Estimating inadequate and excessive iodine intakes from the distribution of urinary iodine concentrations

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This study proposes a new approach to estimating the number of individuals with deficient or excess iodine intakes in a population based on the adjusted UIC distribution from spot urine samples.

Because both deficient and excessive iodine intakes can have adverse health consequences, it is important to assess habitual iodine intakes in populations. The urinary iodine concentration (UIC) is a reliable biomarker of recent iodine intake in populations at all levels of intake, because >90% of ingested iodine is excreted in the urine in the subsequent 24–48 h. But accurate dietary assessment of habitual iodine intake at the individual level is difficult because day-to-day variation in iodine intake is high. In iodine-sufficient countries where most iodine intake comes from iodized salt, UIC (both spot and 24-h urine collections) show an individual day-to-day variation of 30–40% *(1)*.

UIC surveys in school-age children are the recommended method to monitor iodine nutrition in populations, and the median (mUIC) is a reliable population indicator of iodine status; a mUIC of 100–199 μg/L in school-age children indicates adequate iodine nutrition. Unfortunately, the distribution around the mUIC in surveys is often misinterpreted in an attempt to define the number of individuals who are deficient (those with a spot UIC <100 μg/L) or have excess intakes (those with a spot UIC ≥300 μg/L). In an individual whose average daily iodine intake is adequate to maintain euthyroidism, the expected daily variation will result in many individual days when a UIC value will be less than adequate. Thus, even in populations in which iodized salt ensures adequate thyroid stores, there will nearly always be individuals with a UIC <100 μg/L on the day of the survey, but they should not be classified as iodine deficient.

Accounting for within-person variation using repeated urine samples

Nutrient inadequacy of habitual dietary intakes is conventionally assessed by the Estimated Average Requirement (EAR) cutoff method, using the population distribution of intakes; the percentage of individuals with usual intakes below the EAR are at risk of nutrient deficiency, and intake is satisfactory when 97–98% of individuals meet the EAR *(2)*. This method could be applied to the distribution of iodine intakes calculated from UIC distributions *(3)*. However, without accounting for within-person variation, the EAR cutoff method will usually overestimate the prevalence of deficiency *(4)*. Thus, iodine intakes calculated from the UIC distribution need to be adjusted for within-person variation. Within-person variation can be calculated if repeat UIC samples from the same individual in a subset of the study population are collected, and its effect on the distribution can then be adjusted statistically to more closely resemble the distribution of habitual intakes *(4)*. The prevalence of iodine deficiency could then be defined as the proportion of the population below the EAR from the adjusted distribution. A similar approach, applied to the upper tail of the UIC distribution, could be used to compare intakes with the Tolerable Upper Intake Level (UL) for iodine to estimate the prevalence of excessive intakes. The aim of this study was to use the EAR/UL cutoff method and internal within-person variance to develop a new approach to estimate the prevalence of deficient and excessive iodine intakes from distributions of UIC in school-age children.

Estimating iodine intake from UIC

The authors used unpublished data from 4 large national studies of school-age children in Kuwait (carried out in 2014), Oman (2014), Thailand (2012), and Qatar (2014), and a large regional survey in China. The ages of children in these studies were 6–12 y in Kuwait, 6–14 y in Oman, 5–13 y in China and Thailand, and 4–14 y in Qatar. The investigators at each site were asked to collect repeat urine samples in ≥10% of the subjects. According to the WHO classification, Kuwait, Oman, and China with mUICs of 131.6, 191.5, and 198.7 μg/L, respectively, would be classified as having "adequate iodine intakes," Thailand with a mUIC of 261.5 μg/L as having "more-than-adequate" iodine intakes, and Qatar with a mUIC of 333.2 μg/L as having "excessive" iodine intakes. The study used the EAR and UL for iodine established by the US Institute of Medicine (IOM) *(5)*. The EARs for iodine for girls and boys aged 4–8 y and 9–13 y are 65 and 73 μg/d, respectively. The ULs for iodine for girls and boys aged 4–8 y and 9–13 y are 300 and 600 μg/d, respectively. The authors used the following equation to calculate the daily iodine intake from a spot urine sample as proposed by the US IOM *(5)*:

Iodine intake (μg/d) = UIC (μg/L)/0.92 · (0.0009 L · h^{-1} · kg^{-1} · 24h · d^{-1}) · weight (kg)

In this equation, 0.92 refers to 92% bioavailability and 0.0009 L · h^{-1} · kg^{-1} refers to excreted urine volume from studies in children *(6)*.

> **"Adjusting for within-person variability sharply lowers the estimated prevalence of inadequate iodine intakes"**

The iodine intake distributions were extrapolated from the single spot urine sample using the Iowa State University method *(2, 7)*. An estimate of variance from the subsample in which repeated urine samples were collected was applied to the entire population. After this adjustment, the distributions were compared with the EAR and the UL cutoffs (demonstrated in *Figure 1* using data from the Kuwait survey). The resulting proportion of children with daily iodine intakes below the EAR and above the UL are shown by age group and country *(Table 1)*:

(1) without adjustment, based on a single UIC sample,
(2) after adjustment for internal within-person variance.

Improving the estimate of iodine intake in populations

This promising approach to improving iodine monitoring in populations may allow iodized salt program managers to estimate the average increase in daily iodine intake in the population needed to reduce the prevalence of usual iodine intakes below the EAR to <3%, indicating overall adequate iodine intake. Conversely, in countries that have high iodine intakes, a similar approach to compare the UL with the current 97.5th percentiles of intake could predict the decrease in dietary iodine needed to achieve only 2–3% of intakes above the UL. In addition, by accounting for intra-individual variation, it may be possible to reduce the required sample size in UIC surveys to less than the >500 samples now recommended for population assessment. Future studies should determine the minimum number of repeat urine samples needed to estimate within-subject variation. The relation between body weight and daily urine volume should be validated in different settings around the world. Finally, all of these questions need to be tested in other populations with different iodine status and different diets.

FIGURE 1 **The distribution of iodine intakes among children aged 4–8 y in Kuwait (n = 1841) derived from a single spot urine sample (broken line) and after adjustment for within- and between-subject variation (unbroken line). The Estimated Average Requirement (EAR) for children aged 4–8 y is 65 and the Tolerable Upper Intake Level (UL) is 300 μg/d.**

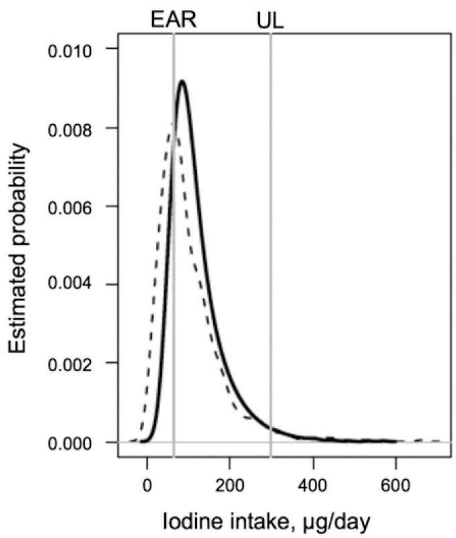

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TABLE 1 **Prevalence of inadequate iodine intake by the EAR and UL cutoff method with the use of internal variance estimates to adjust the usual intake distribution in children aged 4–8 and 9–13 y in Kuwait, Oman, and China. Values are means ± SE.**

Age group of children	Unadjusted prevalence below the EAR	True prevalence below the EAR, adjusted with internal variance	Unadjusted prevalence above the UL	True prevalence above the UL, adjusted with internal variance
4-8 y				
Kuwait	35.3 ± 1.7	19.4 ± 5.7	2.4 ± 0.5	0.2 ± 0.4
Oman	24.3 ± 1.8	7.5 ± 4.7	2.7 ± 0.7	0.2 ± 0.5
China	20.5 ± 2.5	10.1 ± 4.4	10.2 ± 1.9	8.2 ± 4.0
9-13 y				
Kuwait	30.9 ± 1.4	17.4 ± 3.6	0.7 ± 0.2	0.1 ± 0.1
Oman	18.6 ± 1.1	10.5 ± 2.1	0.4 ± 0.2	0.2 ± 0.2
China	24.0 ± 3.9	3.5 ± 7.3	1.7 ± 1.2	0.0 ± ND

EAR, Estimated Average Requirement; ND = SE not determined; UL, Tolerable Upper Intake Level.