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Metabolic mediators of body mass index: Are published results reliable?

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Abstract Text:

In clinical research and epidemiology, there is increasing interest to quantify effects of a given treatment or risk exposure into different causal pathways via the so called mediation analysis. Traditionally, an approach introduced in 1986 by Baron and Kenny was used to decompose the total effect of a given treatment or exposure into a direct and an indirect effect through one or more mediators. Recently, Lange et al. have presented a new framework for mediation analysis based on marginal structural models that is also applicable in the case of survival data. It has been shown that the Baron and Kenny method works well in the special case of linear models without interactions, but is mathematically inconsistent otherwise.

We applied both approaches, Baron and Kenny versus Lange et al., in the field of cardiovascular epidemiology to investigate the relationship between body mass index and coronary heart disease, mediated by metabolic risk factors. We found substantial different results between the two statistical methods, leading to serious concerns regarding recently published results. It appears that the effect of body mass index is mediated to a larger extent by risk factors such as systolic blood pressure, total cholesterol, fasting glucose, and smoking than previously assumed.

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