Meta-analysis of Odds Ratios from Heterogeneous Clinical Studies and Its Shortcomings

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Abstract
Many systematic reviews of randomized clinical trials require meta-analyses of odds ratios. A conventional method estimate the overall odds ratios via weighted averages of the logarithm of individual odds ratios. However, this approach has several deficiencies due to the underlying assumptions and approximations. The goal of this study is to understand and quantify the methodological pitfalls in conducting a meta-analysis of odds ratios. The fixed-effect and random-effect models of pooled odds ratios are compared by applying to a meta-analysis of SNP studies. A popular statistical software R is used for the analysis. The point estimates and confidence intervals for the overall log odds ratio can differ substantially between the traditional and alternative methods, which would affect the resulting statistical inferences. For producing reliable results, the traditional methods for meta-analysis of odds ratios should be discouraged.

Key Words: clinical trials, heterogeneity, meta-analysis, odds ratios, random effect models, randomization

1. Introduction

Many systematic reviews of randomized clinical trials require meta-analyses of odds ratios (OR). A conventional method estimate the overall OR via weighted averages of the logarithm of individual OR's. However, this approach has several deficiencies due to the underlying assumptions and approximations. The goal of this study is to understand and quantify the methodological pitfalls in conducting a meta-analysis of OR.

2. Methods

We considered logistic regression models for meta-regression, and compared fixed-effect and random-effect models of pooled OR via applying to meta-analyses of SNP studies. The popular open-source statistical software R was used for the analysis in addition to SPSS and SAS.

3. Results

The point estimates and confidence intervals for the overall log OR can differ substantially between the traditional and alternative methods, which would affect the resulting statistical inferences; see Figures 1 and 2.

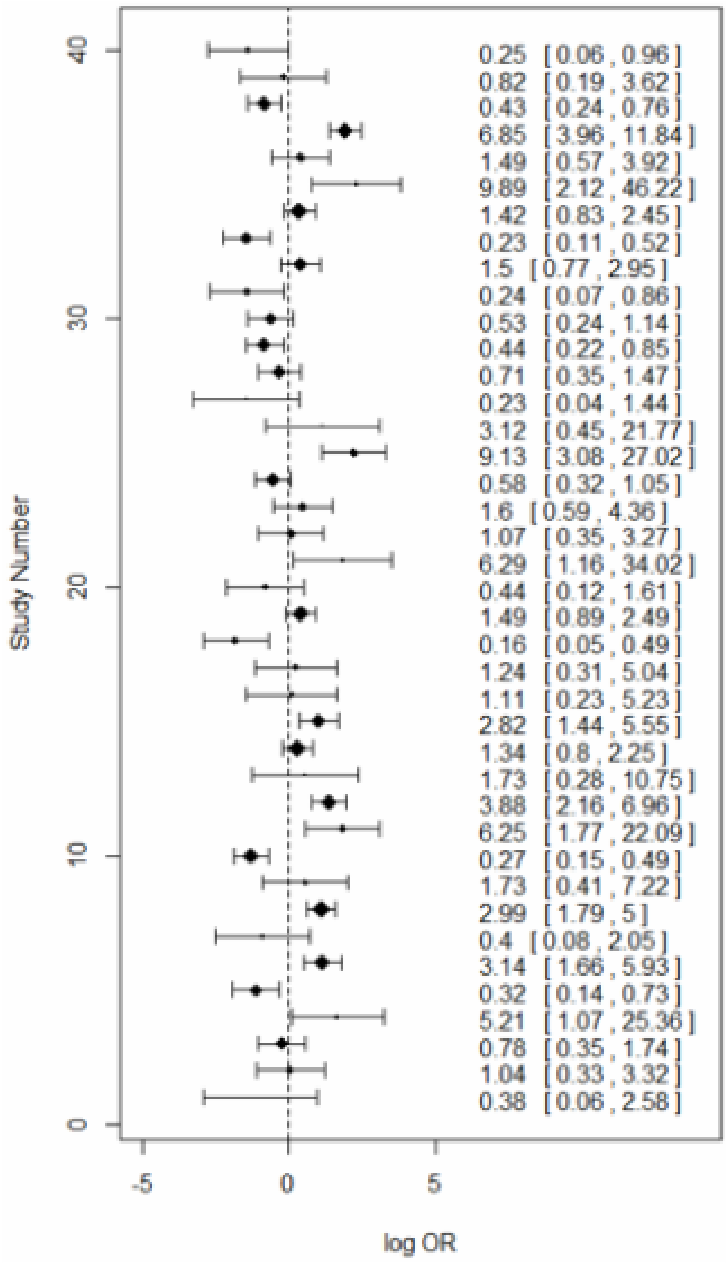

Figure 1: Forest plot of SNP outcome for Alcohol Use Disorder (AUD). The area of each diamond is proportional to the sample size of the study.

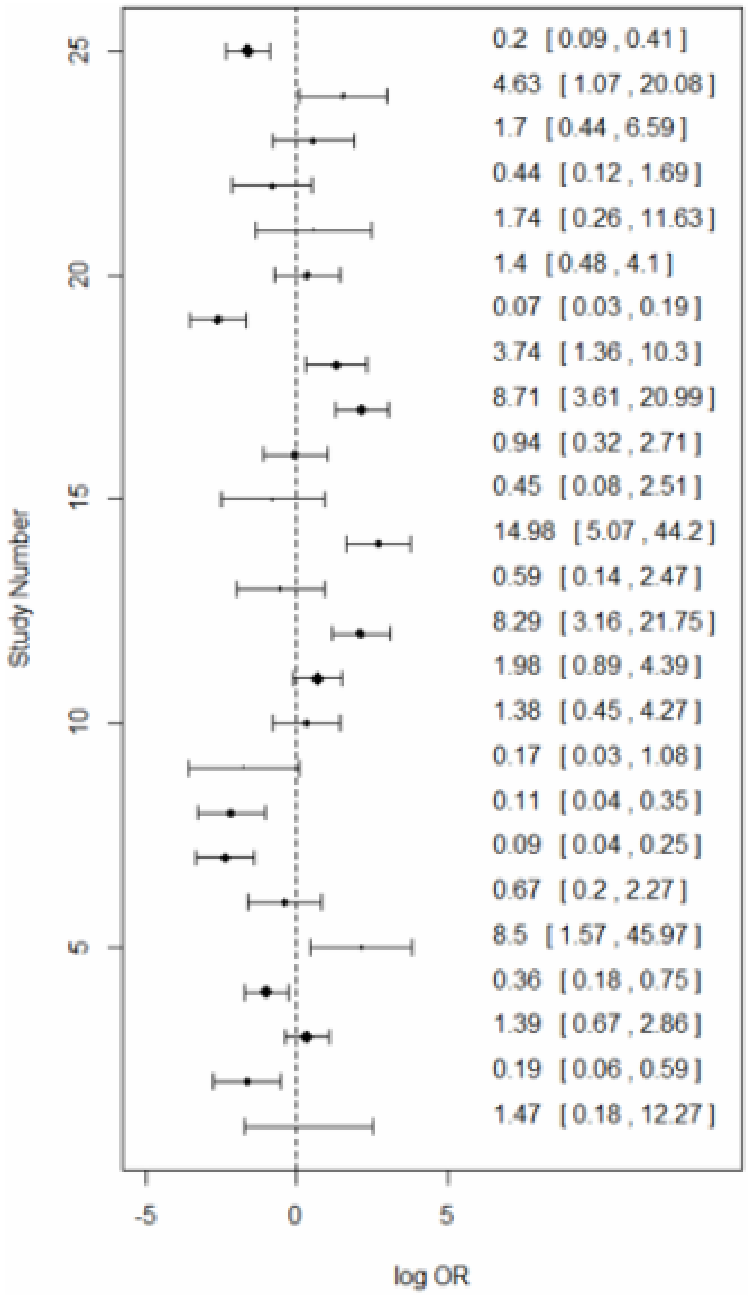

Figure 2: Forest plot of SNP outcome for breast cancer.
The area of each diamond is proportional to the sample size of the study.

4. Recommendation

When the outcome data are available only as study-level summaries such as OR, likelihood ratios (LR), and risk ratios (RR), it is recommended to use the methods that account for the sampling variation in the estimate of the between-study variance (*e.g.*, profile likelihood). Random-effects models are preferred as some degree of heterogeneity exist among different studies unless there is a clear reason to use a fixed-effect model (*e.g.*, identical study setups).

5. Conclusion

As aforementioned, point estimates and confidence intervals for the overall log OR can differ substantially between the traditional and alternative methods. This would affect the resulting statistical inferences. For producing reliable results, the traditional methods for meta-analysis of OR should be discouraged.

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