Antidepressants versus psychological treatments and their combination for bulimia nervosa (Review)

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[Intervention Review]

Antidepressants versus psychological treatments and their combination for bulimia nervosa

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ABSTRACT

Background

Psychotherapeutic approaches, mainly cognitive behavior therapy, and antidepressant medication are the two treatment modalities that have received most support in controlled outcome studies of bulimia nervosa.

Objectives

The primary objective was to conduct a systematic review of all RCTs comparing antidepressants with psychological approaches or comparing their combination with each single approach for the treatment of bulimia nervosa.

Search methods

(1) electronic searches of MEDLINE (1966 to December 2000), EMBASE (1980-December 2000) , PsycLIT (to December 2000), LILACS & SCISEARCH (to 1999)

(2) the Cochrane Register of Controlled Trials and the Cochrane Depression, Anxiety and Neurosis Group Register - ongoing

(3) handsearches of the references of all identified trials

(4) contact with the pharmaceutical companies and the principal investigator of each included trial

(5) handsearch of the International Journal of Eating Disorders - ongoing

Selection criteria

Inclusion criteria: every randomized controlled trial in which antidepressants were compared with psychological treatments or the combination of antidepressants with psychological approaches was compared to each treatment alone, to reduce the symptoms of bulimia nervosa in patients of any age or gender.

Quality criteria: reports were considered adequate if they were classified as A or B according to the Cochrane Manual.

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Data collection and analysis

Data were extracted independently by two reviewers for each included trial. The main outcome for efficacy was full remission of bulimic symptoms, defined as 100% reduction in binge or purge episodes from baseline to endpoint. Dichotomous data was evaluated by the relative risks and 95% confidence intervals around this measure, based on the random effects model; continuous data was evaluated by the average difference and the 95% confidence interval. Number needed to treat (NNT) and number needed to harm (NNH) were calculated using the inverse of the absolute risk reduction.

Main results

Five trials were included in comparison one (antidepressants versus psychological treatments), five in comparison two (antidepressants versus the combination) and seven in comparison three (psychological treatments versus the combination). Remission rates were 20% for single antidepressants compared to 39% for single psychotherapy (DerSimonian-Laird Relative Risk = 1.28; 95% Confidence Interval = 0.98;1.67). Dropout rates were higher for antidepressants than for psychotherapy (DerSimonian-Laird Relative Risk = 2.18; 95% Confidence Interval = 1.09;4.35). The NNH for a mean treatment duration of 17.5 weeks was 4 (95% confidence interval = 3;11). Comparison two found remission rates of 42% for the combination versus 23% for antidepressants (DerSimonian-Laird Relative Risk = 1.38; 95% Confidence Interval = 0.98;1.93). Comparison three showed a 36% pooled remission rate for psychological approaches compared to 49% for the combination (DerSimonian-Laird Relative Risk = 1.21; 95% Confidence Interval = 1.02;1.45). The NNT for a mean treatment duration of 15 weeks was 8 (95% Confidence Interval = 4;320). Dropout rates were higher for the combination compared to single psychological treatments (DerSimonian-Laird Relative Risk = 0.57; 95% Confidence Interval = 0.38;0.88). The NNH was 7 (95% Confidence Interval = 4;21).

Authors' conclusions

Using a more conservative statistical approach, combination treatments were superior to single psychotherapy. This was the only statistically significant difference between treatments. The number of trials might be insufficient to show the statistical significance of a 19% absolute risk reduction in efficacy favouring psychotherapy or combination treatments over single antidepressants. Psychotherapy appeared to be more acceptable to subjects. When antidepressants were combined with psychological treatments, acceptability of the latter was significantly reduced.

PLAIN LANGUAGE SUMMARY

Antidepressants and psychological treatments, alone or combined, for bulimia nervosa

Psychotherapeutic approaches, mainly cognitive behavior therapy, and antidepressant medication are the two treatment modalities that have received most support in controlled outcome studies of bulimia nervosa. Using a more conservative statistical approach, combination treatments were superior to single psychotherapy. This was the only statistically significant difference between treatments. The number of trials might be insufficient to show the statistical significance of a 19% absolute risk reduction in efficacy favouring psychotherapy or combination treatments over single antidepressants. Psychotherapy appeared to be more acceptable to subjects. When antidepressants were combined with psychological treatments, acceptability of the latter was significantly reduced.

BACKGROUND

Bulimia Nervosa is an eating disorder characterized by recurrent episodes of uncontrolled compulsive eating binges, followed by compensatory behaviors to prevent weight gain. These behaviors include self-induced vomiting, the most frequent one, and misuse of laxatives, diuretics, enemas or other medications, fasting or excessive exercise. In addition, body shape and weight unduly influence self-evaluation of individuals with bulimia nervosa. Their self-esteem is regulated in the extreme by these aspects of their appearance. They feel in intense pressure to diet and to avoid weight gain (APA 1994). At least 90% of individuals with bulimia nervosa are female. Surveys indicate that the prevalence among adolescent and young adult females is approximately 1% to 3% .

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Treatments that have received the most support in controlled outcome studies of bulimia nervosa are psychotherapeutic approaches, mainly cognitive behavior therapy, antidepressant medications, and their combination (antidepressants plus psychological approaches). All types of antidepressants seem to be beneficial in the short-term in relieving bulimic symptoms (Wolfe 1995). Short-term abstinence rates (on average 8 weeks) are about 20%, and overall reductions in bulimic behaviors are about 70% (Agras 1992, Bacaltchuk 2000 a, Leitenberg 1994). However, a significant relapse rate (30-45%) is observed in patients followed for 4-6 months (Walsh 1997). There is no clear evidence of a differential effect among the various classes of drugs used relative to placebo. However, there are two unpublished trials showing no benefit of fluvoxamine compared to placebo (Corcos 1996).

Cognitive behavior therapy (CBT) is considered the standard treatment of choice for bulimia nervosa. The CBT model for bulimia nervosa was developed by Fairburn and colleagues (Fairburn 1991) and has the following major features: (1) self monitoring of food intake and of bingeing and purging episodes, as well as the thoughts and feelings that trigger these episodes; (2) regular weighing; (3) specific recommendations designed to normalize eating behavior and curb restrictive dieting; (4) cognitive restructuring directed at habitual reasoning errors and underlying assumptions that are relevant to the development and maintenance of the eating disorder; and (5) prevention of relapse. Numerous randomized controlled trials (RCTs) have shown that CBT is either significantly more effective or at least as effective as any alternative form of psychotherapy (Hay 2000). Nonetheless, CBT is underutilized, mainly due to the relative unavailability of therapists with specialized training in CBT for eating disorders in many countries.

This review assessed the effectiveness and acceptability of antidepressants compared with psychological treatments, including CBT, and of their combination compared to each single treatment, in bulimia nervosa.

OBJECTIVES

The objectives of this review were:

1. to investigate whether using antidepressant medications was clinically effective compared to psychological treatments for the treatment of bulimia nervosa.

2. to investigate whether using a combination of antidepressants plus psychological treatments was more effective compared to each single approach for the treatment of bulimia nervosa.

Where possible, a meta-analytic synthesis of the studies was performed.

METHODS

Criteria for considering studies for this review

Types of studies

We attempted to identify all relevant randomized controlled trials.

Types of participants

People with bulimia nervosa defined by clinical state description or diagnosed by Russell's (Russell 1979), DSM-III (APA 1980), DSM-III-R (APA 1987), DSM-IV (APA 1994) or ICD-10 (WHO 1992) criteria, irrespective of gender, age or treatment setting. Participants with both purging and nonpurging type bulimia nervosa, as defined in DSM-IV (APA 1994), were included.
Exclusion criteria: people with binge-eating/purging type anorexia nervosa or binge-eating disorder as defined in the DSM-IV (APA 1994).

Types of interventions

Trials were included if they compared antidepressants with psychological treatments or their combination to each single approach during at least 4 weeks.
The following antidepressants were included:
a) tricyclic antidepressants (TCA):imipramine, amitryptiline, clomipramine, nortryptiline, desipramine;
b) selective serotonin reuptake inhibotors (SSRI): fluoxetine, sertraline, paroxetine, citalopram, fluvoxamine;
c) monoamine oxidase inhibitors (MAOI): phenelzine, isocarboxazide, moclobemide, brofaromine, tranylcipromine;
d) other antidepressants: bupropion, trazodone, nefazodone, mianserine, mirtazapine, venlafaxine.
The following individual or group, extensive or intensive psychological treatments were included:
i) cognitive-behavior therapy
ii) cognitive therapy
iii) behaviour therapy
iv) psychodynamic/psychoanalytic oriented therapy
v) interpersonal therapy
vi) supportive therapy
vii) family therapy
viii) nutritional counselling
ix) any other psychological approach not specified above

Types of outcome measures

A. Efficacy
(i) the number of people per treatment group who did not show a remission in the bulimic symptoms, defined as 100% reduction in binge or purge episodes from baseline to endpoint
(ii) the number of people per treatment group who did not show a clinical improvement in the bulimic symptoms, defined as at

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least 50% reduction in binge or purge episodes from baseline to endpoint
(iii) the average difference in bulimic symptoms at endpoint
B. Comorbidity
(i) average difference in the severity of depressive symptoms at the end of the trial
C. Acceptability of the treatment
(i) number of people per treatment group dropping out during the trial for any cause

Search methods for identification of studies

See: Collaborative Review Group search strategy
A. Electronic searching
Relevant randomized trials were identified by searching the following eletronic databases by means of the Depression, Anxiety and Neurosis Group Strategy (see CCDAN module):
(i) MEDLINE (January 1966 to December 2000). A subsection of this was obtained by linking the DAN search with the following specific search for this review:
[and ((bulimia in MeSH / explode all subheadings) or (binge*) or (overeating*) or (compulsive near (eating* or vomit*)) or (food* near bing*))]
This downloaded set of reports was searched for possible trials and re-searched, within the bibliographic package, ProCite, with the phrase:
[antidepressant* or tricyclic* or imipramine or amitryptiline or clomipramine or nortryptiline or desipramine or fluoxetine or sertraline or paroxetine or citalopram or fluvoxamine or bupropion or trazodone or nefazodone or phenelzine or isocarboxazid* or moclobemide or brofaromine or tranylcipromine or mianserin or mirtazapine]
(ii) EMBASE (January 1980 to December 2000) was searched by linking the DAN search with the phrase:
[and ((bulimia in theasurus - subheadings, prevention, drug therapy, side effect and therapy) or (binge*) or (overeating*) or (compulsive or eating* or vomit*) or (food* or binge*))]
This downloaded set of reports was searched for possible trials and re-searched, within the bibliographic package, ProCite, with the phrase:
[antidepressant* or tricyclic* or imipramine or amitryptiline or clomipramine or nortryptiline or desipramine or fluoxetine or sertraline or paroxetine or citalopram or fluvoxamine or bupropion or trazodone or nefazodone or phenelzine or isocarboxazid* or moclobemide or brofaromine or tranylcipromine or mianserin or mirtazapine]
(iii) LILACS (January 1982 to December 2000) DAN search was combined with the phrase:
[and (bulimia in theasurus)]
This downloaded set of reports was searched for possible trials and re-searched, within the bibliographic package, ProCite, with the phrase:
[antidepressant* or tricyclic* or imipramine or amitryptiline or clomipramine or nortryptiline or desipramine or fluoxetine or sertraline or paroxetine or citalopram or fluvoxamine or bupropion or trazodone or nefazodone or phenelzine or isocarboxazid* or moclobemide or brofaromine or tranylcipromine or mianserin or mirtazapine]
(iv) PsycLIT (January 1974 to December 2000) was searched combining the DAN search strategy for randomized controlled trials with the phrase:
[and ((explode bulimi* in DE) or (explode binge* in DE) or (overeating*) or (compulsive* near (eating* or vomit*) or (food* near binge*))]
This downloaded set of reports was searched for possible trials and re-searched, within the bibliographic package, ProCite, with the phrase:
[antidepressant* or tricyclic* or imipramine or amitryptiline or clomipramine or nortryptiline or desipramine or fluoxetine or sertraline or paroxetine or citalopram or fluvoxamine or bupropion or trazodone or nefazodone or phenelzine or isocarboxazid* or moclobemide or brofaromine or tranylcipromine or mianserin or mirtazapine]
(v) the Cochrane Depression, Anxiety and Neurosis Group Database of Trials
(vi) the Cochrane Controlled Trials Register was searched with the phrase:
[and ((bulimia in MeSH / explode all subheadings) or (binge*) or (overeating*) or (compulsive near (eating* or vomit*)) or (food* near bing*))]
(vii) SCISEARCH - Science Citation Index
Each of the included studies was sought as a citation on the SCISEARCH database. Reports of articles that had cited these studies were inspected in order to identify further trials.
(viii) Electronic search was performed by the CCDAN Group.
B. A second search was conducted with Clinical Evidence (HAY 2001) and comprised Medline 1966-December 2000, Embase 1980-December 2000, Psychlit 1989-December 2000.Cochrane 2000 Issue 4. The following terms were used: (bulimia or bulimia nervosa or eating disorders or binge eating) and (therapy or treatments or trials or psychotherapy or cognitive-behavioural therapy or pharmacotherapy or antidepressant or SSRI or MAOI).
C. Reference searching. The reference lists of all papers selected were inspected for further relevant studies.
D. Pharmaceutical companies. Companies carrying out comparative studies of their own products with placebo in the treatment of bulimia nervosa were contacted in order to obtain data on unpublished trials.
E. Personal contact. The first authors of all included studies were contacted for further information or information regarding unpublished trials.
F. A handsearch from the first issue of the International Journal of Eating Disorders is ongoing.The first authors of all included studies were contacted for further information or information re-

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garding unpublished trials.
G. Book chapters on the treatment of bulimia nervosa were reviewed.

Data collection and analysis

Selection of trials
The abstract of each reference identified by the search was evaluated by one reviewer (JB) in order to see if the study was likely to be relevant. For this review all trials comparing antidepressants with psychological treatments or combinations of antidepressant medications plus individual or group psychological treatments versus each single treatment were eligible, whether other comparisons were made in the trial or not. For possible RCTs the full article was obtained and inspected by two independent reviewers to assess whether they met criteria to be included.
Quality assessment
In order to ensure that variation was not caused by systematic errors in the design of a study, the methodological quality of the trials eligible to be included in this review was assessed by two independent reviewers. As randomization concealment has been shown to affect trial outcomes (Schultz 1995), quality of trials was graded according to the three categories described in the Cochrane Handbook (Mulrow 1996). The Cochrane Collaboration Handbook criteria is based on the evidence of a strong relationship among potential for bias in the results and allocation concealment (Schultz 1995, Jadad 1996) and are defined as below:
A. Low risk of bias (adequate allocation concealment)
B. Moderate risk of bias (some doubt about the results)
C. High risk of bias (inadequate allocation concealment)
Trials included in this review were those with low or moderate risk of bias (category A or B, respectively). Randomized studies with no information on the allocation concealment process obtained from the authors were included in category B.
Reviewers were not blind to the names of the authors, institutions and journal of publication. Where disagreement could not be resolved by discussion and consensus, further information was sought contacting the authors for clarification. The articles were then added to the list of those awaiting assessment. The same adapted methodology was used for the selection of trials identified by means of reference lists searched and for data on unpublished trials obtained through the pharmaceutical industry or personal contacts with first authors. An inter-rater reliability study between reviewers for the Cochrane Collaboration Handbook grades was performed by means of the kappa.
Data Management
Data from the selected trials was extracted by the same two reviewers. Again, any disagreement was discussed, the decisions were documented and, if necessary, the authors of the studies were contacted for clarification. Justification for excluding references from the review was documented. It was antecipated that many trials would have an inadequate reporting. As the objective was to perform an intention-to-treat analysis, it was assumed a priori that dropouts would be assigned to the worst outcome (no remission or no improvement in their bulimic symptoms).
It was also expected that some trials would have used a crossover design. In order to exclude the potential additive effect in the second or more stages of these trials, only data from the first stage was analysed.
Analysis
Dichotomous outcomes (remission, clinical improvement and dropouts) were analysed by calculating relative risks (RR) and 95% confidence intervals (CI) for each trial. The RR from the individual trials were combined using appropriate methods of meta-analysis. The estimates of RR were based on the random effects model. This model takes into account both within-study sampling error and any between-studies variations in the assessment of the CI of the results (even if there was no statistically significant heterogeneity) and gives the same result as the fixed effects model when there is no between study variance. If the RR equaled 1, this indicated no difference between the groups compared. Additionally, when overall results were significant the number needed to treat statistics (NNT) was calculated by combining the RR with an estimate of the prevalence of the event in the control groups of the trials. The NNT indicates the number of patients who need to be treated to prevent one bad outcome and is the inverse of the absolute risk reduction. In the case of dropouts, the corresponding number needed to harm (NNH) was calculated.
For continuous outcomes the mean and standard deviations of these measures were assessed. They were analysed according to their difference in mean treatment effects and its standard differences, and standardised mean differences calculated. When appropriate, the raw data was log-transformed to improve the distribution of the data and for scales that had similar psychometric properties (for example range and scoring direction) these scores were entered in a meta-analysis.
Heterogeneity in the results of the trials, i.e., whether differences among the results were greater than would be expected by chance alone, was assessed both visually by inspection of graphical presentations and by calculating a chi-square test of heterogeneity. Finally, the possibility of publication bias was visually assessed from funnel graphs and the fail safe-N calculated (Hedges 1985).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.
Five trials fulfilled inclusion criteria and had evaluable data for at least one outcome of comparison one (237 patients in total). Five studies were also included in comparison two (247 patients, 124

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randomised to antidepressants and 123 to the combination), and seven studies were included in comparison three (343 patients, 166 randomised to psychological treatments and 177 to the combination). Thirty-seven studies identified with the search strategy compared antidepressants with placebo, without a psychotherapy control group and/or were subset studies with follow-up or partial data. Therefore, they were not eligible for this review.

All studies were described as randomized. One (Walsh 1997) compared sequential antidepressants (desipramine followed by fluoxetine 60 mg daily for those patients who did not improve after eight weeks on desipramine) to two types of psychotherapy: CBT and supportive therapy, alone and combined to an antidepressant (five comparison groups in total), for 16 weeks. Only the CBT combination group was considered, compared with the sequential antidepressants group (comparison two) or with the single CBT group (comparison three). One study (Mitchell 1990) compared imipramine 200 mg daily with intensive group CBT for 10 weeks, alone and in combination and one study (Leitenberg 1994) compared desipramine 150 mg with individual CBT alone and in combination during respectively 20 weeks. Another study (Goldbloom 1996) compared fluoxetine 60 mg daily to CBT or the combination over 16 weeks. The single antidepressant and the single CBT groups were considered in comparison one and the combined treatment groups in comparisons two or three. One trial (Agras 1992) compared desipramine sixteen and twenty-four weeks to CBT twenty-four weeks or to the combination of CBT twenty-four weeks plus desipramine sixteen or twenty-four weeks. Only the twenty-four week single desipramine, single CBT and combination groups were considered. The sixth study (Fichter 1991) compared the combination of fluoxetine 60 mg daily plus inpatient intensive therapy with inpatient intensive therapy plus placebo over 5 weeks. The seventh study (Russell 1995 b) compared fluoxetine 60 mg daily plus nutritional counselling with nutritional counselling plus placebo for 8 weeks. These last two trials were only considered in comparison three.

In general, adequate description of psychotherapy was provided. Number of individual CBT sessions ranged from sixteen to twenty-two, over a period of sixteen to twenty-four weeks. Four trials were conducted in the United States of America (Mitchell 1990, Agras 1992, Leitenberg 1994, Walsh 1997) one in Canada (Goldbloom 1996), one in Germany (Fichter 1991) and one in Australia (Russell 1995 b). All but the German study recruited outpatients from eating disorders programs and from the community, through advertisements. This study included patients who were undergoing intensive inpatient behavioral psychotherapy, in addition to pharmacotherapy or placebo. Six trials used DSM-III-R criteria for bulimia nervosa, and only one (Mitchell 1990) included bulimic patients diagnosed according to the DSM-III criteria. All patients were purging-type bulimic subjects, according to the DSM-IV definition ("regularly engaged in self-induced vomiting or misused laxatives, diuretics or enemas"). The study populations presented reasonably comparable demographic and behavioral features. They were mostly adult and young adult females; few adolescents were included. The mean number of bulimic episodes per week at baseline ranged roughly from 6 to 9. Patients with comorbid severe major depression, obesity, or substance abuse were usually not included in these studies.

Risk of bias in included studies

All included trials reported the randomisation procedure without adequate information on allocation concealment. Two studies (Leitenberg 1994, Fichter 1991) were classified as "A" according to the methodological quality assessment criteria, thanks to information provided by the authors. The other 5 trials were classified as "B". Agreement between authors for methodological quality grading was 100%. One trial (Russell 1995 b) excluded patients who dropped-out after randomisation from analysis and did not report an intention-to-treat analysis. Data was analysed on an intention-to-treat basis with dropouts being considered as not improved.

Effects of interventions

Meta-analysis 1 (single antidepressants versus psychological treatments)

Remission

CBT was the psychological approach used in the five studies included in this comparison. Remission was reported in all trials. Overall remission rates were 20% for antidepressants and 39% for psychotherapy. Three individual studies showed no significant difference between antidepressants and individual CBT (Agras 1992, Goldbloom 1996, Walsh 1997). Two trials (Mitchell 1990, Leitenberg 1994) showed a statistically significant difference favoring psychotherapy. When the more conservative DerSimonian-Laird estimate of pooled RR was used (random effects model), a clinically relevant but not statistically significant difference favouring psychological treatments was found (DL RR = 1.26; 95% CI= 0.90-1.78).

Clinical Improvement

This outcome was reported in only one trial. Therefore, it will not be considered in this review.

Dropouts

Four trials reported the number of dropouts per treatment group (Mitchell 1990, Agras 1992, Leitenberg 1994, Goldbloom 1996). Overall dropout rates for these short-term trials were higher for antidepressants than for psychotherapy (DL RR= 2.18; 95% CI= 1.09-4.35). Considering dropout rates of 40% for antidepressants and 18% for CBT, the NNH for a mean treatment duration of 17.5 weeks (min-max=10-24) was 4 (95% CI = 3-11).

Difference in bulimic symptoms

The analysis of the mean difference in bulimic symptoms was based on the number of patients who reported the number of bulimic episodes at the end of the trial. No difference was found between

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treatment groups in mean rates of bulimic episodes at baseline. The chi-square test suggested heterogeneity in the results of the studies. SMD was not significant either including or excluding the outlier study (Leitenberg 1994).

Difference in depression

The analysis of the mean difference in depressive symptoms was also based on the number of patients who reported depression scores at the end of the trial. Three trials reported mean and standard deviations for depressive symptoms at endpoint (Leitenberg 1994, Goldbloom 1996, Walsh 1997) and Goldbloom 1996 provided intention to treat data. Most trials did not include depressive patients and baseline mean depression scores were low. No difference between the two treatments was demonstrated. It was not possible to evaluate if the effects of antidepressants on bulimic symptoms were independent of their effect on depressive symptoms because individual patient data was not obtained.

Meta-analysis 2 (antidepressants versus combinations)

Remission

Remission was reported in four trials (Agras 1994, Leitenberg 1994, Goldbloom 1996, Walsh 1997). In general, short-term remission of binge episodes was more likely in the combination than the single antidepressants group (42% versus 23%). DL RR for the four studies reporting this outcome was 1.40 (95% CI = 0.98-1.99) . The NNT for a mean treatment duration of 19 weeks (min-max=16-24), considering the non-remission rate in the antidepressants group of 77% as a measure of the baseline risk, was 5 (95% CI = 3 to 26).

Clinical improvement

As clinical improvement was reported in only one trial, this outcome was not analysed.

Dropouts

Overall dropout rates were high. Forty-one percent of the patients receiving single antidepressant treatment dropped out from the studies, compared to 34% of those randomised to the combined treatment (RR= 1.19; 95% CI 0.69-2.05).

Difference in bulimic symptoms

Four trials were included in the analysis (Leitenberg 1994, Goldbloom 1996, Agras 1994, Walsh 1997). SMD was 0.34 (95% CI= -0.05-0.73) in favour, but just missing significance, of the combined treatment.

Difference in Depression

Three trials reported mean and standard deviations for depressive symptoms at endpoint (Walsh 1997, Goldbloom 1996, Leitenberg 1994). SMD was 0.24 (95% CI = -0.14-0.62). As individual patient data was not available it was not possible to evaluate if the effects of antidepressants on bulimic symptoms were independent of their effect on depressive symptoms.

Meta-analysis 3 (psychological treatments versus combination)

Remission

Remission was reported in six trials (Leitenberg 1994, Agras 1992 , Russell 1995 b, Fichter 1991, Goldbloom 1996, Walsh 1997). In general, short-term remission of binge episodes was more likely on the combination than the single psychological treatments group (49% versus 36%). DL RR was 1.21 (95% CI = 1.02-1.45). The NNT for a mean treatment duration of 15 weeks (min-max=5-24), considering the non-remission rate in the single psychological treatments group of 64% as a measure of the baseline risk, was 8 (95% CI = 4 - 320). Similar results were obtained when nutritional counselling was removed from the analysis (RR = 1.20; 95% CI 1.00-1.44). The RR for the CBT trials was 1.23 (95% CI 0.95-1.60).

Clinical improvement

Clinical improvement could be obtained from two trials (Fichter 1991, Leitenberg 1994). No difference between treatments could be shown (RR= 0.90; 95% CI = 0.30-2.66).

Dropouts

A statistical significant difference in acceptability of treatment was shown. Dropout rates were 16% for the single psychological treatments and 30% for the combined treatment groups (RR= 0.57; 95% CI = 0.38 - 0.88). The NNH for a mean treatment duration of 14 weeks (min-max=10-24) was 7 (95 % CI = 4 - 21).

Difference in bulimic symptoms

SMD for difference in bulimic symptoms was 0.12 (95% CI= -0.21 - 0.46).

Difference in depression

The analysis of mean difference in depressive symptoms included 5 trials (Russell 1995 b, Fichter 1991, Goldbloom 1996, Leitenberg 1994, Walsh 1997). SMD was 0.13(95% CI= -0.27 - 0.53).

Remission and dropout rates were similar for both "single" psychotherapy treatment groups: the one receiving psychological treatment combined to medication placebo and the one receiving psychological treatments without medication placebo (38% versus 33% for remission and 14% versus 18.5% for dropouts). So, results favouring effectiveness of combination of psychological treatments with active antidepressant medications and acceptability of single psychological treatments can not be interpreted as a result of a reduced effectiveness of psychological treatments due to the combined use of medication placebo.

For meta-analysis 1, the fail-safe N for the outcome "dropouts" was 8. This is the number of studies (with null results) needed to overturn the results of the combined significant test. In meta-analysis 2, the fail-safe N for the outcome "remission" was 0; in meta-analysis 3, the fail-safe N for the outcome "remission" was 0 and for the outcome "dropouts" it was 3.

DISCUSSION

Most guidelines for treatment of bulimia nervosa report that psychotherapy in general, and CBT in particular, is the "gold standard" therapeutic approach (Fairburn 1991). Medication is frequently proposed as a supplement to education, nutritional rehabilitation and psychotherapy. CBT alone is generally considered

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superior to antidepressants alone. Reasons for not using medication as the exclusive treatment of bulimia nervosa usually include: the overall effectiveness of well-established psychological interventions is considered to be good; CBT seems more acceptable to patients than antidepressant medication as the dropout rates are higher with the latter; longer term maintenance of change appears to be better with CBT than antidepressant drugs, as relapse rates with drug discontinuation seem to be high. Nonetheless, CBT is under-utilized, mainly due to the relative unavailability of therapists with specialized training in CBT for eating disorders in many countries. Combining psychological treatments with antidepressant drugs is usually considered more effective than using drugs alone, but to produce few consistent benefits over CBT alone.

This review demonstrates the small number of available trials on direct comparisons between medications and psychotherapy or comparing the combination of antidepressants and psychological treatments with each single approach to guide clinical decisions for the treatment of bulimia nervosa. All studies identified by the search strategy were published in the last decade, showing the increasing interest in evaluating combination strategies to improve efficacy and acceptability of treatments for bulimia nervosa.

Four out of seven trials included in this review used classical individual CBT. One trial used an intensive group CBT. Intensive inpatient psychotherapy and nutritional counselling were used in the remaining studies. It could be argued that combining such different treatments is not sensible. However, in this review no difference among these treatments could be shown, as indicated by the sensitivity analysis. Considering the small number of trials, with rather reduced sample sizes, a more conservative statistical approach seemed more appropriate.

All participants were patients with purging type bulimia nervosa. Those with severe comorbid depression, obesity and substance abuse were usually excluded from the trials. Patients were recruited through advertising in the majority of studies. These patients may differ on some demographic, clinical and psychological variables from nonrecruited bulimic patients. It was not possible in this review to determine whether the source of referral influenced treatment outcome. Therefore there may be limitations on the generalisability of the findings from this review.

Remission rates for single antidepressants were equivalent to those found in another meta-analysis comparing different classes of antidepressants with placebo (Bacaltchuk 2000 a). About 20% of the patients were "free" of binge-eating episodes at the end of the short-term trials. Figures were better in the single psychotherapy group, but still not very high (less than 40%). It is possible that the statistical power was insufficient to demonstrate a significant difference in efficacy between the two single approaches. This difference seems, however, clinically relevant. When psychological treatments were combined with antidepressants, efficacy of each single approach was improved. This better outcome may be related to a host of possible factors, including patients and therapists preferences. The increased efficacy of the combined treatments was statistically significant when compared to single psychological treatments and marginally significant but clinically relevant when compared to single antidepressants. Nevertheless, some authors are more cautious about the added value of the combined therapy on the cardinal features of binge eating or purging behaviours in BN (Mitchell 1990, Agras 1992). It must be pointed out that as only one trial reported remission rates for SSRIs, conclusions are necessarily limited with respect to clinical guidance regarding choice of drug.

Data from these seven trials confirmed that single psychological treatments are a better-accepted therapeutic approach. Many patients with BN appear reluctant to take antidepressant medications and even reject participate in trials with madication-only treatment groups (Leitenberg 1994) prefering psychological approaches. The combination of antidepressants with psychological treatments were less accepted than psychological treatments alone.

Only two of these seven comparative studies have reported longer term follow-up (Mitchell 1987 b, Agras 1992). Both suggest a better maintenance of change with CBT.

AUTHORS' CONCLUSIONS

Implications for practice

The current findings are based on a small number of trials, most of them including few patients. According to the fail-safe N calculations, results are not strong and more trials are necessary to confirm these findings. One single trial with null results could overturn the significant results regarding efficacy. For that reason, clinical recommendations at this point in time must be cautious. Another important issue in clinical practice is the effect variation according to dose and compliance. The limited discussion in this review regarding medications dose and assessment of compliance, among other relevant questions, is determined by restricted information available in original studies and the limitations of meta-analysis itself. Such statistical summary can not answer important questions if the original RCTs were not designed for that purpose. As long as new studies are not available, combination of antidepressants and psychological treatments may be recommended as an efficient treatment for bulimia nervosa, particularly when bulimic symptoms are very severe and a single approach has been only partially successful. In many clinical settings where a psychotherapist trained for the treatment of eating disorders is available, single CBT is frequently indicated as a first therapeutic choice. Antidepressant medications may be considered a first-line treatment if a skilled psychotherapist is not available. If an increased efficacy of single CBT is needed, augmentation with antidepressants can be recommended. When adding antidepressants it may be sensible to implement measures to prevent dropouts.

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Implications for research

More studies with higher sample sizes are needed in order to better estimate the differential effectiveness and acceptability of these two therapeutic approaches. Well-designed and unbiased RCTs evaluating short and long-term outcomes, including relapse and maintenance of remission, are necessary. It is also important to better define which is the most adequate outcome to be evaluated and examine predictors of response to each treatment and the effects of combined treatments (psychotherapy plus medication). Meanwhile, trials should systematically report remission rates, the number of patients that do not fulfill diagnostic criteria at the end of the trial, as well as other relevant dimensions of response.

Other psychological interventions, such as interpersonal, psychodynamic, supportive-expressive and focal interpersonal psychotherapies, self-help and behavioral treatments, should also be compared to antidepressants and combined treatments. Further evaluation is needed of longer-term medication trials and of other drug therapies, such as the new antiepileptics, as well as of two stage interventions.

New trials should also include bulimic patients with severe comorbid conditions frequently seen in clinical settings (like depression and substance abuse), as well as adolescent patients. Raters should always be blind to treatments and patients and investigators should systematically be questioned about treatment preferences in order to detect possible bias. A question raised by this data is whether CBT is cost-effective when compared to antidepressants in a short-term. Specifically designed studies allowing for economic analysis should be performed to clarify this point.

It is of note that since the inception of this review (first search dated to 1997) there have been no new trials in this area. As with the research in the area of antidepressant treatment efficacy for bulimia nervosa, there are likely several reasons for this. They include the possible greater acceptance of psychotherapy by clinicians and patients, and the costs of further trials for the use of medication in areas other than that of their first indication. However, the hypothesis that combined approaches improve the acceptability of antidepressants, and appear to be more efficacious than either approach alone, needs to be confirmed.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agras 1992

Methods	RCT, 24 weeks, ITT. Assessor blind to assignment, different from physicians
Participants	DSM-III-R BN; 18-65 years old, mean: 30 years old, recruited from eating disorder clinic + ads. Binges/w: 9,2. Purges/w: 7,5. Beguin BN: 20 years old
Interventions	Desipramine (15 min sessions): 25 mg/3days,, till 300 mg(25-50 mg / 3-5 days. Mean: 167mg/day. versus CBT: 50 min sessions, experienced therapists (5 years) -self monitoring eating behaviors -3 or more meals per day -cognitive restructuring relapse prevention Supervised ttt, 15 sessions/16 weeks, follow-up at weeks 20 and 24k
Outcomes	Remission (at 32 weeks) Change in bulimic symptoms Drop-outs to any cause Depr: BDI, not done
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Fichter 1991 a

Methods	RCT, sealed envelopes and identical capsules, 5 weeks duration
Participants	BN DSM-III-R, 39 female, 1 male.Age: 24.6(pl);26.5(fl). Onset of eating dis: 16 years old.Binges/w: 8.8(pl); 5.6(fl). HDRS: 14.1(pl]); 13.3(fl)
Interventions	Fluoxetine 60mg versus placebo plus intensive inpatient psychotherapy (behavioral)
Outcomes	Remission Clinical Improvement Deterioration Change in bulimic symptoms Drop-outs to any cause Depression (HDRS)
Notes	

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Fichter 1991 a (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Goldbloom 1996

Methods	RCT,16 weeks, not ITT, self assessments, follow-up 4 weeks after the end of the trial, experienced psychiatrists or psychologists, independent assessor
Participants	BN DSM-III-R, 6 month duration, 2 episodes per week, n= 76, referred by health professionals to Eating Disorders Program, females, Age= 18-45 years, mean of completers: 25.8, 85-125% population mean weight, BMI of completers:20
Interventions	Fluoxetine 60 mg versus CBT versus combination. CBT= Fairburn, 16 sessions over 16 weeks, 1 hr. sessions, FL= 10 sessions, 10 min
Outcomes	Remission not ITT Drop-outs due to any cause Depression: Beck
Notes	Author supplied unpublished data

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Leitenberg 1994

Methods	RCT, 20 weeks, self records(diaries)
Participants	BN DSM-III-R + Russell, 4 episodes of vomiting/week/2weeks, women, 18-45 years old, mean 26.7, 80-120% normal weight, newspaper advertisement and referrals, duration=83.48 months, vomiting/week baseline=8.5
Interventions	Desipramine >= 150 mg versus CBT versus combinations. 22 sessions of CBT, 20 weeks, 1 and 1/2 to 2 hours sessions. Fairburn CBT with exposure to eating feared foods plus response prevention (vomiting). DFesipramine alone group sessions: 15 min. Start dose:50 mg/d, increases of 50 mg every 3 days
Outcomes	Remission Clinical improvement Change in bulimic symptoms Drop-outs due to any cause

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Leitenberg 1994 (*Continued*)

Notes	IDD is highly correlated to BDI	
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Mitchell 1990

Methods	RCT, 10 weeks, physicians responsible for medication management were blind to randomization	
Participants	Bulimia DSM-III, 3 episodes/week/6 months, patients being evaluated in ED clinic and advertisements. Age 18-40, mean 24, female, 80-120% ideal body weight, mean 107%, duration of illness 6.5 years, binges/week baseline=7,3(i)/ 8,0(pl)/ 9,2(pt)/ 8.4(comb).HDRS baseline=11	
Interventions	Imipramine versus Intensive CBT versus combinations. Initial dose 50 mg, increments to 200 mg for 2 weeks, maintained for 2 weeks, if necessary 300 mg.CBT= 3 phases. 1= 2 hour sessions for each week 2 weeks: mael planning and CBT techniques. 2=arttempt to interrupt bulimic behaviors begin eating regular meals, use of CBT techniques,5 nights a week, 3 hour sessions, then 2 sessions/week (lecture+diner+psychotherapy). 3= last month: 1 and half hour sessions, exposure and relapse prevention	
Outcomes	Drop-outs due to any cause	
Notes	HDRS	
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Russell 1995 b

Methods	RCT, parallel,DB, 8 weeks. Placebo wash out 7-10 days run in. ITT analysis. Patient diaries. Assessors different from therapists
Participants	DSM-III-R BN. Age: 24,2 (fl) 25,1(pl), BMI: 22. Weight: 60,5(fl),60,9(pl), referrals and patients at the university treatment centers. Objective Binges/w: 5,7(fl); 3,2(pl) + difference statistically significant. HDRS: 11(fl); 11,8 (pl)
Interventions	Fluoxetine plus nutritional counselling program versus nutritional counselling progra plus placebo
Outcomes	Remission Relapse (3 months) Change in bulimic symptoms Drop-outs to side effects and any cause

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Russell 1995 b (*Continued*)

	Depression (HDRS)	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Walsh 1997

Methods	RCT, 16 weeks, single blind placebo wash out run-in,diary, interviewers blinded to treatment, ITT analysis	
Participants	BN DSM-III-R+ 1 year + vomiting(purging type). 18-45 years old, mean=26, 80-120% ideal weight, BMI=21.9, through advertisements, duration of illness=7,91, binges/week baseline:7,43, BDI= 13.4	
Interventions	Desipramine 200 mg till 300 mg followed by fluoxetine 60 mg if not improved versus CBT or SPT or combinations= CBT + med, CBT + Pl, SPT + med, SPT + pl, med. CBT derived from Fairburn, 20 sessions. Medication: desi for 8 weeks. If not better, fluoxetine	
Outcomes	Remission Change in bulimic symptoms Depression: BDI	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Agras 1987	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Alger 1991	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Barlow 1988	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Blouin 1988	RCT comparing antidepressant with placebo. No psychological treatment or combination control group

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(*Continued*)

Box 1983	Not BN patients, antidepressant versus placebo. No psychological treatment or combination control group
FBNCSG 1992	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Fichter 1991	No antidepressant alone group. Fluoxetine + placebo versus psychotherapy plus placebo
Horne 1988	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Hughes 1986 a	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Kanerva 1994	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Kennedy 1986	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Kennedy 1988	No psychotherapy control group.
Kennedy 1993	No psychotherapy control group.
Marcus 1990	Antidepressant plus behaviour modification versus placebo plus behaviour modification. No separate data for BN patients provided by the author
Margittai 1987	Subset of Barlow 1988: RCT comparing antidepressant with placebo. No psychological treatment or combination control group
McCann 1990	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Mitchell 1984	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Mitchell 1987 b	Subset of Mitchell 1990. Sex-month follow-up maintenance data.
Pope 1983	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Pope 1989	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Price 1987	Not RCT. No psychological treatment or combination control group
Rothschild 1994	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Sabine 1983	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Scrimali 1994	RCT comparing antidepressant with diet. No psychological treatment or combination control group
Walsh 1984	Subset of Walsh 1988: RCT comparing antidepressant with placebo. No psychological treatment or combination control group

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(*Continued*)

Walsh 1985	Subset of Walsh 1988: RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Walsh 1991 a	RCT comparing antidepressant with placebo. No psychological treatment or combination control group
Wheadon 1992	RCT comparing antidepressant with placebo. No psychological treatment or combination control group

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DATA AND ANALYSES

Comparison 1. Antidepressants versus psychological treatments

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Remission	5	237	Risk Ratio (M-H, Random, 95% CI)	1.26 [0.90, 1.77]
2 Cinical improvement	1	14	Risk Ratio (M-H, Random, 95% CI)	6.0 [0.95, 37.76]
3 Dropouts	4	184	Risk Ratio (M-H, Random, 95% CI)	2.18 [1.09, 4.35]
4 Difference in bulimic symptoms	4	143	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.26, 0.70]
5 Difference in depression	3	109	Std. Mean Difference (IV, Random, 95% CI)	0.30 [-0.29, 0.89]

Comparison 2. Antidepressants versus combination of antidepressants and psychotherapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Remission	4	141	Risk Ratio (M-H, Random, 95% CI)	1.37 [0.98, 1.91]
2 Cinical improvement	1	14	Risk Ratio (M-H, Random, 95% CI)	2.0 [0.81, 4.96]
3 Dropouts	4	196	Risk Ratio (M-H, Random, 95% CI)	1.19 [0.69, 2.05]
4 Difference in bulimic symptoms	4	136	Std. Mean Difference (IV, Random, 95% CI)	0.34 [-0.05, 0.73]
5 Difference in depression	3	111	Std. Mean Difference (IV, Random, 95% CI)	0.24 [-0.14, 0.62]

Comparison 3. Psychotherapy versus combination of psychotherapy and antidepressants

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Remission	6	257	Risk Ratio (M-H, Random, 95% CI)	1.21 [1.02, 1.45]
2 Cinical improvement	2	54	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.30, 2.66]
3 Dropouts	6	295	Risk Ratio (M-H, Random, 95% CI)	0.57 [0.38, 0.88]
4 Difference in bulimic symptoms	6	247	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.21, 0.46]
5 Difference in depression	5	217	Std. Mean Difference (IV, Random, 95% CI)	0.13 [-0.27, 0.53]

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Comparison 4. CBT versus combination of CBT and antidepressants

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Remission	4	150	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.95, 1.60]
2 Dropouts	4	188	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.33, 0.92]

Comparison 5. Classical psychotherapy versus combination of antidepressants and psychotherapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Remission	5	190	Risk Ratio (M-H, Random, 95% CI)	1.20 [1.00, 1.44]
2 Dropouts	5	228	Risk Ratio (M-H, Random, 95% CI)	0.55 [0.33, 0.90]

Analysis 1.1. Comparison 1 Antidepressants versus psychological treatments, Outcome 1 Remission.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 1 Antidepressants versus psychological treatments

Outcome: 1 Remission

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	7/12	10/23		14.3 %	1.34 [0.69, 2.62]
Goldbloom 1996	20/23	21/24		28.7 %	0.99 [0.80, 1.24]
Leitenberg 1994	7/7	2/7		7.9 %	3.00 [1.06, 8.52]
Mitchell 1990	45/54	17/34		23.9 %	1.67 [1.17, 2.38]
Walsh 1997	20/28	19/25		25.2 %	0.94 [0.68, 1.30]
Total (95% CI)	**124**	**113**		**100.0 %**	**1.26 [0.90, 1.77]**
Total events: 99 (Treatment), 69 (Control)					
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 13.40$, df = 4 (P = 0.01); $I^2 = 70\%$					
Test for overall effect: Z = 1.36 (P = 0.17)					

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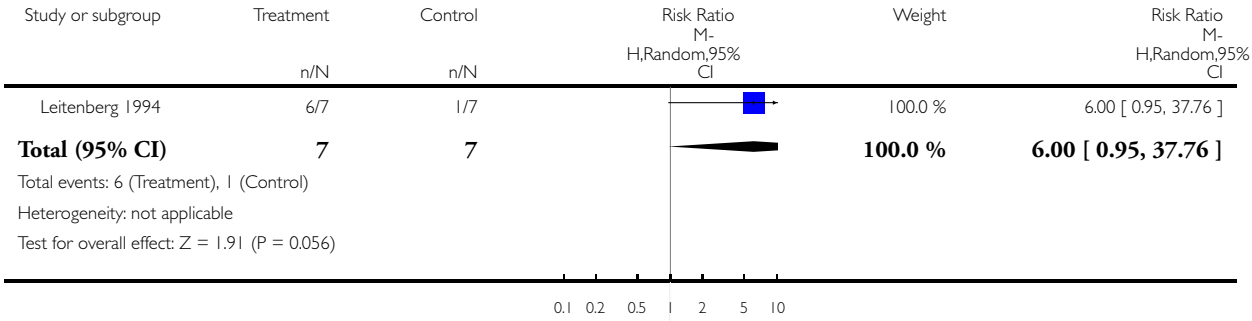
Analysis 1.2. Comparison 1 Antidepressants versus psychological treatments, Outcome 2 Cinical improvement.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 1 Antidepressants versus psychological treatments

Outcome: 2 Cinical improvement

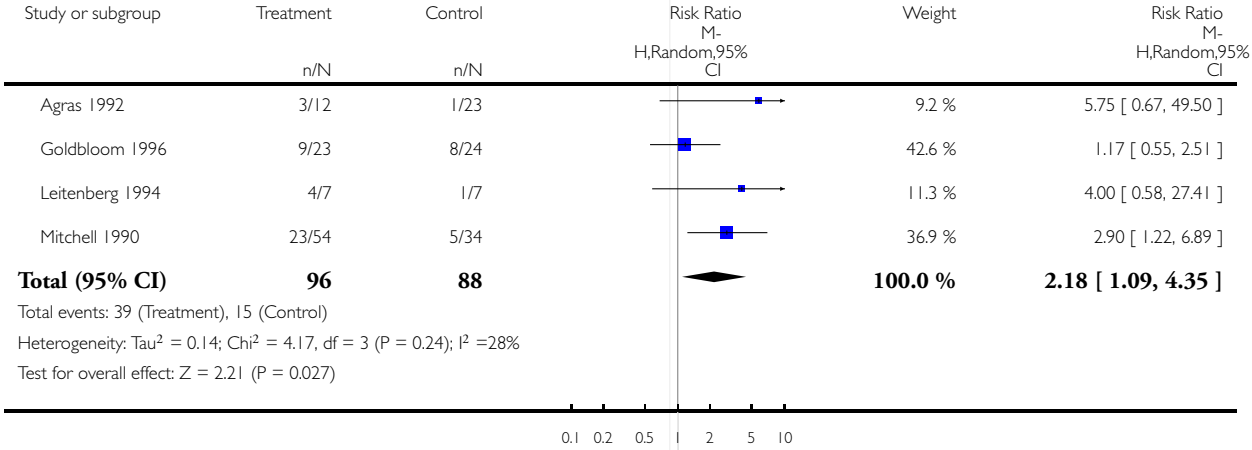


Analysis 1.3. Comparison 1 Antidepressants versus psychological treatments, Outcome 3 Dropouts.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 1 Antidepressants versus psychological treatments

Outcome: 3 Dropouts



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Analysis 1.4. Comparison 1 Antidepressants versus psychological treatments, Outcome 4 Difference in bulimic symptoms.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 1 Antidepressants versus psychological treatments

Outcome: 4 Difference in bulimic symptoms

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Agras 1992	12	2.7 (2.8)	23	2.8 (5.9)		26.9 %	-0.02 [-0.72, 0.68]
Goldbloom 1996	23	22.52 (24)	23	15.91 (19.9)		32.6 %	0.29 [-0.29, 0.88]
Leitenberg 1994	3	8.17 (5.96)	6	0.08 (0.2)		5.4 %	2.25 [0.29, 4.22]
Walsh 1997	28	2.59 (3.5)	25	2.56 (3.3)		35.0 %	0.01 [-0.53, 0.55]
Total (95% CI)	**66**		**77**			**100.0 %**	**0.22 [-0.26, 0.70]**

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 5.14$, df = 3 (P = 0.16); $I^2 = 42\%$

Test for overall effect: Z = 0.89 (P = 0.38)

Analysis 1.5. Comparison 1 Antidepressants versus psychological treatments, Outcome 5 Difference in depression.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 1 Antidepressants versus psychological treatments

Outcome: 5 Difference in depression

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Goldbloom 1996	23	17.04 (12.8)	24	15.63 (14.5)		44.4 %	0.10 [-0.47, 0.67]
Leitenberg 1994	3	21 (10.44)	6	8.17 (1.84)		9.0 %	1.97 [0.13, 3.81]
Walsh 1997	28	8.2 (9)	25	6.8 (7)		46.5 %	0.17 [-0.37, 0.71]
Total (95% CI)	**54**		**55**			**100.0 %**	**0.30 [-0.29, 0.89]**

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 3.66$, df = 2 (P = 0.16); $I^2 = 45\%$

Test for overall effect: Z = 1.00 (P = 0.32)

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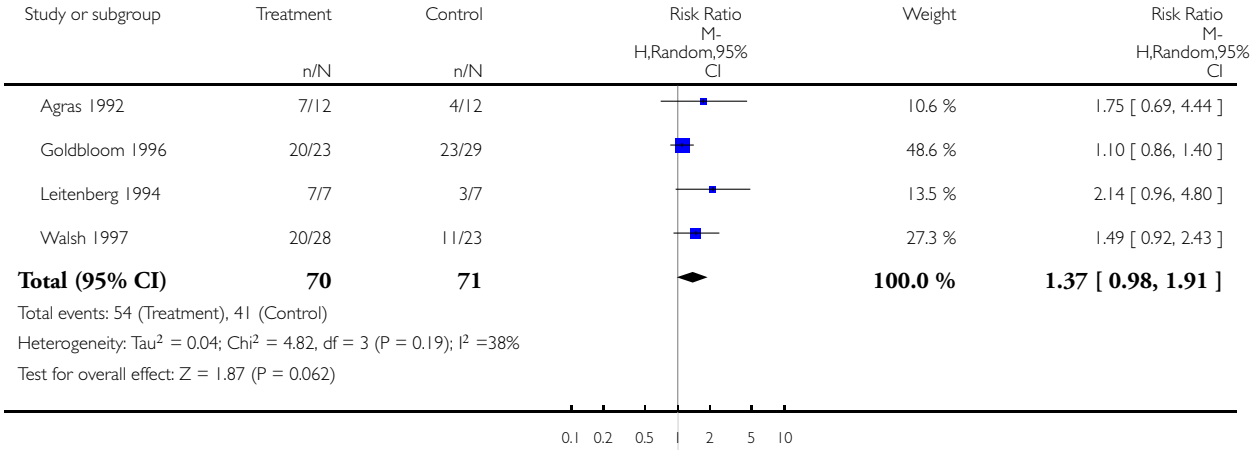
Analysis 2.1. Comparison 2 Antidepressants versus combination of antidepressants and psychotherapy, Outcome 1 Remission.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 2 Antidepressants versus combination of antidepressants and psychotherapy

Outcome: 1 Remission

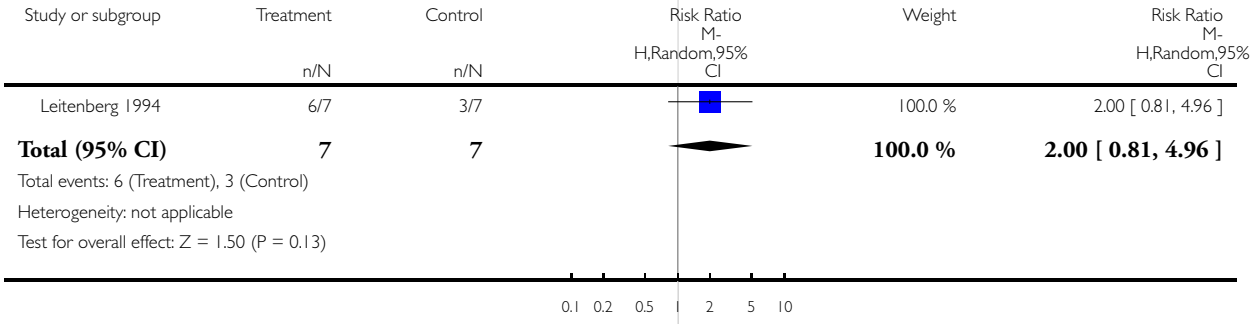


Analysis 2.2. Comparison 2 Antidepressants versus combination of antidepressants and psychotherapy, Outcome 2 Cinical improvement.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 2 Antidepressants versus combination of antidepressants and psychotherapy

Outcome: 2 Cinical improvement



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Analysis 2.3. Comparison 2 Antidepressants versus combination of antidepressants and psychotherapy, Outcome 3 Dropouts.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 2 Antidepressants versus combination of antidepressants and psychotherapy

Outcome: 3 Dropouts

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	3/12	3/12		12.5 %	1.00 [0.25, 4.00]
Goldbloom 1996	9/23	16/29		35.9 %	0.71 [0.39, 1.30]
Leitenberg 1994	4/7	2/7		13.3 %	2.00 [0.53, 7.60]
Mitchell 1990	23/54	13/52		38.2 %	1.70 [0.97, 2.99]
Total (95% CI)	**96**	**100**		**100.0 %**	**1.19 [0.69, 2.05]**

Total events: 39 (Treatment), 34 (Control)

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 5.03$, df = 3 (P = 0.17); $I^2 = 40\%$

Test for overall effect: Z = 0.62 (P = 0.54)

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Analysis 2.4. Comparison 2 Antidepressants versus combination of antidepressants and psychotherapy, Outcome 4 Difference in bulimic symptoms.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 2 Antidepressants versus combination of antidepressants and psychotherapy

Outcome: 4 Difference in bulimic symptoms

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Agras 1992	12	2.7 (2.8)	12	2.3 (4.7)		20.3 %	0.10 [-0.70, 0.90]
Goldbloom 1996	23	22.52 (24)	29	20.34 (25.6)		37.7 %	0.09 [-0.46, 0.63]
Leitenberg 1994	4	9.16 (4.93)	5	2.4 (3.78)		5.9 %	1.39 [-0.18, 2.96]
Walsh 1997	28	2.59 (3.5)	23	0.95 (1.6)		36.1 %	0.57 [0.01, 1.14]
Total (95% CI)	**67**		**69**			**100.0 %**	**0.34 [-0.05, 0.73]**

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 3.56$, df = 3 (P = 0.31); $I^2 = 16\%$

Test for overall effect: Z = 1.73 (P = 0.084)

Analysis 2.5. Comparison 2 Antidepressants versus combination of antidepressants and psychotherapy, Outcome 5 Difference in depression.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 2 Antidepressants versus combination of antidepressants and psychotherapy

Outcome: 5 Difference in depression

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Goldbloom 1996	23	17.04 (12.8)	29	17.07 (12.1)		47.7 %	0.00 [-0.55, 0.54]
Leitenberg 1994	3	21 (10.44)	5	18.2 (10.82)		6.9 %	0.23 [-1.21, 1.67]
Walsh 1997	28	8.2 (9)	23	4.4 (5)		45.4 %	0.50 [-0.06, 1.06]
Total (95% CI)	**54**		**57**			**100.0 %**	**0.24 [-0.14, 0.62]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.58$, df = 2 (P = 0.45); $I^2 = 0.0\%$

Test for overall effect: Z = 1.25 (P = 0.21)

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Analysis 3.1. Comparison 3 Psychotherapy versus combination of psychotherapy and antidepressants, Outcome 1 Remission.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 3 Psychotherapy versus combination of psychotherapy and antidepressants

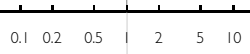
Outcome: 1 Remission

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	13/23	4/12		4.0 %	1.70 [0.71, 4.07]
Fichter 1991 a	16/20	13/20		20.4 %	1.23 [0.83, 1.82]
Goldbloom 1996	21/24	23/29		53.8 %	1.10 [0.87, 1.40]
Leitenberg 1994	2/7	3/7		1.5 %	0.67 [0.16, 2.84]
Russell 1995 b	13/33	10/34		6.9 %	1.34 [0.68, 2.62]
Walsh 1997	19/25	11/23		13.4 %	1.59 [0.98, 2.57]
Total (95% CI)	**132**	**125**		**100.0 %**	**1.21 [1.02, 1.45]**

Total events: 84 (Treatment), 64 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.51$, df = 5 (P = 0.62); $I^2 = 0.0\%$

Test for overall effect: Z = 2.15 (P = 0.032)



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Analysis 3.2. Comparison 3 Psychotherapy versus combination of psychotherapy and antidepressants, Outcome 2 Cinical improvement.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 3 Psychotherapy versus combination of psychotherapy and antidepressants

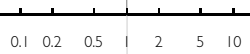
Outcome: 2 Cinical improvement

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Fichter 1991 a	12/20	10/20		77.5 %	1.20 [0.68, 2.11]
Leitenberg 1994	1/7	3/7		22.5 %	0.33 [0.04, 2.48]
Total (95% CI)	**27**	**27**		**100.0 %**	**0.90 [0.30, 2.66]**

Total events: 13 (Treatment), 13 (Control)

Heterogeneity: $Tau^2 = 0.31$; $Chi^2 = 1.55$, df = 1 (P = 0.21); $I^2 = 36\%$

Test for overall effect: Z = 0.19 (P = 0.85)



Analysis 3.3. Comparison 3 Psychotherapy versus combination of psychotherapy and antidepressants, Outcome 3 Dropouts.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 3 Psychotherapy versus combination of psychotherapy and antidepressants

Outcome: 3 Dropouts

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	1/23	3/12		3.9 %	0.17 [0.02, 1.50]
Fichter 1991 a	0/20	1/20		1.8 %	0.33 [0.01, 7.72]
Goldbloom 1996	8/24	16/29		42.5 %	0.60 [0.31, 1.16]
Leitenberg 1994	1/7	2/7		3.9 %	0.50 [0.06, 4.33]
Mitchell 1990	5/34	13/52		20.7 %	0.59 [0.23, 1.50]
Russell 1995 b	7/33	11/34		27.2 %	0.66 [0.29, 1.49]
Total (95% CI)	**141**	**154**		**100.0 %**	**0.57 [0.38, 0.88]**

Total events: 22 (Treatment), 46 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.45$, df = 5 (P = 0.92); $I^2 = 0.0\%$

Test for overall effect: Z = 2.55 (P = 0.011)

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Analysis 3.4. Comparison 3 Psychotherapy versus combination of psychotherapy and antidepressants, Outcome 4 Difference in bulimic symptoms.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

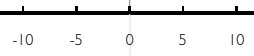
Comparison: 3 Psychotherapy versus combination of psychotherapy and antidepressants

Outcome: 4 Difference in bulimic symptoms

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Agras 1992	23	2.8 (5.9)	12	2.3 (4.7)		15.4 %	0.09 [-0.61, 0.79]
Fichter 1991 a	20	6.6 (6.94)	19	3 (4.77)		17.1 %	0.59 [-0.05, 1.23]
Goldbloom 1996	23	15.91 (19.9)	29	20.34 (25.6)		20.7 %	-0.19 [-0.74, 0.36]
Leitenberg 1994	6	0.33 (5)	2	4 (3.78)		3.7 %	-0.66 [-2.33, 1.00]
Russell 1995 b	32	0.8 (1.7)	33	1.2 (2.7)		23.5 %	-0.17 [-0.66, 0.31]
Walsh 1997	25	2.56 (3.5)	23	0.95 (1.6)		19.5 %	0.57 [0.00, 1.15]
Total (95% CI)	**129**		**118**			**100.0 %**	**0.12 [-0.21, 0.46]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 7.87$, df = 5 (P = 0.16); $I^2 = 37\%$

Test for overall effect: Z = 0.72 (P = 0.47)



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Analysis 3.5. Comparison 3 Psychotherapy versus combination of psychotherapy and antidepressants, Outcome 5 Difference in depression.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

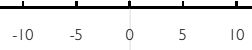
Comparison: 3 Psychotherapy versus combination of psychotherapy and antidepressants

Outcome: 5 Difference in depression

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Fichter 1991 a	20	11.1 (7.4)	19	8.3 (5)		20.4 %	0.43 [-0.20, 1.07]
Goldbloom 1996	23	15.91 (19.9)	29	20.34 (25.6)		23.6 %	-0.19 [-0.74, 0.36]
Leitenberg 1994	6	8.17 (1.84)	5	18.2 (10.82)		7.2 %	-1.25 [-2.60, 0.10]
Russell 1995 b	33	6.8 (6.4)	34	5.3 (5.5)		26.2 %	0.25 [-0.23, 0.73]
Walsh 1997	25	8.2 (9)	23	4.4 (5)		22.5 %	0.51 [-0.07, 1.08]
Total (95% CI)	**107**		**110**			**100.0 %**	**0.13 [-0.27, 0.53]**

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 7.93$, df = 4 (P = 0.09); $I^2 = 50\%$

Test for overall effect: Z = 0.65 (P = 0.51)



Analysis 4.1. Comparison 4 CBT versus combination of CBT and antidepressants, Outcome 1 Remission.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 4 CBT versus combination of CBT and antidepressants

Outcome: 1 Remission

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	13/23	4/12		8.3 %	1.70 [0.71, 4.07]
Goldbloom 1996	21/24	23/29		64.1 %	1.10 [0.87, 1.40]
Leitenberg 1994	2/7	3/7		3.2 %	0.67 [0.16, 2.84]
Walsh 1997	19/25	11/23		24.4 %	1.59 [0.98, 2.57]
Total (95% CI)	**79**	**71**		**100.0 %**	**1.23 [0.95, 1.60]**

Total events: 55 (Treatment), 41 (Control)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.48$, df = 3 (P = 0.32); $I^2 = 14\%$

Test for overall effect: Z = 1.55 (P = 0.12)

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Analysis 4.2. Comparison 4 CBT versus combination of CBT and antidepressants, Outcome 2 Dropouts.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 4 CBT versus combination of CBT and antidepressants

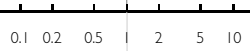
Outcome: 2 Dropouts

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	1/23	3/12		5.5 %	0.17 [0.02, 1.50]
Goldbloom 1996	8/24	16/29		59.8 %	0.60 [0.31, 1.16]
Leitenberg 1994	1/7	2/7		5.5 %	0.50 [0.06, 4.33]
Mitchell 1990	5/34	13/52		29.2 %	0.59 [0.23, 1.50]
Total (95% CI)	**88**	**100**		**100.0 %**	**0.55 [0.33, 0.92]**

Total events: 15 (Treatment), 34 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.22$, df = 3 (P = 0.75); $I^2 = 0.0\%$

Test for overall effect: Z = 2.29 (P = 0.022)



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Analysis 5.1. Comparison 5 Classical psychotherapy versus combination of antidepressants and psychotherapy, Outcome 1 Remission.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 5 Classical psychotherapy versus combination of antidepressants and psychotherapy

Outcome: 1 Remission

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Agras 1992	13/23	4/12		4.3 %	1.70 [0.71, 4.07]
Fichter 1991 a	16/20	13/20		21.9 %	1.23 [0.83, 1.82]
Goldbloom 1996	21/24	23/29		57.8 %	1.10 [0.87, 1.40]
Leitenberg 1994	2/7	3/7		1.6 %	0.67 [0.16, 2.84]
Walsh 1997	19/25	11/23		14.4 %	1.59 [0.98, 2.57]
Total (95% CI)	**99**	**91**		**100.0 %**	**1.20 [1.00, 1.44]**

Total events: 71 (Treatment), 54 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.38$, df = 4 (P = 0.50); $I^2 = 0.0\%$

Test for overall effect: Z = 1.99 (P = 0.046)

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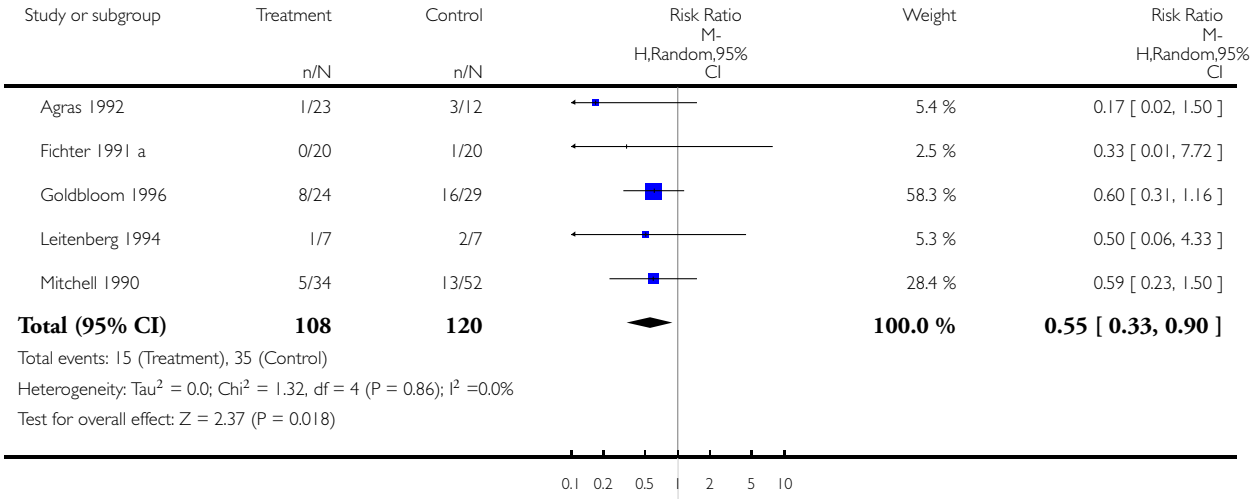
Analysis 5.2. Comparison 5 Classical psychotherapy versus combination of antidepressants and psychotherapy, Outcome 2 Dropouts.

Review: Antidepressants versus psychological treatments and their combination for bulimia nervosa

Comparison: 5 Classical psychotherapy versus combination of antidepressants and psychotherapy

Outcome: 2 Dropouts



WHAT'S NEW

Last assessed as up-to-date: 12 August 2001.

Date	Event	Description
1 November 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 4, 1997

Review first published: Issue 4, 2001

Date	Event	Description
13 August 2001	New citation required and conclusions have changed	Substantive amendment

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DECLARATIONS OF INTEREST

None.

JB has received fees from Janssen-Cilag Farmaceutica, Brazil. PH has received supprot to attend conferences and meetings from Pfizer PTY Ltd, Solvay Pharmaceuticals and Bristol-Myers Squibb Pharmaceuticals.

NOTES

This review is in the process of being updated. We hope to publish the updated version in Issue 2, 2008.

INDEX TERMS

Medical Subject Headings (MeSH)

*Psychotherapy; Antidepressive Agents [*therapeutic use]; Bulimia [drug therapy; *therapy]; Combined Modality Therapy

MeSH check words

Humans

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