

PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	WHO Child Growth Standards in context: The Baby-body Project– Observational study in Tasmania.
AUTHORS	Jayasinghe, Sisitha Herath, Manoja P. Beckett, Jeffrey M. Ahuja, Kiran D.K. Byrne, Nuala M. Hills, Andrew P.

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Dr. Peter Flom Institution and Country: Peter Flom Consulting, United States Competing interests: None
REVIEW RETURNED	15-Apr-2021

GENERAL COMMENTS	<p>I confine my remarks to statistical aspects of this paper. Unfortunately, I don't think the methods chosen were correct.</p> <p>The main point is that none of the continuous measures should be categorized. Categorizing continuous variables is almost always a bad idea. It increases type I and type II error, reduces the number of questions that can be asked of the data, and introduces a kind of "magical thinking" - that something amazing happens at the arbitrary cutoffs. See e.g. Harrell, F. *Regression Modeling Strategies* pub. by Wiley, or my blog post https://medium.com/@peterflom/what-happens-when-we-categorize-an-independent-variable-in-regression-77d4c5862b6c</p> <p>Instead, I would leave all the variables continuous, use splines to look for nonlinearity, and, possibly, use quantile regression to examine quantiles of the dependent variables, rather than examining means with OLS regression (or ANOVA). This is important as results at both extremes may indicate problems.</p> <p>More specific issues:</p> <p>Table 1: The p value column can be eliminated. The important thing here is not significance but effect size. Indeed, the small p values for tiny differences are like a case study in why p values are problematic.</p> <p>In several places both %FM and %FFM are given. These are redundant. Only one needs to be given.</p> <p>It would be nice to see density plots of the important variables.</p> <p>Peter Flom</p>
-------------------------	--

REVIEWER	Reviewer name: Mahenderan Appukutty Institution and Country: MARA Institute of Technology, United Kingdom of Great Britain and Northern Ireland Competing interests: None
-----------------	---

REVIEW RETURNED	24-Apr-2021
------------------------	-------------

GENERAL COMMENTS	<p>The authors work on this research particularly looking at body composition in infants as a preventive measure of malnutrition either overweight or underweight is a highly commendable effort. The manuscript well explained the growth and development of infants that were monitored periodically (at birth, 3 and 6 months) for their weight and length along with body composition (FFM, FM). It would be good if mentioned on the mother's dietary patterns (any plant-based diet). The somatic development at birth as influenced by maternal characteristics can be discussed too with some data of the mothers in the study.</p> <p>These findings certainly will lead to more studies focusing on body composition and obesity matters from birth and serve as a pediatric guidelines for infants on growth and body composition.</p> <p>Good research findings and would be great if the authors can continue the cohort from infants to adolescent age and compare the data.</p>
-------------------------	--

REVIEWER	<p>Reviewer name: Dr. Jon Dorling Institution and Country: Dalhousie University, Canada Competing interests: None</p>
REVIEW RETURNED	27-Apr-2021

GENERAL COMMENTS	<p>Thanks for this interesting paper.</p> <p>The paper gives some interesting data comparing Australian infants with the WHO growth charts in a very specific location in a moderately sized group of babies.</p> <p>The study is well designed and used appropriate methods for the analyses that were undertaken. Growth results given in the table 3 might be easier to visualise if given in a graphical format. Having said that the figures are not easy to read and I suspect they do not meet the DPI requirements for the journal. Figure 2 is very difficult to interpret because of this.</p> <p>I have some very minor suggestions for edits to the text.</p> <p>On page 8, line 46 "The minor variations in averages" should indicate which averages are being compared to what as this is not clear.</p> <p>There is a statement given on page 9 line 38 that needs to be supported by data on feeding; "The fact that a significant proportion (data not shown) of infants in our cohort were breast fed up to 6 months of age may have contributed to the patterns of FM accretion observed". In my view this statement needs support as the reader cannot confirm this interpretation of the data without being given detail on feeding.</p> <p>Page 9 line 45 "is crucial in providing infants" should be "are crucial in providing infants" as it refers to the 1000 days which are plural.</p> <p>Page 10 line 17 states "The modest sample size and the lack of racial and ethnic diversity in our cohort limits the potential to extrapolate findings to the wider Tasmanian population." I think this should be followed by a comment on the very small sample sizes of SGA and LGA infants that make the finding from these groups uncertain.</p> <p>Page 10 line 55 "with a broader study population representative of the wider Tasmanian infant" should be amended to "with a broader, larger study population representative of the wider Tasmanian infant"</p>
-------------------------	--

	<p>Page 12</p> <p>under What is already know on this topic? line 5 appears to be missing a word before minimise;</p> <ul style="list-style-type: none"> • Optimal growth assessment in early life is critical as it minimise the potential for erroneous diagnosis of undernutrition/ overnutrition. <p>Perhaps it should be "Optimal growth assessment in early life is critical as it can minimise the potential for erroneous diagnosis of undernutrition/ overnutrition"?</p>
--	--

VERSION 1 – AUTHOR RESPONSE

Dear Professor Choonara,

RE revised submission of article: WHO Child Growth Standards in context: The Baby-body Project– Observational study.

Thank you for the opportunity to submit a revised version of our manuscript. Detailed responses to Reviewers' comments are included in the Table below and all amendments to the manuscript text are highlighted in yellow.

Please note that we have only made limited improvements to the quality of the illustrations. We would be very happy to explore other ways to further improve these figures if/when the manuscript moves to the next stage of acceptance.

We look forward to your feedback regarding our submission.

Yours Sincerely,

Professor Andrew P. Hills

Professor of Exercise and Sports Science
College of Health and Medicine
University of Tasmania

<p>Reviewer: 1</p> <p>Dr. Peter Flom, Peter Flom Consulting</p>	<p>We thank Dr. Flom for his insightful comments.</p>
<p>The main point is that none of the continuous measures should be categorized. Categorizing continuous variables is almost always a bad idea. It increases type I and type II error, reduces the number of questions that can be asked of the data, and</p>	<p>The World Health Organization recommends cut-off values of ± 2 standard deviations (which correspond to $\sim 3^{\text{rd}}$ and 97^{th} percentiles, to define abnormal growth (https://www.who.int/publications/i/item/924154693 X). There may be merit in leaving all variables continuous, using splines to look for nonlinearity, and, possibly, using quantile regression to examine quantiles of the</p>

<p>introduces a kind of "magical thinking" - that something amazing happens at the arbitrary cutoffs. See e.g. Harrell, F.</p> <p>*Regression Modeling Strategies* pub. by Wiley, or my blog post https://medium.com/@peterflom/what-happens-when-we-categorize-an-independent-variable-in-regression-77d4c5862b6c</p> <p>Instead, I would leave all the variables continuous, use splines to look for nonlinearity, and, possibly, use quantile regression to examine quantiles of the dependent variables, rather than examining means with OLS regression (or ANOVA). This is important as results at both extremes may indicate problems.</p>	<p>dependent variables. However, under routine circumstances, this is uncommon. As such, we respectfully decline Dr Flom's suggestion in this instance. Further, we have included the following sentence in the discussion in acknowledgement of the potential limitations of size-based categorization.</p> <p>"In addition, categorization of infants according to size (i.e., a continuous variable), although widely utilized, may have unintended statistical consequences."</p>
<p>Table 1: The p value column can be eliminated. The important thing here is not significance but effect size. Indeed, the small p values for tiny differences are like a case study in why p values are problematic.</p>	<p>We have now included effect sizes as suggested. However, due to customary practices and for familiarity amongst the BMJ Paediatrics Open readership (e.g., https://bmjpaedsopen.bmj.com/content/5/1/e000881), we did not remove the p values column from Table 1 as suggested.</p>
<p>In several places both %FM and %FFM are given. These are redundant. Only one needs to be given.</p>	<p>We believe there is merit in presenting both parameters in infant body composition reports. FM and FFM accretion can have a differential influence on infant growth (e.g., https://academic.oup.com/jn/article/148/4/607/4965918).</p>
<p>It would be nice to see density plots of the important variables.</p>	<p>Figure 2 contains density plots for length-for-age, WFL, weight-for-age and BMI-for-age for all 3 time points of interest. We have now attempted to improve the visual quality of the Figure.</p>
<p>Professor Mahenderan Appukutty, MARA Institute of Technology</p>	<p>We thank Professor Appukutty for his approval of our work.</p>
<p>The authors work on this research particularly looking at body composition in infants as a preventive measure of malnutrition either overweight or underweight is a highly commendable effort.</p>	
<p>The manuscript well explained the growth and development of infants that were monitored periodically (at birth, 3 and 6 months) for their weight and length along with body</p>	

composition (FFM, FM).	
It would be good if mentioned on the mother's dietary patterns (any plant-based diet). The somatic development at birth as influenced by maternal characteristics can be discussed too with some data of the mothers in the study.	We acknowledge the potential richness that measures of maternal dietary patterns would have added. However, the study design was aligned with many of the elements of the earlier WHO Multi-Centre Growth Reference Study (1) and did not incorporate these measures. However, we have previously shown how maternal characteristics can influence infant body composition (2), and this work has now been cited in the discussion.
These findings certainly will lead to more studies focusing on body composition and obesity matters from birth and serve as a pediatric guidelines for infants on growth and body composition.	
Good research findings and would be great if the authors can continue the cohort from infants to adolescent age and compare the data.	We agree regarding the importance of continuous follow-up of infants into adolescence, and ideally early adulthood. We have now included this as a suggestion for 'future directions' in the discussion.
Dr. Jon Dorling, Dalhousie University	We Thank Dr. Dorling for his approval of our work.
The study is well designed and used appropriate methods for the analyses that were undertaken. Growth results given in the table 3 might be easier to visualise if given in a graphical format. Having said that the figures are not easy to read and I suspect they do not meet the DPI requirements for the journal. Figure 2 is very difficult to interpret because of this.	We have now improved the clarity of all visual representations in the manuscript. However, we prefer the tabular format for skewness/ kurtosis data and have not included a graphical format as suggested.
On page 8, line 46 "The minor variations in averages" should indicate which averages are being compared to what as this is not clear.	We have now referred to the pertinent data as suggested.
There is a statement given on page 9 line 38 that needs to be supported by data on feeding; "The fact that a significant proportion (data not shown) of infants in our cohort were breast fed up to 6 months of age may have contributed to the patterns of FM accretion observed". In my view this statement needs support as the reader cannot confirm this interpretation of the data without being given detail on feeding.	We have now indicated the proportion of breast-fed infants for clarification.
Page 9 line 45 "is crucial in providing infants" should be "are crucial in	We have amended the wording as suggested.

providing infants" as it refers to the 1000 days which are plural.	
Page 10 line 17 states "The modest sample size and the lack of racial and ethnic diversity in our cohort limits the potential to extrapolate findings to the wider Tasmanian population." I think this should be followed by a comment on the very small sample sizes of SGA and LGA infants that make the finding from these groups uncertain.	We have amended the wording as suggested.
<p>Page 12</p> <p>under What is already know on this topic? line 5 appears to be missing a word before minimise;</p> <ul style="list-style-type: none"> • Optimal growth assessment in early life is critical as it minimise the potential for erroneous diagnosis of undernutrition/ overnutrition. <p>Perhaps it should be "Optimal growth assessment in early life is critical as it can minimise the potential for erroneous diagnosis of undernutrition/ overnutrition"?</p>	We have amended the wording as suggested.

1. De Onis M, Garza C, Victora CG, Onyango AW, Frongillo EA, Martines J. The WHO Multicentre Growth Reference Study: planning, study design, and methodology. *Food and nutrition bulletin*. 2004;**25**:S15-S26 Online.
2. Herath MP, Ahuja KD, Beckett JM, Jayasinghe S, Byrne NM, Hills AP. Determinants of Infant Adiposity across the First 6 Months of Life: Evidence from the Baby-bod study. *Journal of clinical medicine*. 2021;**10**:1770 Online.

VERSION 2 – REVIEW

REVIEWER	Reviewer name: Dr. Peter Flom Institution and Country: Peter Flom Consulting, United States Competing interests: None
REVIEW RETURNED	12-May-2021
GENERAL COMMENTS	<p>The authors have responded to my review, but their response is not adequate. I have also checked with editorial staff at the journal.</p> <p>For my remarks about categorizing continuous variables, please leave them continuous. Rather than adding a note that your analysis, "though common, may have unintended statistical consequences" you can then write "our analysis, though uncommon, is superior to the more usual one".</p> <p>For my comment about p value in table 1, please delete them as I requested. It is true that they are common, but they are easy to misinterpret and add nothing to the utility of the table. You can cite https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4245357/</p>

	Peter Flom
REVIEWER	Reviewer name: Mahenderan Appukutty Institution and Country: MARA Institute of Technology, United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	16-May-2021
GENERAL COMMENTS	No further comments.

VERSION 2 – AUTHOR RESPONSE

Dear Professor Choonara,

RE submission of revised article: WHO Child Growth Standards in context: The Baby-body Project– Observational study in Tasmania.

Thank you for the opportunity to submit a revised version of our manuscript. Detailed responses to Dr Flom’s comments are included in the Table below and all amendments to the manuscript text are highlighted in yellow.

We look forward to your feedback regarding our submission.

Yours Sincerely,

Professor Andrew P. Hills

Professor of Exercise and Sports Science
College of Health and Medicine
University of Tasmania

Reviewer: 1 Dr. Peter Flom, Peter Flom Consulting	We thank Dr. Flom for his insightful comments.
For my remarks about categorizing continuous variables, please leave them continuous. Rather than adding a not that your analysis, "though common, may have unintended statistical consequences" you can then write "our analysis, though uncommon, is superior to the more usual one".	We have now included results from a quintile regression analysis (Figure 1) in the main body of the manuscript alongside the suggested wording by Dr. Flom. The clinically relevant categorization-based graph has now been moved to supplementary material to provide context for interested parties.

For my comment about p value in table 1, please delete them as I requested. It is true that they are common, but they are easy to misinterpret and add nothing to the utility of the table. You can cite https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4245357/	We have now removed the p values as suggested.

VERSION 3 – REVIEW

REVIEWER	Reviewer name: Dr. Peter Flom Institution and Country: Peter Flom Consulting, United States Competing interests: None
REVIEW RETURNED	26-May-2021

GENERAL COMMENTS	The authors have addressed my concerns and I now recommend publication.
-------------------------	---

REVIEWER	Reviewer name: Mahenderan Appukutty Institution and Country: MARA Institute of Technology, United Kingdom of Great Britain and Northern Ireland Competing interests: None
REVIEW RETURNED	25-May-2021

GENERAL COMMENTS	No further comments.
-------------------------	----------------------

VERSION 3 – AUTHOR RESPONSE