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Invited Commentary

Do bioactive components in non-animal food sources contribute to the beneficial health effect of a Japanese dietary pattern?

In their article, 'Dietary patterns and abnormal glucose tolerance in Japan' in this issue of *Public Health Nutrition*, Okada *et al.*[1] identified three dietary patterns using factor analysis of data from approximately 100 000 participants in the 2012 Japanese National Health and Nutrition Survey (NHNS) to explore associations with diabetes risk based on glycated Hb (HbA1c) cut-off values. Of three patterns identified, only the predominantly plant-based dietary pattern was significantly and inversely associated with diabetes risk, leading us to speculate that both the amount of specific foods consumed and their bioactive components may afford a protective mechanism against abnormal glucose tolerance. Two foods characterising this 'vegetable pattern' and which are widely consumed in Japan, namely soya/soya products and mushrooms, differ in both quantity of consumption and their bioactive components compared with the plant foods predominant in Western cultures. The objective of our commentary is to delve deeper into these differences and speculate on possible mechanisms through which these foods may reduce disease risk.

Three dietary patterns were found: (i) 'high-bread and low-rice', (ii) 'high-meat and low-fish' and (iii) 'vegetable'. The first pattern, on which bread, milk/dairy products, confectionery, butter/margarine and fruit were positively loaded, and animal meats/poultry and rice were negatively loaded, was weakly inversely associated with elevated HbA1c. The 'vegetable' pattern, with positive loadings for vegetables, fruit, mushrooms, soyabeans/soya products, was significantly inversely associated with elevated HbA1c. No association was seen for the second pattern[1].

It is perhaps no surprise that the first pattern did not show a strong association with HbA1c given that foods loading on this factor included some that would be considered beneficial, such as positive loadings for fruit and negative loadings for meat and poultry; but other items like confectionery with a positive loading would be expected to be associated with a greater risk of elevated HbA1c or diabetes[2]. The strong negative loading for rice and the similar strength positive loading for bread are difficult to interpret without more detail of the main foods consumed within these groups. White rice is low in nutrients, including fibre, and can have a low glycaemic index[3], which might also contribute to diabetes risk[4]. However, even within white rice Atkinson *et al.* report a wide range of glycaemic indices ranging from below 50 for some types to above 100 for others[3]. Bread similarly is reported to have a range of glycaemic indices, both within and between different types of grains[3].

The second pattern, with positive loadings for bread, noodles, animal meats/poultry, butter/margarine, vegetable fats/oils and coffee/cocoa, and inverse associations for rice, pickles, raw fish/shellfish and tea, is similar to other 'unhealthy' dietary patterns that have been associated with increased diabetes risk[5].

The 'vegetable' pattern loads all plant-based foods and mushrooms, and in that respect is similar to other 'healthy' patterns that have been inversely associated with diabetes risk[5]. Although we recognise that mushrooms are fungi and in fact part of a separate kingdom to plants, we refer to them with plant foods here. Due to differences in the sort of foods consumed in Japan compared with Western countries, the actual components of this 'vegetable' pattern may be quite different, in particular the focus on soyabean-derived foods and mushrooms. The positive effects of the 'vegetable' dietary pattern in Japan may relate specifically to the component foods that are consumed at significantly higher levels than in Western cultures.

Soya products are more common in Japanese than Western diets. According to the most recently available FAO data, the soya food supply in Japan for 2013 was about 20 g/capita per d which was the third highest consumption after China and Korea. For Australia, the equivalent figure was 0·53 g/capita per d and for the USA, 0·11 g/capita per d[6]. A recent systematic review and meta-analysis of soya intake and diabetes risk identified weak evidence for an inverse association, but results were heterogeneous, possibly because of the different soya products evaluated and differences between study populations. Subgroup analysis showed that in women, Asian populations and cross-sectional rather than longitudinal studies, there were consistent inverse associations[7]. The significantly higher soya intakes in Asian populations may contribute to the finding of beneficial associations.

The 2015 Japanese NHNS report, cited by Shimizu *et al.*[8], indicated that in Japan the average intake of mushrooms was 15 g/d, including a number of different species rich in a range of nutrients, including B vitamins, vitamin D, fibre and folic acid, and with some reported antidiabetic actions[8]. *Flammulina velutipes*, *Hypsizygus marmoreus*, *Lentinus edodes*, *Grifola frondosa* and *Pleurotus eryngii* are the top five mushroom varieties grown and consumed in Japan[8]. Data presented by Freidman[9] show the variation in nutrient contents (protein, fat, ash, dietary fibre and sugar) between the last three of these and *Agaricus bisporus*, which is the common white button, brown crimini or Portobello mushroom consumed in Western cultures. In comparison, statistics from the USA show that between 2009 and 2017 annual mushroom intake per capita increased from 1·6 to 1·8 kg (equivalent to 4·4 to 4·9 g/d), and 61 % were white mushrooms[10]. Mean mushroom intake for Australia in the 2011–12 nutrition component of the Australian Health Survey was 10·7 g/d[11]. Although there are no readily accessible data on consumption of different mushroom types in Australia, personal observation in shops suggests that most are the common *A. bisporus*. In a review looking at dietary patterns and diabetes risk, Schwingshackl *et al.*[2] noted that inverse associations between 'vegetables' and diabetes risk were observed only in Australian and Asian studies, which may reflect to some extent the different combinations of vegetables consumed.

The Japanese clearly consume more soya and soya products, as well as mushrooms compared with Europeans or North and South Americans. The health benefits of soya and soya products are well established with respect to chronic disease[7,12], while much less is known about the human health effects of mushroom consumption. In a cross-sectional population study in elderly Japanese, high mushroom consumption was associated with lower prevalence of dementia and impaired cognitive function[13]. An important factor to consider in the Japanese 'vegetable' diet pattern is that two of the dominant foods contain high levels of bioactive compounds that have been linked to mechanisms that may protect against chronic diseases such as diabetes and impaired cognitive function leading to dementia.

Both soya and mushrooms are rich in polyphenolic compounds and other bioactive components not found in other non-animal foods, for example ergocalciferol (vitamin D_2) in light-exposed mushrooms, which has been shown to be a potent modulator of inflammation in immune-challenged rats[14]. The Japanese have long been recognised for their higher natural intake of vitamin D, with the contribution from mushrooms second only to fish[15]. Vitamin D is a critical nutrient in the prevention of inflammation, as well as having an important role in calcium and phosphorus homeostasis. Both soya and mushrooms are rich sources of antioxidants, but one potent antioxidant in mushrooms, ergothioneine, is not found in significant quantities in other plant or animal sources and is not synthesised by human or other animal species[16]. In fact, ergocalciferol and ergothioneine are bioactive components unique to mushrooms[17] and their content varies with the type of mushroom, with the varieties consumed in Japan having higher levels of both relative to *A. bisporus*[18]. Retrospective analysis of findings from a 16-week mushroom feeding study in older individuals with metabolic syndrome (pre-diabetes) showed that even *A. bisporus* consumption at the level of 100 g of fresh mushrooms per day was associated with significant increases from baseline in the anti-inflammatory hormone, adiponectin, and decreases in the oxidative stress-inducing advanced glycation end products, carboxymethylysine and methylglyoxal, which like HbA1c are elevated in diabetes[19]. Ergothioneine is proposed by some researchers to be a potent adaptive antioxidant that functions in the protection of injured tissues[20].

Chronic inflammation and oxidative stress are now widely considered to be the underlying mechanisms of most chronic diseases including diabetes[21]. Higher consumption of soya and soya products and consumption of a variety of mushrooms with high levels of ergocalciferol and ergothioneine theoretically provide the Japanese with the anti-inflammatory vitamins and potent antioxidants needed to reduce the risk of chronic diseases.

Notwithstanding these potentially interesting findings and their implications, Okada *et al.*'s study has some important limitations as outlined by the authors; in particular, the dietary data based on a single day and evaluated at the household level is likely to have significant error. The authors adjusted the multivariate models for diet patterns and elevated HbA1c for BMI, but did not show causal diagrams to clarify whether they considered BMI as a confounder or potentially a mechanism linking diet and diabetes. If the latter, it should not have been adjusted for. Given that it is never clear which is the correct causal pathway, it may have been useful to perform the analysis with and without BMI or other body size measure and explain clearly why this had been done.

The new Japanese study supports previous work indicating that healthy, predominantly plant-based dietary patterns may help to reduce diabetes risk and provides insight for hypothesising possible mechanisms of action. This is timely with the recent release of the EAT–Lancet commission report[22] calling for a move away from high consumption of meat, for both health and sustainability reasons. More studies specifically examining the possible benefits of soya products and mushrooms, including variety of species, on glucose metabolism should be conducted to confirm these potential associations.

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