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Commentary: Relative importance of diet vs physical activity for health

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Physical inactivity and poor diet are both commonly reported to be associated with a wide range of chronic diseases, including hypertension, type 2 diabetes, coronary heart disease (CHD) and stroke, and, together, contribute to substantial burden of disease.[1] Although it is well known that those who follow a healthy diet also frequently have higher levels of physical activity, which may lead to confounding, diet and physical activity may also share and affect many common biological disease mechanisms, such as blood pressure, lipids, glucose, inflammation and adiposity. Therefore, some questions still remain whether dietary associations are (i) confounded by physical activity, (ii) causally independent of physical activity and/or (iii) obviated by physical activity superseding dietary effects in mutually shared intermediate disease pathways.

In this issue of the *IJE*, Héroux *et al*.[2] conducted a careful analysis to investigate the association of disease intermediate-derived dietary patterns and risk of mortality, and whether such a derived dietary pattern is associated with risk independent of physical activity. Conducted in a unique cohort comprising participants visiting an aerobic fitness centre, the authors used reduced rank regression (RRR) on a battery of biological intermediates—including body mass index, blood pressure, high-density lipoprotein and total cholesterol, triglyceride, fasting glucose, uric acid and white blood cell levels—to derive a dietary pattern score predictive of adverse levels of these intermediates. They found that adverse dietary pattern score associations were attenuated and the score was not predictive of mortality after controlling for self-reported physical activity and treadmill-assessed cardiorespiratory fitness levels in particular.

The findings, at first glance, appear to suggest that dietary associations with mortality are either confounded or trumped by physical activity. However, such a conclusion should be interpreted in the context of numerous previous epidemiological studies, where dietary factors have been found to be associated with risk of type 2 diabetes, CHD, stroke, cancer and mortality, independent of lifestyle factors including physical activity levels.[3] With a modest number of endpoints (136 cardiovascular deaths and 445 total deaths), statistical power of this analysis is somewhat limited, which may explain the lack of overall significant trends between the RRR dietary pattern and CVD and total mortality, even before adjustment for physical activity or fitness. Conceptually, because dietary factors may influence physical fitness directly or indirectly through body weight, it can be argued that dietary associations are mediated rather than simply confounded by physical fitness.

Diet is a highly complex exposure, which can be analysed in many ways, including macronutrient

composition, micronutrients, food items/groups, food indexes (e.g. glycemic index), certain eating behaviours (e.g. skipping breakfast) and overall dietary patterns.[4] Characterization of overall dietary patterns is not straightforward either, but can be derived through *a posteriori* methods such as principle component analysis, cluster analysis or through construction of dietary quality indices (such as Mediterranean Diet Index or Healthy Eating Index) based on *a priori* knowledge. The RRR is a recently proposed method that takes into account the biological pathway from diet to outcome by identifying dietary patterns associated with specific intermediate biomarkers of a specific disease.[5] One advantage of RRR over traditional methods is that it incorporates information on biological biomarkers into the analysis. However, this method is limited by the availability or selection of biomarkers that are used in the analysis. For example, useful blood biomarkers are lacking for most cancers. Because the RRR analysis is intended to explain maximum amount of variance in the selected biomarkers, the derived dietary pattern reflects only one aspect of dietary exposure that is related to the selected biomarkers. In this study, the selected biomarkers are mainly related to cardiovascular disease, although total mortality is the main focus of the analysis and discussion. Because diet influences cardiovascular disease through multiple pathways, beyond the biomarker intermediates included in the study, the derived dietary pattern cannot be interpreted as a complete global index of all dietary effects on cardiovascular or all-cause mortality.

As complex human behaviours, there are many parallels between physical activity and diet in terms of health effects and assessment.[6] The effects of physical activity go beyond energy expenditure, in the way that diet contributes more than just energy intake. No epidemiological methods are able to capture all dimensions of physical activity in free-living populations, including type, duration, frequency and intensity. Although physical fitness and physical activity are strongly correlated, they are not synonymous and should not be used interchangeably because physical activity consists of behaviour, whereas physical fitness is a functional attribute (like blood cholesterol) that can be influenced not only by physical activity behaviours, but also a wide range of other modifiable and non-modifiable factors including age, sex, genetics, body weight, existing and preclinical diseases and probably diet. Despite substantial measurement errors in assessing physical activity levels using questionnaires, numerous epidemiological studies have demonstrated that increasing physical activity is strongly and consistently associated with decreased risk of diabetes, CHD, stroke, several cancers and mortality.[7] There is no epidemiological or clinical trial evidence, however, to suggest that the benefits of physical activity trump those of other lifestyle factors. Notably, in our recent analysis of a large cohort of women with 24 years of follow-up,[8] poor diet, lack of physical activity, obesity and cigarette smoking were each independently associated with increased risk of mortality. Using repeated measures of physical activity assessed every 2–4 years during follow-up, we found that being physically inactive (<0.5 h/week of exercise vs $\geqslant 5.5$ h/week) was associated with an ~80% increased risk of cardiovascular mortality. The magnitude of this association is compatible with that observed for low cardiorespiratory fitness.[9] A diet quality score remained strongly and significantly associated with mortality after adjustment for repeated measures of physical activity and other lifestyle factors. The estimated population attributable risks were 28% for cigarette smoking, 14% for being overweight, 17% for lack of physical activity (<30 min of physical activity per day), 13% for low diet quality (scored <40 percentile of the cohort for a Healthy Eating Index). Overall, 55% (95% confidence interval 47–62%) of total deaths were attributable to the combination of smoking, being overweight, lack of physical activity and a low diet quality. These results indicate that diet, exercise and other lifestyle factors have additive influences on the risk of premature mortality.

Héroux *et al.*'s analysis reminds us of the complexity of teasing out independent associations of unhealthy diet and physical inactivity, two of underlying modifiable risk factors for chronic diseases and premature death. Similar challenges have arisen from assessing the relative importance of obesity vs physical activity. Because diet, physical activity and adiposity are all multidimensional variables that can influence each other, ranking the relative importance of them through statistical modelling oversimplifies these complex factors. From a public health point of view, promoting a healthy diet and encouraging physical activity are not mutually exclusive, but equally important factors for maintaining healthy weight and reducing the risk of chronic diseases and premature death.

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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.[1] 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.[1] 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*.[2] 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.[2] 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