Author’s response to reviews

Title: Development and Relative Validation of a Food Frequency Questionnaire for French-Canadian Adolescent and Young Adult Survivors of Acute Lymphoblastic Leukemia

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Author’s response to reviews:

Reviewer reports:

Associate Editor: Thank you for resubmitting your work, and thank you for addressing all comments individually. I think the manuscript has been much improved, and one of the reviewers and myself have only a few remarks left that would need to be addressed. Please have a look at our remarks and suggestions below:

We would like to thank the associate editor for his/her encouraging comments regarding our manuscript. He/she will find below the point-by-point answers to his/her comments.

Comment: I'm pleased to see that you addressed the comment of the reviewer and now also present medians and interquartile ranges in Tables 3 and 5. Although I will not insist you will do
so, I strongly recommend you to move these tables to the appendix, and present in the medians and interquartile ranges in the main manuscript.

Response: To follow the editor’s recommendation, we have moved the two tables (originally 3 and 5), presenting means and standard deviation, to the Supplementary data section and have included the tables with medians and interquartile ranges in the main manuscript. The new version of the manuscript is organized as follow:

Main manuscript:

Table 3: Food frequency questionnaires and 3-day food records: Comparison of nutrient median (inter-quartile range) daily intake and correlation coefficients

Table 5: Food frequency questionnaires at visits 1 and 2: Comparison of nutrient median (inter-quartile range) daily intake and intraclass correlation coefficients

Supplementary tables:

Supplementary Table 9: Food frequency questionnaires and 3-day food records: Comparison of nutrient mean daily intake and correlation coefficients

Supplementary Table 10: Food frequency questionnaire visits 1 and 2: Comparison of nutrient mean daily intake and intraclass correlation coefficients

To be consistent with the changes made in the main manuscript, we have also changed the Supplementary tables 1, 2, 3, 4, 5, 6, 7 and 8 (analyses for males vs. females for the entire group and separately in adults and children) to present medians and inter-quartile ranges instead of means and standard deviations.

We have adjusted the result section in the manuscript to reflect the modifications made to these tables.

«The median values of daily energy and nutrient intakes derived from the FFQ and the 3-DFR are reported in Table 3. Two of 3 macronutrients derived from the FFQ showed higher values compared to the 3-DFR (proteins +12.7% and CHO +20.0%), resulting in higher reported energy intake (+12.1%). Reported intakes of dietary fiber and micronutrients (vitamins A, C, E and D, calcium, iron and folate) were also higher with the FFQ, differences ranging between +16.0% (iron) and +52.6% (vitamin C).» (lines 242-247)
Comment: I agree with reviewer 1 that some further clarification regarding the use of energy adjustment in your work is required - it would be great if you could clarify whether the main analyses were based on energy-adjusted values or if they won't (I realise you have used the residual method for Table 3, but I'm not sure whether you used the adjusted values in subsequent analyses that you present. Did you use energy-adjusted nutrients in subsequent analyses? Did using them make a difference?). It would be good to report both type of analyses.

Response: We agree with the associate editor that clarifications regarding the use of energy adjustment are needed through the manuscript and tables. Specifications were added in the text (lines 200, 215, 223-224,) and in Table notes (Tables 4, 5 and 6).

The FFQ was validated using a 3-day food record as a reference tool in 80 cALL survivors while reproducibility was evaluated by comparing FFQs from visit 1 and 2 in 29 cALL survivors. For the validation of the FFQ, Spearman correlation and cross classification analyses between 3-DFR and FFQ were executed. To assess the reproducibility of the FFQs, intraclass correlation and cross classification analyses between FFQ visit 1 and 2 were done.

We used crude data for the cross classification analyses for both the validation and reproducibility testing. We consider that the correlation coefficients computed with the energy-adjusted nutrient intakes exposes to the reader the variations between the FFQ and 3-DFR or between the two FFQs. In our opinion, performing cross classification analyses with energy-adjusted nutrient intakes do not add meaningful information for the reader. Thereby, we did not include these results in the manuscript. However, we have performed the analyses and you will find the results for your consideration (please see additional document). If you believe that it would add substance to the manuscript we will do the needed modifications.

Similarly, we did not initially calculate intraclass correlation coefficients (to test FFQ reproducibility) with energy-adjusted nutrient intakes due to the small sample size. Any modification in the composition of diet would greatly impact the residual values (energy-adjusted nutrient intakes) and the correlation coefficients. We considered it could mislead the conclusion regarding the reproducibility of our questionnaire. You will find the analyses for your appreciation.

The results of the intraclass correlation analyses between FFQ visit 1 and 2 (first and second Tables) for CHO and lipid nutrients support the fact that, even if only a few individuals modify the composition of their diet between the two visits, the correlation coefficient is greatly impacted. After a thorough analysis of the questionnaires for both visits, we identified 3 patients of the 29 that had significantly changed the composition of their diet in CHO and/or lipids at the two visits. These modifications in the composition of the diet are translated into smaller
correlation coefficient for CHO and lipid-related nutrients. The small sample size and these modifications of the diet composition are also reflected in the weighted kappa factors between FFQ visits 1 and 2 for CHO and lipids (fourth Table below).

The weighted kappa factors in the cross classification analyses shown in the third table below (Food frequency questionnaires and 3-day food records: cross-classification analysis of energy adjusted nutrient intakes) show similar variations as the correlation coefficients computed with the energy-adjusted nutrient intakes (shown Table 3 in the manuscript) between the FFQ and 3-DFR, particularly for lipids and CHO.

Finally, in order to complete the supplementary analyses using energy-adjusted nutrient intakes, we did a thorough audit of the data entries. We detected 3 data entries misclassified that impacted mainly the lipid correlation and weighted kappa factors between FFQs visits 1 and 2. We made the necessary corrections in Tables 5 and 6 and the Result section:

"Intraclass correlations assessing FFQ reproducibility between visits 1 and 2 are shown in Table 5. Coefficients for macronutrients ranged between 0.76 (lipids) and 0.81 (CHO), indicating good reliability, which translated into a 0.84 coefficient for energy intake demonstrating good reliability. For micronutrients, intraclass correlation coefficients ranged from 0.68 (vitamin A) to 0.88 (vitamin D) with the indication of moderate to good reliability. Coefficients were found lower for three nutrients: MUFA (0.62), PUFA (0.56) and dietary fiber (0.63), but still indicating moderate reliability." (lines 310-321)

"Our results surpassed 0.7 in most of the nutrients tested even though one year on average separated the administration of the two FFQs." (lines 472-473)

"Weighted kappa values varied from 0.52 (lipid) to 0.66 (CHO) for energy intake and macronutrients and from 0.46 (vitamin C) to 0.66 (vitamin D) for micronutrients, indicating moderate to good agreement for both groups." (lines 319-321)

Note Please see additional document identified as "Reviewer report" to consult the Tables.

Reviewer #1: The authors revised the manuscript following the reviewers’ input but the manuscript still requires further revision:

Comment: The way of calculating the bias at the populational level, without considering the individual level information is not very informative and properly done. It is not because that others have done something uncorrect, that one should do it. To represent a populational level measurement, such as bias, a measure of variability is also needed! That does not mean that one will interpret the individual level information/ dispersion such as Bland Altman. It will simply
give more information around the measure of central tendency (mean or median), which are very important depending of the type of information assessed, such as inadequacy of diets.

Response: As suggested by the reviewer, we have recalculated the differences with a measure of variability: inter-quartile range for the medians and standard deviation for the means. Tables 3 and 5 in the manuscript were modified accordingly. Supplementary tables 1-10 were also modified to reflect the measure of variability.

Comment: As for the correlation classification interpretation, there is no need to say someone else used the classification, when some else proposed. Many others could have used it. Unless, it becomes clear why you think it is important to mention.

Response: As suggested by the reviewer, we have clarified why we selected this specific classification to interpret correlation coefficients. We consider that it is important to mention the reader that Goulet et al. also used this classification to interpret the correlation coefficients because: (1) their questionnaire was developed, like ours, in a population from the Province of Quebec, Canada and; (2): we used their questionnaire to develop ours. We have however rephrased the paragraph and added the appropriate reference:

«The following classification was utilized to interpret correlation coefficients: very well correlated (coefficient 0.7 to 0.9), well correlated (coefficient 0.5 to 0.7) [29] and moderately well correlated (coefficient 0.3 to 0.5). This classification was also used to interpret the correlation coefficients in one of the FFQ that was used to develop our questionnaire [21].» (lines 188-192)

Comment: Still missing original information about energy adjustment.

Response: We added a brief description regarding energy adjustment in the Method section with the appropriate reference:

«The residual method proposed by Willett et al. was used to calculate the energy-adjusted variables [28]. With this method, the nutrient intakes of each individual are regressed on their total energy intakes. The residual from the regression represent the differences between each individual’s actual intake and the intake predicted by their total energy intake [28].» (line 184-188)