

Letter by Doosti-Irani et al. Regarding Article “Associations of variability in blood pressure, glucose and cholesterol concentrations, and body mass index with mortality and cardiovascular outcomes in the general population”

Amin Doosti-Irani, PhD¹, Mohammad Ali Mansournia, MD, MPH, PhD², Gary Collins, PhD³

1 Department of Epidemiology and Modeling of Noncommunicable Diseases Research Center, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

2 Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

3 Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford OX3 7LD, UK.

Corresponding Author

Mohammad Ali Mansournia

Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, PO Box: 14155-6446, Tehran, Iran. Email: mansournia_ma@yahoo.com

Dear editor in chief.

We read with great interest the recently published study by Kim et al (1). The authors investigated the effects of the variability of metabolic parameters, such as body weight, blood pressure, blood glucose, and cholesterol concentration on cardiovascular events and mortality. According to their results, the high variability in the each mentioned metabolic parameter was associated with a higher risk for stroke, myocardial infarction, and all causes of mortality. They used two models for confounding adjustment. Model 1 adjusted for age, sex, alcohol drinking, smoking, regular exercise, and income status. Model 2 adjusted further for baseline fasting glucose levels, total cholesterol, systolic blood pressure, and body mass index (BMI). To account for the possible changes in fasting blood glucose, systolic blood pressure, total cholesterol, and BMI levels. Model 2 also adjusted for the mean values of these variables. Many covariates in the study including systolic blood pressure, smoking status, alcohol consumption, and regular exercise (model 1), and fasting glucose levels, total cholesterol, and BMI (model 2) are time-varying confounders for the effect of the variability of each metabolic parameters on the outcomes of interest. Furthermore, these time-varying confounders can be affected by previous metabolic measurements resulting in "time-varying confounding affected by prior exposure" (2). In other words, there is a feedback between exposure and confounders e.g., BMI can act as a strong confounder for the effect of variability cholesterol as BMI clearly affects cholesterol level, and at same time patients with hypercholesterolemia may decide to lose weight. We think that the effects estimates for variability of parameters may be biased as model 1 did not include time-varying confounders and model 2 traditionally adjusted for time-varying confounders by including the mean values of time-varying confounders which can produce biased effects estimates in the presence of time-varying confounding affected by previous exposure (2-4). The

causal methods including the inverse probability-of-treatment weighting, G-estimation, and parametric G formula have been proposed to appropriately adjust for time-varying confounders (2, 3, 5). In sum, while we admire the authors for addressing an important research question using a large cohort study, we suggest applying casual methods to adjust for time-varying confounders given that repeated measurements on the exposure and confounders are available.

Disclosures: None

References

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