Iodine status of UK schoolgirls: a cross-sectional survey

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Summary

Background **Iodine deficiency is the most common cause of preventable mental impairment worldwide. It is defined by WHO as mild if the population median urinary iodine excretion is 50–99 µg/L, moderate if 20–49 µg/L, and severe if less than 20 µg/L. No contemporary data are available for the UK, which has no programme of food or salt iodination. We aimed to assess the current iodine status of the UK population.**

Methods **In this cross-sectional survey, we systematically assessed iodine status in schoolgirls aged 14–15 years attending secondary school in nine UK centres. Urinary iodine concentrations and tap water iodine concentrations were measured in June–July, 2009, and November–December, 2009. Ethnic origin, postcode, and a validated diet questionnaire assessing sources of iodine were recorded.**

Findings **810 participants provided 737 urine samples. Data for dietary habits and iodine status were available for 664 participants. Median urinary iodine excretion was 80·1 µg/L (IQR 56·9–109·0). Urinary iodine measurements indicative of mild iodine deficiency were present in 51% (n=379) of participants, moderate deficiency in 16% (n=120), and severe deficiency in 1% (n=8). Prevalence of iodine deficiency was highest in Belfast (85%, n=135). Tap water iodine concentrations were low or undetectable and were not positively associated with urinary iodine concentrations. Multivariable general linear model analysis confirmed independent associations between low urinary iodine excretion and sampling in summer (p<0·0001), UK geographical location (p<0·0001), low intake of milk (p=0·03), and high intake of eggs (p=0·02).**

Interpretation **Our findings suggest that the UK is iodine deficient. Since developing fetuses are the most susceptible to adverse effects of iodine deficiency and even mild perturbations of maternal and fetal thyroid function have an effect on neurodevelopment, these findings are of potential major public health importance. This study has drawn attention to an urgent need for a comprehensive investigation of UK iodine status and implementation of evidence-based recommendations for iodine supplementation.**

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See Comment page 1979

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Introduction

WHO estimates that two billion people worldwide including 285 million children of school age have iodine deficiency despite major national and international efforts to increase iodine intake, mainly through voluntary or mandatory iodisation of salt.[1,2] Iodine deficiency is defined as a population median urine iodine excretion less than 100 µg/L, with deficiency classified as moderate if 20–49 µg/L and severe if less than 20 µg/L.[3] Iodine deficiency has substantial effects on growth and development and is the most common cause of preventable mental impairment worldwide. Mild iodine deficiency impairs cognition in children, and moderate to severe iodine deficiency in a population reduces IQ by 10–15 points.[4] Iodine supplementation before pregnancy might prevent this adverse effect on the intellectual development of infants and children.[5] Mild-to-moderate iodine deficiency occurs in areas that are not immediately recognised as iodine deficient.[3] Iodine intake can vary substantially within a region and country because of variations in the natural iodine content of food and water.[6]

Around 45% of the population of continental Europe continues to have evidence of iodine deficiency, although iodine status in several regions has not been documented.[7] No current data are available for the UK population.[8] Although the UK population was historically thought to have sufficient iodine intake,[9] concern has been expressed about current UK iodine intake.[10] We aimed to assess systematically the iodine status of the UK population using the standard approach of targeting the most relevant age group and sex.

Urine iodine excretion is a good marker of dietary intake of iodine over days and is the measure of choice for assessment of iodine status.[3] For epidemiological studies, a population distribution of urinary iodine is required and, because the frequency distribution is typically skewed towards high values, the median rather than the mean is judged the best indicator of iodine status. WHO, International Council for Control of Iodine Deficiency Disorders, and UNICEF recommend that for national surveys of iodine nutrition, the median urinary iodine from representative samples of spot urine collections from children aged 6–12 years can be used to define a population's iodine status.[3] This study focused on female schoolchildren aged 14–15 years from nine UK centres, since those who might proceed to pregnancy in the short-to-medium term (and their

offspring) are the most susceptible to the adverse effects of iodine deficiency.

Methods

Participants

Participants in this cross-sectional survey were recruited from nine centres across the UK (Aberdeen, Belfast, Birmingham, Cardiff, Dundee, Exeter, Glasgow, London, and Newcastle-upon-Tyne), with three different sampling clusters in each centre, broadly in accord with WHO guidance.[3] Multicentre ethics approval was obtained (reference 09/H0720/47). Girls aged 14–15 years attending secondary schools were invited to participate. Members of the survey team made a presentation to participants about the role of the thyroid gland and the effect worldwide of iodine deficiency.

See Online for webappendix

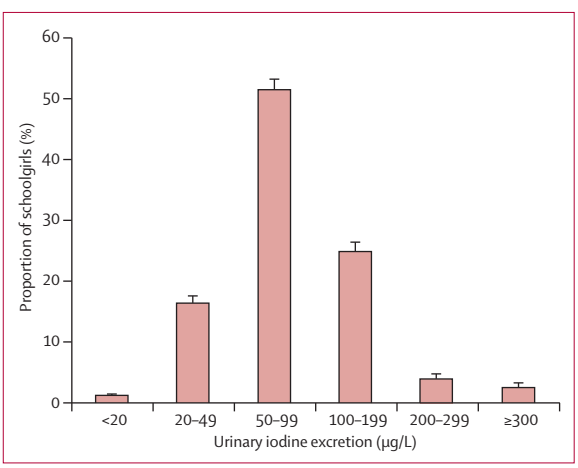

Figure 1: **Urinary iodine concentration in UK schoolgirls, showing the proportions of participants with mild (50–99 µg/L), moderate (20–49 µg/L), and severe (<20 µg/L) iodine deficiency**
Bars show standard error.

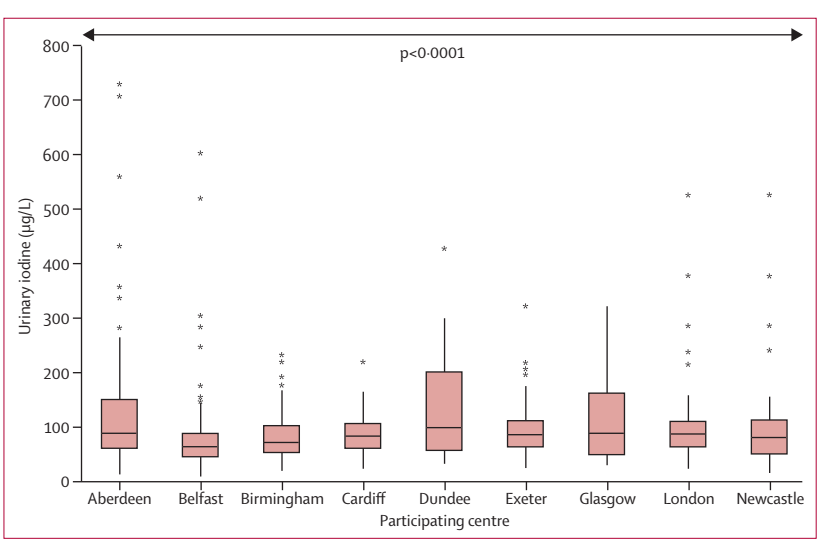

Figure 2: **Median urinary iodine according to participating centre**
Kruskal-Wallis test for global comparison of all centres, p<0·0001.

Procedures

A 20 mL non-fasting sample of early morning urine was obtained for each participant in specimens collected in June–July (summer), 2009, and November–December (winter), 2009. Urinary iodine excretion was measured by a multiplate persulphate digestion method followed by Sandel-Kolthoff colorimetry.[11] The sensitivity of the assay was 5 µg/L and quality control was assessed in a laboratory that participated in the US Centers for Disease Control and Prevention EQUIP programme.[12]

A 5 mL sample of tap water at each sampling site for each centre was taken at the time of collection of urine samples. Iodine was measured by the method of alkaline incineration of the sample followed by resuspension and iodine measurement by the Ceri/As method.[6] With a 2 mL sample, the limit of detection was 1·0 µg/L and all samples were measured in duplicate. The recovery of added iodine was greater than 95%.

Ethnic origin, date of birth, postcode, and a validated diet questionnaire[13] (webappendix p 1) assessing sources of iodine were recorded. Ethnic origin was self-classified as white, Asian, Afro-Caribbean, or other. No assessment of thyroid size or function was made.

Statistical analysis

Minitab (version 15) and SPSS (version 18) software were used for all analyses. We used the Mann-Whitney test and Kruskal-Wallis tests for comparison of two or more groups of non-normal data. The Kolmogorov-Smirnov test was used to test for normality. Binomial tests were used to compare two binomial proportions. We did χ^2 tests to compare the consumption of milk and eggs between Belfast and other UK centres. A non-parametric Spearman correlation test was used to assess the relation between average drinking water iodine content in each centre and urinary iodine. The Spearman correlation test was also used to investigate the relation between dietary habits and urinary iodine. We used binary logistic regression analysis to investigate the association between ethnic origin and dietary habits and to establish the probability of iodine deficiency in different UK centres.

A multivariable analysis using the general linear model was used to establish the effect of dietary habits, ethnic origin, season of sampling, and UK geographical location on urinary iodine. Since residuals for urinary iodine were not normally distributed, we explored the Box-Cox set of transformations. The logarithmic transformation was optimum and the residuals followed a normal distribution after exclusion of the five highest and five lowest urinary iodine measurements as tested by the Kolmogorov-Smirnov statistic. Further analyses also included interaction factors between season of sampling and milk intake and between season of sampling and consumption of eggs. All two-factor interactions were considered, but only these two were retained together with all main effects. Significance was taken as p<0·05.

Role of the funding source
The Clinical Endocrinology Trust provided funding for the cost of the materials and assays used in the study. The corresponding author had full access to all data in the study and had final responsibility to submit for publication.

Results

810 schoolgirls participated in the survey, of whom 737 provided urine samples. Questionnaire data were available for 664 of these 737 participants. 73 participants provided questionnaire data only. 30 tap water samples were obtained to establish iodine concentration in drinking water in participating centres.

The median urinary iodine excretion in our sample was 80·1 µg/L (IQR 56·9–109·0), for which the 95% CI was 76·7–83·6 µg/L, indicating that the sample size was sufficiently large to estimate median urinary iodine to within 7 µg/L. Within the sample of 737 participants, urinary iodine measurements indicative of mild iodine deficiency (50–99 µg/L) were present in 51% (n=379), moderate deficiency (20–49 µg/L) in 16% (n=120), and severe deficiency (<20 µg/L) in 1% (n=8; figure 1). Median urinary iodine concentration differed significantly between centres (p<0·0001) with the lowest measurements recorded in Belfast (64·7 µg/L) and highest in Dundee (98·4 µg/L). Figure 2 shows median urinary iodine by centre.

Table 1 shows the proportions of participants in each participating centre with iodine deficiency (urinary iodine <100 µg/L), as well as the subgroups with mild (50–99 µg/L) and moderate-to-severe iodine deficiency (<50 µg/L). The probability of iodine deficiency was highest in Belfast, where 85% (n=135) of participants had urinary iodine excretion less than 100 µg/L, and odds ratios (ORs) for iodine deficiency were significantly lower in every other centre (table 2). Very low urinary iodine measurements compatible with severe iodine deficiency were found in five participants in Belfast, two in Aberdeen, and one in Newcastle, but not in other centres.

Iodine concentrations were measured in tap water samples from schools at each sampling site for each centre. Iodine concentrations were universally less than 3 µg/L with the exception of London, where measurements varied between 5·2 and 18·2 µg/L. This pattern reflects universally low iodine content in water apart from in London, where tap water contained moderate amounts. There was no positive association between iodine content of tap water and urinary iodine concentration (data not shown).

Table 3 shows the dietary habits of the 664 participants who completed the dietary questionnaire in addition to providing a urine sample. Increasing intake of milk was associated with high median urinary iodine (p=0·002). Low urinary iodine was not associated with intake of cheese, eggs, beef, chicken, or fish. We investigated the dietary habits of the 73 participants who did not provide a urine sample. Dietary habits of these participants, and in particular the intake of milk and eggs, were not significantly different from those of participants who provided a urine sample. Since the highest proportions of participants with iodine deficiency were recorded in Belfast, we compared dietary habits in this centre with those in other UK locations. Dietary habits, and in particular the consumption of milk and eggs, were not significantly different when comparing Belfast with other UK centres.

Urinary iodine concentration was lower during summer (n=537, median 76·2 µg/L, IQR 56·9–100·8) than in winter (n=200, median 95·1 µg/L, 58·3–158·8; p<0·0001). Urine samples were provided by 517 white (median 78·6 µg/L), 33 Afro-Caribbean (77·1 µg/L), and 47 Asian (93·7 µg/L) participants, with 33 belonging to other ethnic groups (79·3 µg/L); ethnic origin was not declared by 34 participants (82·7 µg/L). There was no difference in urinary iodine excretion between ethnic

	n	Participants with iodine deficiency (urinary iodine <100 µg/L)	Participants with mild iodine deficiency (urinary iodine 50–99 µg/L)	Participants with moderate-to-severe iodine deficiency (urinary iodine <50 µg/L)
Aberdeen	110	65 (59%)	54 (49%)	11 (10%)
Belfast	159	135 (85%)	86 (54%)	49 (31%)
Birmingham	127	92 (72%)	70 (55%)	22 (17%)
Cardiff	43	29 (67%)	24 (56%)	5 (12%)
Dundee	38	20 (53%)	15 (39%)	5 (13%)
Exeter	82	53 (65%)	43 (52%)	10 (12%)
Glasgow	21	11 (52%)	8 (38%)	3 (14%)
London	99	65 (66%)	55 (56%)	10 (10%)
Newcastle/Gateshead	58	37 (64%)	24 (41%)	13 (22%)
All centres	737	507 (69%)	379 (51%)	128 (17%)

Data are n (%).

Table 1: **Median urinary iodine concentrations in participating UK centres**

	Probability of iodine deficiency		Probability of moderate-to-severe iodine deficiency	
	OR (95% CI)	p value	OR (95% CI)	p value
Belfast	1·0	..	1·0	..
Aberdeen	0·26 (0·14-0·84)	<0·0001	0·25 (0·12-0·51)	<0·0001
Birmingham	0·47 (0·26-0·84)	0·01	0·47 (0·27-0·83)	0·009
Cardiff	0·37 (0·17-0·80)	0·01	0·30 (0·11-0·80)	0·02
Dundee	0·20 (0·09-0·43)	<0·0001	0·34 (0·13-0·92)	0·03
Exeter	0·32 (0·17-0·61)	<0·0001	0·31 (0·15-0·65)	0·03
Glasgow	0·20 (0·07-0·51)	0·001	0·37 (0·11-1·33)	NS
London	0·34 (0·19-0·62)	<0·0001	0·25 (0·12-0·53)	<0·0001
Newcastle/Gateshead	0·31 (0·16-0·62)	0·0001	0·65 (0·32-1·31)	NS

The probability of overall (urinary iodine <100 µg/L) and moderate-to-severe (<50 µg/L) iodine deficiencies are shown. OR=odds ratio. NS=non-significant.

Table 2: **Probability of iodine deficiency in Belfast compared with other UK centres following binary logistic regression analysis**

	Number of participants	Median urinary iodine concentration (μg/L)	p value
Cows' milk (n=660)			
None	54 (8%)	61·95 (43·50–85·00)	..
Occasionally	254 (38%)	76·60 (53·26–103·45)	..
1 cup per day	244 (37%)	84·95 (57·55–120·85)	..
≥2 cups per day	108 (16%)	87·56 (69·10–123·65)	..
Interaction	..	..	0·002*, <0·0001†
Yoghurt (n=659)			
None	149 (23%)	74·60 (50·60–104·55)	..
1 pot per week	305 (46%)	83·70 (58·35–117·45)	..
>1 pot per week	205 (31%)	78·20 (57·95–108·05)	..
Interaction	..	..	0·08*, 0·38†
Cheese (n=661)			
None	97 (15%)	81·40 (54·25–120·20)	..
Once per week	287 (43%)	83·20 (58·90–115·78)	..
>Once per week	277 (42%)	75·80 (55·45–103·60)	..
Interaction	..	..	0·31*, 0·15†
Beef (n=661)			
None	144 (22%)	85·50 (58·68–111·08)	..
Once per week	288 (44%)	80·09 (55·90–118·90)	..
>Once per week	229 (35%)	78·20 (54·95–106·65)	..
Interaction	..	..	0·76*, 0·39†
Chicken (n=661)			
None	51 (8%)	73·20 (50·60–112·70)	..
Once per week	252 (38%)	81·30 (56·90–107·13)	..
>Once per week	358 (54%)	78·69 (56·30–111·41)	..
Interaction	..	..	0·74*, 0·94†
Eggs (n=660)			
None	176 (27%)	83·80 (57·70–132·05)	..
Once per week	394 (60%)	78·10 (55·65–107·40)	..
>Once per week	90 (14%)	71·00 (52·66–101·11)	..
Interaction	..	..	0·21*, 0·027†
Fish (n=660)			
None	235 (36%)	83·30 (57·80–118·00)	..
Once per week	362 (55%)	76·60 (56·90–107·53)	..
>Once per week	63 (10%)	85·20 (45·60–110·90)	..
Interaction	..	..	0·58*, 0·14†

Data are n (%), median (IQR), or p value. *Kruskal-Wallis test. †Spearman correlation.

Table 3: **Urinary iodine concentrations analysed according to dietary habits**

groups. Assessment of dietary habits established that Asian participants were more likely to consume cheese (OR 4·27, p=0·05) but less likely to consume beef (OR 0·14, p=0·001) and chicken (OR 0·26, p<0·0001) than were white participants. No other differences in dietary intake between ethnic groups were identified.

We established the effect of dietary habits (intake of milk, yoghurt, cheese, eggs, beef, chicken, and fish), ethnic origin, season of sampling (summer or winter), and UK geographical location (one of nine participating centres) on urinary iodine concentrations through general linear model analysis. The R^2 value for the overall analysis was 11·9% (p<0·0001). Sampling during summer (p<0·0001), UK geographical location (p<0·0001), low intake of milk (p=0·03), and high intake of eggs (p=0·02) were all independently associated with low urinary iodine excretion. There was no independent association with other dietary habits or with ethnic origin. Further detailed analysis showed that there was no significant interaction effect between the intake of milk and the season of sampling on urinary iodine excretion. There was a significant interaction between intake of eggs and season of sampling on urinary iodine excretion (p=0·002). During summer, urinary iodine did not differ significantly between participants who consumed eggs (median 76·0 μg/L) and those who did not (75·0 μg/L), whereas during winter, excretion was higher in those who did not consume eggs (131·9 μg/L *vs* 87·3 μg/L).

Discussion

Our findings suggest that the UK is now iodine deficient (panel). Endemic goitre associated with iodine deficiency was at one time widespread in the UK.[9] In 1924, a national survey of 375 000 12-year old schoolchildren in England and Wales found a prevalence of visible goitre of up to 30%.[14] A 1944 Medical Research Council survey reported visible goitre in 50% of adult women and 26–43% of schoolgirls.[15] No salt iodisation programme was adopted in the UK, unlike in other European countries. Several surveys undertaken in subsequent years showed that a high prevalence of thyroid enlargement continued in many areas of the UK well into the 1960s.[9]

Since the 1940s, significant changes in farming practice in the UK were associated with a rise in the iodine content of milk, particularly during winter months when cattle are dependent on iodine-rich artificial feed.[9] The seasonal variation in urinary iodine concentration in our study reflects the greater use of compound feeding stuffs containing iodine during winter. Additionally, successive UK Governments from the 1940s encouraged increased milk consumption in schoolchildren. By the 1980s, this approach resulted in the iodine content of milk alone being almost sufficient to meet the recommended daily requirement of 150 μg per day.[9] In 1995, at the 20-year follow-up of the Whickham survey in northeast England,[16] the median urinary iodine excretion for a random sample of 101 participants aged 38 years and older was 102 μg/L, which suggested that iodine deficiency was not present in that region. Recently, concern has again been expressed about UK iodine status because up to 50% of UK women of childbearing age screened in smaller studies at single centres were iodine deficient.[17–19] A similar pattern of iodine deficiency has been seen in Ireland, with iodine intake being especially low in the summer months.[12]

Our survey has provided evidence that the UK is now iodine deficient. Australia, which had been previously documented as iodine sufficient, has also been reported

to be iodine deficient.[20] Iodine intake can vary substantially within a region or country because of variation in the natural iodine content of water.[6] However, this UK survey has shown no regional differences in water iodine concentrations, apart from slightly raised levels in London. The reason why Belfast had the highest proportion of samples with a low urinary iodine concentration is unaccounted for, since dietary habits were no different to those in the rest of the UK, but the median urinary iodine value found was compatible with previous data from Ireland.[12]

The supplementation of animal feeding stuffs with iodine is controlled by legislation in the UK with a maximum permitted level of 10 mg/kg for dairy cattle.[21] Recent studies of pregnant women in Italy and Spain have confirmed that intake of cows' milk remains the main source of iodine.[13,22] This UK survey has confirmed milk intake to be positively associated with urinary iodine. An assessment of iodine concentrations in cows' milk in 2008 by the UK Food Standards Agency found milk iodine concentrations generally similar to those reported from previous surveys in 1995–1996 and reported that milk contributed 41% of the total iodine intake in the UK.[23] However, UK milk consumption has fallen[24] and, since milk iodine concentration remains unchanged, this study suggests that the reduced amount of milk now drunk by the population is responsible for the decline in iodine status. The inverse relation between egg consumption and urinary iodine is unaccounted for. The major dietary sources of iodine in countries where salt is iodised, such as the USA and Switzerland, are bread and milk.[25,26] Household iodised salt is rarely available to purchase in the UK and few if any manufacturers use iodised salt in the preparation and manufacture of foods.[10]

This study focused on young female participants aged 14–15 years who were prepregnancy, because in the short-to-medium term the children of these young women will be the most susceptible to the adverse effects of iodine deficiency.[4] Epidemiological studies have shown that reduced iodine intake during pregnancy leads to development of goitre, decreased free thyroxine concentrations, and increased serum thyroid-stimulating hormone (TSH) in pregnant women. Because maternal thyroxine is crucial for maturation of the fetal nervous system, especially before development of the fetal thyroid before 13 weeks of pregnancy, even mild iodine deficiency could be harmful. Data from the USA and Netherlands suggest that the children of women with hypothyroxinaemia can have psychoneurological deficits and delayed mental and motor function compared with controls.[27,28] This finding is in accord with those in classic areas of iodine deficiency, for which a range of psychological and neurological deficits in children are described and in which maternal hypothyroxinaemia rather than high serum TSH is the biochemical abnormality.[4] Little is known of the consequences of mild-to-moderate iodine deficiency in older children.[29] A recent randomised, placebo-controlled, double-blind trial in 184 children aged 10–13 years in New Zealand (median urinary iodine 63 µg/L) showed that iodine supplementation (150 µg/L daily) for 28 weeks improved perceptual reasoning, suggesting that mild iodine deficiency might prevent children attaining their full intellectual potential. Similar positive findings have been reported in European children who were moderately iodine deficient.[30]

We believe that the findings of this survey have great public health importance for the UK. Iodine deficiency presents a substantial challenge, as recently addressed in Australia.[31] Salt iodisation remains the most cost-effective way to control iodine deficiency[4] and recent epidemiological studies from Denmark have shown benefits both in terms of goitre prevalence and hyperthyroidism.[32] Although high iodine intake can be associated with very small increases in the incidence of subclinical hypothyroidism and autoimmune thyroiditis,[32] a more important consideration is to ensure that everyone, including young women, has an adequate iodine intake. A comprehensive investigation of UK iodine status and evidence-based recommendations on the need to implement a policy of iodine prophylaxis are urgently needed.

Panel: Research in context

Systematic review

We established from published work with PubMed, Ovid Medline, and Abridged Index Medicus (search terms used were "iodine", "deficiency", "UK", "goitre", and "WHO") and from WHO that no current data exist for the iodine status of the UK, which has no programme of food or salt iodination. Using methods defined by WHO,[3] we recruited participants from nine UK centres to undertake a systematic assessment of the current UK iodine status in schoolgirls aged 14–15 years by measuring urinary iodine concentrations. A multivariable analysis established the effect of dietary habits, ethnic origin, season of sampling, and UK geographical location on urinary iodine concentration.

Interpretation

We found that median urinary iodine excretion was indicative of mild iodine deficiency in the UK. Lower urinary iodine concentrations were recorded in Belfast than in other regions and were independently associated with sampling during summer months, low milk intake, and high egg intake. This study focused on young female participants who were prepregnancy because in the short-to-medium term the children of these young women will be the most susceptible to the adverse effects of iodine deficiency. The findings emphasise an urgent need for a comprehensive investigation of UK iodine status and evidence-based recommendations on the need to implement a policy of iodine prophylaxis.

Contributors
MPJV, JHL, PPS, PL, and JAF contributed to study design. KB, RLH, MPJV, and JAF took part in data analysis. All authors contributed to data interpretation. MPJV, KB, and JAF wrote the report. The British Thyroid Association UK Iodine Survey Group were responsible for data collection.

Conflicts of interest
We declare that we have no conflicts of interest.

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