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: 9 April 2015

Reviewer: Katherine Crew

Reviewer’s report:

This study uses the UK Clinical Practice Research Datalink (CPRD) to evaluate the relationship between pre-diagnostic vitamin D supplementation and all-cause mortality among women with breast, colorectal, lung, or gynecological cancers. Strengths of the study include the large sample size, long-term follow-up, and linkage to pharmacy records. The authors should address the following concerns:

Major revisions:

1. The main measure of exposure is number of prescriptions for vitamin D in the 5 years prior to cancer diagnosis. The authors acknowledge that post-diagnosis supplement use was not included in this analysis. What is the typical duration for one prescription of vitamin D (i.e., 1 month, 6 months, etc.)? The authors also acknowledge that no information on average daily dosage and over-the-counter (OTC) supplement use is not available. Since OTC use may be limited among patients after age 60 due to free prescription coverage, the authors should consider restricting analysis to women over age 60, rather than 55.

2. The authors state that confounding by indication may be limited in their analysis since they evaluated discontinuation (3+ vs. 1-2 prescriptions) rather than initiation of vitamin D use. However, continuation of treatment may also be influenced by the strength of the indication. For example, presence of osteoporosis, which is related to low estrogen levels, may influence vitamin D supplement use and breast cancer prognosis.

3. Another limitation is the lack of information on tumor characteristics and cancer treatments, which affect long-term clinical outcomes. Early discontinuation of vitamin D may be influenced by the severity of their cancer, which would influence prognosis.

4. Is data available on cause of death and were the authors able to assess cancer-specific mortality in relation to vitamin D use?

Minor revisions:

5. Is the Index of Multiple Deprivation (IMD) score a measure of socioeconomic status? If so, the authors should define this and provide a reference for the measure.
**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.