Iodine deficiency among pregnant women living in Northern Ireland

McMullan, P., Hamill, L., Doolan, K., Hunter, A., McCance, D., Patterson, C., Smyth, P., Woodside, J. V., & Mullan, K. (2019). Iodine deficiency among pregnant women living in Northern Ireland. *Clinical Endocrinology*. https://doi.org/10.1111/cen.14065

Published in:
Clinical Endocrinology

Document Version:
Peer reviewed version

Iodine deficiency among pregnant women living in Northern Ireland

Paul McMullan[1], Lesley Hamill[2], Katy Doolan[2], Alyson Hunter[3], David McCance[1], Chris Patterson[2,] Peter Smyth[4], Jayne V. Woodside[2], Karen Mullan[1]

[1]Regional Centre for Endocrinology and Diabetes Royal Victoria Hospital Belfast;

[2]Queens University Belfast

[3]Royal Maternity Hospital Belfast

[4]UCD Dublin

Corresponding author: K Mullan; Regional Centre for Endocrinology and Diabetes Royal Victoria Hospital Belfast; karen.mullan@belfasttrust.hscni.net; 02890633480

Key words: iodine, nutrition, pregnancy, deficiency

Declaration of interest, Funding, Acknowledgements and Data Sharing

We declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

This work was supported by the Metabolic Research Fund, Royal Victoria Hospital, Belfast

We would like to acknowledge the help of Dr S Bath in allowing our use of the iodine specific food frequency questionnaire that she developed.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Abstract

Objective: Mild iodine deficiency has re-emerged among school girls in the UK. We wished to study a contemporaneous pregnant population because a relationship between maternal iodine deficiency and offspring cognitive scores has recently been reported. The WHO have set a median population urinary iodine concentration (UIC) of ≥ 100 and ≥ 150 µg/L to define adequacy outside of and during pregnancy respectively. Iodine creatinine ratio (ICR) is also used to correct for dilution effects (sufficiency ≥ 150µg/g creatinine in pregnancy).

Design and methods: A total of 241 women were followed across trimesters (T) into the postpartum period (PPP) along with 80 offspring with spot urine sampling and food frequency questionnaires.

Results: Median UIC was 71.7µg/L in the 1st T (ICR 102µg/g creatinine) despite 55% taking iodine containing supplements. Median UICs were 94.2, 115.6 and 89.7µg/L in the 2nd T, 3rd T and PPP respectively. Corresponding ICRs were 120, 126 and 60µg/g creatinine. ICR was associated with volume of milk consumed throughout pregnancy. Median UIC among the offspring was 147.9µg/L, with no difference between the breast or formula fed babies.

Conclusions: Pregnant women living in Northern Ireland are at risk of iodine deficiency across pregnancy and into the PPP while the offspring are iodine sufficient. This is the first study of its kind in the UK with data for pregnant women and their offspring. The UK does not provide an iodine fortification programme nor offer routine iodine dietary advice in pregnancy and this requires consideration by public health agencies.

Background

For many years, the population of the British Isles (UK and Republic of Ireland) was thought to have adequate iodine nutrition. From the 1940s onwards, iodine was added to cattle feeds as it was thought to enhance animal fertility and iodine containing disinfectants were used to clean milking parlours. The resulting increase in iodine in the food chain has been described as an "accidental public health triumph".[1] However a re-emergence of mild deficiency across the British Isles has been reported by recent surveys using the gold standard population median urinary iodine concentration (UIC).[2,3] The UK survey of >700 UK teenage girls in 2009 found that 69% were mildly iodine deficient.[2] Causes for the re-emergence of iodine deficiency include possible changing farming techniques and dietary habits.

There is an increase in iodine requirements during pregnancy because of an increase in the production of maternal thyroid hormones; placental transfer of iodine for foetal thyroid hormone production and increased urinary losses associated with the increased glomerular filtration (GF) of later pregnancy. Early infancy is also thought to be an important time for optimal iodine nutrition.[6] Lactating breast tissue is known to concentrate iodine through expression of the sodium/iodide symporter gene and infant formula feeds available in the UK contain iodine, but it is not known whether these meet requirements.[7]

During pregnancy moderate or severe iodine deficiency is associated with poor cognitive outcomes in the offspring.[4] The effect of mild iodine deficiency during pregnancy is much less clear and iodine status is difficult to assess during pregnancy. Difficulties include overly dilute urine samples provided in early pregnancy in preparation for imaging and increased glomerular filtration in late gestation, which

may overestimate and underestimate iodine deficiency respectively. Corrections using urinary creatinine (iodine: creatinine ratio ICR) have been proposed with a cut off level of 150µg/g creatinine in pregnancy.[5] The Avon Longitudinal Study of Parents and Children (ALSPAC) authors reported that lower ICR but not UIC in first trimester was associated with offspring IQ (age 8), reading ability (age 9) and Key Stage 2 scores (age 11) in a dose dependent fashion.

The WHO recommends an intake of 250mcg of iodine per day for mothers to meet these increasing demands while the European Food Safety Authority (EFSA) recommends 200 mcg/day. The American Thyroid Association (ATA) recommends that different regions develop strategies for ensuring adequate iodine intake during preconception, pregnancy and lactation according to dietary patterns and availability of iodized salt.[8, 9] With no formal iodine food fortification program in the UK or ROI, dietary sources are essential to help meet requirements. Iodine supplementation is also not specifically recommended during pregnancy in the UK with the Scientific Advisory Committee for Nutrition calling for further research.[10] This position is at variance with other nations such as Australia and USA who recommend a supplement containing 150 µg iodine daily.[9,11]

Epidemiological surveys assessing iodine nutrition status during pregnancy are limited in the UK and there is none in the geographical area of Northern Ireland (NI). The aim of this study is to assess iodine nutrition status among NI pregnant women in each trimester and the postpartum period and their offspring.

Methods

This survey was carried out in the Royal Jubilee Maternity Hospital Belfast. Participants were recruited at their booking visit and followed up at scheduled second and third trimester hospital clinic review appointments. Exclusion criteria included those participants under 18 years of age and those with known thyroid disease taking thyroid medications. One post-natal visit was undertaken for sampling of both maternal and infant urine from 6 weeks to 6 months post-partum. The study received ethical approval from the Office for Research Ethics Committees Northern Ireland (reference 14/NI/0047) and trust governance (13171KM-AS). Consent has been obtained from each patient or subject after full explanation of the purpose and nature of all procedures used.

~~A history~~ Women were asked to complete a short health and lifestyle questionnaire (Appendix 1). ~~and anthropometric measurements were taken~~. Height was measured to the nearest 0.1cm using a wall-mounted stadiometer. Weight was measured using calibrated digital scales and recorded to the nearest 0.1kg. Body mass index was calculated by dividing weight by height squared and recorded to the nearest 0.1kg/m^2.

Occupation was graded according to the European Socio-economic Classification (ESeC).[12] Deprivation scores were assigned using postcode and national statistics information from the Northern Ireland Statistics and Research Agency.[13]

Iodine specific food frequency questionnaires (FFQ) developed by Bath et al were distributed at baseline; supplementation questions were included and data collected on an ordinal or nominal scale.[14] A random non-fasting spot urine sample was collected from each participant at the booking visit and each subsequent visit when

116 possible. Care was taken to avoid contamination of samples with the use of urine
117 dipsticks which contain iodine-based components. Infant urinary samples were
118 collected using nappy pads inserted into nappies on the morning of the scheduled
119 appointment. All urine samples were frozen at -80 degrees until analysis. Mothers
120 were asked at the postnatal review if they were partially or exclusively breastfeeding.

121 Urinary iodine concentration was measured using a multiplate persulphate digestion
122 method followed by Sandel-Kolthoff colorimetry and expressed as μg/L as
123 previously described. [2, 15] Samples were analysed in triplicate for iodine and the limit
124 of detection was 10μg/L. The laboratory participated in the Ensuring the Quality of
125 Urinary Iodine Procedures (EQUIP) programme at the US Centers for Disease
126 Control and Prevention (CDC Atlanta, Georgia, USA). The intra-assay coefficient of
127 variation (CV) for urinary iodine was 15% for low QC (mean 30.5 μg/L) and 8% for
128 high QC (mean 95.0 μg/L). Urinary creatinine concentration was measured singly
129 using an ILAB 600 chemistry analyser (Werfen, UK) using the Jaffe rate method
130 with CV <4%.

131 **Statistical analysis**

132 Statistical analyses were conducted using the statistical Package for the Social
133 Sciences software (version 23.0; SPSS, Inc. USA) and significance set at $p<0.05$.
134 Median and interquartile range were used to present non-normally distributed data
135 and to allow comparison with other studies. Log transformations were, however,
136 carried out to allow for parametric testing and back transformed for presentation
137 purposes. To compare means between groups an independent t-test and one-way
138 ANOVA were used. Paired samples were compared using a paired samples t-test. eg
139 breast and bottle fed babies, male and female babies and between breast and bottle feeding

mothers. ANOVA was used to compare differences between groups eg groups of mothers with differing milk consumption. Correlations between continuous variables was assessed using Pearson's correlation coefficients. In order to allow comparison with other papers we have presented the unadjusted data. For analyses the first trimester was defined as <14 weeks gestation, second trimester ≥18 ≤22 weeks gestation and third trimester as ≥28≤32 weeks gestation. Iodine: creatinine ratio (ICR) (µg/g creat) was calculated by dividing the UIC (µg/L) by the urinary creatinine (g/L). The 24-h excretion of iodine (UIE) was estimated by multiplying the ICR by the expected daily excretion of creatinine (1.23 g/day) in adult women as per Bath et al.[19]

Results

From July 2014 to March 2015 a total of 241 women were recruited to the study at booking. Twenty-four patients recruited at baseline were re-categorised as being in the 2nd trimester based on scans done for dates. Urine samples were collected from all participants. Two samples were contaminated by urine dip sticking and excluded from analysis. One hundred and thirty-four urine samples were collected at the 20-week scan visit and 153 in the early third. FFQ returns were 240, 130 and 150 at each visit respectively. Baseline characteristics are outlined in Table 1.

The mean gestational age at study baseline was 11 weeks (range 9-17)..~~Most women (71%) were recruited at 11-12 weeks gestation with 10% recruited before 11 weeks and the remainder at 13-14 weeks.~~ The mean age of participants was 30.3 ± 5.4 years with a range of 18-41 years. The mean BMI was in the overweight category (26.2 ±4.9 kg/m^2) with a range of 18-34 kg/m^2. Low deprivation scores (graded 4, 5) and low occupation scores were calculated in 42% and 35% women respectively.

Most reported a planned pregnancy (78%) and a normal diet with just over half reporting that they took a pregnancy supplement which contained iodine. About one quarter had persistent vomiting. Nearly two thirds of participants were recruited during the winter months.

Trimester specific and offspring median UIC (mUIC) are shown in Table 2 along with results corrected for urinary creatinine. The group at booking was iodine deficient (mUIC 72.6 µg/L) with 83% of participants having levels below the current recommendation from the WHO of 150µg/L. The mUIC was also below the threshold even for outside of pregnancy (>100 µg/L). Median UIC at subsequent time points were also less than 150µg/L although ~~values~~ concentrations increased as pregnancy progressed. Figure 1 shows the proportion of participants above and below the WHO cut-off value of 150µg/L at each trimester. Postnatally maternal mUIC was also low.

The median estimated 24-hour urinary iodine excretion (UIE) in pregnancy has been suggested by Bath et al to be >225µg/day assuming the recommended 250µg/day intake of which 90% is excreted. [19] Our cohort excreted 148µg/day (IQR 90-269), 181µg/day (IQR 115-311) and 184µg/day (IQR 117-293) across the three trimesters.

In the first trimester, ~~younger age and~~ pregnancy planning was associated with lower levels of mUIC (r=0.16, p=0.05). In contrast, several characteristics were associated with lower levels of ICR: younger age (<30 years) (r=0.30, p=0.01); persistent vomiting, a regular diet, and lack of family history of thyroid disease (r=0.16, 0.13, and 0.14 respectively, p=0.05). Reported iodine supplementation in first trimester was associated with higher ICRs than in those without supplementation (145 vs 96 µg/g creatinine p<0.001) but this was still below the recommended 150 µg/g

creatinine for pregnancy. Supplementation invariably contained 140-150 µg/day iodine.

Lower and intermediate occupations had ICR of 100 µg/g compared to 149 µg/g creatinine for the higher occupations ($p<0.01$). Most of the ICR associations were lost in later trimesters except first trimester vomiting ($r=0.18$ in 2nd trimester) and lack of family history of thyroid disease ($r=0.18$-0.24) (all $p=0.05$). There were no associations with parity, previous miscarriage, BMI, smoking, or season at booking (results not shown). Only one set of twins were born in this cohort.

There were no significant associations between dietary habits and mUIC across the trimesters. Associations between a selection of dietary habits and first trimester ICR are shown in Table 3. ICR was positively associated with intake of milk (<140mls daily vs ≥140mls) and full fat yoghurt (<1/week vs ≥ 1/week) ($r=0.22$, 0.19 respectively, $p=0.01$); and white fish (<1/week vs ≥ 1/week) ($r=0.17$, $p=0.05$). ICR levels increased in a dose dependent way with volume of milk consumed. Only milk quantity continued to show significant associations with ICR in the second ($p<0.001$) and third trimesters ($p<0.005$). There were too few participants who used milk other than cow's milk to draw any meaningful conclusions about milk type. Increased egg intake was trending to a higher ICR but did not reach significance. There was an increase in consumption of milk, dairy desserts and butter across pregnancy ($p <$ 0.05).

Infant results: The mUIC in (at least partially) breast fed infants (n=49) was 146µg/L (IQR 103-202µg/L) and 156µg/L (IQR 103-247µg/L) in formula fed infants (n=31). There was no significant difference between (at least partially) breast fed and formula fed infants and no difference between male and female infants. Only 24

211 babies were exclusively breastfed and this is below the cutoff recommended by
212 WHO as a sufficient group to analyse. However results were not significantly
213 different from partially breast fed or formula fed babies (147 μg/L, IQR 92-229)
214 There was also no significant difference in mUIC between the breast versus bottle
215 feeding mothers who supplied a postpartum sample.

216

Discussion

This is the first survey of its kind in NI and one of the few studies to survey across pregnancy into the postpartum with offspring iodine status. Results suggest iodine deficiency among this cohort across pregnancy and beyond but not in the offspring.

The ATA has called for population surveys in different geographical regions to take account of differing environmental iodine levels. The UK has an estimated population of ~66 million of which ~20 % are females of childbearing age and there are ~seven million births/year.[27, 28] The regions where iodine nutrition during pregnancy have previously been studied locally include four areas of England, Wales and the Republic of Ireland (RoI) (Table 4). [3, 5, 14, 16-19] A further study in Scotland (which incorporated other UK areas online) relied on FFQ rather than population urinary iodine sampling.[20] The studies span nearly 25 years and are consistent in reporting median UIC below the recommended 150 μg/L in pregnancy with no pointers to improvement over this period.

The median UIC increased across the trimesters in our survey and fell in the postpartum period. The only other UK study, which surveyed across pregnancy showed a similar trend while the RoI study showed no change from a higher baseline but did replicate the precipitous fall as quickly as three days postpartum.[16, 19] We found that, after correction for dilution with urinary creatinine, there was still an increase in urinary iodine across pregnancy. Reasons for this may include a change in iodine intake across pregnancy, lessening iodine sequestration by the maternal thyroid, placenta and breast with time and/or a residual dilution bias in early pregnancy.

Lower SES occupations were associated with lower ICR. The association of lower ICR with lack of family thyroid disease raises the possibility that knowledge about thyroid health may be a factor. We have reported, in abstract form, a separate local pregnant cohort in which 80% of women were not aware of the increased iodine requirements in pregnancy and 45% were unable to identify any iodine rich foods.[21]

Vomiting in 1st trimester was associated with lower levels of ICR throughout all the trimesters. This points to the importance of dietary iodine intake in early pregnancy and a possible legacy effect in later pregnancy.

We found that conventional cow's milk intake increased across pregnancy and correlated with ICR in keeping with other studies. [16,19] Numbers were too small to comment on more expensive organic cow's milk, which is in keeping with our socio-economic cohort, but other studies have demonstrated lower levels of iodine content in organic milk by up to 40%.[22] Although fish is also an iodine rich source in the UK and we found associations with ICR, overall fish consumption was low.

The most commonly used combined pregnancy supplements taken in 1st trimester contain ~140-150 μg iodine /tablet. Although mothers who took this had higher levels of ICR, levels remained below target. This is in keeping with other studies where pregnant women taking iodine supplements but living in an iodine deplete area have higher ICR than those not taking supplements, but their levels remain below that recommended by WHO. Supplementation in an iodine deplete area may therefore not be sufficient without also an iodine fortification or education program.[14, 24-25] In the absence of any successes in improving dietary intake of our population in pregnancy, the argument for fortification at a population level, may become compelling.

We found that iodine status was sufficient in the offspring as a whole at six weeks to six months despite iodine deficiency in their mothers at that stage. There were no differences in iodine excretion between breast and formula feeding mothers. The breast and formula feeding offspring also had similar levels of UIC. These results are at variance with the RoI study which reported that both mothers and their offspring overall were iodine deficient at 3 days postpartum and that the formula fed babies had lower levels than breast fed babies.[16] The authors suggested that the available formula feeds (containing 100-150 μg/L iodine) may be inadequate for iodine deplete regions or was in a form that did not permit satisfactory absorption. The babies in our cohort were sampled from 6 weeks so that feeding would be in the established phase and suggests no disadvantage for the formula fed group. Although the content of iodine in formula feeds have not changed significantly in the intervening years, other changes to the formula may have had a positive impact on absorption.

Strengths of our study include the large sample size including offspring along with dietary information. Weaknesses include recruitment in only one centre, although this is the largest maternity unit in NI serving 25% of all the births in the region. The higher than expected rate of reported planned pregnancy and use of iodine containing supplements at booking may also underestimate the underlying scale of iodine deficiency in our population.

Conclusions

This cohort of pregnant women living in Northern Ireland are iodine deficient across pregnancy and into the post-partum period, while the offspring are iodine sufficient when feeding is established. The UK does not provide an iodine fortification program nor offer routine iodine dietary or supplement advice in pregnancy and this requires consideration by public health agencies.

References

1. Phillips D. Iodine, milk, and the elimination of endemic goitre in Britain: the story of an accidental public health triumph. J Epidemiol Community Health.1997; 51:391–393

2. Vanderpump MP, Lazarus JH, Smyth PP, Laurberg P et al; on behalf of the British Thyroid Association UK Iodine Survey Group. Iodine status of UK schoolgirls: a cross-sectional survey. Lancet 2011 377: 2007–2012

3. Nawoor Z, Burns R, Smith DF, Sheehan S, O'Herlihy C & Smyth PP. Iodine intake in pregnancy in Ireland—a cause for concern? Ir J Med Sci 2006 175:21–24

4. Zimmermann MB. Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. Am J Clin Nutr. 2009 Feb;89(2):668S-72S

5. Bath SC, Steer CD, Golding J, Emmett P & Rayman MP. 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 2013 382:331-337

6. Pearce EN, Lazarus JH, Moreno-Reyes R, Zimmermann MB. Consequences of iodine deficiency and excess in pregnant women: an overview of current knowns and unknowns. Am J Clin Nutr. 2016 Sep;104 Suppl 3:918S-23S

7. Portulano C, Paroder-Belenitsky M, Carrasco N. The Na^+/I^- symporter (NIS): mechanism and medical impact. Endocr Rev. 2014; 35:106–149.

8. World Health Organization/International Council for the Control of the Iodine Deficiency Disorders/United Nations Children's Fund. Assessment of the iodine deficiency disorders and monitoring their elimination. Geneva 2007

9. Stagnaro-Green A. Abalovich M. Alexander E. Azizi F. Mestman J. Negro R. Nixon A. Pearce EN. Soldin OP. Sullivan S. Wiersinga W. Guidelines of the ATA for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid.2011; 21:1081–1125

10. SACN Statement on Iodine and Health. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/339439/SACN_Iodine_and_Health_2014.pdf (last accessed 12/12/2018)

11. Condo D, Huyhn D, Anderson AJ, Skeaff S, Ryan P, Makrides M, Mühlhaüsler BS, Zhou SJ. Iodine status of pregnant women in South Australia after mandatory iodine fortification of bread and the

recommendation for iodine supplementation. Matern Child Nutr. 2017 Oct;13(4)

12. The European Socio-economic Classification ESeC User Guide https://www.iser.essex.ac.uk/archives/esec/user-guide- last accessed 12/12/2018

13. NI Statistics and Research Agency https://www.nisra.gov.uk/- last accessed 12/12/2018

14. Bath SC, Walter A, Taylor A, Wright J, Rayman MP. Iodine deficiency in pregnant women living in the South East of the UK: the influence of diet and nutritional supplements on iodine status. Br J Nutr. 2014 May;111(9):1622-31.

15. Ohashi T, Yamaki M, Pandav CS, Karmarkar MG, Irie M. Simple microplate method for determination of urinary iodine. Clin Chem. 2000 Apr;46(4):529-36

16. Smyth PP, Hetherton AM, Smith DF, Radcliff M, O'Herlihy C. Maternal iodine status and thyroid volume during pregnancy: correlation with neonatal iodine intake. J Clin Endocrinol Metab. 1997 Sep;82(9):2840-3

17. Kibiridge MS, Hutchison S, Owen CJ & Delves HT. Prevalence of maternal dietary iodine insufficiency in the north east of England: implications for the fetus. Arch Dis Child Fetal Neonatal Ed; 2004; 89:436–39

18. Pearce EN, Lazarus JH, Smyth PP et al. Perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant women. J Clin Endocrinol Metab. 2010; 95:3207–15.

19. Bath SC, Furmidge-Owen VL, Redman CWG et al. Gestational changes in iodine status in a cohort of pregnant women from the United Kingdom: season as an effect modifier. Am J Clin Nutr. 2015; 101:1180-1187

20. Combet E, Bouga M, Pan B, Lean ME, Christopher CO. Iodine and pregnancy - a UK cross-sectional survey of dietary intake, knowledge and awareness. Br J Nutr. 2015 Jul 14;114(1):108-17

21. McMullan P, Hunter A, McCance D, Woodside JV, Mullan K. Knowledge about iodine requirements during pregnancy and breastfeeding among pregnant women living in Northern Ireland (In submission)

22. Bath SC1, Button S, Rayman MP Iodine concentration of organic and conventional milk: implications for iodine intake. Br J Nutr. 2012 Apr;107(7):935-40.

23. Alvarez-Pedrerol M1, Ribas-Fitó N, García-Esteban R, Rodriguez A, Soriano D, Guxens M, Mendez M, Sunyer J. Iodine sources and iodine levels in

399 pregnant women from an area without known iodine deficiency Clin
400 Endocrinol (Oxf). 2010 Jan;72(1):81-6.
401
402 24. Vandevijvere S, Amsalkhir S, Mourri AB, Van Oyen H, Moreno-Reyes R.
403 Iodine deficiency among Belgian pregnant women not fully corrected by
404 iodine-containing multivitamins: a national cross-sectional survey. Br J Nutr.
405 2013 Jun 28;109(12):2276-84.
406
407 25. Dold S, Zimmermann MB, Aboussad A, Cherkaoui M, Jia Q, Jukic T, Kusic
408 Z, Quirino A, Sang Z, San Luis TO, Vandea E, Andersson M. Breast Milk
409 Iodine Concentration Is a More Accurate Biomarker of Iodine Status Than
410 Urinary Iodine Concentration in Exclusively Breastfeeding Women. J Nutr.
411 2017 Apr;147(4):528-537
412
413 26. Sarah Coates et al. Office for National Statistics. Overview of the UK
414 population:https://www.ons.gov.uk/peoplepopulationandcommunity/populati
415 onandmigration/populationestimates/articles/overviewoftheukpopulation/nov
416 ember2018 (last accessed 21/05/2019)
417
418 27. World Population Prospects (https://population.un.org/wpp/) (last accessed
419 21/05/2019)
420

Table 1 Baseline Characteristics

Baseline characteristics (n)	
Age (241)	Mean 30.3 years (SD 5.4)
Body Mass Index kg/m2(224) Height cm (224) Weight kg (224)	Mean 26.2 kg/m2(SD 4.9) Mean163.7 cm (SD 6.5) Mean 70.1 kg (SD 13.9)
Occupation - Higher (92) - Intermediate (53) - Lower/UE/ill-defined (77)	 41.4% 23.9% 34.7%
Deprivation Scores - 1 (Most affluent) (61) -2 (48) -3 (31) -4 (18) - 5 (Most deprived) (83)	 25% 20% 13% 8% 34%
Smoking - Never (214) - Current (25) - Ex-smoker (2)	 88.8% 10.4% 0.8%
Ethnicity - White Caucasian (238) - Black African (2) - Indian (1)	 98.8% 0.8% 0.4%
Previous pregnancy - 0 (114) - 1-2 (106) - >2 (21)	 47.3% 44.0% 8.7%
Previous miscarriage - Yes (74) - No (167)	 30.7% 69.3%
Planned pregnancy - Yes (189) - No (52)	 78.4% 21.6%

Diet	
- Normal (225)	93.4%
- Vegetarian (6)	2.5%
- Gluten free (6)	2.5%
- Other	1.6%
Nausea	
- Yes (179)	79.2%
- No (47)	20.8%
Ongoing vomiting	
- Yes (65)	27.0%
- No (160)	66.4%
Family history of thyroid disease	
- Yes (51)	21.2%
- No (170)	70.5%
Iodine containing multivitamin	
- Yes (127)	52.7%
- No (105)	43.6%
Season	
- Winter (151)	62.7%
- Summer (90)	37.3%

Table 2: Trimester specific and offspring median UIC and ICR

Trimester	Number of samples	Median UIC µg/L (IQR)	Median ICR µg/g creatinine (IQR)
First (<14 weeks)	217	72.6 (36.7-122.4)	116.4 (71.0 – 216.2)
Second (18-22 weeks)	134	94.2 (53.0-173.8)	147.2 (93.7 – 252.5)
Third (28-32 weeks)	153	116.7 (62.9 – 194.7)	149.9 (94.2 – 237.0)
Postpartum (6 weeks-6 months)	88	89.7 (52.2-152.5)	60.2 (32.6-92.4)
Baby breastfed (at least partially)	49	146.2 (103.4-202.3)	
Baby formula fed	31	156.5 (102.9-247.0)	

Abbreviations: UIC- urinary iodine concentration; IQR- interquartile range; ICR- iodine: creatinine ratio

478 Table 3: First trimester associations between ICR and dietary habits derived from
479 food frequency questionnaires

480

Food group	% of cohort	ICR Mean (SD)	p value
Milk daily ml (n=197)			
- None	8	66.4 (1.7)	
- < 140	28	107.4 (2.1)	
- 140 – 279	30	126.0 (2.4)	
- 280 – 424	19	157.0 (2.2)	
- >425	15	147.2 (2.1)	
			0.002*
Full fat yoghurt (n=192)			
- Never or <1/month	59	113.1 (2.2)	
- 1/ week - fortnight	20	111.0 (2.3)	
- 2-3 times/week	12	209.5 (2.2)	
- ≥4 /week	9	146.7 (1.9)	
			0.004*
White fish (n=194)			
- Never or <1/month	51	104.3 (2.2)	
- 1/ fortnight	20	131.0 (2.1)	
- 1/ week	29	152.7 (2.2)	
- 2-3 times/week	2	118.1 (2.3)	0.036*
Eggs weekly (n=197)			
- 0	16	95.8 (2.0)	
- 1-2	53	121.7 (2.3)	
- 3- 4	26	128.7 (2.1)	
- >4	7	177.8 (2.7)	
			0.100

481 Mean value back transformed; ICR compared between frequency groups using one-way analysis
482 of variance

483

Table 4: Comparison of comparable iodine surveys of the British Isles (UK and Rep of Ireland)

	Year	No.	Trim.	mUIC	mICR	Milk Intake assoc	I Supp	Offspring UIC µg/L
SW England [5]	1991-2	1040	1st	91	110	-	0%	-
Rep of Ireland[16]	1997	79 67 83 108 122	1st 2nd 3rd PP* PP**	135 124 122 67 74	-	-	0%	n=108* -Breast: 100 -Formula: 43
NE England [17]	2000-1	227	1st	40% "borderline"		-	n/a	-
Wales [18]	2002-6	383	1st	117	-	-	n/a	-
Rep of Ireland[3]	2004-5	54	1st	45-68	-	-	n/a	-
SE England [14]	2009	100	1st	85	123	yes	42%	-
S England [19]	2009-11	230	1st 2nd 3rd	42 52 69	102 120 126	yes	3%	-
N Ireland Current	2014-5	217 134 153 88	1st 2nd 3rd PP***	73 94 118 90	116 147 150 60	yes	53%	n=80*** Breast: 149 Formula:144

Trim-Trimester; mUIC- median urinary iodine concentration (Pregnant sufficiency≥150 µg/L; Not Pregnant ≥ 100 µg/L) ; mICR-median iodine: creatinine ratio (Pregnant sufficiency ≥150 µg/g creatinine); I Supp– iodine supplement; 3d= 3 days postpartum

* Postpartum 3 days; ** 6weeks; ***6 weeks to 6months

Figure: Proportion of cohort with sufficient Urinary Iodine Concentration (UIC) ≥ 150 µg/L in each trimester