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Short Communication

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

Roever L[1]* and Biondi-Zoccai G[2,3]

[1]Department of Clinical Research, Federal University of Uberlândia, Uberlândia, Brazil

[2]Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy

[3]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

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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
Data sources	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
Restrictions	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
Trial-level risk factors	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
Regarding direction of bias	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
Impact of risk factors on intervention effect estimates	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
Impact of risk factors on intervention effect estimates	Between trials within MA		Between trials within networks
	Between MA		Between networks

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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].

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