

# Incorporating Expert Opinions in the Analyses of Binomial Clinical Trials

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## **Abstract**

In the design and analysis of randomized trials, utilization of external information, such as prior information or expert opinions, is an important part of the decision making process. Seeking effective schemes for incorporating expert opinions with the primary outcomes of interest has drawn increasing attention in pharmaceutical applications in recent years. A popular existing scheme is the univariate Bayesian approach which utilizes a normal distribution approximation. Although the univariate Bayesian approach has been applied to binomial trials, there is a serious theoretical problem associated with it in the binomial cases. Motivated by a binomial clinical study on the efficacy of a migraine preventive pharmaceutical agent in enhancing the effect of an acute migraine therapy, we develop in this paper a bivariate full Bayesian approach with an MCMC algorithm as well as a new alternative frequentist approach based on the notion of *confidence distributions* for analyzing binomial outcomes. These approaches, both Bayesian and Frequentist, and a comprehensive comparison are illustrated with analyses of data from the clinical study and simulation. In the case when the prior distribution can be well approximated by a normal distribution, there appears little difference among the univariate Bayesian, the bivariate full Bayesian and the confidence distribution approaches. However, when the prior distribution is skewed, the univariate Bayesian approach based on the normal approximation fails to catch the skewness, the bivariate full Bayesian approach may lead to results that are counter-intuitive, and the confidence distribution approach appears to have an advantage in this setting.

*Key Words:* Bayesian method; frequentist method; confidence distribution; prior distribution; posterior distribution; combining information; expert opinion; MCMC algorithm.

*Running Title:* Incorporate expert opinions in clinical trials