Commentary: Physical fitness: confounder or intermediary variable in the association of diet with health outcomes?

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Observational studies suggest that diet and physical activity are among the main determinants for the risk of the major chronic diseases in Western civilizations, including type 2 diabetes, cardiovascular diseases (CVDs) and cancer. Nevertheless, the exact estimation of the effects of dietary factors and physical activity in epidemiological studies is challenging, for various reasons. While lifestyle variables such as smoking behaviour and alcohol consumption can relatively easily be assessed through questionnaires with sufficiently high validity and reliability, the accurate and precise assessment of diet and physical activity in large-scale epidemiological studies is more difficult and requires sophisticated methods or procedures. Further, diet and physical activity are complex exposures, and there tends to be a close correlation among these and other lifestyle factors, which necessitates the need to take them precisely and accurately into account when estimating their effect on health outcomes. Inaccurate or imprecise assessment may lead to differential or non-differential misclassification not only of the exposure variable but also of the covariates, and the latter could result in residual confounding.

In this issue of the IJE, Héroux et al. studied the impact of adjustment for physical activity or physical fitness on the strength of the association between an ‘unhealthy’ dietary pattern (termed the ‘Unhealthy Eating Index’) and the risk of all-cause mortality. A high consumption of red meat, processed meat, added fat, white potato products and non-whole grains, as well as a low consumption of non-citrus fruits contributed most to have a high Unhealthy Eating Index. Individuals in the highest compared with the lowest quintile of the distribution of the Unhealthy Eating Index had a 1.40-fold increased risk [95% confidence interval (CI) 1.02–1.91] of all-cause mortality after adjustment for age, gender, year of examination, parental history of CVD, history of CVD, history of cancer, smoking and alcohol consumption. Further adjustment for physical activity (assessed through self-report by questionnaire about...
the participant’s physical activity patterns over the preceding 3 months) had little effect on the relationship between the Unhealthy Eating Index and all-cause mortality (relative risk in the highest vs lowest quintile, 1.36; 95% CI 0.99–1.87). In contrast, adjustment for physical fitness (as assessed through a symptom-limited maximal exercise treadmill test) substantially attenuated the relationship (relative risk, 1.18; 95% CI 0.86–1.64).

The study by Héroux et al. suggests that the association of an ‘unhealthy’ dietary pattern with the risk of premature death can largely be explained by physical fitness (but not by physical activity). Does this imply that the unhealthy dietary pattern has no impact on mortality? Does physical fitness confound the association of diet with the risk of premature death, as the authors conclude from their study?

While physical activity can be defined as ‘any bodily movement produced by skeletal muscles that results in energy expenditure beyond resting expenditure’, physical fitness ‘includes cardiorespiratory fitness, muscle strength, body composition and flexibility, comprising a set of attributes that people have or achieve that relates to the ability to perform physical activity’. Physical fitness is typically more strongly related to health outcomes than physical activity, which may be partly related to the fact that fitness is usually assessed more precisely and accurately than physical activity using objective measurements (e.g. treadmill tests). In an immanent effort to use most precise and accurate variables, it may thus be tempting to adjust for physical fitness in epidemiological analyses, as has been done in the study by Héroux et al. However, it should be noted that physical fitness is conceptually different from physical activity.

The relationship between physical activity and physical fitness is complex, partly because both factors may influence each other, and because both may be influenced by other factors as well. Physical activity will generally improve physical fitness, whereas physical fitness may determine to what extent people are physically active. However, physical activity, in contrast to fitness, is largely under direct conscious control, since people may decide to what extent they are physically active. It therefore appears reasonable to consider physical activity as a potential confounder when analysing the diet–disease relationship. Physical fitness much more reflects the status quo of the human body in response to various endogenous or exogenous factors, and it is not under direct conscious control. People engaging in the same type and degree of physical activity may have fundamentally different degrees of physical fitness. Fitness depends on physical activity, but also on other genetic and non-genetic factors. For example, obesity as well as abdominal fat accumulation are strong determinants of impaired cardiorespiratory fitness. It is very likely that dietary or nutritional factors other than obesity affect cardiorespiratory fitness as well, although there is only a limited number of studies available that have looked at dietary determinants of cardiorespiratory fitness. For example, dietary and nutritional factors affect lipid and glucose metabolism, as well as inflammation, which gives indirect support to the hypothesis that diet and nutrition are major determinants of cardiorespiratory fitness.

Based on these considerations, it is more likely that cardiorespiratory fitness is an intermediary variable, rather than a confounder, in the association of an unhealthy dietary pattern with the risk of premature death. If the assumption holds that dietary behaviour affects the risk of mortality, then there must be some mechanisms that mediate these effects. It does not seem unlikely that these mechanisms include physical fitness. Thus, the results from the study by Héroux et al. may also be interpreted in a way that a large proportion of the effects of dietary patterns on the risk of death may be mediated through physical fitness, although one has to consider that the true effects may have been underestimated because of the less precise assessment of diet in contrast to that of physical fitness.

The study by Héroux et al. gives interesting insights into the relationship of dietary patterns, physical activity and physical fitness with risk of mortality. Particularly, Héroux et al. are to be commended for the detailed assessment of cardiorespiratory fitness in their cohort. The article reminds us that the selection of variables and the interpretation of results in epidemiological studies should be based on conceptual considerations as well as on precision and accuracy. Future studies with more detailed and objective information about physical activity (e.g. by using accelerometers or other devices) in addition to fitness are warranted to look in more detail on the relationship among these variables with diet, to more clearly differentiate between confounding and intermediary variables, and to more accurately and precisely estimate their impact on health outcomes.

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References
Author’s Response

Dietary patterns and the risk of mortality: impact of cardiorespiratory fitness

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We would like to thank Drs Ding, Hu and Pischon for their insights and commentaries on our paper ‘Dietary patterns and the risk of mortality: impact of cardiorespiratory fitness’.¹ In the spirit of a healthy debate, there are a few issues that we would like to address in our response. We would first like to highlight that the purpose of our paper was not to argue against the role of an unhealthy diet as a risk factor for morbidity and mortality. We are in full agreement that a healthy diet is important and that there is an abundance of evidence to support this position. Rather, our goal was to highlight that previous studies examining the relation between dietary patterns and health have not properly controlled for the confounding effects of physical activity, which, without exception, have been measured by self-report.

Validation studies have consistently found that self-reported physical activity measures are biased (e.g. most people overestimate their activity) and only modestly associated with objective measures of physical activity.²–⁴ The imprecision of these estimates would result in an underestimated effect of physical activity on the morbidity and mortality outcomes, and in studies of unhealthy dietary patterns and poor health, would result in residual confounding for physical activity. Our study attempted to overcome this limitation by including an objective marker of physical activity as a covariate in the analyses. Indeed, the risk estimates for dietary patterns were substantively smaller when cardiorespiratory fitness was the covariate compared with when self-reported physical activity was the covariate.

Next, we would like to address the concern regarding the use of cardiorespiratory fitness as a marker of physical activity participation. We appreciate that fitness is not a direct measure of physical activity and that other factors such as genetics, age and sex play a role in determining one’s fitness. However, by using age- and sex-specific cut-points to define the different fitness groups, our analyses accounted for some of the most meaningful non-activity determinants of fitness. Furthermore, several studies have shown that fitness is highly related to physical activity participation in recent months²,⁵,⁶ and that fitness is responsive to changes in physical activity.⁷–⁹ Thus, while we recognize that there is not a perfect relation...