Effectiveness of current treatment approaches for benzodiazepine discontinuation: a meta-analysis

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CRD summary
The authors concluded that brief interventions improved benzodiazepine cessation rates compared to routine care. Adding psychological interventions to gradual dose reduction may have increased cessation rates. Evidence appeared to support the authors’ conclusions, but the lack of adequate assessment of differences between studies made it difficult to assess the consistency of treatment effect.

Authors’ objectives
To evaluate the effectiveness of interventions for benzodiazepine cessation in general practice or out-patient settings.

Searching
PsycLIT, MEDLINE and EMBASE were searched from inception to 2005, with a further search conducted in 2007; search terms were reported. Reference lists were searched for further relevant articles.

Study selection
Randomised controlled trials (RCTs) were eligible if they compared adjunctive treatment for benzodiazepine cessation with routine care or gradual dose reduction (GDR) in participants from out-patients who had used benzodiazepines continuously for three months or more before study entry. Studies had to have at least 10 patients in each treatment group at baseline and report sufficient data to permit calculation of cessation rates on an intention-to-treat basis.

Included studies compared routine care with other treatments (a brief intervention that involved a letter from their general practitioner (GP) with or without a self-help booklet, gradual dose reduction or psychological interventions) or compared gradual dose reduction with gradual dose reduction plus additional treatments (psychological interventions or substitutive pharmacotherapy). Where reported, the mean age of patients ranged from 38 to 71 years, the mean duration of taking benzodiazepines ranged from two to 19 years and, in most studies, most patients were women.

Two reviewers independently selected studies and resolved disagreements by discussion or with the help of a third reviewer.

Assessment of study quality
Three reviewers independently assessed validity using an 18-item scale that included criteria related to: patient sampling and description; treatment; follow-up and outcomes; and study design. The maximum possible score was 45 points. Quality ratings were reviewed by two reviewers who reached consensus.

Data extraction
The proportion of patients ceasing benzodiazepines in each treatment group was calculated post-treatment and at follow-up on an intention-to-treat basis. The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The studies were grouped by comparator. Pooled odds ratios and 95% confidence intervals (CI) for each comparison were calculated using the fixed-effect Mantel-Haenszel method. The relationship between study quality score and size of treatment effect was assessed.

Results of the review
Thirty-two RCTs were included. The size of treatment groups ranged from 10 to 129 in studies that randomised individuals and from 1,395 to 7,532 in studies that randomised practices.
Study quality: The median quality score was 19 (range eight to 33) out of 45. Study limitations included inadequate definition of dependency, short-term follow-up (most were less than 12 months) and lack of blinding and independent assessment of outcome.

Treatment versus routine care: Brief interventions, gradual dose reduction and psychological interventions were all associated with a significant increase in benzodiazepine cessation rates compared to routine care.

Brief intervention versus routine care: The odds ratio for the three studies (n=532) that randomised individuals was 4.37 (95% CI: 2.28 to 8.40). The odds ratio for the two studies (n=13,343) that randomised practices was 2.21 (95% CI: 1.92 to 2.55).

Gradual dose reduction versus routine care: The odds ratio was 5.96 (95% CI: 2.08 to 17.11; one study, n=107).

Psychological interventions versus routine care: The post-treatment odds ratio was 3.38 (95% CI: 1.86 to 6.12; three studies, n=354) and the odds ratio at follow-up was 13.5 (95% CI: 1.20 to 152.21; one study, n=20).

Gradual dose reduction versus gradual dose reduction plus additional treatment: Adding psychological interventions to gradual dose reduction slightly but significantly increased benzodiazepine cessation rates compared to gradual dose reduction alone post-treatment (odds ratio 1.82, 95% CI: 1.25 to 2.67; seven studies, n=454) and at follow-up (odds ratio 1.88, 95% CI: 1.19 to 2.97; six studies, n=308).

Gradual dose reduction versus gradual dose reduction plus substitutive pharmacotherapy: There was no significant difference in cessation rates at post-treatment (14 studies, n=927) or follow-up (five studies, n=389).

Psychological treatment plus either gradual or abrupt withdrawal: There was no significant difference in cessation rates at post-treatment or follow-up (one study, n=42).

No evidence was found of a relationship between study quality score and size of treatment effect.

Authors’ conclusions
Brief interventions were more effective than routine care in increasing benzodiazepine cessation rates. Adding psychological interventions to gradual dose reduction may have increased cessation rates compared to gradual dose reduction alone. There was insufficient evidence to support substitutive pharmacotherapies.

CRD commentary
The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched, but no attempts were made to minimise publication bias and it was unclear whether attempts were made to minimise language bias. Appropriate methods were used to minimise reviewer error and bias during study selection and validity assessment, but it was unclear whether similar steps were taken in data extraction. Only RCTs were included. Validity was assessed and results were reported. Studies were appropriately grouped by comparators. Statistical heterogeneity was not assessed, so it was unclear whether it was appropriate to pool data statistically. Much of the review was well conducted and clearly reported. Evidence appeared to support the authors’ conclusions, but the lack of adequate assessment of differences between studies made it difficult to assess the consistency of treatment effect.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future research should include assessment of the cost-effectiveness of benzodiazepine cessation interventions. There was also a need to evaluate additional psychological strategies for benzodiazepine cessation and various durations of gradual dose reduction.

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