# Review and meta-analysis of pharmacotherapy for binge-eating disorder

*Reas DL, Grilo CM*

**CRD summary**
The review evaluated the effectiveness of pharmacotherapy for binge-eating disorder and found some pharmacotherapies reduced short-term binge-eating and gave a limited weight loss. Combination of antiepileptic or anti-obesity drugs with cognitive or behavioural therapy did not reduce binge-eating, but modestly enhanced weight loss. Limited evidence for individual drugs and review process limitations make the reliability of the authors' conclusions unclear.

**Authors' objectives**
To evaluate the effectiveness of pharmacotherapy for binge-eating disorder.

**Searching**
MEDLINE, PsycLIT, Science Direct, and the Cochrane Library were searched from 1985 to January 2008 for published studies. Search terms were reported. Bibliographies of each retrieved article and obesity, eating disorder, psychiatry and pharmacology journals were handsearched.

**Study selection**
Randomised placebo-controlled trials (RCTs) evaluating the effects of a pharmacological agent as a primary treatment for binge-eating disorder (pharmacotherapy only), or RCTs comparing pharmacotherapy or combined with psychosocial treatments (additive or combined designs), were eligible for inclusion. Only trials of binge-eating disorder, or the International Classification of Diseases-10 category 'overeating associated with other psychiatric condition', were eligible for inclusion and not other eating disorders (further details provided). Trials with an additive or open-label design were excluded. Trials were also excluded where the participants had an uncertain diagnosis, a subclinical disorder, or where the primary disorder was bipolar disorder. A trial of d-fenfluramine was excluded as the drug had been withdrawn. Primary eligible outcomes were attrition, remission from binge eating and weight loss.

The included pharmacotherapy-only RCTs were generally of short duration, with an average 12.2 weeks (range six to 24 weeks). The RCTs with pharmacotherapy combined with psychotherapy interventions were generally of moderate duration, with an average 20.1 weeks (range eight to 36 weeks).

There were three main classes of drugs in the included trials: antidepressant serotonin-norepinephrine reuptake inhibitors (SSRIs: atomoxetine, citalopram, desipramine, escitalopram, fluoxetine, fluvoxamine, imipramine and sertraline); antiepileptic medication (topiramate and zonisamide); and obesity medication (orlistat and sibutramine). Details of the dosage and frequency of the specific drugs used were given in the review.

Cognitive behavioural therapy (CBT) was the main psychotherapy intervention in the included trials.

Most of the included trials were carried out in the USA, with two in Brazil, two in Italy, and one in Switzerland. Most of the participants were women (range 59 to 100%); their mean age range was 29.1 to 46.1 years; and their initial mean body mass index (BMI) range was 32.3 to 44.2, where reported.

Two researchers were involved in the literature search, but the authors did not state how the papers were selected for the review.

**Assessment of study quality**
The authors did not state that they carried out a formal assessment of methodological quality, but a number of relevant features which affected trial quality were discussed including: blinding, overall drop-out rate, study design and how participants were recruited.

**Data extraction**
Dichotomous data for remission (binge-eating frequency and binge-eating abstinence rates) and attrition (percentage drop-out rates) were extracted in order to calculate relative risks (RR) (or risk ratios) and 95% confidence intervals (CIs). Weight loss data were extracted in order to calculate mean differences and 95% confidence intervals. Missing data was assumed to have a negative outcome (no remission) and baseline values were carried forward and for continuous data; any completed-only data was clearly labelled to draw a distinction. Intention-to-treat data were extracted where possible.

The authors did not state how the data extraction was carried out or how many reviewers performed the extraction.

**Methods of synthesis**
Trials were grouped according to the intervention. Pooled relative risks and 95% confidence intervals were calculated for dichotomous data. Weighted mean differences (WMDs) and 95% confidence intervals were calculated for weight loss data and a summary variance-weighted effect size was calculated to give more weight to larger trials.

Between trial heterogeneity was determined using $\chi^2$ and $I^2$ tests: an $I^2$ of less than 30% indicated mild heterogeneity; $I^2$ between 30 and 50% indicated some heterogeneity; and an $I^2$ of more than 50% indicated considerable heterogeneity. For heterogeneous data, synthesis using a random-effects model was used. For homogeneous data, synthesis using a fixed-effects model was used. Trials considered to be contributing to heterogeneity were removed in sensitivity analyses.

Subgroup analyses were performed in order to compare different drug classes. A narrative synthesis was provided for the RCTs, with combined therapy due to the heterogeneity of the interventions.

**Results of the review**
Twenty-two relevant RCTs (n=1,962 participants) were included in the review; 20 RCTs were double-blinded.

Pharmacotherapy-only RCTs (14 RCTs; n=1,279 participants):

For attrition/drop-out rate, there was no significant difference between medication and placebo (13 RCTs). For treatment with SSRIs, there was significant heterogeneity ($I^2$=57.7%; six RCTs) but, after omitting one trial, there was a small but significant advantage for the placebo (RR 1.66, 95% CI 1.01 to 2.74; Z=1.99). There were no significant differences for attrition with the other subgroups of drugs versus placebo.

There was a clinically significant benefit for binge-eating remission for medication versus placebo (RR, 0.74, 95% CI 0.66 to 0.84; $I^2$=34.6%; 13 RCTs), which was also significant for the different subgroups of drugs including SSRI (seven RCTs), antiepileptic (three RCTs), obesity (two RCTs), and serotonin-norepinephrine re-uptake inhibitors (SNRIs, one RCT) medication. Of the antiepileptic drugs, topiramate (RRs 0.56 and 0.59), appeared to be more effective than zonisamide (RR 0.88). The pooled meta-analysis also found a significant additional weight reduction for medication versus placebo of 3.4kg (WMD -3.42, 95% CI -4.25 to -2.58; $I^2$=53.2%; eight RCTs), which was also significant for the different subgroups of drugs. However, the effect was greater for antiepileptic medication (WMD -4.58, 95% CI -5.36 to -3.79; $I^2$=0%; two RCTs) and obesity medication (WMD -3.63, 95% CI -4.40 to -2.87; $I^2$=0%; two RCTs) than for SSRIs (three RCTs) and SNRIs (one RCT).

RCTs with pharmacotherapy combined with psychotherapy interventions (eight RCTs; n=683 participants):

The addition of pharmacotherapy to cognitive-behavioural therapy (CBT) did not significantly affect binge-eating outcomes. The addition of antidepressants to CBT or behavioural weight loss did not significantly affect weight loss. However, for four individual RCTs, the addition of topiramate and orlistat to CBT, imipramine to diet counselling, and orlistat to a special diet, significantly enhanced weight loss. Two of these results were clinically significant: CBT plus topiramate; and orlistat with a special diet. CBT without medication was more effective in reducing binge-eating than fluoxetine therapy alone (two RCTs) or fluvoxamine alone (one RCT).

**Authors' conclusions**
Some pharmacotherapies may reduce binge-eating in the short term and increase weight loss to a limited extent. Combining medication with cognitive or behavioural treatment was unlikely to reduce binge-eating, but specific medication with topiramate or orlistat may modestly increase weight loss.

**CRD commentary**
The review addressed a well-defined question in terms of participants, study design and relevant outcomes. The psychosocial treatments, which were classified as eligible for inclusion in combination with pharmacotherapy, were not clearly defined or clearly described for the included trials. Relevant databases were searched. It was unclear whether any language restrictions were used, but it appeared that only English language articles were included in the review, and unpublished trials were not considered, so some relevant trials may have been missed. Publication bias was not assessed.

Some trial quality criteria were assessed as only randomised placebo-controlled trials were eligible for inclusion, but no formal validity assessment was performed and little relative data was reported. It was not clear whether efforts were made to reduce error and bias in the review process, as no relevant information was reported.

Relevant trial details were reported, but minimal details of the included psychosocial treatments were provided and there was little relevant detail regarding the placebo groups. Statistical heterogeneity was assessed and there was evidence for heterogeneity with some outcomes. The statistical method used for the meta-analysis of the RCTs seemed appropriate. The reliability of the subgroup analyses was uncertain due to the small number of relative trials identified. A sensitivity analysis was carried out.

There were some potential limitations, mainly arising from the reporting of the review process, and the review covered a wide variety of classes of drugs resulting in a relatively small number of trials for some drug classes, so the reliability of the authors' conclusions is unclear.

**Implications of the review for practice and research**
Practice: The authors suggested a more limited use of SSRIs and also suggested that specific forms of psychotherapy should be offered, e.g. CBT and behavioural weight loss.

Research: The authors stated that studies representing the general population needed to be performed, and recommended that further larger studies of medications for binge-eating disorder with long-term follow-up should be carried out, which would also provide data relevant to when pharmacotherapy should be stopped.

**Funding**
Donaghue Medical Research Foundation; US National Institutes of Health, grant numbers R01 DK49587, R01 DK073542, and K24 DK070052.

**Bibliographic details**
Reas DL, Grilo CM. Review and meta-analysis of pharmacotherapy for binge-eating disorder. Obesity 2008; 16(9): 2024-2038

**PubMedID**
19186327

**Original Paper URL**
http://www.nature.com/oby/journal/v16/n9/abs/oby2008333a.html

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Anti-Obesity Agents /therapeutic use; Bulimia Nervosa /drug therapy; Female; Humans; Male; Patient Dropouts; Psychotherapy; Randomized Controlled Trials as Topic; Weight Loss /drug effects

**AccessionNumber**

12009104623

**Database entry date**
24/02/2010

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.