

Joint EFSA/EBTC Colloquium

Briefing notes DG3: Quantitative approaches to combining evidence across evidence streams for Hazard Identification

1. Background

The issue of determining the relationship between cause and effect is traditionally referred to in the literature as causality assessment or, when referring to statistical methodologies, causal inference. In recent years a suite of quantitative methods and approaches has been developed to address causal questions (e.g. Pearl, 2009; Imbens and Rubin, 2015; Hernan and Robins, 2017; Greenland, 2017).

In hazard identification in human risk assessment of chemicals, the objective is to draw conclusions about the causal relationship between exposure to a chemical and possible adverse effects in humans, based on evidence from laboratory animals, in vitro and in silico studies and human observational studies.

In the obvious absence of randomised clinical trials, the evidence available on adverse effects of chemicals suffers from uncertainties mainly stemming from the confounding factors affecting the validity of observational data and the external validity/biological relevance issues afflicting the use of animal, in vitro and in silico data. Accounting for these uncertainties and reducing the potential bias in the conclusions about causality represents one of the primary challenges in this context.

2. Objective

As a follow up of lecture 1 and 4, the objective of this group is to discuss the available quantitative approaches to combining evidence across streams accounting for possible sources of uncertainty.

The discussion will focus on:

- Comparing available quantitative approaches for combining evidence across streams: advantages and limitations, possibility to reconcile different theoretical perspectives, identification of contexts in which one method is better than others;
- Identification of issues unaddressed by the currently available approaches;
- Recommendations for future developments in the field.

3. References

Greenland S, 2017. For and against methodologies: some perspectives on recent causal and statistical inference debates, *Eur J Epidemiol.* 2017 Jan;32(1):3-20. doi: 10.1007/s10654-017-0230-6

Hernan MA, Robins JM, 2017. *Causal inference.* New York Chapman & Hall. To appear

Imbens GW and Rubin DB, 2015. Causal Inference for Statistics, Social, and Biomedical Sciences: An Introduction. Publisher: Cambridge University Press, 2015

Pearl J, 2009. Causality: models, reasoning and inference. 2nd edition. Cambridge: UK Cambridge University Press

Rubin DB, 2007. The design versus the analysis of observational studies for causal effects: Parallels with the design of randomized trials. *Statistics in Medicine*, 26, 20–36

DG3	Quantitative approaches to combining evidence across evidence streams for Hazard Identification
Chair	Donald Rubin , Harvard University, USA
Follow-up of lectures 1 and 4	Introduction to evidence integration for HI: overview of qualitative and quantitative methods and challenges Donald Rubin , Harvard University, USA Quantitative approaches to combining evidence across evidence streams Stijn Vansteelandt , University of Ghent (BE)
Rapporteurs	Laura Martino (EFSA) Rob de Vries (EBTC)