Reviewer’s report

**Title:** The effect of pre-diagnostic vitamin D supplementation on cancer survival in women: a cohort study within the UK Clinical Practice Research Datalink

**Version:** 1  
**Date:** 23 January 2015

**Reviewer:** Alison M Mondul

**Reviewer’s report:**

Reviewer’s Comments to Authors:

This was a population-based study in women in the United Kingdom (UK) that investigated whether vitamin D supplementation before a cancer diagnosis affects overall cancer survival. The participants were identified from the UK Clinical Practice Research Datalink (CPRD) with a first diagnosis of breast, colorectal, lung, ovarian or uterine cancer between 2002 and 2009. The participants had to have at least 5 years of CPRD data prior to diagnosis. The study found that vitamin D supplementation prior to cancer diagnosis had no effect on cancer survival comparing women with 3 or more versus 1 to 2 prescriptions of vitamin D. Improved breast cancer survival was found only when they compared women with any prescription versus no prescription at all. The study concluded that there was no evidence that vitamin D supplementation is associated with improved cancer survival. The research question posed by the authors was original, easily identifiable and understandable. It addresses an important issue related to vitamin D supplementation and cancer survival. The large sample size was a strength of this study.

Minor compulsory revisions:

1. It was not mentioned in the article why the authors decided to carry out this study only in women. Please indicate why this decision was made.

2. It is not clear why the authors were concerned about confounding by indication in this study. Because the authors are examining vitamin D prescribed prior to cancer diagnosis, I struggle to envision why cancer prognosis/survival would be an indication for their being prescribed a vitamin D supplement before they were even diagnosed with cancer. Please clarify why confounding by indication was a concern.

3. Are there any current vitamin D supplementation guidelines in the UK? If so, how might they have had an implication in this study. Although there is not clear data on the dose taken by the study participants, if there is a published clinical guideline, mentioning it might give the reader some indication of what is usually recommended in the UK for women in this age range.

4. In regards to the inclusion criteria, the authors mentioned that they included data from those women who had at least five years’ worth of research standard
quality data prior to the date of cancer diagnosis. Please expand on what is meant by “research standard quality data”? What criteria are used to define the research standard quality data?

5. In the results section it was mentioned that there was a strong relationship between period of diagnosis and vitamin D prescription with the proportion of women having had three or more prescriptions. Does “period” refer to calendar year? Was there any evidence of different prescribing patterns by season? Please clarify this in the paper.

6. In the introduction and discussion, the authors cited and compared studies that use blood levels of vitamin D with the current analysis and other studies of vitamin D supplementation. Vitamin D supplement use does not necessarily correlate to vitamin D blood levels due to the component of vitamin D status that is determined by sun exposure. Perhaps the studies of circulating vitamin D should be mentioned only in the discussion, and the authors should mention the limitations of using vitamin D prescription from CPRD instead of blood levels of vitamin D and the fact that the results of this analysis are not directly comparable to the studies using circulating vitamin D as the exposure.

Discretionary Revisions:

1. More information on the UK Clinical Practice Research Datalink should be provided in the methods section. For example, population coverage, inclusion and exclusion criteria, variable measurements, especially for the variables used in this study. Alternatively, providing a reference to a previously published analysis with this detailed information would be sufficient.

2. I would suggest to move the information related to the number of women analyzed in this study to the methods section (currently reported in the first paragraph of the results).

3. Is there any information on adherence for the women prescribed vitamin D in this study?

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.