

Coffee Consumption and All-Cause Mortality: It May Be Premature to Advise Limiting Coffee Consumption in Younger Nonsmokers

To the Editor: I read with great interest the recent article by Liu et al¹ on the health consequences of coffee consumption. Their methodological approach was strong, and their findings were reported clearly. However, I disagree with their conclusion that on the basis of the study's findings, "it seems appropriate to suggest that younger people avoid heavy coffee consumption (ie, averaging >4 cups per day)."

Liu et al reported that at baseline, the coffee drinkers in the Aerobics Center Longitudinal Study cohort, like many other populations, were more likely to smoke cigarettes. The authors did an excellent job in handling this well-recognized association. Their multivariate models (2 and 3) were adjusted for smoking. The authors recognized that residual confounding from smoking could still exist and that this could lead to the appearance of a mortality risk from coffee. Indeed, this was mentioned in their "Limitations" section. To eliminate possible residual confounding, the authors stratified their analysis by smoking status and presented their findings separate from the article as supplemental online material. The authors reported that "we did not observe the significant association between coffee consumption and all-cause mortality both in current smokers and non-current smokers."

The supplemental figures actually show what appears to be an inverse relationship for male nonsmokers between coffee consumption and all-cause mortality for consumption of 8 to 14 through 22 to 28 cups per week, with a hazard ratio below 1 for the latter category. Female nonsmokers in all coffee consumption

categories appear to have hazard ratios that approximate the null value without the appearance of increased risk with increased coffee consumption even in the highest consumption category (>28 cups per week).

Although moderation in all things has historically been good advice, the recommendation for younger people to cut back on their coffee consumption does not appear to be well supported by the data presented.

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1. Liu J, Sui X, Lavie CJ, et al. Association of coffee consumption with all-cause and cardiovascular disease mortality. *Mayo Clin Proc*. 2013;88(10):1066-1074.

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Factors Affecting the Association of Coffee Consumption With All-Cause and Cardiovascular Disease Mortality

To the Editor: We read with great interest the recent article by Liu et al¹ concerning the association of coffee consumption with all-cause and cardiovascular disease mortality. We particularly applaud the thoroughness of their data collection, including 43,727 participants over a median follow-up of 17 years. Considering the pervasive nature of global coffee consumption, studies of this scale are both valuable and ubiquitously relevant. However, we have some concerns regarding the conclusions drawn from the data and would be interested if the authors could clarify some of these points.

One apparent trend was that participants with the highest coffee consumption were less healthy than participants with lower coffee consumption. The authors confirm this by reporting, "Men and women who

consumed higher amounts of coffee were more likely to smoke and had lower levels of [cardiorespiratory fitness]."¹ These participants managed the least time on a treadmill and had the highest level of inactivity, and the men in this category had the highest rate of parental cardiovascular disease. Although it appears that any individual confounding effect from cardiorespiratory fitness was statistically addressed, it is not clear that the cumulative effects of multiple risk factors were accounted for in the statistical analysis.

Most concerning was that the confounding effect from smoking was not adequately addressed. The authors concede this point in their discussion, stating that "smoking is likely to be one of the most important factors to cause residual confounding in this investigation."¹ It is well known that smoking can induce changes in hepatic enzymes and increase the clearance of caffeine, in turn leading to a higher rate of coffee consumption in smokers.^{2,3} It is also widely established that smoking is a strong independent predictor of mortality.⁴ Further, a recent study that evaluated the association of coffee drinking with all-cause mortality confirmed that coffee drinkers were more likely to smoke, and after adjusting for the confounding variable of smoking, coffee consumption was actually associated with decreased mortality.⁵ We question whether the conclusions of the study by Liu et al can be supported without accounting for this "residual confounding" of smoking.

The authors also comment on the homogeneity of the cohort, stating that the uniformity of the participants increases the internal validity of the study.¹ Although this may lend credence to the data, we suggest that external validity may be more critical, because the widespread use of coffee begs the immediate question of how applicable these results are beyond the confines of this study.

The pervasive use of coffee worldwide behooves us as research scientists