Validation of a short food frequency questionnaire specific for iodine in UK females of childbearing age

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Emilie Combet[1], Michael EJ Lean[1]

[1] Human Nutrition, School of Medicine, College of Medical Veterinary and Life Sciences, University of Glasgow, New Lister Building, Glasgow Royal Infirmary, Glasgow G31 2ER

*** Corresponding author:**
Emilie Combet, School of Medicine, College of Medical Veterinary and Life Sciences, University of Glasgow, New Lister Building, Glasgow Royal Infirmary, Glasgow G31 2ER, UK
Tel +44 141 201 8527; Fax. +44 141 201 9275
email: Emilie.CombetAspray@glasgow.ac.uk

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Abstract

Background: Widespread subclinical iodine insufficiently has recent been reported in Europe, particularly amongst young women, based on urinary iodine using WHO/FAO criteria. While urinary iodine concentration is useful measurement of the population iodine status, it does not provide an insight in the habitual iodine intake of this population. This is compounded by the fact that very few iodine-specific food frequency questionnaires (FFQ) have been validated so far.

Aim: to develop and validate a new, simple, rapid survey tool to assess dietary iodine exposure in female of childbearing age.

Methodology: Iodine was measured in duplicate 24-hour urine collection. Iodine intake was measured with duplicate 4-day semi-quantitative food diaries and the FFQ Correlation, cross-classification and Bland Altman analyses were used to estimate agreement, bias and reliability of method. The triangular (triad) method was used to calculate validity coefficients.

Results: 43 women, aged 19-49, took part in the validation of the 17-item FFQ. Median UI was 74 µg/L (IQR 44) indicative of mild iodine insufficiency. The FFQ showed good agreement with food diaries to classify iodine intake (82% of subjects to the same or adjacent quartile). The FFQ was moderately correlated to the food diaries (r_s=0.452, p=0.002) and to urinary excretion in µg/L (r_s=0.341, p=0.025) but not µg/day (p=0.316). The validity coefficients were 0.69, 0.66 and 0.52 for the food diaries, FFQ, and urinary iodine excretion respectively.

Conclusion: The FFQ provides a rapid and reliable estimate of dietary iodine exposure to identify population subgroups at risk of iodine deficiency.

Introduction

Iodine deficiency, which may be clinical or subclinical, is estimated to be responsible for impaired neuro-development which causes a global reduction in IQ of 13.5 points (Bleichrodt and Born, 1994, Zimmermann and Andersson, 2012).

Following recent reports of widespread iodine insufficiency in Britain and other Europeans countries, there has been renewed interest in assessing iodine intake, iodine status and thyroid function in females of childbearing age. Iodine intake is crucial for the neurodevelopment of the fetus and infant, and maternal iodine insufficiency has been linked to lower academic attainment in children of the ALSPAC cohort (Bath et al., 2013). Iodine insufficiency results from low intake of seafood and dairy, especially milk. Consumption of seafood is now generally low in the UK population, (at 37g/day, (Department of Health and The Food Standards Agency, 2011), while milk consumption has been steadily decreasing since 1975 (Elwood, 2005). Many young women avoid these foods, for various reasons (Olsen, 2003). There is further concern that changes in agricultural practices (withdrawal of fortified cattle feeds, and iodophore for sanitization) as well as increased availability and consumption of organically farmed milk (lower in iodine) may affect general status of the population (Flachowsky et al., 2013, Bath et al., 2012).

Following WHO/FAO guidelines, the iodine status of a population relies on measuring iodine concentration in a spot urine sample, and relating the UIC outcome to established thresholds. A median UIC above 100ug/L is the definition of a sufficient iodine status for the population (WHO-UNICEF-ICCIDD, 2007). However, it is important to recognize that spot UIC does not provide a valid representation of habitual iodine exposure of an individual. Indeed, most of the iodine (90%) is excreted within a few hours of intake, and since iodine is extensively stored in the thyroid gland, it can safely be consumed intermittently (Zimmermann, 2009, Zimmermann and Andersson, 2012). There are only two validated food frequency questionnaires to assess iodine intake specifically, one validated for Danish women (DanThyr study, women aged 25-30 and 60-65) (Rasmussen et al., 2001) and the other for Australian older adults (men and women, aged 60-95) (Tan et al., 2013). A separate questionnaire, focusing on iodine awareness and 24hours dietary recall of iodine-rich foods was also published by Leung et al to assess iodine intake in American adults (Leung AM, 2007). Meanwhile, the MoBa study FFQ was validated for iodine intake in Norwegian mothers (Brantsaeter, 2009).

The present study was designed to develop and validate a practical survey tool to assess dietary iodine exposure, using both a Food Frequency questionnaire specific to the main dietary source of iodine in European diets, and a complete Food Diary.

Method

Subjects, samples and measurements

Healthy females were recruited to the study by local advertisement. Inclusion criteria were age between 18 and 50 years, English speaking. Exclusion criteria were known thyroid disease, any other active disease, pregnancy, lactation. A local institutional ethics committee approved the protocol and all participants provided written informed consent. Height was measured to the nearest mm using a stadiometer (Seca 213; Seca, Birmingham), weight was measured to the nearest 0.1kg using portable scales (Tanita B.V., Hoofddorp, The Netherlands) and and waist circumference was measured to the nearest 0.1cm using non-elasticated tape (at the mid-point between the lowest rib and iliac crest, after expiration).

Food frequency questionnaire

A food frequency questionnaire was developed, to assess the intake of iodine rich food over the previous 6 months, using the Dietary Target Monitor questionnaire as a template(Lean et al., 2003). Iodine-rich foods were grouped in eight categories, including milk, oil-rich fish, white sea fish, other seafood, cheese (hard and soft), yoghurts, milk or cream-based puddings, and cheese-based dishes. The milk category was broken down in four sub-categories, to capture the frequency of milk intake consumed with i) tea or coffee, ii) breakfast cereals, iii) in latte, cappuccinos, hot chocolate or iv) just on its own. Specific examples were given for the oil-rich fish category, the seafood category, the milk or cream-based puddings and the cheese-based dishes. Further questions included information on consumption of organic milk (never, sometime, often, always), and salt usage habits and salt brand. Frequency of consumption of goitrogenic foods was also assessed alongside iodine-rich foods consumption (5 separate food categories) however, this does not form part of this report.

Frequencies of intake were recorded per day, or per week, or per month, according to eight categories, from less than once a month to more than 6 times per day. The Windiest 2005 database (Robert Gordon University, UK) was searched for all foods relevant to each category, and average portion size and iodine content of a portion was derived. For each participant, total number of servings per month for all eight food categories was calculated, and the daily estimated iodine intake calculated.

Food diaries

Participants completed an inventory of all food and drink consumed, with semi-quantitative estimation of portion sizes on two occasions for 4 days each with at least one week between each recording. Each 4-day period included at least one weekend day. Food diaries were analysed with the Windiet 2005 software to estimate average daily iodine intake.

Urine collection and iodine measurement

Two 24 hour urine collections were collected, on non-consecutive days. The first urine collection occurred prior to the participant recording their diet on food diaries. The second urine collection occurred on the fourth day of the food diary. The urine collections were kept in an opaque container placed in a cool-bag, aliquoted and stored at -80C until analysis. Urinary iodine was measured using a microplate adaptation of the Sandell-Kolthoff colorimetric method (Ohashi et al., 2000). The CV% of the assay was 2% at 125ug/L, 2% at 62.5ug/L and 19% at 15.5ug/L. Samples were analysed in triplicates, with all samples from the same participant analysed in the same batch.

Statistics

Analyses were carried out in SPSS (v18 SPSS Inc., Chicago IL, USA). Normality was tested using the Shapiro-Wilks test. Descriptive statistics were used to present the outcome variables, using medians and inter-quartile ranges. The Wilcoxon signed rank test was used to test the differences between the FFQ and the food diaries, and between the FFQ and urinary iodine. Relative agreement between methods was measured using correlation coefficients and cross-classification. The Spearman correlation coefficient was used to measure the agreement in ranking between the FFQ and each of the two other tools (food diaries and urinary iodine). To compare the classification of iodine intake according to FFQ, food diaries and urinary iodine, subjects were categorised into defined quartiles. Proportions of subjects categorised in the same, adjacent or extreme quartile were calculated. The Cohen's kappa coefficient was calculated for agreement, using counts allocated to either sufficient or insufficient categories. Subjects were categorised as having sufficient or insufficient iodine intake according to the following threshold: 140µg/day for the FFQ and the food diaries (Department of Health, 1991), and 100µg/L for urinary iodine. Specificity and sensitivity of the FFQ as a tool to measure iodine sufficiency was calculated against food diaries and urinary iodine as "gold-standard methods". Finally, validity coefficients were calculated using the Triad method (Ocke and Kaaks, 1997, Yokota et al., 2010), as implemented by others (Tan et al., 2013, Brantsaeter, 2009, Rasmussen et al., 2001), using a R script to generate the bootstrap sample used to obtain 95% CI (using Maximum Likelyhood Estimations which eliminate issues relative to negative correlations and validity coefficients above one, as explained by Brantstaeter et al. (2007).

Direction and magnitude of bias between FFQ and food diaries and FFQ and UI was assessed via graphical representation using Bland Altman plots (Martin Bland and Altman, 1986).

Results

A total number of 43 adult female participants, aged 19 to 49, took part in the validation study, from June to August 2012. Their median age was 27.0 (IQR 16.5), with a median weight of 60.6 kg and BMI of 22.6 (IQR 4.8). All had resided in Britain for at least 1 year, and were mostly white British (72%) or white Europeans (21%). Five participants reported smoking (average 5 cigarettes a day), and eleven had been pregnant in the previous 10 years. Seven followed a vegetarian diet (6 lacto-ovo-vegetarian and 1 lacto-vegetarian). None of the salt brand listed by participants included iodine, and 19 participants reported never adding salt to food, with a further 22 only occasionally adding it.

The questionnaire took between 3 and 5 minutes to complete. Fish and seafood contributed to only 12% (IQR35%) of the iodine intake measured with the FFQ, with milk contributing to half (47%) of the iodine provided by all dairy products (88%, IQR 35%).Median daily iodine intake was estimated at 110µg (IQR 69), using the FFQ µg and 103µg (IQR 64) with the food diaries (FD). These estimates were not significantly different (p=0.726).

Iodine intake assessed by the FFQ was moderately correlated with the iodine intake assessed by food diaries (r_s=0.452, p<0.001).

The median urinary iodine output was 74ug/L (IQR 44), calculated as 107µg/24hours (IQR 56) based on recorded urine volumes. Using the IOM equation (Institute of Medicine, 2001), this equates to an iodine intake estimated at 104.3µg/day for a population with a median weight of 60kg.

While iodine intake measured by food diaries was correlated with iodine excretion (µg/day) (r_s=0.396, p=0.009), there was no such correlation between UI (µg/day) and FFQ (p=0.316). There was however a significant correlation between FFQ and iodine excretion when expressed in ug/L (r_s=0.341, p=0.025).

Reliability of measures

The biases between FFQ and food diaries, and FFQ and UI are relatively small (11.8 and 16.2, respectively), as shown graphically using Bland Altman plots (Figure 1A&B), but with wide limits of agreement (-139; 163, and -163; 195, respectively).

Comparing classification of individuals to quartiles of iodine intake, there was good agreement between FFQ and food diaries, with 40% allocated to the same quartile, 42% to an adjacent quartile, and only 5% misclassification (allocation to extreme quartiles).The cross-classification agreement was not as good (but still acceptable) for FFQ and urinary iodine (µg/L), with 35% of individuals allocated to the same quartile, 37% to adjacent quartile and no (0%) misclassification.

The Kappa statistic test between FFQ and food diaries estimation of iodine intake was 0.229, indicative of fair agreement between the two methods. Using food diaries as the gold standard measurement, with a threshold of 140µg/day to classify iodine intake as sufficient, the FFQ had a specificity of 81% and a sensitivity of 42%.

Using the triad method, the validity coefficients were calculated for each of the three measurements (FFQ, food diaries and UI) and the true “unknown” Iodine value, according to the equations (1) to (3) outlined below (with U, the iodine defined by biological (urinary) marker; Q, the iodine defined by FFQ; and D, the iodine defined by food diaries. ”I” is the “true unknown iodine intake”) (Figure 2) (Yokota et al., 2010).

(1) $\rho QI = \sqrt{\frac{rQD\ .\ rQU}{rDU}}$

(2) $\rho DI = \sqrt{\frac{rQD\ .\ rDU}{rQD}}$

(3) $\rho UI = \sqrt{\frac{rDU\ .\ rQU}{rQD}}$

The validity coefficients ρ and associated CIs are presented in Table 1.

Discussion

Food frequency questionnaires are useful to gather data on habitual intake of foods relevant to the whole diet or specific micronutrients. Using food composition tables, they enable to estimate the habitual intake of particular micronutrients, with more or less precision, depending on the level of detail included in the questionnaire (portion size, frequencies of intake, number of items) and the quality of the instructions. They are easy to implement, demanding little resources or analytical power. It is however important to validate FFQs against accepted methods of dietary exposure, for a specific population and setting, in order to be able to draw conclusions from the use of the FFQ (Cade et al., 2002).

There are only two known iodine-specific FFQs (Rasmussen et al., 2001, Tan et al., 2013) one validated in Denmark, the other in Australia for older adults. In this paper, we present the validation of an iodine-specific questionnaire developed to measure habitual intake in females of childbearing age in the UK.

This food frequency questionnaire, focusing on selected iodine-rich foods, is short and fits on a single side of A4 representing a low burden for study participants. In comparison, the MoBa FFQ spans 11 pages and assesses total diet (Brantsaeter, 2009), the FFQ developed by Rasmussen et al. (2001) includes 53 items, and the Australian iodine FFQ includes 49-items and took 15 minutes to fill (Tan et al. 2013),. The study participants were young UK females, who, as a group, had a low UIC, indicative of insufficient iodine status, and had a median iodine intake below the recommended 140µg/day (assessed by FFQ and food diaries). This is consistent with previous reports of iodine status in the UK female population (Lampropoulou et al., 2012, Bath et al., 2008, Bath et al., 2010, Vanderpump et al., 2011). A major dietary source of iodine was milk, and fish or seafood only played a minor role for iodine provision, as observed previously (Tan et al., 2013, Rasmussen et al., 2001, Brantsaeter, 2009).

The three methods used to estimate iodine intake were in agreement. Correlation between iodine intake estimated by FFQ and food diaries was moderate (r_s=0.452) and in line with values reported by Tan et al., Brantstaeter et al. and Rasmussen et al. (with r_s between 0.37 and 0.52). The correlation between FFQ and iodine excretion (in µg/day) was not significant, contrary to the findings of Brantstaeter et al. and Rasmussen et al. (r_s 0.42 and 0.66, respectively). It was however significant when iodine excretion was expressed in µg/L. This may be partly explained by timing and number of 24h urine collections performed, as iodine excretion directly depends on short-term dietary intake. The DanThyr study also included PABA ingestion to check for 24-hour urine collection completeness, strengthening the validation protocol (Rasmussen et al. 2001). Similar to this study, Tan et al. did not observe a correlation between iodine intake estimated by FFQ and urinary excretion (µg/L), although this was assessed using repeated (n=3) spot urine samples. The correlation was however significant when excretion was corrected with creatinine.

This validation study is limited by its small sample size, however, the combination of the three methods to assess iodine status led to the use of the Triad (triangulation) method to generate validity coefficients. The validity coefficient generated for iodine intake estimated by FFQ using the Triads method (ρQI=0.66, CI 0.33 - 0.99) is consistent with those of Tan et al. (ρQI=0.40, CI 0.2 - 0.99) and Brantstaeter et al. (ρQI=0.62, CI 0.46 - 0.77). The small bias and large limits of agreement seen on the Bland altman plots however indicate that the FFQ may not be suitable to determine the daily iodine intake of individuals, but is a useful tool to estimate of daily iodine intake at population / group level. The FFQ performed well against both food diaries and iodine excretion for classification of intakes to quartiles, with 82% and 73%, respectively, being classified to the same or adjacent quartile. These results are in line with those obtained for the iodine questionnaire of Tan et al. and Rasmussen et al.

Further limitations include the non-inclusion of specific food items, such as eggs and salt. The contribution of egg to iodine status remains unclear. Vanderpump et al. (2011) showed a negative association between egg consumption and iodine status, while Bath and Rayman (2013) showed a positive association. Neither study, however, used a validated questionnaire for iodine intake. Salt intake was not quantified either in the FFQ, as there is no compulsory iodination of salt in the UK. Moreover, a majority of the study participants indicated to rarely use table salt. A longer, more detailed list of iodine-rich foods could have been drawn to improve accuracy; however, this would have increased the participant burden. No portion size was specified against the items listed, and including indicative portion size may improve accuracy too.

The use of 24-hour urine collection may not have accurately captured the urinary status of the volunteers, depending on days of collection, and several spot urine samples (at least ten, collected on different days) may have been a valid alternative way to estimate iodine status (Koenig et al., 2011). However, a strength of this validation study was its assessment of iodine using three methods. Both food diaries and urine collection were carried out twice, non-consecutively, with food diaries including week-end days. Iodine intake estimation took in consideration the consumption of organic milk, which has been shown to contain significantly lower levels of iodine compared to conventional milk (Bath et al., 2012).

Urinary iodine concentration (UIC) has been extensively used in the past years to study the iodine status of female populations across areas previously believed to be iodine replete. However, there is an inherent risk of over-interpretation when using data generated for a group and relying on a single spot sample. While statistical methods are available to correct for inter and intra—individual variability, these require repeat samples (Mackerras et al., 2011, Subcommittee on Interpretation and Uses of Dietary Reference Intakes and Standing Committee on the Scientific Evaluation of Dietary Reference Intakes, 2003). On the other hand, a simple FFQ can be a powerful tool to estimate habitual iodine intake, over a longer period than can be assessed using UIC or food diaries, and to classify individuals according to their intake.

This FFQ is a useful tool relying on a succinct list of iodine rich-foods. Its restricted number of food item did not translate in compromised performance compared to longer questionnaires. This is particularly advantageous for large population studies which require a rapid method to estimate habitual dietary intake.

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Table 1: Validity coefficients obtained for the three iodine assessment methods, calculated using the Triad method (n=43).

	Validity coefficient	**95% CI (percentage)**	**95% CI (MLE)**
ρ Q.I	0.66	0.20 – 1.00	0.33 – 0.99
ρ D.I	0.69	0.24 – 1.00	0.35 – 0.99
ρ U.I	0.52	0.11 – 0.80	0.21 – 0.80

Q: food frequency questionnaire; D: food diaries; U: biomarker (urinary iodine); I: true "unknown" iodine intake; CI: confidence interval, calculated with either the percentage method, or the Maximum Likelihood Method (MLE).

List of Figures

Figure 1A&B: Bland Altman plots showing bias between FFQ and food diaries (A) and FFQ and UI (B)

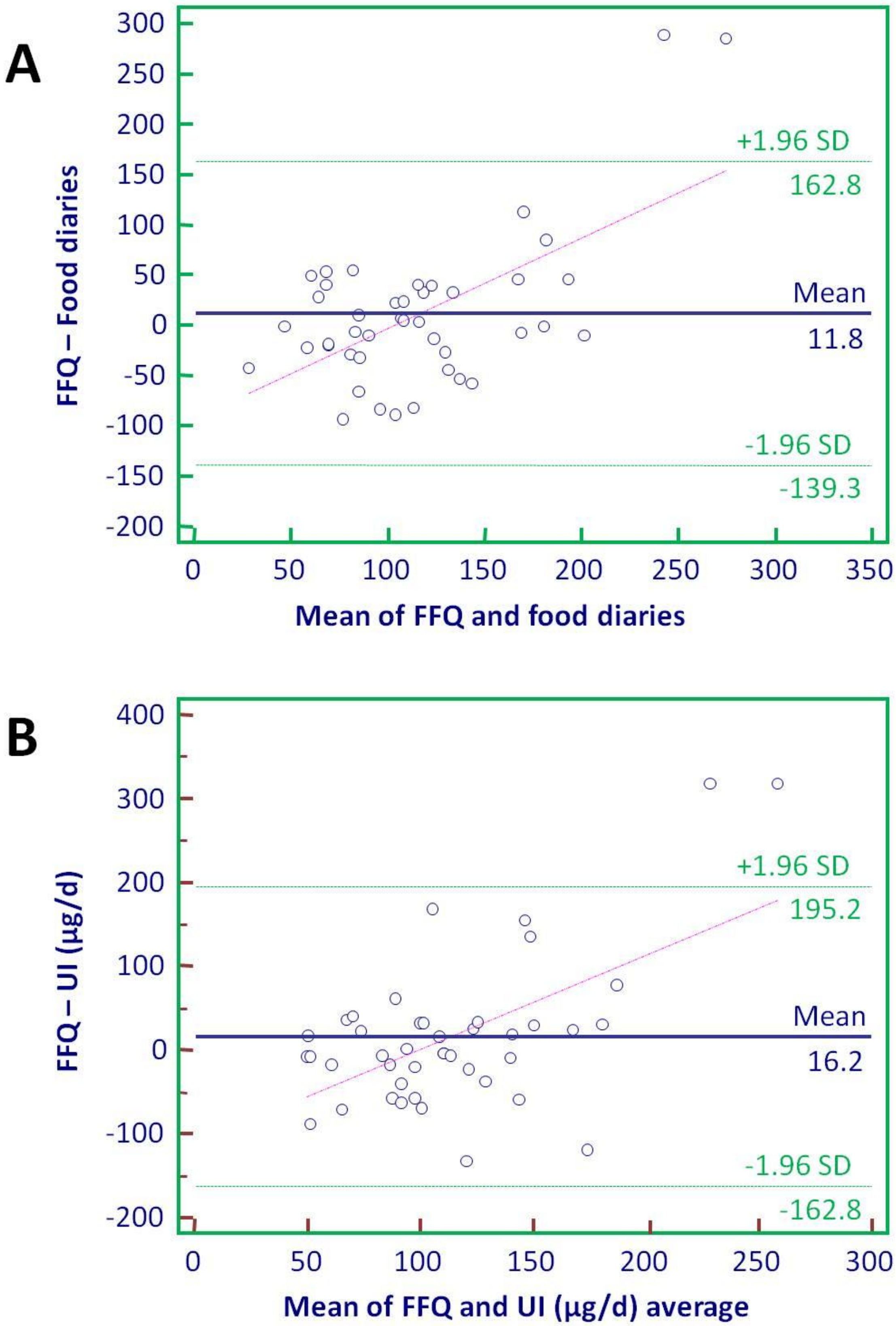

Figure 2: Graphical representation of the Triads methods, with the true iodine intake, I, at the center, and the iodine intake estimated using FFQ (Q), urinary iodine (U) and food diaries (D). The relationships between each two estimation method is denoted by the correlation coefficient r (rQU, rQD, rDU) outside the triangle, while validity coefficients between each estimate and the true intake I are shown inside the triangle (ρQI, ρDI, ρUI) (based on Yokota et al. 2010).