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The author responds

Yuan Lu¹, Kaveh Hajifathalian¹, Eric B Rimm^{2,3,4}, Majid Ezzati⁵, and Goodarz Danaei^{1,3}

¹Department of Global Health and Population, Harvard School of Public Health, Boston, USA

²Channing Division of Network Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, USA

³Department of Epidemiology, Harvard School of Public Health, Boston, USA

⁴Department of Nutrition, Harvard School of Public Health, Boston, USA

⁵MRC-HPA Centre for Environment and Health, School of Public Health, Imperial College London, London, UK

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We had previously considered that the selected mediators (i.e. blood pressure, blood glucose and serum cholesterol) may explain a different proportion of the effect of body mass index (BMI) in the elderly versus younger adults. Therefore, in our prior meta-analysis of 97 cohort studies, we stratified the cohorts by mean age at baseline (<55 versus ≥55 years) and estimated the proportion of excess risk mediated separately. Our results did not indicate any change in proportion of excess risk mediated for coronary heart disease (CHD); and for stroke cohorts with older individuals had a larger proportion of the effect explained by these mediators.¹

Following Fritz et al.'s suggestion², we have now analyzed our individual-level data from seven prospective cohort studies with data on age (ARIC, FHS, FHS offspring, MESA, CHS, HHS, WHI-CT and MRFIT) and added a product term between age and overweight and obesity. The interaction term was not significant in 6 out of 7 cohorts (P values of 0.23 or larger). The only cohort with a significant age interaction was MESA, which has a substantially larger proportion of ethnic minorities as well as younger participants compared with other cohorts. Therefore, data from these large cohort studies does not support a significant interaction between age and overweight/obesity.

Further, results presented by Fritz et al. do not provide strong support for the age interaction either. Firstly, the confidence intervals for the estimated proportion of direct effects among younger and older obese participants overlap substantially: proportion mediated for obesity was 46% (95% confidence interval 28 to 80%) in the younger participants vs 20% (-5 to 60%) in older participants. Second, the model used in these analyses did not include other potential confounders for BMI and CHD such as alcohol use, physical inactivity, diet, and

Corresponding author: Goodarz Danaei, MD ScD, 677 Huntington Avenue, building 1, room 1107, Boston MA 02115, gdanaei@hsph.harvard.edu.

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socioeconomic status, which were included in our models. There are also other minor differences between the two analyses: age was only used as a linear variable whereas we used both linear and quadratic age; the outcome was only fatal CHD whereas we used both fatal and non-fatal CHD combined.

Based on the above, we believe there is not enough evidence to support a significantly different impact of the selected mediators in the elderly versus the younger participants.

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