measured cardiorespiratory fitness in our cohort but have used 10-km race performance as a surrogate measure because this factor correlates well with maximum oxygen consumption. The correlation between 10-km performance and exercise dose in our study was only $r=0.29$ (or 9% of the variance), documenting that exercise performance and habitual physical activity are not tightly related. In our cohort, 15% of the runners exceeded 7.2 metabolic equivalent of task-h/d (MET-h/d) of running and constituted our high-mileage runners, but these individuals were not the fittest runners. Specifically, 70% of the high-mileage runners were in the slowest 85% of the 10-km performance times. Consequently, the differences in results between The FIT Project and our report is likely due in part to our measuring habitual exercise and Hung et al’s measuring cardiorespiratory fitness.

In addition, the greater risk we observed may be specific to cardiovascular disease mortality rather than morbidity and may involve mechanisms other than the traditional heart disease risk factors. We have reported no increased risk for nonfatal coronary heart disease or coronary heart disease risk factors with greater exercise through running at least 39 miles (63 km) per week. In fact, 2 other epidemiological cohorts reporting greater exercise dose in our study but have used 10-km race performance as a surrogate measure and individuals reporting greater exercise dose in our study but have used 10-km race performance as a surrogate measure and have used 10-km performance times. Consequently, the differences in results between The FIT Project and our report is likely due in part to our measuring habitual exercise and Hung et al’s measuring cardiorespiratory fitness.

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Ethanol has been consumed by humans for millennia, and at high doses it can cause well-known adverse effects, such as hepatitis and cirrhosis. Ethanol abuse can lead to addiction and devastating consequences for at-risk individuals. However, many individuals have no propensity for abuse of ethanol or experiencing any other serious adverse effects of a single serving per day. By the age of 40 years, when cardiovascular disease begins to become a major cause of death, most people know whether they have a tendency to abuse ethanol. With latent and overt alcoholics excluded from randomization, a study could be conducted using capsules of ethanol vs placebo capsules of water (to preserve blinding). If taken in the evening with food, effects on driving accidents should be minimized or eliminated.

If the benefits found in this meta-analysis were associated with any pharmaceutical, there would be great excitement about its potential widespread use, and a phase 3 clinical trial would have been conducted long ago. It is time to obtain definitive proof of the alleged benefits of low-dose ethanol consumption or to disprove them in a randomized controlled trial.

**To the Editor:** The meta-analysis by Huang et al in the September 2014 issue of Mayo Clinic Proceedings revealed an association between low to moderate ethanol consumption and reduced risk of cardiovascular disease and all-cause mortality (ACM) in hypertensive patients. This study adds additional observational evidence to support the hypothesis that there is a J-shaped curve for ACM vs ethanol consumption, with minimum ACM observed in persons with a low-level long-term ethanol intake of about 10 g/d (about 1 standard serving or drink). This well-designed study reinforces previous epidemiological data suggesting similar benefits of low levels of ethanol consumption in other populations. What is needed is a large prospective randomized controlled trial comparing ethanol vs placebo to provide the high-quality evidence needed for physicians to prescribe low-dose ethanol for patients who could benefit.

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