Author's response to reviews

Title: Median ages at stages of sexual maturity and excess weight in school children

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Author's response to reviews: see over
Mr. Jose Belizan  
Editor-in-Chief of Reproductive Health  

Article reference number: 5078151719296913  
Title: "Median ages at stages of sexual maturity and excess weight in boys and girls"  

Sao Paulo, October 6th, 2013.

Dear Dr. Belizan,

First and foremost, we would like to thank you and the referees for the invaluable comments. The necessary modifications have been made to the text in order to meet these suggestions.

Sincerely,

Alexandre P. Luciano et al.
Response to the reviewers:

Reviewer 1: Marcelo Ferreira

Dear Dr.,

We thank you for the careful revision of our manuscript and inform you that all suggestions were integrally considered. Below, we detail the modifications we made to the manuscript.

“The authors estimated the median ages at specific stages of sexual maturity stratified by excess weight in boys and girls. They performed an elegant statistical analysis. Their findings are also important for both reproductive and growth and development areas. This is an interesting study that will surely contribute to the scientific area. Some changes I request the authors to do: 1-I suggest the following title: "Median ages at stages of sexual maturity and excess weight in school children" 2-The keyword "schoolar children" is worth to be included. 3-The objective may be changed to "...we aimed to evaluate the estimation of the median ages at the sexual maturation stages stratified by excess weight in boys and girls. 4-I suggest the authors to include an additional paragraph in Discussion that discusses the limitations of the study.”

Answer:

We changed the title based on the referee’s suggestion (1); added the suggested keyword (2); changed the objective according to the referee’s suggestion (3); and included an additional paragraph about the limitations of the study in the discussion session (4). All modifications made to the manuscript are in red.
Reviewer 1: Elise Murowchick

Dear Dr.,

We thank you for the careful revision of our manuscript and inform you that all suggestions were integrally considered. Below, we detail the modifications we made to the manuscript.

1- “The question Luciano et al. seems to be posing is: Does excess weight related to differences in median ages with respect to the different components of pubertal development as measured my Tanner staging. There are a couple questions threading this review, which once addressed and revised may make many of the auxiliary comments clearer and greatly strengthen the article. The use of the median age may need clarification. This is a major clarification and occurs in several places in the article, (Major compulsory revision #1 that infiltrates much of the paper). Once the clarification as to why median age is employed has been established this can be integrated into the revised statement of the research question.

Answer:
As there is no standard definition of early sexual maturity, we used an approach similar to other studies in order to ensure comparability of our results (Ribeiro et al., 2006; Rubin et al., 2009; Belachew et al., 2011; Monteilh et al., 2011; Papadimitriou et al., 2011). To make this point clearer, as suggested by the reviewer, we added a brief explanation and some references to the manuscript methods section.


2- In addition, clarify why this particular area (with better health indices than the rest of the country as a whole) was selected. The authors need to make this point clearer, especially as it relates to the research question (Major compulsory revision #2).

Answer:
The city of Florianópolis was chosen for logistic purposes.

3- While there are a number of potential variables described in the measures section little in the analysis indicates if and how these were used. For example, description of the birth weight, the birth weight categories, maternal weight, etc., are put forth in the methods section but not mentioned again in the analysis or results except briefly in Table 1. Each of the variables described may be linked with pubertal status and/or BMI. Are these variables controls or alternative hypotheses? This needs clarification. (Major compulsory revision #3). It is often the case one includes a bivariate correlation table to see these associations and if some of the variables are not normal and/or interval a Spearman’s correlation table might be appropriate (Major compulsory revision#4)"

Answer:
These covariables were collected only to better characterize the study population, as shown in table 1. As the main aim of the study was just to compare the mean ages of sexual maturity according to excess weight and sex, these covariables were not adjusted for in the analysis.

4- “It is not clear why in multiple instances continuous variables are then categorized. This seems to limit the power of the analysis and may produce spurious findings as has been noted (cf. MacCallum, Zhang, Preacher, & Rucker, 2002) (variation of major compulsory revision #1)”

Answer:

The categorization of variables was based on standard cutoff points, as proposed by the World Health Organization.


5- “From what I can understand the BMI were normalized by age and gender with a z-score. Did this not render this variable normally distributed? How are decisions about normality being made? Be explicit to allow others to replicate the findings. Also if the BMI’s are age normed will that throw out variation due to age in”

Answer:

In order to clarify aspects about the calculation of BMI z-score, a full description of the method was added to the methods section.
6- “p.8. The authors report a higher median pubertal score for boys than girls. There is a large literature that finds girls are usually earlier than boys. If the boys being earlier is not an artifact of the medians then this should be explained. Is there a difference in who gets to go to school, the boys were heavier according the Table 1 and had higher z-score BMI’s. Is this typical of this country? (Major compulsory revision #6). Furthermore, it seems the boys’ have higher weight, higher BMI, and earlier puberty overall although the girls who are categorized as higher BMI were more often in the earlier puberty group compared with the normal weight peers. How does this fit the research question and outside research presented on leptin etc. (Major Revisions #7)”

Answer:

As can be seen in figures 1 and 2, boys achieved sexual maturation later than girls, which is in accordance with the scientific literature:

- Figure 1 for stage 2 of sexual development: 10.8 y (boys) vs. 10.3 (girls) (p = 0.005)
- Figure 2 for stage 2 of pubic hair: 11 y (boys) vs. 10.8 (girls) (p = 0.071)
- Figure 2 for stage 4 of pubic hair: 13.7 y (boys) vs. 13.4 (girls) (p = 0.009)

7- “There may be a typo with the on this page (p. 8) too after the reference 16. The should not be capitalized. Check this paragraph for this type of error. (Minor compulsory revision #1)”

Answer:

We corrected this mistake.

8- “In describing the pattern for boys in Table 2 seems to indicate that 3 of the 10 tests presented are statistically significant at p < .05. This might not qualify as a trend. Were any correction like Bonferonni’s, done for running multiple tests? (Minor compulsory revision #2)”

Answer:
Taking into account the significance level adopted (5%), it would be expected to find less than one significant test by chance in ten tests (0.05*10). Therefore, we do not believe that a Bonferroni correction would be needed. Also, the p values obtained in table 2 that were below the significance level were much smaller than 5%, which means that the probability of finding a difference of these size or more by chance would be very low (1% for p = 0.01; 0.8% for p = 0.008; and less than 0.1% for p < 0.001).

9- “Authors posit a unidirectional hypothesis when it is possible that a lack of body weight could delay puberty as has been seen throughout history with delays in puberty due to famines, excessive exercise, restricted eating due to anorexia (see R. Frisch or J. Brooks-Gunn for examples). (Minor compulsory revision #3)”

Answer:
Although we recognized the importance of the point raised by the reviewer, this is probably not a relevant issue in our study, given the low prevalence of undernutrition in the study population (less than 5% of the children between 7 and 10y had low BMI-for-age) (Assis et al., 2005).


10- “In addition to major revisions suggested above regarding medians and distributions the data reported in tables for the p-values could be reported just to two decimal places. (Minor compulsory revision #4)”

Answer:
Based on the referee’s suggestions, we reported data with two decimal places in the Tables.

11- “On p. 4 If one is looking at sexual precocity why not collect from 7 year olds? (Minor compulsory revision #5)”
As indicated by the reviewer, there is a lack of data on sexual maturity for 7-year-old children. However, we believe this does not have important implications to our results since puberty onset at such a young age has a very low prevalence, and may result from pathologic conditions, such as pituitary tumors, hydrocephaly, perinatal anoxia etc (Longui et al., 2001). In the British ALSPAC cohort (Avon Longitudinal Study of Parents and Children), at age 8, about only 5% of the boys reported Tanner pubic hair stage >1 (Monteilh et al., 2011) and 12% of girls reported Tanner breast stage >1 (Rubin et al., 2009). Several studies aiming to investigate the onset of sexual maturation events include only children older than 7y (Euling et al., 2008; Rubin et al., 2009; Monteilh et al., 2011).


12- “Explain what ASSIS is and provide a reference if needed. (Minor compulsory revision #6)”

Answer:

The complete reference was added to the manuscript (Assis MA, Rolland-Cachera MF, Grossemann S et al. Obesity, overweight and thinness in schoolchildren of the city of Florianopolis, Southern Brazil. *Eur J Clin Nutr.* 2005, 59:1015-1021).
13- “In the abstract two minor modifications are suggested, these are optional. First, the word transversal is unique to some disciplines and adding the cognate cross-sectional would be good. Some explanation as to why medians are used here, are the data not normal? Also the tone of the abstract “excess weight is an important variable in the determination of median age” sounds more causal than a transversal/cross-sectional non-experimental study could conclude. (Discretionary revision #1).”

Answer:
All the proposed changes to the abstract are in red in the manuscript text.

14- “Somewhere in the introduction a brief acknowledgement of puberty can be delayed as well as accelerated by environmental and other types of variables. For example, there can be delayed puberty due to under nutrition or other medical problems. It seems only half of the ways BMI and puberty is considered and this merits an acknowledgement if not a direct test. The lack of pubertal developmental as well as its occurrence can be used to monitor growth. (Discretionary revision #2).”

Answer:
As requested, a brief discussion about the fact that puberty can be influenced by environmental factors was added to the introduction.

15- “The sampling design is a careful one, selecting schools in different areas. The weighting based on this seems appropriate. Since income level is a contributor to BMI in many studies, perhaps an indication of income from the schools (or parents) might be useful. Also are there differences in income level for the schools or for Tanner stages or gender? (Discretionary revision #3).”

Answer:
A stratified analysis performed between children attending public and private schools (a proxy of income level) showed no significant differences in Tanner stages or gender.
16- “a) The discussion of leptin and genetics is interesting but the data presented here do not really address this cellular and hormonal level of analysis. If this line of thinking seems relevant perhaps work on the genetic component of puberty might also be relevant. However since the authors did not report data on leptin or genetic markers this seems to be speculative. More germane might be the data collected on maternal weight but understanding this role could be subsumed in an epigenetic model (e.g. shared genes, stress, contexts, or economics). b) Is there a gender difference in under nutrition in this area? (Discretionary revisions #4)”

Answer:

a) Given the cross-sectional design of the study, it was important to discuss our findings in terms of their biological plausibility, one of the most important Hill’s criteria of causation (Hill, 1965). For that reason, we included a discussion about hormonal and metabolic aspects linking adiposity and sexual maturity.

b) The prevalence of thinness in the study population was similar between boys and girls (less than 5% in children between 7 and 10y) (Assis et al., 2005).


17- “This study was cross-sectional so the discussion points going beyond associative relationships might be speculative. (Discretionary revisions #5)”

Answer:

The discussion section was revised in order to avoid ‘cause and effect’ claims. The implications of the cross-sectional design to the research question were also discussed as a limitation of the study.