Tests of Mediation under a Composite Null Hypothesis

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Abstract

Mediation effect of an exposure on an outcome via a mediator involves of two parameters, one for the exposure-mediator association, α_S, and the other for the mediator-outcome association conditional on the exposure, β_M. Hypothesis tests are conducted under a composite null where at least one of α_S and β_M is zero. This paper studies various hypothesis tests for the mediation effect in the settings of a single test and multiple tests. Under a single test, we show that joint significance test examining the two parameters separately is an intersection-union test with size α, and has smaller *p*-values than normality-based or normal product-based tests for $\alpha_S\beta_M$. However, in the setting with multiple tests, the joint significance test has low power because it fails to account for the composition of different null hypotheses. To this end, we develop a new testing procedure under the composite null hypothesis. We show that the composition of null hypotheses can be adjusted by variances of test statistics without directly estimating the proportion of respective nulls. Advantages of the new test are illustrated in simulation and the epigenomic study.