Author's response to reviews

Title: Trait-specific tracking and determinant of body composition: a 7-year follow-up study of pubertal growth

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Version: 3 Date: 10 December 2008

Author's response to reviews: see over
Dear Dr. Robin Cassady-Cain,

Enclosed is a copy of our responses to the reviewer’s comments along with the revised manuscript (MS: 1681081156230294) entitled “Trait-specific tracking and determinant of body composition: a 7-year follow-up study of pubertal growth” We appreciate the reviewers’ valuable comments and ideas. The point-by-point answers to the reviewers’ suggestions are given identified by number. We have taken every effort to meet the criticisms of each reviewer. As a result, we feel that the paper is stronger and provides superb information for the readers of BMC Medicine. I hope our changes meet with your approval and deem the article worthy of publishing in the BMC Medicine.

We think our article is particularly suited to publication in BMC Medicine because it is deals with the epidemic of unfavorable body composition development during adolescence and factors that potentially important in the prevention of obesity and osteoporosis which has broad interest. It is also worth mentioning that several articles using this same study population are in preparation and that these manuscripts will hopefully cite this current article as a key paper. Therefore, open access publication is important for us.

Our study capitalizes on use of data from a 7-year longitudinal design which captures changes in whole body composition (bone, muscle and fat) as girls transit from early puberty through young adulthood. The clarification of growth patterns is of great importance for early prediction and prevention of obesity, osteoporosis, and sarcopenia in later life. Due to the fact that the biology of bone, muscle and fat tissues and their associated disorders such as obesity, osteoporosis, and sarcopenia, are closely inter-related and share several common origins, including genetic and environmental factors, bone mass, lean mass, and fat mass should be considered together when studying the development of body composition.

The new findings in the paper are that the developments of three components of body composition are inter-related during growth. Bone mass was the most heritable trait while lean mass was the most environmentally modifiable. Using a clustering technique we demonstrate that a habitually higher quality of diet is essential for the development of high bone and muscle mass and while minimizing gain in fat mass during puberty. Physical activity is also important for increasing muscle mass and for preventing high fat mass during the adolescent growth period. The other important point is that we found that girls who are prone to develop low bone mass and lean mass and high fat mass in adulthood can be identified in prepuberty.
RESPONSE TO EDITORIAL COMMENTS:

1. The concerns of referees have been addressed point by point below (the changed part highlighted with yellow color).

2. The title of the article has been modified. The new title is:

   Trait-specific tracking and determinants of body composition: a 7-year follow-up study of pubertal growth in girls

3. The abstract has been reformatted and modified to make it more clear as follows:

   **Background:** Understanding how bone (BM), lean (LM) and fat mass (FM) develop through childhood, puberty and adolescence is vital since it holds key information regarding current and future health. Our study aimed to determine how BM, LM and FM track from prepuberty to early adulthood in girls and what factors are associated with intra- and inter-individual variation in these three tissues.

   **Methods:** The study is a 7-year longitudinal cohort study. BM, LM and FM measured using DXA, self-reported diet, leisure time physical activity (LTPA) and other factors were assessed 1-8 times in 396 girls aged 10-13 years (baseline), and 255 mothers once.

   **Results:** The location of a girl's BM, LM and FM in the lower, middle or upper part of the sample distribution was established before puberty and tracked in its percentile of origin over 7 years (r=0.72 for BM, r=0.61 for LM, and r=0.65 for FM all p < 0.001 first vs. last measurements' ranking). Seventy-three percent of those in the lowest quartile for BM and 69 % for LM, and 79% of those in the highest quartile for FM at baseline remained in their quartile at 7-year follow-up. Heritability was estimated to contribute 69% of the total variance of the BM, 49% of the LM, and 57% of the FM. Besides body size, diet index (explaining 9% of variance), breast feeding duration (6%) and mother’s BM (9%) predicted high BM. Diet index and high LTPA predicted high LM (24% and 14%, respectively), and low FM (25% and 12%, respectively), and low level of parental education predicted high FM (4%).

   **Conclusion:** Individual levels of BM, LM and FM are established before puberty and track in a trait-specific manner until early adulthood. Girls who are prone to develop low BM and LM and high FM in adulthood can be identified in prepuberty. The developments of three components of body composition are inter-related during growth. BM was the most heritable trait while LM the most environmentally modifiable. Diet and physical activity played an important role in increasing LM and preventing the accumulation of excessive FM.

4. Competing interests have been added according to the instruction (page 13 the first paragraph). In addition, we added in the acknowledgements (page 13, last paragraph) and list of abbreviations (page 12)

5. Two appendixes regarding the questionnaires used in this article have been added in the end of the article. The original questionnaires contain over 70 questions 14 pages. Thus we only provided the questions used in this article.

6. The file formats have been changed according to the editor’s suggestion. Each figure has been saved as a separate PowerPoint file. The text part saved as Microsoft Word file.
REPOSE TO REVIEWER 1:

1. *The data are sound. However there is a big loss of participants in the follow up (sometimes almost 50%), this has to be discussed.*

   **Our response:**
   
   The following sentences were added into discussion section regarding the dropouts (page 12 line 8-11):

   “The high drop out in the follow-up assessments was mainly due to a high proportion of girls going to universities or professional schools and relocating at the end of the follow-up period. However, our statistical methods were able to cope with this since hierarchical models allow inclusion of data from every subject regardless of irregularly-spaced and missing data.”

2. *Title and abstract are not convey what has been found: I miss in title: girls and in abstract: which percentile position.*

   **Our response:**
   
   The title of the article and the abstract has been modified to make it more clear (see above response to the editor.

3. *Also the illustrations can not be read independently from the article and need more explanation.*

   **Our response:**
   
   The figure legends have been modified to make it reads independently from the article as follows (Page 17):

   **Figure 1.** Growth curves (left panels) for whole body bone mass, lean mass, and fat mass in girls. The x-axis is the time relative to menarche (months). In the left panel, points and thin linking lines indicate individual measurements and the thick line represents the best fitting line estimated by a hierarchical linear model with random effects. In the right panel, each error-box indicates an age group value (mean ± 1 SD shade area). The error line represents the 95% confidence interval.

   **Figure 2.** Residuals of bone mass, lean mass, and fat mass in girls compared to their pre-menopausal mothers. Each point indicates an individual value. All values are in kg. For girls the value adjusted for time relative to menarche.

   **Figure 3.** Estimated marginal means of fat mass, lean mass, and bone mass adjusted for menarche age, baseline body height and weight in groups by ranking quartiles at the baseline. Lines with different thickness link the baseline and follow-up assessments indicating different quartile groups.

REPOSE TO REVIEWER 2:

1. *More details should be provided for the questionnaire used for dietary assessment.*

   **Our response:**
An appendix has been added regarding the dietary records to provide details of the assessments. In addition, the following information has been added in the methods section page 4 last 2 lines to page 5 first 5 lines. One new reference (13) has been added.

“Dietary information was obtained from a food-intake diary kept for three days (2 ordinary school days and 1 weekend day, see appendix 2) as described elsewhere [12]. The food records contained time of eating, items, and portion of food. The families were given written instructions and an example of how to record food consumption with a help of portion guidebook. Details of all foods and drinks including the type and commercial brand name were filled in the records. In addition, the type of diet (if restricted) was requested in a separate question. During the coding process the food records were checked by the nutritional students. Dietary intakes were analyzed using Micro-Nutrica software (version 2.5), Finland. The program has been validated and gives a reasonably good estimate of the intake of energy and most nutrients compared to chemical analyses of the diet [13]. For this report, on the basis of earlier studies[14-17] , the nutrients related to body composition were chosen to compute a dietary intake index, including intakes of protein (g/day), calcium (mg/day), potassium (mg/day), phosphorus (mg/day), and magnesium (mg/day) (for more details, see statistical methods).”

2. *It is not clear how socioeconomic status has been categorized.*

**Our response:**

The category of socioeconomic status is provided in the questionnaire (see appendix 1).

3. *There are some typos that should be corrected.*

**Our response:**

Typos have been corrected throughout the manuscript.