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ORIGINAL ARTICLE

Evaluation of urinary iodine excretion as a biomarker for intake of milk and dairy products in pregnant women in the Norwegian Mother and Child Cohort Study (MoBa)

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Background/Objectives: Milk and dairy products are the main sources of iodine in the Norwegian diet. This is due to a high consumption of milk and dairy products combined with a relatively high concentration of iodine in milk because of mandatory iodine fortification of cow fodder. The aim of the present study was to investigate the relation between 24-h urinary iodine excretion and estimated dietary intake, and to explore the use of 24-h urinary iodine excretion as a possible biomarker for the intake of milk and dairy products when assessing the validity of a new food frequency questionnaire for pregnant women participating the Norwegian Mother and Child Cohort Study (MoBa).
Subject/Methods 119 women participated in a validation study. Iodine was analyzed in 24-h urine. Dietary intakes were estimated by a food frequency questionnaire (FFQ) and a 4-day weighed food diary (FD). Using linear regression, predictors of urinary iodine excretion were identified. The triangular method was applied to calculate validity coefficients.
Results: Significant predictors of 24-h urinary iodine excretion were: intake of dairy products, iodine-containing supplements and intake of fruit/vegetables. Fish/seafood intake and time of the year influenced 24-h urinary iodine excretion, although not significantly. The validity coefficients observed for total intake of dairy products were 0.65, 0.94 and 0.52 for the FFQ, the FD and the 24-h urinary iodine excretion, respectively.
Conclusions: The present study showed that 24-h urinary iodine excretion may be a useful biomarker for validating the intake of milk and dairy products in pregnant Norwegian women.
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Introduction

Epidemiological studies indicate that fetal nutrition may influence fetal growth, development and the risk of various diseases later in life. Accordingly, the mother's diet during pregnancy is attracting increased interest, and reliable methods to monitor maternal food consumption are more important than ever.

In Norway, as in many other Northern European countries, milk and dairy product consumption is high and contributes significantly to the intake of energy, fat, protein and several vitamins and minerals. Few studies have examined the impact of maternal milk and dairy product consumption on fetal growth and health of the child later in life, but in the wake of several large ongoing pregnancy cohort studies, this can be expected in the future. Finding a biological marker in blood or urine directly reflecting the intake of milk and dairy products could therefore strengthen the validity of dietary assessment methods regarding the intake of this food group.

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Biomarkers for validation of nutrient intake are scarce, the most accurate findings being the recovery biomarkers, that is urinary nitrogen excretion for protein intake and doubly-labeled water for energy intake (Bates *et al*., 1997; Black *et al*., 1997). The fatty acid pentadecanoic acid (15:0), synthesized by bacteria in the rumen, has been used as a biomarker for intake of dairy fat in several studies (Wolk *et al*., 1998, 2001; Brevik *et al*., 2005; Biong *et al*., 2006). As low-fat milk comprises a large part of the total dairy product intake, a biomarker related to milk and total dairy product intake rather than milk-fat would contribute to better validation of this food group.

Iodine is not exclusively found in dairy products, but milk and dairy products are the primary source of iodine in the Norwegian diet due to mandatory fortification of cattle fodder ($2\,mg\ I^{-}\ kg^{-1}$) since 1950 (Frey *et al*., 1993). This has also been documented in other European countries and in the United States (Lee *et al*., 1994; Rasmussen *et al*., 2002; Als *et al*., 2003a; Girelli *et al*., 2004; Remer *et al*., 2006). The only good natural source of iodine is seawater fish and other marine products (Julshamn *et al*., 2001), but the intake of marine foods in Norway has declined over the last decades (Johansson and Solvoll, 1999). The contribution of iodine from drinking water and from iodine-fortified salt is negligible in Norway (Dahl *et al*., 2003b, 2004).

Twenty-four hour urinary iodine excretion is considered to be the best measure of iodine intake in an individual and reflects short-term (24 h) intake. (Thomson *et al*., 1996; Rasmussen *et al*., 1999; Als *et al*., 2003b; Remer *et al*., 2006).

The aim of the present study was to investigate the relation between 24-h urinary iodine excretion and estimated dietary intake, and to explore the use of 24-h urinary iodine excretion as a possible biomarker for intake of dairy products when assessing the validity of a new food frequency questionnaire.

Materials and methods

Subjects and design

The current study was part of a validation study of a new food frequency questionnaire (FFQ) developed for use in the Norwegian Mother and Child Cohort Study (MoBa). MoBa is an ongoing, long-term prospective cohort study that aims to include 100 000 pregnancies by the end of 2007. The objective of MoBa is to examine associations between exposures and diseases, aiming at prevention (Magnus *et al*., 2006). Healthy pregnant women in MoBa referred to Bærum Hospital (Norway) were invited to participate in the validation study when they came for routine ultrasound examination at 17–18 weeks of gestation. Exclusion criteria were hyperemesis and anorexia. Subjects had to have completed the MoBa FFQ before inclusion. The data collection was conducted between 15 January 2003 and 1 February 2004.

The women participating in the validation study were asked to provide one 24-h urine collection and to keep a 4-day weighed food diary (FD). Data on weight, height and age were recorded. Of 120 women included, one dropped out due to illness. The study protocol was approved by the Regional Ethics Committee of Southern Norway, and informed written consent was obtained from all participants.

Food frequency questionnaire

The MoBa FFQ (available online at http://www.fhi.no/dav/22CA50E0D7.pdf) was mailed to all participants around the fifteenth week of gestation. It is a semi-quantitative questionnaire designed to capture dietary habits and intake of dietary supplements during the first 4 months of pregnancy (Meltzer *et al*., 2008). The FFQ included six questions directly related to the use of milk as a beverage, three related to yoghurt, three related to butter, seven related to cheese, and 10 questions related to consumption of foods with a high content of milk or cream. For each food item, the frequency of consumption was reported by selecting one out of 8–10 frequencies, ranging from never to several times monthly, weekly or daily. For milk and yoghurt, portion sizes were given in the questionnaire, while for cheese, butter, desserts and other food items, standard Norwegian portion sizes for women were used. The questionnaires were optically read and, for nutrient calculations, FoodCalc (Lauritsen, 2005) and the Norwegian food composition table (Rimestad *et al*., 2001) were used. For calculation of dietary iodine, data from recent analyses of more than 100 food items were included (Dahl *et al*., 2003b, 2004).

Four-day weighed food diary

Participants in the validation study were asked to weigh and record all food, beverages and food supplements consumed during three consecutive weekdays and one weekend day. Each participant was given an FD and a digital balance and asked to continue with her normal food intake. Upon collection, each FD was checked for completeness by the nutritionist (ALB).

Iodine supplement use

Use of dietary supplements was recorded in both the FFQ and the FD. The amount of iodine provided by iodine-containing vitamin, mineral or herbal supplements was calculated separately. Iodine-containing supplements were recorded by 23 subjects in the FFQ and by 25 in the FD.

Determination of urinary iodine excretion

At the end of the FD period, each participant provided one 24-h urine collection taken on a weekday. An Agilent quadruple ICP-MS 7500c instrument (Yokogawa Analytical System Inc., Tokyo, Japan), which was used as

an iodine-specific detector for urinary determination, was run in the standard mode. In Table 1 the instrumental settings for the ICP-MS are given. Data were collected using the Agilent Chemstation ICP-MS chromatographic software (Julshamn *et al*., 2001; Dahl *et al*., 2003b, 2004). Certified reference material (CRM) (Seronorm Trace Elements; Nycomed, Norway) of iodine in human urine was included in each analytical series of 25 samples to control the systematic errors of the analytical method.

Statistical analysis

Urinary iodine excretion was normally distributed, while dietary intake of most nutrients and food groups were not normally distributed. Mean, median, 5 and 95 percentile values are presented. The mean difference in urinary iodine excretion between iodine and non-iodine supplement users was tested using independent samples *t*-test, while the differences between dietary estimates were tested using Wilcoxon's signed-rank test (paired data) and the Mann–Whitney *U*-test (unpaired data). P for trend in urinary iodine excretion across increasing quintiles of milk and dairy product intake was assessed by regression. Linear regression was also used to examine 24-h urinary iodine excretion as dependent variable, with the intakes of foods and iodine-supplement use as independent variables. Cooks' distance and diagnostic residual plots were computed to check the underlying linearity and constant variance assumptions of the models.

Spearman's correlations were calculated for urinary iodine excretion and intake of various food groups in participants taking no iodine-containing dietary supplements.

Validity coefficients (VC) were calculated according to the method of triads (Ocke and Kaaks, 1997). We used maximum likelihood estimation (Mardia *et al*., 1979) and bootstrap sampling with the statistical program R (R Development Core Team, 2005) to estimate VCs and 95% confidence intervals for these. Use of maximum likelihood estimation eliminated problems related to possible negative correlations or calculating validity coefficients larger than one, as explained elsewhere (Brantsæter *et al*., 2007).

Table 1 Instrumental settings for Agilent 7500c ICP-MS

ICP-MS settings	
RF power (W)	1550
Carrier gas flow (L min^{-1})	1.2
Plasma gas flow (L min^{-1})	15
Auxilary gas flow (L min^{-1})	1
Nebulizer	Babington nebulizer
Spray chamber	Water-cooled double pass
Spray chamber temperature (°C)	2
Interface cones	Platinum
Lens voltage (V)	2–3
Mass resolution (u)	0.8
Integration time (s)	1000

All analyses except bootstrapping were performed with SPSS, version 13 (SPSS Inc., Chicago, IL, USA). *P*-values <0.05 were considered statistically significant.

Results

Among the 119 participants there was large dispersion with regard to age (mean: 31 years, range, 23–44 years), weight (at time of FD: mean 70 kg, range, 52–111 kg), weight prior to pregnancy (mean: 65 kg, range, 47–116 kg) and height (mean: 1.68 m, range, 1.50–1.85 m).

The mean excretion of iodine in the 24-h urine collection was 146 μg (s.d. ± 87) in non iodine-containing supplement users ($n=94$) and 217 μg (s.d. ± 111) in iodine supplement users ($n=25$) at the time of the FD. The contribution of iodine from supplements significantly increased both iodine intake ($P<0.001$) and excretion ($P=0.001$) (Table 2). In one urine sample iodine was below the level of quantification.

The increase in urinary iodine excretion with increasing iodine supplied by dairy products is shown in Figure 1.

No statistically significant differences were found between the FFQ and the FD regarding daily intake of milk, butter or total dairy products (Table 3). The FFQ estimated higher intake of yoghurt and lower intake of cheese and milk foods (desserts, ice-cream, porridge, pancakes) compared with the FD ($P<0.05$ for all). The differences between intake estimates remained significant when adjusted for total energy intake.

Dietary sources of iodine calculated by the FFQ and the FD are shown in Figure 2. Dairy products contributed on average 58% of dietary iodine estimated both with the FFQ and the FD (s.d. ± 17%), with milk contributing 35%, cheese 12%, yoghurt 9% and butter/milk in other foods 2%.

Significant correlations between FFQ and FD measures were found for intake of dairy products, energy and nutrients (Table 3). The highest correlations were found for milk ($r=0.66$) and cheese ($r=0.51$). Correlation coefficients only improved slightly when intakes were adjusted for total energy intake (Table 3).

Urinary iodine excretion was significantly correlated to total intake of iodine, milk and total dairy products estimated with both the FFQ and FD. The correlation between intake of dairy products and urinary iodine excretion was higher for the FD ($r=0.48$) than for the FFQ ($r=0.34$) (Table 4). Urinary iodine excretion increased significantly with increasing quintiles of milk and total dairy product intake for the FFQ as well as for the FD ($P<0.05$ for all). This was found independent of whether iodine supplement users were excluded or not.

Using urinary iodine excretion as the dependant variable in a multivariable regression model and FD intakes as explanatory variables, significant predictors of urinary iodine excretion were intake of dairy products ($P<0.001$), intake of fruit/juice ($P<0.001$), iodine-containing supplement use ($P<0.001$) and season ($P=0.008$). Intake of fish/seafood and eggs influenced urinary iodine excretion, but

Table 2 Urinary iodine excretion and dietary iodine intake in non-iodine and iodine containing supplement users recorded by the food frequency questionnaire (FFQ) and the food dairy (FD)

		Non-iodine supplement users (n = *96 FFQ*, n = *94 FD*)						*Iodine supplement users* (n = *23 FFQ*, *n* = *25 FD*)						P-*value*[b]
		Median	*Mean*	*Min*	*Max*	*P5*[a]	*P95*[a]	*Median*	*Mean*	*Min*	*Max*	*P5*[a]	*P95*[a]	
Iodine excretion[c]														
Iodine in 24-h urine	μg per 24 h	118	146	0[d]	388	44	321	219	217	22	477	73	416	0.001
Iodine intake														
Iodine in diet, FFQ	μg day^{-1}	122	138	25	340	48	304	120	142	78	451	88	223	
Iodine in supplements, FFQ	μg day^{-1}	0	0					65	69	13	150	18	129	
Iodine total FFQ	μg day^{-1}	122	138	25	340	48	304	215	211	106	526	113	282	<0.001
Iodine in diet, FD	μg day^{-1}	120	117	42	222	54	196	113	125	72	205	82	184	
Iodine in supplements, FD	μg day^{-1}	0	0					94	89	8	150	15	150	
Iodine total FD	μg day^{-1}	120	117	42	222	54	196	213	214	103	355	107	323	<0.001

[a]P5 = 5th percentile, P95 = 95th percentile.
[b]Test of difference between iodine supplement users and non-iodine supplement users.
[c]Suppement users at the time of the FD.
[d]Below the level of quantification.

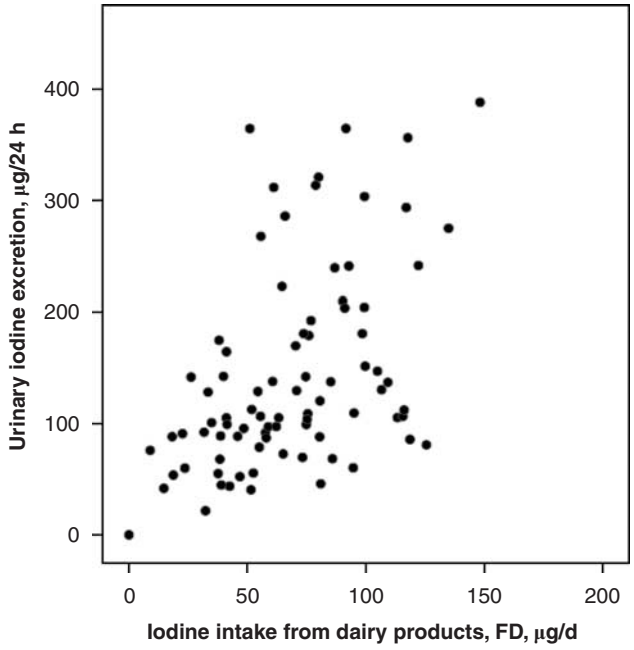

Figure 1 Urinary iodine excretion (*y* axis) plotted against iodine intake from dairy products assessed by the food diary in non-iodine supplement users (*n* = 84).

were not significant predictors (Table 5). When FFQ intakes were used in the model significant predictors were intake of dairy products ($P = 0.003$), intake of fruit/juice ($P = 0.032$) and iodine-containing supplement use ($P < 0.001$). When the dairy food category was divided into separate variables for milk, cheese and yogurt, milk was the only significant predictor and nearly identical betas as for total dairy products were obtained (data not shown).

Validity coefficients for FFQ, the FD and urinary iodine excretion were calculated (Table 4). The highest validity coefficients were found for the food diary. For iodine intake, the validity coefficient was higher for urinary iodine excretion (UIE) than for the FFQ ($VC_{UIE} = 0.68$, $VC_{FFQ} = 0.62$), while for dairy product intake the validity coefficient was higher for the FFQ than for UIE ($VC_{FFQ} = 0.65$, $VC_{IUE} = 0.52$).

Discussion

A significant association between urinary iodine excretion and intake of milk/dairy products was seen with both FD and FFQ intake estimates. This enabled the calculation of a sound triangular validity coefficient for the FFQ dairy product intake. The practical use of this biomarker is not for prediction of milk and dairy product intake as a substitute for dietary assessment, but as an independent reference measure in addition to the dietary method. The advantage of the biological reference is that it does not depend on the respondents' ability to recall or report dietary intake correctly, a major source of error in all dietary assessments (Kaaks, 1997; Willett, 1998).

Dietary iodine is rapidly absorbed and more than 90% is excreted by the kidneys, making urinary iodine excretion a sensitive marker to recent changes in iodine intake. Urinary iodine excretion varies over 24 h and peaks after the main meals. Consequently, 24-h urine rather than spot urine samples are required to assess individual iodine intake (Als *et al*., 2003b).

To our knowledge, urinary iodine excretion has not previously been evaluated as a potential biomarker for dairy product intake. However, correlations between urinary iodine excretion and milk/dairy product intake have been reported in many countries (Rasmussen *et al*., 2002; Als *et al*., 2003a; Girelli *et al*., 2004; Remer *et al*., 2006). The

Table 3 Intake of dairy products and nutrients by the food frequency questionnaire (FFQ) and the food diary (FD), $n=119$

	FFQ per day, Median (P5, P95)[a]	*FD per day, Median (P5, P95)*[a]	*Spearman,* $r_{FFQ\text{-}FD}$	*FFQ Per 10MJ, Median (P5, P95)*[a]	*FD Per 10MJ, Median (P5, P95)*[a]	Spearman, $r_{FFQ\text{-}FD}$
Milk for drinking (g)	260 (0, 1200)	210 (16, 660)	0.66**	290 (0, 900)	260 (18, 690)	0.67**
Yoghurt (g)	34 (0, 220)[††]	31 (0, 130)	0.48**	38 (0, 240)[††]	39 (0, 160)	0.51**
Cheese (g)	20 (3, 50)[††]	36 (4, 68)	0.51**	24 (4, 55)[††]	41 (4, 82)	0.43**
Milk in foods[b] (g)	28 (10, 72)[†]	33 (0, 130)	0.27**	31 (12, 73)[††]	38 (0, 130)	0.23*
Butter (g)	2 (0, 31)	3 (0, 26)	0.45**	2 (0, 26)	3 (0, 31)	0.45**
Total dairy products (g)	450 (66, 1330)	370 (140, 830)	0.58**	460 (88, 1080)	410 (160, 850)	0.59**
Energy (kJ)	9340 (6330, 14200)	9160 (6720, 11100)	0.27**			
Calcium (mg)	930 (495, 1890)[††]	920 (556, 1360)	0.37**	1040 (706, 1550)[††]	780 (723, 1400)	0.33**
Riboflavin (mg)	1.8 (1.0, 3.5)[†]	1.7 (1.1, 2.5)	0.43**	2.0 (1.3, 2.7)[†]	1.9 (1.3, 2.6)	0.35**
Phosphorous (mg)	1610 (1130, 2730)[††]	1510 (1050, 2020)	0.43**	1780 (1350, 2260)[††]	1710 (1320, 2080)	0.48**
$Iodine_{diet}$ (μg)	120 (54, 300)	120 (54, 200)	0.46**	130 (67, 260)	130 (64, 200)	0.42**
$Iodine_{diet+supplements}$ (μg)	140 (54, 300)	130 (54, 250)	0.48**	150 (57, 260)	140 (65, 300)	0.40**
Protein, % of energy	16.1 (12, 20)[†]	15.5 (12, 20)	0.44**			
Fat, % of energy	30 (22, 36)[††]	33 (24, 41)	0.39**			
Carbohydrate, E%	53 (47, 65)[††]	51 (44, 60)	0.36**			

[a]P5 = 5th percentile, P95 = 95th percentile.
[b]Milk in foods = pancakes, porridge, desserts, ice-cream.
[†]Difference between FFQ and FD, $P<0.05$.
[††]Difference between FFQ and FD, $P<0.01$.
*$P<0.05$.
**$P<0.01$.

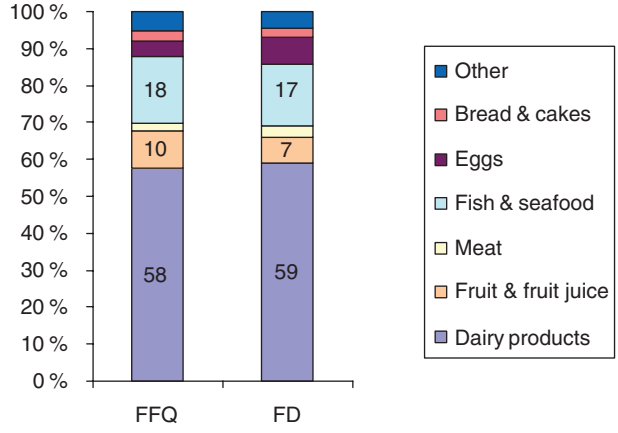

Figure 2 Contribution (%) of different food groups to the total intake of iodine recorded by the food frequency questionnaire (FFQ) and the food diary (FD) in the validation study.

contribution of iodine from milk/dairy products in these studies is primarily attributed to iodine fortification of industrially produced animal feed. The mandatory iodine fortification of cow fodder, leading to relatively high concentration of iodine in milk and dairy products, combined with a high consumption of milk and dairy products, has resulted in this food category being the major source of iodine in the Norwegian diet (Figure 2) (Dahl *et al*., 2003a, 2004).

Linear regression analysis of urinary iodine excretion against intake of various food groups identified dairy food intake as the major contributor to urinary iodine excretion, apart from iodine supplement use, whether FFQ or FD data were used in the model. Intake of fish/seafood was related to urinary iodine excretion, but did not reach statistical significance, while the intake of fruit/juices did. This was surprising, as the iodine content per 100 g is substantial in seafood (range, 10–120 μg) compared to fruit/juice (~2 μg). For comparison, the average iodine content per 100 g is 15 μg in milk and 45 μg in eggs (Dahl *et al*., 2004). The increase in urinary iodine excretion by a 1 g increased intake of a food category predicted by the β values in the model (Table 5) reflect higher iodine content per gram of fish and eggs than of milk/dairy products in proportion to the actual iodine content of these foods, while the β for the fruit/juice category was higher than expected from the actual iodine content. The results found for fish and fruit/juice could be due to the large variation in iodine contributed by fish compared to dairy foods and fruit/juice. There will be a day to day variation in urinary iodine excretion reflecting day to day variation in dietary iodine intake (Rasmussen *et al*., 1999). The highest correlation between FFQ and FD intakes was found for milk ($r=0.66$). Milk and dairy products are consumed with high regularity, if part of the diet, and are easier to recall than foods consumed less regularly.

Historically, the consumption of fish was high in Norway, and greater in coastal areas than inland (Frey *et al*., 1993). Lean seawater fish, such as cod, has the highest content of iodine (Julshamn *et al*., 2001). However, the consumption of fish, especially cod, has declined over the last decades, with young women being the lowest consumers (Norwegian Scientific Committee for Food Safety, 2007). In this study,

Table 4 Spearman's correlation coefficients and validity coefficients (VC) for urinary iodine excretion (UIE) and the intake of iodine, milk and dairy products recorded by the food frequency questionnaire (FFQ) and the food diary (FD)

Spearman's r (*95% CI*)			
n[a]	UIE vs FFQ	UIE vs FD	FFQ vs FD
119 Iodine	0.42** (0.26, 0.56)	0.52** (0.38, 0.64)	0.48** (0.33, 0.61)
84 Milk	0.32** (0.11, 0.50)	0.41** (0.21, 0.57)	0.70** (0.57, 0.80)
84 Total dairy products	0.34** (0.14, 0.52)	0.48** (0.30, 0.63)	0.61** (0.46, 0.73)
Triangular VCs (95% CI)			
n[a]	VC_{UIE}	VC_{FD}	VC_{FFQ}
119 Iodine	0.68 (0.51, 0.85)	0.76 (0.62, 0.91)	0.62 (0.46, 0.77)
84 Milk	0.43 (0.22, 0.64)	0.96 (0.77, 1.00)	0.73 (0.61, 0.93)
84 Total dairy products	0.52 (0.33, 0.69)	0.94 (0.76, 1.00)	0.65 (0.48, 0.85)

[a]119 = all participants, 84 = non-iodine-supplement users at the time of either the FFQ or the FD.
**$P<0.01$.

Table 5 Predictors of 24-h urinary iodine excretion in 119 pregnant women recruited between January 2003 and February 2004. Results are presented separately for the food diary (FD) and for the food frequency questionnaire (FFQ)

	FD estimates[a]		*FFQ estimates*[a,b]	
	Regression coefficient β	P	*Regression coefficient* β	P
Dairy products, g day^{-1}	0.26	<0.001	0.09	0.003
Fish, fish products, seafood g day^{-1}	0.30	0.086	0.50	0.096
Eggs g day^{-1}	0.50	0.154	1.24	0.053
Fruit/fruit juice, g day^{-1}	0.16	<0.001	0.08	0.032
Intake of an iodine-containing dietary supplement[c]	77.8	<0.001	94.3	<0.001
Season with highest use of iodine fortified cow's fodder[d]	52.0	0.008	33.0	0.106

[a]Adjusted for total energy intake.
[b]Adjusted for time between assessment methods.
[c]Supplement use: Yes/No.
[d]November to June.

participants consumed mainly fatty fish, and the total intake was moderate. Hence, intake of fish did not significantly influence the 24-h urinary iodine excretion.

There is a seasonal variation in the iodine content of Norwegian milk due to differing feeding practice in summer and winter. The average content in low-fat milk was 88 μg l^{-1} in summer and 232 μg l^{-1} in winter months (Dahl *et al.*, 2003b). An intake of 300 ml milk would supply 70 μg of iodine during winter months and 26 μg of iodine during summer months, resulting in a seasonal difference in iodine intake of 44 μg. The predicted seasonal difference in urinary iodine excretion in our study (Table 5) seems a reasonable estimate in relation to this.

Iodine from table salt enriched with iodine (5 μg g^{-1} NaCl) was not included in the assessment of iodine intake in our study, because use of this salt is very limited in private households and not allowed in the food industry in Norway (Dahl *et al.*, 2004). However, we cannot exclude that iodinated salt have been used in private households and therefore may be a confounding factor in our analysis.

Urinary iodine excretion was more closely correlated to FD than to FFQ intake estimates, due to the concurrent timing of the FD compared to the FFQ. This was evident also for the validity coefficients. The correlations between urinary iodine excretion and iodine intake ($r_{FFQ}=0.42$, $r_{FD}=0.52$) were similar to the correlation between urinary iodine excretion and iodine intake reported by a Danish study (Rasmussen *et al.*, 1999). Higher correlation coefficients were obtained between FFQ and FD intakes of milk and dairy products than between each of the dietary estimates and urinary iodine excretion (Table 4). Associations between biomarkers and a FFQ covering a long time span are weakened by variation in dietary intake as well as by factors not related to intake, for example biological and analytical variability, and correlations will tend to be modest even if the dietary measurement is accurate (Willett and Lenart, 1998; Cade *et al.*, 2002). Consequently the strength of the correlations found between 24-h urinary iodine excretion and the intake of milk and dairy products in this study provides qualitative documentation of validity.

Validity coefficients estimated for each of the three methods were higher than the three pairwise correlations that formed the basis for the validity coefficient (Table 4). The highest validity coefficient for the urinary iodine excretion was seen for total iodine intake ($VC_{UIE}=0.68$) as expected, because iodine from all food sources and dietary

supplements were included. VCs for milk and dairy products were higher for the FFQ than for the biomarker, and the strongest VCs were observed for the FD. The VCs obtained for FFQ intakes of milk and dairy products in this study were higher than the corresponding VCs found in a study where the fatty acid 15:0 was used as biomarker (Brevik *et al*., 2005).

The combined use of biomarkers and FD may strengthen the validation of epidemiological instruments like the MoBa FFQ, and the triangular method has been used in several studies (Kaaks, 1997; Daures *et al*., 2000; Andersen *et al*., 2005; McNaughton *et al*., 2005). However, the method also has limitations. It is based on the assumption that errors associated with each of the three measures are independent, and that estimates from the FFQ, FD and biomarker are linearly related to the common true intake. Yet, correlation of errors between the FFQ and the FD can not be ruled out, and the reported validity coefficients should be regarded as the upper limits of the true validity coefficients (Ocke and Kaaks, 1997).

The group of women in this study was not a random sample. In planning the validation study, we did not aim for a representative sample, as the purpose of the validation was to investigate the agreement between the FFQ and reference measures within the same individuals. It was however, important to get a broad range of intakes within the sample, and this was achieved (Table 3). The range of intakes was larger with the FFQ than with the FD. This could be due to the FFQ covering a larger time span than the FD and to the fact that the food frequency method is less precise than food registering (Willett, 1998).

Studies of day-to-day variation in urinary iodine excretion have indicated that ideally, more than one 24-h urine sample should have been used (Rasmussen *et al*., 1999). However, 24-h urine samples are inconvenient for the subjects, difficult to collect accurately and repeated 24-h urine samples could have reduced the participation rate.

Conclusion

We conclude that 24-h urinary iodine excretion may be a useful biomarker for validating the intake of milk and dairy products in a situation like the Norwegian, where this food group is the main contributor to dietary iodine intake. When using 24-h urinary iodine excretion as an independent biomarker of dairy product intake, the validity of the MoBa FFQ could be assessed by the triangular method.

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