Author's response to reviews

Title: Development of waist circumference percentiles for Japanese children and an examination of their screening utility for childhood metabolic syndrome - a population-based cross-sectional study

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Author's response to reviews: see over
We would like to thank the reviewer for the valuable suggestions and comments. Based on which we modified our manuscript. Please note that the modified parts are indicated in red in the revised version.

Major Compulsory Revisions

1. The validity of using the WC and WC/Ht percentile curves based on data collected in 2012-2012 from children aged 4.5-12.75 years to identify Metabolic syndrome among the obese children aged 6-12 years olds who visited pediatric outpatients department in 2005-2007. In addition, the percentile curves were generated based data from non-nationally representative sample (as authors had mentioned in page 10, line 10).

Response: This claim is reasonable. Ideally, validity using the WC and WC/Ht should have been determined on the basis of data collected in the same period or in close succession. We added some sentences aimed at explaining this limitation in the Discussion (page 11, line 9). Considering that the incidence of childhood obesity in Japan has remained the same since 2000 (Yoshinaga et al., Pediatric International 2009), our retrospective trial should be acceptable. We added this reference in the revised manuscript. In addition, we did not use the data form a nationally representative sample, as mentioned in the first submitted version as well as in the revised version (page 10, line 24). This is another limitation of our study. We would like to emphasize that this study does not demonstrate solid evidence of the utility of the WC and WC/Ht across the country. However, it shows significant potential of WC and WC/Ht in screening childhood MetS in Japan. We intend to compile a proposal for national surveillance, using the new WC percentiles. Subsequent data will provide sufficient evidence for the utility of those WC percentiles for national health promotion.

2. The validity (such as sensitivity and specificity) of using cut-off point >90th, >95th or >97th value from the newly developed WC percentile curves in identifying obesity among Japanese children is unknown since these cut-offs were not cross-checked with other indicators such as BMI and VAT.

Response: The main reason for use of the >90th percentile cutoff point was that childhood MetS criteria(s), including those of the International Diabetes Federation (IDF), NCEP/ATP-III, and Cook et al. employed WC >90th percentile as the cutoff value; many studies on the incidence of childhood metabolic syndrome have also used this cutoff point. We did not use >95th percentile in this study. A 90th percentile cutoff for WC might lead to an over-diagnosis of central obesity, when applied to Japanese children, whose WC is relatively smaller than that of children in western countries; therefore, we tested the cutoff point of WC >97th percentile. This explanation appears on page 7, line 23. We had confirmed the strong correlation between WC and BMI values in our samples (r > 0.8: data not shown in the text). On the other hand, when using the BMI percentile as the cutoff point, then no statistical significance is observed between the BMI percentile and the cluster (two or more) of metabolic abnormalities. Unfortunately, we did not have any data of the participants' VAT data.

3. ROC curve analysis should be used in determining the optimal WC percentile value for predicting childhood MetS.
Response: We strongly agree with the reviewer’s noteworthy comment. Actually, we had performed ROC curve analysis (explanatory variable: 50–75th WC percentile, 75–90th WC percentile, 90–97th WC percentile, and 97–100th WC percentile: supervised variable: two or more metabolic abnormalities), however, statistical significance was not obtained because of an extremely small number of non-obese subjects (50–75th WC percentile), and a marginal number of subject in the 75–90th WC percentile. Then, we changed the explanatory variable to be higher or lower than the cutoff WC percentile (75th, 90th, or 97th) and re-performed the ROC analysis. When we analyzed each group, categorized by sex and age, statistic difference was not obtained because of the relatively small sample size. Then, we combined the data of boys and girls, regardless of age. When a single explanatory variable (higher or lower) was set, the confidence intervals for the area under ROC the curve (AUC) was 0.5054 (95% CI: 0.501–0.51) for a cutoff of WC at the 75th percentile, 0.5386 (95% CI: 0.528–0.55) for a cutoff of WC at the 90th percentile, or 0.4816 (95% CI: 0.387–0.576) for cutoff of WC at the 97th percentile. Therefore, we concluded that WC at the 90th percentiles is very likely to be suitable for screening childhood MetS. We added some explanations in the Methods, Results and Discussion sections (page 6, line 21, page 8, line 15, and page 10, line 8), and the description about the limitation of the ROC analysis in this study (page 11, line 14).

4. Previous studies did not find a significant influence of WC measurement site on the relationships with visceral adiposity and cardiometabolic risk factors. Therefore, the authors claimed that WC percentile from WC measured at the level of umbilicus was more useful than other measurement sites for screening childhood MetS is questionable.

Response: We understand the reasoning behind his comment. The main advantage of the new WC percentiles based on data measured at the umbilical level is as follows. In Japan, the standard WC measurement site is the umbilical level. Therefore, the WC data from school health checkups should be measured at this position. Considering this, for wide usage of WC percentiles, especially in view of health promotion, it is the best way to measure WC at the umbilical level.

5. Please consult statistician on the likelihood ratio #2 tests that were performed in this study. Few cells with expected frequency < 5 and observed frequency= 0 were noted in table 1 to 4. Therefore, the likelihood ratio #2 test may not be appropriate.

Response: Following your suggestion, we consulted several statisticians and, as you have indicated, we concluded that the likelihood ratio (G test) may give inaccurate results if the expected frequency of observations in any category is too small (<5), as refereed in the Handbook BioStat First (John H. McDonald, University of Delaware 2001). We once again conducted statistical assessment on the utility of the new WC and WC/Ht percentiles for screening MetS, integrating all participants’ data, and obtained statistical significance when the cutoff was set WC at the 90th percentile. Then, we modified Table 2–5 (deleted the column, “p value”) and added explanations in the Results section (page 7, line 19, page 8, line 2, 10 and 13). We do appreciate your observation.

Response:

Minor Essential Revisions
1. What were the inclusion and exclusion criteria for data collection from children in Shizuoka prefecture? What is the total number of eligible children and response rate?
Response: The children’s WC measurements were taken at as an optional assessment during the annual health checkups. All the children’s height and weight were measured at the same time WC was measured among children who, and whose parents had agreed to participate in the study through written consent (N = 7,418). In total, 229 children were not eligible because written consents were not obtained. The data from children who had foreign nationalities (N = 210), in active treatment, or with a severe handicap (N = 38) were excluded. Eventually, data for WC percentiles were obtained from 7,170 children (3,634 boys and 3,536 girls). The response rate was 100% because written consent (or disapprovals) was obtained from 100% of the children. We added these explanations in the methods section (page 5, line 6).

2. Is the equation correct? : POW was calculated as 100×(the measured weight - normal weight)/normal weight (\%)

Response: This was a careless mistake. We corrected the formula. We appreciate your careful observation.

3. Error: To change the ‘table 1 and 2’ to ‘figure 1 and 2’ (page 6, line 17).

Response: We show the LMS parameters in Supplemental Table 1 and Table 2. We changed “Tables 1 and 2 of the Additional files’ to Supplemental Table 1 and Table 2 to avoid misreading (page 7, line 1).

4. For comparisons of WC and WC/Ht percentile curves between boys and girls (page 6, 19-24) please present the boys and girls percentile curve in one figure (to combine figure 1a and 1b, figure 2a and 2b).

Response: Following this comment, we added new figures, in which boys’ and girls’ percentile curves are combined, namely Figure 1c and 2c.

5. In page 8, line 1: “In the group aged 10–12 years, 16 (11%) of the 140 boys and 3 (4.4%) of the 68 girls”, the figures did not tally with the figures showed in table 4.

Response: This was a careless mistake. We corrected this description, to correspond with the contents of Table 4 (page 8, line 5).

6. Table 4 and 5, the girls’ column subheading should be ‘WC/Ht percentile’, not ‘WC percentile’.

Response: We made the corrections. We appreciate your advice.

Discretionary Revisions

Results section is too lengthy. Please highlight the important points that authors would like to share with the readers.

Response: Following this comment, we re-wrote the Results section, and sent the revised manuscript for professional proofreading.
<Reviewer #2>

We are very grateful for your supportive comments on our paper. We performed revisions on our paper following your comments. Please note that the modified parts are shown in red in the revised version.

**Minor essential revisions:**

1. In the methods; line 24, the formula has double ‘/normal weight’

**Response:** This was a careless mistake. We corrected the formula.

2. The references are appropriate for the manuscript. But there are some writing mistakes in the name of literatures (numbers of literatures are: 15, 20, 23, 30, 47).

**Response:** We carefully corrected those mistakes.

3. On the table 1; table legend (201?1), (‘BW’ for girls may change to ‘Weight’ as boys)

**Response:** This was a careless mistake. We corrected this mistake.
<Reviewer #3>

We are very grateful for your helpful comments on our paper. We performed revisions on our paper following your comments. Please note that the modified parts are shown in red in the revised version.

INTRODUCTION

1. The first paragraph is too long. It would be interesting to divide into two or more paragraphs.

Response: We rewrote this paragraph for easy reading (page 4, line 2). We appreciate the reviewer’s comment.

2. Exclude this paragraph from introduction section. It should be described in methods section: “The LMS method of summarizing growth standards, which monitors changing skewness (L), medians 20 (M), and coefficients of variation (S) in childhood distributions, was used on a representative dataset from 21 Japanese children whose WC was measured at the umbilical site.”

Response: We agree with your claim. Following this comment, we deleted this paragraph.

METHODS

Include the number of ethical committee How many measurements of WC was taken each children? Please describe it in this section.

Response: Thank you so much for your observation. We added the numbers in the text (page 5, line 5 and page 5, line 4). We measured the children’s WC once and clarified this in the text (page 5, line 15).

TABLES

Table 5 is in poor quality. It need to be redone

Response: Following this comment, we revised Table 5.