Author's response to reviews

Title: Pre-Invasive And Invasive Disease In Women With A Cytological Diagnosis Of High-Grade Lesion And High Grade Lesion Can Not Exclude Microinvasion

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Author's response to reviews: see over
Covering Letter

Dear Ms. April Rada,

Regarding the paper named *Pre-Invasive and Invasive Disease in Women With a Cytological Diagnosis of High-Grade Lesion And High Grade Lesion Can Not Exclude Microinvasion*, we are resubmitting a new version with the issues addressed in your e-mail dated Feb 20th, as follows.

Regards,

Nina Kuperman.

**REFEREE 1:**

**Minor Essential Revisions**

1. *If you are going to select the cut-offs for age from a ROC-curve, it is necessary to make sure that they are appropriate for the desired purpose, which I don’t think they are in this situation. The selected cut-offs split the women with HSIL-micro into groups of size 1, 4 and 42 – it is difficult to place much trust in results based on 1 and 4 women in the HSIL-micro group. Age categories which split the data for both HSIL and HSIL-micro women more equally make the results more reliable. Your previous response to comment 8 (“The age categories for Table 3 and 4 are not sensible, as they do not split the HSIL-micro women (42/47 are in the 35+ category).”) explains why you chose the categories, but did not address the fact that the cut-offs do not result in reasonable numbers in each category.*
We accepted the reviser’s suggestion and decided not to split patients by age groups. We analyzed them as a single group.

2. Not everything in the abstract is mentioned in the main paper (for example, cervical cancer is the 3rd most common cancer in Brazil).

Done. Please, see lines 77-89.

3. ETZ, AIS, EJC should be spelt out before first use (in the text, not just as footnotes to a table).

Done. We revised all the abbreviations.

4. Please name the confounders adjusted for in the statistical analysis paragraph.

Done. Please, see lines 168-169.

5. In the last paragraph of the discussion, you say that the cPR was 5.45 for women under 25 – no cPR was calculated for women under 25, and 5.45 is the overall cPR.

We changed our analysis.

Discretionary Revisions

1. In the last paragraph of the discussion, you say the cPR for women 35+ was similar to the overall aPR – this may be a result of age 35+ being the baseline category when the age variable was adjusted for – if so you would expect the cPR for women 35+ to be the most similar to the aPR, and it is an artifact of the analysis, rather than something to comment on.

We changed our analysis.
Minor issues not for publication

1. In the statistical analysis paragraph, the test is a Student’s t-test (there is currently a typo), and there are words missing from this sentence so it currently doesn’t make sense – Student’s t-test was used to do what to numerical variables?

   Done. Please, see lines 160-167.

2. It is more usual to present results in order of increasing age when split by age, rather than decreasing age, as in Tables 3 and 4.

   We did not split the analysis by age in the new version.

REFEREE 2:

I have read the revised manuscript.

I still do think the discussion is too weak on this subject. Even as the goal of the authors was to compare HSIL to HSIL-Micro in Brasil, a proper discussion regarding prevalence of (pre)-invasion in their population is warranted and would make the manuscript more valuable.

Additionally, I notice that the conclusion in the abstract has not changed regarding a more aggressive approach in HSIL-Micro, although this has now been explained in the manuscript. I would suggest to use the conclusion of the manuscript also for the abstract.

I also notice that the authors have difficulty with the remark of the other reviewer that this is a selected population, and not just a sample out of mass screening in the population. If they persist in stating this a screening population, than they have to comment on screening advise and attendance in their region. I suppose this is an underscreened population, resulting in a high prevalence of invasive disease, and not a screened population.

Finally the English has not improved yet, indeed, the added parts are even worse.
If the journal will correct the English than this is not appoint of concern, but if the authors will do it as they state in their cover letter, than this needs to be corrected before acceptance.

We added some more references in the discussion, but it is difficult to find studies with information similar to ours, in order to compare.

The same conclusion is now shown in the abstract and in the manuscript.

We believe the population in our study is now more clearly explained. We also removed the key-word “mass screening”.

Another language reviser will revise the manuscript after all questions had been addressed.