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Iodine deficiency in pregnant women living in the South East of the UK: the influence of diet and nutritional supplements on iodine status

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Abstract

Iodine is a key component of the thyroid hormones which are crucial for brain development. Adequate intake of iodine in pregnancy is important as *in utero* deficiency may have lifelong consequences for the offspring. Data on the iodine status of UK pregnant women are sparse, and there are no such data for pregnant women in the South East of the UK. A total of 100 pregnant women were recruited to a cross-sectional study carried out at the Royal Surrey County Hospital, Guildford, at their first-trimester visit for an ultrasound scan. The participants provided a spot-urine sample (for the measurement of urinary iodine concentration (UIC) and creatinine concentration) and 24 h iodine excretion was estimated from the urinary iodine:creatinine ratio. Women completed a general questionnaire and a FFQ. The median UIC (85·3 μg/l) indicated that the group was iodine deficient by World Health Organisation criteria. The median values of the iodine:creatinine ratio (122·9 μg/g) and of the estimated 24 h iodine excretion (151·2 μg/d) were also suggestive of iodine deficiency. UIC was significantly higher in women taking an iodine-containing prenatal supplement (*n* 42) than in in those not taking such a supplement (*P*<0·001). In the adjusted analyses, milk intake, maternal age and iodine-containing prenatal supplement use were positively associated with the estimated 24 h urinary iodine excretion. Our finding of iodine deficiency in these women gives cause for concern. We suggest that women of childbearing age and pregnant women should be given advice on how to improve their iodine status through dietary means. A national survey of iodine status in UK pregnant women is required.

Key words: Iodine: UK: Pregnancy: Diet

Iodine deficiency, once endemic in the UK, was eradicated by the concurrent increase in milk-iodine concentration and milk consumption in the post-war years, though neither was aimed at improving human iodine status[1]. From the 1960s, the UK was considered to be an iodine-sufficient country, but data are now emerging that suggest that this may no longer be the case, at least in women of childbearing age[2–5] and pregnant women[6–8]; indeed, the WHO now classifies the UK as mildly iodine deficient[9].

Iodine is a key component of the thyroid hormones, which are crucial for brain development, particularly during gestation and early life[10]. The WHO iodine recommendation for pregnant women is 250 μg/d, which is considerably higher than the 150 μg/d recommendation for adults. Pregnant women are at a higher risk of developing iodine deficiency as their iodine requirement is higher than that of non-pregnant women. Severe iodine deficiency during pregnancy is well known to cause cretinism and severe mental retardation[10]. We have recently found mild-to-moderate iodine deficiency in a large UK cohort of pregnant women and that children of those who have a low iodine status in early pregnancy are more likely to have significantly lower intelligence quotient and reading scores[11].

Though it is vital that pregnant women meet their iodine requirements, this is not always achieved even in developed countries such as the USA[12,13]. Strategies such as salt iodisation programmes that exist in many countries may provide enough iodine for adults but not necessarily for pregnant women[14]. Therefore, it is important to monitor the iodine status of pregnant women in a population; for this purpose, the WHO recommends collecting spot-urine samples from a group of pregnant women and comparing the median urinary iodine concentration (UIC) with the cut-off value for adequacy (150–249 μg/l)[15].

The UK has never introduced a national iodine-fortification programme to ensure adequate population iodine intake, as has been done in many countries worldwide[10]. Furthermore, advice to pregnant women from the UK Department of Health makes no mention of the need for iodine in pregnancy and nor does it list dietary sources[16]. Results from the National

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Abbreviations: EAR, estimated average requirement; UIC, urinary iodine concentration.

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Diet and Nutrition Survey suggest that milk (and milk products), fish and eggs are the main dietary sources of iodine (estimated from food diary analysis) in UK adults[17]; certain groups of women may not consume these iodine-rich foods. Not all UK prenatal supplements contain iodine and, in contrast to the situation in the USA, Australia and New Zealand, there is no official recommendation for pregnant women to take an iodine supplement[18,19].

Iodine deficiency has been demonstrated in studies carried out in pregnant women in Scotland[7], the North East of England[6] and Cardiff[8], but all these studies have limitations: one was only published as an abstract[7], two came out before the publication of the updated WHO iodine requirements for pregnancy[6,7], and one reported iodine status of women recruited to a trial[8] who may not be representative of pregnant women in general. There are no data on the iodine status of pregnant women from the South East of the UK or any information on the dietary sources that contribute to iodine status in pregnant women, as none of the previous studies collected dietary data. Furthermore, there is no information on the effect of taking a UK prenatal iodine-containing supplement on iodine status. Therefore, the present study aimed to evaluate iodine status in pregnant women in the South East of the UK and to explore factors that influence iodine status at this critical life stage. On the basis of the sparse UK literature, we hypothesised that women would be iodine deficient by WHO criteria.

Experimental methods

Recruitment of subjects

Pregnant women were recruited consecutively to a cross-sectional study at the time of their first-trimester ultrasound scan (around 12 weeks of gestation) at the Royal Surrey County Hospital, Guildford. Women were not eligible for inclusion if they had a history of thyroid disease or were taking thyroid medication. Owing to budget and time constraints, it was not possible to recruit throughout the year and a decision was made to recruit only in the summer season (July to September 2009). This removed the complication of straddling seasons as milk-iodine content exhibits a seasonal variation[1] that affects iodine status; other UK studies have found lower UIC in samples collected in summer than in winter[4,20].

The participants were asked to provide a spot-urine sample at the ultrasound clinic; all clinics were conducted in the morning, though the timing of sample collection is unlikely to affect the concentration of iodine or creatinine[21]. The participants were also required to complete a short FFQ and a general questionnaire that collected demographic and nutritional information. One of the authors was present during the completion of the questionnaires, giving an opportunity for clarification (e.g. the meaning of 'iodised salt'). The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the NRES Ethics Committee (South East Coast – Surrey, ref 08/H1109/140)

and the University of Surrey Ethics Committee (ref EC/2009/39/FHMS). Written informed consent was obtained from all the subjects.

Analysis of dietary intake and nutritional supplement use

The general questionnaire collected details on participant age, smoking status and time since previous delivery (birth in the last 3 years). It also collected information on whether the participant was a vegetarian or vegan and whether she took a prenatal nutritional supplement. The dose of iodine in the supplement, if any, was determined by conducting a shelf-survey of prenatal supplements available in the UK in November 2009.

The forty-six-item semi-quantitative FFQ was designed to obtain detailed information only on foods that were iodine rich or had potential goitrogenic properties. It was intended not to calculate the intake of nutrients, but rather to estimate the quantity of iodine-rich foods consumed (e.g. g of fish/week). The FFQ design was based on the FFQ used in the European Prospective Investigation of Cancer (EPIC) study[22]. There were nine frequency options for all the foods, except for milk; in the latter case, daily consumption had six frequency options. With the exception of eggs (kept as a frequency coding), all other food items were recoded to the estimated weekly intake (in g). Estimated intake was computed by combining information on the number of weekly portions with the estimated food weights of each portion; medium portion sizes were used[23] and an average portion weight was computed for composite food groups, such as 'white fish'. The coding of weekly portions was based on that used for the FFQ completed by pregnant women in the Avon Longitudinal Study of Parents and Children (ALSPAC)[24]. The weekly portions were as follows: $0 =$ none/rarely; $0·5 =$ once a fortnight; $2 =$ one to four times/week; $5·5 =$ five to seven times/week; $10 =$ more than once daily[24].

The individual food items were collapsed into seven food categories: milk (daily intake); seafood (total of processed fish, white fish, oily fish, shellfish and fish roe); meat and poultry (total of all processed meat, red meat and poultry); dairy products (total of all cream, yogurts, butter and cheese); eggs (once/fortnight or less or once/week or more); iodised salt; seaweed; goitrogens (total soya products (soya milk, tofu and other soya products), cruciferous vegetables (broccoli/kale/spring greens, cabbage, Brussels sprouts, cauliflower, turnip/swede, radish) and sweet potatoes). For the purposes of statistical analyses, daily milk consumption was recoded as follows: (1) none; (2) <140 ml; (3) $140–280$ ml; (4) >280 ml. Weekly estimated intake (in g) of seafood, meat/poultry and dairy products was divided into tertiles. For seaweed and iodised salt, the participants were dichotomised into either 'consumers' or 'non-consumers' due to the low numbers of consumers (n 13 and n 4, respectively).

Laboratory analysis

UIC was measured on a ThermoElemental X-Series ICP-MS (ThermoFisher Scientific) in the Trace Element Laboratory at the University of Surrey. The samples were diluted with an

alkaline diluent prepared by dissolving 3·32 g $NH_4H_2PO_4$ and 1·16 g $(NH_4)_2H_2EDTA$ (Analar grade; Sigma-Aldrich) in deionised water, adding 10·0 ml ammonia solution (specific gravity 0·88) and making up to 1000 ml with deionised water. Using the alkaline diluent, 400 µl of each participant's urine sample were made up to 10 ml. Standard iodine solutions were prepared with potassium iodide solution (Analar grade; Romil Limited) for the construction of calibration curves. To obtain matrix-matched standards, 400 µl of control urine were added to 400 µl of each standard. An internal standard was added to all the samples: rhodium (^{103}Rh) and iridium (^{192}Ir) (both obtained from SPEX Certiprep Limited) were made up in a working standard solution of 1 mg/l (parts per million) in 1% v/v HNO_3 (Trace analysis grade; Fisher Scientific). This solution was made up in a ratio of 1 in 10 with the diluent. In the analysis, 150 µl of this solution were added to every tube. To evaluate the accuracy of the method, certified reference materials were obtained through quality-assurance programme of the Centre for Disease Control, entitled 'Ensuring the Quality of Urinary Iodine Procedures' (EQUIP). Our observed mean values for the EQUIP-certified reference materials were as follows: 27·6 (SD 2·3, n 3) for U02 (certified mean 28·7 µg/l, range 20·1–37·3); 47·4 (SD 2·1, n 4) for U05 (certified mean 45·0 µg/l, range 31·5–58·5); 301·8 (SD 7·5, n 4) for U09 (certified mean 296·3 µg/l, range 251·9–340·7); 9·6 (SD 0·8, n 2) for U10 (certified mean 12·2 µg/l, range 8·5–15·9). Urinary creatinine concentration was measured in the Biochemistry Department at the Royal Surrey County Hospital on the ADVIA Chemistry System (Siemens Healthcare) by the Jaffe rate method.

Classification of iodine status

The UK Dietary Reference Values for iodine were published in 1991, and they are outdated as they do not reflect the need for additional iodine during pregnancy[10,25]. For the present study, we therefore used WHO criteria to assess iodine status in pregnancy[15]. The iodine status of the group was described by comparing the median UIC value with the WHO UIC cut-offs for iodine adequacy in pregnancy[15]. However, these cut-offs cannot be used to identify iodine deficiency in an individual owing to the large intra-individual variation in iodine excretion from day to day in a spot-urine sample; it is often incorrectly assumed that anyone with UIC in a spot-urine sample that is below the cut-off for adequacy (150 µg/l in the case of pregnancy) is iodine deficient, which may well not be the case[10].

Using urinary creatinine concentration in a spot-urine sample to correct UIC for intra-individual variation in daily urine volume produced, we can more closely approach individual iodine status, especially when the age and sex of the individual are taken into account[26–28]. Therefore, we report iodine status in three ways: as the simple iodine concentration (µg/l), as the iodine:creatinine ratio (µg/g), and as the estimated 24 h iodine excretion (µg/d). The 24 h iodine excretion was estimated by multiplying the iodine:creatinine ratio by the expected daily creatinine excretion, which is 1·23 g/d[26] for our cohort of women

aged from 19 to 47 years (on the basis that the value for non-pregnant adults can be used as creatinine excretion is unaltered in pregnancy[29,30]). To explore relationships between participant characteristics (such as age) and dietary intake (estimated from the FFQ), we used the estimated 24 h iodine excretion value for each participant as a proxy for individual iodine status, though we recognise the limitations of this method.

Statistical analyses

UIC and the estimated 24 h iodine excretion values were not normally distributed and therefore medians with the 25th and 75th percentiles are reported. The estimated 24 h iodine excretion values were log-transformed using the natural logarithm to allow parametric testing. Maternal age was recoded as a categorical variable: 19–34 and 35–49 years. The log-transformed data were subjected to independent t tests or one-way ANOVA to compare two groups or two or more groups, respectively. Spearman's rank correlation was used to explore relationships between continuous data.

Multiple linear regression (using the general linear model in the Statistical Package for Social Sciences) was used to evaluate associations between dietary and demographic factors and the (log-transformed) estimated 24 h iodine excretion; variables that were significantly related to the estimated 24 h iodine excretion in the unadjusted analyses were entered into the model. The model was then used for the calculation of the estimated geometric means with their 95% CI of the estimated 24 h iodine excretion for each category of milk intake; the geometric means were computed by back-transformation of the adjusted means and 95% CI of the log-transformed estimated 24 h iodine excretion values.

Significance was set at $P < 0.05$, and analyses were conducted using the Statistical Package for Social Sciences (version 19.0; SPSS, Inc.).

Results

During the defined study period (July to September 2009), 100 women were recruited to the study. The mean age of the women was 32·4 (SD 4·7) years with a range of 19–47 years. The median UIC was 85·3 µg/l, classifying this group of pregnant women as mildly to moderately iodine deficient[15,31] (Table 1). The median iodine:creatinine ratio (122·9 µg/g) was also low, and the median estimated 24 h iodine excretion value (151·2 µg/d) was considerably less than the value that would have been expected (i.e. 225 µg) if 250 µg iodine (the dietary requirement for pregnant women) had been consumed/d of which 90% was excreted.

Describing the prevalence of iodine deficiency within the cohort of the present study is challenging. Many authors report the percentage of values below the WHO cut-off of 150 µg/l, which in the present study would be 76% (or 67% if using the iodine:creatinine ratio with a cut-off of 150 µg/g). However, this may lead to an overestimation of the extent of deficiency; strictly speaking, the estimated average requirement (EAR), and not the reference nutrient intake,

Table 1. Iodine status of pregnant women from the South East of the UK (*n* 100), reported as iodine concentration (μg/l), iodine:creatinine ratio (μg/g) and estimated 24 h excretion (μg/d)*

(Median values with their 25th−75th percentiles)

	Median	25th−75th percentile
Iodine concentration (μg/l)	85·3	39·6−145·5
Iodine:creatinine ratio (μg/g)	122·9	79·5−163·6
Estimated 24 h iodine excretion (μg/d)*	151·2	97·8−201·2

*Age- and sex-adjusted iodine:creatinine ratio on the basis of an expected daily urinary creatinine excretion value of 1·23 g/d[26].

should be used to report the prevalence of deficiency of a nutrient in a population[32]. Hence, it may be more correct to report the percentage with values below the EAR, which we estimated to be 180 μg/d (calculated by converting the pregnancy reference nutrient intake of 250 μg/d to an EAR using the published reference nutrient intake-to-EAR conversion factor for iodine of 1·4[32]). Therefore, the expected 24 h urinary excretion value would be approximately 160 μg/d (assuming a 90 % excretion of the EAR of 180 μg/d). By these calculations, 53 % (*n* 53) of the women in the present study were found to have an estimated 24 h iodine excretion value below the EAR.

Participant characteristics and iodine status

Table 2 summarises the effect of participant characteristics on maternal iodine status. There was no significant difference in iodine excretion by smoking status, consumption of a vegetarian diet (there were no vegans) or time since last birth (Table 2). The estimated 24 h iodine excretion value was significantly higher in women aged above 35 years than in those aged 19−34 years (*P*=0·01; Table 2). We explored the relationship between maternal age and urinary creatinine excretion to investigate whether the higher iodine status at older age was explained by lower creatinine excretion[33]; we did find a significant negative correlation between maternal age and urinary creatinine concentration (*r* −0·21, *P*=0·01). To test whether older women consumed more iodine-rich foods, we explored correlations between dietary food groups and maternal age and found a positive association with seafood (*r* 0·22, *P*=0·03) and cheese (*r* 0·30, *P*=0·003) (data not shown).

Use of an iodine-containing nutritional supplement

A total of seventy-five (75 %) participants were taking a nutritional supplement at the time of recruitment (including single folic acid supplements); fifty-one (51 %) women were taking a multivitamin or mineral supplement, but only forty-two (42 %) women were using a prenatal vitamin and mineral formulation that contained iodine. The median content of iodine in the supplements reported by the participants was 140 μg/dose

Table 2. Estimated 24 h iodine excretion* (μg/d) according to participant characteristics

(Number of participants, percentages and median values with their 25th−75th percentiles)

	n	%	Estimated 24 h iodine excretion (μg/d)*		*P*†	Adjusted *P*‡
			Median	25th−75th percentile		
Age (years)					0·01	0·007
19−34	66	66	131·8	86·3−198·5		
35−49	34	34	178·1	134·1−241·3		
Smoking status					0·57	N/A
Non-smoker	95	95	154·9	97·1−201·4		
Smoker	5	5	118·7	88·9−202·3		
Time since last gave birth (in the last 3 years)					0·86	N/A
< 1 year	4	4	84·2	71·8−338·0		
< 2 years	24	24	158·4	92·9−195·6		
< 3 years	13	13	133·0	94·1−258·8		
No birth in past 3 years	59	59	154·9	105·4−227·4		
Vegetarian status					0·89	N/A
Omnivore	94	94	151·2	96·4−202·2		
Vegetarian§	5	5	139·2	94·4−293·0		
Use of iodine-containing supplement					<0·0001	<0·0001
Yes	42	42	183·6	132·9−294·7		
No	58	58	124·9	82·0−175·6		

N/A, variable not entered into the multivariate analyses.
*Age- and sex-adjusted iodine:creatinine ratio on the basis of an expected daily urinary creatinine excretion value of 1·23 g/d.
† *P* value for comparison between the groups from independent *t* test or ANOVA conducted on log-transformed estimated 24 h iodine excretion data.
‡ Adjusted *P* value from the general linear model with the following variables: maternal age; supplement use; milk, seafood and egg intake.
§ One woman was classified as a pescatarian, but was excluded from the statistical analysis that compared vegetarians and omnivores.

(range 75–150 μg). The iodine status of women who took an iodine-containing supplement was significantly higher than that of those who did not take such a supplement; this relationship was demonstrated both by the simple iodine concentration measure ($P < 0.0001$) and by the estimated 24 h iodine excretion ($P < 0.0001$; Table 2). Fig. 1 shows the result obtained in the present study in comparison with the WHO recommended levels for a population of pregnant women[15]. The median UIC of women taking an iodine-containing supplement (111 μg/l) was closer to the WHO adequate range for pregnant women (150–249 μg/l) than was that of women not taking such a supplement (61 μg/l), which was close to the severe-deficiency level (≤ 50 μg/l)[31].

Dietary influences on iodine status

Iodised salt was rarely or never used by 96 % of the women, and there was no significant difference in iodine excretion between consumers and non-consumers (Table 3). There was no difference in iodine status between consumers (n 13) and non-consumers of seaweed ($P = 0.23$; data not shown). Weekly estimated intake of goitrogens or meat and poultry was not significantly associated with iodine excretion (Table 3). Although iodine excretion was higher in the top tertile of dairy-product intake than in the bottom tertile (Table 3), the difference was not significant ($P = 0.10$).

By contrast, the intakes of milk, eggs and seafood were positively associated with the estimated 24 h-iodine excretion (Table 3). The difference in iodine status between the categories of milk consumption was highly significant ($P = 0.007$), and post hoc tests indicated that women who did not consume milk had significantly lower iodine excretion than those consuming more than approximately 280 ml/d ($P = 0.008$). Consumption of up to approximately 570 ml of goats' milk/d was reported by one woman; she was an outlier with an estimated 24 h iodine excretion value of 1414·0 μg/g. The estimated 24 h iodine excretion differed significantly between the tertiles of seafood intake ($P = 0.04$), and the post hoc test indicated that iodine excretion was significantly

lower in the bottom tertile than in the top tertile ($P = 0.03$; Table 3). Iodine excretion differed significantly with the frequency of egg consumption ($P = 0.04$); higher iodine excretion was associated with a greater frequency of weekly egg consumption (Table 3).

In the adjusted analyses (which included significant variables from univariate analyses), the only factors significantly associated with the estimated 24 h iodine excretion were categories of milk consumption ($P = 0.002$), use of an iodine supplement ($P < 0.0001$) and maternal age ($P = 0.007$). There were no significant interactions between the variables. The model explained 31·1 % of the variance in the estimated 24 h iodine excretion (adjusted R^2 0·311); milk 15·1 % (partial $\eta^2 = 0.151$), iodine supplement use 14·5 % (partial $\eta^2 = 0.145$) and maternal age 7·8 % (partial $\eta^2 = 0.078$). The intakes of eggs ($P = 0.24$) and seafood ($P = 0.42$) were not significantly associated with iodine excretion in the adjusted model. When all the other factors were controlled for, there remained evidence of a trend of increasing estimated 24 h iodine excretion with increasing daily milk consumption (Fig. 2).

Discussion

The present results support our hypothesis that pregnant women in the South East of the UK would have an inadequate iodine status as the median UIC classified the women as mildly to moderately iodine deficient[15,31]. The present results, together with those from earlier UK studies[6–8], suggest that UK pregnant women are not meeting the higher iodine requirements of pregnancy; this may be having a negative effect on fetal brain development[10]. Indeed, the level of deficiency found in the present study (median UIC 85·3 μg/l) is similar to that in an Australian study (in women recruited before mandatory iodine fortification of bread in 2009)[34] and in our own recent UK study[11] (median UIC 81 and 91·1 μg/l, respectively); these studies found associations between iodine status in pregnancy and poorer cognition (intelligence quotient, reading ability and spelling) in children up to the age of 9 years.
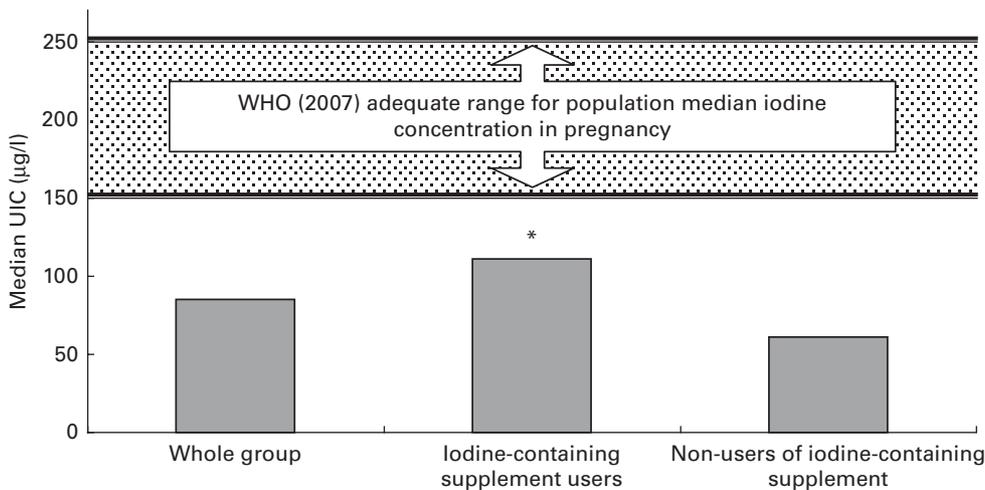
Fig. 1. Iodine status of women by the use of iodine-containing supplements. *Urinary iodine concentration (UIC) was significantly higher in women taking an iodine-containing supplement than in non-users ($P < 0.0001$; analysis on log-transformed data).

Table 3. Estimated 24 h iodine excretion* (μg/d) according to maternal diet

(Median values with their 25th−75th percentiles)

Food group	Estimated 24 h iodine excretion (μg/d)*		P†	Adjusted P‡
	Median	25th−75th percentile		
Daily milk intake (n)			0·007	0·002
None (n 7)	83·4	53·7−123·6		
<140 ml (n 24)	132·1	88·2−199·5		
140−280 ml (n 41)	156·6	101·4−200·9		
>280 ml (n 28)	171·4	127·2−357·9		
Dairy produce intake/week (g)			0·10	N/A
Bottom tertile (0−406 g)	139·1	85·3−203·9		
Middle tertile (406−829 g)	130·6	93·5−203·3		
Top tertile (830+ g)	173·6	121·3−203·0		
Seafood intake/week (g)			0·04	0·42
Bottom tertile (0−238 g)	133·0	64·9−173·3		
Middle tertile (239−401 g)	157·5	89·6−212·1		
Top tertile (402+ g)	165·8	115·8−219·8		
Meat and poultry intake/week (g)			0·54	N/A
Bottom tertile (0−628 g)	140·6	101·6−183·3		
Middle tertile (629−821 g)	154·9	95·5−203·0		
Top tertile (822+ g)	167·8	95·7−233·1		
Egg intake (n)			0·04	0·24
Once/fortnight or less (n 32)	118·7	87·2−173·1		
Once/week or more (n 68)	165·8	105·7−226·3		
Goitrogen intake/week (g)			0·97	N/A
Bottom tertile (0−333 g)	147·7	94·1−218·5		
Middle tertile (334−640 g)	158·4	102·1−198·5		
Top tertile (641+ g)	137·6	90·5−216·0		
Iodised salt use			0·75	N/A
Yes (n 4)	184·0	100·0−200·7		
No (n 96)	151·2	81·9−360·4		

N/A, variable not entered into the multivariate analyses.

* Age- and sex-adjusted iodine:creatinine ratio on the basis of an expected daily urinary creatinine excretion value of 1·23 g/d.

† Results from ANOVA on the log-transformed estimated 24 h iodine excretion data.

‡ Adjusted P value from the general linear model with the following variables: maternal age; supplement use; milk, seafood and egg intake.

As we collected only one urine sample from each woman, we cannot accurately describe the prevalence of iodine deficiency in the present study; ideally, multiple urine samples from each woman should be collected to adjust the iodine concentration distribution for intra-individual variation[14]. However, while recognising the limitation that one urine sample from each woman may not reflect usual iodine status, we feel that reporting the percentage of women below the EAR threshold (53 %) is a more accurate reflection of the extent of iodine deficiency than the traditional approach of reporting the percentage below the WHO cut-off (150 μg/l)[15] (which reflects the reference nutrient intake for pregnancy). In our opinion, the methodology for the use of the EAR cut-point method during pregnancy needs further development.

We found that maternal age was positively associated with the estimated 24 h iodine excretion. There are two potential explanations for this: older women consume more iodine-rich foods and urinary creatinine excretion decreases with age (which we found), thus increasing the iodine:creatinine ratio. Data from the 2000/01 Adult National Diet and Nutrition Survey suggest an increased dietary iodine intake with advancing age, as older women had a significantly higher iodine intake (estimated from food diaries) than younger women[17].

Women who reported taking an iodine-containing supplement had a significantly higher iodine status than those who did not take such a supplement, which is consistent with other research findings in Europe[35−37] and New Zealand[38]. Health authorities in America, Australia and New Zealand recommend that all pregnant (and lactating) women take a supplement containing 150 μg/d of iodine during pregnancy[18,19]. There are just two trials that supplemented pregnant women with iodine in regions of mild-to-moderate iodine deficiency that included child cognitive outcomes[39,40]; while these suggest a benefit for child cognition, further good-quality evidence from a randomised controlled trial is needed. In the present study, we obtained no data on maternal or neonatal thyroid function or on long-term cognitive outcomes in the offspring that would support benefit (or indeed lack of harm[41,42]) of initiating iodine supplementation in pregnancy. Despite the fact that 51 % of the women in the present study were taking a prenatal multivitamin and mineral supplement, only 42 % were taking a supplement that contained iodine – a reflection of the fact that, at the time, only 67 % of UK prenatal supplements contained iodine and that there is no
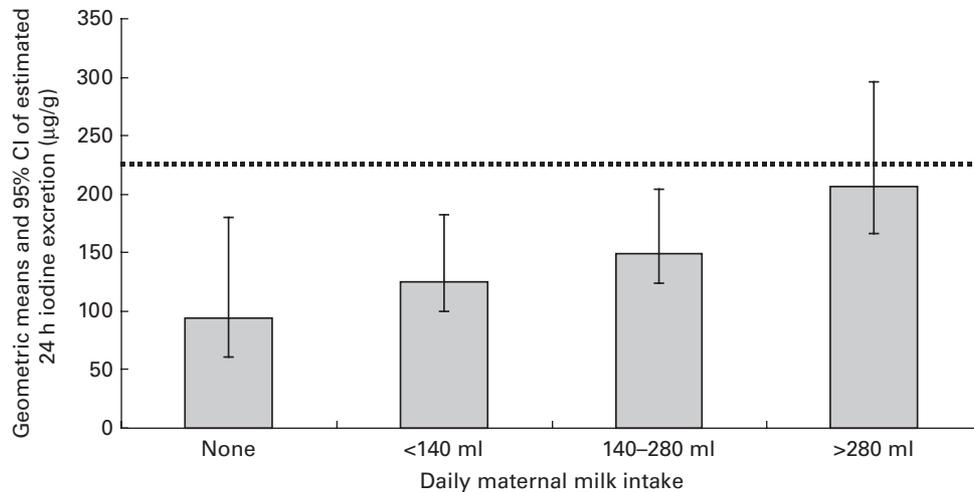
Fig. 2. Adjusted geometric means and 95 % CI of estimated 24 h iodine excretion (computed by back-transformation of the log-transformed 24 h iodine excretion data) by maternal milk intake (variables included in the model: frequency of egg intake; maternal age (years); use of iodine-containing supplement; tertiles of weekly seafood intake (g)). ···· represents the expected value (225 µg) for 24 h iodine excretion if 250 µg iodine (the dietary requirement for pregnant women) were consumed per d of which 90 % was excreted.

official UK advice to take an iodine supplement during pregnancy. A higher percentage of women in the present study were taking an iodine-containing supplement than were women in the USA[43,44], Switzerland[45], New Zealand[38] or Australia[46]. Most UK pregnant women are unaware of the need for iodine[47], so the presence of iodine in the supplement is unlikely to influence choice, but the leading UK prenatal supplement brand does contain iodine. In addition, Surrey is an affluent area[48] and therefore supplement use may be higher than that in other, less-affluent, UK regions[49].

The finding that a higher intake of milk was related to higher urinary iodine excretion is consistent with the findings of studies in pregnant women in other countries[35,43,50,51]. The present results suggest that women consuming more than approximately 280 ml of milk per d had an iodine status greater than the cut-off for iodine adequacy in pregnancy, even after adjusting for other factors. However, it needs to be remembered that this milk-volume value is related to the intake of summer milk (as we recruited participants over the summer), which has a lower iodine content than the winter milk. The inaccuracies of a FFQ for collecting dietary intake data should also be kept in mind.

We have shown a positive association between egg intake frequency and maternal iodine status, although the significance disappeared in the adjusted analyses. This is in contrast to the findings of the UK study of iodine status of teenage schoolgirls, which surprisingly found that a high intake of eggs was associated with low urinary iodine excretion[4], though we have previously suggested that failings in the FFQ in that study (ambiguous and unquantified frequency options) resulted in spurious associations[52]. Iodine status was higher in women in the top tertile of fish intake, but the relationship was no longer significant when adjusted for other dietary factors. The intake of seafood also failed to exhibit associations with the iodine status of pregnant women in

Spain[35,53] and teenage girls in the UK[4]. The lack of a strong relationship between fish intake and iodine status (compared with the relationship with the intake of milk, despite its lower iodine concentration) may be explained by the insensitivity of an FFQ (see limitations) and the relatively poor consumption of fish by many UK women[49]. The fact that such a low percentage of pregnant women in the present study reported the use of iodised salt may reflect its poor availability in UK supermarkets[54].

The present study was limited by the relatively small sample size; however, a study of adults has estimated that 100 spot-urine samples (if corrected to estimate 24 h iodine excretion) are sufficient to give a population estimate of urinary iodine excretion (within a 95 % CI) with a precision of ±10 %[55]. Nevertheless, the stratified analyses in the present study (e.g. by age or dietary pattern) are based on a small sample size and therefore the results should be treated with caution. The other major limitation of the study is the fact that recruitment was conducted only in the summer months and in only one region of the UK (Surrey). Given the known seasonal variation in the iodine content of dairy products[1], it is likely that the present study represents a worst-case scenario. On the other hand, with Surrey being an affluent county, the women in the present study are likely to have a higher socio-economic status than those in many other UK regions. Thus, results may be biased towards a higher iodine status, as the intake of iodine-rich foods, particularly fish, may be greater in more-affluent women. A large multi-centre study is needed to provide a more comprehensive view of the iodine status of UK pregnant women as Surrey women may not be representative of UK women in general. The evaluation of the impact of diet on iodine status is limited by the inherent limitations of a FFQ. It is perhaps unsurprising that some dietary items failed to exhibit associations with iodine status, given that iodine excretion reflects recent (previous 24–48 h) dietary iodine intake[28] and FFQ evaluate intake over a longer time

period. Thus, consumption of foods consumed regularly, such as milk, is more likely to affect the iodine concentration of a spot-urine sample than food items consumed irregularly and in low amounts within the cohort, such as fish; this is likely to be especially true in studies with small sample sizes, such as the present study. We are aware that there are limitations of using a single spot-urine sample for individual iodine status assessment, and although we have attempted to overcome some of these limitations by use of the age- and sex-adjusted iodine:creatinine ratio, this method still has limitations[27]; future studies might explore the use of body weight for further adjustment of the iodine:creatinine ratio and the collection of repeated urine samples for the measurement of iodine status in the same individual[27].

In conclusion, we have demonstrated iodine deficiency in pregnant women in the South East of the UK – a cause for concern, given the need for adequate iodine for fetal brain development[10]. The intakes of milk and iodine-containing supplements were the most important predictors of iodine status in UK pregnant women. Women who follow the current government generic pregnancy healthy eating advice of consuming 2–3 portions of dairy products per d, together with the recommended 1–2 portions of fish per week, should receive an adequate supply of iodine. However, for women who do not consume these iodine-rich foods, an appropriate prenatal iodine-containing supplement is probably appropriate (although kelp supplements should be avoided); indeed, in the present study, we have demonstrated that the use of such a supplement is associated with a higher iodine status. Ensuring adequate iodine intake is likely to be particularly important before pregnancy to ensure that stores of iodine are optimised so that there is no shortfall in early gestation[42,56]. The dietary advice to UK pregnant women needs to be revised to explain why increased iodine intake during pregnancy is important and good dietary sources should be clearly signposted.

References

1. Phillips DI (1997) Iodine, milk, and the elimination of endemic goitre in Britain: the story of an accidental public health triumph. *J Epidemiol Community Health* **51**, 391–393.
2. Bath S, Walter A, Taylor A, *et al.* (2008) Iodine status of UK women of childbearing age. *J Hum Nutr Diet* **21**, 379–380.
3. Rayman MP, Sleeth M, Walter A, *et al.* (2008) Iodine deficiency in UK women of child-bearing age. *Proc Nut Soc* **67**, E399.
4. Vanderpump MP, Lazarus JH, Smyth PP, *et al.* (2011) Iodine status of UK schoolgirls: a cross-sectional survey. *Lancet* **377**, 2007–2012.
5. Lampropoulou M, Lean M & Combet Aspray E (2012) Iodine status of women of childbearing age in Scotland. *Proc Nutr Soc* **71**, E143 Abstr.
6. Kibirige MS, Hutchison S, Owen CJ, *et al.* (2004) Prevalence of maternal dietary iodine insufficiency in the north east of England: implications for the fetus. *Arch Dis Child Fetal Neonatal Ed* **89**, F436–F439.
7. Barnett C, Visser T, Williams F, *et al.* (2002) Inadequate iodine intake of 40 % of pregnant women from a region in Scotland. *J Endocrinol Invest* **25**, Suppl. 7, 90.
8. Pearce EN, Lazarus JH, Smyth PP, *et al.* (2010) Perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant women. *J Clin Endocrinol Metab* **95**, 3207–3215.
9. Andersson M, Karumbunathan V & Zimmermann MB (2012) Global iodine status in 2011 and trends over the past decade. *J Nutr* **142**, 744–750.
10. Zimmermann MB (2009) Iodine deficiency. *Endocr Rev* **30**, 376–408.
11. Bath SC, Steer CD, Golding J, *et al.* (2013) Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). *Lancet* **382**, 331–337.
12. Caldwell K, Pan Y, Mortensen ME, *et al.* (2013) Iodine status in pregnant women in the National Children's Study and in U.S. women (15–44 years), National Health and Nutrition Examination Survey 2005–2010. *Thyroid* **23**, 927–937.
13. Brough L, Jin Y, Shukri NH, *et al.* (2013) Iodine intake and status during pregnancy and lactation before and after government initiatives to improve iodine status, in Palmerston North, New Zealand: a pilot study. *Matern Child Nutr* (Epublication ahead of print version 18 June 2013).
14. Zimmermann MB & Andersson M (2012) Assessment of iodine nutrition in populations: past, present, and future. *Nutr Rev* **70**, 553–570.
15. Secretariat WHO, Andersson M, de Benoist B, *et al.* (2007) Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. *Public Health Nutr* **10**, 1606–1611.
16. NHS (2011) NHS choices. Your health during pregnancy. Vitamins, minerals and special diets. In *The Pregnancy Care Planner*. http://www.nhs.uk/Planners/pregnancycare planner/pages/Vitaminsmineralsdiets.aspx (accessed 19 July 2011).
17. Henderson L, Irving K, Gregory J, *et al.* (2003) *The National Diet & Nutrition Survey: Adults Aged 19 to 64 Years. Volume 3: Vitamin and Mineral Intake and Urinary Analytes.* London: HMSO.
18. National Health and Medical Research Council and New Zealand Ministry of Health (NHMRC) (2010) Iodine supplementation for pregnant and breastfeeding women.

http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/new45_statement.pdf (accessed 10 October 2011).

19. Stagnaro-Green A, Abalovich M, Alexander E, et al. (2011) Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid* **21**, 1081–1125.

20. Nelson M, Phillips DI, Morris JA, et al. (1988) Urinary iodine excretion correlates with milk iodine content in seven British towns. *J Epidemiol Community Health* **42**, 72–75.

21. Wang CY, Cogswell ME, Loria CM, et al. (2013) Urinary excretion of sodium, potassium, and chloride, but not iodine, varies by timing of collection in a 24-hour calibration study. *J Nutr* **143**, 1276–1282.

22. Bingham SA, Welch AA, McTaggart A, et al. (2001) Nutritional methods in the European Prospective Investigation of Cancer in Norfolk. *Public Health Nutr* **4**, 847–858.

23. Food Standards Agency (2002) *Food Portion Sizes*, 3rd ed. London: The Stationary Office.

24. Rogers I & Emmett P (1998) Diet during pregnancy in a population of pregnant women in South West England. ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and Childhood. *Eur J Clin Nutr* **52**, 246–250.

25. Delange F (2007) Iodine requirements during pregnancy, lactation and the neonatal period and indicators of optimal iodine nutrition. *Public Health Nutr* **10**, 1571–1580, discussion 1581–1573.

26. Knudsen N, Christiansen E, Brandt-Christensen M, et al. (2000) Age- and sex-adjusted iodine/creatinine ratio. A new standard in epidemiological surveys? Evaluation of three different estimates of iodine excretion based on casual urine samples and comparison to 24 h values. *Eur J Clin Nutr* **54**, 361–363.

27. Konig F, Andersson M, Hotz K, et al. (2011) 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* **141**, 2049–2054.

28. Rasmussen LB, Ovesen L & Christiansen E (1999) Day-to-day and within-day variation in urinary iodine excretion. *Eur J Clin Nutr* **53**, 401–407.

29. Mojtahedi M, de Groot LC, Boekholt HA, et al. (2002) Nitrogen balance of healthy Dutch women before and during pregnancy. *Am J Clin Nutr* **75**, 1078–1083.

30. Pahl MV, Culver BD, Strong PL, et al. (2001) The effect of pregnancy on renal clearance of boron in humans: a study based on normal dietary intake of boron. *Toxicol Sci* **60**, 252–256.

31. Zimmermann MB (2007) The adverse effects of mild-to-moderate iodine deficiency during pregnancy and childhood: a review. *Thyroid* **17**, 829–835.

32. WHO (2006) Part IV: implementing effective and sustainable food fortification programmes. Annex C. In *Guidelines on Food Fortification with Micronutrients*, [L Allen, B de Benoist, O Dary and RF Hurrell, editors]. Geneva: World Health Organization.

33. Haddow JE, McClain MR, Palomaki GE, et al. (2007) Urine iodine measurements, creatinine adjustment, and thyroid deficiency in an adult United States population. *J Clin Endocrinol Metab* **92**, 1019–1022.

34. Hynes KL, Otahal P, Hay I, et al. (2013) Mild iodine deficiency during pregnancy is associated with reduced educational outcomes in the offspring: 9-year follow-up of the gestational iodine cohort. *J Clin Endocrinol Metab* **98**, 1954–1962.

35. Alvarez-Pedrerol M, Ribas-Fito N, Garcia-Esteban R, et al. (2010) Iodine sources and iodine levels in pregnant women from an area without known iodine deficiency. *Clin Endocrinol* **72**, 81–86.

36. Marco A, Vicente A, Castro E, et al. (2010) Patterns of iodine intake and urinary iodine concentrations during pregnancy and blood thyroid-stimulating hormone concentrations in the newborn progeny. *Thyroid* **20**, 1295–1299.

37. Andersen SL, Sorensen LK, Krejbjerg A, et al. (2013) Iodine deficiency in Danish pregnant women. *Dan Med J* **60**, A4657.

38. Pettigrew-Porter A, Skeaff S, Gray A, et al. (2011) Are pregnant women in New Zealand iodine deficient? A cross-sectional survey. *Aust N Z J Obstet Gynaecol* **51**, 464–467.

39. Berbel P, Mestre JL, Santamaria A, et al. (2009) Delayed neurobehavioral development in children born to pregnant women with mild hypothyroxinemia during the first month of gestation: the importance of early iodine supplementation. *Thyroid* **19**, 511–519.

40. Velasco I, Carreira M, Santiago P, et al. (2009) Effect of iodine prophylaxis during pregnancy on neurocognitive development of children during the first two years of life. *J Clin Endocrinol Metab* **94**, 3234–3241.

41. Rebagliato M, Murcia M & Alvarez-Pedrerol M (2013) Iodine supplementation during pregnancy and infant neuropsychological development: INMA mother and child cohort study. *Am J Epidemiol* (Epublication ahead of print version 1 April 2013).

42. Moleti M, Di Bella B, Giorgianni G, et al. (2011) Maternal thyroid function in different conditions of iodine nutrition in pregnant women exposed to mild-moderate iodine deficiency: an observational study. *Clin Endocrinol* **74**, 762–768.

43. Perrine CG, Herrick K, Serdula MK, et al. (2010) Some subgroups of reproductive age women in the United States may be at risk for iodine deficiency. *J Nutr* **140**, 1489–1494.

44. Gregory CO, Serdula MK & Sullivan KM (2009) Use of supplements with and without iodine in women of childbearing age in the United States. *Thyroid* **19**, 1019–1020.

45. Andersson M, Aeberli I, Wust N, et al. (2010) The Swiss iodized salt program provides adequate iodine for school children and pregnant women, but weaning infants not receiving iodine-containing complementary foods as well as their mothers are iodine deficient. *J Clin Endocrinol Metab* **95**, 5217–5224.

46. Charlton KE, Gemming L, Yeatman H, et al. (2010) Suboptimal iodine status of Australian pregnant women reflects poor knowledge and practices related to iodine nutrition. *Nutrition* **26**, 963–968.

47. Williamson C, Lean MEJ & Combet E (2012) Dietary recommendations and iodine awareness among mothers in the UK. *Proc Nutr Soc* **71**, E141 Abstr.

48. Office of National Statistics (2011) *Indices of Deprivation 2010 for Super Output Areas*, ONS. http://www.neighbourhood.statistics.gov.uk/dissemination/instanceSelection.do?JSAllowed=true&Function=&%24ph=60_61&CurrentPageId=61&step=2&datasetFamilyId=2307&instanceSelection=127506&Next.x=17&Next.y=8 (accessed 22 January 2012).

49. Henderson L, Gregory J & Swan G (2002) *The National Diet & Nutrition Survey: Adults Aged 19 to 64 Years. Volume 1: Types and Quantities of Foods Consumed*. London: The Stationary Office.

50. Mian C, Vitaliano P, Pozza D, *et al.* (2009) Iodine status in pregnancy: role of dietary habits and geographical origin. *Clin Endocrinol* **70**, 776–780.

51. Brantsaeter AL, Haugen M, Julshamn K, *et al.* (2007) 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). *Eur J Clin Nutr* **63**, 347–354.

52. Bath S & Rayman MP (2011) Iodine deficiency in UK schoolgirls. *Lancet* **378**, 1623; author reply 1624.

53. Costeira MJ, Oliveira P, Ares S, *et al.* (2009) Iodine status of pregnant women and their progeny in the Minho Region of Portugal. *Thyroid* **19**, 157–163.

54. Bath S, Button S & Rayman MP (2013) Availability of iodised table salt in the UK – is it likely to influence population iodine intake? *Public Health Nutr* (Epublication ahead of print version 16 January 2013).

55. Andersen S, Karmisholt J, Pedersen KM, *et al.* (2008) Reliability of studies of iodine intake and recommendations for number of samples in groups and in individuals. *Br J Nutr* **99**, 813–818.

56. Moleti M, Lo Presti VP, Campolo MC, *et al.* (2008) Iodine prophylaxis using iodized salt and risk of maternal thyroid failure in conditions of mild iodine deficiency. *J Clin Endocrinol Metab* **93**, 2616–2621.