Author's response to reviews


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Author's response to reviews: see over
August 14th, 2014

RE: Submission of revised manuscript (#9498040941323195, “Health Initiative Program for Kids: Effects of a 1-year, multidisciplinary, lifestyle intervention on adiposity and quality of life in obese children and adolescents - a longitudinal pilot intervention study”)

Dear Mrs. Parkinson, dear reviewers:

Thank You very much for taking the time to review our manuscript and for the opportunity to submit a revised version to BMC Pediatrics for further consideration. We would like to thank the reviewers for their valuable comments, and have made revisions to the manuscript based on the reviewers' reports. In the following, we would like to address the reviewers’ comments and concerns in a point-to-point fashion:

Response to Reviewer 1

Major Compulsory Revisions

One major comment is related to the analysis of dietary data. Since 3-day dietary records were collected, it would have been useful to present results on energy and macronutrient intake pre and post intervention. Data on other food group that form part of the Canadian Food Pyramid would have been also useful, as it will be useful to observe if participants switched from having white bread to wholegrain bread, full-fat milk to semi-skimmed milk…etc

➔ We would like to thank the reviewer for this excellent comment, and we wholeheartedly agree that it would have been useful and interesting to have collected and analyzed more nutritional data, such as energy- and macronutrient intake. Since funding of the project was limited, and the main purpose of the current study was to assess the feasibility of this novel intervention based on the 2008 Provincial Council for Maternal and Child Health recommendations, and to obtain initial data on our primary research question, whether HIP Kids is effective in preventing further increase in BMI and BMI z-score, and in improving QoL, we unfortunately haven’t been able to perform detailed analyses on energy- and macronutrient intake.
With regards to other food groups, "Canada's Food Guide", released in its current form in 2007, only contains, and is based on, 4 food groups, "Vegetables and Fruits", "Grain Products", "Milk and Alternatives", and "Meat in Alternatives" (http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/food-guide-aliment/print_eatwell_bienmanger-eng.pdf). Based on the relevance for childhood obesity, we have also collected and are presenting data on sugar-sweetened beverage consumption. In addition to that, however, we also have collected data on juice consumption and snack frequency that we originally hadn't included. We further realized we hadn't included data for the "Meat & Alternatives" food group. We now have added this information to the manuscript.

We have revised Table 4 accordingly and have entered these data as follows:

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>Median (RANGE)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meat &amp; Alternatives (servings/day)</td>
<td>1.86 (0.86)</td>
<td>1.74 (1.01)</td>
<td>-0.27 to 0.50</td>
</tr>
<tr>
<td>Snack consumption (servings/day)</td>
<td>1.82 (0.77)</td>
<td>1.59 (0.95)</td>
<td>-0.14 to 0.60</td>
</tr>
<tr>
<td>Juice consumption (servings/day)$^1$</td>
<td>0.33 (0.00 – 5.33)</td>
<td>0.33 (0.00 – 3.00)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

We also have revised the results section (line 239) by adding "other nutrition or" into the following sentence: "None of the other nutrition or laboratory parameters assessed during the study showed any statistically significant improvements (Table 4)."

**Minor Essential Revisions**

**Eating patterns were not assessed as no mention of meal skipping, meal frequency or regularity** (Line 166).

Thank you very much as well for mentioning this important aspect. Indeed, we haven't reported on, but did assess meal frequency / frequency of meal skipping. The reason we didn't report these data is that the number of events as per our statistician was too low to perform a meaningful statistical analysis.

However, we are more than happy to share these results with you for your information and review:

On study entry, 12 of 38 children with available data (4 missing values) had skipped any number of meals during the 3-day food record assessment period: breakfast was skipped once by 7 children, twice by 2 children, three times by 1 child; lunch was skipped once by 3 children; dinner was skipped once by 3 children. Overall, 20 meals were skipped.

On final (12-month) assessment, 8 of 31 children (11 missing values) had skipped meals: breakfast was skipped once by 3 children, and twice by 2 children; lunch was skipped once by 4 children; dinner was skipped once by 1 child. Overall, 12 meals were skipped.

In total, 8 (40%) less meals were skipped at study end compared to study entry.
Response to Reviewer 2

Major Revisions

1) Title: What does “HIP” stand for?
   ➔ Thank you for pointing out this oversight! We have replaced the abbreviation in the title with the full name of the intervention ("Health Initiative Program for Kids").

2) Authors: Role of Ralf Rauch? ➔ Dr. Rauch participated in data collection prior to relocating to Germany; i.a., he conducted entry and exit exams of study participants at our centre. He also participated in data entry and critically reviewed the manuscript drafts.

3) Introduction: Line 99-107: A clear formulation of a hypothesis is missing
   ➔ We clarified this by adding (line 107-109): "We hypothesized that the HIP Kids program will prevent further BMI and BMI z-score increase, and will increase standardized QoL scores in intervention subjects over the 1-year study period."

4/5) Methods: Line 124, Line 120-141:
   a) Counseling by whom? Who participated in these sessions? How did the authors involve parents/other family members? How was attendance monitored?
   b) How was compliance of parents/caregivers monitored?
   ➔ We thank the reviewer for raising these excellent questions and agree that including the requested clarifications may be of benefit to the readership. We have revised the paper as follows:
   • a) we have added (lines 130-137): "These educational blocks were led by a dietitian, exercise specialist, and social worker, respectively. A pediatrician provided medical counseling including discussion of laboratory results during the initial and exit visits, and on an as needed basis. Sessions were attended by the participant and at least one parent, but participation of both parents, as well as of siblings and other caregivers was continuously encouraged. Attendance was recorded at each session. Family involvement was central to the program design, and included jointly developing short and longer term goals, and strategies to accomplish these."
   • b) Previously set goals and adherence to mutually agreed on approaches to achieve those goals were reassessed at every visit, and counseling was tailored to the identified needs.
   We further clarified this by adding the following to the respective statement contained in the paper (lines 146-148): "Struggling families were continuously encouraged and received focused support directed at guiding them to overcome the challenges that had impacted on achieving their goals."

6) Line 120-141: How were subjects/families recruited? Please comment on whether the actual recruitment model could have introduced a bias how representative the population studied is?
   ➔ Family physicians and pediatricians were informed about the program and were invited to refer potentially eligible obese patients (page 5, lines 113-115). Since we did not recruit out of a
specialized obesity clinic, but enrolled eligible participants prospectively in the order they were referred by community physicians, we believe that our sample should be largely reflective of the targeted population of obese Canadian children and adolescents who have not been successful with initial office-based counselling.

7) Line 155: was there a variation in ethnicity? If yes, how was this reflected in the growth charts used?
   ➔ The vast majority of our study population was of Caucasian ethnicity. 2 participants were of African American, 2 of Hispanic, 1 of Aboriginal, and 3 of Arabic decent. In order to maintain comparability and due to the fact that BMI z-score calculations were based on U.S. Centers for Disease Control and Prevention reference data, only one set of growth charts was used. However, the reference population these charts are based on does also include children of non-Caucasian ethnicity.

8) Line 156-158: a reference describing the validation of the BIA analyser in this age population should be quoted.
   ➔ Reference to the Pediatric validation study done on the model directly preceding ours was added (Nuñez C, Ref. 17). As per manufacturer, the body fat analyzer of our model (TBF-300) is based on the one used in the cited validation study.

In addition, while conducting the study we as well were curious about the correlation between BIA and DXA, and have assessed this in a subsample of our study population. 17 out of the 42 patients who completed the study also have complete DXA data available (unpublished): correlation analysis showed a very high correlation between change in body fat (baseline to exit at 12 months) measured by BIA and DXA (r=0.96, p=0.013).

9) Line 166-174: How was time point/date for assessment of dietary intake and Physical Activity Questionnaire standardized/defined?
   ➔ All assessments were performed at baseline and 12 months (end of program). Anthropometric and body composition measures were also obtained at 3 months.

10) Line 184: Sample size calculation is missing
   ➔ Thank you for pointing this out. Indeed, due to the pilot nature of our study a formal sample size calculation was not performed. The purpose of this pilot study was to 1) assess the feasibility of this novel intervention based on the 2008 Provincial Council for Maternal and Child Health recommendations, and to 2) obtain initial data on our primary research question, whether HIP Kids is effective in preventing further increase in BMI and BMI z-score, and in improving QoL. The data of
this study will inform the development of a larger study, which will include a formal sample size calculation.

Results

11) Line 191 – 193: How does the interaction with staff changes impact the validity of the data?

→ Thank you for this comment, as it shows that we formulated this sentence too vaguely. We have revised it as follows (line 205-207): "Of those who withdrew, multiple participants verbally indicated to have found it challenging to build a trustful relationship with new members of the research team following staff changes."

→ We do not believe the validity of our data was compromised by staff changes, since concerns with staff changes were mainly raised by those participants who prematurely withdrew from the study. Also, all new staff members underwent a thorough pre-hiring interview process to ensure the individual meets the professional standards and requirements of the respective positions they applied for, and, once hired, received standardized training preparing them for their respective roles.

12) Line 206 -214: the study subjects are growing during the study period. This might change their body composition/BMI z-score. How do the authors account for the changes in BMI z-scores due to natural growth?

→ We completely agree with the reviewer, that natural growth has an impact on body composition, especially in pubertal children. Given our population consisted of still growing children (mean [SD] growth of our sample population from study entry to exit 4.25 cm [3.07]), it is for that reason that we chose to include not just BMI, but rather BMI z-score as main outcome parameter, since it accounts for growth- and gender-related changes in body composition.

Tables

13) Too many significant digits. Rounding to three digits would be fully sufficient

→ Based on the reviewer’s request we have revised our tables to display p-values with only three digits.

14) Also give fat mass in absolute values, not only in percent

→ We appreciate the reviewer’s suggestion, and would like to address it as follows: since body fat percentage has been the most commonly used variable to report body fat and its change over time in the Pediatric literature, we only have included this variable in our database. Also, reference curves for children are available for that measure. Compared to absolute body fat, body fat percentage has been much more frequently reported as the only body fat variable in research studies, systematic reviews and meta-analyses on childhood obesity, and has been used as one factor to determine the
effectiveness of Pediatric weight loss interventions (i.a. in systematic reviews with meta-analyses (e.g. Mandy Ho and colleagues, published in Pediatrics 2012, and JAMA Pediatrics in 2013); in various RCTs (e.g. Baan-Slootweg et al., JAMA Pediatrics 2014), and even in the study cited below by Fush G, et al. on nutritional status in sick children and adolescents).

We therefore hope it will be acceptable to our reviewer to proceed with body fat percentage, the body fat variable included in our dataset.

Discussion
15) Lines 231 – 240: the paragraph should be omitted. No new aspects, all information has been given in introduction. The discussion may start with a modified line 241.

→ Thank you for this suggestion. We acknowledge that this first paragraph reflected a summary of previously stated content, which increased the length of the discussion. We therefore have removed this paragraph and have modified the first three sentences of the discussion as follows (line 245-250): “The present study assessed whether the HIP Kids program prevented further increase in participants’ BMI and BMI z-score, and improved QoL. We demonstrated that during the initial phase of the program BMI increase was prevented and BMI z-scores decreased in our study population. During the subsequent, less intensive 9-month maintenance phase BMI z-scores continued to decrease, but further increase in BMI was not prevented.”

We also have deleted the last sentence of the discussion (lines 326-327 of original manuscript) since it merely repeated what was already mentioned in the results.


→ We would like to thank the reviewer for sharing the citation to the above article, which we read with great interest. We agree with the reviewer, that neither BMI nor BMI z-score are ideal measures of body composition, and that it would be preferable to obtain DXA data on everyone who requires an assessment of nutritional status, and pre- / post every intervention aiming to influence nutrition and body composition. While radiation associated with modern DXA scanners is very low but may still be a concern to some, unfortunately, the cost and limited availability of DXA scanners, and even of alternative devices such as bioelectrical impedance analysis as used in our study, poses a significant limitation to their utility. It is based on these limitations of the "gold standard", that research done in the field, including the study of Barnow et al. cited by the reviewer below, has
commonly been using more readily available proxies of body composition as outcome measures, such as BMI and BMI z-score. While both measures have been found to correlate with adiposity, we clearly agree that their biggest limitation is their inability to differentiate between lean body mass and body fat. This is even more important in children, were growth naturally goes along with increasing BMI trajectories from the age of BMI rebound on. BMI z-score, however, accounts for growth- and gender-related changes in body composition in children, and therefore is the more preferable outcome measure for Pediatric weight management interventions compared to BMI. This is in keeping with current recommendations, and, for example, is reflected by the UK's National Obesity Observatory's 2009 "Standard Evaluation Framework for weight management interventions" (http://www.noo.org.uk/uploads/doc/vid_3534_NOOSEFreportJuly09.pdf).

The interesting study by G. Fusch et al. cited by the reviewer demonstrated in a cross-sectional sample of sick children, classified as under- normal, and overweight/obese by their BMI and by %BF assessed by DXA, that BMI-SDS significantly correlated with %BF, but that especially underweight subjects in their population (defined in the study as %BF under the 10\textsuperscript{th} percentile) had a high misclassification rate using BMI-SDS when compared to %BF. This finding is most relevant when developing or interpreting data on children with poor (underweight) nutritional status. Interestingly, BMI-SDS misclassification was lowest in overweight/obese subjects, and the authors state that BMI-SDS may be a useful tool for identifying overweight and obese children and adolescents. Since the study was cross-sectional, no data on the performance of BMI-SDS to accurately reflect change in %BF over time was generated.

In summary, we feel that using BMI z-score as an outcome for Pediatric weight management interventions, in spite of its limitations, is in line with current recommendations and research practice, and allows for better comparison of results with other studies in the field.

Of note, in our study we have not solely relied on BMI or BMI z-score, but also measured body composition (and waist circumference, even though less reliable), to overcome the discussed limitations.

17) A decrease in fat mass paralleled by an increase in muscle mass (a typical effect of such intervention programs) would not necessarily result in a change of BMI or its z-scores – despite the fact that it leads to a more appropriate body composition.

→ We completely agree with the reviewer that if the decrease in fat mass during a weight management intervention is paralleled by an equivalent increase in muscle mass no change in BMI would be expected. However, such balanced change with muscle mass increasing during the intervention to the same extent as fat mass is decreasing, is not always happening in practice.
18) Lines 257-269: Similar findings also in:

Line 301: the two papers above report a positive effect on self esteem, comparable to what this study shows.

→ Thank you for citing this interesting study, and a prior paper reporting initial results. Since we had only included English-language articles in our literature review we unfortunately have missed this study. We now have added a reference to this study to line 275 (new reference #28).

19) Line 274-275: Self reporting is often charged with underreporting. However, this effect should be equally present during all assessment periods.

→ While we only have discussed recall bias as one potential reason for our physical activity-related findings, we agree that recall bias in physical activity questionnaires filled in by the same individual may have a similar extent of error across multiple assessments when caused by a systematic error (e.g., a 60-minute gym class may be accounted for as 1 hour of physical activity, while the child truly was only active for 30 minutes during that time). However, there are factors known to potentially lead to a more substantial recall bias when measures are repeated to assess for intervention effects. Some of these factors may include i.a. shame when not reaching set goals, self-perceived poor adherence with a medication whose effect is to be evaluated by a questionnaire, "last-minute" completion of a questionnaire under time pressure, or perceiving the task of repeatedly filling in a questionnaire as personally not beneficial.

20) Line 279: as a consequence this would mean that the authors have applied an inappropriate tool? Please comment.

21) Line 285: was the study powered to detect a difference?

→ Thank you for raising these questions. The "Physical Activity Questionnaire for Older Children" and the "Physical Activity Questionnaire for Adolescents" are well-validated, cost-effective and easily administrable tools developed to discriminate between low- and higher levels of physical activity in the respective age groups (e.g. Kowalski KC, et al. Validation of the Physical Activity Questionnaire for Older Children. Pediatric exercise science 1997, 9:174-186). While utilizing a more objective
measure like accelerometry for this study would have been more ideal, we have chosen this questionnaire-based tool because of its validation and cost-effectiveness, and in assuming the intervention may lead to a more significant increase in participants' physical activity levels. Generally, since our primary research question was to investigate whether HIP Kids is effective in preventing further increase in BMI and BMI z-score, and in improving QoL, assessing physical activity changes was not one of our primary outcomes. As such, and in consideration of our sample size, all results regarding secondary outcomes should be seen as hypothesis-generating only. Also, in response to the second, related question listed at the beginning of this paragraph, our study was not specifically powered to detect any influence of physical activity changes on blood lipids or insulin sensitivity. Therefore, we have only speculated briefly in the discussion that based on data in the literature a more pronounced increase in PA and decrease in %BF may have been necessary to produce positive effects on laboratory outcomes.

Minor Essential Revisions

Title:
22) Two colons in a row is quite unusual. Replace the second one by a dash: “…adolescents – a longitudinal pilot intervention study”
→ We have revised the title as recommended.

Abstract
23) Line 36 and 43: abstract should contain minimum information about QoL method used
→ We have revised the abstract as recommended, the respective sentence now read as follows (line 36-37): "Anthropometric measures, body composition, and QoL (using the Pediatric Quality of Life Inventory 4.0), were assessed at baseline, 3, and 12 months, and laboratory values were assessed at baseline and 12 months."

24) Line 41: “…21 girls, mean age….” Is misleading. Reads like mean age given only for girls. Please revise.
→ Thank you for pointing this out. We have revised the abstract as recommended, the respective sentence now read as follows (line 42-43): "42 obese children and adolescents (21 girls) completed the 12-month intervention (mean age 12.8 ± 3.14 years)."

25) Line 43: give z-score as “…+ 2.19….” → Changed as requested.
26) Line 44: four significant digits is too much as there is no 1‰ precision of this measurement; giving two or three would be by far sufficient: “74.45”, better “74.5” or “74”. This applies to all sections of the abstract and text body where figures are given.

  → We have revised abstract and text body as requested. All QoL values in the text are now shown with only one decimal.

27) Line 44: the figures make only sense of a normal range is given. Not all readers will be familiar with these test tools.

  → We agree with the reviewer that it may be easier for the reader to interpret the absolute QoL values if reference ranges based on the validation studies were given for each item. We have added the published means and standard deviations for healthy children for all four items (parent- and self-reported physical and emotional functioning scores) to the "Methods" section now read as follows (lines 180-185): "The Pediatric Quality of Life Inventory 4.0 (PedsQL) Child (age 8-12) and Teen (age 13-18) Report and the respective Parent Reports were used to assess QoL and consisted of validated 23-item self-report questionnaires (maximum total score 100). Reported scores [SD] for Physical and Emotional Functioning for healthy children are 84.4 [17.3] and 80.9 [19.6] (Child Report), and 89.3 [16.4] and 82.6 [17.5] (Parent Report), respectively [19]."

Because of the quantity of this new additional information we hope that it is acceptable to our reviewer that we have included this only into the “Methods” section of the text body, as including this in the abstract as well would exceed the 350 word maximum for the abstract. Thank you.

Introduction:

28) Line 104: “hospital-based” and “outpatient intervention” sounds somewhat contradictory. Please clarify and revise.

  → Thank you, we agree that our wording may have sounded ambiguous. "Hospital-based outpatient intervention" referred to the program occurring within the hospital premises with patients attending the program as outpatients rather than as inpatients.

  We have clarified this in the manuscript by rewording the above into "hospital outpatient clinic-based intervention".

Methods:

29) Line 118: give reference for charts used

  → We originally had cited this reference in line 153 of the original manuscript where we discussed the calculation of BMI z-scores (reference 16 of the original reference list). We now have revised the
reference order and list to make reference to this publication where requested by the reviewer (line 121, new reference # 13).

30) Line 163 and line 201: definition of hypertriglyceridemia
   → We clarified this in the "Methods" section as follows (line 176-177): "Hypertriglyceridemia was defined as triglycerides ≥ 1.50 mmol/L."

31) Line 165: give reference for HOMA → Reference added as requested (Ref. 18 in reference list).

Results:
32) Line 206: “15” for SD → Revised as requested

Discretionary Revisions
33) Line 34: “intervention” instead of “program” → Revised as requested

34) Line 35” “fifteen 90- minute educational …” instead of 15 19-minute educational…” → Revised as requested

35) Line 152: “…were calculated using the U.S. Centers…” → Revised as requested

36) Line 166: “Three-day food…” → Revised as requested

Thank you very much for the opportunity to submit a revision of our manuscript, and we hope that our response is adequately addressing the reviewers’ concerns.

Sincerely,

Dirk E. Bock M.D.