PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Intra-individual variation in urinary iodine concentrations: effect of adjustment on population distribution using two and three repeated spot urine collections
AUTHORS	Charlton, Karen; Batterham, Marijka; Buchanan, LiMin; Mackerras, Dorothy

VERSION 1 - REVIEW

REVIEWER	Sheila A Skeaff Dept Human Nutrition University of Otago Dunedin
REVIEW RETURNED	16-Sep-2013

GENERAL COMMENTS	This is a well-written paper illustrating how multiple spot urine samples can adjust the distribution of urinary iodine concentration (UIC). The authors are clear that the study was originally designed to assess the relationship between iodine status and cognition in elderly adults. Thus, the study was powered for another outcome (i.e. cognition). In conducting the original study, the authors collected 3 spot urine samples from the participants, and have now taken the opportunity to ascertain the effect of adjusting the distribution of intakes. The adjustment undertaken by the authors is commonly undertaken in the adjustment of dietary data, for example, the adjustment of 24-hour recall data by obtaining another 24-hour recall from a subset of participants. (i) Spot urine samples do not represent iodine intake for a 24-hour period, thus the variation associated with a spot urine sample is likely to be larger than if the authors had collected 24-hour urine samples. The CV of spot versus 24-hour urine samples with regard to UIC has been reported by Konig et al; this should be acknowledged in the manuscript. (ii) The authors requested the participants collect urine on the same day of the week for three consecutive weeks, however, do not report for how many participants followed this protocol. (iii) The participants in this study were elderly adults, probably one of the least studied groups with regard to UIC. (iv) Did the authors collect information on use of iodine containing medications or supplements that may have impacted on UIC? (v) The inclusion of some of the data in Table 1 such as cognition is irrelevant to this study and should be removed. (vi) The authors report the % of participants with a UIC >100

	ug/L when the WHO/UNICEF/ICCIDD recommendation is for the percentage of participants with a UIC <100 ug/L: Table 1 should be altered accordingly.

REVIEWER	Danijela Ristic-Medic University of Belgrade Institute for Medical Research Centre of Research Excellence in Nutrition and Metabolism Belgrade, Serbia
REVIEW RETURNED	03-Nov-2013

GENERAL COMMENTS	Well done. You have conducted paper in interesting discussion in the field of intra-individual variation in collecting the single spot urine samples from each survey Australia participants. Manuscript provides a useful contribution in iodine status biomarkers research. There are some minor suggestions to improve the paper. Abstract Methods: First long sentence, write in two clearer sentences Line 35 and 36 – corrected ug/L u micro (µg/L) Introduction Line 19-21 and 28 – corrected ug/L u micro (µg/L) Divided Methods parth in 3 subheadings: 1. Participants 2. Biochemical data 3. Statistically analyses

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: This is a well-written paper illustrating how multiple spot urine samples can adjust the distribution of urinary iodine concentration (UIC). The authors are clear that the study was originally designed to assess the relationship between iodine status and cognition in elderly adults. Thus, the study was powered for another outcome (i.e. cognition). In conducting the original study, the authors collected 3 spot urine samples from the participants, and have now taken the opportunity to ascertain the effect of adjusting the distribution of intakes. The adjustment undertaken by the authors is commonly undertaken in the adjustment of dietary data, for example, the adjustment of 24-hour recall data by obtaining another 24-hour recall from a subset of participants.

(i) Spot urine samples do not represent iodine intake for a 24-hour period, thus the variation associated with a spot urine sample is likely to be larger than if the authors had collected 24-hour urine samples. The CV of spot versus 24-hour urine samples with regard to UIC has been reported by Konig et al; this should be acknowledged in the manuscript.

The following has been added into the Discussion: “Another consideration is the use of spot urine samples as a proxy for assessment of iodine status on a population level. A spot sample does not reflect intake over an entire day for which a 24-hour collection would be needed. Konig et al. [25] have reported a trend for higher intra-individual variation for spot UIC (38 %) versus measured 24-hour urinary iodine excretion (32 %).
New reference added: Konig F, Andersson M, Hotz K, et al. Ten Repeat Collections for Urinary Iodine from Spot Samples or 24-Hour Samples Are Needed to Reliably Estimate Individual Iodine Status in Women. J Nutr. 2011;141:2049-54.

(ii) The authors requested the participants collect urine on the same day of the week for three consecutive weeks, however, do not report for how many participants followed this protocol.

We do not have data on compliance with this protocol. However, all participants were reminded by telephone the day before their scheduled urine collections and fieldworkers visited participants in their homes on the day of collection to fetch the samples.

(iii) The participants in this study were elderly adults, probably one of the least studied groups with regard to UIC.

Yes, we agree with this comment. The following has been included in the discussion as follows: “Our study sample comprised older adults, an age group who have been studied least for iodine status, and who also often have impaired renal function.

(iv) Did the authors collect information on use of iodine containing medications or supplements that may have impacted on UIC?

Thyroxine use was an exclusion criterion as stated in the methods. No other medications or supplements were considered in the analysis. The purpose of the paper is to assess intra-individual variation in repeated spot urine collections for assessment of population distribution of iodine status, using statistical adjustment. The absence of data on medications (other than thyroxine) should not affect the study outcomes.

(v) The inclusion of some of the data in Table 1 such as cognition is irrelevant to this study and should be removed.

This has been removed from the Table, as suggested. However, nutritional status (MNA categorization) is described in the text, as is independence (Barthel index). For generalizability of the findings, it is necessary to demonstrate that the group, despite being elderly, were highly functional and mostly well nourished.

(vi) The authors report the % of participants with a UIC >100 ug/L when the WHO/UNICEF/ICCIDD recommendation is for the percentage of participants with a UIC <100 ug/L: Table 1 should be altered accordingly.

This has been done, both in the Table and the text: “The percentage of participants with UIC < 100 µg/L increased decreased from 79 % to 83 % following adjustment.”

Reviewer 2:
Well done. You have conducted paper in interesting discussion in the field of intra-individual variation in collecting the single spot urine samples from each survey Australia participants. Manuscript provides a useful contribution in iodine status biomarkers research. There are some minor suggestions to improve the paper.

Abstract
Methods: First long sentence, write in two clearer sentences
This sentence has been shortened as follows:
“Between May and September 2009, 110 adults aged 60 - 95 years volunteered for a study that investigated the association between iodine status and cognition. English-speaking men and women were recruited from a random selection of aged care facilities (independent, assisted and low care living) in the Illawarra region, south of Sydney in Australia.”

• Line 35 and 36 – corrected ug/L u micro (µg/L)
This has been done.

• Introduction, Line 19-21 and 28 – corrected ug/L u micro (µg/L)
This has been done.

• Divided Methods part in 3 subheadings: 1. Participants 2. Biochemical data 3. Statistically analyses
This has been done.

We trust that we have addressed all of the reviewers' comments and that the manuscript has been improved.

VERSION 2 – REVIEW

REVIEWER	Sheila A Skeaff Department of Human Nutrition University of Otago
REVIEW RETURNED	02-Dec-2013

GENERAL COMMENTS	You describe the MNA and Barthel Index in methods but have removed the associated data from results section, thus the information in methods could also be removed.