Reviewer’s report

Title: Association Between Delayed Initiation of Adjuvant Chemotherapy and Survival in Breast Cancer: A Systematic Review and Meta-analysis

Version: 2 Date: 8 February 2013

Reviewer: Dorte Lisbet Nielsen

Reviewer’s report:

Is the question posed by the authors new and well defined? Yes

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work? Yes

3. Are the data sound and well controlled? Yes (see comment)

4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes, use PRISME criteria

5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes; however, see comments

6. Do the title and abstract accurately convey what has been found? Yes

7. Is the writing acceptable? Yes

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

I suggest: Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

I think the article is of sufficient importance to be published in BMC Medicine.

In general, this is a well written systematic review and meta-analysis of data concerning delayed initiation of adjuvant chemotherapy in early breast cancer. The topic is very important and highly relevant. The majority of studies included into the meta-analysis are retrospective reducing the impact of the results and making firm conclusions impossible. However, I agree with the authors; it is unrealistic to expect a randomized trial.

Major comments:

The authors state that only “high validity” studies are included in the meta-analysis, however, they include the study by Samur et al. (reference 4). It seems that this study has no adjustment and does not fulfil the inclusion criteria stated. Accordingly, I suggest that the study is excluded.

Totally 34,193 patients are included in the analysis. Because of heterogeneity the authors exclude the study by Cold et al. leaving 28,128 patients back in the final analysis. However, at least 19,383 of the patients are # 65 years (57% of all patients; 69% of patients included in the final analysis) (inclusion criteria in
Hershman (reference 6) and Nurgaliev (reference 20)). The median age for breast cancer diagnosis is 61 years. The authors need to comment/discuss the age distribution of the patient population, including potential impacts on the conclusion.

Minor comments:
Reference 14 is not mentioned in the manuscript?
Estrogen receptor status should be included in Table 1.
Several typographical errors should be corrected.

**Quality of written English:** Needs some language corrections before being published

**Declaration of competing interests:**
I have no competing interests