New Advances in Fixed-effects Meta-analysis and a New Measure for Heterogeneity

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Abstract

Meta-analysis is a statistical tool for evidence-based practice, which aims to synthesize multiple studies and produces a summary conclusion for the whole body of research. In the literature, there are three main statistical models for meta-analysis including the common-effect model, the random-effects model, and the fixed-effects model. Chapter 1 gives a brief introduction on the above three models for meta-analysis, followed by several real data examples that will be applied in the later chapters.

Among the three models, the common-effect model and the random-effects model are more commonly used in the literature. To choose a proper model between them, the Q statistic and the I^2 statistic are frequently employed as the criteria. Recently, it is recognized that the fixed-effects model is also essential for meta-analysis, especially when the number of studies is small. With this new model, the existing methods are no longer sufficient for model selection in meta-analysis. In view of the demand, we propose a novel method for model selection between the fixed-effects model and the random-effects model in Chapter 2. Specifically, we apply the Akaike information criterion (AIC) to both models and then select the model with a smaller AIC value. A real data example is also presented to illustrate how the new method can be applied. Noticing that the AIC value of REM often has a large variation, especially when the number of the studies is small, we further propose the generalized AIC (GAIC) to reduce the large variation in the AIC value, and demonstrate its superiority through real data analysis and simulation studies. To the best of our knowledge, this is the first work in meta-analysis for model selection between the fixed-effects model and the random-effects model.

In Chapter 3, we propose a new measure for quantifying the heterogeneity in meta-analysis. To achieve the goal, we first show that the I^2 statistic was, in fact, defined as problematic or even be completely wrong from the very beginning. We then present a motivating example to show that the I^2 statistic is heavily dependent on the study sample sizes, and more seriously, it may also yield contradictory results for the amount

of heterogeneity. We further draw a connection between meta-analysis and analysis of variance (ANOVA) to demonstrate that the I^2 statistic has, mistakenly, applied the sampling errors of the estimates but not the variances of the study populations. Inspired by this, we propose an Intrinsic measure for Quantifying the heterogeneity in meta-analysis, referred to as the IQ statistic, to overcome the limitations in the I^2 statistic. "Intrinsic" means the IQ statistic is not affected by the number of studies. Finally, we demonstrate by simulations and real data analysis that the IQ statistic provides a nearly unbiased estimate for the true heterogeneity, and it is also independent of the individual sample sizes.

Combining the p-values is an important statistical approach for the fixed-effects meta-analysis. Existing methods and their statistical properties for combining the p-values rely on the assumption that the individual p-values are independent of each other. In Chapter 4, we propose new methods that are able to combine the p-values derived from dependent tests. And for this purpose, we first derive the joint distribution of the bivariate p-values that are derived from testing two dependent normal means. Like Birnhaum's adimissibility for methods of combining the independent p-values, we also propose the criterion of admissibility for combining the dependent p-values and derive the set of methods combining the bivariate p-values that satisfy such criterion. The theoretical results for the bivariate p-values are further generalized to the multivariate p-values. It is shown that for dependent case, Stouffer's combination method is also admissible subject to an adjustment on the critical values. By simulations and an application to meta-analysis, we show that the adjusted Stouffer's combination method can achieve its nominal type I error rate more accurately than the unadjusted competitor.

Keywords: Common-effect model, Dependent p-values, Fixed-effects model, Heterogeneity, Meta-analysis, Model selection, Random-effects model

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