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Invited Commentary

In defence of phytochemical-rich dietary patterns

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There is widespread acceptance that consuming whole grains is good for overall health[1]. Evidence from epidemiological cohort studies suggests that greater whole-grain consumption is inversely related to total mortality, CVD and other diseases[2]. Several observational studies also find that whole-grain consumption is inversely related to CVD risk factors, including excess body weight, abdominal obesity, hypercholesterolaemia and insulin resistance[3,4]. Some whole-grain supplement or feeding studies, which have varied in duration from weeks to months, support a beneficial effect of whole-grain consumption[5–8], while others do not[9,10].

In this issue of the *British Journal of Nutrition*, Brownlee *et al.*[11] present data from a large-scale intervention study that examined the effect of supplemental wholegrain foods on CVD risk factors in 316 overweight adults. Across the 16-week intervention, no significant improvements were observed in blood lipids, insulin sensitivity, inflammatory status, coagulation status, endothelial function, or blood pressure. Despite the many strengths of this study – the large sample size, the intervention length, and the intervention itself, which involved increasing whole-grain intake in non-consumers to approximately four to eight servings/d – the authors nevertheless observed no significant improvements in risk factors. With all these strengths, why were no changes observed in CVD risk factors?

First, concerning compliance with the intended study protocol, it appears that participants included wholegrain foods as additions, rather than substitutions, to their regular diets. Such a problem is not unique to this type of study; others have observed compliance difficulties in dietary regimens in free-living conditions. For instance, in a study designed to test whether consuming wholegrain foods in a hypoenergetic diet enhanced weight loss and improved CVD risk factors[8], the initial nine study participants averaged only a 7 kcal (about 29 kJ) deficit from baseline, leading to 1·0 kg weight loss. When investigators emphasised to the subsequent fifteen participants to avoid refined grains and include only whole grains, participants averaged a 430 kcal (about 1800 kJ) deficit from baseline and a 5·3 kg weight loss. Thus, adding whole-grain foods while failing to compensate by omitting other foods may have affected the findings in Brownlee *et al.*[11].

Second, the 60 g and 120 g whole-grain intervention groups did not gain weight, despite increased reported average daily energy intake of approximately 900 and 650 kJ/d, respectively, relative to the control group. Assuming 32 238 kJ intake per kg body-fat gain, body-weight increases of 2–3 kg over 16 weeks were expected, yet no differences in body weight were observed[11]. While unreliable energy intake estimates from self-report FFQ could be an issue, it is possible that decreases in several risk factors related to whole-grain intake would have been observed if the interventions had been isoenergetic.

Third, this study was specifically designed to test the impact of increasing whole-grain intake in overweight or obese (mean BMI 30 kg/m^2) individuals who habitually consume refined grains, but who are otherwise relatively healthy (i.e. participants had no previous diagnosis of CVD or diabetes, and were not taking lipid-lowering medication). The question then becomes whether improvements in risk factors would have been observed if the participants had more pronounced metabolic abnormalities, such as hyperinsulinaemia or dyslipidaemia. Many metabolic risk factors improved in a large sample of older individuals with diabetes or CVD after supplementation of a Mediterranean diet with extra-virgin olive oil or tree nuts (walnuts, hazelnuts and almonds)[12–14]; like whole grains, these foods are phytochemical-rich. Similarly, isoenergetic replacement of refined rice with whole grains and other plant products in powdered form improved risk factors in Koreans with CHD[6]. These studies suggest that risk profiles of 'at-risk' individuals can be ameliorated through intake of phytochemical-rich foods or diets. It is possible that more pronounced effects of increasing whole grains would be observed in individuals with more severe metabolic challenges.

The epidemiological observational studies of whole-grain intake are numerous[2], consistent and impressive: whole grains appear to benefit health. Yet it is impossible to declare unequivocally that the observed benefits of whole grains are due to the whole grains *per se*, and not due to 'the company they keep'. For example, individuals who eat more wholegrain foods tend to live healthier lifestyles and choose healthier foods[3,4]. As such, characteristics such as physical activity, smoking, socio-economic status and other dietary components are typically accounted for in observational studies, but residual confounding is nevertheless possible[15–17]. However, observational studies of dietary patterns and clinical outcomes[18–22] may have less potential for residual confounding because dietary patterns include a wide variety of dietary behaviours. It follows that dietary or lifestyle confounding that might exist in nutrient- or food-specific studies, such as those investigating whole grains, may be minimised in studies of dietary patterns. In these types of studies, we consistently observe that certain patterns (typically called Mediterranean or 'prudent', and typically heavily weighting whole grains) are linked with fewer clinical events, while alternative, less healthy patterns (typically called Western) are linked with

more clinical events. Mediterranean or prudent dietary patterns seem to emphasise quantity, abundance, and variety of biologically active phytochemicals, while the Western pattern seems to be oriented towards high animal food intake. These studies of dietary pattern are very attractive in terms of translating dietary recommendations because they capture the way food is eaten – in great variety, several times a day, throughout the lifetime. Furthermore, individual components in foods and individual foods in dietary patterns are likely to act synergistically[23]. This synergy would seem to be especially pertinent for wholegrain foods, which contain a wide variety of biologically active constituents that are intentionally discarded in the refining process.

Randomised controlled trials (RCT) of foods or nutrients are considered insufficient to answer all the questions that need to be answered. RCT work well embedding a drug in a pill that can be mirrored in a placebo, with replication in different populations over long time frames. On the other hand, testing foods in RCT is much more difficult for several reasons: (i) 'no exposure' is typically not a possibility – everyone is exposed to some extent; (ii) the study requires a high degree of compliance, a large sample size and a long duration; and (iii) disease events, as outcomes, are rarely possible. Diet is not the same as treatment with isolated compounds found in diet[24,25]. While it would be imprudent not to consider results of RCT of foods and nutrients as we try to further understand their effects on intermediate risk factors, disease and health, it is important that we carefully interpret and recognise the power of observational cohort studies.

Do these new findings[11] 'put a halt to our gallop'? Should we question the established belief of many nutrition and scientific experts that increasing whole-grain intake to three or more servings/d has a substantial and positive impact on health? Brownlee *et al.*[11] are reluctant to draw this conclusion. They suggest instead a note of caution concerning specific health claims. Nevertheless, we agree with them that their finding 'does not undermine more general efforts to promote whole grains as part of a healthy diet for the general population across the life course, based on data from observational studies'. The concept of phytochemical-rich dietary patterns, in which whole grains are a natural fit, is an attractive paradigm on which to base dietary recommendations for the public. For now, let's hedge our bets with variety and abundance in whole grains as well as in other phytochemical-rich plant foods.

Conflicts of interest

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