

The Critical Role of Biological Plausibility in Evidence Integration

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Abstract:

Increasing reliance on epidemiological evidence for risk characterizations also increases the need for systematic evidence integration practices that merge disparate streams of health hazard information. Systematic tools for critical appraisal are well-established for epidemiological and in vivo toxicological evidence; however there is no systematic "one-size-fits-all" method for direct cross-comparison of the strength of evidence supporting a causal association for all evidence streams. Critically, a systematic process for addressing scenarios in which there is a lack of concordance between epidemiological and toxicological findings is needed. Biological plausibility is a long-established consideration in causal analysis, but its potential role as a key piece of evidence in evidence integration is often overlooked. Case studies using a blend of GRADE-based methodology with Bradford-Hill considerations will exemplify the important role of biological plausibility in gluing together disparate evidence streams to improve confidence in hazard and risk characterizations. The evidence used to inform these systematic integrations (i.e. risk of bias, magnitude of effect, etc.) is then directly applicable to development of subsequent evidence-based uncertainty assessments.