



Benchmark dose risk analysis with mixed-factor quantal data in environmental risk assessment

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Abstract:

Benchmark analysis is a general risk estimation strategy for identifying the benchmark dose (BMD) past which the risk of exhibiting an adverse environmental response exceeds a fixed, target value of benchmark response (BMR). Estimation of BMD and of its lower confidence limit (BMDL) is well understood for the case of an adverse response to a single stimulus. In many settings, however, one or more additional, secondary, qualitative factor(s) may collude to affect the adverse outcome, such that the risk changes with differential levels of the secondary factor. We extend the single-dose BMD paradigm to a mixed-factor setting with a secondary qualitative factor possessing two levels. With focus on quantal-response data and using a generalized linear model with a complementary-log link function, we derive expressions for BMD and BMDL. We study the operating characteristics of six different multiplicity-adjusted approaches to calculate the BMDL, using Monte Carlo evaluations. We illustrate the calculations via an example data set from environmental carcinogenicity testing.

Keywords:

benchmark analysis; lower confidence limits; quantal response data; quantitative risk assessment; simultaneous inferences