Author's response to reviews

Title: Effects of interval between age at first birth and age at diagnosis on breast cancer survival according to menopausal status: A register-based study in Korea

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Version: 4
Date: 24 July 2014

Author's response to reviews: see over
April Joy U. Rada  
Editor-in-Chief  
BMC women health  
23 July 2014

Dear Dr April,

Re: Manuscript reference No. 1862859438122536

Please find attached a revised version of our manuscript “Effects of interval between age at first pregnancy and age at diagnosis on breast cancer survival according to menopausal status: A register-based study in Korea”, which we would like to resubmit for publication as a original article in BMC women health.

Your comments and those of the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers as well as your own comments.

Revisions in the text are shown using yellow highlight for additions. In accordance with reviewer ’s suggestion, we insert changes according to suggestions. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in BMC women health.

We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

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Responses to the comments of Reviewer #1

1. Please indicate what proportion of Korean breast cancer patients are registered in the Korean Breast Cancer Society Registry.

Response: 71% of breast cancer patients in Korea has been registered in the Korean Breast Cancer Society registry. We inserted this sentence using yellow highlight for additions.

2. First sentence would be better expressed thus: “T1,T2 staged breast cancer was more frequent in postmenopausal than in premenopausal breast cancer patients (84.9% versus 82.3%, p<0.001). And similarly throughout.

Response: We changed all previous sentences like your recommendations in the result session using yellow highlight for additions.

3. Abbreviations should be listed alphabetically

Response: We changed it like your recommendations using yellow highlight for additions.

4. Authors’ contribution: “Both authors…” rather than “ all authors…..”

Response: We changed it like your recommendations using yellow highlight for additions.

Responses to the comments of Reviewer #2

1. (a) Age at breast cancer diagnosis is missing( the terms pre- and postmenopausal are fine but we need age at diagnosis.(b) Did they exclude women who had neoadjuvant treatment/primary metastatic disease?

Response:
(a) We inserted this sentence in the result session using yellow highlight for additions.
(b) We didn’t exclude women who had neoadjuvant treatment/primary metastatic disease.

2. Please provide us with data for breast cancer mortality by breast cancer subtype( ER- status) to make these conclusions more understandable. This is important as reproductive factors affect these different type breast cancer differently. They describe to have these variables but why were these not included in the results/outcome apart from being descriptive?

Response: We previously reported the data for breast cancer mortality by breast cancer subtype in other journal; Clinical breast cancer. ER positive breast cancers, such as luminal A or luminal B breast cancer, have significantly different correlations with breast cancer mortality according to reproductive factors. We inserted these informations into the introduction using yellow highlight for additions.

3. 2/3 rd of the population had another or other pregnancies after the first one. 1) please provide us with date on the effect of time intervals since last pregnancy and breast cancer outcome.2) the authors didn’t include breast cancer patients who had another pregnancy after breast cancer treatment which
proportion and how might this affect results (is selection bias possible as they mainly premenopausal in their analysis)

Response: 1) This registry didn’t include the date of last pregnancy. We couldn’t report the effect of time intervals since last pregnancy and breast cancer outcome.
2) In 21126 premenopausal breast cancer patients, 63 patients (0.3%) had another pregnancy after breast cancer treatment. We considered this proportion had little effects on the clinical outcomes, and then we excluded these patients in this study.

4. Please provide us with data on adjuvant breast cancer treatment during throughout the study period.

Response: The topic (data on adjuvant breast cancer treatment during throughout the study period) is being analyzed for another manuscript by other authors, and then we couldn’t provide these data in this manuscript.

5. How clinically relevant is a significant HR of 1.03(table 6)

Response: We changed that sentence using yellow highlight for additions.

6. 1) Please explain the large number of premenopausal/postmenopausal breast cancer diagnosis in this database from Korea.

Response: We can’t give a detailed explanation why the majority of the patients were premenopausal in Korea. There were several epidemiologic reports about the age distribution of Korean breast cancer. Several genetic studies are currently underway.

Reference:

2) How do they explain 617/14387 non-breast cancer deaths in premenopausal and 440/6781 in postmenopausal being related with reproductive factors?

Response: Non breast cancer death in premenopausal women included that trauma, liver cirrhosis, leukemia, multiple myeloma, and other malignancy (ovary, pancreas, lung, hepatocellular carcinoma, colorectal cancer, stomach cancer) and in postmenopausal women included that pneumonia, chronic obstructive pulmonary disease, cerebral infarction, intracranial hemorrhage, congestive heart disease, end-stage renal disease, myocardial infarction, Parkinson’s disease, other malignancy (ovary, pancreas, lung, hepatocellular carcinoma, colorectal cancer, stomach cancer). Postmenopausal women had non breast cancer death correlated with chronic disease with complications, or cerebral disease.

7. Please shorten the background as there is some repetition in this part of the paper.

Response: We didn’t shorten the background.
8. Be consistent when defining early AFP/ Please be consistent with using AFP(AFB)

Response: We changed that sentence using yellow highlight for additions.

9. Follow-up duration differs between AFP and parity (table 2-3)

Response: We changed that sentence using yellow highlight for additions.