

# A review of the iodine status of UK pregnant women and its implications for the offspring

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**Abstract** Iodine, as a component of the thyroid hormones, is crucial for brain development and is therefore especially important during pregnancy when the brain is developing most rapidly. While randomised controlled trials of pregnant women in regions of severe iodine deficiency have shown that prenatal iodine deficiency causes impaired cognition, less is known of the effects in regions of mild deficiency. This is relevant to the UK as the World Health Organisation now classifies the UK as mildly iodine deficient, based on a national study of 14–15 year old schoolgirls in 2011. We have previously published a study using samples and data from the UK-based Avon Longitudinal Study of Parents and Children (ALSPAC) that found an association between low iodine status in early pregnancy (urinary iodine-to-creatinine ratio  $<150 \mu\text{g/g}$ ) and lower verbal IQ and reading scores in the offspring. Though the women in ALSPAC were recruited in the early 1990s, the results of the study are still relevant as their iodine status was similar to that reported in recent studies of UK pregnant women. This review discusses the evidence that mild-to-moderate iodine deficiency during pregnancy has deleterious effects on child neurodevelopment and relates that evidence to the data

on iodine status in the UK. It has highlighted a need for nationwide data on iodine status of pregnant women and that a randomised controlled trial of iodine supplementation in pregnant women in a region of mild-to-moderate iodine deficiency with child outcomes as the primary endpoint is required.

**Keywords** Iodine · Nutrition · Pregnancy · UK · Cognition

## Role of iodine and intake recommendations for adults and pregnant women

Iodine is important during pregnancy and early life as it is required for the production of thyroid hormones, T4 and T3; these hormones are required for brain and neurological development of the foetus (Zimmermann 2009). The World Health Organisation (WHO) considers iodine deficiency to be “the single most important preventable cause of brain damage” worldwide (WHO et al. 2007). The “Iodine Deficiency Disorders” are largely the result of an inadequate production of thyroid hormones.

According to WHO/UNICEF/ICCIDD, the recommended iodine intake for adults ( $>12$  years) is  $150 \mu\text{g/day}$  (WHO et al. 2007). As iodine can be stored in the thyroid, it is important that women of childbearing age, and particularly those planning a pregnancy, meet their iodine requirement prior to

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conception to ensure that they have adequate iodine stores in the thyroid (Glinoe 2004). Recent evidence suggests that prolonged supply of iodine prior to the pregnancy is associated with lower probability of thyroid failure during pregnancy than a sudden supply of iodine at the start of pregnancy (e.g. through use of iodine supplements) (Moleti et al. 2011); this highlights the importance of an adequate iodine intake in women of childbearing age.

During pregnancy and lactation, the recommended iodine intake rises from 150 to 250 µg of iodine per day (WHO et al. 2007). The UK iodine recommendations, set in 1991, do not include an increment for pregnant or lactating women (Department of Health 1991) and are therefore outdated. There are three reasons for the higher recommendation in pregnancy: (1) to facilitate the 50 % surge in thyroid hormone production that occurs during early pregnancy, (2) to cover potential increased renal loss of iodine during pregnancy and (3) to supply iodine to the foetus so it can produce its own thyroid hormones after the onset of thyroid function in mid-gestation (Zimmermann 2009). In theory, it may be possible to utilise thyroidal iodine stores, and potentially placental iodine stores (Burns et al. 2011), to meet the higher iodine requirement of pregnancy (i.e. in addition to dietary iodine intake). However, in regions of iodine deficiency, thyroidal iodine stores would not have been maximised prior to the conception, and therefore cannot be drawn upon during pregnancy when demands on the thyroid are high. As brain development continues post-natally, ensuring an adequate supply of iodine during lactation is also essential as breast milk is the sole source of iodine for the exclusively breast-fed infant; the recommendation for lactating women is the same as for pregnancy (250 µg/day) (WHO et al. 2007).

It is clear that iodine excess should be avoided as there may be deleterious consequences for thyroid hormone production (both hypo- and hyperthyroidism) (Burgi 2010). A safe upper limit of 17 µg/kg body weight/day or 1,000 µg/day for adults has been suggested in the UK (Department of Health 1991). The tolerable upper intake level of iodine for adults (>12 years) and pregnant women has been set at 600 µg/day by the European Commission (Scientific Committee on Food 2002) and at 1,100 µg/day by the Institute of Medicine (IOM) (Food and Nutrition Board Institute of Medicine 2001). The upper limit

for iodine intake is a somewhat arbitrary cut-off as some individuals, particularly those with longstanding iodine deficiency, may respond adversely (i.e. develop iodine-induced hypo- or hyperthyroidism) to iodine intakes below the suggested safe level (Zimmermann 2009; Burgi 2010).

### Assessment of iodine status

Dietary assessment is not recommended for the estimation of iodine intake (Ovesen and Boeing 2002) because the iodine content of foods varies considerably, and therefore food-table values for iodine are not likely to reflect accurately the amount of iodine consumed. The iodine content of foods varies as a result of farming practice or soil iodine concentration; for example, winter milk has a higher iodine concentration than summer milk because cattle are more reliant on mineral-fortified feed in the winter (when housed indoors) than in the summer when they are out to grass (Phillips 1997). The high variation in iodine content of foodstuffs can result in inaccurate estimates of iodine intake from dietary analysis (Rasmussen et al. 2002). Furthermore, in many countries, iodised salt added during cooking and at the table can contribute to iodine intake and, as salt intake is difficult to quantify in dietary assessment, and this adds another complication to assessing iodine intake.

Urinary iodine concentration is considered to be a good biomarker of iodine status for groups or populations and reflects recent iodine intake (Zimmermann 2009). WHO/UNICEF/ICCIDD recommend comparing the median urinary iodine concentration from spot urine samples against cut-offs for describing population iodine status; a median below 100 µg/L in school-aged children and adults, or 150 µg/L in pregnant women is suggestive of iodine deficiency in the population (WHO et al. 2007). The disadvantage of urinary iodine excretion is that it does not directly assess thyroid function but a low (or indeed high) median urinary iodine concentration in a population may predict risk of thyroid disorders in a population (Zimmermann 2009).

Care should be taken that urine samples used for iodine analysis should not have been previously exposed to urine test strips as they may have contaminated the sample with iodine (Pearce et al.

2009; Chanoine et al. 1987). This may be of particular concern in studies of pregnant women that utilise samples collected during routine appointments, and indeed potential contamination has occurred in two studies of UK pregnant women (Pearce et al. 2010; Bath et al. 2013b).

It is important to highlight the fact that the urinary iodine concentration from a spot urine sample cannot be used to diagnose iodine deficiency in an individual. This is because of substantial intra-individual variation in daily urine volume excreted and in iodine intake (Zimmermann 2009). The variation in urine volume can largely be overcome by measuring urinary creatinine concentration, particularly if adjusted for the age and sex of the individual (Knudsen et al. 2000). However, even if the iodine-to-creatinine ratio is used, at least ten repeat urine samples would be required for assessment of iodine status in an individual (Konig et al. 2011). The iodine-to-creatinine ratio is not considered to be reliable in malnourished subjects, where a low protein intake, and thus low creatinine excretion, means that the iodine-to-creatinine ratio would mask iodine deficiency (Zimmermann 2009). However, in countries such as the UK, where subjects are well nourished, the iodine-to-creatinine ratio in pregnant women has potential epidemiological utility as it has been shown to relate to both child outcomes (Bath et al. 2013b) and diet (Bath et al. 2014b).

### Relationship between iodine status in pregnancy and child cognition in regions of mild-to-moderate iodine deficiency

It is known that severe iodine deficiency is related to the development of cretinism, either neurological or hypothyroid (myxedematous). The symptoms of neurological cretinism include hearing defects, spastic movements of arms and legs and mental retardation; hypothyroid cretinism leads to symptoms of thyroid insufficiency, such as dry skin and stunted growth but is associated with less severe mental insufficiency than is neurological cretinism (Zimmermann 2009). The effects of mild-to-moderate iodine deficiency on cognition are less well known than are those of severe iodine deficiency but are important as mild-to-moderate iodine deficiency is prevalent in many developed countries, including the UK.

### Iodine supplementation during pregnancy

Three iodine intervention studies, all Spanish, conducted in mildly to moderately iodine-deficient pregnant women, have included child cognitive outcomes (Berbel et al. 2009; Velasco et al. 2009; Santiago et al. 2013). However, none of these studies was a randomised placebo-controlled trial (RCT) and all have limitations. Berbel and colleagues supplemented women with 200 µg KI (150 µg iodine) from various stages of pregnancy until the end of lactation: 4–6 weeks (Group 1,  $n = 92$ ), 12–14 weeks (Group 2,  $n = 102$ ) and from term (Group 3,  $n = 151$ ). The neurocognitive performance of children from Group 1 was significantly higher than that of children in Group 2 or 3, suggesting a benefit of early iodine supplementation. However, it is important to note that the women were selected on the basis of their fT4 level at recruitment—Group 1 comprised women with fT4 above the 20th percentile, while Groups 2 and 3 had fT4 below the 10th percentile. Therefore, the study evaluates the effect of iodine supplementation on hypothyroxinaemic mothers and not the general population so interpretation is limited and the findings may reflect differences in fT4 in early pregnancy rather than the effect of delayed iodine supplementation. Furthermore, only small numbers of children in each group ( $n = 13$ , 12 and 19, respectively) were selected for neurocognitive testing. Velasco et al. (2009) supplemented women ( $n = 133$ ) with 300 µg KI (230 µg iodine) in the first trimester and, as the ethics committee did not permit a control group, they compared child neurodevelopment with those born to a group of women who had not received iodine during pregnancy ( $n = 61$ ). Unfortunately, neurological testing was conducted at significantly different ages in the offspring of treated and control women (5.47 and 12.44 months, respectively), and the length of gestation was significantly different between the groups (38.90 and 40.27 weeks, respectively). Though the psychomotor scores were significantly higher in offspring born to iodine-supplemented women than to controls, the results need to be interpreted with caution (Velasco et al. 2009). In another study in Spain, Santiago et al. (2013) randomly assigned 131 women to one of three groups: iodised table salt, 200 µg KI/day (150 µg iodine) or 300 µg KI/day (230 µg iodine). There was no significant difference in either maternal thyroid function or child

neurodevelopment (assessed between 6 and 18 months), though this may be because there was no control group that did not receive iodine, and there were small numbers in each group ( $n = 38$ ,  $n = 55$  and  $n = 38$ , respectively).

Other research has queried the benefit of iodine supplementation in pregnancy on cognition in the offspring following findings that the use of a supplement containing over 200  $\mu\text{g}$  iodine per day was associated with a higher risk of raised thyroid stimulating hormone (TSH) than that of a supplement containing less than 100  $\mu\text{g}/\text{day}$  (Rebagliato et al. 2010). The same group has evaluated the relationship between reported iodine supplement use and neurodevelopment at 12 months. In the Valencia cohort of the INMA study, psychomotor scores, particularly in girls, were found to be lower in the offspring of women who were taking a daily supplement containing  $\geq 150$   $\mu\text{g}$  iodine than in those taking a supplement containing less than 100  $\mu\text{g}/\text{day}$  (Murcia et al. 2011). However, in a follow-up study that included a larger number of children ( $n = 1,519$ ) from three cohorts in Spain, the results from the Valencia cohort were only partly confirmed (Rebagliato et al. 2013). While the relationship between use of a supplement containing  $\geq 150$   $\mu\text{g}$  iodine and higher odds of scores below 85 for both psychomotor (OR 1.5, 95 % CI 0.8–2.9), and mental development (OR 1.7, 95 % CI 0.9–3.0) was not significant in the whole group, in one region (Asturias), there was a significant association with lower psychomotor scores (Rebagliato et al. 2013). It is important to note that these studies (Rebagliato et al. 2010; Murcia et al. 2011; Rebagliato et al. 2013) were observational studies, and the iodine was part of a multivitamin/mineral supplement so the effects may not be iodine specific.

It is evident that a well-designed RCT is required in regions of mild-to-moderate iodine deficiency with child cognitive outcomes. However, the feasibility of conducting RCTs is becoming increasingly difficult as more countries recommend iodine supplements to pregnant women (National Health and Medical Research Council 2010; Stagnaro-Green et al. 2011), and there is concern over the ethical implications of a placebo-controlled trial (Stagnaro-Green et al. 2012). The ongoing MITCH trial (Maternal Iodine Supplementation and Effects on Thyroid Function and Child Development) is an RCT in regions of mild-to-moderate iodine deficiency (India and Thailand) that

is randomising pregnant women to iodine (200  $\mu\text{g}$  KI) or placebo and measuring maternal and infant thyroid function as well as child development up to 24 months of age (Zimmermann and Melse-Boonstra 2008). The results are expected in 2015 and will help to determine whether iodine supplementation during pregnancy is beneficial, and indeed safe, in regions of mild-to-moderate deficiency (Melse-Boonstra et al. 2012). However, further evidence will likely be required, particularly in the UK. We have previously argued that the UK is one of the few countries that could ethically conduct an RCT, as there are no official recommendations for a higher intake of iodine, or recommendation for iodine supplementation during pregnancy and lactation, and no salt-iodisation policy (Bath et al. 2013a).

#### Observational studies of iodine in pregnancy and child cognition

As mentioned above, the effect of in utero mild-to-moderate iodine deficiency on child cognition is relatively unexplored, especially in the UK. Though many studies have investigated the relationship between maternal thyroid function and child cognitive development (Melse-Boonstra and Jaiswal 2010), this is not the same as exploring the effect of iodine per se, as maternal thyroid function may be affected by other factors, not just iodine intake. For the first time in the UK, in collaboration with researchers at the University of Bristol, we were able to explore this relationship by measuring iodine status (from stored urine samples collected in the first trimester) in 1,040 pregnant women that were recruited to the Avon Longitudinal Study of Parent and Children (ALSPAC) in the 1990s (Golding et al. 2001) and relating it to IQ at age 8 years and reading ability at age 9 years. The results, published in the *Lancet* in May 2013, showed that the women were classified as mildly to moderately iodine deficient, with a median urinary iodine concentration of 91.1  $\mu\text{g}/\text{L}$  (iodine-to-creatinine ratio: 110  $\mu\text{g}/\text{g}$ ) (Bath et al. 2013b). Using the WHO/UNICEF/ICCIDD criteria for iodine deficiency or sufficiency in pregnancy, we dichotomised women on the basis of their iodine-to-creatinine ratio to one of two groups,  $<150$  or  $\geq 150$   $\mu\text{g}/\text{g}$ . Following adjustment for up to 21 potential confounding variables (including maternal and paternal education, gender and maternal age) children of women with an iodine-to-creatinine ratio

of less than 150 µg/g were significantly more likely to be in the bottom quartile of scores for verbal IQ at age 8 (OR 1.58, 95 % CI 1.09–2.30;  $p = 0.02$ ), reading accuracy (OR 1.69, 95 % CI 1.15–2.49;  $p = 0.007$ ) and reading comprehension (OR 1.54, 95 % CI 1.06–2.23;  $p = 0.02$ ) at age 9 years, (Bath et al. 2013b). Furthermore, when the <150 µg/g group was subdivided, scores for IQ, reading accuracy and reading comprehension worsened across the categories, with lower scores in the <50 µg/g group than the 50–150 µg/g group or the ≥150 µg/g group.

A number of other studies have also evaluated the relationship between urinary iodine status in pregnancy and child development. Researchers in Spain assessed iodine status (urinary iodine concentration) in the first and third trimester of pregnancy and related the measurements to child neurodevelopment, as assessed by the Bayley Scale of Infant Development (Costeira et al. 2011). The study found that pregnant women with a urinary iodine concentration below 50 µg/L had children with a significantly lower Psychomotor Development Index (PDI) at 18 months and a significantly lower Mental Development Index at both 18 and 24 months than children born to mothers with status above 50 µg/L. The study was limited by the small number of children assessed ( $n = 86$ ) and the relatively low cut-off applied to indicate iodine deficiency (i.e. assessing status closer to severe iodine deficiency than mild-to-moderate deficiency).

In the Netherlands ( $n = 692$ ), the association between urinary iodine excretion in early pregnancy (median 13.2 weeks gestation) and executive function in children up to the age of 4 years was evaluated as part of the Generation R study (van Mil et al. 2012). The researchers defined low iodine status as an iodine-to-creatinine ratio in the bottom 10th percentile, which was equivalent to iodine-to-creatinine <136 µg/g. They found that, after adjusting for potential confounders, children born to mothers with low iodine status had impaired working memory, though the effect was modest ( $\beta = 0.06$ , 95 % CI 0.01, 0.10) and other effects (e.g. inhibition scores—i.e. ability to stop own behaviour) were attenuated after adjustment for maternal psychological symptoms (van Mil et al. 2012). It is perhaps not surprising that this study found minimal effects of low iodine status, as the group as a whole was iodine sufficient, and therefore the number of women with low iodine status was relatively small.

A study in Australia has found an association between maternal iodine status (measured throughout pregnancy) and educational outcomes up to the age of 9 years (Hynes et al. 2013b). The median urinary iodine concentration was 81 µg/L. Using a similar methodology to our ALSPAC study, the pregnant women were dichotomised according to their urinary iodine concentration, on the basis of the WHO/UNICEF/ICCIDD cut-off for pregnancy (i.e. above or below 150 µg/L), although in contrast to our study, iodine excretion was not corrected for urinary creatinine concentration. Children born to mothers with urinary iodine concentration below 150 µg/L had poorer scores for spelling, grammar and English literacy, although only the association with spelling was significant after complete adjustment for confounders (i.e. including maternal socio-economic status) (Hynes et al. 2013a). The number of mother-child pairs was much lower in this study than in the ALSPAC study (228 vs. 1,040, respectively), and therefore a lack of power may explain the null results for some of the educational outcomes. Interestingly, as a result of a voluntary iodine fortification programme, the children grew up in an iodine-sufficient environment, showing that the negative effects of iodine deficiency during pregnancy cannot be completely overcome by a sufficient intake of iodine in childhood.

In contrast to the studies outlined above, a recent study of iodine-sufficient pregnant women in the Netherlands has found no significant association between maternal iodine status (mean 13.2 weeks gestation) and child cognition at age six (Ghassabian et al. 2014). That study also dichotomised women according to their iodine-to-creatinine ratio on the basis of WHO criteria (above and below 150 µg/g) and unlike the Hynes et al. study, did correct the iodine measured in the spot urine sample for creatinine concentration. Though children born to women with low iodine status were more likely to have scores in the bottom quartile for non-verbal IQ, this was attenuated after adjustment for confounders (OR 1.33, 95 % CI 0.92, 1.92). Women in Generation R had a higher median urinary iodine concentration than ALSPAC women (229.6 vs. 91.1 µg/L or 296.5 vs. 110 µg iodine/g creatinine), and a much smaller percentage of women had low iodine status (i.e. <150 µg/g) (12.3 vs. 67.4 %). Lack of power may therefore explain the null result in the Netherlands as, although the overall sample size was larger (1,525 vs. 1,040), the number

of women with low status was smaller (188 vs. 646 women). Furthermore, although 12.3 % of women in the Netherlands were assigned to the low iodine group, it is possible that they were misclassified on the basis of the single spot urine sample, and that they were in fact iodine sufficient having adequate stores of iodine in the thyroid (Ghassabian et al. 2014).

### Iodine status in the UK

Iodine deficiency was historically common in the UK, with a goitre belt that extended from the West Country and included Derbyshire, where goitre was so common it was called “Derbyshire neck” (Phillips 1997). Iodine deficiency persisted until the 1960s but was subsequently eradicated, not by the usual practice of an iodised-salt programme, but through an adventitious increase in milk-iodine concentration and concurrent increase in milk consumption (Phillips 1997). Milk-iodine concentration increased as a result of changes in the dairy-farming industry when dairy farmers began to add iodine to cattle feed to improve the health of the herd and also as a result of the use of iodine-containing disinfectants (iodophors). Iodine intake increased threefold between the 1950s and the 1980s (Wenlock et al. 1982) and was sufficient to eradicate goitre. After the eradication of goitre, there was an assumption that iodine deficiency was no longer a problem in the UK (Phillips 1997). In the years that followed goitre eradication, there were very few surveys of the iodine status of the population using recommended methods (i.e. goitre prevalence or urinary iodine concentration). In fact, until 2011, the UK was one of the few countries worldwide that was classified by WHO as having “no data” on population iodine status (de Benoist et al. 2008).

The National Diet and Nutrition Survey monitored iodine intake (from food diary analysis) but as mentioned above, this is not considered to be an accurate method of assessment. Nevertheless, the data suggested that milk and dairy products were the principal source of iodine in the UK diet, contributing up to 42 % in the adult 2000/01 survey (Henderson et al. 2003). The NDNS data have suggested that intake has fallen over time—iodine intake in the 2000/01 adult survey was significantly lower than in the 1986/87 survey (Henderson et al. 2003). This fall in iodine intake appears to be continuing, although as a

result of methodological differences between the surveys, the latest results from the NDNS rolling programme (2008/09–2011/12) do not report the statistical differences in iodine intake between the historical and current NDNS results (Bates et al. 2014).

Concern for the iodine status of UK women was heightened in 2011 when the first national survey of iodine status for more 60 years was conducted (Vanderpump et al. 2011). The study collected spot urine samples from over 737 schoolgirls (14–15 years) from nine locations across the UK as well as administering a dietary questionnaire. The median urinary iodine concentration, at 80.1 µg/L, revealed mild iodine deficiency in the cohort (Vanderpump et al. 2011) on the basis of the WHO cut-off for adequacy in adults of 100 µg/L (WHO et al. 2007). The median urinary iodine concentration was significantly higher in the winter months (November–December;  $n = 200$ ) than in the summer months (June–July;  $n = 537$ ) (95.1 vs. 76.2 µg/L;  $p < 0.0001$ ). Low iodine concentration was associated with sampling in the summer, low intake of milk, geographical location (lowest iodine status in Belfast) and high intake of eggs. However, caution has been urged over the inverse relationship between eggs and urinary iodine concentration as a result of the ambiguous food frequency questionnaire (Bath and Rayman 2011).

A Lancet Comment (Stagnaro-Green and Pearce 2013) published with our ALSPAC paper (Bath et al. 2013b) suggested that the finding of iodine deficiency in UK schoolgirls (Vanderpump et al. 2011) in combination with the evidence of the deleterious effects of iodine deficiency in pregnancy on child cognition, should be seen as “call to action to public health policy makers in the UK”. Indeed the UK Scientific Advisory Committee on Nutrition (SACN) has reviewed the evidence for iodine deficiency in the UK and published a position paper in February 2014 (Scientific Advisory Committee on Nutrition 2014). The review was a scoping exercise, rather than a full risk assessment, and the committee did not make public health recommendations. From April 2013, spot urine samples for the purpose of iodine measurement have been collected as part of the National Diet and Nutrition Survey, and these will provide representative data on the iodine status of adults and children over the age of 4 years (Scientific Advisory Committee on Nutrition 2014) from 2015. Unfortunately, NDNS does not include pregnant women and

SACN recognise that more data on this vulnerable group are required (Scientific Advisory Committee on Nutrition 2014).

Current iodine status in UK pregnant women: do the results from the ALSPAC study apply to the present day?

There are relatively few recent studies of iodine status (i.e. using urinary iodine excretion) in UK pregnant women but all five, from locations across the UK, have found a degree of deficiency (Table 1).

We have evaluated iodine status in pregnant women in both Surrey (Bath et al. 2014b) and Oxford (Furmidge-Owen et al. 2014). In Surrey, we recruited 100 first-trimester pregnant women during the summer months. The median urinary iodine concentration (85.3  $\mu\text{g/L}$ ) was considerably lower than the WHO/UNICEF/ICCIDD cut-off, as was the iodine-to-creatinine ratio (122.9  $\mu\text{g/g}$ ), suggesting deficiency; women who were not taking an iodine-containing prenatal supplement had significantly lower iodine status than those taking such a supplement (Table 1) (Bath et al. 2014b). In Oxford, women recruited to a selenium and pre-eclampsia trial (Rayman et al. 2014) provided urine samples at 12, 20 and 35 weeks of gestation, and the median urinary iodine concentration was 42.0, 52.0, 69.4  $\mu\text{g/L}$ , respectively, suggesting mild-to-moderate deficiency (Furmidge-Owen et al. 2014). However, the urinary iodine concentration values here are misleading; women gave urine samples at their 12 and 20 week ultrasound scan appointments and were required to attend with full bladders, hence the urine samples were very dilute. This means that the iodine-to-creatinine ratio, which takes account of urine volume, is more meaningful; the median values at each visit were 102.5, 120.0 and 126.0  $\mu\text{g/g}$ , respectively. The median value for all urine samples collected, regardless of week of gestation ( $n = 662$ ) was 56.8  $\mu\text{g/L}$  or 116  $\mu\text{g/g}$ .

A study in the North East of the UK reported that up to 47 % of 228 pregnant women had a urinary iodine concentration below 100  $\mu\text{g/L}$ , indicating inadequate iodine status; as that paper was published prior to the recommendations that the median should be between 150 and 249  $\mu\text{g/L}$  (WHO et al. 2007), and the prevalence of deficiency in the cohort may have been underestimated. Unfortunately, the paper does not present a median urinary iodine concentration, and the

iodine-to-creatinine ratio is reported in unconventional units ( $\mu\text{g}$  iodine/ $\text{mmol}$  creatinine). Conversion of the iodine-to-creatinine ratio to  $\mu\text{g}$  iodine/ $\text{g}$  creatinine, using the molecular weight of creatinine, produces results that are not credible, suggesting that there are errors in the reporting of the data—for example, the median of 0.11  $\mu\text{g}/\text{mmol}$  converts to a figure of 0.97  $\mu\text{g/g}$ .

Up to 40 % of pregnant women in Scotland ( $n = 433$ ) were reported have inadequate iodine intake (Barnett et al. 2002). In Cardiff, 480 euthyroid women enrolled in the Controlled Antenatal Thyroid Study (Lazarus et al. 2012) had a median urinary iodine concentration of 117  $\mu\text{g/L}$ , which, by WHO/UNICEF/ICCIDD criteria, denotes iodine deficiency (Table 1) (Pearce et al. 2010).

These studies all have several limitations: (1) use of inappropriate units and errors in reporting of iodine status (Kibirige et al. 2004), (2) use of urine test strips during sample collection (Pearce et al. 2010), which may contaminate the sample with iodine (Pearce et al. 2009), (3) measurement of iodine status in women recruited to trials (Lazarus et al. 2012; Furmidge-Owen et al. 2014) who may not be representative of UK women, (4) recruitment only in the summer months (Bath et al. 2014b), when iodine content of milk [the UK principal dietary source of iodine (Bates et al. 2014)] is at its lowest (Food Standards Agency 2008) and (5) the fact that two studies are only (as yet) published in abstract form (Barnett et al. 2002; Furmidge-Owen et al. 2014).

Despite these limitations, the evidence suggests that a sizeable number of UK pregnant women are iodine deficient. Furthermore, as shown in Table 1, the urinary iodine concentration (and iodine-to-creatinine ratio, where available) in the UK studies that have reported a median are close to the value found in the UK ALSPAC study (Bath et al. 2013b); this is particularly so in women who were not taking an iodine-containing supplement (as was the case in ALSPAC). This suggests that although the ALSPAC results are over 20 years old, iodine status then was similar to current UK status. The median UIC (81  $\mu\text{g/L}$ ) from the Australian study that also found an association between urinary iodine status and child cognition up to 9 years (Hynes et al. 2013a) is similar to that reported in recent UK studies.

The iodine status in UK women of childbearing age is also suboptimal, as revealed in the nationwide study

**Table 1** Iodine status of UK pregnant women from all available studies

Study location and name	Year of urine sample collection	Time-point of urine collection during pregnancy	Number of women	Season of recruitment	Use of iodine-containing supplement (%)	Median urinary iodine concentration ( $\mu\text{g/L}$ )	Median iodine-to-creatinine ratio ( $\mu\text{g/g}$ )	References
Bristol (ALSPAC)	1991–1992	$\leq 13$ weeks	1,040	All year	0	91.1	110	Bath et al. (2013b)
North East	2000–2001	15 weeks	227	All year	Not reported	Not reported <sup>a</sup>	Not reported <sup>a</sup>	Kibirige et al. (2004)
Cardiff (CATS)	2002–2006	$< 16$ weeks	480	All year	No information	117	Not reported	Pearce et al. (2010)
Scotland	Not reported	11.5 <sup>b</sup>	433	Not reported	Not reported	137 <sup>b</sup>	Not reported	Barnett et al. (2002)
Surrey	2009	12 weeks (approx.)	100	Summer	42	Whole Group: 85.3 Supplement users: 111 Non-supplement users: 60.9	Whole Group: 122.9 Supplement users: 149 Non-supplement users: 101	Bath et al. (2014a)
Oxford (SPRINT)	2009–2011	12 (approx.) 20 (approx.) 35 (approx.)	228 222 212	All year	3	42.0 52.0 69.4	102.5 120.0 126.0	Furmidge-Owen et al. (2014)

<sup>a</sup> A median value (0.11) is provided for the iodine/creatinine ratio in unconventional units ( $\mu\text{g}/\text{mmol}$ ), which if converted to  $\mu\text{g/g}$ , gives a median of 0.97  $\mu\text{g/g}$ ; as this is not a credible value, it suggests errors in reporting

<sup>b</sup> Figures are mean values

of 14–15 year olds, who may become pregnant in the short-to-medium term (Vanderpump et al. 2011). We have recently found borderline iodine status in a small ( $n = 57$ ) group of women of childbearing age (Bath et al. 2014a). The median urinary iodine concentration (63.1  $\mu\text{g/L}$ ) suggested mild deficiency, whereas the median value calculated from the 24-h urine samples (149.8  $\mu\text{g}/24$  h) suggested a minimal risk of iodine deficiency. However, it is important to note that that study likely represents a UK best-case scenario as the women were mostly nutrition-degree students with quite good diets, and the study was conducted during the winter, when milk-iodine concentration is at its highest (Bath et al. 2014a). Mild iodine deficiency has also been found in women of childbearing age in Scotland ( $n = 381$ ) with a median of 75  $\mu\text{g/L}$  (Lampropoulou et al. 2012), though these data have only been published as an abstract. These three studies of women of childbearing age give cause for concern as

they suggest that a considerable percentage of young women may be entering pregnancy with suboptimal iodine status and thus low stores of iodine in the thyroid. This may put them at higher risk of thyroid dysfunction during pregnancy, which might have deleterious consequences for foetal brain development.

## Summary

Mild-to-moderate iodine deficiency appears to be associated with poorer child cognitive development and educational attainment. However, the evidence is largely based on observational studies which may be subject to residual confounding or on intervention studies with limitations. Therefore, further research in this area is required, particularly well-designed RCTs. In view of the evidence of iodine deficiency in UK pregnant women and the fact that women do not



currently receive advice on iodine requirements in pregnancy, we recommend that official dietary advice to pregnant women, and those planning a pregnancy, should be updated to include information on iodine intake. In the meantime, an Iodine Food Fact Sheet, prepared by us, is now available from the British Dietetic Association (Bath and Rayman 2013). Furthermore, given both the lack of studies of iodine status in UK pregnant women and the limitations of those studies, iodine status needs to be measured in a nationally representative sizeable cohort of pregnant women.

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