THE AUTHORS REPLY

We thank Mesrine et al. (1) for their interest in our article (2) on dairy-food intake and incident, laparoscopically confirmed endometriosis in the Nurses’ Health Study II (NHSII). Mesrine et al. make a thoughtful point that a potential explanation for the stronger inverse association with milk intake among women with endometriosis who had never reported infertility, and who thus were likely "symptomatic" with respect to pain, could be the avoidance of milk by women with pain symptoms because of self-diagnosis of lactose intolerance or irritable bowel syndrome. To evaluate this hypothesis, we have conducted further analyses, the results of which suggest that reverse causation by gastrointestinal symptoms does not explain the inverse associations that we observed.

The long-term, prospective follow-up of the NHSII, including dietary data collected every 4 years, allows for enhanced analysis of the uncertain temporal relationships between dietary factors and endometriosis with respect to symptom onset. To evaluate whether the association between diet and endometriosis was influenced by alteration of intake because of prediagnosis symptoms, we conducted a latency analysis (3), described previously (4), examining a latency period of 4–8 years before endometriosis diagnosis. This time span encompasses the average duration of symptoms of 7 years prior to surgical diagnosis of endometriosis in the general population (5), which is slightly longer than in this medical professional cohort. For a latency period of 4–8 years, we used dietary intake in 1991 for cases diagnosed in 1995–1999, intake in 1995 for cases diagnosed in 1999–2003, and so forth. By using this approach, we found that the adjusted hazard ratios were not materially different from those reported in the publication. Specifically, with a 4- to 8-year latency period, we found that women who consumed more than 2 servings per day of any type of milk had hazard ratios of 0.79 (95% confidence interval (CI): 0.58, 1.07) ($P_{\text{trend}} = 0.19$) for all women and 0.84 (95% CI: 0.60, 1.16) ($P_{\text{trend}} = 0.46$) for never infertile women compared with women who consumed milk 4 or fewer times per week. The original hazard ratios from the cumulative average approach were 0.83 (95% CI: 0.67, 1.04) ($P_{\text{trend}} = 0.07$) and 0.81 (95% CI: 0.63, 1.03) ($P_{\text{trend}} = 0.08$), respectively. In addition, we compared baseline intake (in 1991) with the most recently reported dietary intake and cumulative average intake and did not observe materially different results among these 3 approaches.

In addition, to address the hypothesis regarding gastrointestinal symptoms and reverse causation, we performed analyses excluding women who self-reported inflammatory bowel disease. The adjusted hazard ratios differed by less than 0.05 from those reported in the publication. Specifically, when we excluded women who self-reported inflammatory bowel disease, we found that women who consumed more than 2 servings per day of any type of milk had a hazard ratio of 0.87 (95% CI: 0.70, 1.09) ($P_{\text{trend}} = 0.16$) for all women and 0.84 (95% CI: 0.66, 1.08) ($P_{\text{trend}} = 0.14$) for never infertile women compared with women who consumed milk 4 or fewer times per week. Results were similar when we excluded only women with physician-confirmed diagnoses of inflammatory bowel disease.

Mesrine et al. are correct that gastrointestinal symptoms are reported in women with endometriosis, although robust prevalence has not been established. It is also unclear what proportion of these women with self-diagnosed lactose intolerance, or physician-diagnosed inflammatory bowel disease, avoid milk as a result. Subjects in the NHSII are predominantly Caucasian (96%), and the prevalence of lactose intolerance is approximately 21% in North American Caucasians (6); thus, the number of women who make permanent changes to their milk intake is unlikely to be driving the associations that we observed. Unfortunately, because reports on gastrointestinal pain and/or self-reported lactose intolerance are not available within our data, we are unable to assess precisely the temporal relationships between these events as suggested by Mesrine et al.

Ideally, future studies of diet and endometriosis will include the collection of data on a variety of gastrointestinal symptoms in addition to pain, with details of onset, pain classification, duration, and consequential lifestyle changes.

ACKNOWLEDGMENTS

Conflict of interest: none declared.

REFERENCES


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DOI: 10.1093/aje/kwt152; Advance Access publication: July 23, 2013