60 women with bulimia nervosa In review [67]	**Serious adverse effects** with topiramate 250 mg daily with placebo The RCT reported that no psychotic symptoms, suicidal be-			

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		haviour, or other "serious" adverse events were observed			
[68] RCT	60 women with bulimia nervosa In review [67]	**Sedation** 2/30 (7%) with topiramate 250 mg daily 3/30 (10%) with placebo	Statistical assessment not performed		
[68] RCT	60 women with bulimia nervosa In review [67]	**Dizziness** 1/30 (3%) with topiramate 250 mg daily 2/30 (7%) with placebo	Statistical assessment not performed		
[68] RCT	60 women with bulimia nervosa In review [67]	**Headache** 3/30 (10%) with topiramate 250 mg daily 2/30 (7%) with placebo	Statistical assessment not performed		
[68] RCT	60 women with bulimia nervosa In review [67]	**Paraesthesia** 2/30 (7%) with topiramate 250 mg daily 2/30 (7%) with placebo	Statistical assessment not performed		

Further information on studies

[68] The RCT found that 11 people (18%) did not complete treatment, although the reasons for this were not reported.

Comment: Topiramate is a mood-stabilising anticonvulsant treatment (for partial-onset or primary generalised seizures), and is also used in migraine prophylaxis.

The review reported that one included RCT (not meeting *Clinical Evidence* inclusion criteria because of a low follow-up rate and so not reported here) found that adverse effects were reported more frequently with topiramate compared with placebo (e.g., paraesthesia: 8/34 [24%] with topiramate *v* 2/34 [6%] with placebo). However, it reported that adverse effects were not more frequent in the RCT [68] reported above (see above). The participants in this other RCT were older (mean age about 30 years) than the participants in the RCT reported above (mean age about 21 years), and thereby possibly more susceptible to and less tolerant of adverse effects. [67]

Clinical guide:
Topiramate may have a role in bulimia nervosa treatment, but adverse effects may be problematic. Long-term outcome is unknown.

OPTION MIRTAZAPINE

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether mirtazapine can improve symptoms or remission in people with bulimia nervosa.

Benefits and harms

Mirtazapine:

We found no systematic review or RCTs.

Further information on studies

Comment: For further information about harms of antidepressants see harms of antidepressants in review on depression in children and adolescents, and harms of antidepressants in review on depression in adults.

Mirtazapine is a noradrenergic and specific serotonergic antidepressant.

Clinical guide:
Mirtazapine is not an evidence-based treatment in bulimia nervosa and should not be used as a first-line treatment for this condition. It is associated with weight gain, making it problematic for treating people with eating disorders. Where other antidepressants are not tolerated or appropriate, it may be tried on an empirical basis as adjunct to psychotherapy.

OPTION REBOXETINE

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether reboxetine can improve symptoms or remission in people with bulimia nervosa.

Benefits and harms

Reboxetine:

We found no systematic review or RCTs.

Further information on studies

Comment: For further information about harms of antidepressants see harms of antidepressants in review on depression in children and adolescents, and harms of antidepressants in review on depression in adults.

Reboxetine is a noradrenergic antidepressant.

Clinical guide:
Reboxetine is not an evidence-based treatment in bulimia nervosa and should not be used as a first-line treatment for this condition. Where other antidepressants are not tolerated or appropriate, it may be tried on an empirical basis as adjunct to psychotherapy.

OPTION VENLAFAXINE

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know whether venlafaxine can improve symptoms or remission in people with bulimia nervosa.

Benefits and harms

Venlafaxine:

We found no systematic review or RCTs.

Further information on studies

Comment: For further information about harms of antidepressants see harms of antidepressants in review on depression in children and adolescents, and harms of antidepressants in review on depression in adults.

Venlafaxine is a serotonin and noradrenaline reuptake inhibitor.

Clinical guide:
Venlafaxine is not an evidence-based treatment in bulimia nervosa and should not be used as a first-line treatment for this condition. Where other antidepressants are not tolerated or appropriate, it may be tried on an empirical basis as adjunct to psychotherapy.

OPTION PHARMACOTHERAPY PLUS PSYCHOTHERAPY

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .
- We don't know if combining pharmacotherapy with psychotherapy enhances outcome. Trials that have suggested combinations may enhance outcomes have been limited in power.

Benefits and harms

CBT for bulimia nervosa (CBT-BN) plus tricyclic antidepressants (TCAs) versus TCAs alone:

We found two systematic reviews (search dates 2001 [57] and 2005 [41]), which identified the same two RCTs. [65] [66]

Symptom improvement

CBT for bulimia nervosa (CBT-BN) plus tricyclic antidepressants (TCAs) compared with TCAs alone We don't know how effective imipramine plus group-based CBT-BN and imipramine alone are, compared with each other, at reducing binge eating. We don't know how effective desipramine plus CBT-BN (16 weekly sessions with 2 follow-up sessions) and desipramine alone are, compared with each other, at improving binge-eating remission rates or bulimic symptoms (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[65] RCT **4-armed trial**	171 people In review [57] [41] The remaining arms evaluated group-based CBT for bulimia nervosa (CBT-BN) alone and placebo alone	**Mean reduction in number of binges a week** 7.7 with imipramine plus CBT-BN 3.6 with imipramine 200 mg to 300 mg daily	Significance assessment not performed		
[66] RCT **3-armed trial**	71 people In review [57] [41] The remaining arm evaluated CBT-BN (16 weekly sessions with 2 follow-up sessions) alone	**Bulimic symptoms , at 24 weeks** with CBT-BN plus desipramine with desipramine (mean 167 mg/day) Absolute results not reported	SMD +0.10 95% CI –0.70 to +0.90	⟷	Not significant
Remission					
[66] RCT **3-armed trial**	71 people In review [57] [41] The remaining arm evaluated CBT-BN (16 weekly ses-	**Remission rate , at 24 weeks** 67% with CBT-BN plus desipramine 42% with desipramine (mean 167 mg/day)	RR 1.75 95% CI 0.69 to 4.44	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	sions with 2 follow-up sessions) alone	Absolute numbers not reported			

Adverse effects

No data from the following reference on this outcome. [65] [66]

CBT-BN plus TCAs versus CBT-BN alone:

We found one systematic review, [57] which identified two RCTs. [65] [66]

Symptom improvement

CBT for bulimia nervosa (CBT-BN) plus tricyclic antidepressants (TCAs) compared with CBT-BN alone CBT-BN plus TCAs seems as effective as CBT alone at improving binge-eating remission rates and bulimic symptoms (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[65] RCT **4-armed trial**	171 people In review [57] The remaining arms evaluated imipramine alone and placebo alone	**Mean reduction in number of binges a week** 7.7 with imipramine plus CBT for bulimia nervosa (CBT-BN) 8.2 with CBT-BN plus placebo	P = 0.67	⟷	Not significant
[66] RCT **3-armed trial**	71 people In review [57] The remaining arm evaluated de-sipramine alone	**Bulimic symptoms , after 24 weeks** with CBT-BN plus desipramine with CBT-BN alone Absolute results not reported	SMD +0.09 95% CI –0.61 to +0.79	⟷	Not significant
Remission					
[66] RCT **3-armed trial**	71 people In review [57] The remaining arm evaluated de-sipramine alone	**Remission rate , after 24 weeks** 67% with CBT-BN plus de-sipramine 44% with CBT-BN alone Absolute numbers not reported	RR 1.70 95% CI 0.71 to 4.07	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [65] [66]

CBT-BN plus fluoxetine versus fluoxetine alone:

We found two systematic reviews, [57] [41] which identified one RCT. [58]

Symptom improvement

CBT for bulimia nervosa (CBT-BN) plus fluoxetine compared with fluoxetine alone We don't know how effective CBT-BN plus fluoxetine and fluoxetine alone are, compared with each other, at improving binge-eating remission rates, bulimic symptoms, and depression scores (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[58] RCT **3-armed trial**	76 people In review [57] [41] The remaining arm evaluated CBT for bulimia nervosa (CBT-BN) alone	**Bulimic symptoms** with CBT-BN plus fluoxetine with fluoxetine Absolute results not reported	SMD +0.09 95% CI –0.46 to +0.63	⟷	Not significant
Remission					
[58] RCT **3-armed trial**	76 people In review [57] [41] The remaining arm evaluated CBT-BN alone	**Remission rate** 21% with CBT-BN plus fluoxetine 15% with fluoxetine Absolute numbers not reported	RR 1.10 95% CI 0.86 to 1.40	⟷	Not significant
Depression					
[58] RCT **3-armed trial**	76 people In review [57] [41] The remaining arm evaluated CBT-BN alone	**Depression** with CBT-BN plus fluoxetine with fluoxetine Absolute results not reported	SMD 0 95% CI –0.55 to +0.54	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [58]

CBT-BN plus fluoxetine versus CBT-BN alone:

We found two systematic reviews, [57] [41] which identified one RCT. [58]

Symptom improvement

CBT for bulimia nervosa (CBT-BN) plus fluoxetine compared with CBT-BN alone We don't know how effective CBT-BN plus fluoxetine and CBT-BN alone are, compared with each other, at improving binge-eating remission rates, bulimic symptoms, or depression scores (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Improvement in bulimia symptoms					
[58] RCT **3-armed trial**	76 people In review [57] [41] The remaining arm evaluated fluoxe-tine alone	**Bulimic symptoms** with CBT for bulimia nervosa (CBT-BN) plus fluoxetine with CBT-BN alone Absolute results not reported	SMD –0.09 95% CI –0.74 to +0.36	⟷	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[58] RCT **3-armed trial**	76 people In review [57] [41] The remaining arm evaluated fluoxetine alone	**Remission** 21% with CBT-BN plus fluoxetine 12% with CBT-BN alone Absolute numbers not reported	RR 1.10 95% CI 0.87 to 1.40	⟷	Not significant
Depression					
[58] RCT **3-armed trial**	76 people In review [57] [41] The remaining arm evaluated fluoxetine alone	**Depression** with CBT-BN plus fluoxetine with CBT-BN alone Absolute results not reported	SMD –0.19 95% CI –0.74 to +0.36	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [58]

Pure self-help CBT plus fluoxetine versus fluoxetine alone:

We found one RCT. [43]

Symptom improvement

Pure self-help CBT plus fluoxetine compared with fluoxetine alone We don't know how effective pure self-help CBT plus fluoxetine and fluoxetine alone are, compared with each other, at improving remission rates (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[43] RCT **4-armed trial**	91 women with bulimia nervosa The remaining arms evaluated placebo plus a self-help CBT manual, and placebo alone	**Remission rate , after 16 weeks** 6/21 (26%) with self-help CBT plus fluoxetine 4/26 (16%) with fluoxetine 60 mg alone Data provided upon personal communication with author	RR 1.86 95% CI 0.60 to 5.73	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [43]

Pure self-help CBT plus fluoxetine versus self-help CBT alone:

We found one RCT. [43]

Symptom improvement

Pure self-help CBT plus fluoxetine compared with self-help CBT alone We don't know how effective pure self-help CBT plus fluoxetine and self-help CBT alone are, compared with each other, at improving remission rates in the last 2 weeks of treatment (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Remission					
[43] RCT **4-armed trial**	91 women with bulimia nervosa The remaining arms evaluated fluoxetine 60 mg daily alone and placebo alone	**Remission rates , after 16 weeks** 6/21 (26%) with self-help CBT plus fluoxetine 5/22 (24%) with pure self-help CBT plus placebo Data provided upon personal communication with author	P >0.15	⟷	Not significant

Adverse effects

No data from the following reference on this outcome. [43]

Further information on studies

[65] The RCT found that TCAs increased withdrawal rate compared with combination treatment, although the difference was not significant (43% with TCAs *v* 25% with combination treatment; RR 1.70, 95% CI 0.97 to 2.99). It found no significant difference in withdrawal rates between combination treatment and CBT-BN alone (15% with CBT-BN alone *v* 25% with combination treatment; RR 0.59, 95% CI 0.23 to 1.50).

[66] The RCT found no significant difference in withdrawal between combination treatment and TCAs alone (25% in both groups; RR 1.00, 95% CI 0.25 to 4.00). It also found no significant difference in withdrawal rate between CBT-BN and combination treatment (4% with CBT-BN *v* 25% with combination treatment; RR 0.17, 95% CI 0.02 to 1.50).

[58] The RCT found no significant difference in withdrawal rates between combination treatment and CBT-BN alone (33% with CBT-BN *v* 55% with combination treatment; RR 0.60, 95% CI 0.31 to 1.16). The RCT also found no significant difference in withdrawal rates between combination treatment and fluoxetine alone (39% with fluoxetine *v* 55% with combination treatment; RR 0.71, 95% CI 0.39 to 1.30).

[43] In trials with a drug-treatment arm, people randomised to self-help plus placebo were seen regularly by healthcare professionals, and so results may not generalise to self-help, in which there is no contact with healthcare professionals. The results of this RCT should be regarded with caution.

Comment: Modest effect sizes in these analyses may be clinically relevant, but the small number and size of trials limit conclusions.

Clinical guide:
Evidence is insufficient to support the use of pharmacotherapy plus psychotherapy. In clinical practice pharmacotherapy may be added to psychotherapy as adjunctive treatment to enhance a partial response to treatment.

QUESTION What are the effects of discontinuing treatment in people with bulimia nervosa in remission?

OPTION DISCONTINUING ANTIDEPRESSANTS

- For GRADE evaluation of interventions for Bulimia nervosa, see table, p 41 .

- We don't know whether continuation of antidepressant treatment may maintain a reduction in vomiting frequency compared with withdrawing treatment in people in remission.

Benefits and harms

Discontinuing antidepressants:

We found no systematic review or RCTs in people with bulimia nervosa in remission (see comment).

Further information on studies

Comment: We found no RCTs assessing the effects of discontinuing treatment in people in remission (complete abstinence from bingeing). We found one RCT (150 people who had responded to 8 weeks' treatment with fluoxetine [response defined as decrease of at least 50% from baseline in vomiting frequency]) comparing continued treatment with fluoxetine 60 mg daily versus placebo. [69] Results must be interpreted with caution because of high attrition rates, especially during the first 3 months (43% with fluoxetine *v* 74% with placebo). The RCT found that time to relapse (a return to baseline vomiting frequency for 2 consecutive weeks) was significantly prolonged with fluoxetine compared with placebo at 1 year (time to relapse not reported; P <0.02). It found a similar rate of discontinuation caused by relapse in both groups. Rhinitis was significantly more common with fluoxetine than with placebo.

Clinical guide:
Continuing treatment with antidepressants in treatment responders is likely to prevent relapse, but there is insufficient evidence to support this, and no evidence to support this beyond 1 year. Provided the medication is well tolerated and no problematic adverse effects emerge, the balance of benefits and harms favours benefit for continuation of fluoxetine.

GLOSSARY

Cognitive orientation therapy The cognitive orientation theory aims to generate a systematic procedure for exploring the meaning of a behaviour around themes, such as avoiding certain emotions. Therapy for modifying behaviour focuses on systematically changing beliefs related to themes, rather than beliefs referring directly to eating behaviour. No attempt is made to persuade the people that their beliefs are incorrect or maladaptive. [73]

Dialectical behavioural therapy A type of behavioural therapy that views emotional dysregulation as the core problem in bulimia nervosa, with binge eating and purging understood as attempts to influence, change, or control painful emotional states. People are taught a repertoire of skills to replace dysfunctional behaviours. [52]

Exposure therapy In bulimia nervosa, this is a modification of the exposure and response prevention therapy developed for obsessive compulsive disorder. It involves, for example, exposure to food, and then psychological prevention strategies to control weight behaviour, such as vomiting after eating, until the urge or compulsion to vomit has receded. [71]

Beck Depression Inventory A 21-item ordinal scale of symptoms of depression. Scores less than 10 are normal or minimal depression: 10–18 indicates mild to moderate depression, 19–29 indicates moderate to severe depression, and greater than 30 indicates severe depression. A short version has 13 items; scores above 4 indicate increasing levels of depression.

Beck Depression Inventory Standardised scale to assess depression. This instrument consists of 21 items to assess the intensity of depression. Each item is a list of 4 statements (rated 0, 1, 2, or 3), arranged in increasing severity, about a particular symptom of depression. The range of scores possible are 0 = least severe depression to 63 = most severe depression. It is recommended for people aged 13 to 80 years. Scores of more than 12 or 13 indicate the presence of depression.

Binge eating Modified from DSM-IV. [1] Eating, in a discrete period (e.g., hours), a large amount of food, accompanied by a lack of control over eating during the episode.

Bulimia nervosa The DSM-IV [1] criteria include recurrent episodes of binge eating; recurrent inappropriate compensatory behaviour to prevent weight gain; frequency of binge eating and inappropriate compensatory behaviour, with both occurring, on average, at least twice a week for 3 months; self-evaluation unduly influenced by body shape and weight; and disturbance occurring not exclusively during episodes of anorexia nervosa. Types of bulimia nervosa, modified from DSM-IV, [1] are purging (using self-induced vomiting, laxatives, diuretics, or enemas) and non-purging

(fasting, exercise, but not vomiting or other abuse as for the purging type). However, many studies evaluate efficacy for samples that may include people with subthreshold bulimia nervosa or binge eating disorder. Where possible, only data for bulimia nervosa participants are reported in this review.

Cognitive behavioural therapy A specific form of cognitive behavioural therapy (CBT) has been developed for bulimia nervosa (CBT-BN), [70] which uses three overlapping phases for 19 sessions over 20 weeks. Phase one aims to educate the person about bulimia nervosa. People are helped to increase the regularity of eating and resist the urge to binge or purge. Phase two introduces procedures to reduce dietary restraint (e.g., broadening food choices). In addition, cognitive procedures supplemented by behavioural experiments are used to identify and correct dysfunctional attitudes, beliefs, and avoidance behaviours. Phase three is the maintenance phase. Relapse-prevention strategies are used to prepare for possible future setbacks. [36] [70] Although many studies have used variants of CBT for bulimia nervosa, for the purposes of this review only those that resemble CBT-BN are cited unless otherwise specified. In this review, CBT-BN refers to all treatments that closely resemble CBT-BN.

Guided self-help cognitive behavioural therapy A modified form of cognitive behavioural therapy, in which a treatment manual is provided with support, usually from a non-professional or professional without specialist expertise in eating disorders. A good discussion of the development and types of self-help can be found in Williams (2003). [72]

Hypnobehavioural psychotherapy Therapy that uses a combination of behavioural techniques, such as self-monitoring, to change maladaptive eating disorders, and hypnotic techniques to reinforce and encourage behaviour change.

Interpersonal psychotherapy (IPT) In bulimia nervosa, this is a three-phase treatment. Phase one analyses in detail the interpersonal context of the eating disorder. This leads to the formulation of an interpersonal problem area, which forms the focus of the second stage; this is aimed at helping the person to make interpersonal changes. Phase three is devoted to the person's progress and an exploration of ways to handle future interpersonal difficulties. At no stage is attention paid to eating habits or body attitudes. [39]

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Remission Sustained abstinence (longer than 1 month) from binge eating.

Short-Form Health Survey-36 items (SF-36) A scale that assesses health-related quality of life across eight domains: limitations in physical activities (physical component), limitations in social activities, limitations in usual role activities due to physical problems, pain, psychological distress and wellbeing (mental health component), limitations in usual role activities because of emotional problems, energy and fatigue, and general health perceptions.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

CBT for bulimia nervosa One systematic review updated, no new RCTs added from this systematic review. [34] Categorisation unchanged (Likely to be beneficial).

CBT plus exposure/response prevention therapy One systematic review updated, [34] no new evidence found. Categorisation unchanged (Unknown effectiveness).

Dialectical behavioural therapy One systematic review updated, [34] no new evidence added. Categorisation unchanged (Unknown effectiveness).

Guided self-help CBT One systematic review added. [34] It found one RCT, [50] which did not meet *Clinical Evidence* inclusion criteria for this review. Categorisation unchanged (Unknown effectiveness).

Interpersonal psychotherapy One systematic review, which reported adverse effects, updated. [34] No new evidence added. Categorisation unchanged (Unknown effectiveness).

Pure or unguided self-help CBT One systematic review updated, [34] no new RCTs found. Categorisation unchanged (Unknown effectiveness).

Topiramate One systematic review added. [67] It found no new RCTs meeting *Clinical Evidence* inclusion criteria. Categorisation unchanged (Unknown effectiveness).

Pharmacotherapy plus psychotherapy No new evidence added, but evidence re-evaluated. Categorisation changed from Unlikely to be beneficial to Unknown effectiveness.

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Disclaimer

TABLE 1 **Comparison of non-remission rates between active drug and placebo by class of antidepressant** [54]

Class: drug(s)	Number of RCTs	Number of people	Absolute non-remission rates (drug *v* placebo)	RR (95% CI)
TCA: desipramine, imipramine	3	132	79% *v* 91%	0.86 (0.70 to 1.07)
SSRI: fluoxetine	3	467	81% *v* 89%	0.89 (0.76 to 1.03)
MAOI: phenelzine, isocarboxazid	2	98	76% *v* 94%	0.81 (0.68 to 0.96)

MAOI, monoamine oxidase inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

GRADE **Evaluation of interventions for Bulimia nervosa.**

Important outcomes			Quality of life, Symptom improvement						
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of treatments for bulimia nervosa in adults?									
1 (<77) [34] [35]	Symptom improvement	CBT for bulimia nervosa (CBT-BN) versus waiting list control, no treatment, or placebo	4	–3	0	0	0	Very low	Quality points deducted for sparse data, no intention-to-treat analysis, and incomplete reporting of results
1 (<77) [35]	Symptom improvement	CBT plus exposure/response prevention therapy (CBT-ERP) versus waiting list control	4	–3	0	0	0	Very low	Quality points deducted for sparse data, no intention-to-treat analysis, and incomplete reporting of results
1 (39) [35] [34]	Symptom improvement	CBT-ERP versus CBT-BN	4	–3	0	0	0	Very low	Quality points deducted for sparse data, no intention-to-treat analysis, and incomplete reporting of results
2 (101) [42] [43]	Symptom improvement	Pure or unguided self-help CBT versus waiting list, no treatment, or placebo medication	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and baseline differences in purging between groups. Directness point deducted for inclusion of co-intervention (contact with health professionals)
1 (48) [43]	Symptom improvement	Pure or unguided self-help CBT versus fluoxetine	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of co-intervention (contact with health professionals)
2 (143) [38] [46] [47]	Symptom improvement	Guided self-help CBT versus CBT for bulimia nervosa (CBT-BN)	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
2 (295) [30]	Symptom improvement	IPT versus CBT for bulimia nervosa (CBT-BN)	4	–1	–1	0	0	Low	Quality point deducted for incomplete reporting of results. Consistency point deducted for different results for different outcomes
1 (<78) [51]	Symptom improvement	Hypnobehavioural therapy (HBT) versus no treatment, placebo, or waiting list	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and significant differences between groups at baseline
1 (<78) [51]	Symptom improvement	HBT versus CBT for bulimia nervosa (CBT-BN)	4	–3	0	0	0	Very low	Quality points deducted for sparse data, unbalanced groups at baseline, and incomplete reporting of results
1 (31) [52]	Symptom improvement	Dialectical behavioural therapy versus placebo, no treatment, or waiting list	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and unclear measurement of outcomes
1 (68) [53]	Symptom improvement	Motivational enhancement therapy versus CBT for bulimia nervosa (CBT-BN)	4	–3	0	0	0	Very low	Quality points deducted for sparse data, short-term follow-up, and no intention-to-treat analysis
at least 5 (at least 706) [54] [55] [56]	Symptom improvement	SSRIs versus placebo or no treatment	4	–2	0	0	0	Low	Quality points deducted for incomplete reporting of results and for different results for different outcomes
2 (<111) [58] [59]	Symptom improvement	SSRIs versus CBT for bulimia nervosa (CBT-BN)	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and no intention-to-treat analysis

Important outcomes			Quality of life, Symptom improvement						
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
4 (156) [54]	Symptom improvement	Monoamine oxidase inhibitors (MAOIs) versus placebo or no treatment	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consistency point deducted for different results for different outcomes
3 (132) [54]	Symptom improvement	Tricyclic antidepressants (TCAs) versus placebo	4	–2	–1	0	0	Very low	Quality points deducted for sparse data and incomplete reporting of results. Consistency point deducted for different results for different outcomes
2 (<211) [65] [66]	Symptom improvement	TCAs versus CBT for bulimia nervosa (CBT-BN)	4	–1	–1	–1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results. Directness point deducted for different regimens between studies
1 (60) [68]	Symptom improvement	Topiramate versus placebo	4	–2	0	–1	0	Very low	Quality points deducted for sparse data and short-term follow-up. Directness point deducted for composite outcome
1 (60) [68]	Quality of life	Topiramate versus placebo	4	–3	0	0	0	Very low	Quality points deducted for sparse data, short-term follow-up, and incomplete reporting of results
2 (<242) [65] [66]	Symptom improvement	CBT for bulimia nervosa (CBT-BN) plus tricyclic antidepressants (TCAs) versus TCAs alone	4	–2	0	–1	0	Very low	Quality points deducted for incomplete reporting and no statistical test between groups. Directness point deducted for conflicting results
2 (<242) [65] [66]	Symptom improvement	CBT-BN plus TCAs versus CBT-BN alone	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
1 (<76) [58]	Symptom improvement	CBT-BN plus fluoxetine versus fluoxetine alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (<76) [58]	Symptom improvement	CBT-BN plus fluoxetine versus CBT-BN alone	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (47) [43]	Symptom improvement	Pure self-help CBT plus fluoxetine versus fluoxetine alone	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for inclusion of co-intervention (contact with health professionals)
1 (43) [43]	Symptom improvement	Pure self-help CBT plus fluoxetine versus self-help CBT alone	4	–3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and inclusion of co-intervention (contact with health professionals)

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.