**Author's response to reviews**

**Title:** Temporal trends in female breast cancer mortality in Brazil and correlations with social inequalities: Ecological time-series study.

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**Author's response to reviews:** see over
Dear Reviewers,

We prepared this letter in order to respond each of your considerations.

Editorial requests:

(1) Please remove the author's qualifications (i.e., PhD) in the submission system.

We have deleted the author’s qualifications in the submission system.

(2) Data availability: Please document within the Methods section of your manuscript as to whether the data used for the study is openly available or as to whether you received permission (and by who) to use this.

The information about the data used for the study was documented to methods section. Lines 141 and 142.

Referee 1:

(1) In general, for better reading, report rates and APCs with one decimal.

We have accepted and adopted this suggestion in the manuscript.
(2) Line 45: specify that APC=0.3 is calculated for the period 1994-2011.

The period 1994-2011 was added to the abstract section.

Materials and methods section:

(3) State the software used to compute APCs. Presumably Joinpoint (Seer).

Joinpoint was added to the methods.

(4) Lines 130-133: Instead of mortality rates, correlations were computed between variations in mortality rates and SEI or HDI.

“Mortality rates” was substituted by “variations in mortality rates”.

(5) Lines 130-133: Specify how variations in mortality rates were computed. They seem different from APCs.

Variations in mortality were added to the lines 111-114.

(6) Lines 131-132: Replace IDH with DHI.

“IDH” was substituted by “HDI”.

Results section:

(7) APCs are often calculated for two different periods. Report APCs and corresponding period.

We have accepted and adopted this suggestion in the manuscript.
(8) Line 146-148: APCs are reported by age groups. Specify that they are calculated for all country (I presume).

“In Brazil” was added to the line 153.

(9) Line 161: Repeat that the correlation between SEI and variation of mortality is computed for the overall period.

“For the overall period” was added to the line 171.

Table 1:

(10) In title add “(world)” after age-standardized. Replace “age group” with “age-specific”.

“World” was added after age-standardized and “age group” was substituted by “age-specific”.

Table 2:

(11) “Trend 1” and “Trend 2” likely correspond to the segments of Joinpoint. Specify better.

“Joinpoint analyses with up to 1 joinpoints yielding up to 2 trend segments (Trends 1-2)” was added to table 2 in footnote.

(12) (13) Presumably mortality rates are computed for the first and last year displayed. Report it in footnote. State that mortality rates are age-standardized mortality rates.

The mortality rates in each state were presented as a Figure 2.
(14) Specify the lowest and the highest range of SEI in legend.

**Figure 2 was transformed in Figure 1b, the lowest and the highest range of SEI were added in legend.**

(15) Report correlation and p-value.

**There is no correlation and p-value for Figure 2 (1a).**

Figure 3:

(16) Create a fig 3a and 3b that display variations in mortality and HDI-2000 (fig 3a), or HDI-2010 (fig 3b).

**We created figure 3a and 3b.**

(17) Report also correlations and p-values.

**Correlations and p-values were reported.**

(18) Figure 4: correct 20011 with 2011.

“20011” was substituted by “2011”.

**Referee 2:**

(1) It is advised that the authors provide more details in the methods section regarding the choice and the definition of the trend 1 and the trend 2, the number of joinpoint used in the regression analysis, and perform additional analysis to present the AAPC. Given the 'slope' of the age-standardised mortality rates in some states was constant, the
authors might want to compare the significance of the test results by alternatively allowing 0 joinpoint to each state.

**We have accepted and adopted this suggestion in the manuscript. Lines 116-122.**

For our analysis, up tp 3 joinpoints were used, however the best model was chosen by program itself, whit a maximum of 2 trends.

(2) It is advised that the authors provide further details on the variation in the mortality rate.

**We provided more details on the variation in the mortality rate, lines 111-114.**

(3) Analysis of the temporal trend by the SEI and the HDI - The findings of the study could be far clearer, and the greater significance as a result, if the authors analysed the trend by the SEI and the HDI categories (i.e. use aggregated number of deaths from states in the same SEI or HDI level instead of analyzing number of deaths in individual state. Results for individual state can be included in the appendix). Then the authors can calculate the standardized rate ratios (and 95% Cis) of the mortality rates using the highest SEI or the HDI category as the reference group to see how much variation in mortality rate can be explained by social inequalities. The authors could also consider incidence to mortality ratio by the SEI and the HDI categories, respectively, if breast cancer screening program is in place in Brazil and the participation rates vary by those indices.

**The breast cancer incidence rates in Brazil are estimated by multiplying the observed mortality rate in the region by the ratio between the values of incidence and mortality of the town where there is single record of population based cancer registry.**

(4) It is suggested the authors perform the trends in the age-standardised mortality rates by different age groups. Graphical presentation, rather than the tabular format, will be more informative.
The trends in the age-standardised mortality rates by age groups were in lines 153-157.

(5) Table 2, Figure 1 and Figure 2 – I understand the number of tables and figures are limited. However, the results will be clearer if the authors present some part of the results from the Table 2 in a graphical format, and combine the Figure 1 and 2 as Figure 1.(a) and Figure 1.(b). This is that the period columns could be omitted from the Table 2 and the age-standardised mortality rate in each state could be presented as a figure.

We have accepted and adopted this suggestion in the manuscript. Figure 1 and 2 combined as Figure 1a and 1b. The age-standardised mortality rates were presented as a figure 2 and were deleted from the Table 2.

(6) Line 110 – please change >20 years to #20 years

“>20 years” was substituted by “20 years of age or more”.

(7) Line 131 – IDH (2000)? Did you mean HDI (2000)?

“IDH” was substituted by “HDI”

(8) Line 132 – IDH (2010)? Did you mean HDI (2010)?

“IDH” was substituted by “HDI”

(9) Results (line 137-154) – The study firstly described the results in terms of age-adjusted mortality rate, followed by individual state, then describe the age effect again. It is suggested the authors describe the results in line with the results tables, i.e. describe the mortality rates by age group as per Table 1 then describe the mortality rate and the associated trend by individual state as per Table 2.
We have accepted and adopted this suggestion in the manuscript.

(10) Line 192-197 – although this is a relevant discussion point, this paragraph is rather hanging between the previous paragraph (line 185-190) and the next paragraph (line 199-207). It is suggested the authors restructure this paragraph (perhaps after line 207).

We have accepted and adopted this suggestion in the manuscript.

(11) Line 209-214 – how is this relevant to the current study finding?

We have deleted this sentence.

Sincerely,

Prof. Ruffo Freitas-Junior, MD, PhD.