

## Short Communication

# Features of Meta-Epidemiology, Meta-Meta-Epidemiology and Network Meta-Epidemiology in Emergency Medicine

Roever L<sup>1\*</sup> and Biondi-Zoccai G<sup>2,3</sup>

<sup>1</sup>Department of Clinical Research, Federal University of Uberlândia, Uberlândia, Brazil

<sup>2</sup>Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

<sup>3</sup>Department of Angio Cardio Neurology, IRCCS Neuromed, Pozzill, Italy

\*Corresponding author: Leonardo Roever, Department of Clinical Research, Av. Pará, 1720–Bairro, Umuarama, Uberlândia-MG-CEP 38400-902, Brazil

Received: September 27, 2016; Accepted: October 04, 2016; Published: October 06, 2016

## Introduction

The effectiveness of treatments ideally comes from randomized clinical trials (RCTs) or systematic reviews of trials that assess final endpoints. Many aspects of the design and conduct of RCTs have been shown to lead to overestimation of treatment effect size. These include [1-7]:

1. Inappropriate random sequence generation
2. Inadequate allocation concealment
3. Lack of blinding
4. Single center status
5. Use of composite outcomes
6. Inadequate intention to treat analysis
7. Inadequate double blinding/placebo control

8. Meta-Confounders, such as genotype, study design, and the number of participants

The definition of meta-epidemiology was introduced with considering the methodological limitations of systematic review for intervention trials. Meta-epidemiology study aims to describe the distribution of research evidence for a specific issue, to examine the heterogeneity and associated risk factors, and also to control bias between studies and summarize evidence. Diverse methods, such as meta-regression, imputation, informative missing odds ratio, two statistical models, and others, were attempted, and the term meta-epidemiology [8-15].

Meta-epidemiology is focused as a research paper not being a simple meta-analysis or narrative review we usually encounter in the literature; it is clearly though a sort of meta-review. In meta-epidemiology, one restriction is that informative meta-analyses must include at least one trial with and one without the risk factor of interest, and a minimum number of trials per meta-analysis may be required, depending on how heterogeneity is modelled and multivariable analyses are undertaken [8-15].

The meta-epidemiological, the point of analysis are meta-analysis of randomized controlled trials; for meta-meta-epidemiology, the point are meta-epidemiologic studies, and for network epidemiology, the point are meta-analysis (MA) of randomized controlled trials published where data had been analyzed with a valid statistical method for indirect comparisons or network meta-analysis(NMA) [8-16].

The meta-epidemiology is based on the combination of two concepts: epidemiology and meta-analysis. To fit the purposes

Table 1:

	Meta-epidemiology	Meta-meta-epidemiology	Network meta-epidemiology
<b>Data sources</b>	A collection of MA of randomized trials	A collection of meta-epidemiologic studies, combined into a harmonized dataset without overlap between MA	Networks of RCTs
<b>Restrictions</b>	Informative MA must include at least one trial with and without the risk factor of interest	The different meta-epidemiologic studies investigate various sets of risk factors, potentially assessed with different methods	Eligible networks must include more trials than interventions
<b>Trial-level risk factors</b>	Reassessment from individual trial reports or reliance on assessment from each selected MA	Assessment from each meta-epidemiologic study	Reassessment from individual trial reports or reliance on assessment from each selected NMA
<b>Regarding direction of bias</b>	In active–inactive comparisons, a risk factor is expected not to favor the inactive comparator		In star-shaped networks, a risk factor is expected not to favor the common comparator
	In active comparisons, an assumption regarding direction of bias is needed		In networks with closed loops, an assumption regarding direction of bias is needed
<b>Impact of risk factors on intervention effect estimates</b>	Effect estimates are compared between trials with and without the risk factor within each meta-analysis; the mean impact of the risk factor is estimated across all MA		Effect estimates are compared between trials with and without the risk factor within each network; the mean impact of the risk factor is estimated across all networks
<b>Impact of risk factors on intervention effect estimates</b>	Between trials within MA		Between trials within networks
	Between MA		Between networks

of these two concepts, meta-epidemiology strives to achieve the following [16]:

- To describe the distribution of research evidence for a specific question;
- To examine heterogeneity and associated risk factors; and
- To control bias across studies and summarize research evidence as appropriate.

More differences are shown in Table 1 [8-16].

## References

1. Moher D, Schulz KF, Altman D. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA*. 2001; 285: 1987-1991.
2. Herbison P, Hay-Smith J, Gillespie WJ. Different methods of allocation to groups in randomized trials are associated with different levels of bias. A meta-epidemiological study. *J Clin Epidemiol*. 2011; 64: 1070-1075.
3. Wood L, Egger M, Gluud LL, Schulz KF, Jüni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ*. 2008; 336: 601-605.
4. Dechartres A, Boutron I, Trinquart L, Charles P, Ravaud P. Single-center trials show larger treatment effects than multicenter trials: evidence from a meta-epidemiologic study. *Ann Intern Med*. 2011; 155: 39-51.
5. Ciani Oriana, Buysse Marc, Garside Ruth, Pavey Toby, Stein Ken, Sterne Jonathan AC et al. Comparison of treatment effect sizes associated with surrogate and final patient relevant outcomes in randomised controlled trials: meta-epidemiological study. *BMJ*. 2013; 346: f457.
6. Bafeta A, Dechartres A, Trinquart L, Yavchitz A, Boutron I, Ravaud P. Impact of single centre status on estimates of intervention effects in trials with continuous outcomes: meta-epidemiological study. *BMJ*. 2012; 344: e813.
7. Ferreira-Gonzalez I, Busse JW, Heels-Ansdell D, Montori VM, Akl EA, Bryant DM, et al. Problems with use of composite end points in cardiovascular trials: systematic review of randomised controlled trials. *BMJ*. 2007; 334: 786.
8. Biondi-Zoccai G. *Umbrella Reviews: Evidence Synthesis with Overviews of Reviews and Meta-Epidemiologic Studies*. Springer. 2016.
9. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Social Res Method*. 2005; 8: 19-31.
10. Colquhoun HL, Levac D, O'Brien KK, et al. Scoping reviews: time for clarity in definition, methods, and reporting. *J Clin Epidemiol*. 2014; 67: 1291-1294.
11. Biondi-Zoccai G, Landoni G, Modena MG. A journey into clinical evidence: from case reports to mixed treatment comparisons. *HSR Proc Intensive Care Cardiovasc Anesth*. 2011; 3: 93-96.
12. Ioannidis JP. Evolution and translation of research findings: from bench to where? *PLoS Clin Trials*. 2006; 1: e36.
13. Knottnerus JA, Turgwell P. Knowledge synthesis to improve practice requires up-to-date definitions, methods, and techniques. *J Clin Epidemiol*. 2014; 67: 1289-1290.
14. Glasziou PP, Shepperd S, Brassey J. Can we rely on the best trial? A comparison of individual trials and systematic reviews. *BMC Med Res Methodol*. 2010; 10: 23.
15. Bae JM. Meta-epidemiology. *Epidemiol Health*. 2014; 36: e201401.
16. Zhang W. Meta-epidemiology: building the bridge from research evidence to clinical practice. *Osteoarthritis Cartilage*. 2010; 18: S1.