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To the editor:

We thank Kim et al for their interest in our recent work (1). They suggest that our finding of an association between weight loss during midlife and increased dementia-related mortality risk more than 3 decades later could be due to release of organochlorine pesticides (OCPs) from adipose tissue to the blood stream during a period of weight loss (2). Our study cohort born during 1925–45 were growing up in a time period when OCPs were much used in agriculture, and it is likely that they have been exposed to OCPs, especially from fatty animal food and fatty fish (3,4). Levels of OCPs measured in foods were peaking during the lifetime of our study cohort (4, 5).

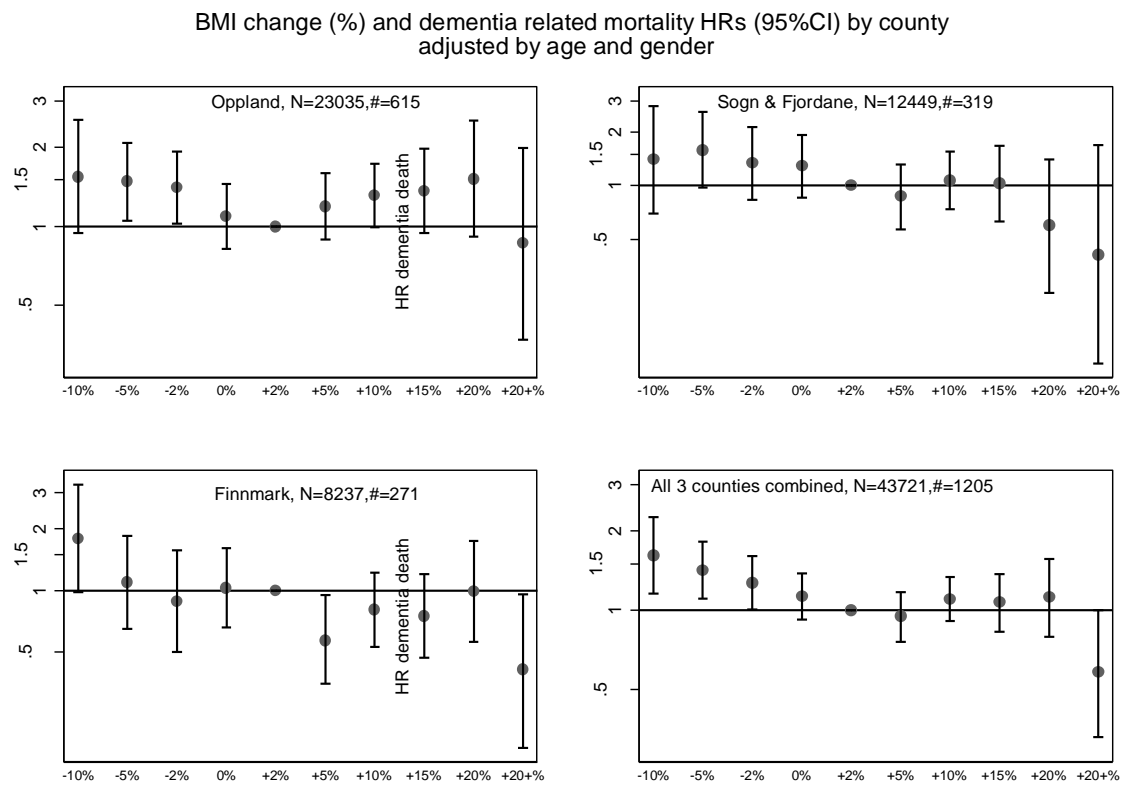
Our cohort members originate from three counties in Norway; Finnmark, Sogn & Fjordane, and Oppland. Finnmark is the northernmost county with a long coastline, and fishing is the main occupation. Sogn & Fjordane, lies in west, also with a coastline and fishing as one of the main industries. Lastly, Oppland, is an inland county with farming as the main industry. The prevalence of meat consumption for dinner at least once a week was similar in these counties; 35% in Finnmark, 37% in Sogn & Fjordane and 40% in Oppland. The pattern of minimum weekly fish consumption for dinner, however, differed significantly; 72% in Finnmark, 59% in Sogn & Fjordane and 23% in Oppland. A remarkable difference was found in consumption of the part of the fish which contained the higher levels of OCPs (4), namely the liver. In Finnmark, 35% reported weekly fish liver dinners compared to only 3% in Oppland and 11% in Sogn & Fjordane. In Finnmark, 2.3% reported fish liver dinners three times or more per week, whereas 0.4% in Oppland and 1.7% in Sogn & Fjordane had such high consumption. It is likely that these high fish liver consumers have

been exposed to levels above recommended values of OCP⁴. Thus, it is likely that Finnmark residents have been more exposed to OCPs than Oppland residents. On this basis, one could hypothesize that Finnmark residents also had higher OCP levels in their fat mass. Following from this, they would also release more OCP into their blood circulation with weight loss. Under the OCP hypothesis, we'd thus expect weight loss to be stronger associated with dementia risk in Finnmark than in Oppland. However, in additional analyses with county specific results, there seems to be no weight loss by county interaction (see Figure 1). Furthermore, fish liver intake did not attenuate the weight loss–dementia association. Kim et al's hypothesis (2) might still be valid as the difference in OCP levels between individuals from the three counties of Norway might be too small to detect an association. Furthermore, the causality of dementia is multifactorial where the contribution of OCPs might be modest. Mechanisms linking weight loss and dementia are complex and not fully understood (6). For example weight loss could lead to lack of essential vitamins, fatty acids and hormones which in turn affect dementia risk (7). Another mechanism is the glucocorticoid cascade hypothesis (8), which links depression to both loss of weight and dementia (9, 10), that is as a confounder. The hypothesis contends that depression leads to release of glucocorticosteroids to the blood, which in turn lead to hippocampal damage and neuronal death (11).

Kim et al propose an interesting mechanism (2), but it has yet to be investigated in epidemiological studies having all of the bits of the puzzle, including weight loss, OCP exposure, and dementia outcome.

Figures

Figure 1. BMI change (%) and dementia related mortality hazard ratios (HR) with 95% confidence interval bands, by county. Adjusted by age and gender.



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