A Bayesian Method for Cross-Trial Inference in the Non-Inferiority Setting

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In settings where a placebo-controlled clinical trial is unethical, experimental therapies are often compared to an active control. When a new therapy offers advantages over the old, such as a reduction in adverse events, regulatory approval may not hinge on proof that the new therapy is superior in efficacy to the old but, rather, on a determination that it is not meaningfully worse. Clinical trials designed to investigate this question are called non-inferiority studies. Often, researchers would also like to show that, in addition to being “non-inferior” to the active control, the new therapy would have been proven superior to placebo, had one been included in the trial. Such proof requires cross-trial inference, which previously required strong, often unrealistic assumptions. For example, most traditional methods require that the constancy assumption holds, i.e., that the effect of any one therapy remains constant from trial to trial. In therapeutic settings with changing patient populations, however, this assumption is often highly suspect. We present a Bayesian method for cross-trial inference when treatment effect changes as a function of the study population. The performance of this method is examined under a variety of circumstances.