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PURE study challenges the definition of a healthy diet: but key questions remain

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Graphical Abstract

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The relationships between diet, cardiovascular disease, and death are topics of major public health importance, and subjects of great controversy.^{1,2} In European and North American countries, the most enduring and consistent diet advice is to restrict saturated fatty acids, by replacing animal fats with vegetable oils and complex carbohydrates (and more recently

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whole grains).^{1,3} In *The Lancet*, Mahshid Dehghan and colleagues⁴ echo the views of a growing number of scientists by stating that advice to restrict saturated fatty acids “is largely based on selective emphasis on some observational and clinical data, despite the existence of several randomised trials and observational studies that do not support these conclusions”. This lack of definitive evidence has left clinicians, scientists, and the public uncertain about the best foods to advise and to eat.²

Dehghan and colleagues⁴ add to this uncertainty by publishing the initial results of the Prospective Urban Rural Epidemiology (PURE) study, an ambitious undertaking involving over 200 investigators who collected data on more than 135 000 individuals from 18 countries across five continents for an average of 7.4 years. As the largest prospective observational study to assess the association of nutrients (estimated by food frequency questionnaires) with cardiovascular disease and mortality in low-income and middle-income populations, the PURE findings make an important contribution to the field. The PURE team report that higher intakes of fats (including saturated fatty acids, monounsaturated fatty acids, and total polyunsaturated fatty acids) and animal protein were each associated with lower mortality, whereas carbohydrate intake was associated with increased mortality.⁴ Here we provide context and highlight questions that need to be answered to move the field forward.

Do meats and dairy reduce mortality? Animal products (including beef, lamb, and dairy) are the major sources of saturated fatty acids and monounsaturated fatty acids in most populations studied in PURE. Since saturated fatty acids, monounsaturated fatty acids, and animal protein were all inversely associated with mortality, is the real finding simply that meat and dairy intakes were associated with increased survival? To answer this question, the PURE team needs to complete a thorough analysis relating intakes of different animal products to mortality.

Micronutrient malnutrition is an important problem in many of the countries included in PURE. Animal products are rich sources of zinc, bioavailable iron, vitamin K2, and vitamin B12, which might be suboptimal in populations consuming high carbohydrate diets. Therefore, one potential explanation for the PURE results is that nutrient-dense meats corrected one or more nutrient deficiencies. Since the PURE study collected blood for lipoprotein analyses,⁵ this potential role of micronutrient deficiency in PURE could be investigated further.

Which carbohydrates are associated with increased mortality? Dehghan and colleagues⁴ report that high intake of total carbohydrates was associated with increased mortality. In a concurrent *Lancet* Article,⁶ the PURE group reports that intakes of fruits, legumes, and raw vegetables (three major carbohydrate sources) were associated with lower mortality. This discrepancy suggests that processed carbohydrates, including added sugars and refined grains, are likely driving this association. In a future paper, the PURE group should report associations between added sugars, refined grains, whole grains, and mortality.

Is PURE less confounded by conscientiousness than observational studies done in European and North American countries? Conscientiousness is among the best predictors of

longevity.⁷ For example, in a Japanese population, highly and moderately conscientious individuals had 54% and 50% lower mortality, respectively, compared with the least conscientious tertile.⁸ Conscientious individuals exhibit numerous health-related behaviours ranging from adherence to physicians' recommendations and medication regimens,⁹ to better sleep habits,¹⁰ to less alcohol and substance misuse.¹¹ Importantly, conscientious individuals tend to eat more recommended foods and fewer restricted foods.¹² Since individuals in European and North American populations have, for many decades, received influential diet recommendations, protective associations attributed to nutrients in studies of these populations are likely confounded by numerous other healthy behaviours. Because many of the populations included in PURE are less exposed to influential diet recommendations, the present findings are perhaps less likely to be confounded by conscientiousness.

The PURE study is an impressive undertaking that will contribute to public health for years to come. Initial PURE findings challenge conventional diet–disease tenets that are largely based on observational associations in European and North American populations, adding to the uncertainty about what constitutes a healthy diet. This uncertainty is likely to prevail until well designed randomised controlled trials are done. Until then, the best medicine for the nutrition field is a healthy dose of humility.

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