Longitudinal examination of 24-h urinary iodine excretion in schoolchildren as a sensitive, hydration status–independent research tool for studying iodine status1–3

Thomas Remer, Nadine Fonteyn, Ute Alexy, and Shoma Berkemeyer

ABSTRACT
Background: Because worldwide iodine status (IS) depends on continuous fortification, the adequacy of IS needs to be regularly monitored.

Objective: Our study aimed to evaluate IS in a longitudinal sample of healthy schoolchildren who regularly used table salt iodized with 20 μg I/g.

Design: Urine osmolality (Uosm) and 24-h urinary excretion rates of iodine (24-h UI), sodium, creatinine, and total urine volume (24-h Uvol) were measured in 1046 specimens that were collected at repeated intervals from 1996 to 2003 in a sample of 358 German children aged 6–12 y. Energy intake and food consumption were calculated from 3-d weighed dietary records that were collected in parallel to the urine samples.

Results: During the 4-y period from 1996 to 1999, the median 24-h UI increased from 87 to 93 μg I/d (P = 0.017), whereas urinary iodine concentration (UIC), Uosm, and 24-h Uvol did not change significantly. Thereafter (from 2000 to 2003), UIC stagnated and Uosm decreased (P = 0.004), whereas 24-h Uvol (P = 0.008) and 24-h UI (P = 0.002) increased. The final median 24-h UI reached 120 μg I/d. Milk, fish, egg, and meat intakes and 24-h sodium excretion were all significant predictors of IS, with an almost doubled contribution from milk intake during the second 4-y period.

Conclusions: Our study shows a continuous improvement of IS in a longitudinal sample of German schoolchildren. This improvement was masked when UIC was used as an IS index, especially from 2000 to 2003 because of changes in hydration status. Thus, in research-oriented studies that focus on UIC measurements, hydration status can be a relevant confounder. Longitudinal analyses of 24-h UI in cohort studies may represent an alternative hydration status–independent tool to examine trends in IS and the contribution of relevant foods to IS. Am J Clin Nutr 2006;83:639–46.

KEY WORDS Children, iodine status, long-term trend, sodium excretion, dietary intakes, 24-h urine sample, urinary iodine concentration, urine osmolality, animal foods

INTRODUCTION

Iodine is an essential nutrient required for normal thyroid function, growth, and development. Even mild iodine deficiency seems to be causally involved in hearing impairment (1) and in the reduction of the intelligence quotient (2) in children. Despite such consequences, iodine deficiency is still a worldwide health problem (3). The adequacy of iodine status (IS), which depends on continuous fortification measures, needs to be regularly monitored (4, 5). The decrease in IS seen in New Zealand (4, 6) and the United States (7) underlines the importance of systematic checks.

Until recently, even Germany was an iodine-deficient area (8). A nation-wide study in 1996 showed that, although iodine concentrations in the population had improved compared with previous surveys, a ≈30% deficit in the recommended iodine intake still remained (8). Improved legislation in 1993 regarding the use of iodized salt in industrial food production was primarily responsible for the improvement in IS seen in 1996 (9). Accordingly, a clear decrease in the thyroid gland size of adolescents was discernible between 1993 and 1997 (10). In Germany, the use of iodized salt is voluntary. For more than a decade, both table salt and salt used in the food industry were iodized according to food legislation at a constant level of 20 μg I/g salt (allowed range: 15–25 μg I/g). Additionally, from 1995 until now, consumption of iodized salt in German households was shown to be relatively constant, ie, between 70–80% of total table salt consumption (11, 12). The food production industry in Germany has also kept to an almost constant yearly usage of 35% iodized salt in their total salt usage since 1995 (11, 12). Despite this, a recent publication that summarized spot urine measurements of different cross-sectional studies reported an abrupt increase in urinary iodine concentration (UIC) in German schoolchildren from a median level of 83 μg I/L in 1996 to 148 μg I/L in 1999, which was then followed by a decrease to 125 μg I/L in 2003 (12).

To specifically examine the long-term trends in IS from 1996 to 1999 and from 2000 to 2003, we studied the 24-h urinary iodine excretion (24-h UI) in a sample of German schoolchildren who were followed longitudinally over the respective 8-y period. This allowed us to compare the UIC, which is the most commonly measured variable for the assessment of IS, with the actual 24-h UI. Additionally, the hydration status and the contributions of urinary sodium output and energy-adjusted intakes of foods particularly relevant to daily iodine excretion were examined. In

1 From the Research Institute of Child Nutrition, Dortmund, Germany.
2 Supported by the Ministry of Science and Research North Rhine-Westphalia, Germany.
3 Reprints not available. Address correspondence to T Remer, Research Institute of Child Nutrition, Department of Nutrition and Health, Heinsteuck 11, D-44225 Dortmund, Germany. E-mail: remer@fke-do.de.
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the present analysis of a subsample of the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study, our objective was also to examine the suitability of a longitudinal analysis of 24-h urine samples and dietary records as a potential research tool for studying the relevant trends in IS and identifying the major foods contributing to IS.

SUBJECTS AND METHODS

Subjects

The children were selected from the ongoing longitudinal DONALD study on the basis of age (6–12 y) to exclusively study school-aged children. DONALD is a longitudinal (open cohort) study that collects data on anthropometric measurements, 3-d weighed dietary records, and 24-h urine samples. The children visit the Research Institute of Child Nutrition, Dortmund, once a year for examinations and assessments. At each evaluation, interviews on lifestyle and health-related issues, such as the use of iodized salt at home, and a medical examination are conducted. Because of the open cohort design of the DONALD study, the number of subjects of the present subsample varied each year, with new 6-y-olds entering and older 13-y-olds leaving the study during the 1996 to 2003 period under consideration. Within this time period, each subject had a minimum of 1 and a maximum of 7 potential measurements. Generally, in the DONALD study, children provide a 3-d weighed dietary record and collect a 24-h urine sample around their birthday. Because of the voluntary character of the DONALD study, some children provide either only a dietary record with no urine sample or vice versa or they provide both but not at the same time. Total dropout rates (no dietary record and no urine collection at all) are low in young (school-age) children compared with adolescents (13). Furthermore, not all families use iodized table salt. Thus, additional inclusion criteria for the present study were the use of iodized table salt at home and a 3-d weighed dietary record collected in parallel with a 24-h urine sample. Four hundred thirty-two children were eligible according to the criterion of age and the criterion that they had ≥1 dietary record within the 8-y observation period. Six of the 432 children did not regularly use iodized table salt and were excluded from the study. Of the remaining 426 children with a total of 1545 three-day dietary records, 68 children did not have simultaneous 24-h urine collections and dietary records and were excluded from the study. All 358 remaining subjects (178 boys and 180 girls), with a total of 1046 complete observations (both 24-h urine samples and dietary records), were included in the study. The number of dropouts, whether because of older age or a lack of both urinary and dietary data, was relatively evenly spread during the study period. The number of included observations (corresponding to the number of subjects) in 1996 and 1997 was 136 and 129, respectively, and was 132 and 126 at 2002 and 2003 (the end of the 8-y period), respectively. All examinations and assessments for DONALD are performed with both parental and children’s consent. The study was approved by the institutional review board of the Research Institute for Child Nutrition Dortmund.

Urine collection

For the 24-h urine collection, the children and their caregivers received personal and written instructions on how to collect complete samples. The children were instructed to void their bladder in the morning after arising. This micturition was completely discarded and the time was noted as the start time of urine collection. For the next 24 h, all micturitions were collected, including the first void of the following morning. The samples were immediately stored in preservative-free, Extran-cleaned (Extran, MA03; Merck, Darmstadt, Germany) 1-L plastic containers at −12 °C before transfer by a dietitian to the research institute. The dietitian reviewed the child’s compliance with the family and discussed the completeness of the urine collection (14). At the institute, the urine samples were stored at ±20 °C until analyzed.

Measurements

Body weight was measured with an electronic scale (Seca 753E; Seca Weighing and Measuring Systems, Hamburg, Germany) to the nearest 0.1 kg, and standing height was measured to the nearest 0.1 cm with a digital telescopic wall-mounted stadiometer (Harpenden, Crymch, UK). UIC was measured by a modified Sandell–Kolthoff method after acidic wet-washing of the samples (15, 16). Creatinine was measured by the Jaffé method with the use of a Beckman-2 creatinine analyzer (Beckman Instruments Inc, Fullerton, CA), and sodium was measured by flame atomic absorption spectrometry with a Perkin Elmer 1100 Spectrometer (Perkin Elmer, Überlingen, Germany). Additionally, urine osmolality (Uosm) was measured in all samples (Osmometer OM 802-D; Vogel, Giessen, Germany). Uosm and 24-h urine volume (Uvol) were used to assess hydration status (17, 18).

Dietary survey

Three-day weighed dietary records were used to collect information on food and nutrient intake from the participants of the DONALD Study. The dietary record started 2 d before the 24-h urine collection; ie, the third day of the dietary record corresponded to the day of the urine collection. The children decided themselves what day of the week they would begin to collect the diet record. In the present sample, all days of the week were nearly equally represented; representation ranged from 11% to 14%, and Fridays had 18% representation. The record comprised all food and beverage intake, including tap and mineral water, as well as out-of-home food consumption. The parents and children were instructed on how to use digital food scales and to record the weight of foodstuffs to the nearest 1 g. Recording comprised not only the quantity of food, but also product information, such as brand name, time and location of eating, and recipes. After the 3 d, a dietitian visited the families to pick up the dietary records and, as mentioned before, the 24-h urine samples.

The dietary records were coded and linked to the institute’s own nutrient database, named LEBTAB, to calculate the energy and nutrients intakes (19). Salt intake could not be quantitatively recorded. Therefore, salt intake was calculated from urinary sodium measurements.

Statistical analysis

SAS version 6.12 (SAS, Cary, NC) was used for the data analysis. Food and nutrient intakes were calculated as individual mean values of the 3 record days. Data are presented as means ± SDs with the exception of the iodine excretion variables,
Urine osmolality (mosm/kg) 772.5

which—according to standard practice—are also given as median values with interquartile ranges. In this context, the 20th and 80th percentiles were additionally presented for UIC measures to directly check whether <20% of the children were below the World Health Organization (WHO) lower UIC cutoff of 50 µg/l/L. All statistical analyses, including those on the iodine variables, were performed by using the arithmetic mean values. Sex differences (for the initial description of the sample characteristics) were tested with an unpaired t test. Preliminary analyses of age dependency of different iodine excretion variables were done cross-sectionally (with only one urine sample randomly selected for each child) with the use of simple regression analysis. The chi-square test was used to assess whether the urine specimens and parallel dietary data, which were collected throughout the year, were evenly distributed across the seasons. Because the proportions were not equally distributed (P = 0.0024; n = 1046)—with 23.8% attributable to the January-March season, 20.8% to April-June, 26.9% to July-September, and 28.5% to October-December—all subsequent analyses that used PROC MIXED (see below) were carried out including season as a covariate.

To avoid correlated measurement errors for the association between urinary sodium excretion and urinary iodine excretion (measurements in the same urine sample), 24-h urinary sodium output was corrected for 24-h creatinine excretion. From this sodium-to-creatinine ratio, daily sodium excretion was estimated with the use of published anthropometric-based reference values for renal 24-h creatinine output for healthy children and adolescents (14). A correction of dietary intakes and 24-h urinary analyte excretion rates for total energy intake was performed with division of individual intakes or excretions with individual energy intake. Standardization of dietary intakes and 24-h urinary excretions was performed by multiplying the energy-corrected values with the age group and sex specific reference energy intake (20).

For the longitudinal analysis of time trends of 24-h Uvol, Uosm, and IS (energy-corrected 24-h UI, energy-standardized 24-h UI, and UIC), the mixed linear model PROC MIXED was used, which included the covariates sex, age, season, and y (trend) in all cases. This model allowed for the inclusion of time-varying covariates in the mean structure and repeated measurements in the same subjects. In contrast to other models, eg PROC GLM for balanced longitudinal data, the PROC MIXED model uses all available data and not only the complete cases (21). Hence, children for whom measurements are lacking at certain time points are still taken into account in the analysis. The main strength of PROC MIXED is that it does not assume that an equal number of repeated observations is taken from each person or that all persons should be measured on the same time points (21). Accordingly, the measurements can be viewed as being taken at a continuous, rather than a discrete, time scale (21). The level of significance was set at P < 0.05.

RESULTS

Mean (±SD) age, weight, height, dietary intakes, and urinary excretion variables for the children at the time of their first 24-h urine collection within the 1996 to 2003 period (when the children were aged ≥6 and ≤12 y) are shown in Table 1. Median values and interquartile ranges of the iodine excretion variables are presented in the footnotes of Table 1. The boys did not differ significantly from the girls with regard to age, weight, height, or
energy-corrected 24-h UI and sodium excretion. For the foods examined, only absolute daily milk intake differed significantly between the sexes. The median UICs of the boys and girls were slightly above the target minimum of 100 μg I/L, as recommended by the WHO for the median UIC in populations with sufficient IS.

As discernible in Figure 1, a significant age dependency existed for urinary iodine when expressed as absolute daily excretion rate and after correction for creatinine excretion. No variation with age was present for UIC or energy-corrected 24-h UI in this preliminary cross-sectional analysis. The inclusion of all samples, analyzed with the PROC MIXED procedure, yielded a small but significant improvement in iodine supply (assessed as the energy-corrected 24-h UI) between 1996 and 1999 and a clear increase between 2000 and 2003 (Figure 2). The corresponding time trend is also shown together with additional predictors of iodine status in Table 2. All dietary variables, but not sex, age, or season, were significantly and independently associated with 24-h UI for the whole observation period. During the first 4-y period, 1-g sodium excretion increase was associated with a rise in the 24-h UI (12.75 μg I/d; Table 2) that was ≈3-fold that observed after a 100-g milk consumption increase (0.04 μg

**FIGURE 1.** Cross-sectional analysis of age dependency of different urinary iodine (UI) variables during 1996 to 1999 (n = 186) and 2000 to 2003 (n = 172). Each point represents one randomly selected urine sample per child. Each child is represented only once in one or the other set of graphs; boys •; girls ○. UIC, urinary iodine concentration.
iodine · d\(^{-1}\) · g milk\(^{-1}\); Table 2). The contribution of egg intake (on a 100 g/d basis) to the 24-h UI corresponded to 1 g sodium excretion, whereas meat intake appeared to contribute less. The contribution of animal food intakes to IS, as shown by the regression coefficient $\beta$, nearly doubled for milk intake and rose about 1.5-fold for egg intake in the 2000 to 2003 period compared with the 1996 to 1999 period. When the model, which additionally included milk-by-time and eggs-by-time interactions, was run again for the whole observation period, the change in the contribution of milk and eggs to IS (as indicated by their interaction terms) was significant for milk ($P = 0.0001$), but not for eggs ($P = 0.9$).

The 24-h UI of the children, after standardizing to the average energy intake of 12-y-old children (9 MJ/d) (20), was compared with the WHO recommendation of daily iodine intake for 6–12-y-old children (Figure 3). Apart from the trend already seen in Figure 2, it is evident from Figure 3 that, until 1999, >50% of the children had 24-h UIs <100 $\mu$g I/d (which approximately corresponds to the recommended daily intake of 120 $\mu$g I/d for 12-y-olds). According to the population-based WHO criteria for adequacy of IS, which is expressed in UIC, >50% and 80% of the children had a UIC of >100 and 50 $\mu$g I/L, respectively, for most of the years studied (Figure 3). Between 1996 and 1999, UIC, Uosm (Figure 3B), and 24-h Uvol (Figure 3) did not significantly change. During the following 4 y, the UIC stagnated and Uosm fell significantly (Figure 3B), whereas the 24-h Uvol clearly increased (Figure 3A).

**DISCUSSION**

Twenty-four-hour urine samples are considered to be the most reliable specimen for assessing the IS of persons (22–25). Both UIC and energy-corrected 24-h UI proved to be unrelated to age and qualified especially these variables—and not primarily the absolute 24-h UI and the iodine-to-creatinine ratio—for a direct age-independent assessment of IS. Our 24-h UI measurements corrected for energy intake did not confirm the abrupt increase in UIC in schoolchildren between 1996 and 1999 and the subsequent fall in 2003, as reported by Hampel and Zöllner (12). Other cross-sectional, mostly regional, studies from Germany that also examined spot urine samples found continuous improvements in IS in schoolchildren after 1996 (11, 26), which agrees with our longitudinal 24-h UI data.

Even so, longitudinal studies are inherently nonrepresentative; the analyzed 24-h UI of our children in the year 1996 corresponded closely to the mean 24-h UI of 125 $\mu$g I/d that was

### TABLE 2

Predictors of energy-corrected 24-h urinary iodine excretion ($\mu$g · MJ\(^{-1}\) · d\(^{-1}\)) in 358 children with multiple urine samples collected between 1996 and 2003\(^1\)

<table>
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<tr>
<td></td>
<td>(n = 255 children; 552 samples)</td>
<td>(n = 231 children; 494 samples)</td>
<td>(n = 358 children; 1046 samples)</td>
</tr>
<tr>
<td>β(^2)</td>
<td>P</td>
<td>β(^2)</td>
<td>P</td>
</tr>
<tr>
<td>Sex</td>
<td>−0.30</td>
<td>0.40</td>
<td>0.05</td>
</tr>
<tr>
<td>Age (y)</td>
<td>−0.02</td>
<td>0.79</td>
<td>−0.13</td>
</tr>
<tr>
<td>Season(^2)</td>
<td>—</td>
<td>0.83</td>
<td>—</td>
</tr>
<tr>
<td>Time (y, since 1996)</td>
<td>0.39</td>
<td>0.004</td>
<td>0.56</td>
</tr>
<tr>
<td>Sodium excretion (g · MJ(^{-1}) · d(^{-1}))(^4)</td>
<td>12.75</td>
<td>&lt;0.0001</td>
<td>12.03</td>
</tr>
<tr>
<td>Fish (g · MJ(^{-1}) · d(^{-1}))(^5)</td>
<td>0.30</td>
<td>0.0006</td>
<td>0.39</td>
</tr>
<tr>
<td>Milk (g · MJ(^{-1}) · d(^{-1}))(^6)</td>
<td>0.04</td>
<td>&lt;0.0001</td>
<td>0.07</td>
</tr>
<tr>
<td>Eggs (g · MJ(^{-1}) · d(^{-1}))(^7)</td>
<td>0.12</td>
<td>0.08</td>
<td>0.18</td>
</tr>
<tr>
<td>Meat (g · MJ(^{-1}) · d(^{-1}))(^8)</td>
<td>0.06</td>
<td>0.03</td>
<td>0.07</td>
</tr>
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\(^1\) 128 children (35.8% of the total number of children) were represented in both time periods.

\(^2\) β denotes the regression coefficient based on PROC MIXED statistic.

\(^3\) Season 1–4: January to March, April to June, July to September, and October to December.

\(^4\) Estimated by the sodium:creatinine ratio by using age- and sex-specific creatinine reference values corrected for body weight (14).

\(^5\) Only saltwater fish products.

\(^6\) Only whey-based milk products.

\(^7\) Eggs and egg products.

\(^8\) Meat and meat products.
estimated from spot urine samples of a military conscripts subgroup in a 1996 representative German survey (8) (the average 24-h UI of the DONALD children was 130 μg I/d after standardization to an energy intake of 12.5 MJ/d for young men). This, and the fact that our iodine excretion data for the year 2000 were pronounced between 2000 and 2003 than during the preceding years (Figure 2 and Figure 3). However, no corresponding increases were discernible for UIC, the recommended biomarker for the assessment of a population’s iodine nutrition (27–29). Because UIC, similar to the concentrations of other urinary analytes, can vary with fluid intake, the hydration status may have confounded the measurements. In fact, compared with international data, the total water intake of German children was still suboptimal in the late 1990s (30). The 24-h Uvol and Uosm analyzed in the present study strongly suggest that the modest positive trend observed for fluid intake until 1999 (30) continued. The culturally influenced and traditionally unfavorable drinking habits in Germany, which are comprehensively described by Manz and Wentz (31), appear to have begun to change consistently during the past years. Thus, the significant decrease in Uosm and increase in 24-h Uvol in our sample during the second period shows—contrary to what is generally assumed (27, 28)—that fluid intake–dependent variations in UIC do not necessarily level out. In accordance with this, Rasmussen et al (32) observed significant negative associations between thyroid volume and different measures of iodine intake, except for UIC.

In the period from 1996 to 1999, which was characterized by a more unfavorable hydration status than from 2000 to 2003, median UICs were mostly >100 μg I/L; however, in the same years, the 24-h UI was 100 μg I/d, which corresponds to the recommended daily iodine intake of 120 μg I/d (27, 33), for <50% of the children. Correspondingly, the present longitudinal research study showed, by means of 24-h urine analyses, that hydration status can confound the UIC-based assessment of IS.

In this context, however, it must be stated that 24-h urine collections are not a practical alternative to spot urine collections when large epidemiologic surveys are conducted. This is especially true when compliance to 24-h urine collections cannot be guaranteed, as, for example, in low-income areas, where appropriate freezing of the 24-h urine samples may not be possible but where iodine deficiency is probably most prevalent. The spot UIC method, which is recommended by WHO/UNICEF/IHCCD, has been successfully used to monitor the public health implications of iodine fortification measures worldwide, and this would have not been possible with 24-h collections given their marked financial, logistic, and compliance-related implications. Nevertheless, the hydration status should not be ignored if, for scientific purposes, more in-depth analyses of IS are performed, eg, if spot UICs of target groups with potentially different nutritional behavior or varying physiological water losses are compared. For this, the additional measurement of Uosm in spot samples would be an option, but it is time-consuming, relatively expensive, and requires trained laboratory technicians (17). Therefore, for detailed analyses on IS in low-income countries, low-cost hydration assessment techniques (eg, the determination of urine color or conductivity together with UIC measurements) could provide an alternative (17). Whether these relatively easily performed methods are sufficiently accurate to identify actual differences in hydration status between population groups needs to be tested in additional studies.

Our findings suggest that longitudinal studies such as the DONALD study—although not representative in an epidemiologic sense—can provide valuable research information on IS for specific population groups. This is not only because the analyses of 24-h specimens in a longitudinal cohort allow a more accurate assessment of IS, particularly the trends in IS, than do

![Figure 3](image-url)
the usual examinations of spot samples in cross-sectional surveys, but also because additional biomarkers can be examined for their relation to IS, which thereby avoids the problems due to confounding circadian rhythms (34). In our children, a relative constant portion of ≈12 μg of the daily excretion of iodine could be attributed to 1 g sodium excretion during both the 1996 to 1999 and the 2000 to 2003 periods. In Germany, the use of iodized salt is voluntary, and its iodine content, as regulated by food legislation (20 μg I/g table salt and salt used in the food industry), did not change during the total observation period.

Apart from salt intake (assessed via renal sodium excretion), intakes of fish, milk, eggs, and meat were all significant dietary predictors of the 24-h UI. Despite a very low average ingestion per day, saltwater fish proved to contribute the most to the iodine supply per 1-g food item ingested. The importance of milk as another major source of iodine was confirmed in different countries, including the United States (34–36). The contribution of milk intake to IS was one-third that of egg intakes; and between 1996 and 1999, intakes of ≈300 g milk or 100 g eggs were associated with almost the same increase in 24-h UI as was 1 g renal sodium excretion. Although the regression coefficients of sodium excretion, fish intake, and meat intake for 24-h UI were similar for both observation periods, it nearly doubled from 1996–1999 to 2000–2003 for milk intake. Accordingly, an increase in the iodine content of milk may have substantially contributed to IS improvement during the second 4-y observation period. Given an average milk intake of 300 mL/d (Table 1), the rise in the 24-h UI from 4 to 7 μg I/d for each 100-g increase in daily milk intake (Table 2) could explain one-third (9 μg I/d) of the average increase in iodine excretion observed between the end of the first and the second 4-y periods. Recent iodine measurements in cow milk samples (37, 38) confirmed concentrations of ≈70 μg I/L (compatible with the β of 0.07 observed for the period from 2000 to 2003; Table 2).

Animal feed legislation (which allowed a maximum of 10 mg I/kg of feed on a voluntary basis) did not change from 1997 to 2004; the milk processing and milk hygiene legislation also has not changed in the past 10 y. The teat sanitizer allowed in Germany has a relatively low iodine content (maximum: 0.3%), and only minor increases in milk iodine concentrations result from the regular practice of solely postmilking teat dipping (39). Thus, the observed increase in the iodine content of cow milk may arise from other reasons. In Germany, meat-and-bone meal (which has a low iodine content) has been prohibited for cattle feeding since 1996, but it was still allowed for nonruminant feed until 2000. Because meat-and-bone meal is an inexpensive source of protein and minerals, it could have been used not only for pigs and poultry, but illegitimately also for dairy cattle. Actually, in a regional Bavarian survey, 20% of the quality-controlled feed for dairy cattle still contained animal constituents even at the end of the year 2000 (40). Simultaneously, the production of commercial iodized mineral feed for cattle increased after 2000 (41), which would explain at least a part of the positive trend in the iodine content of milk.

A limitation of this longitudinal study was that the subjects moved in and out of the data pool over the observation period. However, the use of PROC MIXED analysis, which accounts for incomplete cases, reduces the potential biases due to this limitation. Taken together, repeated analyses of 24-h UI in longitudinal cohorts may allow a sensitive, research-based examination of trends in iodine nutrition and the contribution of relevant foods to it. If UIC is compared between different samples for scientific purposes, hydration status may confound the IS assessment and should be controlled for.

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TR, SB, and NF participated in the study conceptualization. UA and NF were primarily responsible for the statistical data analysis. TR and NF wrote the manuscript. Each of the authors made substantial contributions to the interpretation of the results. SB edited the manuscript. None of the authors had any conflicts of interest with regard to this study.

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