

## Live Longer with Fermented Soy...Or Not

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### ***Caution Urged in Looking at Clinical vs Observational Studies with Fermented vs Non-Fermented Soyfoods***

Periodically, research involving soy gets picked up by the media. Sometimes, the journal in which the research is published also invites a commentary linked to that research to be written and published in the same issue. Such is the case with recent research that generated media headlines like this one: "To Live Longer Eat Fermented Soy." These types of headlines are certainly good press for soy, something I always welcome. But a closer look at the basis for these recent headlines raises some questions about the strength of the data upon which they are based.

The research in question comes from the Japan Public Health Centre-based Prospective Study, which includes 11 public health center areas in Japan.<sup>1</sup> The analysis was based on 92,915 participants (42,750 men and 50,165 women) aged 45 to 74 years who were enrolled in the early 1990s and followed for nearly 15 years. During that time there were 13,303 deaths.

In the multivariable adjusted models, intake of total soy products was not significantly associated with total mortality. However, when comparing extremes of intake, fermented soy intake was associated with a reduced risk of mortality. More specifically, the hazard ratio (95% confidence interval, CI) for fermented soyfood intake among men and women when comparing the fifth intake quintile with the first, was 0.90 (0.83 to 0.97) and 0.89 (0.80 to 0.98), respectively. In contrast, the corresponding values for non-fermented soyfood intake were 1.01 (0.94 to 1.09) and 1.00 (0.92 to 1.10), respectively.

Natto and miso were the two fermented soyfoods examined individually. Among men, there was no statistically significant association with either food, although for each food the hazard ratio was below 1.0. Among women, when comparing intake extremes, the hazard ratios (95% CI) for natto and miso were 0.84 (0.76 to 0.93) and 0.89 (0.81 to 0.97), respectively.

There are differences between fermented and non-fermented soyfoods that could account for why the former were associated with a decreased risk of mortality and the latter were not. For example, although quite variable, in fermented soyfoods, more of the isoflavones are present as aglycones,<sup>2,3</sup> which may mean they are absorbed more quickly.<sup>4</sup> In addition, some antioxidants are created by fermentation.<sup>5,6</sup> But it's not clear these differences provide clinically relevant health advantages. Furthermore, several previously published observational studies have found non-fermented soyfood intake, but not fermented soyfood intake to be associated with reductions in cancer risk.<sup>7,8</sup>

There is, however, another more pressing issue related to data interpretation that needs to be highlighted. Among women, the fifth intake quintile cutoff for natto and miso intake was 26.3 and 26.2 g/day, respectively. At that intake level, natto and miso would provide only about 5 and 3.5 g protein, respectively, and an estimated 18 and 12 mg isoflavones, respectively. It is difficult to imagine that consuming so little soy could reduce mortality by 10%. Typically, clinical studies involving soy intervene with  $\approx 25$  g/d soy protein and/or 50 to 100 mg/d isoflavones. Clinical studies are necessarily relatively short term, whereas soyfood intake assessment in the Japan Public Health Centre-based Prospective Study may have captured lifelong intake. In theory, when consumed over a lifetime, lower amounts of soy may be needed to exert physiological effects than estimates from clinical studies suggest.

Importantly, in another recent analysis from the Japan Public Health Centre-based Prospective Study, in multivariable adjusted models, total, soluble, and insoluble fiber intakes were inversely associated with all-cause mortality.<sup>9</sup> The hazard ratios (95% CI) for total mortality in the highest quintile of total fiber intake compared with the lowest quintile were 0.77 (0.72, 0.82) in men and 0.82 (0.76, 0.89) in women. Fiber from beans was significantly inversely related with total mortality in men and women, total cardiovascular disease and heart disease mortality in men, and cerebrovascular and respiratory disease mortality in women. Beans included soy products such as tofu, miso, and soymilk. Tofu and soymilk contain very little fiber (

Could it be that natto and miso intake simply reflects an overall lifestyle that is protective against disease, whereas tofu intake does not? That is, do consumers of fermented soyfoods differ from non-consumers in ways that reduce mortality? In the model generating the hazard ratios cited above, the data were adjusted for quite a few factors including geographical area, smoking, frequency of alcohol intake, body mass index, sports or physical exercise, history of diabetes or taking drugs for diabetes, taking antihypertensives, health check-up, total energy intake, and intake of green tea, coffee, fish, meat, fruit, and vegetables. Nevertheless, it is impossible to control for all potentially confounding variables, especially because some may be unknown. This is precisely why observational studies do not form a basis for establishing cause and effect relationships.

On the other hand, in some sense, the potential benefit of soy may be undervalued in studies like the Japan Public Health Centre-based Prospective Study, when the primary endpoint of interest is mortality. There are undoubtedly many causes of mortality that no single food such as soy, or even diet in general, can prevent. Therefore, when looking at total mortality, the causes of mortality that soy does combat are not as evident.

Finally, none of the above discussion is meant to suggest that soyfoods do not contribute to health. Rather, the point is that observational studies are most insightful when they focus on

dietary pattern analysis, which describes "... the overall diet; the foods, food groups, and nutrients included; their combination and variety; and the frequency and quantity with which they are habitually consumed."<sup>10</sup> In contrast, clinical studies are best suited for identifying the effects of

single foods or food components. Based on the results from the Japan Public Health Centre-based Prospective Study, an interesting clinical study would be to directly compare the effects of fermented with non-fermented soyfoods on different health outcomes.

## References

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