THE PRIMARY CARE COMPANION
FOR CNS DISORDERS

Supplementary Material

Article Title: Effectiveness of Gabapentin in Reducing Cravings and Withdrawal in Alcohol Use Disorder: A Meta-Analytic Review

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List of Supplementary Material for the article

1. Supplementary Appendix 1

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Supplementary Appendix 1

Design-specific standardized mean difference (SMD) scores were calculated for each study, using one (or more, when a study provided data that could be used in more than one of the meta-analyses conducted) of three formulas. For studies that examined single group pretest-posttest changes, Formula 13 in Morris and DeShon[1] was used. For studies that examined posttest differences between independent groups, Formula 2 in Morris and DeShon[1] was used. Finally, for studies that examined differences in pretest-posttest change scores between independent groups, we used Formula 6 in Morris and DeShon.[1] In all cases of effect size calculations, the direction was coded so that negative effect sizes reflect favorable outcomes for the gabapentin group (either from pretest to posttest, relative to placebo at posttest, or amount of pretest-posttest change relative to placebo, depending on the design-specific meta-analyses).

In most cases, these calculations were done using means and standard deviations.[1] In one case[2] these data were not available. As a result, the between-group t-statistic was converted into SMD using Formula 27 from Morris and DeShon.[1]

Calculation of effect sizes were generally straightforward, with some exceptions. Three studies[3–5] involved independent groups, pretest-posttest designs, in which gabapentin treatment groups were compared to another drug instead of placebo. For the purposes of the present meta-analysis, only data from the gabapentin treatment group were extracted (as detailed in the text's Methods section), and the study was treated as a single-group pretest-posttest design in computing effect sizes. In addition, the baseline data for an independent groups' pretest-posttest study was unreported in one publication.[6] Consequently, only the posttest data was extracted, and the study was treated as an independent groups posttest study to compute its effect size.

Given the variability in types of trial designs, we aggregated only design-specific effect sizes across studies. That is, we meta-analyzed separately the (a) single-group pretest-posttest, (b) independent groups posttest, and (c) independent groups pretest-posttest results.

The sampling variances for the independent groups posttest effect sizes were calculated using formula A1.[1] An adapted version of this formula was used for the single-group pretest-posttest effect sizes, but—in contrast to the formula A1 in Morris and DeShon[1]—the effect size term was specifically defined by Formula 13 rather than Formula 4 in Morris and DeShon.[1] The rationale for this adaptation was that Formula 4 in Morris and DeShon[1] requires the standard deviation of the difference scores of outcome variables (or the pretest-posttest correlation of the relevant outcome variable, which can be algebraically transformed into the standard deviation of the difference score), which is information that is almost never reported by primary studies. As a result, it was preferable to use an adapted sampling variance formula for single-group pretest-posttest effect size that does not require this information, rather than impute an arbitrary estimate for the standard deviation of the difference scores. Calculation of sampling variances requires input of the sample size of study participants. As a result of attrition or missing data, however, the pre-test and posttest sample sizes for some studies with single-group

pretest-posttest effect sizes were different. We, therefore, used the pre-test sample sizes for calculation of the sampling variances.

For independent groups pretest-posttest studies, we first calculated single-group pretest-posttest sampling variances separately for the treatment and placebo arms of the study, using the calculations detailed above; both sampling variances were then summed to obtained the sampling variance for the independent groups pretest-posttest effect size.[7] As above, for instances in which pre-test and post-test sample sizes differed from each other, the sampling variances for each of the study arms were calculated using the pre-test sample sizes.

Effect sizes and their sampling variances were meta-analyzed with a random effects model using the metafor package in R.[8] Heterogeneity was measured using the Q and I^2 statistics. A significant Q statistic suggests that the variability among the effect sizes is larger than what is expected from participant sampling error alone. An I^2 value of 75% and above indicates a high degree of heterogeneity.[9] Publication bias was assessed by funnel plots. In addition, trim and fill analysis[10] was conducted to assess the degree to which publication bias may have influenced the meta-analytic results. Specifically, the trim and fill analysis use an iterative procedure to correct for potential publication bias by adjusting the weighted mean effect for studies at the extreme positive side of the graph until the distribution of studies is symmetric. Leave-one-out analyses were carried out for each of the three meta-analyses to assess the replicability and robustness of the results.

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