Introduction: Generalized Anxiety Disorder (GAD) is a common psychiatric disorder, and benzodiazepines (BZD) are effective in its short-term management. This analysis studied the influence of a range of variables on response to BZD in placebo controlled studies in GAD.

Methods: We performed a systematic review of placebo-controlled RCTs with BZDs in GAD as described in a Cochrane Protocol (Gale 2012). We extracted the baseline Hamilton Anxiety (HAM-A) score, change in HAM-A score at endpoint, drop-out rate, year of study publication, diagnostic criteria, dose of benzodiazepines (in diazepam equivalents), study size and duration. The influence of individual variables on the primary endpoint (change in HAM-A) was assessed by ANOVA, and covariate relationships were explored using structural equation modeling (Arbuckle, 2012).

Results: We included 56 studies between 1979 and 2009. In 39 (70%) of these studies, commercial sponsorship was indicated: 15 by a company marketing the BZD. BZD treatment showed consistently greater changes in HAM-A scores than placebo, although these differences decreased in more recent studies (Fig A). Baseline anxiety severity was strongly associated with change in HAM-A scores, but only for BZD-treated study arms (Fig B). Dose did not influence change in HAM-A change. Dropouts tended to increase in BZD-treated arms in more recent studies, and decrease in placebo-treated arms. The size of study arms increased in more recent studies (Fig C), presumably to deal with smaller BZD-placebo differences, and altered dropout rates. ANOVA of individual variables on change in HAM-A identified a number of significant findings (Table D). Structural equation modelling (Fig E) identified a number of direct and indirect influences of variables on change in HAM-A ratings.

Conclusions: This analysis confirms the activity of BZDs in GAD. In addition to treatment allocation to BZDs, baseline anxiety severity has a major direct influence on change in HAM-A ratings.

References