Author's response to reviews

Title: Quantification of the energy gap in young overweight children. The PIAMA birth cohort study

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Author's response to reviews: see over
1. Modeling of energy gap differs between the different studies cited. This may add to between-studies-differences in results. The authors should use their own data to calculate energy gap using the different strategies. Specifically the percentile-based approach used in ref.8 (Plachta-Danielzik et al.) should be compared with their own strategy.

Re: The reviewer correctly states that the calculation of the energy gap differs between studies and suggests that we should use our data and calculate the energy gap by using different models. We think this would be a nice approach. However, in some cases it is not possible to calculate the energy gap similarly.

Butte & Ellis (Science 2003) used actual changes in body composition in children aged 5-19 and used more specific energy efficiencies of 85% for fat and 42% for protein storage. As in our study population measured data on body composition was not available it is not possible to apply their strategy to our data. Additionally, they did not take into account the energy required for healthy growth. Therefore, applying there approach to our data is in our opinion not so relevant.

Wang et al (Pediatrics 2006) and Plachta-Danielzik et al. (Obesity 2008) applied a more or less similar approach based on changes in percentiles of body weight or fat mass and fat-free mass. Wang et al. used cross sectional data of two different groups of children (2-11 of age and 12-17 years of age) obtained from two NHANES surveys (1988-1994 and 1999-2002). For all the children aged 2-7, they calculated the expected body weight 10 years later at the same weight-for-age percentile, assuming stability in height and weight distribution. This body weight distribution was compared with the actual weight distribution obtained with the data from 1999-2002 and differences were calculated. Plachta-Danielzik et al. applied a quite similar approach using longitudinal data. For normal weight children at baseline they calculated sex-specific differences in z-scores between baseline and after 4-years for measured fat mass and fat free mass. Because of the similarity between the methods of Wang et al. and Plachta-Danielzik et al. we applied the latter approach to our data. Since we have no measured data on body composition we used changes in z-scores for body weight. Applying this approach resulted in an only slightly lower median excess body weight gain among NO children compared to the estimate reported in the manuscript (1 kg/year vs 1.2 kg per year; see table 1 rebuttal) and subsequently a slightly lower energy gap. The similarity between these findings shows that our estimate of the energy gap is rather robust. We have added a paragraph on the comparison of the results obtained by the percentile approach with our own strategy in the discussion section of our manuscript at page 15, lines 10-19. In addition, as z-scores give more insight in growth compared to mean BMI we replaced BMI by BMI z-scores in table 2.
Table 1. Yearly weight change and z-score for weight at baseline (age 2) and follow (age of 5-7) of 2190 children divided in four groups based on BMI status.

<table>
<thead>
<tr>
<th>Method manuscript²</th>
<th>Additional method³</th>
<th>z-score body weight Baseline</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>NN</td>
<td>2.2 (1.9-2.6)</td>
<td>-0.27 (-0.84-0.36)</td>
<td>-0.2 (-0.8-0.4)</td>
</tr>
<tr>
<td>NO</td>
<td>3.4 (3.0-3.9)</td>
<td>0.95 (0.44-1.63)</td>
<td>0.6 (0.2-0.9)</td>
</tr>
<tr>
<td>OO</td>
<td>3.3 (2.8-4.0)</td>
<td>-1.04 (-0.62-0.35)</td>
<td>1.8 (1.5-2.1)</td>
</tr>
<tr>
<td>ON</td>
<td>2.2 (2.0-2.5)</td>
<td>-1.30 (-1.74-0.78)</td>
<td>1.6 (1.5-1.9)</td>
</tr>
</tbody>
</table>

²NN= normal weight/normal weight; NO= normal weight/overweight; OO=overweight/overweight; ON=overweight/normal weight.
³Yearly weight change ((weight follow-up-weight baseline)/follow up time)

2. Regarding their own approach a number of questions remained to be answered. Since weight and height were based on self reports from the parents and a number of BMI data were missing these methodological drawbacks should be addressed more systematically. I assume that these problems may add a considerable error which should be at least quantified.

Re: We agree with the reviewer on this point. The issue self-report of weight and height, has already extensively been described and quantified in the discussion at page 13. In addition, we have now more extensively discussed the issue of missing BMI data in our revised manuscript (page 13, lines 20 – page 14, 5). We have added the following text “Children with missing BMI data at age 2 more often had a lower educated mother than children with BMI data at age 2 (data not shown). As obesity is more common among people with lower SES, we may have underestimated the percentages of overweight and obesity at age 2 However, there were no differences in BMI z-scores at age 1 between these groups. Furthermore, mothers of children with known BMI at age 2 and missing BMI data at age 6 also were also more often lower educated than mothers of children with known BMI data at age 2 and age 6. However, there were no differences in BMI at age 2 between those groups. In addition, we observed no difference in weight gain during the study between children grouped by educational level of their mother. Therefore, we think that missing values in BMI has not materially influenced our energy gap estimates.”

3. A further question is that for my feeling energy gap was calculated by two different strategies (i.e. from NN to NO and from OO to ON). These data should compared with each other.

Re: We thank the reviewer for this useful comment. The difference in positive energy balance between NN and NO indeed reflects the daily energy gap responsible for the excess body weight gain among children who develop overweight when being normal weight at the beginning. The difference in positive energy balance between OO and ON more or less reflects the daily energy gap among OO children responsible for maintaining their excess body weight. The estimated median energy gap in NO children was slightly higher compared to OO children, which is logical, due to their slightly higher median excess weight gain (Table 3 manuscript). We have clarified this in the revised version of the manuscript and stated the differences between the two types of energy gaps in the methods part (page 8, lines 7-8).
4. The authors assumed a linear model. Faced with the normal percentiles of weight and height this cannot be really true. Thus I recommend to use a more sophisticated model taking into account changes in P50 (for NN) and P90 (for OO). This will give a more detailed view on age-dependent changes in energy gain.

Re: the reviewer suggests a more sophisticated model to calculate differences in weight. We agree with the reviewer that the percentiles for weight and height between birth to adulthood do not follow a linear distribution. Therefore, studying long term changes in body weight requires a more sophisticated model. However, in this study we used relatively short term changes in body weight between age 2 and age 6. Therefore, we think that assuming a linear model has not largely influenced our results. Furthermore we respectfully disagree with the reviewer that the use of a more sophisticated model will give more insight in age-dependent changes in energy gain in our case. We have studied only one time period (age 2 to age 6). In our opinion changes in different time periods (e.g. differences between age 2 and 6, differences between age 6 and 10 etc.) should be compared to get a more detailed view on age-dependent changes in energy gain.

5. My major concern is on author's calculation of body composition from the weight data. First, the reference data base of FM used is outdated and is not population-specific (i.e. it cannot be used for Dutch children). There are more recent data bases for FM in European populations of children.

Second, using the mean data of percentage FM per weight (or BMI) does not take into account the considerable inter-individual variance in the weight-FM relationship.

Third, percentiles of weight and FM should be compared with each other and the dynamics of changes in either FM or weight should be taken into account in the model used to calculate energy gap. Following Hill's approach (i.e. using BMI plus a mean energy equivalent of weight changes) may provide an alternative approach. A more systematic analysis of body composition at least in a subgroup of children is recommended.

Re: We agree with reviewer that a more systematic analysis of body composition at least in a subgroup of children would be valuable. Unfortunately we do not have information on body composition. Therefore, we had to make assumption regarding the composition of the weight gain. We are aware of the limitations of using the body composition of reference children published by Fomon et al in 1982. Wells et al. reported, a higher absolute fat mass for a given BMI as compared with those reference children for children 1-11 years of age living in the UK (Int J Obesity 2002;26:1323-1328). Unfortunately, this paper does not report exact fat mass percentages by age and sex. As far as we know, more recent information on fat mass percentages for Dutch or European boys and girls at age 2 and age 6, specified for those with a normal weight as well as those with overweight has not been reported in literature. Most studies did not report at both ages or reported fat mass percentages combined for sex or age groups or report data in figures which makes it difficult to extract the correct values. Although the absolute fat mass has increased in children over the last decade, the difference in fat mass percentages are relatively small. Therefore, we think that this has not materially influenced our results.
6. In children at age 2 to 5 years there is high remission rate in overweight compared to children at age 6-10 years. This should be taken into account in any future recommendations on prevention of childhood overweight.

*Re: We fully agree with the reviewer that the high remission rate in overweight in children between age 2 and age 6 is an important issue, which should be taken into account in any future recommendations on prevention of childhood overweight. We have added this remark to the discussion part of the revised manuscript (page 16, lines 22-24).*

7. The authors refer to considerable differences in energy gaps published so far. Taking a lifelong view on the overweight issue the different numbers should be compared with each other and specific recommendations for specific life periods should be considered. My question is whether these differences reflect real life course specific problems in energy balance. Alternatively they may be more likely due to the differences in the methodological approaches used to calculate the energy gap in the different studies.

*Re: We agree with the reviewer that this is an interesting issue which needs further study. Besides the different methodological approaches used in literature so far to calculate the energy gap, the observed differences could also reflect real life-course specific differences in energy balance. This could imply specific recommendations for specific life periods and it’s worthwhile to study this issue further. We have added this recommendation for further study to the discussion part of our manuscript (page 16, lines 16-21).*