Author’s response to reviews

Title: Modern dietary pattern is prospectively associated with earlier age at menarche: data from the CHNS 1997-2015

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Author’s response to reviews:

RESPONSE TO NUTRITION JOURNAL COMMENTS

Manuscript No. NUTJ-D-20-00172

Title of Paper: Modern dietary pattern and plant-based diet pattern, but not animal food pattern, are prospectively associated with age at menarche: data from the CHNS 1997-2015

Point-to-point reply

EXPLANATION TO ALL REVIEWERS
We appreciate the suggestions made by the editors and reviewers since we believe that they helped to improve our manuscript. We addressed each of the points raised by the reviewers and changed the text accordingly. All the changes are highlighted in yellow.

Editor Comments:
Comment #1) What was the average follow-up period for the participants? It seems that there shouldn't be any girls who should be censored since they haven't yet started menarche, but it is not clear in the manuscript. For example, at line 111 it says "many of them have not yet experienced menarche." Does this mean at baseline many had not yet experienced menarche? If for some reason there are participants who haven't yet started menarche by the end of follow-up, then a survival analysis would be the appropriate way to analyze these data. I don't think this is the case since the cohort began in 1989, but it should be written more explicitly in the methods.

We thank the reviewer for pointing out this issue. The average follow-up period for the participants was 2.4 years. We had added the information in the Results section.
Location: line 224

We agree with the reviewer that if there are participants who haven’t yet experienced menarche by the end of follow-up, a survival analysis would be the appropriate way to analyze these data. However, the CHNS is an ongoing longitudinal cohort study which is conducted every 3-4 years to obtain nationally representative information on economy, socio-demography, nutrition, lifestyle and health issues. Participants were not followed up every year, and data on menarcheal age in the CHNS was limited. As we were interested in the prospective relevance of premenarcheal dietary patterns on age at menarche by similar biological time range, i.e. 1-4 y prior to menarche onset, only girls who had experienced menarche by the time of this analysis were included in the present study. As suggested by the reviewer, we have described the study design more explicitly in the Methods as follows:
“For this study, girls who were initially recruited into the CHNS differed considerably in age (6-14 years old), and they have not yet experienced menarche. As we were interested in the prospective relevance of premenarcheal dietary patterns on age at menarche by similar biological time range, girls who had experienced menarche by the time of this analysis were included in the present study. Between the 1997 and the 2015 survey, there were 1367 girls with plausible data on menarcheal age. Of these, 843 provided dietary intake information at least once during the visits 1-4 y prior to menarche onset (baseline).”

Comment #2) For the 3 consecutive 24-hour recalls, were two of them on the weekdays and one on the weekend?
We thank the reviewer for pointing out this issue. Essentially the CHNS is a community and household based study, and all household members were interviewed. Individual data are highly detailed, including dietary intake, physical activity, anthropometry, blood pressure and limited clinical nutrition and physical functioning data. For the dietary data, it was collected for three random and consecutive days, which was not designed to include two weekdays and one weekend day initially. Based on the actual diet interview date of the 711 participating girls, we found that 49.2% of them had three weekdays, 28.9% had two weekdays and one weekend day, and 19.9% had one weekday and two weekend days. We have added the information in the text as follows: “The majority of participants had a complete three-day 24-hour recalls (n = 697, 98.0%, i.e. 49.2% had three weekdays, 28.9% had two weekdays and one weekend day, and 19.9% had one weekday and two weekend days); the reminder had either one or two recalls (n = 4 and n = 10, respectively).”

Comment #3) Line 152- What do you mean that the factor scores were calculated by a multiple regression method? Aren't they computed by multiplying the factor loadings by the food intake frequency and then summing?
We thank the reviewer for pointing out this issue. Actually, as the reviewer said, the factor scores of each dietary pattern were calculated for each participant by summing the product of a standardised gram of each item consumed by its factor loading. We have removed “by multiple regression method”, and changed the sentence to “by summing the product of a standardized gram of each item consumed by its factor loading” in the text.

Comment #4) Line 287- You discuss the importance of thinking about dietary patterns as a whole, but then in your interpretation you insinuate that the findings must be explained by individual food items/micronutrients. Isn't this a bit contradictory?
We thank the reviewer for pointing out this issue. Since biologic knowledge concerning health/disease outcomes is based on the role of nutrients, the explanation of the associations between dietary patterns and menarche could be confirmed by the correlations between nutrients/foods and
menarche as in other studies (Nutr Res, 2018 August; 56: 41-50; Public Health Nutr, 2020 Apr; 23(6): 1020-1030; Int J Endocrinol, 2018 Jan 16; 2018:4528704). Compared with individual nutrients or food items, dietary pattern analysis examines the effects of diet as a whole, i.e. it takes the interactions of nutrients and foods into account, and thus could have important public health implications because the overall patterns of dietary intake might be easier for the public to interpret or translate into daily diets. However, it would not replace nutrient or food analysis, but instead serves as a complementary approach to traditional analysis. Evidence could be enhanced when the results from multiple lines of research (i.e. nutrients, foods, and dietary patterns) are consistent (Curr Opin Lipidol, 2002 Feb; 13(1):3-9).

Comment #5) In the discussion you mention some additional analysis where you examined individual foods in relation to age at menarche. I think this additional analysis needs to be described in both the methods and results rather than appearing for the first time in the discussion.

We thank the reviewer for this important comment, which helped us to rethink the interpretation and discussion of our results. In theory, additional analysis of examining individual foods in relation to age at menarche could be conducted and added to the text. However, dietary pattern analysis is the crucial point addressed by this article. If the description of statistical analysis on the associations of 18 food groups with menarche was added to both the Methods and Results section, the theme of the manuscript might be poorly focused. Therefore, we determined to remove the $\beta$ and $p$ values from the Discussion, and rewrote the interpretation and discussion of the relationship of modern dietary pattern with menarcheal timing as follows:

“The modern dietary pattern we identified showed some similarities with results previously reported by Zhang et. al, which was characterized by high intakes of fast foods, milk, fruits, ethnic foods and cakes, and sugary foods. We observed that modern dietary pattern was associated with an increased risk for accelerated menarche. This pattern was implicated in the timing of menarche probably in any of the three ways: high consumption of milk, high fat intake, and high sugar intake. Previous studies have shown that consumption of milk contributed to high IGF-I concentrations in prepubertal children, which was found to be associated with earlier menarche. Also, high consumption of fat and sugar were associated with an increase in insulin secretion that could increase IGF-I. Taken together, these evidence suggest that modern dietary pattern has potential influence on menarcheal timing through metabolic changes in insulin-mediated pathway mechanisms and upregulation of hormones. Since mid-1990s, a marked transition to the modern dietary pattern with increased consumption sugary and fat-rich foods has occured in China. Ouyang el al. reported that fruits, milk, and fast foods were the three most consumed snacks among Chinese children. Moreover, calories from fast foods account for 26%-40% of total energy intake. Although more research is needed to determine the effects of modern dietary pattern on Chinese children's health, the present public health recommendations include the necessity to limit consumption of fast foods and sugary foods.”

Location: line 296-305

Comment #6) Line 359: "researches are needed" should be changed to "research is needed".

We are grateful to the reviewer for this suggestion. We have changed "researches are needed" to "research is needed".
Comment #7) It's interesting that you did not observe any associations with the Animal Food pattern, but I can see that it loads positively with both red meat and with fish/shellfish. It may be possible that these two types of meat are associated with menarche in opposite ways, as has been reported in other literature.

We thank the reviewer for pointing out this issue. In the manuscript, we explained the null association of animal food pattern with age at menarche by age-specific effects since some researchers have proposed that animal food intake at younger ages (e.g. early childhood) may be more relevant to occurrence of menarche than peripubertal intake (Annu Rev Public Health, 2016;37:33-46). We are especially thankful for the reviewer’s suggestion, and have added another potential explanation to the Discussion section as follows:

“Another potential explanation is that the animal food pattern in our study was loaded heavily for both red meat and fish/shellfish, and these two types of meat may be associated with timing of menarche in opposite ways. For example, a prospective study conducted in 456 US girls aged 5-12 y showed that red meat was inversely related to age at menarche while tuna/sardine intake frequency was positively associated with age at menarche.”

Reviewer #2:
This paper is the first to assess the associations between different food patterns (modern, vegetative or animal) and age at menarche in a Chinese population. The authors use data from 711 girls with food recalls in the China Health and Nutrition Survey. This is a well written manuscripts and I only have a few comments that are found below.

Comment #1) Please describe the design of the cohort study in a bit more detail so that it becomes clear how old the children/girls were when they entered the cohort and how they were recruited.

We are grateful to the reviewer for this suggestion. The CHNS is an ongoing longitudinal cohort study which was started in 1989. A multistage, random cluster procedure was used to obtain nationally representative information on economy, socio-demography, nutrition, lifestyle and health issues in both urban and rural areas in 15 provinces and municipal cities in China. The CHNS is a community and household based study. In each community, 20 households were randomly selected, and all household members were invited to participate in the study. For this study, girls with plausible data on menarcheal age and dietary intake information at least once during the visits 1-4 y prior to menarche onset (baseline) were included for the present analyses. They were 6-14 years old when they entered the cohort (baseline). As suggested by the reviewer, we have added the information to the Method section as follows:
“In brief, a multistage, random cluster procedure was used to obtain nationally representative information on economy, socio-demography, nutrition, lifestyle and health issues in both urban and rural areas in 15 provinces and municipal cities in China. The CHNS is a community and household based study. In each community, 20 households were randomly selected, all household members were invited to participate in the study.”

“For this study, girls who were initially recruited into the CHNS differed considerably in age (6-14 years old), and they have not yet experienced menarche. As we were interested in the prospective relevance of premenarcheal dietary patterns on age at menarche by similar biological time range, girls who had experienced menarche by the time of this analysis were included in the present study. Between the 1997 and the 2015 survey, there were 1367 girls with plausible data on menarcheal age. Of these, 843 provided dietary intake information at least once during the visits 1-4 y prior to menarche onset (baseline).”

Comment #2) English is not my native tongue but should it not be a "are" instead of an "is" in the title, also, add a comma after "but not animal food pattern".

We thank the reviewer for pointing out this issue. We have changed the title to “Modern dietary pattern and plant-based diet pattern, but not animal food pattern, are prospectively associated with age at menarche: data from the CHNS 1997-2015”.

Comment #3) Abstract: I find this sentence somewhat strange: "Multivariate regression analyses were performed in 711 China Health and Nutrition Survey (CHNS) girls with three-day 24-hour recalls and information on potential confounders at baseline (i.e. 1-4 y before the onset of menarche)." Do you perform analyses on data or on girls? I would rephrase to "analyses on data from 711 girls participating in the CHNS".

We thank the reviewer for pointing out this issue. We have changed the sentence in the manuscript, i.e. “Multivariate regression analyses were performed on data from 711 girls participating in the China Health and Nutrition Survey (CHNS) with three-day 24-hour recalls and information on potential confounders at baseline (i.e. 1-4 y before the onset of menarche).”

Comment #4) Abstract: Consider presenting mean (95% CI) as 12.50 y (95% CI: 12.29-12.70) instead of "mean (95% CI) 12.50 y (12.29, 12.70))" if this is in accordance to the journal guidelines.

We are grateful to the reviewer for this suggestion. We have presented the data as “mean AAM: 12.50 y, 95%CI: 12.29-12.70” in accordance with the journal guidelines. Also, we have presented RR (95%CI) as “RR: 1.79, 95% CI: 1.09-2.93” in the Result section.
Comment #5) Is vegetative food pattern different from vegetarian or vegetable-rich food patterns? To me "vegetative" is not as commonly used.

We thank the reviewer for this important comment, which helped us to rethink the labeling of dietary patterns identified in this population. As factor 3 was characterized by high intakes of legumes, nuts, fungi and algae, beverages, fats and oils, and condiments instead of vegetables, we think that “vegetable-rich food patterns” may not be appropriate. In addition, it has been mentioned in other studies that a vegetarian diet is mostly based on plant foods such as cereals, legumes, fruits, leafy vegetables, nuts, seeds, and sea vegetables, with eliminations of animal products such as meat or chicken, fish, eggs, and dairy products (Nutrients, 2017 Jun 14; 9(6): 603; Nutr J. 2014 Sep 5; 13:89). And the meaning of “vegetative” is relating to plant life. Thus, “vegetarian diet pattern” or “vegetative food pattern” may also not be felicitous in the present study. Having conducted further literature search on the topic of dietary patterns, we decided to change the labeling of factor 3 to “plant-based diet”, which was defined in terms of high quality plant foods and low frequency of animal food consumption, including generally less animal-food intensive, vegetarian, or vegan diets (Trends Cardiovasc Med. 2018 Oct;28(7):437-441; Nutrients. 2018 Dec; 10(12): 1841). We have changed the word in the text, Tables and Figure 2 accordingly. Location: title; line 44; line 50; line 57; line 236; line 251; line 252; line 263; line 272; line 274; line 283; line 288; line 312; line 322; line 370; Table 3; Table 4; Figure 2

Comment #6) Line 181: "based on the Chinese reference curves" should it be "based on a Chinese reference population"?

We are grateful to the reviewer for this suggestion. We have changed “based on the Chinese reference curves” to “based on a Chinese reference population”. Location: line 189

Comment #7) Table 1: Why is lollipops and ice cream described under beverages? Lollipop also occurs under sugar and preserves (where I would think it sits better).

We thank the reviewer for pointing out this issue. In fact, “lollipops” under beverages should be “popsicle”. The dietary intake data in the present study were divided into 18 categories based on Chinese Food Composition, in which popsicle and ice cream are classified as beverages considering that their nutrient profiles are similar to beverages. We have changed “lollipops and ice cream” to “popsicle and ice cream” under beverages in Table 1. Location: Table 1

Comment #8) Table 2: I suggest including n=711 at the top of the table under Values, and next to values (mean ±SD/n (%)). Include numbers before % in the table. In the legends it does not say that you used Cole et al to calculate BMI z-score only the Chinese reference data. Please correct here or in the manuscript.
We thank the reviewer for this suggestion. We have included “n, 711” at the top of the table, and added (mean ±SD/n (%)) next to values. Data were presented as means±SD or n (%) in Table 2.

In addition, we have added “using the equation by Cole et al. based on a Chinese reference population” to the footnotes of Table 2.

Comment #9) The authors do not say anything about the fish and shellfish being included in the Animal food pattern. Could this be of importance as to why you did not see an association with age at menarche?

We thank the reviewer for pointing out this issue. In the manuscript, we explained the null association of animal food pattern with age at menarche by age-specific effects since some researchers have proposed that animal food intake at younger ages (e.g. early childhood) may be more relevant to occurrence of menarche than peripubertal intake (Annu Rev Public Health, 2016; 37:33-46). As suggested by the Reviewer #1, we have added another potential explanation to the discussion section as follows:

“Another potential explanation is that the animal food pattern in our study was loaded heavily for both red meat and fish/shellfish, and these two types of meat may be associated with timing of menarche in opposite ways. For example, a prospective study conducted in 456 US girls aged 5-12 y showed that red meat was inversely related to age at menarche while tuna/sardine intake frequency was positively associated with age at menarche.”

Location: 338-344

Comment #10) Line 214, 222, 235: change "were" to "are"

As suggested by the reviewer, we have changed "were" to "are" in the text.
Location: line 222; line 231; line 244; line 258

Comment #11) Line 359: change to research

We have changed “researches are” to “research is” as suggested by the reviewer.
Location: line 373

Comment #12) References: Are there page numbers missing in references 6 and 20?

We thank the reviewer for pointing out this issue. We have checked reference 6 and 20, and corrected the reference format according to the journal style.
Location: line 452-454; line 498-500
References cited in the response: