Author's response to reviews

Title: Physical activity, cardiorespiratory fitness, and metabolic syndrome in adolescents: a cross-sectional study.

Authors:

Antonio Stabelini Neto (asneto@uenp.edu.br)
Rodrigo Bozza (rdbozza@gmail.com)
Anderson Z Ulbrich (anderson_u@hotmail.com)
Luis Paulo G Mascarenhas (luismsk@gmail.com)
Margaret Cristina S Boguszewski (margabogus@uol.com.br)
Sergio G da Silva (sergiogregorio@ufpr.br)
Wagner de Campos (wagner@ufpr.br)

Version: 2 Date: 2 June 2011

Author's response to reviews: see over
Reviewer’s report

Title: Physical activity, Cardiorespiratory fitness, and Metabolic syndrome in Adolescents: A Cross-Sectional Study

Version: 1 Date: 31 March 2011

Reviewer: Carla Moreira

1. The authors may consider to use the word “sex” instead of “gender”.
The word gender was used by professional English proof reader

2. The authors may consider being consistent in the use of the terminology when referring to cardiorespiratory fitness: “aerobic fitness”, “VO2máx”, “physical fitness”. Similar comment about the use of “subjects” and “participants”. Please choose one and be consistent throughout the manuscript.
Were used the terminologies cardiorespiratory fitness and subjects.

3. The authors may consider removing the word “the” before Metabolic Syndrome along the manuscript.
The word “the” was removed.

4. Abstract:
- Background: A word is missing between “known” and “adolescents”.
The word “in” was included.

- Abstract, Methods: Eliminate “VO2máx” and write “cardiorespiratory fitness”.
We replaced VO2máx for cardiorespiratory fitness.

5. Background:
- First paragraph: need to add a sentence to clarify the definition of metabolic syndrome in children and adolescents.
We rewrite the Background wiht the definition of metabolic syndrome in children and adolescents.

- Third paragraph “…about MetS in youths.” suggests “…about MetS in youth.”
Fifth paragraph “…to analise” suggest “to analyze”
Replaced for “youth” and “analyze”.
6. Methods,
a) Sample
- First paragraph: the authors say that “schools were randomized according to type (age range and gender), location (urban, suburban, and rural), and the socioeconomic characteristics.” I would like to be informed about the socioeconomic characteristics.

The city of Curitiba has a population of 1,678,965 inhabitants with a human development index by 0.763. The sample size consisted of school children registered in the education system (approximately 45,000 students). The following parameters were used to estimate the sample size: an error of 5%; an estimated Mets prevalence of 20%; a design effect of 1.5; a 95% confidence interval; and an additional 10% for losses and refusals. A conglomerate sample of 456 adolescents (223 girls [49%] and 233 boys [51%]) was evaluated. The schools were randomly selected, and the proportion of students was established according to the number of students in each of the nine administrative areas of the city (Santa Felicidade 6.6%; Matriz, 12.3%; Boa Vista, 14.7%; Cajuru, 12%; Portão, 10.6%; Boqueirão, 13.1%; Bairro Novo, 9.6%; Pinheirinho, 9.5%; and CIC, 11.6%). Data collection from schools took place between April and November 2009.

b) Measurements

- The measurements should be rewritten for a more logical structure and an easier understanding. The variables are mixed and the information it is not clear.

The measurements were rewritten for a more logical structure:

1. Anthropometric measures
2. Blood pressure
3. Blood sampling
4. MetS definitions
5. Physical activity
6. Cardiorespiratory fitness
manufacturer information.
The brand and manufacturer information were included.

- Measurements, Physical Activity

First paragraph: need to add a sentence to better explain the questionnaire used to estimate physical activity (i.e., that classifies physical activity in terms of energy expenditure). The authors say that “…physical activity scale of 1-9 (1 being sedentary active, and 9 being very active).” Please, clarify.
The sentence was rewritten for easier understanding. We added more information about the physical activity intensity (1-2, sedentary activity [lying down and seated]; 3-5, light activity [taking a shower, cooking, taking a walk, and light manual work]; 6-8, moderate activity [sports or leisure activities and moderate manual work; 9, vigorous activity [intense manual work and intense sport or leisure activities]).

- “(MVPA) expressed in minutes for day” suggests “(MVPA) expressed in minutes per day. Replaced for “minutes per day”.

- Fifth paragraph: information about cardiorespiratory fitness test is lacking. Although the name of the test is mentioned, more information about the protocol and the measurement must be included.
More information about the cardiorespiratory fitness test were included. (The required speed was continuously increased each minute by 0.5 km/h by a beep. The velocity in the exhaustion moment was recorded).

- Measurements, Blood Samples
Third paragraph: rewrite both sentences: "All the measurements…. same sequence" and “The data used … scholl site.”
The sentences were removed of the manuscript.

- Measurements, MetS definitions
“…waist circumference # 90th..” suggests “…waist circumference # 90th percentile..”
“…SBP or DBP> 90th ..” suggests “SBP or DBP> 90th percentile..”
The terms were corrected in the text.
c) Statistical procedures
- First paragraph: rewrite the sentence "Independent … the genders groups."
First paragraph was rewritten. “To compare the continuous variables between the genders we used Student’s t-test, and the chi-squared test was used for categorical variables.”

The physical activity tertiles were present and the cardiorespiratory fitness tertiles should be presented as well for a more logical structure.
The cardiorespiratory fitness tertiles were included. “boys: low < 46 ml.kg\(^{-1}\)min\(^{-1}\), moderate 46-51 ml.kg\(^{-1}\)min\(^{-1}\), and high > 51 ml.kg\(^{-1}\)min\(^{-1}\); girls: low < 38 ml.kg\(^{-1}\)min\(^{-1}\), moderate 38-43 ml.kg\(^{-1}\)min\(^{-1}\), and high > 43 ml.kg\(^{-1}\)min\(^{-1}\)”

7. Results
- First paragraph: “Table 1 presents….evaluated in both genders by sex.”
suggests: “Descriptive characteristics of the data by sex are shown in Table 1”
We replace the sentence by the reviewer suggestion.

- Third paragraph: “…MetS was observed in the sedentary adolescents and with low fitness levels” suggests “…MetS was observed in the sedentary adolescents and in those with low cardiorespiratory fitness”
We replace the sentence by the reviewer suggestion.

- Fourth paragraph: eliminate the sentence “The prevalence of MetS increased significantly with reduction in physical activity and cardiorespiratory fitness levels”. The idea has already been mentioned in the preceding sentence.
The sentence was eliminated.

- Fifth paragraph: the authors say that “Significantly higher ratios (p<0.05) were found for high and low VO\(_{2}\)máx.” Please, clarify.
The sentence was rewritten for easier understanding. “Significant associations were demonstrated between MetS and cardiorespiratory fitness (Table 3). The subjects with low cardiorespiratory fitness had an odds ratio for MetS of 3 (CI, 1.13-7.94) compared with subjects with high cardiorespiratory fitness.”
8. Discussion

- Fourth paragraph “…with higher physical activity levels and higher VO2max had less MetS.” suggests “with both higher physical activity and cardiorespiratory fitness levels had lower prevalence of MetS”.
We replace the sentence by the reviewer suggestion.

- Eighth paragraph: discussion of the physiological process of the muscle fiber metabolism is not necessary that is out of the focus of this paper.
The sentence was eliminated.

- Table 1
Remove “.. values are the mean (SD)” from the title and write down the table.
“1th, 2th and 3th tertile” suggests “1st, 2nd and 3rd tertile”
Eliminate ,000 and write <0.001.
The table 1 was rewritten in accordance with the reviewer suggestions.

Major Compulsory Revisions

1. Measurements, Resting Blood Pressure
- Third paragraph: when the blood pressure was taken? How many measurements of the blood pressure were taken? How did the authors get the SBP and DBP values presented in Table 1? There should be more details about the measurement of resting blood pressure.
The sentence was rewritten for easier understanding and more information about the blood pressure protocol was included.
“Two measurements were obtained after 5 and 10 min of rest. The mean of the two measurements was considered. If the two measurements differed by > 2 mmHg, a third measure was obtained.”

2. Measurements, MetS definitions
- The authors say that “Abdominal obesity was considered as waist circumference # 90th for age and gender19.” However, accordingly to the reference the waist circumference
percentile was defined for children and adolescents aged 5-17. The sample of this study encompasses children and adolescents between 10-18 years old. Please, clarify.

The sentence was rewritten for easier understanding. The term “hypertension” was replaced by “high blood pressure”, and the word “height” was included on the sentence, since this variable is necessary for blood pressure classification in pediatrics population.

3. Results
- Statistics are poorly presented.
More information about the statistics tests were included in the text.

- First paragraph: the authors say that “Apart from height, weight, VO2max, SBP, and glucose, which were higher for the males, no other parameters differed by genders”. What about waist circumference and MVPA? In the table 1 these variables showed significant differences between sexes. Please, clarify.

The sentence was rewritten for easier understanding. The term “hypertension” was replaced by “high blood pressure”, and the word “height” was included on the sentence, since this variable is necessary for blood pressure classification in pediatrics population.

The text was corrected:
“Boys had higher levels of height, weight, waist circumference, cardiorespiratory fitness, physical activity, SBP, and glucose than girls (p<0.005 for all), whereas girls had higher HDL-C values. No differences in age, DBP, and triglycerides levels were observed between the genders”.

Second paragraph: the authors say that “the prevalence of MetS was more common in males than females”. Was this a significant difference?
Yes, the difference was significant. So, the information was included.
- Second paragraph: it will be important to add more information about the individual risk factors. What was the most prevalent? I will suggest adding a table with this information.

The table 2 was added with the prevalences by gender.

- Third paragraph: after “...increased prevalence of MetS was observed in the sedentary adolescents and with low fitness levels” the numeric results and p value should be included.

- Fourth paragraph: the same comment for the sentence “The males showed higher prevalences of MetS than females in all levels of physical activity and fitness.”

The sentence was rewritten and more information was included.

“A higher prevalence of MetS was observed in the inactive adolescents and in the adolescents with low cardiorespiratory fitness (p<0.05); there was no difference with respect to genders.”

- Fifth paragraph: the authors should add numeric results in parenthesis (OR, CI) at the end of the sentence “significantly ....VO2max”. The authors divided the physical activity into tertiles, however, the logistic regression showed only 2 categories. Please, clarify.

The sentence was rewritten for easier understanding. The data for the three physical activity categories were added in the text (table 3).

“Significant associations were demonstrated between MetS and cardiorespiratory fitness (Table 3). The subjects with low cardiorespiratory fitness had an odds ratio for MetS of 3 (CI, 1.13-7.94) compared with subjects with high cardiorespiratory fitness. No significant relationships were observed between MetS and physical activity.”

4. Discussion

- The discussion must be reorganized in order to achieve a clear exposure of the main findings.

The discussion was reorganized for easier understanding.

- Third paragraph: the authors say “there are not others studies pertaining to the prevalence of the MetS in Brazilian children and adolescents with which to
compare”. I suggest the authors to search more carefully in PubMed, because there are some manuscripts regarding this issue.

Studies pertaining the prevalence of MetS in Brazilian children and adolescents were included.

“Rodrigues et al.\textsuperscript{29} evaluated 380 subjects (Vitoria, ES, Brazil) and reported a prevalence of MetS in 1.3% of adolescents. Cavali et al.\textsuperscript{30} evaluated 80 obese adolescents (São Paulo, SP, Brazil) and reported a prevalence of 13.7% using the International Diabetes Federation criteria and 15% by Jolliffe and Janssen criteria.”

- The authors may consider discussing the work of Jonathan Ruiz and Filipe Lobelo although it is not possible to make direct comparisons because they used accelerometers however, they published this research area.

The study was not included, but others studies were included in the discussion.

It is imperative to introduce one or more references in the end of the paragraph “Future intervention…an unhealthy condition”.

The references were added.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

The manuscript was reviewed by a professional English proof reader.

**Statistical review:** No, the manuscript does not need to be seen by a statistician.
Suggestion: Minor Essential Revisions.

1. Are the methods appropriate and well described?
The methods are appropriate but the description is not clear enough and needs to be modified in order to answer the following points:
- We don’t know the rationale for sample size calculation (e.g. why 456 adolescents in 7 schools were selected). The sampling procedures are not clear as well, this should be more described. I am not certain about the proportion of schools in urban, suburban and rural areas and if weighted methods are needed to address this issue. The authors should provide more details regarding this point.

This cross-sectional study was carried out in Curitiba, Paraná, Brazil. The city of Curitiba has a population of 1,678,965 inhabitants with a human development index by 0.763. The sample size consisted of school children registered in the education system (approximately 45,000 students). The following parameters were used to estimate the sample size: an error of 5%; an estimated Mets prevalence of 20%; a design effect of 1.5; a 95% confidence interval; and an additional 10% for losses and refusals. A conglomerate sample of 456 adolescents (223 girls [49%] and 233 boys [51%]) was evaluated. The schools were randomly selected, and the proportion of students was established according to the number of students in each of the nine administrative areas of the city (Santa Felicidade 6.6%; Matriz, 12.3%; Boa Vista, 14.7%; Cajuru, 12%; Portão, 10.6%; Boqueirão, 13.1%; Bairro Novo, 9.6%; Pinheirinho, 9.5%; and CIC, 11.6%). Data collection from schools took place between April and November 2009.

- Describe the process of administration of the questionnaires, e.g. self-completed in classroom setting, researcher led etc
The sentence was rewritten for easier understanding and more information about the administration of the questionnaires was included. “The Three-Day Physical Activity Record\textsuperscript{18} was used to self-record daily activities over 3 days (2 weekdays and 1 weekend day)….. The questionnaires were self-completed in the classroom with orientation by the researcher.”

- How was age recorded, e.g. self-reported? Or data collection included date of birth and date of measurement, and the calculation was decimal age, please clarify?

The date of birth was recorded by adolescents. So, using the date of measurement, we calculate the decimal age. When the adolescents don't remember the date of birth, the information was solicited to school administration.

- It is not clear determine which exercises had moderate to vigorous intensity (# 3 MET). Did the authors base on the Ann Worth’s Compendium? This should be clarified.

The sentence was rewritten for easier understanding. We added more information about the physical activity intensity:

“(1-2, sedentary activity [lying down and seated]; 3-5, light activity [taking a shower, cooking, taking a walk, and light manual work]; 6-8, moderate activity [sports or leisure activities and moderate manual work; 9, vigorous activity [intense manual work and intense sport or leisure activities]). The subject fills in the boxes corresponding to physical activities performed during the specific time periods.

The questionnaires were self-completed in the classroom with orientation by the researcher. The time spent doing exercises with moderate-to-vigorous intensity ($ \geq 6 $ in a physical activity scale) was added, then used to determine the total moderate-to-vigorous physical activity (MVPA) expressed in minutes per day. The mean value from the 3 days was considered for the analysis.”

- The authors need to describe more on statistical tests used to define the significance. The Statistical procedures were rewritten and more information to define the significances were included.

“To compare the continuous variables between the genders we used Student’s $ t $-test, and the chi-squared test was used for categorical variables.”…” The association between physical activity and cardiorespiratory fitness with the diagnosis of MetS was
calculated using binary logistic regression models, adjusting for age and gender. The outcome variable was the presence of MetS. The statistical analyses were performed using SPSS (version 15.0 for Windows; Chicago, IL, USA)\textsuperscript{21}. A $P$ value $< 0.05$ denoted statistical significance.

-I don’t feel comfortable with the word “parameters” here. Are they the values? The word “parameters” was removed.

In the method part, the authors pointed that “Since there are no prescribe thresholds for aerobic fitness, the lowest and highest tertiles of these two variables were used in the analyses” but in the results not much text was described about aerobic fitness, and until the end of the manuscript I am not quite sure which levels are the lowest, the middle and the highest tertiles of aerobic fitness.

The information was included in the text.

“…the subjects were separated in tertiles of cardiorespiratory fitness (boys: low $< 46$ ml.kg$^{-1}$ min$^{-1}$, moderate 46-51 ml.kg$^{-1}$min$^{-1}$, and high $> 51$ ml.kg$^{-1}$min$^{-1}$; girls: low $< 38$ ml.kg$^{-1}$min$^{-1}$, moderate 38-43 ml.kg$^{-1}$min$^{-1}$, and high $> 43$ ml.kg$^{-1}$min$^{-1}$”

- The description in result part is too short providing very little information.

Furthermore, one of the main outcomes of this study is the prevalence of metabolic syndrome among adolescents were not described in details, I even can not see the prevalence of metabolic syndrome in each gender and age group (if applicable).

The sentence was rewritten for easier understanding, and a new table was include with the prevalences of the individual risk factors by gender (table 2).

- All titles of the tables need to be improved.

All titles were replaced.

Table 1 needs footnotes to explain the statistical test used and also meaning of the abbreviation. The presentation of “,000” should be replaced by “$<0.0001$”

The same for Table 2, please indicate the test used to get the $p$-values.

The footnotes and the statistical test were included in both tables.
Are the discussion and conclusions well balanced and adequately supported by the data?
Yes, but the authors should recognize that this work is based on a cross-sectional study and cause-effect cannot be determined. In some instances, “risk” and “relationship” is used inappropriately. Because of the cross-sectional design of the study, the conclusions can only indicate possible associations and not explain entirely how the biologic processes are developing.

The sentence was rewritten and the information was added.
“...the cross-sectional study design does not guarantee the temporal precedence of variables and limit the extrapolation of observations.

In this study, sedentary lifestyle was not mentioned and also discussed. I just wonder if the screen time including computers, TV and videogames were considered to be collected in this study.
No, these information were not considered during the data collect.

The differences in the prevalence of metabolic syndrome should be discussed in light of different definitions applied making the comparison difficult.

The information was added in the text.
“...a problem inherent to any extrapolation of the adult definition to a pediatric population and the lack of consensus about the criteria for diagnosing MetS in a paediatric population, making it difficult to compare studies.”

6. Are limitations of the work clearly stated?
Not entirely.
Firstly, the limitation of a cross-sectional study was not mentioned. Reverse causality could be more explored (i.e. obesity causes physical inactivity – physical inactivity causes obesity).
Secondly, the limitation coming from the lack of a standard definition for the metabolic syndrome in adolescents should be discussed and compared. In fact, the authors realize the study limitation but it was explained by applying adult definition to a pediatric population. I am not quite sure why ATP III’s definition was selected to use while other definitions such as IDF’s which were modified to use among adolescents were not applied.
The limitation sentence was rewritten.
“The primary limitation of this study was that MetS outcomes were dependent on our
definition of MetS, a problem inherent to any extrapolation of the adult definition to a
pediatric population and the lack of consensus about the criteria for diagnosing MetS in a
paediatric population, making it difficult to compare studies. Another limitation of the study
was the use of self-reported instruments to measure physical activity, partly due to the
intermittent nature of youth physical activity. However, the 3-day physical activity record is
considered a valid instrument for physical activity evaluation in population-based studies.
Finally, the cross-sectional study design does not guarantee the temporal precedence of
variables and limit the extrapolation of observations.”

The ATP III’s definition was selected in agreement with other Brazilian researchers that
develop collaborative research with us.

- English editing is needed. The authors should check the spelling throughout the
manuscript, especially the word “Waist circumference”
I would recommend that the authors have their manuscript proof read by a
professional English proof reader.
The manuscript was reviewed by a professional English proof reader.

- The word “sedentary” used to define for the threshold <60 mins/day is
confusing. I would suggest to use “inactive” because sedentary lifestyle should
be related to screen time (computers, TV and videogames) rather than having
physical activity <60 mins/day
The word “sedentary” was replaced by “inactive”.
1) The introduction of the paper needs to be made more explicit. The author(s) mentions that physical inactivity or low CRF is mainly related to MetS in adulthood, but less in youth. In fact, there are several reviews have shown that metabolic risk factors are readily detectable in children and adolescents, but the results of some previous studies are controversial. Also, the definition of metabolic syndrome and its components have not yet been formally established for either children or adolescents. The author(s) should offer some comments on it when reading following references.


More information were included in the introduction. The suggested references were read and some comments added in the manuscript.

2) Methodological issues:
a) MetS definitions. The defined MetS in this study may have a great reduction of risk information, because all risk factors are dichotomized. I would suggest the authors add a single linear regression model, where they use risk as a continuous variable by summing z scores of the different risk factors.

The authors have knowledge about the application of single linear regression model, used to analyze the risk as a continuous variable by summing z scores. But, in this study, we prefer to maintain the dichotomized classification in ours analyses.

b) Definition term. In youth, a clustered metabolic risk score may be used to replace metabolic syndrome, because fasting insulin in this study is missing.
Many researchers used the term metabolic syndrome yet that the fasting insulin has been replaced by fasting glucose.

c) In statistical procedures, physical activity is not clear classified. What kinds of criteria are used to assess the three categories? If youth participated in physical activity during 30 to 60 min/day, do they belong to sedentary (I prefer to inactive)? In general, the participants in the study shall be grouped as inactive < 30min/day, moderate active ≥30 to 60min/day, and active >60min/day owing to a relatively small sample.
The Statistical procedures were rewritten and more information about the cut points was included.

3) Results
a) The text for Table 1 is not clarified. In Table 1, age, DBP and TG are not significant different between boys and girls. Importantly, the clustered MetS score is also missing in table 1.

The sentence was rewritten for easier understanding. But, the clustered MetS score was not applied.

“Boys had higher levels of height, weight, waist circumference, cardiorespiratory fitness, physical activity, SBP, and glucose than girls (p<0.005 for all), whereas girls had higher HDL-C values. No differences in age, DBP, and triglycerides levels were observed between the genders”.

b) Figure 1 not clarified. It should be analyzed using the new classification.

The clustered MetS score was not applied.

c) Table 2 is not clarified. It should be calculated using the new classification. In addition, living environment (urban/rural) and socioeconomic status (high/low) shall be considered as covariates in CRF and physical activity levels separately.

The clustered MetS score was not applied.

4) The discussion section tends to reflect the lack of a clear rationale for studying the relationship between physical activity/CRF and MetS among boys and girls. Consideration should be given to the issues relating to the methods and statistical analysis. Some clarifications are required in the results section and the author(s) needs to qualify some of their comments based on the weight of evidence provided by their statistical findings. The discussion was reorganized for easier understanding and more information was added.