Reviewer’s report

Title: Epidemiology and Outcomes of Undiagnosed Diabetes in Older Women with Breast Cancer: An Observational Cohort Study Based on SEER-Medicare

Version: 1 Date: 24 October 2012

Reviewer: Anjali Deshpande

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Minor Essential Revisions

1. On page 5 in the first paragraph, the statement “there is also evidence many diabetes cases may remain undiagnosed until breast cancer” requires a reference.

2. In the Inclusion/Exclusion criteria—does the term “had only one primary cancer diagnosed” refer to a single primary during the study period (2001-2005) or ever (so a sequence number of 00)?

3. In the definition of physician outpatient visits, where would OB/GYN visit fall? Is that a primary care physician or medical specialist? Studies have shown that women who see OB/GYNs are more likely to get better preventive care especially for “female” issues.

4. Since you don’t have any information in your analysis about length of time with diabetes or treatments for diabetes, I think that the discussion about hyperinsulinemia as a cause of advanced stage of cancer at diagnosis should be tempered somewhat. We don’t know that the newly diagnosed cases had uncontrolled glucose for long enough to result in aggressive tumor growth, etc.

5. On page 15, at the end of the second paragraph please remove the sentence “This is consistent with prior research showing that limited health system contact is associated with advanced cancer stage at diagnosis.” It seems irrelevant in this place and is used on the next page more appropriately anyway.

Major Compulsory Revisions

6. I think that the study of “undiagnosed” diabetes as it relates to breast cancer and breast cancer outcomes is important given the previously reported relationship between diabetes and breast cancer as well as (as the authors point out) the high prevalence of undiagnosed diabetes in the US. However, unlike other studies that have done across the board testing of individuals to see who has diabetes and who doesn’t, this study relies on the presence of a diagnosis code for diabetes around the same time as the cancer diagnosis—the authors point out the limitations of this method. My concern is with the use of the term “previously undiagnosed” or even sometimes just “undiagnosed” throughout the text. I would suggest that either you stick to “previously undiagnosed” or change throughout to “newly diagnosed”.

7. You created an index of preventive services that included a variety of
screenings, tests, immunizations. Did you consider looking at each service separately—in particular mammography and perhaps Pap test?

8. I found the causal diagram piece particularly interesting and Fig 2 clearly shows the complex nature of the relationships under study. In that regard and given that this is an observational study, did the authors consider using a propensity score analysis to account for shared risk factors and additionally unmeasured confounders related to being previously undiagnosed that may also be related to mortality—BMI, smoking, other access to healthcare variables?

9. Also with regard to the causal diagram, though the authors indicate that previously undiagnosed diabetes is a “cause” or precedes advanced stage cancer diagnosis, they could not actually answer that question in their data as diagnosis of diabetes in the “previously undiagnosed” diabetes group was happening at the same time as cancer diagnosis/workup/treatment whereas in the previously diagnosed group diabetes actually did precede cancer diagnosis. They are clearly related and likely due to shared behavioral or access to care risk factors.

10. As for tables and figures—I did not think that Fig 1 or Fig 3 added much. I felt the timeline was well described in the text. And though Table 2 provides a great deal of information already, it was not immediately clear to me if these were multivariate models with prior health system contact not included on the left and prior health system included on the right. I would suggest adding the bivariate associations to either Table 1 or more likely to Table 2 where there is one column for bivariate OR, then multivariate model w/o prior health system contact, then multivariate model w/prior health system contact.

**Level of interest:** An article of importance in its field

**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.