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# Contemporary challenges and opportunities for iodine nutrition

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to
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*To my parents*

*Dimitris & Rania*

# Abstract


Iodine deficiency has been a public health concern for many decades in countries of the developing world. Recently renewed concern was expressed in industrialised countries over mild insufficiency in high-risk groups of the population (pregnant and lactating women and their infants). The main sources of iodine in the UK diet are dairy, and fish and seafood products, while iodised salt is not widely available and does not contribute to iodine intake, contrary to most countries in Europe and globally. Iodine is essential for thyroid hormone synthesis, which are crucial for the neurodevelopment of the fetus and infant. Goiter is a visible symptom of severe iodine deficiency (ID), and consequences of ID during pregnancy vary from development of hypothyroidism to cretinism. Consequences of mild-to-moderate deficiency are less well described, with a reduction of IQ in children born to mothers with mild iodine deficiency. As such, pregnant women, lactating mothers and their infants are at risk of the irreversible consequences of low iodine intake. The World Health Organisation (WHO) recommends an iodine intake approximately 80% higher during pregnancy and lactation. The proposed strategy to combat ID worldwide has been universal salt iodisation. The UK has not implemented any prophylactic measures for ID and the female population in the perinatal period of life remain at risk, with up to 60% of women in pregnancy having insufficient iodine intake. The aim of this thesis was to explore the role that dietary guidance can play in tackling iodine insufficiency in women of childbearing age (pregnant and lactating) in the UK.

The MABY study (Chapter 2) examined the iodine intake of pregnant women in the UK and its association with mother's (postpartum) and infant's iodine status. This longitudinal study of 609 pregnant women in the 28$^{th}$ week of gestation showed that only 34% achieved the recommended daily iodine intake during pregnancy (recommendation 250 μg/day; median 199 μg/day; IQR 121-274). The iodine status of infants was sufficient, as measured in spot urine samples five days postpartum (median 118 μg/l; IQR 71–201). However, 41% of the group remained below the 100 μg/l cut-off point for sufficiency. Breastfed infants had 37% higher UIC compared to formula fed infants (p=0.002), although lactating mothers had 34% lower UIC compared to formula feeders (p=0.002), highlighting a potentially protective effect in newborns. Overall, iodine insufficiency in pregnant and lactating women in the UK remains an existing public health concern, which requires actions to address it.

To explore effective ways to eliminate iodine insufficiency using food and educational strategies, Chapter 3 presents a systematic review of the intervention studies that aimed to increase iodine-rich foods consumption (milk, fish, seaweed), with iodine status as an outcome. Only three studies were included in the review, one of which was a published protocol for an intervention. None of the studies reported improved iodine status. However, knowledge, attitude and practice scores (measured with a questionnaire) improved after an educational intervention in Iran. Chapter 3 confirmed a lack of intervention studies using dietary guidance, education, or provision of iodine-rich foods to increase iodine status, showing a gap in the literature.

Awareness and knowledge on iodine are low in women and healthcare professionals. Chapter 4 tested perceptions on dietary guidance related to iodine and pregnancy, using a mixed-methods design in 48 women. Participants in the perinatal period of life were unaware of the importance, sources and recommendations for iodine intake. Attitudes to dairy product consumption were positive, but increased fish consumption was considered less achievable. Barriers included taste, smell, heartburn and morning sickness in pregnancy. The main recognised provider of dietary advice were community midwives, although the dietary advice received focused most often on multivitamin supplements rather than food sources. Thematic analysis highlighted a clear theme of commitment to change behaviour, motivated by pregnancy, with a desired focus on user-friendly documentation.

Two cross-sectional questionnaire surveys, described in Chapters 5 and 6, investigated the perception, knowledge, awareness and practice towards dairy and seafood products in UK residents. The Theory of Planned Behaviour informed the design of the questionnaires. Less than two dairy servings per day were consumed by 46% of the population (median daily servings 2.2; IQR 1.2-3.5) and less than two fish and seafood servings per week were consumed by 53% (median daily servings 1.9; IQR 0.9-3.7). Knowledge, intentions and attitudes towards behaviour were higher both for "high" consumers (defined as those consuming >2 servings of dairy per day or >2 servings of fish per week). Main factors influencing the choice of these iodine-rich foods were the sensory attributes of the products, both as barriers and as facilitators of consumption, due to the variety and different characteristics of dairy and seafood products.

An intervention was designed based on the findings of Chapters 4, 5 and 6, to increase the iodine status of pregnant women and women trying to conceive. The PICk study, a single-blind randomised control trial was conducted in Glasgow, UK, and a feasibilityanalysis of

the first 33 participants completed was performed. The educational intervention, based on regular text messages on iodine nutrition, was well-accepted by women. Burden was low, although dropout rates have been higher than those initially calculated (24% versus 15%). The study has been shown to be feasible and acceptable in these population groups. At the moment, the sample size limits interpretation of the interim findings, and further analysis after the completion of the study will indicate whether iodine status can be improved through the intervention.

It is important that iodine insufficiency should be tackled, to avoid the irreversible consequences on the population. To address iodine insufficiency effectively, solutions should be designed and work synergistically. Changing dietary patterns is challenging, but pregnancy offers the opportunity for implementation of changes, due to higher motivation and health consciousness. Increasing awareness and knowledge of the population, healthcare professionals and government organisations might be the key for future action. High quality and consistent results from research studies are needed to inform policy changes. This thesis identifies that knowledge and intentions of the population are important targets for public health interventions and offers suggestions on different approaches for the elimination of ID in the UK.

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I left for the end Kyriakos, the greatest support I could ever imagine. Thank you for your patience, for being always next to me, understanding and encouraging me every single day.

# Author's declaration

I declare that the work contained in this thesis is original, and is the work of the author Maria Bouga. I have been solely responsible for the organisation and day-to-day running of this study as well as the laboratory analysis and data processing, unless otherwise referenced. This dissertation has not been submitted for any other degree at the University of Glasgow or any other Institution.

Maria Bouga

# Supervisors' declaration

I certify that the work reported in this thesis has been performed by Maria Bouga and that during the period of study she has fulfilled the conditions of the ordinances and regulations governing the Degree of Doctor of Philosophy, University of Glasgow.

Dr. Emilie Combet Aspray                Prof. Michael EJ Lean

# Publications achieved during the present thesis

## Abstracts

**Bouga M**, Lean MEJ, Combet E (2018) Dairy products as a source of iodine in the UK, and consumers' perceptions. *Proceedings of the Nutrition Society* **77**:OCE2, E30

**Bouga M** and Combet E (2016) Dietary interventions and increase of dietary iodine intake-a systematic review. *Proceedings of the Nutrition Society* **75**:OCE3, E211

**Bouga M**, Lean MEJ, Combet E (2016) Dietary guidance during pregnancy and iodine nutrition: a qualitative approach. *Proceedings of the Nutrition Society* **75**:OCE3, E83

## Full papers

**Bouga M**, Lean MEJ, Combet E (2018) Contemporary challenges to iodine status and nutrition–the role of foods, dietary recommendations, fortification and supplementation. *Proceedings of the Nutrition Society* **(first view – published online)**

**Bouga M**, Lean MEJ, Combet E (2018) Iodine and pregnancy – a qualitative study focusing on dietary guidance and information. *Nutrients* **10**:4, 408

# List of abbreviations

| | |
|---|---|
| ADHD | Attention deficit- hyperactivity disorders |
| ALSPAC | Avon Longitudinal Study of Parents and Children |
| ATB | Attitudes towards behaviour |
| BCTs | Behaviour change techniques |
| BMI | Body mass index |
| CATS | Controlled Antenatal Thyroid Screening |
| CI | Confidence interval |
| CSIRO | Commonwealth Scientific and Industrial Research Organisation |
| DBS | Dried blood spot |
| DIT | Diiodotyrosine |
| DoH | Department of Health |
| DONALD | Dortmund Nutritional and Anthropometric Longitudinally Designed |
| EAR | Estimated average requirement |
| EFSA | European Food Safety Authority |
| ELISA | Enzyme-linked immunosorbent assay |
| FFQ | Food frequency questionnaire |
| GEC | Global executive composite |
| GP | General practitioner |
| GW28 | 28$^{th}$ gestational week |
| GW36 | 36$^{th}$ gestational week |
| HCP | Healthcare professional |
| HNC | Higher National Certificate |
| HND | Higher National Diploma |
| I | Iodine |
| $I^-$ | Iodide |
| ID | Iodine deficiency |
| IDD | Iodine deficiency disorders |
| IGN | Iodine Global Network |
| INT | Intentions |
| IoM | Institute of Medicine |
| IQ | Intelligence quotient |
| IQR | Interquartile range |
| KAP | Knowledge, awareness and practice |
| LDL | Low-density lipoprotein |
| LRNI | Lower reference nutrient intake |
| MABY | Mothers and Babies at Yorkhill |
| MIT | Monoiodotyrosine |
| MoBa | Norwegian Mother and Child Cohort |
| NDNS | National Diet and Nutrition Survey |
| NHS | National Health Service |
| NIS | Sodium / iodide symporter |
| NVQ | National Vocational Qualification |
| Ops | Organochlorine pesticides |

| | |
|---|---|
| PAHs | Polycyclic aromatic hydrocarbons |
| PBC | Perceived behavioural control |
| PBDEs | Polybrominated diphenylethers |
| PCBs | Polychlorinated biphenyls |
| PDI | Psychomotor Development Index |
| PN | Postnatally |
| Pr | Pregnant |
| PRISMA | Preferred Reporting Items for Systematic Reviews and Meta-Analyses |
| PROSPERO | Prospective register of systematic reviews |
| R&D | Research and Development |
| REC | Research Ethics Committee |
| RCT | Randomised controlled trial |
| RNI | Reference Nutrient Intake |
| SACN | Scientific Advisory Committee on Nutrition |
| SBR | Scottish Birth Record |
| SD | Standard deviation |
| SN | Subjective norms |
| SPRINT | Se in PRegnancy INTervention |
| T3 | L-triiodothyronine |
| T4 | L-tetraiodothyronine |
| Tg | Thyroglobulin |
| TgAb | Thyroglobulin Antibody |
| TPB | Theory of Planned Behaviour |
| TPO | Thyroid peroxidase |
| TSH | Thyroid Stimulating Hormone |
| TTC | Trying to conceive |
| TUL | Tolerable upper level |
| UIC | Urinary iodine concentration |
| UK | United Kingdom |
| UNICEF | United Nations Children’s Fund |
| US | United States |
| USI | Universal salt iodisation |
| WHO | World Health Organisation |

# Chapter 1 - General introduction

## 1.1 Iodine, thyroid function and the diet

Iodine (I) was accidentally discovered in 1811 by the French chemist Bernard Courtois (Saintrestitut, 1988). The atomic number of this chemical element is 53, and its name was derived from the Greek word ιοειδής (ioeidēs), which means purple or violet. Iodine is found mainly in seawater but can also be present in some rocks and some types of soil.

### 1.1.1 Thyroid hormones synthesis and control

Iodine is essential for the synthesis of the thyroid hormones T3 (L-triiodothyronine) and T4 (L-tetraiodothyronine) in the thyroid gland. As the major component of these hormones, it comprises 58% and 65% of their weight, respectively, as T3 contains three atoms of iodine and T4 contains four atoms. Approximately 10% of the iodine consumed through the diet is absorbed from the small intestine in the form of iodide ($I^-$). Iodide is then transferred through circulation (serum) and is cleared by the thyroid gland (Rousset et al., 2000). Seventy to eighty percent of the 15-29 mg iodine contained in the human body of a healthy adult is stored in the thyroid gland (with thyroid hormone synthesis requiring approximately 91-97 ± 19 μg of iodine per day based on iodine turnover (Fisher and Oddie, 1969, Zimmermann and Andersson, 2012)). Iodine is also absorbed in small but detectable amounts from the gastric mucosa, salivary glands and choroid plexus. During lactation, the alveolar and ductular cells of the mammary gland also contain iodine which is excreted in the breast milk (Zimmermann, 2009a). More than 90% of ingested iodine is excreted in urine.

Iodide is transported into the thyrocytes, through the protein sodium / iodide symporter (NIS), which is located at the basolateral plasma membrane of thyrocytes. When the thyroid gland has a normal activity (not being under- or overactive), a concentration of free iodide 20-50 times higher than that of plasma is maintained. In the thyrocyte, two proteins, thyroid peroxidase (TPO) and thyroglobulin (Tg) are produced. Iodine, and Tg, are transferred to the lumen of follicles. Iodine, after its oxidation to iodinating form by $H_2O_2$ and TPO, is attached to the tyrosyl groups of Tg. The precursors of thyroid hormones, monoiodotyrosine (MIT) and diiodotyrosine (DIT) are produced following the coupling of iodine to Tg. The final step of thyroid hormone synthesis is the coupling of two iodotyrosyl residues to form iodothyronine. Two DIT form T4, while 1 MIT and 1 DIT form T3 (Rousset et al., 2000).

Thyroid hormone synthesis is controlled by two main factors; Thyroid Stimulating Hormone (TSH) and availability of iodine. A lack of iodine leads to decreased thyroid hormone production. TSH secretion by the pituitary increases to compensate the low production of thyroid hormone, as a regulatory factor. Increase of TSH secretion causes stimulation of the thyroid. Goitre is developed as an attempt to compensate, which is the enlargement of the thyroid gland, and is detectable through palpation or thyroid ultrasonography. Excess iodide acutely inhibits thyroid hormone synthesis, and is known as the Wolff-Chaikoff effect (Rousset et al., 2000). $H_2O_2$ generation blocks Tg iodination, but autoregulative mechanisms inhibit iodide transport and the thyroid usually escapes Wolff-Chaikoff effect within weeks (Wiersinga, 2016).

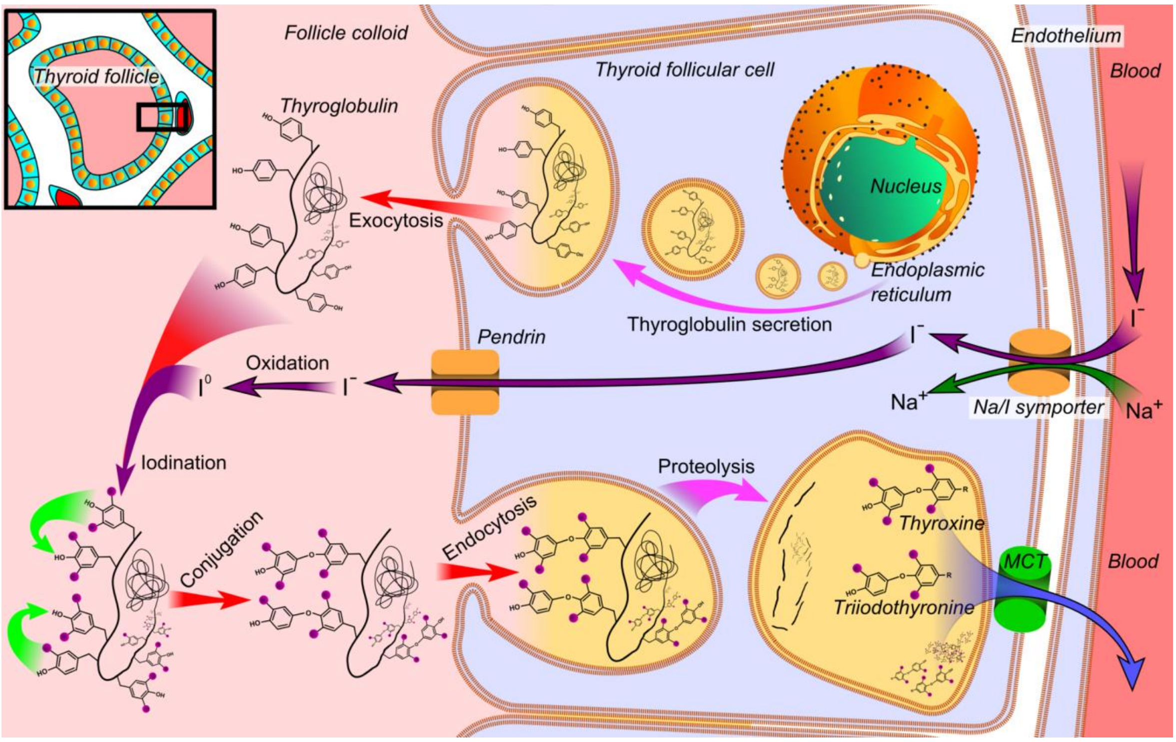


Figure 1.1 Synthesis of thyroid hormones. Adapted from Häggström (2014)

### 1.1.2 Iodine sources and fortification

Dietary choices are critical for an adequate iodine intake. The main dietary sources of iodine in the UK in terms of iodine content are marine fish, seafood, seaweed and dairy products. Their consumption varies among women (Figure 1.2) and their iodine content depends on season, processing and farming practices (Bates et al., 2016). In most countries, the main dietary source of iodine is fortified salt (Figure 1.3) (World Health Organisation, 2014). Many believe that iodine status is potentially compounded by consumption of cruciferous vegetables and soya products (collectively known as goitrogenic foods), but evidence in humans is weak. In a crossover intervention in healthy women of childbearing age with low habitual iodine intake, we did not find differences in thyroid function in women with increased intake of those foods (Bouga et al., 2015a).

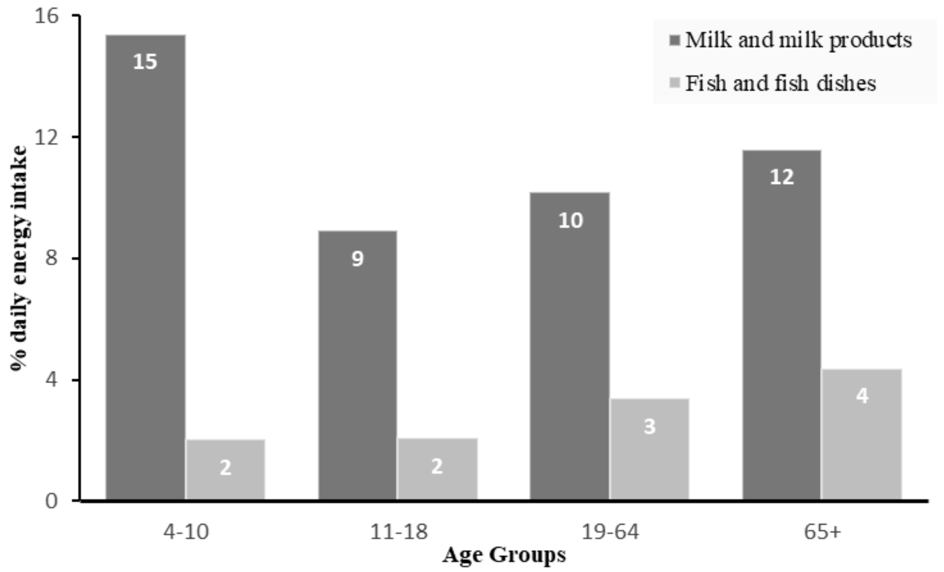


Figure 1.2 Iodine-rich foods percentage contribution to daily average total energy intake in women in the UK, based on their age group, based on the National Diet and Nutrition Survey (NDNS) Rolling program (Years 5-6) (Bates et al., 2016).

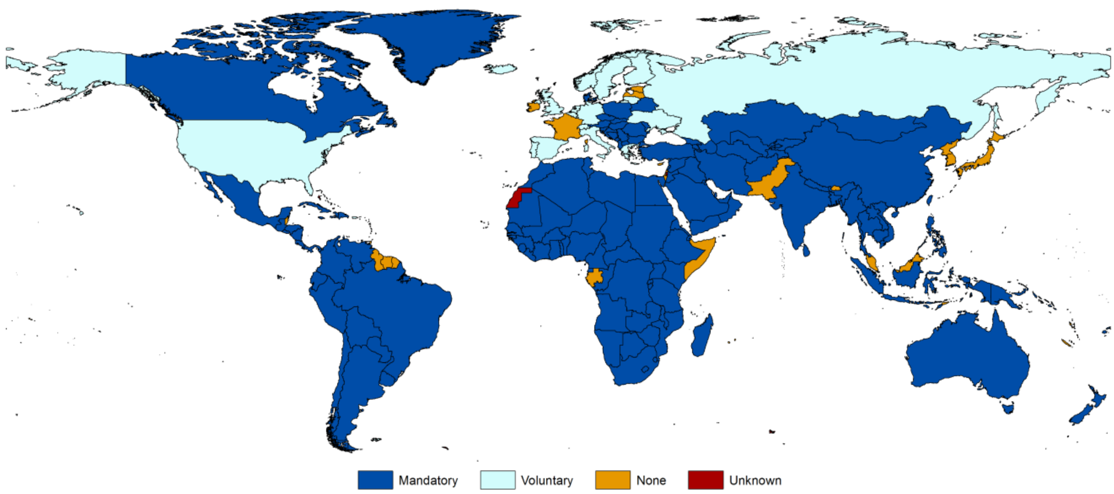


Figure 1.3 Global legislation for salt iodisation (June 2016) (Adapted from IGN).

The elimination of iodine deficiency (ID) and related disorders is a priority for the World Health Organisation (WHO) and United Nations Children's Fund (UNICEF). Universal salt iodisation (USI) has been adopted by over 120 countries globally (World Health Organisation, 2014). USI is the main method of iodine prophylaxis worldwide. Although initially proposed in 1820, salt fortification with iodine was attempted for the first time 100 years later (World Health Organisation, 2014). The proposed iodisation of salt is 20-40 mg/kg and is based on an average salt intake of 10g daily. Salt has been chosen as a vehicle as it combines characteristics that make it suitable, including its stable consumption throughout the year, low cost ($0.02–$0.05 annually per child covered), consumption by everyone in a population, ease in implementation, quality, odour and taste not being affected and monitoring of production (Venkatesh Mannar et al., 1995).

Salt iodisation is not unanimously considered a good practice for the control of ID and there is still a debate on its success and potential risks, which might contribute to the lack of legislation for salt fortification in the UK. The perceived conflicting messages that USI would convey remains at odds with public health campaigns for salt reduction to less than 5 g/day (Tonacchera et al., 2013, Charlton et al., 2014). Experts from the WHO, UNICEF and Iodine Global Network (I) aim to work together to overcome any counterproductive effects of the two public health campaigns and find a common ground for their parallel success (Webster et al., 2014). According to the WHO, salt iodisation and salt intake reduction (in less than 5 g/day), are both important and can be compatible (World Healh Organisation, 2014). Iodine fortification could increase in line with the decrease of salt intake and mandatory fortification would remove the positive bias of iodised salt as "healthier" (Webster et al., 2014). Further argument need to be considered, including (lack of) freedom of choice in the context of mandatory fortification and the risk of high exposure / toxicity for a sub-group of the population (mainly older people with undiagnosed thyroid autonomy).

Iodine deficiency disorders (IDD) have been successfully eliminated or controlled in many countries, via salt fortification in combination with diet diversification (in the US (Leung et al., 2012) and Ghana (Nyumuah et al., 2012), with exceptions in European countries (van der Haar et al., 2011)). However, consumption of fortified salt to increase iodine intake may not be a sufficient measure in pregnancy (Iodine Global Network, 2016). Studies in Italy (Marchioni et al., 2008), Turkey (Kut et al., 2010, Anaforoglu et al., 2016) and Tasmania (Burgess et al., 2007) showed that ID in pregnant women persisted even after the application of USI, with measured urinary iodine concentration (UIC) being 74 μg/l, 87-150 μg/l and 86 mg/l in pregnant women in each country, respectively. Salt fortification with iodine is voluntary in the UK; iodised salt therefore does not contribute to the iodine intake of the population, with restricted availability in the market (weighed availability in market share 21.5%) (Bath et al., 2014a).

Fortification of other foods is also an option, although the IGN does not support individual food iodisation, such as crops or bread (Charlton and Skeaff, 2011). In Bangladesh and Pakistan, fortification of processed foods with iodised salt increased the availability of iodine in the population. Manufacturers use it when legislation permits, as it does not negatively affect the food characteristics (Spohrer et al., 2012). Fortification of bread with iodised salt in Australia resulted in increased iodine intake in pregnancy (median UIC 124.2 μg/day, IQR 121.1-127.2) and postpartum (median UIC 123.4 μg/day, IQR 119.7-127.1) compared to non-pregnant women (median UIC 102.9 μg/day, IQR 101.4-104.4), due to reported higher bread consumption (Mackerras et al., 2011). The choice of bread was the result of extended modelling for the identification of be the best vehicle for the increase of iodine intake (Charlton and Skeaff, 2011). Recently, biofortification of vegetables with iodine was also proposed as an opportunity to increase iodine intake. Positive results have been published after the consumption of fortified vegetables in 50 healthy volunteers in Italy, with UIC increased by 19.6% ($p=0.035$) (Tonacchera et al., 2013). Although UIC was measured in a single morning spot urine sample, which is not indicative of the iodine status of the individuals, there is still a clear increase on iodine intake, which indicates the potential of vegetables as vehicles of bioavailable iodine. Turmeric, being a widely used condiment, can also help in the elimination of goitre as an alternative to salt by increasing iodine intake, based on a study in Pakistan. The authors of this study suggest that the use of iodine fortified salt should not be overemphasised, as alternatives (such as turmeric) could be implemented (Jawa et al., 2015), an opinion which is not widely accepted considering the usefulness of iodised salt in the correction of IDD (Elahi et al., 2015).

A meta-analysis of nine RCTs (1990-2012) looked at the effect of iodine-fortified foods on UIC of children aged 7-10.5 years. Fortified foods included biscuits, meals and milk and the contained dose of iodine ranged from 25 to 200 μg/l, consumed for 4-30 months. At baseline, the UIC was similar in both intervention and controlled groups (heterogeneity $I^2=99\%$, $Q=942.47$, $df=13$). No carry-over effect was observed in crossover trials, so trials with both crossover and parallel designs were included in the meta-analysis. The standard mean UIC was significantly higher in the fortified group when compared to the control group (standard mean difference=2.02 µg/l, 95% CI: 1.30-2.73; $I^2$=99%, p <0.001) with iodine fortified foods effective at improving UIC in children (Athe et al., 2015).

Acceptance of biofortified foods by populations and wider production of these foods should be considered prior to implementing strategies using biofortified foods. Based on the Protection Motivation Theory, parents and school heads in Uganda were surveyed regarding their reactions to adopting iodine biofortified staple foods in the school feeding programs. Knowledge of parents and school heads about micronutrients, IDD and biofortification was low, with iodine and salt iodisation being the only two topics with higher awareness. Conversely, threat appraisal (perceived severity, vulnerability and fear to evaluate ID) and coping appraisal (response efficacy, cost response and self-efficacy to deal with ID through biofortified foods) were high for both sub-samples, which favours the protection motivation. The intention to adopt biofortified legumes was high and depended on factors including cost of the products, age and gender of the respondents. Key aims of a feeding program should include increased awareness of the health effects of ID and low cost of the biofortified foods (de Steur et al., 2015).

### 1.1.3 Iodine recommendations

The WHO/ UNICEF/ IGN recommended daily intake for adults is 150 µg/day, increasing to 250 µg/day for pregnant women (World Health Organisation et al., 2007). The European Food Safety Authority (EFSA) proposed in 2014 a new reference value of adequate intake for pregnant women of 200 µg/day (EFSA NDA Panel, 2014). The United State Institute of Medicine (IoM) and the Food Standards Australia New Zealand (FSANZ) also propose an increase in iodine intake for pregnancy and lactation. However, in the UK, the Department of Health Reference Nutrient Intake (RNI) is for adults 140 µg/day, with no proposed increment for pregnancy and lactation (Table 1.1) (Committee on Medical Aspects of Food Policy, 1991).

Table 1.1 Existing iodine recommendations (μg/day)

| | FAO/WHO (2004) | EFSA (2014) | US IOM (2001) | FSANZ (2006) | UK DoH (1991) |
|---|---|---|---|---|---|
| Preschool children | 90 | 70-90 | 90 | 90 | 60-70 |
| Schoolchildren | 120 | 90-120 | 90-120 | 90-120 | 100-130 |
| Adolescents | 150 | 150 | 150 | 150 | 140 |
| Pregnancy | 250 | 200 | 220 | 220 | 140 |
| Lactation | 250 | 200 | 290 | 270 | 140 |

There is an ongoing debate regarding the thresholds of sufficiency in pregnancy and the different existing recommendations for tolerable upper level (TUL) of intake, which ranges from 600 μg/day in Europe (Scientific Committee on Food) to 1,100 μg/day in the US (Institute of Medicine) (Scientific Committee on Food, 2002, Food and Nutrition Board, 2001). A large-scale cross-sectional study in Chinese pregnant women suggested that UIC in pregnant women should not exceed 250 μg/l in iodine sufficient regions, due to high risk of subclinical hypothyroidism (1.75-fold increased risk in UIC 250-500 μg/l compared to 150-249 μg/l). UIC exceeding 500 μg/l is also associated with isolated hypothyroxinaemia (2.85-fold increased risk compared to 150-249 μg/l). Levels of autoimmunity follow a U-shape curve and are lowest in women with UIC 150-250 μg/l. This leaves a potentially narrow margin of sufficient intake, which would be difficult to control around the world, due to the different iodine content of foods, salt and lack of labelling (Shi et al., 2015). Accordingly, Lee and Pearce (2015) proposed that the upper level of sufficiency in pregnancy should be an intake of 250 μg/day.

Since 15-20 mg of iodine is stored in the body of a healthy adult (defined by short-term clearance studies and chemical analysis of thyroid glands) (Fisher and Oddie, 1969), intermittent consumption is acceptable. Thyroid hormone synthesis requires approximately 60-80 μg of iodine per day, a quarter of which comes from recycling endogenous iodide (Zimmermann et al., 2008). The lower reference nutrient intake (LRNI) of 70 μg/day, which was set as the minimum required iodine to avoid goiter in population level, is in agreement to the daily requirement for thyroid hormone synthesis (Stanbury et al., 1974). The recommended WHO intake of 250 μg/day could be met by: weekly consumption of two portions of white fish (~126 μg per portion) and a portion of oily fish or seafood (~57-74 μg) and daily dairy consumption equivalent of two glasses of milk (as it is, in drinks, in cereals ~54 μg/portion), plus one yoghurt (~44 μg) and a cheese serving (~15-35 μg) (approximate iodine content of foods retrieved from McCance and Widdowson (2002) Foods Composition Database). However, many women avoid these foods and lack guidance on how to include them in their diet (Olsen, 2003).

## 1.2 Iodine status

### 1.2.1 Assessment of iodine status

#### *1.2.1.1 Iodine status at population level*

The gold standard method for iodine intake determination at a population level is urinary iodine excretion. UIC was first utilised in the 1980s and is the most widely used method for assessment of iodine status of a group or a population (Zimmermann and Andersson, 2012). The mean UIC for adequacy of iodine intake for different groups of the population are shown in Table 1.2. In addition, no more than 20% of samples in a population should have an iodine concentration less than 50 μg/l. Although lactating women have higher iodine requirements, UIC for adequate iodine status is lower than in pregnancy, as iodine is also excreted in breast milk, which is used for assessment of iodine status in combination with UIC in breastfeeding women (World Health Organisation et al., 2007, Mulrine et al., 2010).

Table 1.2 Median Urinary Iodine Concentration for adequate intake in different groups of the population (World Health Organisation et al., 2007)

| **Population Group** | **Median UIC (**μg/l) |
|---|---|
| Children <2years old | 100 |
| School-age children (≥6 years old) | 100 - 299 |
| Pregnant women | 150 - 249 |
| Lactating women | 100 |

Almost 90% of ingested iodine intake is excreted in urine, making UIC an indicator of recent iodine intake. However, measuring UIC in 24-hour urine samples is not always possible and practical, so spot urine samples are used instead. . Results from a longitudinal study in an iodine insufficient area on 16 healthy adults in Denmark proposed that almost 500 spot urine samples are required in a population level in order to assess iodine status of the population with 5% precision and 95% confidence intervals, and 125 samples for 10% precision (Andersen et al., 2008).

UIC, however, does not consider the hydration status and iodine volume. For this reason, correcting iodine with creatinine was proposed, although the WHO does not suggest its use (World Health Organisation, 2007). Meanwhile, there are no official cut-off values for assessment of iodine status sufficiency. A cross-sectional study held in 180 subjects of the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) cohort, aged 6-18 years, measured UIC (μg/l) and a creatinine-scaled estimate of 24-h iodine excretion [est24hUIEcrea (μg/d)] against measured 24-h urinary iodine excretion rates (24h-UIE, μg/d). A clearly better comparability of real 24h-UIE was found with est24h-UIEcrea (Pearson correlation for 13-18 years $r=0.47$, $p=0.0002$) than with UIC ($r=0.22$, $p=0.09$) (Montenegro-Bethancourt et al., 2015).

The accuracy of current iodine status assessment methods was questioned in an iodine status study of the German population. UIC in that population, which included men and women (n=6978) aged 18 to 79 years, was found to be lower than the WHO recommendation (54 μg/l in women versus 69 μg/l in men). However, 24-hour iodine excretion and intake were also estimated with the contribution of creatinine, age and gender. After taking these variables into consideration, 24-hour excretion and intake were found to be higher than UIC from spot samples. The recommended daily intake was still not achieved, as 30% of the population was below the Estimated Average Requirement (EAR). In samples where osmolality was also measured as a marker of hydration, differences were found in iodine excretion, even in samples in which estimated daily iodine excretion did not differ. Osmolality was significantly lower ($p<0.0001$) in samples with UIC<100 μg/l compared to samples with higher values (UIC>100 μg/l). In conclusion, the authors suggested that the WHO UIC cut-off for sufficiency of 100 μg/l is high and should be reduced to 60-70 μg/l (for populations with comparable hydration status and daily urine volume approximately 2 litres) as hydration impacts on the UIC epidemiological iodine assessment parameter (Johner et al., 2016).

Tg is the most abundant intrathyroidal protein. In people with sufficient iodine intakes, small amounts are secreted from the thyroid cells to circulation and serum Tg remains low (≤10 μg/l), while in cases of endemic goiter, Tg increases due to higher stimulation of TSH and greater thyroid cell mass (Zimmermann and Andersson, 2012). Tg correlates well with ID when compared with UIC (10.9 μg/l; IQR 0.2-75.0) in an area with mild ID compared to 14.6 μg/l (IQR 0.3-110.0) in an area with moderate ID, $p<0.001$) and is more sensitive to changes than TSH, which does not correlate with Tg (correlation coefficient $r=0$) (Knudsen et al., 2001). Recently, as the determination of an effective biomarker in iodine status assessment remains challenging, health surveys introduced the method of Tg measurement in dried blood spot (DBS) samples collected in filter paper, which has been proposed from the WHO for monitoring of iodine status in children (World Health Organisation, 2007). This new, more practical way for Tg measurement allows wider use in research, as overcomes the burden of serum blood collection in surveys.

Another method of assessment of iodine status is the collection of dietary iodine intake data, which allow the calculation of the mean iodine intake of a population (Cade et al., 2007). Food Frequency Questionnaires (FFQ) are widely used for dietary assessment in research and national surveys, as a rapid, practical and inexpensive estimate of iodine intake (Serra-Majem et al., 2010). A validated FFQ for women of childbearing age, correlated well with 4-day semi-quantitative food diaries ($r=0.45$, $p=0.002$) and duplicate 24-hour urine samples ($r=0.34$, $p=0.025$) (Combet and Lean, 2014). FFQ method validity ($\rho QI=0.66$, CI 0.33–0.99) was similar to Tan et al. (2013) which was validated in older Australians, and Brantsaeter et al. (2009), validated in Norwegian women. However, these FFQs and the ones validated from Rasmussen et al. (2001) in women 25-30 years and 60-65 years in Denmark and Condo et al. (2015) in Australian pregnant women contained more items and needed more time to complete, compared to the 3-5 min required for the FFQ developed by Combet and Lean (2014). Iodised salt intake assessment was not included in the 44-item FFQ of Condo et al. (2015), a limitation for a country with mandatory salt iodisation. In the present thesis, the FFQ developed by Combet and Lean (2014) has been used to assess iodine intake. Although this is a validated tool against food diaries and double 24-hour urine samples, limitations exist. Iodine excretion in two 24-hour urine samples might not depict the iodine status of an individual, and more samples would provide a more accurate measurement. At the same time, food items, such as eggs which are an iodine-rich source, are missing from the questionnaire. Overall, the questionnaire being short allows higher compliance of respondents and provides a useful estimation of habitual iodine intake, both for individuals and for populations.

Dietary assessment is challenging, and every method has limitations, but, depending on the application of the method, unique advantages might make it appropriate to use. FFQs are inexpensive, have a low participant burden, and provide data that represent both past and long-term dietary intake. However, when using an FFQ for dietary assessment attention should be paid in the food composition tables used (changes in nutrients depend on seasonality, location, processing, storage, cooking etc.). Accurate estimation of nutrients intake from FFQ depend on available food composition databases, which need to have all foods and recipes, without missing data (Cade et al., 2007). Extensive use of the FFQ in industrialised countries other than Australia might be limited due to the lack of food composition data. A database of standardised portion sizes for foods and drinks is also important for the use of FFQ, although portions vary within the population and FFQ lack sensitivity compared to weighted records (Cummings et al., 1987). Other disadvantages include long-term recall error, omission of foods from the FFQ list and application of the FFQ depending on the validated population (ethnicity, culture, age etc.) (Satija et al., 2015). Estimated and weighed food records are time consuming, expensive and pose a higher burden for participants, although providing data that are more detailed. Twenty-four-hour dietary recall is also expensive and needs more than one day of recall and an interviewer at the same time with having the recall bias (Shim et al., 2014). All those methods are subjective and are used depending on each occasion and specific aim.

#### *1.2.1.1 Iodine status of individuals*

Assessment of iodine status of individuals remains a challenge. UIC in spot urine samples is only indicative of the iodine status at population level, due to the large intra-individual variability of iodine intake and excretion throughout the day. A total of 10 or more spot samples or 24-hour urine samples are proposed as more reliable method of assessment of iodine status of an individual with 20% precision, based on data from 22 women who provided 24-hour and corresponding spot samples in a 15-month period. Calculation of the required number of samples was based on the intra-individual variation of the different methods (Konig et al., 2011). Recently, alternative biomarkers have been proposed, such as measurement of iodine in hair and toenail, are not yet validated (Pearce and Caldwell, 2016). Developing a biomarker for assessing iodine status of individuals would be of great value for research, public health and patient care. The lack such a biomarker makes the combined use of a validated FFQ and UIC an opportunity for a better determination of the iodine status.

## 1.2.2 Adverse effects of iodine excess

Iodine is excreted through the kidney in urine, and excess intake appears to be safe for the general population. Excess iodine obstructs $H_2O_2$ generation and acts as an inhibitor in crucial steps of the thyroid hormones synthesis, such as iodine organification, synthesis of Tg, release of thyroid hormones and thyroid growth (Smith et al., 2006). High risk groups of the population which are vulnerable to iodine excess include autoimmune thyroid disease patients, patients with history of a previous surgery and antithyroid therapy for Grave's disease (Leung and Braverman, 2014).

Failure to escape the Wolff–Chaikoff effect can lead to iodine-induced hypothyroidism and in patients with goiter, treatment with iodine can lead to iodine-induced hyperthyroidism, with risk factors such as nontoxic or diffuse nodular goitre and latent Graves' disease (Leung and Braverman, 2014). Allergic reactions in the form of skin rashes and acne have been associated with high intakes of iodised salt. Goitre and Hashimoto's thyroiditis with hypothyroidism have been also observed in susceptible individuals after the ingestion of 500-3000 μg/day (World Health Organization, 1994). After the induction of mandatory salt iodisation in China, detection rate of thyroid carcinoma increased significantly, from 0.71% to 1.31% ($\chi^2$=30.64, P<0.001) (Dong et al., 2013). Data from Denmark agree that incidence of thyroid cancers increased 1.7-1.8% annually from 1943 to 2008, with the main increase in the last 16 years. A potential cause might be mandatory iodine supplementation which started in 2000 (Blomberg et al., 2012).

During pregnancy and lactation, high amounts of iodine intake can be a cause of iodine-induced thyrotoxicosis and hypothyroidism to the fetus and neonates (Shumer et al., 2013, Connelly et al., 2012). A case study in infants whose mothers consumed very high amounts of iodine during pregnancy and postnatally, presented iodine-induced neonatal hypothyroidism, which is not always transient as it was in these cases (Emder and Jack, 2011). This was also reported in a case study in a preterm infant (Smith et al., 2006) and in a Korean study in preterm infants of mothers with high iodine intake, which showed that excessive iodine intake through breast milk (>100 μg/kg per day) contributed to development of subclinical hypothyroidism (Chung et al., 2009).

### 1.2.3 Adverse effects of iodine insufficiency

ID, through impairment of synthesis, can lead to a range of adverse effects, defined in the 1980s as IDD. IDD encompass a range of disorders caused by iodine insufficiency, affecting the different lifecycle stages with a variety of symptoms, including hypothyroidism, stillbirth, impaired mental function, congenital anomalies and iodine-induced hyperthyroidism (Li and Eastman, 2012). ID is the most preventable cause of brain retardation for the infant (World Health Organisation et al., 2007) and consequences range from loss of intelligence quotient (IQ) to cretinism. The main visible symptom of severe ID is goiter.

Impairment of fetal / infant neurological development is irreversible and has lifelong consequences. Neuronal myelination and migration both require thyroid hormones during the early stages of pregnancy and infancy, which depend on iodine availability. Insufficient intake of iodine during pregnancy can adversely affect both maternal thyroid health (iodine-induced hyperthyroidism or hypothyroidism) and the infant neurological development. In its most extreme form, deficiency can lead to cretinism, growth retardation and intellectual impairments, pregnancy losses as well as increased mortality in infants (World Health Organisation et al., 2007). Children born to moderately iodine deficient mothers can have neurological and psychological problems, hyperactivity and decreased IQ scores (Leung et al., 2011b). In a meta-analysis of interventions and cohort studies, ID in children aged 5 years old and under was associated with 6.9-10.2 points lower IQ, although high heterogeneity in the evidence calls for cautious interpretation (intervention studies $Q=54.81$, $df=15$, $p<0.0001$; prospective cohort studies $Q=4.85$, $df=12$, $p<0.001$). The same study concluded that maternal iodine status is positively associated with infant neurological development (no effect size calculated due to different outcomes) and that supplementation with iodine (via intramuscular injection, which seldom occurs nowadays) appears beneficial in early pregnancy compared to late pregnancy (effect size for mental development $d=0.82$) (Bougma et al., 2013). After birth, if the infant is exclusively breastfed, the mother remains its sole source of iodine until weaning, with the offspring potentially exposed to sub-optimal iodine levels for at least 13-15 months, 29-33% of the critical first 45 months of neurodevelopment (depending on weaning age, subsequent complementary feeding).

Iodine insufficiency, even marginal (UIC in population 50-99 μg/l), has been shown to affect children’s cognition and their school performance in the UK. The offspring of mothers taking part in the ALSPAC study had verbal IQ in the lowest quartile (odds ratio 1.58, 95%

CI 1.09-2.30; p=0.02) at 8 years when maternal UIC during pregnancy was below 150 μg/g of creatinine (Bath et al., 2013). The use of a single urine iodine measurement only provides a crude categorisation of iodine exposure, which nonetheless resulted in an unexpected outcome for 21st century Britain.

### 1.2.4 Global iodine status

Global iodine status has improved from 1993 to date. In 1993, 110 countries had and insufficient iodine status, in 2003 the number of insufficient countries fell to 54 and based on the latest Global Scorecard of iodine nutrition, 20 countries are iodine insufficient at population level in 2017 (Figure 1.4), a 5.5-fold decrease in less than 25 years. In pregnant women, the number of countries with insufficient iodine status (UIC<150 μg/l) remains higher (33 countries in 2017) (Figure 1.5) (Iodine Global Network, 2017). These countries include, among others, Norway (Henjum et al., 2018), Turkey (Anaforoglu et al., 2016), Denmark (Andersen, 2015), Iran (Delshad et al., 2016), Austria (Lindorfer et al., 2015), Greece (Koukkou et al., 2017) and the UK (Bath et al., 2015).

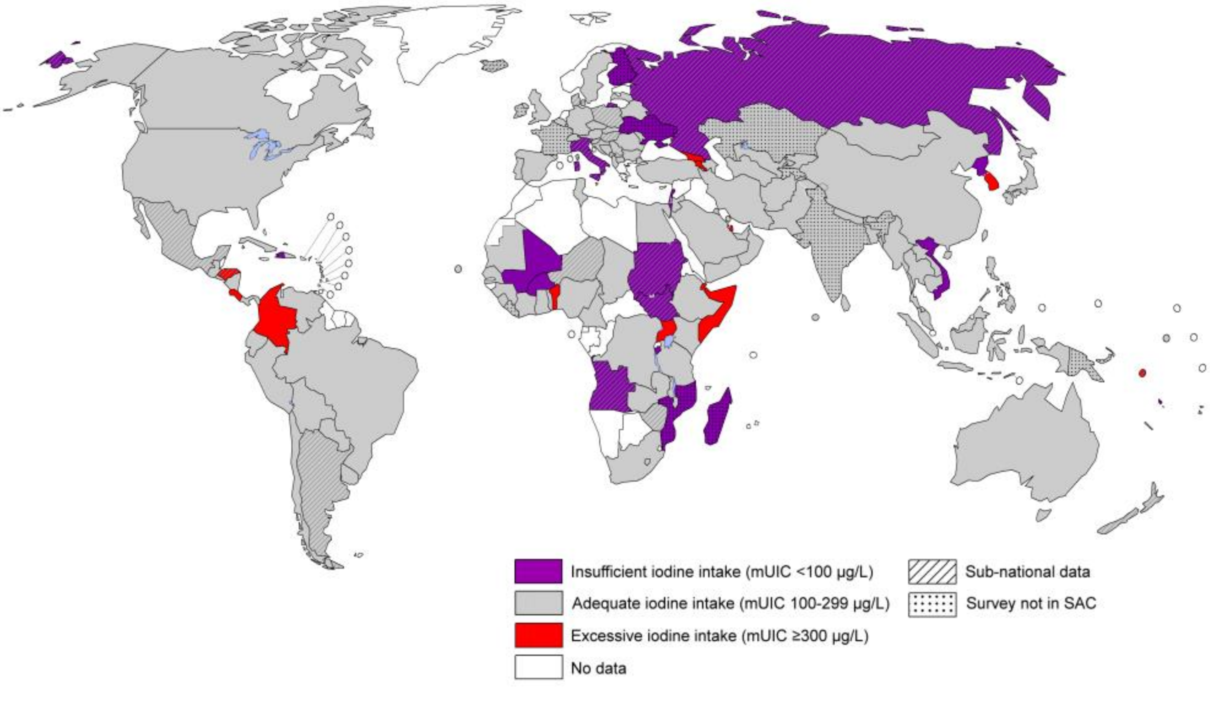


Figure 1.4 Global map of iodine nutrition 2017 in adults and school-aged children, based on median UIC (adapted from IGN).

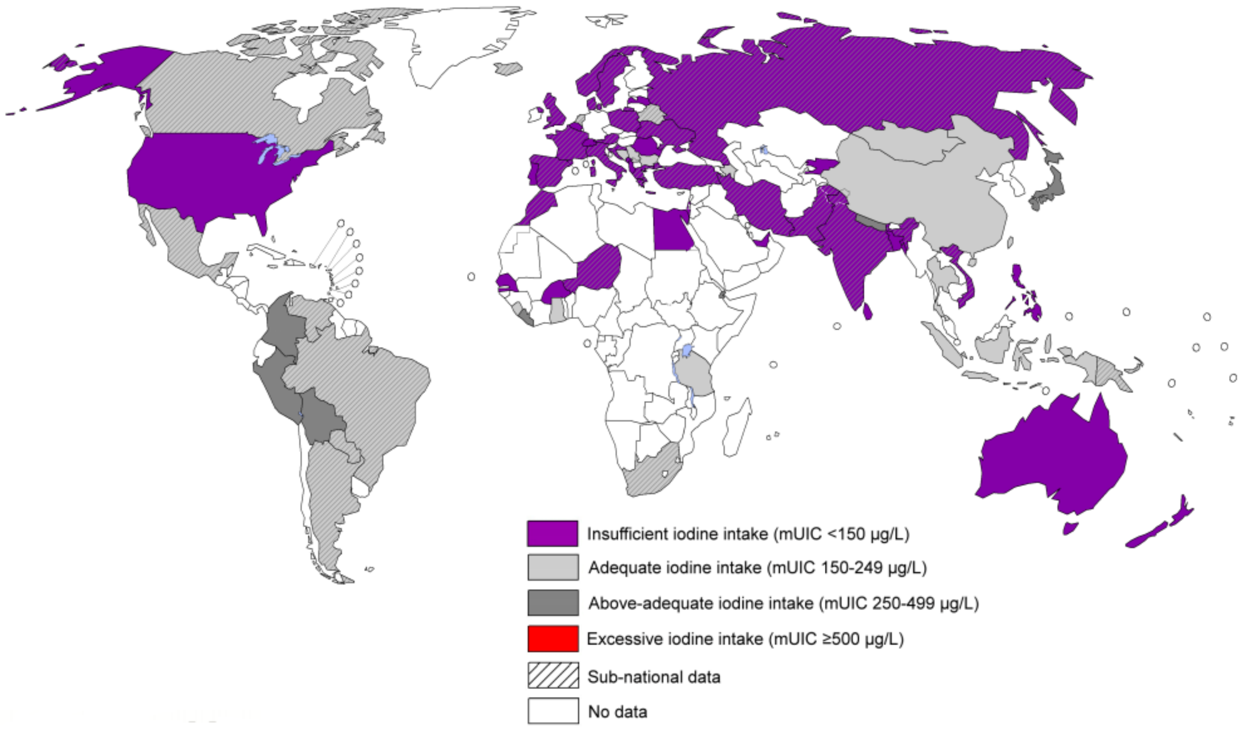


Figure 1.5 Global map of iodine nutrition 2017 in pregnant women, based on median UIC (adapted by IGN).

Mild iodine insufficiency in the UK is therefore a renewed public health concern, after reported insufficient status in schoolgirls in 2011, based on median urinary iodine concentration (80 μg/l, IQR 57–109) (Vanderpump et al., 2011). Previously believed to be iodine-replete, women in the UK have been shown to be iodine insufficient at population level (Vanderpump et al., 2011, Kibirige et al., 2004). In Scotland, females of childbearing age (cross-sectional survey) have been also shown to be iodine insufficient (median 75 µg/l) (Lampropoulou et al., 2012). However, recently (2013) measurement of the iodine status of the population was introduced in the National Diet and Nutrition Survey (NDNS) Rolling Program. The UK population was characterised as iodine sufficient, based on measured UIC in spot urine samples. Pregnant and lactating women have been excluded though from the analysis, and although results agree that he general population is iodine sufficient, women of childbearing age do not meet the criteria for pregnancy and lactation (median UIC 102 µg/l) (Roberts et al., 2018). Pearce (2015), based on the Condo et al. (2015) FFQ validation study for pregnant women, highlighted the importance of assessing iodine intakes in pregnancy, as adequate levels of iodine are essential for normal fetus neurodevelopment.

## 1.3 Iodine supplementation in pregnancy

Supplementation is a strategy to address iodine insufficiency in pregnant and lactating women. However, Healthy Start supplements, provided by the UK health services do not contain iodine, and commercial alternative are expensive (>£10 per 60 tablets). Similarly to the US (Leung et al., 2012), marketed pregnancy supplements are not required to contain iodine, although their use has been associated with a 40% higher urinary iodine concentration in Spanish pregnant women (Alvarez-Pedrerol et al., 2010). The American Thyroid Association, the Endocrine Society and the US National Academy of Sciences have proposed that all prenatal supplements should include 150 μg of potassium iodide (Leung et al., 2012). The WHO also recommends iodine supplementation in pregnancy and lactation in all countries where iodised salt is available in less than 20% of the households (World Health Organisation et al., 2007).

A recent Cochrane review of positive and negative health effects of iodine supplementation in preconception, pregnancy and lactation, for the mother, the infant and the child highlighted inconclusive evidence (Harding et al., 2017). There was indication both of harm and benefit in places of mild to moderate deficiency. The number of available studies, set in Denmark, Germany, Morocco, New Zealand, Thailand and Zaire was limited (14 studies), potentially due to the ethical difficulties implementing studies with a placebo / control group in pregnancy. Potential benefits included lower likelihood of insufficient iodine status in pregnancy, congenital abnormalities, postpartum hyperthyroidism, neonatal goiter and neonatal insufficient iodine intake (Harding et al., 2017). Potential harm included overactive thyroid function, nausea and vomiting during pregnancy. A cohort study in pregnant women with mild to moderate ID, included women receiving prenatal iodised (150 μg) supplements (n=168), women who regularly used iodised salt (n=105) and a control group of women (n=160). Results indicated that TSH was higher in women taking supplements than in the women who used iodised salt ($\chi^2$=3.9, p=0.048, OR 1.97, 95% CI 1.05–3.72), and 26% of women had TSH higher than the upper limit for gestation. Mild ID women that take daily a 200 μg iodine supplement from the beginning of their pregnancy might have an increased TSH and risk of maternal hyperthyrotrophinaemia. Consequently, supplementation with iodine for a long period prior to conception is suggested for women living in mild to moderate deficient areas (Moleti et al., 2011). Iodine supplementation did not influence thyroid dysfunction in a mild to moderate deficient area in Denmark, in thyroid peroxidase antibody (TPO-Ab) positive pregnant women. Women who participated in a placebo controlled RCT received a daily mineral and vitamin tablet with or without 150 μg iodine (group A: no iodine, group B: iodine during pregnancy only, group C: iodine during pregnancy and postpartum). Postpartum thyroid dysfunction developed in 55% of the participants, without any difference between the three groups (Nohr et al., 2000).

Beside impact on iodine status and thyroid function, the effect of iodine (supplementation) on neurodevelopment is critical and should be the key outcome for assessment of supplementation efficacy. Iodine intervention studies in pregnancy have measured an actual cognitive outcome in children from 3 months to 5.4 years (Kevany et al., 1969, Santiago et al., 2013, Berbel et al., 2009, Rebagliato et al., 2013, Murcia et al., 2011, Velasco et al., 2009, Gowachirapant et al., 2017, Pharoah et al., 1971, Thilly et al., 1978). In India and Thailand, iodine supplementation in pregnancy did not lead to a measurable difference in verbal IQ, performance IQ or the global executive composite (GEC) score from the Behaviour Rating Inventory of Executive Function Preschool Version (BRIEF-P), assessed in children at 5.4 years (200 µg daily iodine or placebo during pregnancy) (Gowachirapant et al., 2017). The results of this study need to be interpreted with caution, as UIC of women in India at baseline was not indicative of deficiency (>150 µg/l). The fact that women in the placebo group had sufficient UIC in the second and third pregnancy trimesters along with the small sample size and the sufficient UIC of women in India at baseline, might have prevented the detection of differences in IQ scores, which are anyway challenging, The Spanish multicentre mother-and-child cohort (INMA cohort, Valencia, Sabadell, Asturias and Gipuzkoa) in 1519 1-year-old infants showed a lower Psychomotor Development Index (PDI) score (-4.9 and -5.5 points respectively) in children whose mothers were taking ≥150 µg/day from supplements compared to children whose mothers consumed <100 µg/day iodine from supplements (Bayley scales of Infant Development for psychomotor and cognitive development) in the regions of Asturias and Valencia. When the results of all the areas were put together for comparing these two groups (≥150 µg/day versus <100 µg/day from supplements) a 1.5-fold increase in the odds of a psychomotor scale score less than 85 was found (which might indicate a slight delay in neuropsychological development). There was no difference for the Mental development index or UIC (Rebagliato et al., 2013, Murcia et al., 2011). Furthermore, no significant differences in children's neurological development were shown in iodine supplementation studies in pregnant women in Spain (Santiago et al., 2013) and Australia (Zhou et al., 2015). A key factor in the interpretation of these studies is the age of assessment, since neurocognitive testing is not reliable in the youngest groups (preschool children) (Baron and Leonberger, 2012). However, the Australian study stopped without recruiting the required number of participants and results may be underpowered. The funding body of the trial discontinued financial support, due to the inconsistency of the recommendations for supplementation in pregnancy with a placebo-control group, highlighting once again the ethical difficulties of such studies in pregnancy.

Severe ID, mainly in early pregnancy, was shown to lead to cretinism in a quasi-random trial of iodine supplementation through intramuscular injection (Pharoah et al., 1971). Positive associations between supplementation in mild-to-moderate deficient areas and children's neurodevelopment was shown in Spain. Daily potassium iodide supplementation (300 μg/day) in the first trimester led to an increased PDI score in children assessed at age 3-18 months (108.74±13.74 vs 102.65±14.60, p=0.02) (Velasco et al., 2009). However, the study was not an RCT, and the control group attended only in the last month of gestation in contrast to the intervention groups that was in the study from the first trimester. Confounding factors, such as lactation, were not controlled and results were characterised as preliminary. Higher neurodevelopmental quotient (mean±SD) 101.8 ± 9.7 vs. 87.5 ± 8.9, p<0.001) was found in 18-month-old children born to women with hypothyroxinaemia in early pregnancy who took iodine supplements in pregnancy (200 μg KI/day) (Berbel et al., 2009). IQ score was also 11.2 points higher (95% CI, 7.96- 14.46) in 4-23 months old children of women that received iodine via intramuscular injection during pregnancy (after the prenatal consultation between 20 and 36 weeks of gestation) or delivery; however, those studies were published 40-50 years ago, in areas with severe ID and endemic goiter (Thilly et al., 1978, Kevany et al., 1969).

From those intervention studies, there is overall a neutral or positive impact of supplementation during pregnancy on neurological development of the infant, with evidence not being consistent in the interventions included in a systematic review performed by Zhou et al. (2013). The reliability of the different assessment methods of neurodevelopment in a very early age might be a potential reason for the non-conclusive results (Baron and Leonberger, 2012). More well designed and longer-term randomised controlled intervention studies are needed to draw conclusions, assessing neurological development in older children (Zhou et al., 2013).

## 1.4 Iodine knowledge and awareness

The low profile of iodine in the UK Public Health and media arena can potentially influence the overall level of knowledge and awareness about the nutrient amongst mothers and healthcare professionals (HCPs). Pregnant women receive general dietary guidance during pregnancy, which is usually delivered by the community midwives during the first antenatal care appointment. These recommendations focus on following a balanced diet with limited specific practical recommendations on foods to include/ increase/ decrease/ exclude or portion size (NHS, 2015).

### 1.4.1 Healthcare professionals

Nutritionists and dieticians are the educated and accredited specialists to provide advice on dietary recommendations for pregnancy. However, midwives are usually the HCPs, along with general practitioners and obstetricians that are the primary providers of nutritional advice in pregnancy and their educative background should correspond to this need (Arrish et al., 2014). HCPs have low awareness of iodine in childbearing age, its importance, sources and recommendations (Lucas et al., 2014a). In the US, recommendations include daily prenatal vitamins containing 150 μg of iodine during preconception, pregnancy, and lactation. Obstetricians and midwives (web-based survey, n=476) recognised (60%) that supplementation in childbearing age and pregnancy is useful, but most (75%) reported to rarely or never prescribe iodine containing supplements (de Leo et al., 2016). Australian guidelines also recommend iodine supplementation and although 71% of the HCPs were aware of the recommendation, knowledge regarding the recommended dose and duration was low among 61 nurses and general practitioners (Lucas et al., 2014b) and 396 HCPs (Guess et al., 2017). Iodine supplements were recommended by 73% of the respondents during pregnancy, but only by ~50% in preconception and lactation. Reasons not to recommend supplements were the existence of fortification programs (28%) and lack of awareness of the recommendation (25%). Midwives who took part in the survey reported lack of knowledge (40%) and were less likely than dietitians to discuss dietary sources of iodine, which only 40% of the HCPs reported discussing with women. In New Zealand, where public health nutrition has focused on iodine for several decades, almost 100% of healthcare workers (pharmacists, midwives and hospital nurses, n=25) reported a high knowledge of iodine supplementation and fortification (but the sample of this survey was smaller compared to the rest of the surveys) (Nithiananthan et al., 2013). Knowledge has also been associated with the speciality of the HCPs in Turkey. Endocrinologists had significantly higher knowledge and awareness on iodine supplementation, recommended duration of supplementation, and iodised salt compared to family practitioners and obstetricians. However, in the same survey, knowledge was very low for all three specialities (endocrinologists, family practitioners and obstetricians) when asked whether supplementation in pregnancy should be recommended during the existence of food and salt iodisation programs, as only 23% answered positively in the question (Kut et al., 2015).

In the UK, only 46% of midwives could correctly identify seafood as a source of iodine, and 23% dairy products (Williamson et al., 2012b). This is not surprising since nutrition is still not a significant part of the curriculum. Most midwives (67%) reported not mentioning iodine in antenatal care, as only 20% could link it to fetal development and 10% were aware of the increased iodine requirements during pregnancy. More studies are needed to assess the level and quality of HCPs education who advise women in preconception, pregnancy and lactation, as data are limited and highlight a lack of training and resources to further education (Heyes et al., 2004).

A need and strong interest for further education on iodine was expressed by the majority of HCPs interviewed, focussing on pregnancy, guidelines and sources (Williamson et al., 2012b, Guess et al., 2017, Lucas et al., 2014b).

### 1.4.2 Women of childbearing age

Globally, both iodine knowledge and awareness are low among women of childbearing age (pregnant, lactating or not). In a cross-sectional survey of 1026 UK mothers, 55% were unable to identify sources of iodine, commonly mistaking salt (21%) and vegetables (54%) as iodine-rich foods. However, most (87%) reported willingness to modify dietary behaviour if they received information related to the importance of iodine in pregnancy. In this study, only 9% of women surveyed could recognise milk as a source of the micronutrient (Combet et al., 2015). In Australia, a country with mild iodine insufficiency in pregnancy and mandatory iodine fortification of salt and bread as well as recommendations for iodine supplementation in pregnancy, knowledge regarding the adverse outcomes of ID and the importance of iodine has been found to be consistently poor in pregnant women (Charlton et al., 2012, Charlton et al., 2010a, Lucas et al., 2014b, Malek et al., 2016, Martin et al., 2014). Low self-confidence on whether women met the iodine requirements (20%) could be explained from the lack of knowledge of dietary sources of iodine. Seafood, the most commonly recognised iodine source, was correctly identified by 23-55% of the women, depending on the survey. However, milk was only recognised as a rich source of iodine by 15-29% of pregnant women. Finally, supplementation with iodine was not considered necessary by 41% of pregnant women, but only from 19% when they followed a diet perceived to be "healthy". In Australia, knowledge (defined as knowledge on iodine sources and importance in pregnancy) was identified as a predictor of iodine supplementation. Women who perceived intake of iodine supplements in pregnancy as being important, regardless how healthy a diet they follow, were more likely to take supplements containing iodine (Martin et al., 2014). The likelihood is not quantified though, as the study does not provide any tangible data (e.g. coding of predictors, odds ratios, actual likelihood), which is a limitation. Poor knowledge did not improve after introduction of the mandatory iodine fortification program (Charlton et al., 2010b). In Iran, similarly, women of childbearing age have low knowledge, awareness and practice in relation to ID (Mirmiran et al., 2013, Moraveji et al., 2013, Nazeri et al., 2015). In a study in the UK, lower knowledge was recently linked to lower iodine status (O'Kane et al., 2015). As a result, increasing awareness and knowledge would be potentially a cost-effective way of increasing iodine intake.

## 1.5 Public health and health promotion

Nutritional epidemiology provides data about the nutritional status of the population examines the role of nutrition in the aetiology of disease and develops and evaluates interventions to achieve and maintain healthy eating patterns among populations. Health promotion, defined by the WHO as 'the process of enabling people to increase control over, and to improve, their health' (World Healh Organisation, 2017), moves beyond the focus on individual behaviour towards a wide range of interventions. It is the aim of all Public Health structures worldwide, from the WHO to local authorities that contribute to health policy-making, including all decisions, actions and plans undertaken for health improvement. Public health nutrition research focuses on gathering the evidence required to influence policy-making and contribute to the improvement of health and wellbeing.

## 1.6 Hypothesis and objectives

There is a sustained debate on the ethical implication of a randomised controlled trial of iodine supplementation in pregnancy, in parallel with concerns over the conflicted message that salt iodisation would convey. This absence of prophylaxis in the UK provides an ideal terrain to study the impact of simple health promotion strategies, based on iodine-rich food, and to tackle iodine insufficiency in pregnancy and lactation and its endocrine and neurodevelopmental consequences. In face of the current debate surrounding the relevance and morality of fortifying salt in a country striving to limit it in its diet, we hypothesise that focusing on dietary guidance could be part of the solution of this public health concern. Identifying the level of knowledge and awareness on iodine nutrition and perceptions and practices on iodine rich-foods could potentially aid towards educating pregnant and lactating women on ways to reposition those dietary components in their diets and enhance the improvement of their iodine status.

Specific research questions that will be tested in the thesis include:

1. What is the iodine status of pregnant women and their newborn in the UK?
2. Can neonatal iodine status be associated with maternal iodine intake or urinary iodine excretion in pregnancy or postnatally?
3. Are there any intervention studies in pregnant women which aim to increase iodine intake through dietary guidance or iodine-rich foods provision?
4. What is the current perceived level and quality of dietary guidance received by expectant mothers and new mothers?
5. What are the perceived barriers to increasing or maintaining an adequate intake of dairy and seafood pre-conception and during pregnancy / lactation?
6. What would be the most effective delivery of dietary guidance to expectant and new mothers?
7. What is the contribution of dairy and seafood products in the daily iodine intake of the UK population?
8. What are the main perceived barriers and influential factors in the consumption of dairy and seafood products?
9. Can behaviour towards dairy and seafood products consumption be predicted through the constructs of the Theory of Planned Behaviour (TPB) and sociodemographic characteristics?

10. Is an intervention with simple dietary guidance on iodine feasible, acceptable and effective in pregnancy?

# Chapter 2 - Iodine status of pregnant women and neonates in the UK – The Mothers and Babies at Yorkhill (MABY) study

## Abstract

Low iodine intake during pregnancy can cause a wide range of neurodevelopmental consequences in newborn. Pregnant women in the UK have been described as iodine insufficient, but there is lack of evidence on the contemporary iodine status during gestation and its association with the iodine status of their newborn. We aimed to examine the level of iodine intake of pregnant women and its association with postpartum iodine status and the iodine status of infants.

A longitudinal cohort study in pregnant women took place between January 2015 and September 2017 in antenatal clinics in Glasgow area. Women, recruited in the 28th week of pregnancy, were followed in the 36th-38th gestational week and 5 days postpartum, along with their babies. In the first and last appointments, participants filled in a food frequency questionnaire (FFQ). During the study meetings spot urine samples and blood samples were collected from the mothers and the babies. Iodine intake and excretion were calculated through the FFQ and the Sandell-Kolthoff colorimetric assay respectively.

In total, 710 women were recruited, of which 609 completed the study, with median age 33 years (interquartile range (IQR) 30-35). Median iodine intake at recruitment was 199 μg/day (IQR 121–274) with 34% (n=207) above the World Health Organisation (WHO) recommendation for intake (250 μg/day). After delivery, 38% (n=178) of women with increased iodine demands (breastfeeding or mix feeding), achieved the recommended intake in contrast to 55% (n=69) of those with normal adult demands (formula feeding). Urinary iodine concentration (UIC) results agree with the FFQ, as from women with increased demands, those who achieved the cut-off were 41% (n=186) and for those with basic demands 52% (n=62). Out of the 468 neonates that provided a urine sample, 59% (n=274) met the cut-off point of 100 μg/l (median UIC 118 μg/l, IQR 71-201). Breastfed infants had higher UIC compared to formula fed infants (p=0.002), but lactating mothers had lower UIC compared to formula feeders (p=0.002).

Iodine insufficiency remains a concern in the UK, as pregnant and lactating women struggle to achieve the recommended iodine intake set by the WHO. There is a need for public health strategies aiming to address this concern, as neonates might be affected by maternal low iodine intake, both during pregnancy and lactation. Randomised controlled trials are needed on the effect of mild iodine insufficiency in pregnancy and its relation to children thyroid function and brain development.

## 2.1 Introduction

Iodine deficiency is highlighted as a global public health concern by the WHO and represents a particular threat for pregnant women and their infants (World Health Organisation, 2007). Iodine is an essential component of thyroid hormones T3 and T4, which are critical for normal neurodevelopment in infancy and early childhood (Zimmermann and Boelaert, 2015, Velasco et al., 2018). Suboptimal intellectual performance has been associated with iodine deficiency, including maternal iodine insufficiency during pregnancy and offspring neurodevelopment (Bleichrodt and Born, 1994, Qian et al., 2005). In severe iodine deficiency, the effects on children have been well documented (Pearce et al., 2016), but less clear are the consequences of mild-to-moderate deficiency. Low iodine from foods during pregnancy (<200 μg/day) has been associated with increased risk of attention deficit-hyperactivity disorders (ADHD) in children at the age of 8 years (beta coefficient 0.05 (0.02-0.09), confidence interval (CI) 95%, for iodine from food 100 μg/day, overall adjusted model p=0.001), born in Norway from mothers recruited between 1999-2008 (Norwegian Mother and Child Cohort (MoBa) Cohort). A negative effect of short-term use of supplements in this case was evident (29% increased risk of ADHD diagnosis, 95% CI, p=0.053) for the first pregnancy trimester (Abel et al., 2017). Based on the data of Santiago-Fernandez (Spain), the prevalence of children with UIC 50-100 μg/l who had an intelligence quotient (IQ) score in the bottom quartile was 26%, with an odds ratio of 1.83 of being in the bottom group compared to those with UIC>150 μg/l (Santiago-Fernandez et al., 2004). Bath et al. (2013) (UK) showed relationships between maternal UIC in pregnancy and infant cognition. Based on their data, the prevalence of infant with suboptimal results (bottom quartile of scores – non-specified thresholds) were 29%, 29% and 30% for verbal IQ, reading accuracy and reading comprehension, respectively, when maternal UIC was below the pregnancy threshold (150 μg/g). The probability of having suboptimal results was 58%, 69% and 54% respectively greater for children born from mothers with UIC<150 μg/g compared to UIC<150 μg/g. Long term, educational outcomes remain reduced in children born from mothers with UIC< 150 μg/l compared to UIC≥150 μg/l, which do not always ameliorate in iodine replete children during adolescence (Hynes et al., 2013, Hynes et al., 2017). It is therefore highly desirable for pregnant women to be iodine sufficient before and during pregnancy, primarily through diet and subsequently through the use of iodine-containing supplements (Glinoer, 2007, Mian et al., 2009, Zimmermann, 2009b, Führer, 2011).

Public health strategies have focused on salt iodisation for the elimination of iodine deficiency worldwide and have partially succeeded in improving iodine status in the general population (for example in the US (Leung et al., 2012) and Ghana (Nyumuah et al., 2012)). However, pregnant women remain iodine insufficient, not only in developing countries, but also in the industrialised world (IDD Newsletter, 2017a). Previously, the UK has been assumed to be iodine replete, but a survey of British school girls in 2011 indicated that school-aged girls were iodine insufficient (UIC ~80 μg/l, with threshold for sufficiency set at 100 μg/l) (Vanderpump et al., 2011). Meanwhile, a Scottish survey in women aged 18-48 revealed similar low UIC (Lampropoulou et al., 2012). Recently, based on the latest National Diet and Nutrition Survey (NDNS) data, the UK was classified again as iodine replete for the general population, but no data exist for pregnant and lactating women in the survey (Roberts et al., 2018). Despite the WHO recommendations to increase daily iodine intake from 150 µg/day to 250 µg/day during pregnancy (World Health Organisation and International Council for the Control of Iodine Deficiency Disorders, 2007), up to 40% of pregnant women in Scotland have been shown to be at risk of iodine deficiency (Barnett et al., 2002) (data from published abstract – not peer-reviewed). Similar results for pregnant women in the UK have been published since 2002, presented in Table 2.1. Apart from the UK, pregnant women in other countries also have an insufficient iodine status (UIC<150 μg/l), including Norway (Henjum et al., 2018), Turkey (Anaforoglu et al., 2016), Denmark (Andersen, 2015), Iran (Delshad et al., 2016), Austria (Lindorfer et al., 2015) and Greece (Koukkou et al., 2017).

Table 2.1 UK studies assessing iodine status of pregnant women.

| | **Location** | **Year** | **Gestational weeks** | **Number of women** | **Median UIC (µg/l)** |
|---|---|---|---|---|---|
| Bath et al. (2013) | Bristol (ALSPAC) | 1991-92 | ≤13 | 1040 | 91.1 |
| Kibirige et al. (2004) | Middlesbrough | 2000-01 | 15 | 227 | Not reported[¥] |
| Pearce et al. (2010) | Cardiff (CATS) | 2002-06 | <16 | 480 | 117.0 |
| Barnett et al. (2002)[1] | Scotland | | 11.5 | 433 | 137.0* |
| Bath et al. (2014b) | Surrey | 2009 | 12 | 100 | 85.3 |
| Bath et al. (2015) | Oxford (SPRINT) | 2009-11 | 12<br>20<br>35 | 228<br>222<br>212 | 42.0<br>52.0<br>69.4 |
| Knight et al. (2017) | South-West England | 2016 | 37 | 308 | 88.0 |

[1] Only abstract published (not peer-reviewed); * Mean UIC; [¥] Iodine/creatinine ratio: 0.11 µg/mmol

There are currently no data on iodine status in mother and healthy term infant pairs in the UK, and this information is required. In the context of the existing published work, it is essential that the possibility of iodine insufficiency in UK infants is rigorously investigated given the risk of hampered neurological development.

The aim of the study was to determine whether pregnant women and their infants in the UK have an insufficient iodine status. Research questions included:

1. What is the iodine status of pregnant women and their newborn in the UK?
2. Can neonatal iodine status be associated with maternal iodine intake or urinary iodine excretion in pregnancy or postnatally?

## 2.2 Methods

### 2.2.1 Study design

A longitudinal cohort study in pregnant women took place between January 2015 and September 2017.

Pregnant women were recruited from antenatal clinics at their 28th gestational week appointment (GW28) and were followed up in the antenatal clinics at their 36-38 gestational weeks appointment (GW36), and postnatally (PN) along with their babies. At GW28 and GW36, an aliquot of the routine spot urine sample was collected, prior to the dip-test, which is known to introduce exogenous iodine to the sample (Pearce et al., 2009). An extra tube of blood was also collected during the routine blood sampling (no more than 4 mL). A short (one page), validated FFQ (Combet and Lean, 2014) focusing on iodine-rich food intake, supplement usage and smoking habits was also completed at GW28.

Contact occurred again between days 4-7 after the baby's birth. At this timepoint, a community midwife was performing a home visit to the participants, at which the newborn blood spot (or "Guthrie") screening occurs using the heel prick method. A member of the research team accompanied the midwife on the day. A spot urine sample and a finger prick dried blood spot sample were collected from the mother. Mothers were also asked to complete a new FFQ, same as the one filled in antenatally in the clinic. Two further optional samples were collected: if the mother was breastfeeding or mixed feeding she was asked to provide a few milliliters of breast milk. A hair sample was also collected with a pair of scissors from the left or right temporal area of the mother's scalp. A spot urine sample was collected from the baby, using a pad which was placed in the baby's nappy. Part of the newborn blood spot taken from the midwife was provided for the study. Figure 2.1 shows the study procedures and the samples collected in each appointment.

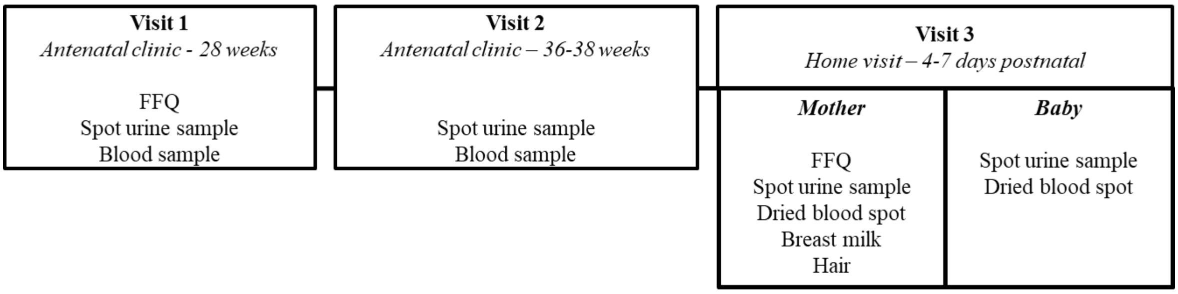


Figure 2.1 Study timeline and samples collected at each time point.

Information was collected from the National Health Service (NHS) records of the participants. This included contact details of the participants; participants' body measurements, postnatal haemoglobin, estimated due date, date and time of delivery, way of delivery, week of delivery, way of baby's feeding, baby's Apgar score and baby's birth weight.

The study was approved by the NHS Greater Glasgow and Clyde Research Ethics Committee (REC reference: 14/WS/1125) and was registered to ClinicalTrials.gov (NCT02390128). All study documents are presented in Appendix 1.

### 2.2.2 Recruitment and participants

Healthy pregnant women were recruited from two Glasgow maternity units – the New Victoria Hospital antenatal clinic and the Western Infirmary antenatal clinic. All women identified from the National Healthcare System to have a 28-week antenatal appointment in the clinics were sent a written invitation to participate in the study, 2 weeks before their appointment, which included the participant information sheet. Women were then approached in the clinic before their appointment with the midwife. The study was again explained to them and interested women signed an informed consent. All participants had the option to withdraw from the study at any time.

Exclusion criteria included abnormal pregnancies, mothers with known thyroid disorders, preterm infants (born before 37 completed weeks), multiple births and infants with postnatal problems such as infection or malformation. Mothers with multiple pregnancies have higher iodine and thyroid hormones demands compared to singleton pregnancies (Dashe et al., 2005). Women with thyroid disorders are also excluded due to being treated as patients taking thyroid therapies and having different iodine requirements. Exclusion of participants could emerge after the consent in the study, in cases of preterm deliveries or the development of a health condition during pregnancy (e.g. gestational diabetes). It was considered important to exclude ill infants and those with significant congenital anomalies (e.g. cardiac, gastrointestinal) from the study since they are known to be prone to developing transient thyroid stimulating hormone (TSH) elevation (Oakley et al., 1998).

Deliveries were identified through the Scottish Birth Record (SBR) system and midwives were contacted to arrange a home visit. In cases where the visit with midwife and the research team was missed or could not be coordinated, participants were contacted directly to arrange a visit, without performing the newborn dried blood spot (DBS). If the baby's urine sample was not collected during the appointment, mothers were provided with pads and the contact details of the researcher to collect the sample in a later time and provide it to the research team.

### 2.2.3 Samples and outcome measures

For the purposes of the present chapter, all urine samples were analysed for iodine concentration and mothers' blood samples were analysed for presence of thyroglobulin antibody. DBS, hair and breastmilk samples were not analysed for the purposes of the present PhD.

UIC was determined in all mothers' and newborns' urine samples by the ammonium persulfate digestion on microplate colorimetric method (APDM) based on the Sandell-Kolthoff reaction, as explained by (Ohashi et al., 2000). In the wells of a polypropylene 96-

well plate were pipetted 50 μl of either a blasted urine sample or potassium iodate calibrators. Ammonium persulfate solution (100 μl) was added with a multichannel pipette. Each sample was measured in triplicates. The plate was sealed and placed into a metal cassette, which was put for digestion tightly closed in an oven adjusted to 100°C for 60 minutes. After the digestion, the bottom of the plate was cooled with iced water to stop the digestion and 50μl of the digested aliquots were transferred to the corresponding wells of two polystyrene 96-well plates (Plate 1 and Plate 2), in order to have duplicate measurements. Plate 2 was sealed carefully until use and the multichannel pipette was used to add 100μl of arsenious acid solution and 50μl of ceric ammonium sulfate solution. The plate was put in a Multiscan reader for 15 minutes and absorbance was measured at 405 nm every 1 minute. The same procedure was repeated for Plate 2. Calculations were based on the iodine standard curve and he UIC results were presented as μg iodine/l. The laboratory has participated in the 'Ensuring the Quality of Urinary Iodine Procedures – EQUIP' program (rounds 45 and 46).

Habitual dietary iodine intake was calculated through the validated food frequency questionnaire (Combet and Lean, 2014). Presence of thyroglobulin antibody (TgAb) in mothers' blood samples (measured at GW28 for 94% (n=563) of participants and at GW36 for 6% (n=34) of participants, due to missing baseline samples) was measured by an enzyme-linked immunosorbent assay (ELISA) immunoassay (RSR™). TgAb is usually measured along with Thyroglobulin (Tg), to identify potentially unreliable serum Tg measurements. As Tg has not been measured for the purposes of the present thesis, TgAb results are presented only for descriptive reasons. The primary outcome measure was the relationship between maternal iodine status (UIC and iodine intake) and neonatal iodine excretion.

### 2.2.4 Data analysis and statistics

The sample number required was calculated as 697 mothers and infant pairs. This number allows for an approximate even mix of gender in the offspring cohort. It is necessary to collect at least 120 samples for each gender (boys / girls) / feeding mode (breastfeeding / formula feeding) (n=480) to establish robust reference ranges. To carry out a basic comparison of infant iodine status between two groups (feeding mode, gender, maternal iodine status), using a sample size of n=488 (n=697 after 30% drop-out), we would be able to detect a difference between group of approximately 17 μg/l (effect size 0.30, $\alpha$=0.05, $\beta$=0.9, two-tailed Wilcoxon test assuming 1:1 distribution between groups).

Normality of data was tested using the Shapiro-Wilks test. Descriptive statistics performed included frequencies (n) and proportions (%) for categorical data and mean and standard deviation (SD) for parametric continuous data or median and interquartile range (IQR) for non-parametric continuous data. Proportions with iodine intake / excretion lower than the recommended threshold were reported. Differences in the iodine status between groups of infants (according to feeding mode, gender, maternal iodine status) were compared. Differences for categorical variables were explored with Pearson Chi-Square test, for continuous parametric variables with independent samples t-test and for continuous non-parametric variables with Mann-Whitney U test or Kruskal-Wallis test (for more than 2 groups). Determination of agreement in the classification of women as having an insufficient iodine status was checked with Cohen's kappa test. Multiple linear regression was performed to identify predictors of infants' iodine status. The following variables were tested as potential prediction factors: Feeding mode (breastfeeding or mixed feeding, formula feeding), use of supplements at GW28, number of FFQ with sufficient iodine intake (0, 1 or 2), maternal UIC at GW28 and GW36. These factors were assumed to be able to influence infant's iodine status, due to the available iodine for the neonate both during pregnancy and postnatally. Data analysis was performed with the statistical software SPSS version 20.0 (IBM Corporation). Level of significance was set at 0.05.

## 2.3 Results

### 2.3.1 Recruitment data

Recruitment started in February 2015 and 710 participants were recruited until May 2016. Follow ups were completed in September 2017.

Over 16 months, 54% of eligible women approached were enrolled (n=710). Urine and blood samples were collected from 99 and 93% (GW28) and 94 and 93% (GW36), respectively. A total of 609 women completed the study (86%), as it is shown in Figure 2.2, and are included in the current analysis. Two women requested to withdraw from the study after consenting to participate, 29 women dropped out, 35 women were excluded from this analysis based on the study's exclusion criteria (23 delivered before the $37^{th}$ GW, 8 developed gestational diabetes, 3 had non-declared hypothyroidism, 1 baby was born with health condition) and 35 women were not followed due to other reasons (14 lack of communication, 10 moving to a new city or country, 1 baby staying on hospital for nasal surgery, 6 being unwilling to continue, 1 delivery non-identified before the 7th postnatal day, 2 changing hospitals, 1 baby moving to foster carer). Maternal and infant sample and data collection (n=609) is shown in Table 2.2.

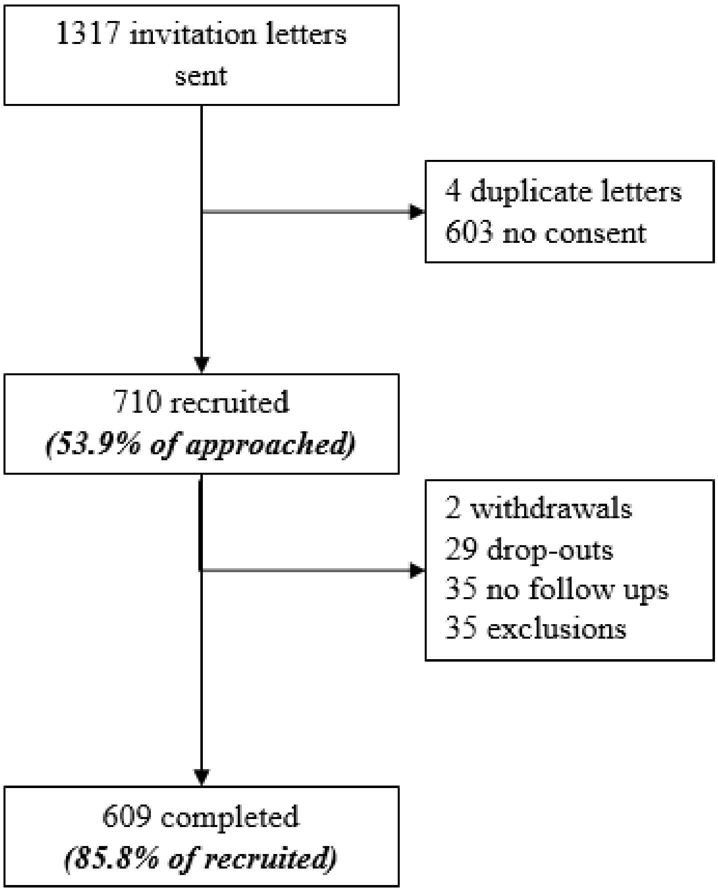


Figure 2.2 Participants' flow chart
No consent includes women who refused to participate and who did not attend the clinic on the day expected.

Table 2.2 Samples collected during the study

| | GW28 | | GW36 | | PN Mother | | PN Baby | |
|---|---|---|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| FFQ | 608 | 100 | - | | 603 | 99 | - | |
| Urine | 574 | 94 | 503 | 83 | 580 | 95 | 463 | 76 |
| Blood | 570 | 94 | 478 | 78 | - | | - | |
| DBS | - | | - | | 597 | 98 | 540 | 89 |
| Breast milk | - | | - | | 218 | 36 | - | |
| Hair | - | | - | | 321 | 53 | - | |

GW28: 28th gestational week; GW36: 36th gestational week; PN: Postnatal

### 2.3.2 Participants' characteristics

Participants' characteristics are shown in Table 2.3. Mothers' median age was 33 years (IQR 30–35), with the majority being normal weight (Body mass index (BMI) 23.8 kg/m3, IQR 21.6-27.2) and white Scottish (70%, n=425). Babies' median birthweight and gestational age were 3535 g (IQR 3242-3848) and 40.1 weeks (IQR 39.3-41.0).

TgAb was positive in 27 women (4.5%). Postnatal haemoglobin of mothers, measured within the first 24 hours after delivery in the hospital, was 10.8 g/dl (SD 1.5), an indicator of mild postpartum anaemia.

Table 2.3 Participants' demographic characteristics

| **Demographic data** | **Median** | **IQR** |
|---|---|---|
| Maternal Age (years) | 33 | 30-35 |
| Maternal BMI (kg/m$^2$) | 23.8 | 21.6-27.2 |
| GW of delivery | 40.1 | 39.3-41.0 |
| Baby birthweight (g) | 3535 | 3242-3848 |
| | **n** | **%** |
| Ethnicity | | |
| White Scottish | 425 | 70 |
| Other white British | 102 | 17 |
| Other ethnic groups | 82 | 14 |
| SIMD Quintile | | |
| 1: most deprived | 79 | 13 |
| 2 | 89 | 15 |
| 3 | 126 | 21 |
| 4 | 92 | 15 |
| 5: less deprived | 221 | 36 |
| Smoking (GW28) | | |
| No, never | 450 | 74 |
| No, I stopped | 143 | 24 |
| Yes | 16 | 3 |
| History of thyroid disease[a] | 92 | 15 |
| Following specific diet[b] | 67 | 11 |
| Way of delivery | | |
| Vaginal | 337 | 55 |
| Cesarean | 179 | 29 |
| Forceps | 68 | 11 |
| Ventouse | 14 | 2 |
| Other[c] | 9 | 2 |
| Baby feeding mode at postnatal visit | | |
| Breastfeeding | 396 | 65 |
| Bottle feeding | 129 | 21 |
| Mixed feeding | 82 | 14 |
| Baby gender | | |
| Boy | 278 | 46 |
| Girl | 331 | 54 |

[a.] Self-reported qualitative description of disease and family member; [b.] Self-reported qualitative data of ype of special diet (e.g. avoid dairy, vegetarian, vegan); [c.] Way of delivery described as "other" on Scottish Birth Records (SBR) system; GW28: 28th gestational week

### 2.3.3 Mothers' iodine intake

Median iodine intake at recruitment from food sources was 136 μg/d (IQR 101–191), up to 199 μg/day (IQR 121–274) when iodine-containing supplements (reported by 40%, n=246) were included (Table 2.4). Only 34% (n=207) of women at GW28 met the WHO recommendation for iodine intake, based on the FFQ (Figure 2.3). Almost half (49%, IQR 35-62) dietary iodine came from milk, which was the main contributor of dietary iodine intake.

Postnatally, women with increased iodine demands (i.e. breastfeeding or mixed feeding) achieved 148 μg/day (IQR 113-201) iodine intake from food sources. Iodine intake increased to 208 μg/day (IQR 134-289) when supplements were also included (reported by 43%, n=205 of women in this group), leading to 38% (n=178) achieving the WHO iodine recommendation. More than half women with normal adult iodine demands achieved the WHO recommendation (55%, n=69): 150 μg/day versus 250 μg/day for women with increased demands. Iodine intake from food sources was 141 μg/day (IQR 89-226) in this group, or 168 μg/day (IQR 98-269) when iodine-containing supplements were also included (reported by 17% (n=22) in this group).

Table 2.4 Iodine-rich foods and iodine intake of women at GW28 and postnatally, based on the FFQ.

| | **FFQ GW28** | | **FFQ PN** | | | |
|---|---|---|---|---|---|---|
| | | | **Increased demands (n=478)** | | **Basic demands (n=129)** | |
| | **Median** | **IQR** | **Median** | **IQR** | **Median** | **IQR** |
| Milk (g/day) | 227 | 140-393 | 240 | 153-400 | 245 | 158-422 |
| Other dairy (g/day) | 93 | 56-148 | 93 | 63-154 | 76 | 40-148 |
| Fish (g/day) | 33 | 19-65 | 37 | 19-71 | 24 | 9-57 |
| Total daily iodine from dairy | 113 | 78-157 | 121 | 113-201 | 114 | 75-190 |
| Total daily iodine from milk | 62 | 38-107 | 65 | 42-109 | 67 | 43-115 |
| Total daily iodine from fish | 21 | 8-36 | 24 | 12-40 | 17 | 7-34 |
| % daily iodine from dairy | 85 | 73-93 | 84 | 73-91 | 88 | 77-95 |
| % daily iodine from milk | 49 | 35-62 | 49 | 34-61 | 53 | 39-68 |
| % daily iodine from fish | 15 | 7-27 | 16 | 9-27 | 12 | 5-23 |
| Total daily iodine from food | 136 | 101-191 | 148 | 113-201 | 141 | 89-226 |
| Total daily iodine with supplements | 199 | 121-274 | 208 | 134-289 | 168 | 98-269 |
| | **%** | **n** | **%** | **n** | **%** | **n** |
| % below LRNI (70μg/day) | 8 | 48 | 5 | 22 | 13 | 17 |
| % achieved WHO recommendation | 34 | 207 | 38 | 178 | 55 | 69 |

GW28: 28th gestational week; PN: Postnatal; IQR: Interquartile range; FFQ: Food frequency questionnaire; LRNI: Lower reference nutrient intake

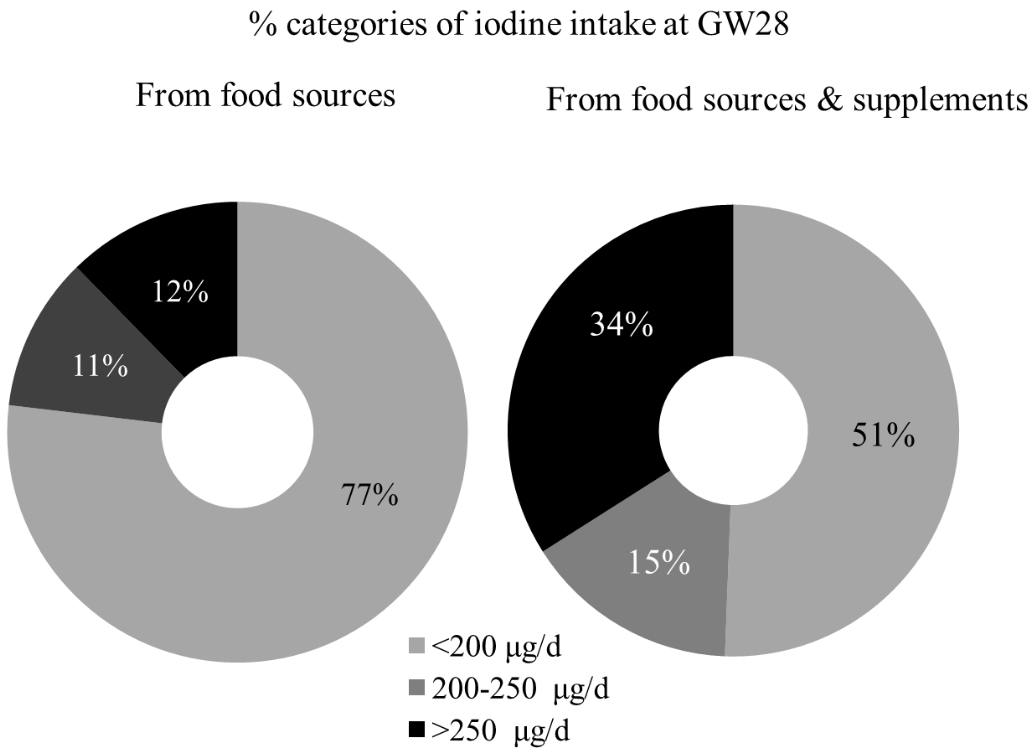


Figure 2.3 Percentage of women in different categories of iodine intake at 28th gestational week (GW28), based on the FFQ.

The left circle refers to iodine intake only from food sources and the right circle refers to total iodine intake (including iodine form supplements).

According to the FFQs, 24% (n=145) were meeting the WHO thresholds for sufficiency in both timepoints, although 49% (n=299) never achieved iodine sufficiency. The rest, 27% (n=165), were meeting the sufficient iodine intake in one timepoint (either GW28 or PN).

### 2.3.4 Urinary iodine concentration of mothers and babies

UIC analysis indicated a maternal median UIC of 121 μg/l (IQR 61–206) at GW28 (n=574); 123 μg/l (IQR 62–201) at GW36 (n=503), and 77 μg/l (IQR 32–166) postnatally (n=580). At GW28, 19% (n=109) of women had a UIC below 50 μg/l, and at GW36 20% (n=99) of women who had provided a urine sample. There was no difference in neonatal birthweight between mothers with UIC $<50$ μg/l and women with UIC $>50$ μg/l at any time point (GW28 $p=0.535$; GW36 $p=0.444$, PN $p=0.933$).

Neonatal UIC was 118 μg/l (IQR 71–201) (n=463). There was no significant difference between UIC of boys and girls (p=306). However, there was significant difference between the different feeding modes ($p=0.002$). The Bonferroni post hoc analysis revealed statistically significant differences in median UIC between formula feeding (UIC 91 μg/l; IQR 67–137) and breastfeeding (UIC 125 μg/l; IQR 75–232) infants ($p=0.002$). This difference remained when breastfeeding and mixed feeding infants were grouped together (UIC 124 μg/l; IQR 74–232) compared to formula feeding (UIC 91 μg/l; IQR 67–134) infants ($p=0.001$). There was no difference between UIC of infants whose mothers had a sufficient or insufficient iodine status (based on UIC) ($p=0.407$).

Women who did not have increased iodine demands postnatally (formula feeding, n=119) had UIC 108 μg/l (IQR 51–192), significantly higher compared to women with increased demands (breastfeeding, mixed feeding, n=457), who had UIC 71 μg/l (IQR 30–160) ($p=0.002$). According to the WHO set cut-off points for sufficient UIC, at GW28 42% (n=239) were meeting the 150 μg/l UIC and at GW36 41% (n=209).

Postnatally, 43% (n=249) of mothers were meeting the 100 μg/l cut-off point, but 36% (n=206) had a UIC less than 50 μg/l. For those with increased demands, those who achieved the cut-off were 41% (n=186) and for those with basic demands 52% (n=62). Out of the 468 neonates that provided a urine sample, 59% (n=274) met the cut-off point of 100 μg/l, and only 11% (n=53) were below the 50 µg/l (Figure 2.4).  Median UIC of mothers and babies in relation to the set cut-off points for sufficiency are presented in Figure 2.5.

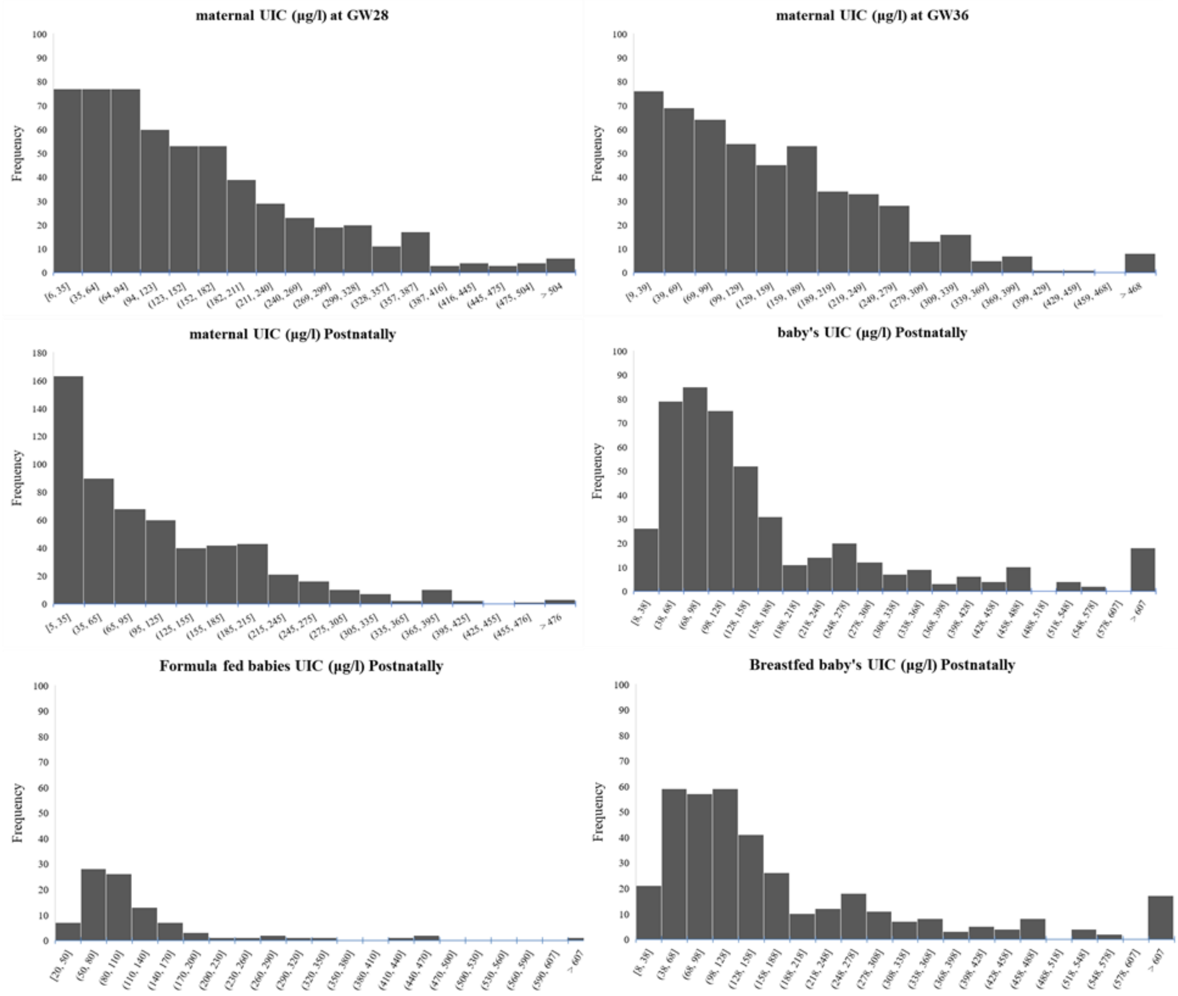


Figure 2.4 Histograms of maternal and baby's UIC at GW28, GW36 and postnatally.  Each bar represents 30 µg/l.
GW28: 28th gestational week;  GW36: 36th gestational week;  PN: Postnatal;  UIC: Urinary iodine concentration

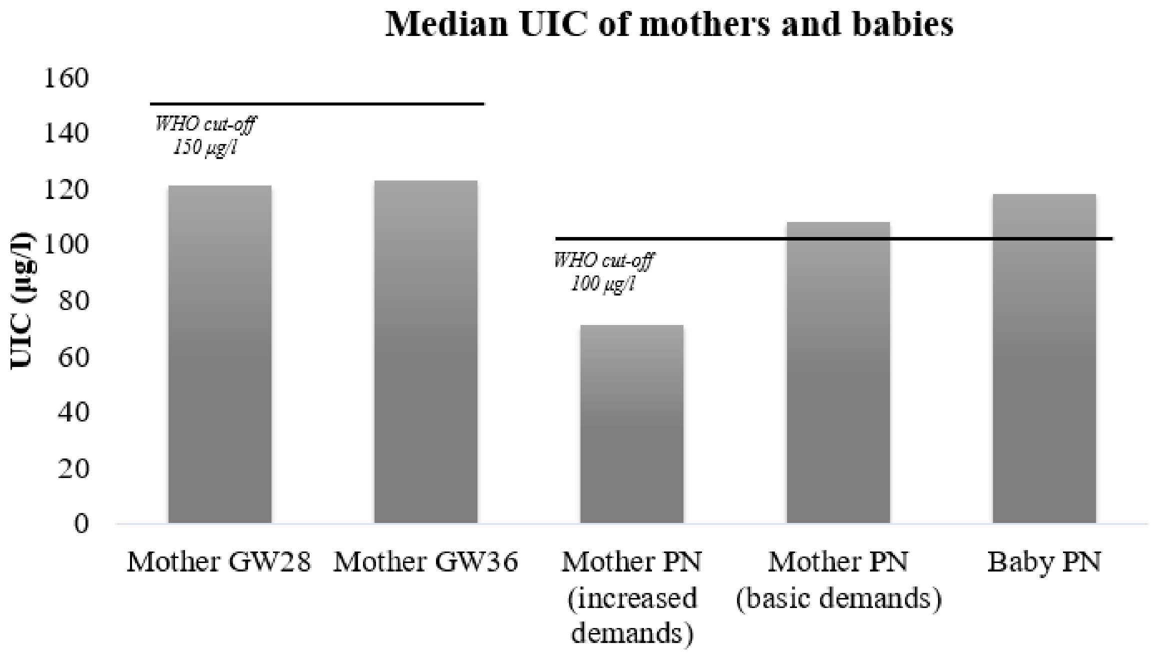


Figure 2.5 Median UIC of mothers and babies (µg/l) in comparison with the set WHO cut-offs for iodine sufficiency

Cut-offs: UIC GW28 and GW36 150 µg/l, Mother and baby PN 100 µg/l; FFQ: Food frequency questionnaire; UIC: Urinary iodine concentration; GW28: 28th gestational week; GW36: 36th gestational week; PN: Postnatal

Classification of participants as meeting the WHO criteria of sufficiency differed between FFQ and UIC at GW28 (p=0.018) but did not differ postnatally (p=0.956). Agreement was tested between UIC and FFQ classification of women as having a sufficient or insufficient iodine status (Cohen's kappa). For GW28 there was no agreement on classification of women between UIC and FFQ (κ=0.009, p=0.819; WHO cut-offs: UIC<150 µg/l and FFQ iodine intake<250 µg/day). Postnatally, UIC and FFQ did not agree in the classification of sufficiency neither for women with normal adult demands (κ=-0.201, p=0.029; UIC<100 µg/l and FFQ <150 µg/day) nor for women with increased demands (κ=-0.019, p=0.685; UIC<100 µg/l and FFQ <250 µg/day).

Out of the number of samples that each participant had provided during the study, only 15% (n=88) of the participants had a UIC which indicated sufficiency at all timepoints, which dropped to 10% (n=63) when baby's UIC was included.

### 2.3.5 Predictive factors of newborn babies' iodine excretion

A multiple linear regression model was created to assess whether neonatal UIC could be predicted. UIC was squared, to follow a normal distribution, and treated as a continuous dependent variable. The assumption of normality was met, as assessed by a Q-Q Plot. Independent variables entered to the model included: feeding mode (breastfeeding or mixed feeding, formula feeding), use of supplements at GW28, number of FFQ with sufficient iodine intake (0, 1 or 2), maternal UIC at GW28 and GW36.

The overall model explained 10.1% (adjusted $R^2$ of 8.9%) of the variation in neonatal UIC. The independent variables explained above statistically significant predicted neonatal UIC, $F(5, 373)=8.389$, $p<0.0005$. However, only three out of the five variables added significantly to the model (UIC at GW28, use of supplements at GW28 and feeding mode). Regression coefficients and standard errors are shown in Table 2.5.

Table 2.5 Multiple linear regression on the prediction of neonatal UIC from number of FFQ sufficiency result, UIC of GW28 and GW36, feeding mode and supplements intake at GW28.

| | **B** | **$SE_B$** | **β** | ***p*** | **95% CI for B** | |
|---|---|---|---|---|---|---|
| | | | | | **Lower** | **Upper** |
| N of FFQ with sufficient intake | 0.535 | 0.324 | 0.083 | 0.099 | -0.102 | 1.173 |
| UIC GW28 (μg/l) | 0.010 | 0.002 | 0.218 | 0.000 | 0.005 | 0.014 |
| UIC GW36 (μg/l) | 0.002 | 0.002 | 0.047 | 0.364 | -0.003 | 0.007 |
| Feeding mode | 2.028 | 0.686 | 0.147 | 0.003 | 0.680 | 3.377 |
| Supplements intake GW28 | 1.613 | 0.811 | 0.100 | 0.047 | 0.019 | 3.207 |
| Constant | 6.774 | 0.985 | | 0.000 | 4.836 | 8.711 |

B=unstandardized regression coefficient; $SE_B$=standard error of coefficient; β=standardised coefficient

## 2.4 Discussion

### 2.4.1 Main findings

The present study in pregnant women and their infants indicates that iodine status remains insufficient both during pregnancy and during lactation (based on data from FFQ and measured iodine excretion). Although not meeting the UIC cut-off point of sufficiency in a spot sample does not indicate deficiency for an individual and does not translate to women or infants being iodine deficient, results were presented as percentages in relation to reference values to allow a description of the study population. Furthermore, results showed that neonates are at risk of insufficiency, mainly if they are not breastfed. Feeding mode, as well as use of supplements and maternal iodine status at the beginning of the third pregnancy trimester can partially predict neonatal iodine status 5 days postpartum. Measurement of UIC in infants remains challenging, due to the difficulty in collecting a non-contaminated urine sample. The pad collection system, used in this study, has been well-accepted, as in a previous study in Swiss infants (Dorey and Zimmermann, 2008). Due to the difficulty in urine samples collection, iodine status in the first week of life has not been researched extensively, and TSH is often measured instead in infants (Travers et al., 2006, Kung et al., 1997). Reference values might not be representative, as iodine excretion has been shown to increasing from day 1 to day 4, and potentially lower reference values should be set for newborn infants, up to a week old (Dorey and Zimmermann, 2008). A balance study in infants aged 2 to 5 months, indicated balance between intake and excretion of iodine, without retention, at a daily intake of 70 μg (95% CI 60-80 μg), proposing an Estimated Average Requirement (EAR) of 72 μg/day for infants up to 6 months old (Dold et al., 2016).

Our results are in agreement with previous findings (presented in Table 2.1), that pregnant women living in the UK have insufficient iodine intake, which might be influencing the development of their infants. More than 60% of mothers and their children in Cambodia have a UIC<100 μg/l, being at risk of iodine deficiency, due to the lack of legislation on iodised salt, which is also the case in the UK (Laillou et al., 2016) However, low intakes are less frequently present in newborns, and mothers who do not breastfeed. Similar results have been published in a study in Iran, where mothers 3-5 days postnatally had a UIC which indicated iodine insufficiency (68 μg/l; IQR 39–134) but their newborns had a sufficient iodine status (UIC 213 μg/l; IQR 92–307) (Nazeri et al., 2016).

After delivery, increased need for iodine continues for lactating mothers in comparison to mothers who formula feed their infants (World Health Organisation, 2007). However, there is a population who combines formula and breastfeeding, and there is lack of data on the needs of this subgroup. In this case, neonates might be covering iodine needs through formula milk, which will also depend on the proportion of the supplied formula and breastmilk. Our results indicated that breastfed infants have higher UIC compared to formula fed, a difference which remained even after grouping breastfed infants with mixed feed (combination of breastmilk and formula). Lactating mothers (exclusively or with complementary formula feeding) had lower UIC compared to women who did not breastfeed. The parallel increased UIC of breastfed newborns though might explain this difference, indicating that low iodine status of lactating mothers might be due to increased iodine concentration of breastmilk, being a protective effect to newborns (Dror and Allen, 2018). Despite the compensation of iodine uptake for adequate iodine provision in infants, low status of mothers raises implications for their thyroid health and supplementation with iodine in lactation should be considered. Breastmilk iodine concentration has been previously associated with infant's UIC (r=0.526, p=0.000) (Wang et al., 2009) and has been suggested as a more accurate biomarker for iodine status during lactation (Dold et al., 2017). Sodium-iodide symporter (NIS) is expressed more during lactation and mediates the transport of iodine in the mammary gland (Spitzweg et al., 1998). Measuring breastmilk iodine concentration could assist the deeper exploration of this result, although studies on breastmilk iodine concentration show a big variation in the population (Dror and Allen, 2018). In areas of iodine sufficiency, breastmilk iodine concentration should be 100-150 μg/dl to provide the optimal iodine intake for thyroid hormones stores to infants (Azizi and Smyth, 2009). Challenges of iodine quantification in breastmilk include the stage of lactation, differences between foremilk and hindmilk and potentially use of unreliable methods (colorimetric assays) (Dror and Allen, 2018, Azizi and Smyth, 2009).

Measurement of UIC is the suggested way to characterise the iodine status at population level (World Health Organisation, 2007). However, individual iodine status is harder to define, as UIC in casual or spot urine samples is only indicative of recent iodine intake and is not interchangeable with 24-hour urine collection (Konig et al., 2011, Laurberg et al., 2007). Our study found differences between the FFQ and UIC in the classification of women's iodine status, which might highly depend on the lack of representation of iodine status from a single spot urine sample. Iodine expressed as concentration per gram of creatinine is another way used to assess iodine status, taking hydration and urine volume into account, but is not supported by the WHO (World Health Organisation, 2007). Apart from its cost, using creatinine to express iodine concentration might add an additional error and enlarge the scatter of iodine concentration, due to variation in creatinine excretion within and between individuals (Bourdoux, 1997, Furnee et al., 1994, Grimes et al., 2017). Due to the renal function of newborns being immature and changing over the first weeks of life (Blackburn, 1994), iodine to creatinine ratio is not also applicable to infants and has therefore not been used in the study. Pregnant women, in the third trimester of pregnancy, have been found iodine insufficient based on UIC (median UIC 140.0 μg/L; IQR 126.0-268.0)) but neonatal TSH was weakly correlated with maternal UIC ($r$=0.06, $p$=0.13) (Yoganathan et al., 2015). As a result, there is a need for other biomarkers, reliable and easily measurable, to identify individuals with insufficient iodine status before irreversible consequences appear.

Elevation of TSH, produced in the anterior pituitary gland, is a surrogate for insufficient exposure of the central nervous system to thyroid hormones. However**,** methods for detecting increased TSH concentrations, and in particular the method for detecting elevated capillary TSH used for newborn screening are geared to detect a significant rise in this hormone and may not be sensitive enough to distinguish subtle perturbations in TSH level due to insufficient dietary iodine. The use of TSH as surrogate for central nervous system effect from iodine insufficiency is particularly important. This is because subtle differences between iodine insufficient and iodine sufficient infants by IQ testing cannot be reliably detected until about 8 years of age (Calaciura et al., 1995). Thus, the early evidence for a neurological effect of iodine deficiency at the level of the thyroid hormone effect on the anterior pituitary gland of the brain is the preferred area of study. This study has the potential to assess the TSH levels of newborns, which is beyond the scope of the present thesis.

Recently, analysis of the ALSPAC Cohort study in pregnant women concluded that mild-to-moderate iodine deficiency or excess iodine intake in pregnancy is not associated with adverse obstetric outcomes, based on UIC/creatinine ratio (Torlinska et al., 2018). Potential lack of power, small number of pregnancy loss and UIC measurement in single spot urine samples might explain the contrast with previous studies that have associated iodine insufficiency with higher rates of preterm birth (17.5% vs. 10.0% ($p = 0.031$)) and low birthweight (19.9% vs. 12.3% ($p = 0.042$)) (Charoenratana et al., 2015). Similar results have been published from (Alvarez-Pedrerol et al., 2009) pregnant women in Spain, where maternal UIC <50 μg/l was associated with higher risk of infant's low birthweight compared to UIC between 100-149 μg/l (adjusted OR (95%CI): 0.15 (0.03-0.76)). Our study did not find any significant differences in neonate's birth weight between mothers with UIC<50 μg/l UIC>50 μg/l at any timepoint.

### 2.4.2 Strengths and limitations

Our study is the largest study in Scotland and second, although most recent, in the UK (after ALSPAC study in 1991) up to date, exploring the risk of iodine insufficiency for pregnant mothers and their newborns. The drop-out, exclusion and missing samples rates were low and allowed to create a cohort of pregnant women with a representative sample. The plethora of collected samples from mothers and their newborns during pregnancy and postpartum offers a unique opportunity for a multilateral exploration of iodine status, through iodine excretion in urine, thyroid hormones and proteins in blood samples, iodine in breastmilk, iodine in hair and data from the FFQ. For the purposes of the present PhD, only samples relating to iodine status were analysed, but there is the opportunity for future analysis of more samples and biological markers.

Collection of spot urine samples from mothers and babies has been an effective way to characterise the iodine status of the population during the study timepoints. However, the differences in classification of iodine status of women between the methods of iodine status assessment (UIC and FFQ) might lie to the application of UIC only to populations, so more spot samples or 24-hour samples collection would be more reliable, although practically harder to collect in these pregnancy stages and in early postnatal days. However, due to UIC at GW28 correlating and being a predictor for neonatal UIC, focussing more on determining it accurately and exploring its association with neonatal UIC could be an opportunity to identifying risk groups for iodine insufficiency and intervening early. Earlier measurement of UIC in pregnancy might be a better approach of future neonate's iodine status and neurodevelopmental outcomes, due to iodine being key in neuronal myelination and migration, which happens in the first weeks of gestation (Volpe, 2000).

Pregnant women had a median age of 33 years, which is comparable to the national statistics, as more than half (53%) of women who gave birth in England and Wales in 2015 were older than 30 years (average age 30.3 years) (Office for National Statistics, 2016). Breastfeeding rates decrease with age (49% at day 10 in 2015-16) and our study documented the way of feeding only 5 days after birth, being very early and agreeing with the 2017 Scottish statistics that 63% on infants were "ever breastfed" (ISD Scotland, 2017). Sixty-five percent were breastfeeding, which would further decrease in comparison to the Scottish breastfeeding rate (39%) 6-8 weeks postpartum in 2015-16 (ISD Scotland, 2016a). However, Participants were of a high socioeconomic status based on the SIMD index in comparison to national statistics: most births in this study occurred in families from the least deprived quintile, although in Scotland (in 2015) most births occurred in the most deprived quintile (ISD Scotland, 2016b). This result could be due to the areas where the antenatal clinics were located. All women in these antenatal clinics who had a 28$^{th}$ gestational week appointment were contacted to take part in the study, however women who agreed to participate were of higher SIMD, which is usual in research studies. The study results though indicate that even women of higher socioeconomic level have a low iodine status, which is worrying for the general population.

## 2.5 Conclusions

Iodine insufficiency in pregnancy and lactation is a contemporary public health concern persisting in many countries, including the UK. Pregnant and lactating women are still susceptible to low iodine status, which might be posing threats for the neurodevelopment of the fetus and infants. A protective effect might exist though for breastfed infants, as the low iodine status of their mothers but sufficient status of infants might imply a protective effect through lactation for neonates. Further research is needed to determine the neurological effect on the babies from the low maternal iodine status during pregnancy. Public health strategies are required to address the concern of iodine insufficiency and its consequences for the groups of the population that are more in risk.

## 2.6 Human resources of research team

The study design was performed before the start of the present PhD, with input from the PhD candidate. Recruitment and follow-ups, samples collection, storage and analysis were performed by the PhD candidate, with the help of two Research Assistants and Master students. Study coordination, data input, data analysis and write -up of the Chapter were performed by the PhD candidate.

# Chapter 3 - Increase iodine intake through diet – a systematic review of interventions during pregnancy

## Abstract

Iodine is mainly found in dairy products, fish and seafood and is particularly important during pregnancy and lactation. Iodine insufficiency has resurfaced in pregnant women in the UK, with no statutory or routine prophylactic measures to address this issue, such as food-based delivery of iodine through food fortification or provision of supplements.

We conducted a systematic review to identify interventions that aimed specifically to increase iodine-rich foods consumption (milk, fish, seaweed) and to improve iodine status. A systematic search of databases (Web of Science, PubMed, EMBASE, Epistemonikos) was conducted from 1990 to 2016. Specific interventions focusing on iodised salt and/or supplements were excluded, due to the absence of these strategies in the UK. Only three studies met the inclusion criteria, as the majority focused on salt iodisation or supplementation, or did not include iodine as an outcome. In total three interventions were included in the review. The studies populations were pregnant women in their first or second trimester and only one of the studies focused on iodine as a main outcome. Only two of the identified studies included results, as the third one only included the protocol of a designed intervention in Spain, with no results presented. Iodine status did not improve in any of those studies, however, knowledge, attitude and practice scores measured from a questionnaire improved after the intervention in Iran, and iodine intake significantly increased in obese women in the intervention group of the LIMIT study in Australia.

Overall, there is lack of interventional studies relying on dietary guidance, education, or provision/repositioning of iodine-rich foods to increase iodine status. Pregnancy nutrition should focus more on dietary guidance, as a safe and easily applicable way for the population to increase micronutrients' status, and studies on its effectiveness are needed.

## 3.1 Introduction

Iodine is a micronutrient found particularly in milk and dairy products, fish and seafood. These iodine-rich foods are the greatest contributors of iodine intake in the UK diet (Bates et al., 2011). However, most countries worldwide have adopted IGN guidelines for mandatory salt iodisation as an effort to correct the insufficient iodine status of the population and eliminate the consequent iodine deficiency disorders (IDD). This has made salt and other high-salt foods, such as most commercial breads, important dietary contributors of iodine and allowed reduced emphasis in advice to eat seafood and to some extent dairy foods (World Health Organisation, 2014).

According to the National Diet and Nutrition Survey (NDNS), dairy products contribute approximately only 9% in the total energy intake of the UK adolescent and adult population, which is less than in children below 11 years and older adults (older than 65 years). Oily fish consumption also remains lower than the recommended minimum of 2 portions per week (Bates et al., 2014). At the same time as increasing vegetarian (8%) and vegan (1%) sub-populations, exclusion diets are becoming more popular (e.g. excluding lactose, gluten). These changes pose risks of nutrient insufficiencies to increasing numbers of the population (Gaesser and Angadi, 2012, Baroke, 2016).

To date, there has been no focus on iodine-rich foods in guidance for dietary advice, and barriers to the consumption of those foods are common. Family preferences, texture, taste, heartburn and lack of knowledge and awareness of exclusion diets all contribute to decreased intake of those foods among pregnant and lactating women (Bouga et al., 2018a). Lack of knowledge and awareness about iodine, with exclusion or decreased intake of such foods, have grave consequences for pregnant and lactating women.

Iodine, as a component of the thyroid hormones, is important for thyroid function and neurodevelopment. Adequate intake is critical, particularly in utero and during infancy (Skeaff, 2011). Although there has been progress in ameliorating the global iodine status, 14 countries in Europe still have suboptimal iodine status in pregnancy (Lazarus, 2014). While the UK was long considered iodine replete, several cross-sectional surveys have highlighted mild insufficiency in the general population (Bath et al., 2016, Bath et al., 2014b, Lampropoulou et al., 2012, Vanderpump et al., 2011) and specifically during pregnancy (Bath et al., 2013, Bath et al., 2014c, Bath et al., 2015). Recently, the NDNS results indicated a median UIC of women of childbearing age which is sufficient for non-pregnant populations (UIC 102μg/l), measured in spot urine samples (Roberts et al., 2018).

The lack of prophylactic measures in the UK contributes to this public health issue, which may pose a socioeconomic burden (The Lancet Diabetes, 2016). Salt iodisation is not mandatory in the UK due to the mixed message, tending to oppose the campaign for salt reduction which has been a successful component of efforts against hypertension and cardiovascular disease risk (Bath et al., 2014a). It has been argued, without great traction, that sodium reduction can be compatible with salt iodisation strategies, by adjusting the level of fortification or by decreasing non-iodised salt used in the food industry (Cappuccio et al., 2011, Harvard Health Publications, 2011). There is a dominant view though, that iodised salt might be perceived as "good for health", so fortification would be preferred for foods that are encouraged as part of a healthful diet.

Supplements provided during pregnancy by the UK national health services (Healthy Start vitamins for women) do not currently contain iodine, in contrast to other westernised countries, such as the US, that recommend iodine-containing supplements for pregnant women. The UK Department of Health has not reviewed the iodine recommendations for pregnancy and lactation since 1991 and proposes no increment (Committee on Medical Aspects of Food Policy, 1991), which is now outdated and in disagreement with the WHO/ IGN (World Health Organisation, 2007) and EFSA (EFSA NDA Panel, 2014) recommendations, proposing an increment in iodine intake from 150 μg/day to 250 μg/day and 200 μg/day respectively. As a result, pregnant and lactating women mainly rely on their diet for an adequate iodine intake for themselves and their infants.

The UK, as well as other countries, faces a significant challenge in improving the iodine status of the population, focusing on pregnancy, lactation and infancy as the most critical stages. However, knowledge and awareness on iodine remain low amongst mothers (Combet et al., 2015) but also healthcare professionals (Lucas et al., 2014a, Williamson et al., 2012a). In a web-based survey of obstetricians and midwives in the US - a country where current recommendation is for women to receive daily prenatal vitamins containing 150 μg of iodine during preconception, pregnancy, and lactation - respondents were also found to have limited knowledge about iodine, with 66-72% reporting rarely or never prescribing iodine-containing supplements for these groups of women (de Leo et al., 2016). Similar findings have been revealed following a detailed survey in Australian healthcare providers (Guess et al., 2017). In the UK, pregnant women receive general dietary guidance during pregnancy, which is usually delivered by the community midwives during their first antenatal care appointment. These guidelines are focused on following a healthful balanced diet without giving specific practical recommendations focusing on foods to include, increase, decrease or exclude and daily or weekly portion sizes (NHS, 2015). This is at booking, so usually around the $12^{th}$ week of pregnancy. The discussion with the midwife differs between cases and depends on both midwife's knowledge, education and personal interest in nutrition as well as woman's needs, is inconsistent and focuses on foods to avoid rather than healthy eating (Lee et al., 2012).

Without prophylaxis, there is a need to explore ways to increase iodine provision in pregnancy and lactation through simple interventions. Women are usually more receptive to changes in behaviours during pregnancy for the benefit of fetal health. Research has focused on behaviour change interventions during this period, for example interventions for weight gain, physical activity and smoking cessation, which have all been shown to be effective (Thangaratinam et al., 2012, Lumley et al., 2009, Oteng-Ntim et al., 2012). Increasing iodine awareness and iodine-rich foods consumption could help reach a sufficient iodine intake in pregnancy and lactation. Therefore, we conducted a systematic review of the literature to identify human interventions in pregnancy that measured iodine status or intake as a result of a dietary or behavioural intervention, excluding those that used iodised salt and supplements, to explore their effectiveness as a potential way to improve iodine status in pregnancy.

## 3.2 Materials and Methods

### 3.2.1 Protocol and registration

The methodology for the present review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher et al., 2009). The search strategy, methods, inclusion and exclusion criteria were specified in advance and documented in a protocol. The review was registered with the international prospective register of systematic reviews (PROSPERO) (Review number: CRD42016039430).

### 3.2.2 Search strategy

A broad search of electronic databases (Web of Science, PubMed, EMBASE and Epistemonikos) from 1990 to November 2016 was conducted. Five different searches on the topic were conducted and combined with the use of AND function in order to give the final results. Keywords used in Cochrane reviews or other relevant reviews for relevant topics were searched in order to finalise our search terms. The five searches included (Appendix 2): [1] a search regarding the exposure of the intervention and the exclusion of animal studies; [2] a search regarding the outcome; [3] a search regarding the study design; [4] a search regarding iodine nutrition; and, [5] a search regarding gestational period. The final results from the 4 databases were collated in a single file on EndNote and duplicate title entries were removed first automated and then manually. The remaining titles were screened from two independent researchers. The results from that step were collated again and the abstracts of the remaining records were screened again from the same two researchers. The remaining records were collated again for full-text screening and the eligible studies were included in the review.

### 3.2.3 Eligibility criteria

Only dietary interventions were included in the review, including counselling and/or educational studies and studies with food provision. Randomised or non-randomised trials, with or without a control group were considered. Animal, cross-sectional, case control and ecological studies were excluded. Studies were also excluded if they were supplementation studies (using tablets, pills or oil) and studies with iodised salt. Any duration, frequency and timing of the interventions were accepted.

The eligible studies for inclusion in the systematic review were interventions in pregnant women, at any stage of pregnancy, without any health conditions that may influence dietary intake, thyroid function or urinary excretion (such as kidney disease, gestational diabetes, thyroid disorders, thyroid cancer etc.). Only studies in singleton pregnancies were included.

The main outcome measures for this systematic review were iodine intake, measured in any dietary assessment method, and/or iodine excretion in urine. Secondary markers of iodine status included were plasma thyroglobulin (Tg) and thyroid function markers (thyroid hormones and thyroid stimulating hormone (TSH)).

### 3.2.4 Quality

Quality was assessed evaluated using the Jadad scale (Jadad et al., 1996). When results were not reported, the study protocol was assessed for quality, based on the described intended procedures. Three components were scored in the published studies or protocols (randomisation, blinding and withdrawals/ dropouts description), from which a quality score was calculated (0-5 points), as follows:

- Given a score of 1 point for each "yes" answer and a score of 0 points for each "no" answer in the questions below (maximum of 3 points):
    - Was the study described as randomised?
    - Was the study described as double blind?
    - Was there a description of withdrawals and dropouts?
- Given 1 additional point if in questions 1 and/or 2 the methods were described and/or were appropriate.
- Deducted 1 point if in questions 1 and/or 2 the methods used were inappropriate.

## 3.3 Results

### 3.3.1 Study selection

A total of 3,021 titles were reviewed by two independent reviewers; 241 publications were considered for abstract screening and 39 for full-text screening. The information of every step of the systematic review is described in Figure 3.1, in the adopted PRISMA flow chart (Moher et al., 2009). Three studies met the criteria for inclusion in the present review (Dodd et al., 2014, Prieto et al., 2011, Amiri et al., 2017).

### 3.3.2 Study characteristics

The studies that were selected for final inclusion in the systematic review are interventions in pregnancy that have measured iodine intake or status before and after the intervention. The interventions were only based on diet or education, and the primary aim of the study was not always focussing on iodine. Although other studies have focused on increasing iodine-rich foods (oil-rich fish), they are not included in the review as iodine status was not a measured / reported outcome. Supplementation studies using lipiodol, fortified bread and salt and other supplements were also excluded, as the aim of the study was to explore whether iodine status can ameliorate through dietary choices or supplementation with foods naturally-rich in iodine such as fish, milk or seaweed.

### 3.3.3 Results of individual studies

Table 3.1 shows in detail the included studies in the systematic review. The three studies were designed for different geographical areas (South Australia (Dodd et al., 2014), Spain (Prieto et al., 2011) and Tehran, Iran (Amiri et al., 2017)), resulting in different approaches depending on the characteristics of the country and the population. Two out of the three studies (Prieto et al., 2011, Amiri et al., 2017) had iodine as the main focus, in contrast to the LIMIT study (Dodd et al., 2014), which had general behavioural, dietary and physical activity advice focus, and iodine as a secondary outcome. In the latter study, obese and overweight pregnant women were only included in the study population, rather than healthy pregnant women with no restriction in the body mass index (BMI).

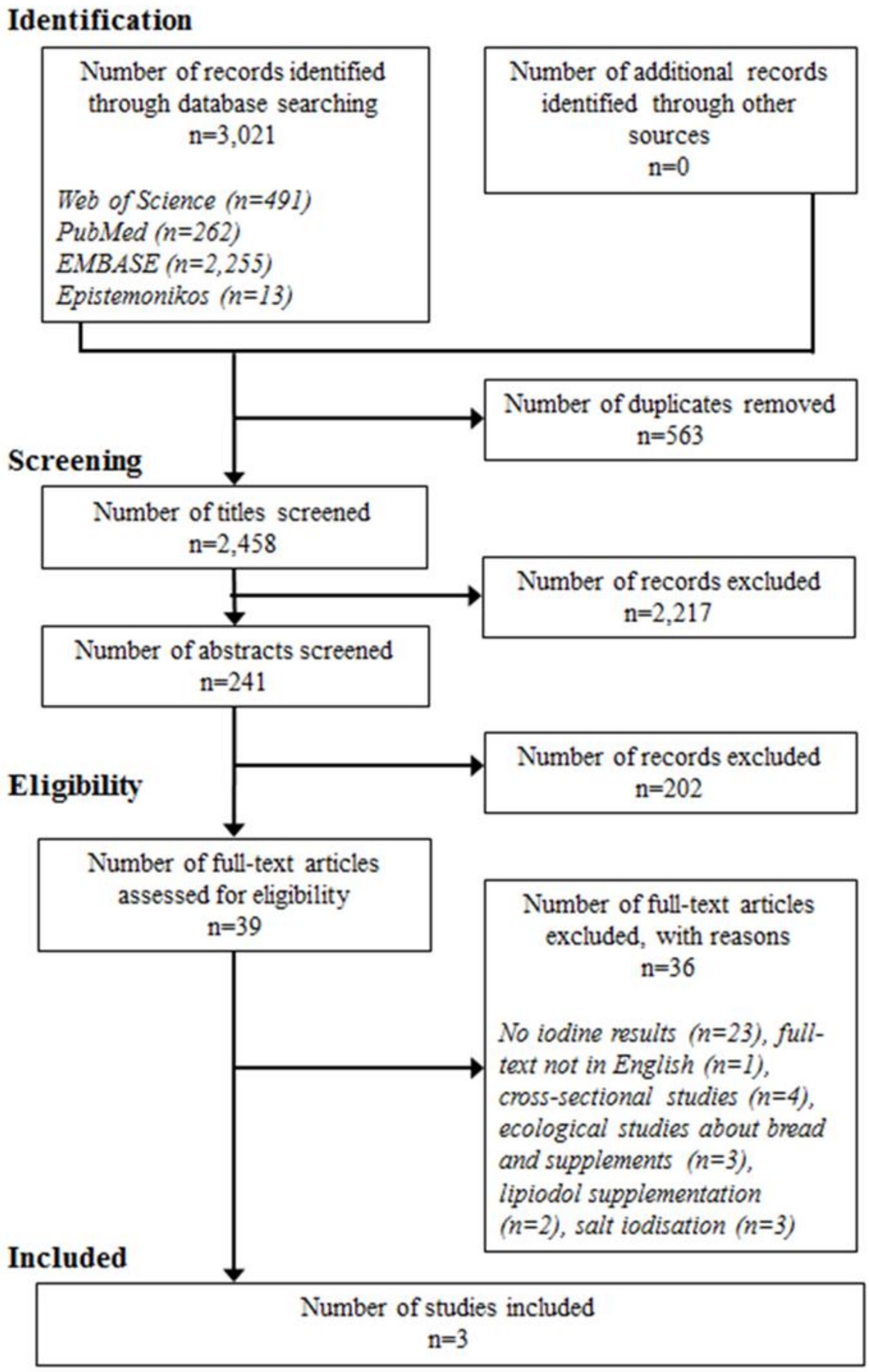


Figure 3.1 Summary of search for selected articles (modified from PRISMA flowchart, (Moher et al., 2009))

All studies aimed to recruit women to their first or second trimester. The LIMIT study was an intervention in overweight and obese women, at 10-12 weeks of gestation and followed-up to 4 months postpartum (Dodd et al., 2014). The dietary guidance provided during the study was consistent with the Australian standards and was tailored to each individual woman through meal plans, recipes and food substitutions. Amiri et al. (2017) recruited pregnant women, between the 4th and 18th weeks of pregnancy, for a randomised controlled trial (RCT). This RCT aimed to assess the effectiveness of an education program on the amelioration of iodine status. The educational program (4 months long) included two face-to-face educational sessions, using a leaflet in the second and the third trimesters, followed by two telephone calls between educational sessions to answer any potential questions the mothers had. The final study (Prieto et al., 2011) was a study protocol for a cluster randomised controlled multicentre trial in pregnant women, to be recruited in the first trimester of pregnancy to their last antenatal appointment in the third trimester (ClinicalTrials.gov NCT01301768, registered in 2011). Women in the intervention group would receive group education on healthy hygiene-dietetic habits and the importance of an adequate iodine nutritional status during the first trimester of pregnancy. The consumption of iodine-rich foods and prevalence of iodine deficiency were described as the outcomes of the study. Iodine status was defined as median urinary iodine concentration (UIC) of the groups, measured from a single spot urine sample.

For the study protocol, findings are not published to this date, and results are not expected, as the intervention could not be completed (Manresa, personal communication). Dodd et al. (2014) did not assess iodine status by measuring UIC, in contrast to Amiri et al. (2017). Based on dietary assessment with the use of a food frequency questionnaire (FFQ), the authors found no significant differences on iodine intake between intervention and control groups (adjusted treatment effect 3.54 μg, 95% CI -4.36-11.44, p=0.38). Iodine intake, however, increased in obese but not overweight women, but data were not provided on the published article (Dodd et al., 2014). Amiri et al. (2017) concluded that the intervention increased knowledge, attitude and practice (KAP) scores, but not iodine status.

The quality scores of the studies above are presented in Table 3.1. Scores were low to medium for both studies (Amiri et al., 2017, Dodd et al., 2014) and the protocol. The protocol was rated based on the design described and the range on the score is due to the question “was there a description of withdrawals and dropouts?”, which is not described on the protocol and would need the study to be completed in order to identify the way it would be reported.

Table 3.1 Included studies characteristics

| Study | Population/ Setting | Sample Size | Intervention | Outcomes | Results | Quality |
|---|---|---|---|---|---|---|
| Dodd *et al*, 2014<br><br>LIMIT study | Randomised controlled trial<br><br>Inclusion criteria: 10-20 weeks pregnant women, singleton pregnancy, BMI≥25kg/m$^2$<br><br>Exclusion criteria: Type 1 or 2 diabetes, multiple pregnancies | N= 1,873<br><br>Intervention group: n=945<br><br>Control group: n=928 | Dietary and lifestyle intervention over the course of pregnancy, including dietary, physical activity and behavioural strategies, delivered by a research dietician and trained research assistants<br><br>Time points: recruitment, and at 22, 24, 28, 32 and 36 weeks of pregnancy by phone or face-to-face | Micronutrients intake estimated from a 126 items FFQ at the time of study entry, at 28 and 36 weeks' gestational age, and at 4 months postpartum | The effect of the intervention on iodine was modified by maternal BMI category (interaction $P < 0.05$ in all cases), with overall intake significantly increased in obese but not overweight women randomised to the intervention group.<br><br>No significant difference on iodine intake when compared between groups (p=0.38). | 2 |
| Amiri et al, 2016 | Randomised controlled trial<br><br>Inclusion criteria: 4-18 weeks pregnant women without history of thyroid disease (goiter, hypo- or hyperthyroidism)<br><br>Exclusion criteria: thyroid diseases during pregnancy, premature labour | N= 63<br><br>Intervention group: n=29<br><br>Control group: n=34 | Two face-to-face educational sessions with the use of an educational pamphlet designed by the researcher. Two follow-up calls between educational sessions. Information included: iodine deficiency definition and consequences, | Iodine knowledge, attitude and practice (KAP) scores, urinary iodine concentration (UIC) in spot samples, iodine in salt | KAP scores were significantly increased at follow up in the intervention group (p<0.01). Median UIC and iodine content of salt did not differ between the 2 groups at follow up (p=0.30 and p=0.40 respectively) | 3 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | importance of iodine and use of iodised salt<br><br>Time points: second (30-60 min) and third (20-30 min) pregnancy trimesters | | | |
| Prieto *et al*, 2011 | Cluster randomised, controlled multicentre trial<br><br>Inclusion criteria: pregnant women over 17 years old<br><br>Exclusion criteria: Pregnant women in the second or third trimester of gestation; diagnosed thyroid disease, pregnant women without a telephone, communication difficulties (cognitive or sensory deterioration, language barrier) | N= 898 | Group education during the first trimester of gestation on healthy hygiene-dietetic habits and the importance of an adequate iodine nutritional status.<br><br>Time points: each trimester of the gestation | Consumption of iodine-rich foods and iodine deficiency | Only protocol – no results published | 0-1 |

## 3.4 Discussion

### 3.4.1 Main findings

After the conduction of the present systematic review, there is noticeably, a lack of studies that have focused on diet and iodine in pregnancy, without looking at supplementation or fortification of salt and other foods (such as bread). With only two studies, in one of which iodine intake was not the primary outcome, it has not been feasible to draw conclusions on the efficacy of these interventions. The study set in Iran, a country with low iodine intake in pregnant women, concluded that the intervention increased KAP scores, but not iodine status. Beyond the large attrition within groups (32% and 42% for control and intervention groups, respectively), iodine status was defined as median UIC of the groups, measured from a single spot urine sample. While collecting 24-hour urine samples or a large number of spot samples from the same subject can be difficult, it is recognised that at least 10 urine samples are required to obtain reliable results and assumptions at individual level (Konig et al., 2011). Spot urine samples, in the meantime, are appropriate iodine status assessment of a population (World Health Organisation et al., 2007). The lack of effect of the intervention over time, in term of iodine status, is therefore not surprising. Spot samples are very unlikely to be representative of the iodine status of these women at individual level, as they highly depend on the recent dietary iodine intake. As renal function changes in pregnancy and clearance increases, adjustment of UIC with creatinine could possibly have corrected for this dilution effect over time (Knudsen et al., 2000).

Defining iodine status is still challenging in individuals. For this reason, a combination of markers and approaches could increase the validity of such study. Dietary assessment of the participants would also have been potentially useful when assessing iodine intake, before and after the intervention to assess any differences in the intake of iodine-rich foods. The questionnaire that was used also focuses on iodised salt only, meaning that much remains unknown in term of knowledge, awareness and practice (e.g. iodine rich foods, use of supplements) in the participating women.

Many trials have focused on the improvement of thyroid health with antithyroid therapies, having measured both maternal and neonatal outcomes (Earl et al., 2010), or micronutrients supplementation (e.g. iron, folic acid, vitamin D) in women, in pregnancy or not, but iodine in those studies has been overlooked.

During the search for the present review, interventions with fish supply in pregnancy were identified (Oken et al., 2013, Rossary et al., 2014). However, these studies focussed mainly on fatty acids, without reporting iodine measurement. There is a potential opportunity, depending on the study design, the available data and samples, to take advantage of these existing studies and measure iodine. However, not all iodine-rich foods are equal with oil-rich fish containing less iodine in comparison to white fish (approximately 48 μg/100 grams in oily fish versus 105 μg/100 grams in white fish) (McCance and Widdowson, 2002).

Dietary choices (of fish and dairy products) are associated with improved iodine status of pregnant women, and thus it is important to focus on iodine-rich foods for improvement of iodine status. In Iceland, a cross-sectional survey in 162 pregnant women found a higher iodine status in women who consumed the recommended minimum of two portions of fish/week and dairy/day (UIC 220 μg/l) in comparison to women who did not meet those levels of intake (UIC 160 μg/l) (Gunnarsdottir et al., 2013). Similar were the findings in adolescent females, in which milk consumption was associated with higher UIC (265 μg/l in tertile 3 in vs 170 μg/l in tertile 1, significantly different in grams of milk intake per day) (Gunnarsdottir et al., 2010). Despite the limitations of the study design and the sufficient iodine status of the examined populations, the importance of dietary choices on iodine intake was evident in these studies, but intervention studies are needed to draw clear conclusions.

One of the three studies (Prieto et al., 2011) was only a published protocol. Based on personal communication with the authors, the intervention was not completed, revealing the difficulties behind pregnancy intervention studies. Similarly, a study in Australia on the effectiveness of iodine supplementation in pregnancy stopped after the funding body withdrew support on the trial (Zhou et al., 2015), as a placebo group was considered inconsistent with the Australian and New Zealand's recommendations for supplementation in pregnancy. While ethical issues arise from placebo-controlled studies in pregnancy, the authors supported that the lack of grounded evidence behind recommendations also poses risks and raises issues of ethical responsibility.

The present review revealed a serious paucity of research examining ways to increase iodine intake through dietary means, highlighting the importance for future research within this area. Interventions with iodine-based supplements and iodised salt can successfully improve the iodine status both of the general population and pregnant women, but salt fortification is unlikely to prevent low intakes in pregnancy and lactation (Fumarola et al., 2008, Isa et al., 2000, Charlton et al., 2012). However, almost 30% of the global households are not covered by salt iodisation (World Health Organisation, 2014), and the concerns over public health risks of this method, by confusing messages about salt, may outweigh its greatest strength of simplicity.

### 3.4.2 Strengths and limitations

The present systematic review identified only three studies that met the inclusion criteria. As one of them was only a protocol of a planned intervention, there was lack of data to quantify the results and continue to a meta-analysis. Quality of the studies was also low to moderate. However, even in this case, the present investigation is useful in identifying this gap in the literature and the need for further research in this field and has all the strengths of a systematic review.

A study protocol was also included in this systematic review. Although the current evidence and guidance regarding using RCTs protocols in systematic reviews is not clear (Boden et al., 2017), we believe that this inclusion provides a more complete overview of the topic and should be encouraged, along with the inclusion of trials from study registries, in order to avoid study bias.

## 3.5 Conclusions

Overall, there is lack of interventional studies that aim to increase the iodine intake of pregnant women by simple dietary guidance, education, increased awareness or provision/repositioning of iodine-rich foods in the diet. RCTs are needed to explore whether the public health concern of iodine insufficiency can be solved with simple dietary guidance and increase of awareness, rather with expensive and time-consuming national public health interventions and legislations. The UK consists an ideal terrain for the investigation of dietary guidance's effectiveness on improving iodine status, due to the lack of recommendations, salt fortification and supplementation with iodine. A synergetic public health approach might be needed to achieve the increase of iodine status in such a population group, due to the high requirements and its importance of sufficiency.

# Chapter 4 - Dietary guidance and recommendation received during pregnancy – a mixed methods study focusing on iodine nutrition

The qualitative part of this Chapter has been published in *Nutrients*

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## Abstract

Iodine is essential for thyroid hormone synthesis and normal neurodevelopment; however, about 60% of pregnant women do not meet the WHO recommended intake.

Using a mixed methods design (qualitative and quantitative), we explored perceptions, awareness and experiences of pregnancy nutrition, focusing on iodine. Women in the perinatal period (n=48) were interviewed and completed a questionnaire, which included a food frequency questionnaire for iodine. Participants were recruited by snowball sampling across the UK, to get a wide representation across various UK regions in order to improve generalisability.

Almost all participants (99%) achieved the recommended 150 μg/day intake for non-pregnant adults, a fact that questions the representativeness of the study sample. However only 81% met the requirement for the increased demands of pregnancy (250 μg/day). Most were unaware of the importance, sources and recommendations for iodine intake. Attitudes to dairy products consumption were positive (e.g. helps with heartburn; easy to increase). Increased fish consumption was considered less achievable, with barriers around taste, smell, heartburn and morning sickness. Community midwives were the main recognised provider of dietary advice. The dietary advice received focused most often on multivitamin supplements rather than food sources. Analysis highlighted a clear theme of commitment to change behaviour, motivated by pregnancy, with desired focus on user-friendly documentation and continued involvement of the health services.

This study highlights the importance of refining current advice about dietary requirements in pregnancy and offers practical suggestions gathered from women in the perinatal period.

## 4.1 Introduction

Iodine is required for synthesis of the thyroid hormones, which play a vital role in normal brain development in fetal and postnatal life. Iodine deficiency (ID) during pregnancy (defined as a median population urinary iodine concentration (UIC) less than 150 μg/l) or neonatal life (<100 μg/l) (World Health Organisation, 2013) is the most preventable cause of brain retardation for the infant (World Health Organisation, 2007). The consequences of ID range from subtle loss of intelligence quotient (IQ) to cretinism. Recent evidence indicates that there is mild iodine insufficiency in several European countries (Finland, Italy, Latvia) with some evidence that this may have adverse consequences for children's cognitive development (e.g. reduced verbal IQ, poorer educational attainment, reduced reading speed) (Bath et al., 2013, Bath and Rayman, 2015). In the United Kingdom (UK) recent data showed that ID is not a concern for the general population (based on measured iodine excretion in spot urine samples) (Roberts et al., 2018), but remains an issue for pregnant and lactating women (Chapter 2).

ID is a global issue (World Health Organisation, 2007), not limited to developing countries or high-altitude areas where endemic cretinism was classically found. Based on the 2017 Iodine Global Network (IGN) global map and scorecard of ID, Europe has a high number of countries where iodine intakes are of concern, including Denmark, Estonia, Finland, Ireland, Italy, Lithuania, and the UK. Women in the UK have been shown, in national and sub-national studies, to be iodine insufficient at population level (Lampropoulou et al., 2012, Kibirige et al., 2004, Vanderpump et al., 2011). The UK Reference Nutrient Intake for adults is 140 μg/day and the recommended level of intake according to the WHO/United Nations Children's Fund (UNICEF)/ IGN is 150 μg/day (World Health Organisation, 2007), which is not met by schoolgirls in the UK (68% below threshold) (Vanderpump et al., 2011). After conception, the WHO recommendation rises to 250 μg/day, which is only met by 40% of pregnant women (Combet et al., 2015). The European Food Safety Authority (EFSA) recently proposed a new reference value for adequate intake for pregnancy (200 μg/day). In the UK, there is no proposed increment for iodine intake during pregnancy and lactation.

Although recommendations focus on daily consumption, adequate status may also be achieved through intermittently greater intakes, to reach an average intake that meets the recommended intake. Iodine is stored in the thyroid (~75% of the total body iodine content of 15-20 mg), and daily usage from the thyroid store is estimated at between 60 and 80 μg in non-pregnant adults (Zimmermann, 2012).

The main dietary sources of iodine in the UK are dairy and seafoods, which together make up 13% of energy intake in adult women (Bates et al., 2016). However, many women avoid these foods and lack knowledge about how to include them in their diet. Including milk in the diet is the factor that contributes most toward iodine status, as found in a Danish study with more than 4500 participants (Rasmussen et al., 2002). Rasmussen et al. (2002) showed that the risk of a low iodine intake is higher in those whose diets do not include at least 0.5 l milk per day and 200 grams of fish per week. Stricter forms of the vegetarian diet, which excludes fish and seafood products consumption, are also associated with higher risk of iodine insufficiency, based on measured urinary iodine excretion (Remer et al., 1999). Although seaweed is an acceptable iodine-rich food for vegetarians, it is not widely consumed, and 25% of vegetarians and 80% of vegans have an insufficient iodine status compared to 9% of non-vegetarians (Combet, 2017, Krajčovičová-Kudláčková et al., 2003). Vegans also have been shown to have a lower urinary iodine excretion compared to vegetarians (78.5 μg/l vs 147 μg/l, $p<0.01$) (Leung et al., 2011a).

The consequences of an iodine insufficient population include personal and societal costs. The absence of prophylactic fortification in the UK, combined with the low knowledge and awareness of iodine nutrition has led to iodine insufficiency becoming a serious public health concern. In a recent meta-analysis, ID children aged 5 years and under had an IQ 6.9 to 10.2 points lower compared to iodine replete children (Bougma et al., 2013). In the Mother and Child Cohort Study (MoBa) study, a recent large prospective cohort study in Norway, children born from mothers who consumed insufficient iodine from foods during pregnancy had significantly higher attention-deficit / hyperactivity disorder symptom scores (Abel et al., 2017). The cost effectiveness of iodine supplementation in pregnancy has been modelled, suggesting a saving of £199 in healthcare costs and £4476 societal costs for an increase of 1.22 IQ points per offspring (Monahan et al., 2015).

There is a sustained debate on the ethical implications of a randomised controlled trial of iodine supplementation in pregnancy, in parallel with concerns over the adverse effects of salt and the conflicted message that salt iodisation would convey (Zhou et al., 2015, He et al., 2016). There are a range of other strategies to tackle iodine insufficiency, including updating dietary recommendations, introducing mandatory salt fortification, and new nutritional education strategies aiming to increase awareness and promote iodine rich foods

(The Lancet Diabetes, 2016, Bouga et al., 2018b). In a UK survey, over half of mothers (55%) could not identify correct sources of iodine, commonly mistaking salt (21%) and vegetables (54%) as iodine-rich foods. Moreover, healthcare professionals could not recognise iodine-rich foods either (Lucas et al., 2014b). Most women (87%) reported willingness to modify their dietary behaviour if they received information related to the importance of iodine in pregnancy (Combet et al., 2015).

To find an effective way to address iodine insufficiency, there is a need to explore the current level of awareness about iodine in pregnancy and related dietary recommendations. Few studies in the UK have explored the level of knowledge and awareness of iodine (Combet et al., 2015, O'Kane et al., 2016) and highlighted the need to understand in-depth the perceptions of women in relation to dietary guidance, the way these are provided and the most endorsed approach for provision of such recommendations.

This mixed methods study is articulated around three main research questions, engaging stakeholders to canvass current perceptions and experiences of dietary guidance and recommendations relating to iodine in pregnancy:

1. What is the current perceived level and quality of dietary guidance received by expectant mothers and new mothers?
2. What are the perceived barriers to increasing or maintaining an adequate intake of dairy and seafood in preconception and during pregnancy / lactation?
3. What would be the most effective delivery of dietary guidance to expectant and new mothers?

## 4.2 Methods

### 4.2.1 Study design and choice of methods

A cross-sectional design was used to explore stakeholders' experiences, views and attitudes. Mixed methods, the combination of qualitative and quantitative approaches, were applied. Participants' perceptions, opinions, beliefs, and attitudes were captured through interviews, either face-to-face or by phone. Topic guides included elements relevant to the Health Belief

Model (Rosenstock, 1990). A food frequency questionnaire (FFQ) (validated for iodine-rich food intake in this section of the population (Combet and Lean, 2014)) was used to explore demographic characteristics, iodine intake and practices related to pregnancy. The combination with the qualitative approach was chosen as it provides a better understanding and allows the exploration of issues that have not been deeply investigated by the existing research (Ritchie et al., 2014). It aims to give voice to people talking about their beliefs and expectations, instead of focusing only on a range of pre-determined questions in semi-quantitative surveys (Braun and Clarke, 2013).

All study documents are listed in Appendix 3.

### 4.2.2 Participants

Recruitment took place from May to December 2015 in a community setting, by snowball sampling. Women were recruited through social media, fora, online advertisement and by word of mouth. Snowball sampling is a non-probability sampling technique, which does not allow representativeness but is used in qualitative studies to identify small groups of participants (Biernacki et al., 1981). Participants were provided with the study information and gave informed consent.

The inclusion criteria were English-speaking women (fluency level sufficient to follow an active conversation), of childbearing age, living in the UK, having a baby (younger than 2 years old), being pregnant or planning to start a family. There were no further restrictions in terms of selection.

### 4.2.3 Questionnaire

Socio-demographic characteristics were recorded in the first part of the questionnaire, including smoking status (those answering “yes” to the question “Are you currently a smoker?” were categorised as smokers), use of medication and self-reported anthropometric measures (pre-pregnancy weight, current weight, height). Education level was categorised as school level (School certificate, standard grade / GCSE, Highers / A levels), college level (HND / HNC, NVQs, other higher education diploma), undergraduate degree (Bachelor degree) and postgraduate degree (Master's degree, PhD). To assess iodine intake with minimal participant burden, we used our previously validated short FFQ which captures the intake frequencies of iodine-rich foods in eight categories (i.e. milk, oil-rich fish, white sea fish, other seafood, cheese (hard and soft), yoghurts, milk or cream-based puddings, cheese-based dishes) (Combet and Lean, 2014). Participants were categorised according to their iodine needs: participants with "increased demands" (250 μg/day, pregnant and breastfeeding) and "basic demands" (normal adult demands, 150 μg/day). Mothers/ mothers-to-be provided quantitative and qualitative data (via questionnaire) relating to their pregnancy/ lactation diet and the changes they have made to it as well as the factors that have influenced their choices. They also provided feedback on the dietary advice received pre, during and post pregnancy, via traditional and non-traditional sources (midwives, healthcare professionals, media, social media). Questions on nutrients' and pregnancy guidelines' awareness, iodine confidence, knowledge of iodine's role and source, and dietary changes during pregnancy (increased, decreased or maintained intake of a list of foods) were also included as part of the questionnaire, as previously described (Combet et al., 2015). Finally, participants were asked about preferred ways of getting informed about nutrition. Multiple choice, 7-point Likert scales and open questions were mainly used.

### 4.2.4 Interviews

All interviews were conducted by the same researcher, either in person or over the phone. Participants were already in possession of the study information sheet and had provided informed consent. Prior to the start of the interview, the overall process was explained again, and participants were notified that interviews would get recorded.

A narrative focussing on current barriers to adequate dairy, seafood and ultimately iodine intake as well as desired content and mode of delivery for dietary guidance / recommendation was obtained through interviews with the recruited participants. Outcome measures were qualitative and analysed using thematic analysis.

Interviews were structured and followed a topic guide based around the Health Belief Model:

1. Form of dietary guidance received before pregnancy/ during pregnancy/ lactation.
2. The role of received dietary guidance in shaping food choices.

3. The perceived recommended levels of intake for iodine in pregnancy.
4. Knowledge on how the recommended intake of 250 μg per day iodine in pregnancy can be met.
5. Barriers and facilitators in meeting an adequate intake of dairy and seafood in preconception and during pregnancy and lactation.
6. Opinions on the best way to deliver dietary recommendations which are understandable and practical, regarding iodine nutrition.

As part of the interview process, participants were given (or sent by post) coloured photos of different foods (dairy products, milk, salt, red meat, sushi, vegetables, fish and seafood) and were asked to name the sources of iodine. They were also provided with pictures of iodine-rich foods portions (a glass of milk, milk in drinks, a portion of cheese, a pot of yoghurt, portions of fish), to estimate a combination that would cover their requirement for iodine in pregnancy. Participants were asked by the researcher to propose a combination of foods and portions (from the pictures they were sent by post/were given) that would cover the iodine needs of a pregnant woman (proposing daily or weekly frequency of foods consumption).

The interview topic guide was pre-tested for clarity and comprehension in a group of women that did not take part in the main study. Validity and reliability were secured in the study during the design of the topic guide, the interviews process and analysis, by following Yardley's (Yardley, 2000) principles for assessment of qualitative research (i.e. sensitivity to context, commitment and rigour, transparency and coherence, impact and importance). In every step of the study, the authors followed the criteria of quality assessment, from the level of design to the level of data presentation.

Interviews were completed after reaching saturation in the upcoming themes. Interviews stopped when lack of novel contributions was evident; the data collected were transcribed verbatim. Transcripts were reviewed by two researchers; after agreement that data saturation was reached, study recruitment closed.

### 4.2.5 Data analysis and statistics

All quantitative data from the socio-demographics and FFQ questionnaires were entered in an SPSS database. Descriptive statistics were calculated. Parametric data were described as mean and standard deviation (SD) and non-parametric as median and interquartile range (IQR). The FFQ data were analysed according to Combet and Lean (Combet and Lean, 2014). The statistical software SPSS version 21.0 (IBM Corporation, New York, NY, USA) was used.

All interviews were audio-recorded, transcribed verbatim and analysed with thematic analysis by following the four stages of the analysis: familiarisation with transcripts and data, generation of initial codes, searching for themes and reviewing themes. NVivo version 11 (QSR International) was used in the analysis.

## 4.3 Results

### 4.3.1 Participants' characteristics and awareness of iodine importance

Only women meeting all inclusion criteria were recruited in the study. A total of 54 women were recruited in the study, of whom 6 failed to complete the interviews and the short questionnaire, resulting in 48 women providing data. At the time of their participation 38% were pregnant, 35% were breastfeeding, 10% were planning to start a family or were actively trying to conceive and 17% had a baby or a toddler (younger than 2 years old) but were not breastfeeding. A minority were following a vegetarian diet (8%, n=4), and 17% had BMI $>30kg/m^2$. All participants' characteristics are shown in Table 4.1. Out of the 48 interviews, 40 were phone and 8 face-to-face interviews with an average duration of 10:46 min (range 06:33 – 18:06 min).

## 4.3.2 Quantitative results

### *4.3.2.1 Received dietary guidance and awareness*

In this study (n=42), most (88%) of the participants reported an interest in pregnancy and lactation nutrition and in a 7-point Likert scale 29% (n=14) reported being aware of dietary and lifestyle guidelines specific for pregnancy and lactation (mode 7). Awareness of specific pregnancy recommendations is displayed in Table 4.2. More than half of the participants (52%, n=25) reported being aware of all 9 recommendations and found them mostly easy to understand (88%, n=42) and to follow (73%, n=35). Preferred sources of information included the internet (69%, n=33), followed by written advice (60%, n=29) and verbal advice (54%, n=26) information from a healthcare professional (HCP) (doctor, nurse or midwife), family or friends (46%, n=22), books or magazines (35%, n=17) antenatal classes (17%, n=8) and other sources (21%, n=10) which were mainly related to education, profession and personal general knowledge.

Table 4.1 Participants' characteristics

| **Demographic data** | **Mean** | **SD** |
|---|---|---|
| Maternal Age (years) n=48 | 30.8 | 4.3 |
| Pregnant n=18 | 31.6 | 3.5 |
| Breastfeeding / with baby n=25 | 31.0 | 4.7 |
| Planning a pregnancy n=5 | 27.2 | 3.0 |
| Child Age (weeks) n=23 | 39.7 | 24.5 |
| | **Median** | **IQR** |
| Maternal BMI (kg/m$^2$)[1] | 24 | 21-29 |
| % WHO iodine recommendation achieved | | |
| Increased demands (250 µg/day) (n=35) | 81 | 56-122 |
| Basic demands (150 µg/day) (n=13) | 99 | 57-134 |
| Total daily iodine intake (µg/day) | | |
| Increased demands (n=35) | 203 | 140-304 |
| Basic demands (n=13) | 148 | 85-202 |
| Ethnicity | **n** | ***%*** |
| White Scottish | 16 | *33* |
| Other White British | 26 | *54* |
| Other ethnic groups | 6 | *13* |
| Residence | | |
| Scotland | 27 | *56* |
| England, Wales, Northern Ireland | 21 | *44* |
| Education | | |
| School level | 3 | *6* |
| College level | 6 | *13* |
| Undergraduate degree | 24 | *50* |
| Postgraduate degree | 14 | *29* |
| Number of children | | |
| 0 (or expecting first) | 15 | *31* |
| 1 | 27 | *56* |
| 2 or more | 6 | *13* |
| Use of supplements | | |
| Iodised | 17 | *35* |
| Non-iodised | 12 | *25* |
| *Increased demands (n=35)* | | |
| Iodised | 16 | *67* |
| Non-iodised | 8 | *33* |
| *Basic demands (n=13)* | | |
| Iodised | 1 | *20* |
| Non-iodised | 4 | *80* |
| Smokers | 1 | *2* |
| Aware about iodine[2] | 11 | *23* |
| Low iodine confidence (1-3 points)[3] | 34 | *72* |

[1.] For pregnant women the BMI has been calculated based on the pre-pregnancy weight reported by the participants. [2.] Iodine awareness was defined as positive when the answer to the question "When it comes to healthy eating in pregnancy and lactation, have you heard of, or were you informed about iodine" was "yes". [3.] Iodine confidence referred to confidence on how to achieve an adequate iodine intake in pregnancy and lactation and was measured with a 7-point Likert scale (1: very low confidence – 7: very high confidence).

Table 4.2 Awareness and compliance to specific recommendations for pregnancy / lactation nutrition (n=48)

| | **Awareness** | | **Following** | |
|---|---|---|---|---|
| | **n** | *%* | **n** | *%* |
| Stop smoking | 46 | *96* | 33 | *75* |
| Stop or limit alcohol | 47 | *98* | 39 | *91* |
| Limit caffeine | 45 | *94* | 39 | *91* |
| Limit vitamin A intake | 34 | *71* | 25 | *58* |
| Avoid certain foods due to bacterial infection risk | 47 | *98* | 38 | *88* |
| Avoid certain fish due to toxins | 41 | *85* | 29 | *67* |
| Limit oily fish to two portions per week | 31 | *65* | 23 | *54* |
| Avoid raw meat, fish or poultry | 44 | *92* | 37 | *86* |
| Wash all fruit and vegetables before consumption | 43 | *90* | 30 | *70* |

Participants' awareness of iodine was poor. Only 23% (n=11) had heard about iodine, lower than for other nutrients: folic acid 100% (n=48), iron 92% (n=44), calcium 85% (n=41), vitamin D 75% (n=36) and vitamin A 63% (n=30). Correspondingly, only 25% (n=12) were aware of the role of the nutrient iodine in the development of the unborn baby. Confidence on how to achieve adequate iodine intake during pregnancy was low (score 1, 2 or 3 in a 7-point Likert scale) in 72% (n=34) of the participants (mode=1).

Exploration of iodine knowledge also included asking participants which foods (amongst potatoes, oil-rich fish, white fish, milk, yoghurts, eggs, table salt, wheat, bread, dark green vegetables) are rich sources of iodine. Oil-rich fish was identified by 71% (n=34) of the participants as an iodine rich source, white fish and yoghurts by 40% (n=19), milk by 56% (n=27), and eggs by 31% (n=15). The most commonly mistaken source was table salt which was wrongly reported as an iodine source from almost 20% (n=9) of the participants. The mode was finding three correct iodine sources out of the 5.

#### *4.3.2.2 Dietary choices*

This section of the questionnaire was only answered by women that were pregnant at the time of the study or had already had a baby /toddler, as it referred to their choices during pregnancy. In a 7-point Likert scale (1 not at all, 7 very much), women were asked to rate how much they feel they changed their diet during pregnancy, mode was 5. Table 4.3 shows the pattern of participants' diet during pregnancy. Most diet components' consumption remained the same, with some people decreasing them and a few more increasing them. However, those components which more women increased were milk (40%, n=18), fruits (56%, n=25) and vegetables (36%, n=16). Women's main reasons for elimination of a food from their diet were taste / smell (39%, n=17), specific recommendations (36%, n=16), morning sickness (34%, n=15), heartburn (18%, n=8), uncertainty of being harmful (18%, n=8), time (5%, n=2), cost (2%, n=1) and other reasons (18%, n=8), which mainly included health conditions and family preferences. Table 4.2 shows which recommendations were followed during pregnancy from the study participants. The mode was following 7 out of 9 recommendations. The parameters that influence participants' choices were also examined and the predominant was the internet, which influenced 64% (n=28) of the respondents, followed by written information from a HCP (59%, n=26), talking to HCP (50%, n=22), books or magazines (41%, n=18), family or friends (46%, n=20) and antenatal classes (18%, n=8).

Table 4.3 Pattern of changes in pregnancy diet

| | **Reduced** | | **Maintained** | | **Increased** | |
|---|---|---|---|---|---|---|
| | **n** | ***%*** | **n** | ***%*** | **n** | ***%*** |
| Yoghurts | 3 | *7* | 31 | *69* | 11 | *24* |
| Milk | 1 | *2* | 26 | *58* | 18 | *40* |
| Cheese & spreads | 7 | *16* | 25 | *56* | 13 | *29* |
| Cheese-based dishes | 5 | *11* | 33 | *73* | 7 | *16* |
| Milk based puddings | 7 | *16* | 32 | *71* | 6 | *14* |
| White fish | 5 | *11* | 33 | *73* | 7 | *16* |
| Oil-rich fish | 8 | *18* | 30 | *67* | 7 | *16* |
| Seafood other than fish | 10 | *22* | 32 | *71* | 3 | *7* |
| Eggs | 4 | *9* | 29 | *64* | 12 | *27* |
| Meat | 6 | *13* | 30 | *67* | 9 | *20* |
| Bread, rice, cereals, pasta | 2 | *4* | 30 | *67* | 13 | *29* |
| Soya products | 4 | *9* | 38 | *84* | 3 | *7* |
| Brassicas | 3 | *7* | 32 | *71* | 10 | *22* |
| Other vegetables | 3 | *7* | 26 | *58* | 16 | *36* |
| Fruits | 3 | *7* | 17 | *35* | 25 | *56* |

When reading / receiving information about diet and nutrition, 87% (n=41) of the women prefer information focusing on both foods and specific elements (e.g. vitamins, fat, proteins etc.), whereas 9% (n=4) prefer foods only and 4% (n=2) specific elements only. In cases where women receive information focussing on specific food elements, 76% (n=35) only know sometimes how to relate this to foods and how to modify their diet, with only 20% (n=9) being confident that they always do.

Finally, 55% (n=26) of the women used some resource in particular to gain information regarding diet around the time of conception, pregnancy and breastfeeding, which were mainly the internet (general websites, healthcare services website, social media), books and advice from the HCPs.

#### *4.3.2.3 Iodine intake*

Out of the 48 participants, 73% (n=35) had increased daily iodine demands according to WHO/UNICEF/IGN and EFSA as they were pregnant or breastfeeding. Table 4.4 shows the median iodine intakes in those with basic or increased demands and the contributions of a range of food sources, as well as the proportion of the WHO/UNICEF/IGN recommended intake achieved in each group, through diet and supplements. Figure 4.1 shows the contribution of milk, other dairy products, fish and supplements on the total daily iodine intake of women, depending on their needs.

Table 4.4 Iodine and iodine-rich foods intake in participants with increased demands (250 μg/day, pregnant and breastfeeding) and normal adult demands (150 μg/day).

| | **Increased demands (n=35)** | | **Basic demands (n=13)** | |
|---|---|---|---|---|
| | **Median** | **IQR** | **Median** | **IQR** |
| Milk (g/day) | 200 | 100-500 | 113 | 11-270 |
| Other dairy (g/day)[1] | 119 | 86-192 | 106 | 80-233 |
| Fish (g/day) | 39 | 9-65 | 43 | 0-101 |
| Total daily iodine from dairy (μg/day) | 120 | 90-185 | 121 | 62-146 |
| Total daily iodine from milk (μg/day) | 54 | 27-136 | 31 | 3-73 |
| Total daily iodine from fish (μg/day) | 21 | 8-31 | 29 | 0-53 |
| % daily iodine from dairy | 83 | 75-97 | 77 | 68-99 |
| % daily iodine from milk | 45 | 23-54 | 24 | 5-47 |
| % daily iodine from fish | 16 | 3-24 | 22 | 0-32 |
| Total daily iodine from food (μg/day) | 152 | 120-199 | 148 | 85-202 |
| Total daily iodine with supplements (μg/day) – whole sample | 203 | 140-304 | 148 | 85-202 |
| Total daily iodine with supplements (μg/day) only in those taking supplement | 299 [2] | 215-233 | 550 [3] | 550-550 |
| % WHO recommendation achieved | 81 | 56-122 | 99 | 57-134 |

[1].Other dairy includes all dairy products listed in the FFQ excluding milk (i.e. cheese (hard and soft), yoghurts, milk/cream-based puddings, cheese-based dishes). [2] n=16, [3] n=1

Dietary change in pregnancy varied among participants, with up to 16% reporting to decrease at least one type of dairy product, 22% reporting to cut-out a type of fish or seafood product, while 40% and 16% reported increasing dairy or fish / seafood, respectively.

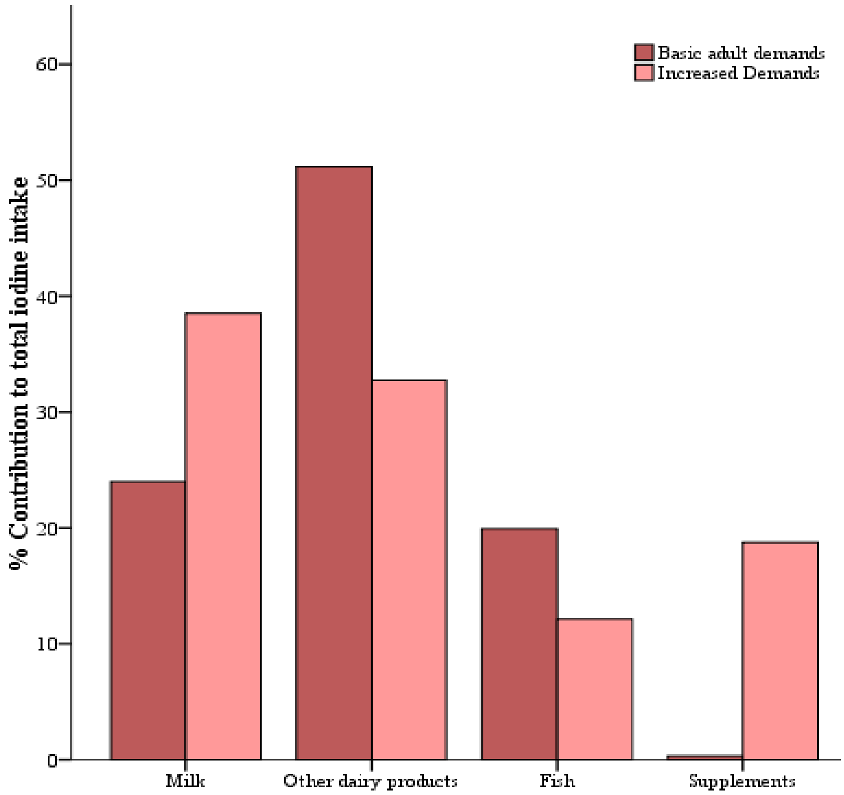


Figure 4.1 Percentage of contribution of food categories and supplements on total daily iodine intake for women with basic adult needs and women with increased needs.

### 4.3.3 Qualitative results

Five main themes emerged from the analysis of the 48 interviews, summarised in Figure 4.2 with associated subthemes and their inter-relationships. The first theme included views about information received during the periods of preconception and pregnancy and focused on sources, content and form of information, as well as perceived problems related to this information and attitudes of participants towards this advice. The second theme focused on the level of participants' iodine knowledge as a nutrient and the recommendations for pregnancy. The third theme was around the exploration of the acceptance of iodine sources and any barriers related to their intake. The fourth theme included views on preferred ways of dietary information delivery in the perinatal period of life. In parallel, the emotional dimension of receiving nutritional guidance in pregnancy emerged throughout the interviews.

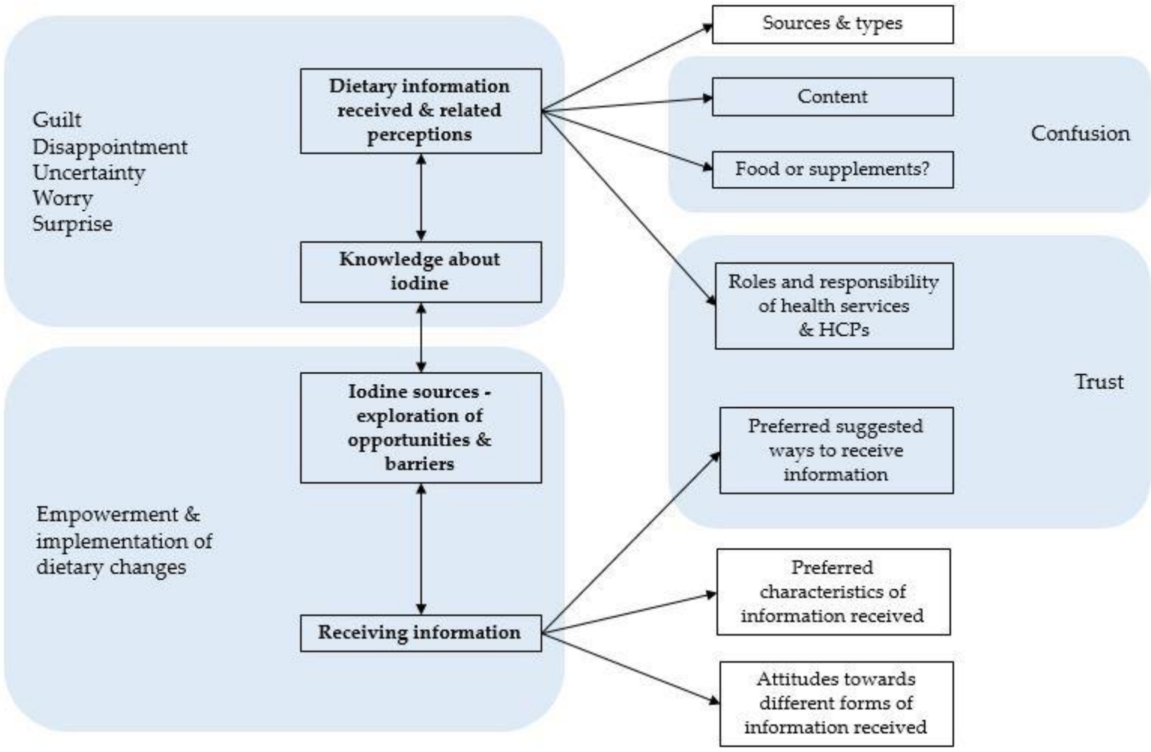


Figure 4.2 Themes and main subthemes of the analysis and their relationships.
HCPs: healthcare professionals

### *4.3.3.1 Dietary information received and related perceptions*

*Sources and form of received dietary information*

There were differences in the type of informational support that participants had received in pregnancy nutrition, by case and between UK regions. Most had received written guidance (leaflets/ booklets) from community midwives, mainly during the first antenatal care appointment (IT39: "*It was really only some leaflets that I was given by the midwife. I don't think she actually talked to me through or anything, it was just literature she handed over.*"). Those living in Scotland mentioned the "Ready Steady Baby" as a source of information about pregnancy nutrition either as a book, a website or an application. No similar resource was mentioned by participants from other geographical areas.

Verbal information was seldom commented on (IT14: "*My midwife on my first appointment asked whether I was aware [about dietary guidelines for pregnancy], I said I was generally aware but then she gave me general points.*"). Short discussions with the midwives regarding nutrition were less frequent and included mainly a brief summary of the written information, mostly after participants' personal enquiry (IT05: "*It was I who brought it up with my midwife on one of the first visits. I had a couple of questions about how cheese and various things like that and it was me that actually brought it up with her. She didn't bring it up with me and really she answered a couple of questions but then told me to refer to this folder I've been given.*"). Apart from the community midwives, who were mostly providing nutrition-related advice, general practitioners were also mentioned in providing verbal guidance, as well as friends and family. A quarter of the participants said that no one has spoken to them about nutrition in pregnancy. Participants interested in learning more about nutrition, including those that have received some form of information, did personal research, either online or using books.

*Nutrition information content*

Pregnancy nutrition-related information fell under three themes: eating a healthy balanced diet, avoiding certain foods and taking folic acid and/or other multivitamin supplements. Most participants could not remember or list specific received nutrition information, and when they could, it was mainly about i) avoiding uncooked and unpasteurised foods, alcohol, caffeine, and ii) taking supplements. Lack of information regarding diet during lactation was also reported.

Around half of the participants highlighted how the information received during pregnancy was mainly related to the foods and other things to avoid (e.g. smoking, alcohol, raw fish and meat, vitamin A, certain types of cheese) rather than foods to increase or maintain in their diet (IT21: "*It was more about what you couldn't eat though than what you should eat. It was more about avoiding things like caffeine and certain types of food rather than what was the best to eat.*"). A part of the participants who reported having received information on what should be eaten during pregnancy believed that messages regarding foods to avoid were most powerful.

Multiparous participants reported having received less information in subsequent pregnancies compared to their first one, as prior knowledge was assumed (IT42: "*I think I didn't receive a lot this time round, because this is my second pregnancy I think they kind of assumed I that I knew it from before.*").

*Foods or supplements?*

A minor theme focused on multivitamins and folic acid with little information or knowledge on the foods that contain the required micronutrients (IT15: "*When I was told in the beginning from my midwife you shouldn't have too much vitamin A, nothing was really explained why and I am still not really clear what foods vitamin A is in, how I should avoid vitamin A.*"). Many participants reported knowing that they should be taking supplements during pregnancy (mainly folic acid, vitamin D or a multivitamin), having received this advice from their midwife, without information about food sources of the nutrient. A suggestion made was that iodine should be included to pregnancy supplements to cover needs, especially for those who do not know how to eat a balanced diet. Worryingly, some participants taking multivitamins felt confident that needs are covered, justifying not paying attention to their diet (IT42: "*Since I became pregnant I've just been taking a multivitamin designed for pregnancy, so I am hoping that kind of covers most things.*"). Only one participant reported that she forgot her supplements and was not taking them regularly, so found food recommendations easier to implement.

*Role and responsibility of health services and healthcare professionals*

Participants usually referred to the health services (including the midwife, the general practitioner, the obstetrician, the health services literature, tools and services) for guidance during pregnancy. There was high expectation that the health services would provide all the required dietary information during the first (booking) appointment or an earlier appointment, through verbal discussions, leaflets, booklets and referrals to online sources, websites and applications. Most participants received this at their first antenatal care appointment with the community midwife (around 8-12 weeks of pregnancy). Midwives were recognised to have experience in the field of pregnancy nutrition and were usually the first port of call when pregnant women were unsure about their diet (IT37: "*I trust very much* *what the midwife has to say in terms of my nutrition regarding my pregnancy, because they are quite experienced in that field.*"). However, expectations were not always met, as described below (see 4.3.3.5 "Trust").

#### *4.3.3.2 Knowledge about iodine*

Iodine was an unknown nutrient for most participants, with a minority linking it to infant brain development (through personal interest, reading or research, and seldom through their community midwife). Knowledge of the relation between iodine nutrition and the thyroid hormones was limited, without any deeper specific knowledge of its importance in pregnancy.

Most participants admitted not knowing the dietary sources of iodine and attempted to guess the correct iodine-rich foods from a selection of foods depicted. Most answers were chosen randomly and were often incorrect. Only a minority identified the iodine-rich foods being dairy and seafood products.

Participants were also asked to estimate the food combination that would cover requirements for iodine in pregnancy, using pictures with portions of iodine-rich foods (a glass of milk, milk in drinks such as tea, chocolate or coffee, a portion of cheese, a pot of yoghurt, a portion of white fish and a portion of salmon). Most food combinations proposed would not have provided a sufficient iodine intake for pregnancy and lactation. The exercise triggered surprise and hesitation in the participants (evident through their expressions, pauses and frequent change of answers).

#### *4.3.3.3 Iodine sources - opportunities and barriers*

Attitude towards dairy products were generally positive as half of the participants reported finding it quite easy to include or increase dairy in the diet in substantial amounts if necessary. Milk was believed to alleviate heartburn symptoms and was often craved during pregnancy (IT25: "*Milk, I probably, I had quite a lot of milk when I was pregnant, a lot of it was because of heartburn but I would say I could drink a lot of milk*."). In cases of dislike, participants still tried to increase dairy consumption via yogurts and/ or cheese (IT36: "*I do not drink milk but I do take a lot of cheese and yoghurts*."). The main barriers towards dairy consumption included taste (mainly of milk), lactose intolerance or other health conditions believed to be associated with dairy products (such as eczema), morning sickness in the first months of pregnancy and perceptions about unhealthfulness of cheese in products (fat, processed foods) (IT33: "*I think with cheese I try not to each too much because I think it is quite fat…*").

Fish and seafood consumption was perceived as harder to increase or maintain during pregnancy. Less than a fifth reported finding this easy and the barriers were further explored. For most, the main barrier was general dislike of fish and seafood products. During pregnancy, this was exacerbated by heartburn, morning sickness and change in taste and smell. Another major cause of fish exclusion was partners' and familial preferences as well as lack of cooking skills and low knowledge (IT30: "*Well, I don't eat a lot of fish probably because my husband doesn't enjoy it and I don't like to cook more than one meal at once.*"; IT09: "*People probably don't have as much knowledge on how to cook fish"*). However, even for participants with high intention to consume fish and seafood, confusion regarding the recommendations, compounded by the worry of eating the wrong fish species prevented the consumption of any fish and seafood type. Cost implications, low availability and habit of not buying or eating these products regularly were also described barriers (IT42: "*We are not in a habit of eating a lot of fish and that's one of the things we often say to ourselves we should have a little bit more of...*"). Vegetarians did not generally intend to change habits by including fish in their diet during pregnancy.

#### *4.3.3.4 Receiving dietary information*

*Receiving dietary information - attitudes towards different formats*

The majority of views around verbal information were positive, with only a couple of participants stating not finding a discussion helpful regarding something important about pregnancy (IT48: "*If I was to go to the doctors and ask for advice there I don't think that would be as beneficial because […] I feel it would be quite overwhelming […] so if the midwife mentioned something to me I would remember but wouldn't really know too much about it so I would have to go and look into it for myself*"). During discussions with midwives, the participants recalled the opportunity to ask questions and get more in-depth knowledge regarding the importance of the advice received, even when the discussion was short. Discussion with an expert was proposed as more useful if accompanied by a leaflet, booklet or another visual source to refer to later, as a reminder and prompt. However, it was agreed by most that such discussions rarely happen, with leaflets usually given without going through them verbally (IT05: "*So for me, the best thing for me would have been if the midwife had given me a brief overview and then maybe given me a leaflet or a web, specific web address to take away that I could then look into more depth afterwards*").

A common theme that emerged was also around the written information received, especially leaflets and booklets. Leaflets were read by many participants, but too many were received during pregnancy and subsequently lost, thrown out or misplaced when required (IT48: "*I was also given information in leaflet form but during pregnancy the amount of leaflets you get is unbelievable so you don't really pay attention, well I don't really pay attention to a lot of the hand out stuff I was given*."). However, participants self-characterised as "old school" find written information in form of bright, colourful leaflets with pictures that catch the attention, mainly given from the midwife or combined with verbal advice, a good and practical way of receiving information about pregnancy, diet and specific nutrients. The information expected to appear on leaflets should be "clear", "specific", "comprehensive" and "straight forward". Leaflets were perceived as useful to remind participants about a key piece of information, more practical, smaller and easier to read compared to books. If the leaflets were not brightly designed, participants mentioned forgetting them or not reading them (IT22: "*Basically kind of brightly designed or whatever, I would definitely pay attention to*.").

Most participants (who were often highly educated) referred to the internet as a source of information in pregnancy. Participants admitted using simple "Google" searches to obtain information about nutrition and pregnancy, and combining information from several online sources, including several websites, BabyCentre (BabyCentre® L.L.C., New York, NY, USA) and healthcare services websites, fora, social media and weekly emails with leaflets, booklets and verbal advice. However, the use of social media and other online sources is not always reliable, and often prompted by excitement about the new pregnancy and the intention to do everything right (IT05: "*These days obviously everybody goes straight on the internet, and that's what was one of the first things that I did, but the problem I think with that is that you google various phrases and it's more luck than judgement which websites you come up on.*"; IT02: "*Well the first thing I do is look on the internet, but then you cannot really rely on that.*"). Participants preferred the internet when looking for information, but recognised that a reliable source, complete with all the required information and presented by an expert is needed (IT30: "*I like to look online and read things of a reliable source. I* *might use the NHS website or something similar rather than a forum. But you need to know to look, that's the problem.*"). The combination with other sources (leaflets, discussions) was also perceived as an effective way of getting information, as well as the weekly emails that healthcare services or other reliable sources send to pregnant women (IT37: "*The emails from the NHS, once you are registered for your pregnancy are really good because you get an email like once a week or something like that […] they are really helpful.*").

Mobile applications were considered an interactive way of dealing with nutritional requirements and increasing knowledge and awareness about specific dietary needs. For many participants, an application on a smartphone would be useful, easy and innovative if they needed to get informed about a nutrient (e.g. iodine) and try to increase it on their diet. As technology is progressing and smartphones and tablets are becoming mainstream, especially in young women, participants suggested mobile applications during pregnancy and lactation to meet an information gap related to healthy eating, supplements reminder, fitness tips, and information about fetus development. Participants proposed that if the information relating to the importance of a nutrient was integrated with one of these mobile applications, or if a new specific mobile application could be developed, that would be useful, easy and practical, especially if endorsed by the doctor or the midwife (IT25: "*You can get apps now for everything, so maybe an app that you could give out like different ideas on how you can get that nutrient you need in the right amount, maybe like meal ideas or something like that*."; IT05: "*The best thing for me would have been if the midwife had given me a brief overview and then maybe given me a leaflet or a web, specific web address to take away that I could then look into more depth afterwards*."). Tracking dietary intake by adding or ticking a checklist of foods commonly consumed daily via a mobile application was highlighted, with a view to tailor advice on dietary needs, directions on what to consume to increase intake of a specific nutrient. A minority disagreed with the use of mobile applications, which they found overwhelming and burdensome (search, download, usage), preferring information from a booklet, a leaflet or a conversation with their midwife instead (IT08: "*I found the most useful just conversation really I suppose rather than apps and research cause that's how I think you can get a bit overwhelming for pregnant mums and for first time pregnant mums*.").

*Receiving dietary information - preferred formats and stakeholders' suggestions*

Half of the participants interviewed stated that the information should be easier, quicker, clearer, more practical, basic, straight forward and easy to remember and understand. They expressed the view that if the information was presented in a more visual, bright and colourful way, including pictures or easy infographics, charts and associations of nutrients with foods and portion sizes, it would stand to attention and be more likely to be remembered.

While understanding which nutrients are important in pregnancy, a gap was identified regarding portion size, and the quantity of food required to obtain the correct amount of a nutrient (IT42: "*I think having something visual that kind of shows you clearly what, like what the portions equate to is really helpful*"). While some participants were confident about the nutrients of importance in pregnancy, they were unable to translate dietary requirements to a balanced meal. There was specific uncertainty on where to get nutrients from the diet, which and how much food, and the impact of different cooking methods.

Participants were asked what they consider the best way to convey or receive information about a specific nutrient. A clear majority believed that the healthcare services were best placed to deliver this advice. The midwife, general practitioner, other healthcare professionals (health visitors, nurses, and pharmacists), dieticians and nutritionists were in most cases considered as the best sources of nutrition information. A face-to-face discussion, early in pregnancy or at the first booking appointment, or even in an antenatal class, was often suggested. Many participants proposed that a combination of this discussion alongside written and/or online information (a leaflet, a website) would be ideal – providing the choice to return to that information later for reference. The healthcare services website and emails were also suggested, as well as the internet in general (other websites, Google search, social media, fora).

For practical advice on how to increase iodine intake, some participants reported that advice from their midwife or doctor, in combination potentially with a reference to a website, a leaflet or a booklet would be sufficient. For others, knowledge of key nutritional focus points was also enough – with the future health of their child an incentive to take the required steps to initiate change. Many other ideas were discussed, including iodised supplements use, iodised salt consumption, a tick sheet or a pin board with reminders for main foods, portions and importance of iodine, internet websites, recipes or meal plans online and in books, fridge magnets and small reference cards, supermarket magazines, advertisements, food packaging information and the use of a mobile application with relevant information. Understanding the portion sizes and the iodine content of the foods was considered important to manage an increased need in iodine during pregnancy.

When thinking innovatively, participants proposed different tools that could be designed to deliver information regarding iodine, nutrition and pregnancy. Approximately half of the participants preferred a mobile application for their smartphone or tablet, accessible at all time to track dietary intake and get reminders when to adapt their diet. Mobile application tailored meal plans were also suggested, as well as improved knowledge on portion sizes, recommended intakes and needs; a comparator was mobile applications focussing on weight management. Visual prompts were identified as important for those with low literacy. Others preferred an easy, pictorial based and quick to refer to tool. Recipes, meal plans ideas, pictorial-based bright leaflets and association of foods and portions with nutritional requirements were described as desirable ways of delivering information. Other proposals included TV programmes and advertisements, public health campaigns, weekly healthcare services emails and infographics. A minority still supported a one-to-one discussion with their midwife or doctor and a referral to a reliable website, booklet or leaflet, as sufficient sources of information.

#### *4.3.3.5 Emotional dimensions of receiving dietary advice and information*

*Confusion*

Confusion about the information received was often observed. Participants reported finding different pregnancy recommendations between the UK and other countries, getting different advice between different UK areas and receiving conflicting information from different healthcare professionals (IT09: "*And then a different midwife had a completely different attitude*."). The lack of a single reference place with comprehensive information about all nutrients was also reported (IT26: "*They should tell you exactly what you need to have, you need to have a leaflet or like a website… It should be clearer, now it is not clear at all.*"). Some recommendations were perceived as difficult to understand and implement in term of know-how (e.g. vitamin A content of foods, recognising unpasteurised products), and overwhelming in the context of all other dietary recommendations available.

*Empowerment - implementation of dietary changes*

Analysis highlighted a theme of clear commitment to change behaviour if prompted or made aware (IT06: "*If I knew how important it was, I would increase it.*"). Almost half of the participants highlighted the fact that if they had the knowledge, the information and the awareness about the importance of a factor during their pregnancy (in this case mainly referring to increasing their iodine intake) they would make a conscious effort to change behaviour or practice. The intention was already high, even from the period of preconception, as participants believed that those at that stage of life want the best for their baby and themselves. Proactivity was also evident in many cases, as nutrition was a topic often brought up by participants to their midwives. Participants asked questions and ended-up looking online for advice when they did not get the level of advice they required or expected. All participants reported having read or considered the information given to them, with the majority stating that they adjusted their diet (with a minority not changing habits through belief of already achieving a balanced diet). To feel confident of meeting all nutrients' recommended intake, multivitamin supplements were frequently adopted.

*Trust*

A trustful source of information was very important for most participants. A clear theme of trust emerged towards the health services and the healthcare professionals. The health services were very often mentioned during the interviews and were considered as the norm for the provision of trustful dietary and pregnancy advice. The most trustful and suitable advisors were "an expert", "the midwife" and "the general practitioner/ doctor" as well as the staff running antenatal classes (IT47: "*I think probably is verbally so that we could ask questions rather than just written information, and maybe not necessarily one to one but along with those pre-antenatal type classes.*"). However, although initial attitudes expressed towards the health services were high expectations and trust, they were followed by disappointment regarding the actual amount of advice received. Similar feelings arose towards the general practitioner surgeries that did not provide nutrition information, which had been an expectation from several participants.

The internet and smartphone applications were considered useful sources of information, but the issue of source reliability emerged. As a result, the healthcare services website or websites proposed by experts were the online sources that participants trusted most. Moreover, the health services application and the BabyCentre application (BabyCentre® L.L.C., New York, NY, USA) were widely used as reliable sources.

*Negative feelings*

Pregnancy is a stage of life when the fetus depends totally on its mother for the supply of nutrients - a fact appreciated by most participants. For this reason, participants were usually positive in making dietary and lifestyle changes (as mentioned above in "*Empowerment - implementation of dietary changes*"), but at the same time this responsibility triggered negative feelings. Apart from the disappointment mentioned above, uncertainty regarding the dietary recommendations was expressed. This triggered, in some cases, worry and lack of confidence on adequate adherence to guidance (example of fish recommendations, as mentioned in 4.3.3.3.)

Towards the end of the interview, the importance of iodine for fetal development, and the richest dietary sources of iodine were presented to the participants, alongside an indicative food combination selected to achieve the pregnancy daily recommended iodine intake. Some participants expressed surprise and disappointment at that point, and questioned why iodine had not been mentioned to them in peri-natal care. Worry and stress were also apparent through tone of voice and expressions, when participants realised the importance of iodine and were unsure whether needs had been covered (IT27: "*There is not enough guidance. As I say I felt I am quite surprised, even a little bit disappointed I didn't know how important iodine, how important the role is it plays in the fetal development.*"). In a couple of cases, participants reported feeling overwhelmed and under pressure to follow the pregnancy recommendations, resulting in guilt for not "getting everything right" (IT08: "*That put a lot of pressure and a lot of guilt on me, but the second time round I decided to be a bit more relaxed and trust my body a bit more.*").

## 4.4 Discussion

### 4.4.1 Main findings

ID is a global public health concern, with the latest IGN data highlighting the general populations in as many as 20 countries, and the pregnant populations of as many as 39 countries being mildly to severely deficient (IDD Newsletter, 2017a). Correcting ID is especially important in high-risk groups, such as pregnant women and their infants. To achieve this, it is essential to understand the underlying causes of ID, and the understanding of iodine nutrition by the populations concerned (Bouga et al., 2018b).

We explored the lack of iodine awareness and knowledge in pregnancy and the dietary and nutrition information received in and around pregnancy, to identify potential ways to improve information delivery at that stage of life. After an in-depth discussion with stakeholders, around the themes of dietary advice received in pregnancy, preferred ways of information delivery, and the knowledge and awareness of iodine nutrition, we identified gaps related to dietary advice in pregnancy and the way it is provided. Our results support and strengthen the previous finding that awareness and knowledge are low amongst pregnant women (Combet et al., 2015), even though more pregnant women achieved the WHO recommended iodine intake (World Health Organisation, 2007) in this sample compared to previous results (81% in this study vs 46% in 1$^{st}$ trimester / 40% in 2$^{nd}$ and 3$^{rd}$ trimesters previously (Combet et al., 2015)). Dietary guidance during pregnancy was described as confusing, focusing mostly on foods to avoid, supplements and selected nutrients of interest (not iodine), and was not always perceived as sufficient or helpful enough to trigger effective dietary changes. Participants highlighted the need for clearer recommendations, with clearer focus on foods and portion sizes, but also emphasised their trust in the health services.

### 4.4.2 Barriers to iodine sufficiency

Until recently, the UK was thought to be iodine replete; the inadequate iodine status of the British population was however highlighted in a multi-centre survey of school girls (Vanderpump et al., 2011). The reasons behind the re-emergence of iodine insufficiency are multiple and need to be explored systematically.

Pregnant women depend on community midwives during antenatal care. The health services are the main providers of dietary and lifestyle advice in pregnancy, in agreement with previous findings from Australia (Charlton et al., 2010a). Consequently, dietary guidance starts around the 10th week of pregnancy, possibly too late for addressing the impact of any iodine insufficiency on fetal neurodevelopment, as the myelination process is complete in the first trimester. Our results highlight the role and importance of the health services in the provision of dietary information around pregnancy. Two contrasting feelings – one of trust, the other of disappointment, were apparent in respect to the relationship with the healthcare professionals and the delivery of information on nutrition and iodine. Awareness and knowledge regarding iodine nutrition in pregnancy have been previously found to be low amongst healthcare professionals in the UK (Williamson et al., 2012b) and other countries (de Leo et al., 2016, Guess et al., 2017, Kut et al., 2015, Lucas et al., 2014b, Nithiananthan et al., 2013), and may partially contribute toward the shift from trust to disappointment. The lack of nutrition education that midwives receive is an important area to tackle (Moore et al., 2000, Arrish et al., 2014), while recognising the stresses and burdens experienced by this group of healthcare professionals, especially the restricted time to cover several complex aspects of pregnancy care and related advice.

As healthcare professionals lack nutritional knowledge, the iodine and nutrition information pregnant women receive is limited, fostering poor knowledge and awareness (Combet et al., 2015). We highlighted divergent experiences of receiving dietary guidance in pregnancy (depth and breadth), with variations between healthcare teams, geographical areas, parity, but also personal interest of the pregnant women, previous pregnancy experience and educational background. These findings confirm our previous results, showing that although information on pregnancy guidelines comes from several sources, confusion and uncertainty prevail, under the need of a reference source of reliable information. The way dietary guidance was delivered during pregnancy, and the level of depth covered also varies between UK geographical areas with inconsistencies amongst antenatal care teams, and large influence of the personal interest of the pregnant women, their previous experience of pregnancy and their educational background. As a result, our study highlights a clear need for a trustful, more comprehensive source of dietary advice in pregnancy for women to follow without feeling confused by different conflicting or unclear guidelines.

An important aspect in the landscape of strategies to address iodine insufficiency is the availability and choice of iodine-rich foods (dairy products, fish and seafood, including seaweed, iodised salt) and the potential barriers to their consumption. In this study, a single participant used iodised salt and 60% reported rarely or never using salt at the table – meaning that voluntary fortification is not likely to effectively address iodine insufficiency through consumption of table salt alone, since most sodium is consumed through ready-meals and processed foods. Since the 1970s, the demand for milk and milk products has decreased steadily (Revoredo-Giha, 2013), but barriers to their consumption are often overlooked. In an area without known ID (Sabadell, Catalonia, Spain), the iodine status of 600 pregnant women was found to be inadequate, based on their UIC (104 µg/l). The FFQ results associated milk and supplements intake with 41% and 78% lower risk respectively of having UIC levels below 150 µg/l (Alvarez-Pedrerol et al., 2010). In this study, we highlight the organoleptic (aspects that an individual experiences via the senses) and behavioural dimensions linked to milk and other dairy products avoidance, including taste and smell, and, less often, adherence to a strict vegetarian or vegan diet, or its association with health-related issues (perceived or diagnose lactose intolerance). Other studies which have explored drivers of dairy food choices also identified family members' taste preferences and needs, cost and health benefits (Hammond and Chapman, 2008, Richardson-Harman et al., 2000, Hagy et al., 2000) but also gender, age and socioeconomic status (Ares and Gambaro, 2007). Choice behaviours regarding milk and dairy products in the context of iodine nutrition are compounded by environmental factors: milk iodine concentration is lower in the spring and summer and in organic milk products (Payling et al., 2015, Bath et al., 2012); therefore seasonality and milk type should be taken into consideration when making recommendations and measuring intake (Bath et al., 2011), as milk remains the main source of iodine in the UK (Bates et al., 2016).

Attitudes were generally more negative towards fish and seafood products. Main barriers included general dislike due to taste and smell, followed by family's preferences, lack of cooking skills, cost and availability, in agreement with previous results (Verbeke and Vackier, 2005). However, an important barrier for fish and seafood consumption in pregnancy lay in the confusion in the dietary recommendations in pregnancy, namely restricting the intake of certain fish species due to heavy metals, toxins and bacterial risk. In extreme cases, this confusion and perception of a risk led to total avoidance of fish, despite two portions of fish per week (one of which oil-rich) being advised (Public Health England, 2016). This is consistent with the findings of Bloomingdale *et al.* in Boston, who found that women would rather exclude fish intake in pregnancy than risk harming themselves or their infant's health (Bloomingdale et al., 2010).

Even though dietary information received during pregnancy is plenty, the way this information is delivered is a key factor in facilitating their implementation (including memorisation, understanding, behaviour change). Clear information, with more focus on portion sizes and foods rather than nutrients, are some of the main characteristics desired by participants. With 90% of people aged 16-24 and 87% of those aged 25-34 owning a smartphone in the UK in 2015 (Statista, 2016), technologically-based information delivery should be reinforced. However, the use of technology can alienate minorities (e.g. women of low socioeconomic status, low education, homeless, socially deprived, urban migrant groups) and care should be taken to avoid exclusion of those groups from accessing information, since they are often the groups needing advice the most (Adams, 2000). Although technology usage, broadly, and internet access is increasing, the quality of information available online is often questionable, and quality control is needed (Eysenbach, 2000). The BabyCentre (BabyCentre® L.L.C., New York, NY, USA) website and application, for example, belong to the Johnson & Johnson group, a commercial entity, which participants still trusted despite the lack of affiliation to the health services. Overall, health information technology can be effective for preventive health and increasing adherence to guidelines, but cost-effectiveness data are limited and inconclusive (Chaudhry et al., 2006). In Scotland, a nutrition education intervention in pregnancy was found to be acceptable in 16-18 years old pregnant women, however, with limited effectiveness in term of changing dietary habits (Symon and Wrieden, 2003). There is scope to build on such an intervention to improve iodine status in pregnancy.

### 4.4.3 Strengths and limitations

The present study used a mixed methods design, combining quantitative and qualitative data that strengthen the results, to deeply investigate the topic of iodine nutrition in pregnancy and perceptions on received and desired dietary guidance, which quantitative data alone would not be enough to explore in depth. The choice of qualitative design helped in the deep investigation of the topic of iodine nutrition in pregnancy and perceptions on the way dietary guidance is delivered in the perinatal period of life. This deep understanding of the reasons why iodine insufficiency is present in those life stages is needed to effectively address this public health issue.

This type of study is time-consuming, and thus the relatively small number that could be studied does potentially limit the generalisability of the results, as does the snowball method of recruitment that can result in an unrepresentative sample if participants tended to be amongst friends and colleagues of similar socioeconomic characteristics and thus similar diets. Recruitment took place mainly online, to reach a population across the UK. As a result, women residing in England, Scotland, Wales and Northern Ireland were recruited, increasing the sample's representativeness. The study population is highly educated, with less than 30% of the participants not having a Bachelor's degree or higher. This is in agreement with the national statistics, as the level of education improves with the years and is higher in females of that age (childbearing age) compared to males. The 16 to 24 year olds Not in Education, Employment or Training in 2014-2015 have decreased by three points since 2010-2011, accounting for only 15.3% in females of that age (Department for Education, 2015). Comparing the study population with the British population, the education level is higher but worryingly, even in that educated young population which could also be biased in terms of interest in pregnancy nutrition, the lack of awareness regarding iodine nutrition in pregnancy remains low.

Our sample also did not include a high percentage of obese women with BMI>30 kg/m$^2$ (17% versus 26% prevalence in the UK (NHS Digital, 2017)) or smokers (1% versus 14% of women in the UK (Office for National Statistics and Public Health England, 2017)), and had no drug or alcohol dependent women, but included 13% of non-British women. In more vulnerable groups, it is possible that dietary advice would be supplanted by focus on areas deemed more pressing – such as tobacco or alcohol dependencies. This is a dimension not explored in this study.

Iodine status is difficult to ascertain. The iodine intake was quantified with our previously validated iodine specific FFQ for women of childbearing age (Combet and Lean, 2014), as a suitable way to classify participants based on their habitual intake of micronutrients, giving us the opportunity to know whether the perceptions of the study population would represent women with a range of different levels of intake.

Lastly, information about iodine was already in the information sheet participants had received, and the question regarding the sources of iodine was asked both in the questionnaire they filled in and during the interviews. As a result, their answers were potentially influenced by these factors.

## 4.5 Conclusions and recommendations

The lack of iodine fortification in the UK provides an unusual, highly appropriate, ecological terrain in which to study the impact of a simple food or education-based intervention to tackle iodine insufficiency and its endocrine and neurodevelopmental consequences. The approach used in this study assumed that evaluating needs and expectations of stakeholders (mothers and women planning a pregnancy or breastfeeding) would enhance the design of suitable and impactful dietary recommendations and information packages, ultimately to improve iodine sufficiency.

Iodine nutrition is important during pregnancy and lactation, but awareness and knowledge is low amongst women of childbearing age, even with high educational attainment, and among healthcare professionals in the UK.

Dietary guidance received in pregnancy is not clear, leading to confusion over recommendations. Future work should incorporate users' input to design and implement tailored health promotion approaches. It is however likely that, to tackle iodine insufficiency in and around pregnancy, a multi-sprung approach will be required, tackling several different angles of the problem. Mobile health tools open an existing range of opportunities for personalised health, which, combined with regulatory steps, conventional dietary advice through health care professionals and targeted awareness campaigns, would form a comprehensive approach to the public health challenge iodine has become.

Although women are willing to change behaviour during pregnancy, existing recommendations in the way these are provided disallow changes. There is a need to focus on specific foods and portion sizes, rather than nutrients, supplements and specific recommendations that are not tethered to a balanced diet and the associated know-how, that many assume is in place (such as cooking skills and knowledge of foods). Healthcare professionals, mainly midwives, should be educated to provide dietary guidance in pregnancy, due to being the most trustful source of information for women around pregnancy. Supportive material, effectively designed and including clear guidelines, should be available and easily accessible to women after referral from healthcare professionals. Such material could incorporate technology, which offers new solutions in the way information are spread, such as the Internet, mobile applications and emails, with links for further information for those women who would like to expand their knowledge behind the recommendations they receive.

# Chapter 5 - A survey on UK consumers' consumption and factors affecting their choice of dairy products

## Abstract

Consumption of dairy products has been related to health benefits, and milk is the main source of iodine in the UK, a country re-categorised as iodine insufficient. Dairy intake tends to decrease with age and a large proportion of women of childbearing age avoid dairy despite their nutritional importance. The aim of this study is to investigate the perceptions (knowledge and awareness) and practice towards dairy products of UK residents.

A cross-sectional survey was carried out by the use of a validated questionnaire, informed by the Theory of Planned Behaviour (TPB). The questionnaire was disseminated online and in the community to English-speaking UK residents aged 14 years and over, between June and November 2016. The drivers for choosing dairy products were rated using 5-point Likert scales. Iodine intake from dairy products was estimated.

In total, 2040 participants completed the questionnaire. The median dairy product servings per day were 2.2 (IQR 1.2-3.5) and the median iodine intake from dairy products was 85 μg/day (IQR 44-147), with 45 μg/day (IQR 10-83) derived from milk. Two servings or more of dairy per day were only consumed by 54% (n=1104) of the population ("high" consumers). The main reported factors identifiable as barriers to dairy consumption in "low" consumers, included taste (78%, n=716), freshness (60%, n=550) and texture (55%, n=508). "High" consumers of dairy products (54%, n=1104) had significantly higher iodine intake compared to "low" consumers ($p<0.01$) – drivers for consumption included taste (89%, n=980), freshness (71%, n=785) and smell (61%, n=676).

Increased intake of dairy products could help in the prevention of nutritional insufficiencies, such as iodine, and adverse health effects both in the general population and in pregnant and lactating women. Barriers to dairy consumption should firstly be addressed to potentially encourage increased consumption.

## 5.1 Introduction

Dairy product consumption has been linked to health benefits (Tunick and Van Hekken, 2014). Robust evidence has demonstrated an association of dairy products intake with muscle building and improvement of body composition (Miller et al., 2014, Katsanos et al., 2008), prevention of tooth decay, due to the presence of calcium, casein-derived bioactive peptides and proteose-peptone (Merritt et al., 2006). Observational studies, partially supported by interventions, have also linked the consumption of milk and yoghurt with reduced risk of obesity, weight gain and cardiovascular disease (Astrup, 2014). Protein, vitamins (vitamin A, B1, B2, B5, B12) and minerals (calcium, magnesium, phosphorus, potassium, iodine) are present in dairy products, although their concentration and contribution to the daily intake varies depending on the product (McCance and Widdowson, 2002).

The current UK recommendations for dairy product intake differ from the recommendations provided by other countries (e.g. United States, New Zealand, Japan, Australia). Furthermore, there is no set easy-to-use portion size guidance for dairy intakes in the UK. The recommendation in the updated "Eatwell Guide" is to *"have some dairy or dairy alternatives (such as soya drinks); choosing lower fat and lower sugar options*" which does not differ from the previous UK recommendations. However, the size of the segment dedicated to dairy products in the depicted form of the new "Eatwell Guide" is slightly smaller compared to the previous "Eatwell Plate" (Public Health England, 2016). In addition, the serving size for milk and other dairy products is not specified (Dror and Allen, 2014) with no differentiation in the dairy product type suggested (apart from the recommendation of choosing lower fat and sugar). The inclusion of dairy alternatives to the recommendation (lacking for example in protein, calcium, iodine, riboflavin and vitamin B12 if they are not fortified) is also concerning for iodine status (Ma et al., 2016, Heaney et al., 2000, Sethi et al., 2016, Chambers, 2018). Plant-based milk alternatives do not contain iodine naturally and are rarely fortified, resulting in very low iodine concentrations ($3.1 \pm 2.5$ μg/250 ml; approximately 2% of the iodine content of conventional milk). Long-term consumption of non-conventional, non-cow's milk can place individuals at risk of iodine insufficiency (Ma et al., 2016, Bath et al., 2017).

Adolescence is a transition period when dairy intake drops, and contributes less to daily energy and nutrient intake (e.g. protein, calcium, fats, iodine) (Roberts et al., 2018) failing to meet the recommendations and leading to subsequent insufficiencies. Despite the fact that dairy products contribute to children's nutrient intake, health and growth, their consumption appears to be lower in developed countries, with a trend towards decreasing with age (Dror and Allen, 2014). It is accepted that public health promotion of health behaviours should be initiated in adolescence and continued through to adulthood, as it is relevant to pregnancy nutrition.

Milk and other dairy products are the main sources of iodine for the UK population, contributing toward 34% of the dietary iodine intake of adults, with semi-skimmed milk being the main contributor (15%) (Roberts et al., 2018). In lactating and pregnant women milk alone contributes toward 38% and 40% of the dietary iodine intake (Bouga et al., 2015b). Meanwhile, in pregnancy iodine is also provided by other dairy (31%) (Combet et al., 2015). The UK population, and in particular women of childbearing age, have been shown to have insufficient iodine intake (Vanderpump et al., 2011), placing at risk their health and the health of their children. Salt iodisation is implemented in more than 120 countries around the world, and has contributed to the elimination of iodine insufficiency in children and adults, but not in pregnant and lactating women (The United Nations Children's Fund, 2008). However, in the UK this prophylactic measure is not in place and iodine intake depends on the traditional dietary sources and their selection from the consumers. However, the level of awareness and knowledge regarding iodine importance and iodine rich foods remains low amongst UK mothers (Combet et al., 2015, Bouga et al., 2018a), leading to low intakes, due to knowledge being correlated with iodine intake (O'Kane et al., 2016). Taking these into account, iodine deficiency is a problem with multifaceted causes and milk, as a rich iodine source, could form part of the solution to this public health concern, which requires a synergistic approach (Bouga et al., 2018b).

It is important to know any perceived influential factors in people's choice of dairy products, barriers and facilitators, due to their contribution to the iodine intake of the UK population (Roberts et al., 2018). Perceptions of healthiness are closely related to dietary behaviour and food choice; attitudes to healthy eating are influenced by factors such as sensorial characteristics, culture, food availability, child feeding and energy density (Carrillo et al., 2011). The identification of barriers, facilitators and perceptions towards iodine-rich food consumption is important, considering their potential input in increasing iodine intake, and evidence is limited mainly to other countries (not in the UK), or specific aspects of dairy characteristics (low fat products, welfare, creaminess) (Hagy et al., 2000, Hammond and Chapman, 2008, Richardson-Harman et al., 2000, Ares and Gambaro, 2007). Consumers' perceptions towards some aspects of dairy products have been previously investigated - with their perceived healthiness ranked as *relatively healthy* (Johansen et al., 2011). There is a lack of studies which examine factors influencing the choice of dairy products and predictors of consumers' behaviour. Such a study is needed in the UK, as increasing dairy intake to the recommended levels would have a positive impact on nutritional insufficiencies (decreasing percentage of people below the LRNI for nutrients such as calcium, iodine, vitamin A, magnesium and potassium) (Roberts et al., 2018). Several health-related interventions are based on the theory of planned behaviour (TBP), as it has been shown to have the potential for the development of interventions which aim in changing behaviour (Hardeman et al., 2002). The TPB is a social cognition model that explores how *attitudes towards a behaviour*, *perceived behavioural control* and *subjective norms* can influence and predict *intentions* over a *behaviour*, and how these constructs can potentially predict a specific behaviour, which is mainly influenced by *intentions* (Ajzen, 1991).

The aim of this study is to investigate the i) behaviour (positive/ negative attitudes, type of products purchased), ii) perception (knowledge and awareness) and iii) practice towards dairy products of people living in the UK. The research questions explored were:

1. What is the contribution of dairy products in the daily iodine intake of the UK population?
2. What are the main perceived barriers and influential factors in the consumption of dairy products?
3. Can behaviour towards dairy products consumption be predicted through the constructs of the TPB and sociodemographic characteristics?

## 5.2 Methods

### 5.2.1 Questionnaire design

A cross-sectional survey was carried out by the use of a validated questionnaire. The questionnaire designed for this study was based on the TPB. Questions were modified and used from the previous questionnaire on mothers' awareness about nutrition guidelines for pregnancy (Combet et al., 2015) and the Commonwealth Scientific and Industrial Research Organisation (CSIRO) health sciences and nutrition, diet and health survey 2004 (focussing on selenium) along with additional questions (Pirog, 2004). Modifications included phrasing alterations and the addition of potential options for responses, in order for the questionnaire to be applicable to the general population and for dairy products. In addition to the TPB constructs (*attitudes towards behaviour*, *subjective norms*, *perceived behavioural control*, *intention* and *behaviour*) that were included in the questionnaire, a section with knowledge and awareness questions and a section of sociodemographic characteristics were developed.

Knowledge questions included those where participants had to complete a sentence, questions with multiple options, yes / no questions and true/ false/ not sure questions. *Attitudes towards behaviour* included a 7-point Likert scale question (completely agree / completely disagree) and true, false / not sure questions. *Perceived behavioural control* included a 7-point Likert scale question (completely agree / completely disagree). *Subjective norms* included a 7-point Likert scale question (completely agree / completely disagree) and 5-point Likert scale questions (not at all / very much, strongly disagree / strongly agree). *Intention* included a yes / no question, a multiple options question and a 7-point Likert scale question (completely agree / completely disagree). Finally, *behaviour* was determined through the FFQ. Four open questions were also part of the questionnaire as well as questions regarding participants' cooking habits, preferred dairy types, potential factors influencing their preferences, health status, special diets and sociodemographic characteristics, with pre-specified options.

The drivers for choosing dairy products were also explored, by listing them on the questionnaire and asking participants to rate in a 5-point Likert scale (1: not at all, 5: very much) how much each factor influences their choice of dairy products (what they buy or order).

All study documents are presented in Appendix 4.

### 5.2.2 Questionnaire validation

A face and content validation of the questionnaire was performed before the initiation of recruitment. A total of 19 volunteers filled in the questionnaire, aiming to identify questions with mistakes, missing options, vagueness or uncertainties. Volunteers were also timing themselves while filling in the questionnaire to be able to provide an approximation of the time required for completion to potential participants. All comments were taken into consideration and were incorporated in the final version of the questionnaire. Mistakes were corrected; ambiguities were clarified (by changing wording or defining terms) and extra possible options were added to answers of questions.

### 5.2.3 Recruitment and participants

Participants were recruited between June-December 2016 by the research team at selected private and public locations in the Greater Glasgow area and online. Eligible participants were UK residents older than 14 years who were able to read and write in English fluently. Face-to-face recruitment took place in libraries, cafes, day centres, community centres, help centres, museums, trains, a rugby match, door to door and canteens. Online recruitment focused on social-networking sites (Facebook, Instagram, Twitter etc.), forums and websites targeting the general population across the UK.

All potential participants, both online and face-to-face, were provided with the information of the study and were asked to consent to take part before completion of the questionnaire.

The proposed sample size of this study was 1979, based on the total UK population taken from the 2011 census data (Office for National Statistics, 2012), and using a 99% confidence level and 2.9% confidence interval.

### 5.2.4 Data cleaning

After the completion of the study, data were cleaned to detect and exclude duplicate and inaccurate entries, based on certain set criteria. Implausibility criteria included: [1] maximum milk and/or other dairy intake: people who reported higher milk and/or other dairy intake more than the maximum milk and other dairy intake reported values on the National Diet and Nutrition Survey Years 5-6 (2013/14) (2450 g of milk and 770 g of other dairy) were excluded (n=21 with daily milk intake between 2550-3510 g and/or other dairy 824-1722 g); [2] age and education: people who reported being 19 years or younger and having a University degree equal to or higher than a Bachelor’s degree and people being 21 years or younger and having a University degree equal to or higher than a Master’s degree were excluded (n=24); [3] vegetarians consuming dairy: people who reported being vegans (avoiding meat, fish, all other types of seafood and all dairy products including eggs) or ovo-vegetarians (avoiding all meat, fish, seafood and all dairy products except eggs) and reported consuming any quantity of dairy were excluded (n=31). Definitions of different types of vegetarians were provided on the questionnaire.

### 5.2.5 TPB constructs scoring

The TPB consists of five variables: three variables (*attitudes towards behaviour*, *perceived behavioural control*, *subjective norms*) which predict *intention* ($4^{th}$ variable) and this affects the performed *behaviour* ($5^{th}$ variable). The questions that consist each section of the questionnaire were scored, and a score was created for each variable according to Francis et al. (2004).

The questionnaire aimed to explore whether the TPB can predict dairy product consumption (targeted behaviour). Self-reported dietary intake, which emerged from the FFQ, formed the behavioural part of the questionnaire. Daily dairy product servings were calculated, and this made up the score for the behaviour section of the questionnaire. Servings were considered as follows: milk 200 ml, cheese 40 g, yoghurt 125 g, milk or cream-based pudding portion of 100 g of which 50 g is dairy, and cheese-based dish portion of 170 g of which 50 g is dairy. Iodine concentration of milk was also calculated based on a year-around average value of iodine in milk (27.2 μg/100 g), derived from a search of all relevant drinks in Windiets 2005 database (Robert Gordon University, Aberdeen, UK) (Combet and Lean, 2014).

The *intention* was assessed via three questions. The first question had a 7-point Likert scale type response (scored 0 to 6 points). The second question was a direct measurement of *intention*, where participants were asked whether they intend to increase, decrease or keep their dairy intake at the current levels and these were scored as 6, 0 or 3 respectively. These scores corresponded to the scoring of the Likert scale and prevented positive intentions from being underestimated compared to the Likert scale. The last question was a scenario in which participants were asked to answer with a “yes” or “no”, so these were scored as 6 and 0 respectively, as they either favour or do not favour the behaviour, as above. Percentage of the maximum score was the *intention* score.

The *attitudes towards behaviour* construct included one question in which the response was in a 7-point Likert scale (scored from 0 to 1.5 points) format and 18 True / False / Not sure questions. For those questions any positive attitude towards increasing / including dairy products (mainly in adulthood and women) was scored as 0.25 and any negative response or “not sure” answer was scored as 0. The total score for this construct was the percentage of the maximum of all the responses.

The *perceived behavioural control* only consisted of one question (7-point Likert scale) and the score for *perceived behavioural control* was this question’s score, normalised in a 0 to100 scale.

The *subjective norms* consisted of nine questions. Eight of the questions were 5-point Likert scale type questions and the other question was a 7-point Likert scale question. This question was reversed as it was a negative question. For *subjective norms* the score was the percentage of the maximum score obtained for the nine questions based on the construct.

Knowledge is an external construct to the TPB, which is also used to predict behaviour with the previously mentioned four constructs. The questionnaire included questions assessing participants’ knowledge and awareness on dairy products. The answers to these questions were rated as correct (given from 0.25 to 2 points, depending on the importance of the question) or wrong (included “not sure” answers, given 0 points) to create a knowledge score for each participant. Twenty-six questions or sub questions were included in the scoring. The percentage of the maximum score was calculated for each participant.

For all the TPB constructs (including knowledge), the median (interquartile range (IQR)) score was calculated. The total population was categorised as “low” consumers of dairy products (those who do not achieve the minimum recommendation of 2 servings/day of dairy products) and “high” consumers of dairy products. Scores were compared between “low” and “high” dairy consumers.

### 5.2.6 Statistics

Data analysis was performed with the statistical software SPSS version 21.0 (IBM Corporation). Normality was tested with Shapiro-Wilk normality test. Descriptive statistics were expressed as median and IQR for continuous non-parametric data and as frequencies (n) and percentages (%) for categorical data. From the FFQ, iodine intake from dairy products was calculated as described by Combet and Lean (2014). Group differences for continuous non-parametric variables were tested with Independent samples Mann-Whitney U test and for categorical data with Pearson Chi-Square test. Binominal logistic regression was also performed to predict a dichotomous dependant variable. Scores were handled both as continuous variables, to find the differences between the” low” and “high” consumers, and as interval variables, in quartiles, for the purposes of the regression.

## 5.3 Results

### 5.3.1 Participants’ characteristics

The survey was opened between June and November 2016. Until September 2016, 1535 valid responses had been gathered. However, the study reopened a month later in order to increase the sample’s representativeness, as only 18% of the initial respondents were males. A total of 2138 responses were gathered, after entering the paper questionnaire responses (n=300). However, after cleaning the database for duplicate entries (n=23) and implausible responses (n=75), the final sample that was included in the analysis was n=2040 participants, from which 59% (n=1209) were females and 41% (n=831) males. In the final included sample, 86% (n=1746) filled in the online questionnaire and 14% (n=294) the paper form of the questionnaire.

The median age of the respondents was 26 years (IQR 21-39) with the youngest participant being 14 and the oldest 95 years old. Twenty-six percent (n=533) of participants were living with their partner, 20% (n=416) with friends, 19% (n=377) with their family, 12% (n=252) with their parents, 11% (n=231) in a student accommodation and 11% (n=230) alone. In each household there was a median of 2 adults (IQR 2-3) and no children (IQR 0-1).

Table 5.1 Participants' characteristics

| **Demographic data** | **n** | **%** |
|---|---|---|
| Age groups | | |
| 16-29 years | 1204 | *59* |
| 30-49 years | 580 | *28* |
| ≥50 years | 255 | *13* |
| Ethnicity | | |
| British | 1494 | *73* |
| Other European | 338 | *17* |
| Other ethnic groups | 207 | *10* |
| Education | | |
| School level | 700 | *34* |
| College level | 314 | *15* |
| Undergraduate degree | 603 | *30* |
| Postgraduate degree | 417 | *21* |
| Educational background | | |
| Nutrition | 223 | *11* |
| Food Sciences | 94 | *5* |
| Health Sciences | 323 | *16* |
| Annual household income | | |
| <£15,000 | 855 | *42* |
| £15,001 - £30,000 | 544 | *27* |
| £30,001 - £50,000 | 370 | *18* |
| >50,000 | 253 | *13* |
| Main grocery shoppers | 1332 | *65* |

### 5.3.2 Special diets, preferences and health status

In the total study sample, 6% (n=113) of the participants were following a vegetarian diet (lacto-ovo-vegetarian, lacto-vegetarian or ovo-vegetarian) and 5% (n=105) were following a vegan diet. From this population, only vegans and ovo-vegetarians were avoiding dairy products, consisting the 5% (n=111) of the total population.

Participants were asked whether they were lactose intolerant and 8% (n=171) reported being lactose intolerant, yet only 37% of those people (n=63) or 3% of the total population were actually diagnosed by a GP. From a 5-point Likert scale, 77% (n=1566) selected that they strongly disagree (1 out of 5) with the statement "*I am allergic to dairy products*", indicating that the 23% perceive that they have an allergy to a certain level. Furthermore, 12% (n=248) were following a weight loss diet, and 2% (n=44) were pregnant or breastfeeding when completing the survey.

When asked about their health status, 6% (n=125) of participants reported having anaemia due to iron deficiency, while 5% (n=98) reported high blood pressure, 4% (n=74) high cholesterol, 1% (n=25) diabetes and 8% (n=160) other health conditions (most often reported being Inflammatory Bowel Syndrome, Crohn’s disease, Coeliac disease and thyroid related diseases, such as hypothyroidism or hyperthyroidism).

Preferences (like / dislike) were expressed for milk, yogurt and cheese. Seventy three percent (n=1491), 83% (n=1688) and 87% (n=1773) reported that they like milk, yoghurt and cheese respectively. On the other hand, 20% (n=404), 14% (n=281) and 11% (n=215) reported that they do not like milk, yogurt and cheese respectively, so they do not consume them and the remaining 7% (n=144), 3% (n=69) and 3% (n=51) reported that they don’t like milk, yoghurt and cheese respectively, but they try to include them in their diet.

### 5.3.3 Dairy consumption

The median dairy servings per day, calculated from the FFQ, were 2.2 (IQR 1.2-3.5), of which milk was 0.8 servings (IQR 0.2-1.5) and other dairy products 1.2 (IQR 0.6-1.9) servings.

Translating servings into g and ml of dairy products, total dairy products consumption was calculated being a median of 260 g (IQR 124-446). Milk consisted 65% (IQR 39-80) of the total dairy consumed and amounted to 167 ml (IQR 36-307) daily. The median of the remaining dairy (including yoghurts, cheese, and milk or crème-based puddings) consumed was 76 g (IQR 36-136) daily.

From the total population, 45% (n=922) did not achieve an intake of 2 portions of dairy per day, the minimum recommended by the American heart Association (Eckel et al., 2013), 22% (n=444) were consuming the recommended 2-3 portions per day and 32% (n=660) were above the recommended. “Low” consumers of dairy products were 45% (n=922) and “high” consumers 54% (n=1104). Education did not differ significantly between low and high consumers (p=0.801).

Cow's pasteurised milk was the most frequently consumed type of milk, followed by plant milk (soya and other plant milks) (Table 5.2). Organic milk was also reported to be used by 39% (n=774) of the participants, either always or occasionally. Milk is the dairy product most often replaced by low fat alternatives (Table 5.3).

Table 5.2 Frequency of usage of different milk types.

| | Always | | Often | | Sometimes | | Never | |
|---|---|---|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| Cow's pasteurised milk | 1016 | *50* | 322 | *16* | 270 | *13* | 338 | *19* |
| Cow's UHT milk | 29 | *1* | 80 | *4* | 321 | *16* | 1481 | *73* |
| Evaporated milk | 6 | *0* | 20 | *1* | 267 | *13* | 1684 | *83* |
| Organic milk | 92 | *5* | 175 | *9* | 507 | *25* | 1219 | *60* |
| Goat's milk | 9 | *0* | 23 | *1* | 159 | *8* | 1815 | *89* |
| Soya milk | 93 | *5* | 157 | *8* | 372 | *18* | 1393 | *68* |
| Other plant milks | 182 | *9* | 254 | *13* | 478 | *23* | 1093 | *54* |
| Flavoured milk | 28 | *1* | 95 | *5* | 510 | *25* | 1379 | *68* |
| Milk powder | 8 | *0* | 18 | *1* | 154 | *8* | 1829 | *90* |
| Lacto-free milk | 40 | *2* | 37 | *2* | 110 | *5* | 1817 | *89* |

Percentages are based on the total population. Option "I don't know" is not included in the table.

Table 5.3 Frequency of replacement of "full fat" dairy products with "low fat" or "fat free" dairy alternatives.

| | Always | | Often | | Sometimes | | Never | |
|---|---|---|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| Low fat yoghurts | 272 | *13* | 283 | *14* | 575 | *28* | 909 | *45* |
| Skimmed milk | 197 | *10* | 155 | *8* | 285 | *14* | 1400 | *69* |
| Semi-skimmed milk | 679 | *33* | 281 | *14* | 332 | *16* | 746 | *37* |
| Low fat cheese | 154 | *8* | 247 | *12* | 601 | *30* | 1035 | *51* |

The cooking and eating habits were also explored by asking participants how often they cook / eat homemade food, ready meals and sandwiches. The mode for cooking and for eating homemade food made by a family member or friend was 1-2 times / day and was 1-2 days / month for eating ready meals, eating in a restaurant or canteen and eating fast food or sandwiches.

### 5.3.4 Iodine intake

Median total daily iodine intake from dairy products was 85 µg/day (IQR 44-147), and 45 µg/day (IQR 10-83) was iodine from milk. “High” dairy consumers had significantly higher iodine intake compared to “low” dairy consumers (137 µg/day; IQR 102-195 vs 41 µg/day; IQR 13-61, p<0.01).

### 5.3.5 Drivers of choice

Taste was reported as the main driver for choosing dairy products, with 84% (n=1708) of the participants selecting 4 and 5 in the scale, followed by freshness (66%, n=1344) and smell (58%, n=1185). Dairy consumption behaviours were rarely influenced by a healthcare professional (GP, nutritionist, dietician, other) (35% in agreement, n=716), or health expert in the media (16% in agreement, n=322). Marketing was the last factor to consciously influence consumers (7%, n=148) (Figure 5.1).

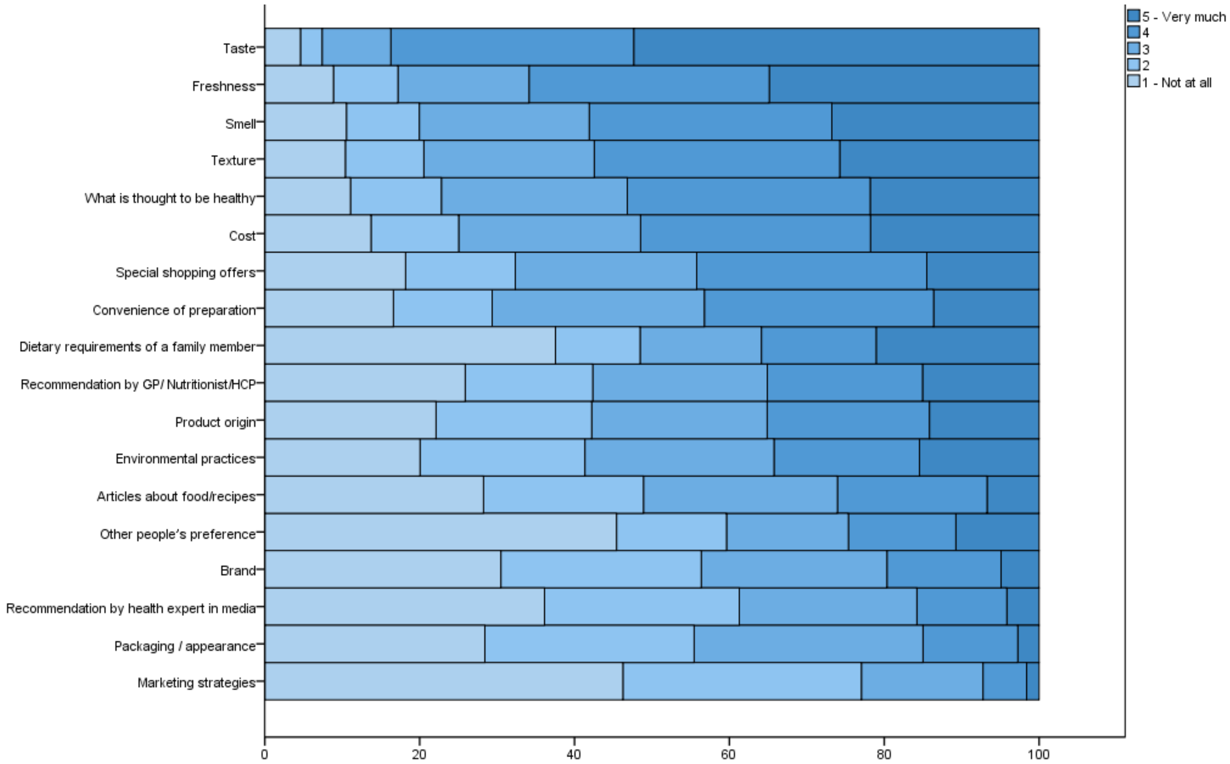


Figure 5.1 Factors influencing choice of dairy products.

The main reported factors identifiable as barriers to dairy consumption (Likert scale 4 & 5) in "low" consumers, included taste (78%, n=716), freshness (60%, n=550) and texture (55%, n=508). For "high" consumers, drivers for consumption included taste (89%, n=980), freshness (71%, n=785) and smell (61%, n=676). Sustainability of dairy food production was a concern to "low" consumers, with 41% (n=376) perceiving a negative impact on the environment, against 19% (n=218) of the "high" consumers. From a health perspective, 25% (n=233) of "low" consumers believed that dairy products should be avoided to limit saturated fats intake.

### 5.3.6 TPB constructs scores

*Knowledge*, *attitudes towards behaviour* and *intention* were found to be significantly higher in the high consumers group of the population compared to the low consumers (Table 5.4, Figure 5.2).

Table 5.4 TPB constructs' scores in the low and high dairy consumers' groups

| | **Low consumers** | | **High consumers** | | |
|---|---|---|---|---|---|
| | **Median** | ***IQR*** | **Median** | ***IQR*** | **p** |
| Knowledge | 50 | *36-61* | 55.6 | *47-67* | *<0.01* |
| ATB | 46 | *33-58* | 54 | *42-67* | *<0.01* |
| PBC | 67 | *50-83* | 67 | *50-83* | *0.304* |
| SN | 34 | *21-45* | 34 | *24-45* | *0.396* |
| INT | 33 | *17-56* | 50 | *22-61* | *<0.01* |
| Behaviour (serv/day) | 1.1 | *0.4-1.6* | 3.3 | *2.5-4.8* | *<0.01* |

ATB: Attitudes towards behaviour, PBC: Perceived behavioural control; SN: Subjective norms; INT: Intention

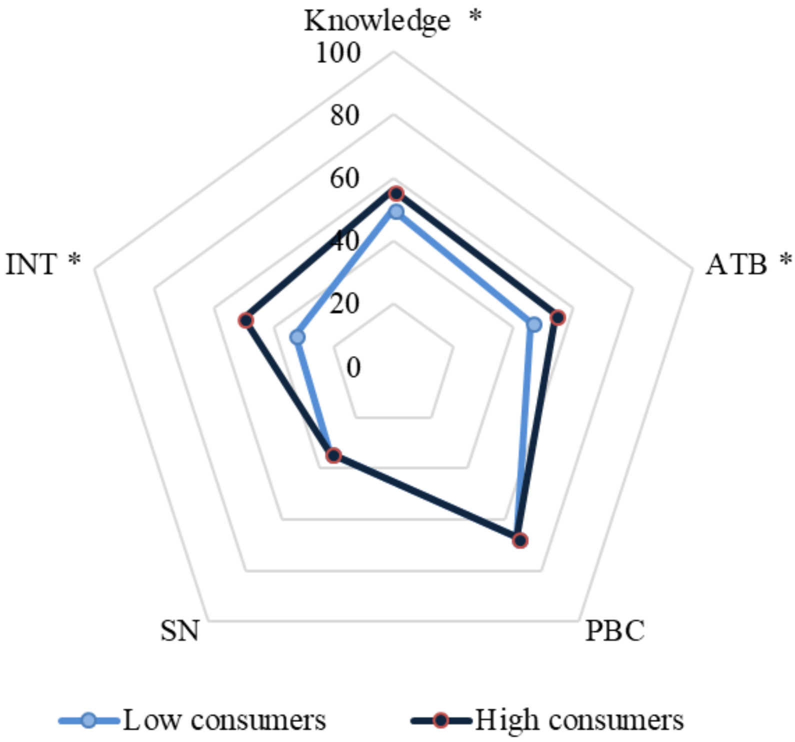


Figure 5.2 Spider graph of TPB constructs' scores for low and high consumers of dairy products.
Constructs with * are significantly different between the low and high consumers (p<0.01); ATB: Attitudes towards behaviour, PBC: Perceived behavioural control; SN: Subjective norms; INT: Intention

A binomial logistic regression was performed to ascertain the effects of *attitudes towards behaviour*, *perceived behavioural control*, *subjective norms*, *intention* and *knowledge* on the likelihood that participants reach the recommendation for dairy intake. The logistic regression model was statistically significant, $\chi^2(15)=166.153$, $p<0.0005$. The model explained 10.5% (Nagelkerke $R^2$) of the variance in meeting the recommended dairy intake and correctly classified 62.1% of cases. Sensitivity was 47.9%, specificity was 74%, positive predictive value was 63% and negative predictive value was 60.6%. Of the five predictor variables only three were statistically significant: *attitudes towards behaviour*, *intention* and *knowledge* (Table 5.5). Increasing those scores (falling to a higher quartile compared to the first quartile which was set as a reference) was associated with an increased likelihood of achieving the recommended dairy intake. Similar results were found when corrected for age and gender and when dairy avoiders were excluded from the analysis (results not shown). The model did not control for any other variables (e.g. income, education).

Table 5.5 Binary logistic regression on TPB constructs' effect on the likelihood to achieve the recommended 2 portions of dairy per day.

| | B | SE | Wald | df | *p* | Odds ratio | 95% CI for odds ratio | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| **Knowledge Quartile 1 (ref)** | | | **36.46** | **3** | ***0.000*** | | | |
| Knowledge Quartile 2 | -0.714 | 0.15 | 24.116 | 1 | *0.000* | 0.49 | 0.37 | 0.65 |
| Knowledge Quartile 3 | -0.181 | 0.14 | 1.719 | 1 | *0.190* | 0.84 | 0.64 | 1.09 |
| Knowledge Quartile 4 | 0.043 | 0.14 | 0.098 | 1 | *0.754* | 1.04 | 0.80 | 1.36 |
| **ATB Quartile 1 (ref)** | | | **32.883** | **3** | ***0.000*** | | | |
| ATB Quartile 2 | -0.802 | 0.14 | 30.885 | 1 | *0.000* | 0.45 | 0.34 | 0.60 |
| ATB Quartile 3 | -0.586 | 0.14 | 17.928 | 1 | *0.000* | 0.56 | 0.42 | 0.73 |
| ATB Quartile 4 | -0.489 | 0.14 | 13.181 | 1 | *0.000* | 0.61 | 0.47 | 0.80 |
| **SN Quartile 1 (ref)** | | | **2.473** | **3** | ***0.480*** | | | |
| SN Quartile 2 | 0.191 | 0.14 | 1.943 | 1 | *0.163* | 1.21 | 0.93 | 1.59 |
| SN Quartile 3 | 0.061 | 0.13 | 0.208 | 1 | *0.649* | 1.06 | 0.82 | 1.38 |
| SN Quartile 4 | 0.009 | 0.13 | 0.004 | 1 | *0.947* | 1.01 | 0.78 | 1.31 |
| **PBC Quartile 1 (ref)** | | | **4.082** | **3** | ***0.253*** | | | |
| PBC Quartile 2 | 0.253 | 0.13 | 3.569 | 1 | *0.059* | 1.29 | 0.99 | 1.67 |
| PBC Quartile 3 | 0.143 | 0.13 | 1.153 | 1 | *0.283* | 1.15 | 0.89 | 1.50 |
| PBC Quartile 4 | 0.208 | 0.13 | 2.425 | 1 | *0.119* | 1.23 | 0.95 | 1.60 |
| **INT Quartile 1 (ref)** | | | **42.622** | **3** | ***0.000*** | | | |
| INT Quartile 2 | -0.797 | 0.14 | 33.337 | 1 | *0.000* | 0.45 | 0.34 | 0.59 |
| INT Quartile 3 | -0.317 | 0.13 | 5.651 | 1 | *0.017* | 0.73 | 0.56 | 0.95 |
| INT Quartile 4 | -0.051 | 0.13 | 0.142 | 1 | *0.706* | 0.95 | 0.73 | 1.24 |
| Constant | 0.948 | 0.17 | 30.987 | 1 | *0.000* | 2.58 | | |

ATB: Attitudes towards behaviour, PBC: Perceived behavioural control; SN: Subjective norms; INT: Intention

## 5.4 Discussion

### 5.4.1 Main findings and barriers exploration

Dairy products in the UK adolescent and adult population contribute approximately 9% in the total energy intake, which is decreased in comparison to children below 11 years and older adults (older than 65 years), according to the National Diet and Nutrition Survey (NDNS)data (Bates et al., 2014). However, the nutritional value of milk and milk products is high, having been related to health benefits not only in childhood but also in adulthood and adolescence (Muehlhoff et al., 2013). The present study explored the factors that influence the choice of dairy products in the UK population, based on the TPB, and the level of their consumption.

With the lack of set recommendations for the daily intake of milk and milk products in the UK, we set the cut-off for sufficient intake at 2 portions per day, as this is the minimum recommended amongst other international organisations (Eckel et al., 2013) and a realistic target for a population. However, in the study sample, 45% did not achieve the 2 servings/day. Exploring the external factors that might contribute to this low intake of dairy products in the UK, the lack of specific quantified recommendations and the confusion over the ambiguous "Eatwell Guide" statement *"have some dairy or dairy alternatives"* (Public Health England, 2016) might be part of the explanation. At the same time, with 28% of the population considering dairy alternatives to be dairy products, and 23% reporting having some level of dairy allergy, the low dairy intake is better explained. Vegan and strict vegetarian diets are also becoming more popular worldwide and in the UK, with 9% of the British population following a vegetarian diet, and 10% of them a vegan diet. Veganism is also increasing more rapidly than vegetarianism (Leitzmann, 2014). Exclusion diets, such as lactose and gluten free diets, are also increasing in popularity in the general population, as shown by the increase in global sales of lactose and gluten-free products (Gaesser and Angadi, 2012, Baroke, 2016). From the respondents, 5% followed a strict vegetarian or vegan diet and consequently were excluding any milk and milk products from their diet while 8% reported being lactose intolerant, with the 5% not being diagnosed from a healthcare professional. As a result of those internal and external factors, milk and milk product consumption is decreasing and plant-based milk alternatives are becoming more popular, as we also found that soya and other plant milks are the most frequently preferred milks after cow's pasteurised milk for consumption (Sethi et al., 2016). The lack of robust and evidence based information from health experts and the confusing, abundant, uncontrolled nutrition information in the media has driven people's perceptions on dietary choices for decades (Turner, 1984). The abundance of information in the media has also been found to affect even children's perceptions on healthy eating, increasing misconceptions and decreasing trustworthiness, even in cases of health promotion initiatives and robust delivery of information (Dorey and McCool, 2009). As a result, marketing has contributed to the increase of milk alternatives in the market, which lack the nutritional value of milk and can lead to nutrient insufficiencies, such as calcium, vitamin D and iodine (Sethi et al., 2016).

Education and available reliable information are again emerging influential factors in dietary choices. The actual behaviour of choosing to consume dairy products has been found to be related to higher intention in the population that achieves a daily intake of 2 portions per day. This intention based on the TPB is mainly influenced by 3 factors, *attitudes towards behaviour*, *perceived behavioural control* and *subjective norms*, and is also related to knowledge, as a barrier in performing certain behaviours (Ajzen, 1991). However, in the present study only knowledge and the *attitudes towards behaviour*were found to be significantly higher in people with a higher intake of dairy. The TPB is only partially explaining the behaviour and is indicating that knowledge and attitudes related to dairy products are the factors that could be targeted in an attempt to increase the consumption of a population.

Taste, smell, texture and perceptions on healthiness have been described in this study as the top factors that influence the choice of dairy products, agreeing with previous studies (Hagy et al., 2000, Hammond and Chapman, 2008, Richardson-Harman et al., 2000). However, one of the strengths of this food group is the diversity of the available products, with a range of sensory characteristics and nutrient profiles, which allows consumers to compensate their dislike of a product with the choice of another of similar nutritional value. Women's perceptions of dairy foods have been also examined through focus groups, which highlighted their awareness of dairy's high calcium content and high fat content. In this study the taste of some products, including low fat, was reported as unsatisfying. This is in agreement with the present results, that taste is the barrier which most frequently discourages consumption in low dairy consumers. Convenience was reported as an important factor, potentially partly compounded by increased cost of such products, factors that, following the sensory attributes, are also important in the choice of dairy within our sample. Dairy products, however, are considered as staples in the everyday life of many, and neither cost nor convenience would affect purchasing decision of 30-55 year old Caucasian women residing in Virginia (Hagy et al., 2000). Other drivers of dairy food choices include not only taste, but also perceived health benefits and the preferences and needs of other family members (Hammond and Chapman, 2008, Richardson-Harman et al., 2000) as well as gender, age and socioeconomic status, which in turn determine the acceptance of functional and enriched foods (Ares and Gambaro, 2007).

### 5.4.2 Iodine in dairy products

The role of iodine in the healthy metabolism and normal thyroid function is well known, and its importance during pregnancy and lactation for the fetal development is highlighted by the WHO (de Benoist et al., 2004). Milk and milk products are the main dietary source of iodine in the UK, contributing 35% for men and 42% for women, followed by fish and seafood, which contribute by 11% in the total intake (Henderson et al., 2003, Bates et al., 2011). The present study showed that even in a population with low dairy intake, milk can contribute to the coverage of the adult iodine needs by 30%, reaching close to 60% when all dairy products contribute. As a result, increasing dairy products by a serving per day can help in increasing the iodine intake of the population and decreasing the proportion of people, mainly women, that do not achieve the recommended iodine intake of 150 μg/day.

Iodine concentration in milk varies depending on several factors. Seasonality and farming practices affect milk iodine concentration, as summer milk and organic milk have been found to have lower iodine compared to winter and conventional milk (Bath et al., 2012). Processing is also a factor that can affect the iodine concentration, as Ultra High Temperature (UHT) milk has lower iodine compared to conventional milk, although fat content of milk has no effect on iodine (Payling et al., 2015). Plant-based milk alternatives also do not contain iodine naturally and are not fortified with it, resulting in very low iodine concentrations (Ma et al., 2016, Bath et al., 2017). The long-term consumption of non-conventional, non-cow's milk can place individuals at risk of iodine insufficiency. A recent UK cross-sectional survey on available milk-alternative drinks showed that only three out of fourty-seven products in the UK market (~50% of the identified products sold in 2015) were fortified with iodine. Measuring iodine content of the unfortified drinks resulted in an iodine concentration 1.7% (range 0.9%-4.9%) of cow's milk value (Bath et al., 2017).

Healthcare professionals and mothers in the UK have been found to have very low awareness on the dietary sources of iodine. In a previous study, only 9% of women surveyed could recognise milk as a source of the micronutrient, commonly mistaking salt as the main dietary source of iodine (Combet et al., 2015). Dairy alternatives, which were considered part of dairy product food group by 28% of the population, have also been found to lack iodine if they are not fortified. In the present study, half of the population reported always choosing cow's pasteurised milk. Soya milk, other plant-based milks and organic milk showed a relative popularity and therefore increase the concern of emerging nutritional deficiencies, including iodine, with their increased popularity.

In the public health interest of mitigating iodine insufficiency in all population groups in the UK, focussing on pregnant and lactating women, milk and other dairy products could be part of the solution, by promoting their health benefits, informing the general public in a robust and evidence-based way on their nutrient profile and targeting the elimination of misconceptions and myths surrounding them.

### 5.4.2 Strengths and limitations

The present study was a cross-sectional survey which explored consumers' perceptions on dairy products. The sample size of more than 2000 people living in the UK, of different ethnicities, educational and socio-demographic backgrounds allowed a representative picture of the UK population's dairy intake and perceptions. Ninety percent of the study population were British and other Europeans which is comparable to the national statistics (87% white ethnic group) (UK Government, 2018). However, more young people were included in the study as online dissemination was wider, reaching younger age groups more than the older population who were recruited mainly via face-to-face interactions. The questionnaire was administered both online and in paper to reach people of all ages and backgrounds. In addition, the use of a validated FFQ (Combet and Lean, 2014) enabled the quantification both of the behaviour of consuming milk and milk based products and the iodine intake from this food group for the population, as one of the best ways to capture habitual intake of foods and nutrients. Using the TPB cognition model, perceptions related to the consumption of dairy products were explored for the first time in the UK population. The sample included a high vegetarian population; however only 5% of the sample was following a vegetarian diet which also excluded dairy products. As such, the more extreme views on dairy products existed but did not influence the final study results. This has been a consequence of the study design, as surveys available online can often attract only a sample with specific characteristics (Wright, 2005). To an extent, this survey was initially influenced by this limitation, attracting a higher proportion of females compared to males and a non-representative vegetarian population, but the re-advertisement of the study targeting non-vegetarian males balanced the final included sample.

The survey was conducted through a self-administered questionnaire online and in paper. The online questionnaire was designed in a way that prevented individuals from leaving unanswered questions, or from providing multiple answers to a question, in an attempt to minimise the amount of missing data. However, with regards to paper copy responses, although all questionnaires were checked by the researcher, mistakes in the completion of the questionnaires could not be avoided and missing data occurred. The dataset was cleaned based on implausible combination of responses, aiming to exclude any questionnaires with randomly answered questions.

Finally, perceptions were captured quantitatively, which does not allow deep exploration of all the angles of people's beliefs and thoughts on a topic. However, a qualitative design would not allow the recruitment of a large sample size and the study would not be representative for the UK population.

## 5.5 Conclusion

The consumption of milk and milk products in the UK population remains low, with 45% consuming less than 2 servings per day. The lack of specific, quantified recommendations has discouraged the general population to include dairy products as part of a healthy balanced diet. Knowledge, attitudes and intentions towards their consumption are higher among people who achieve an intake of 2 or more portions daily. Recommended iodine intake for adults (150 μg/day) is highly achievable based on results for "high" consumers, as the median iodine intake for people consuming more than 2 dairy portions per day is only less than 65 μg below the recommendation, not having measured iodine intake from fish and seafood. As such, by reassuring the consumption of at least two portions of dairy, there is only a very small amount of iodine to cover by other sources that might be less often consumed.

With the sensory attributes and perception of healthiness described as the main influential factors in the choice of milk products, and the variety in the available products of this food category, the barriers can easily become facilitators of choice. Increasing knowledge of the population using information from trustworthy sources may aid dairy products' acceptance amongst women of childbearing age, in order to include these in their diet and concurrently increase their dietary iodine intake.

# Chapter 6 - Fish and seafood products intake in the UK – barriers and facilitators

## Abstract

Consumption of fish and seafood products has been related to cardiovascular and cognitive health benefits, due to their rich nutrient profile. Iodine, which is key in the production of thyroid hormones, is present in fish in high, but variable concentrations (0.4 - 6.9 μg/g). It is a food group which is a promising dietary source for the elimination of the re-emerged iodine insufficiency in pregnant and lactating women in the UK. However, fish intake remains lower than the recommended and conflicting messages regarding risks in pregnancy discourage its increase. The aim of this study was to explore perceptions and factors influencing dietary choices related to seafood products in the UK population.

A cross-sectional survey based on the Theory of Planned Behaviour (TPB), in electronic and paper form, was conducted in a sample of the UK population. A total of 1511 UK residents, older than 14 years, were included in the survey. The median age of the population was 31 years (IQR 21-37), with 5% following a vegetarian or vegan diet. Fish intake was 1.9 (IQR 0.9-3.7) servings/week, with more than half (53%) of the respondents consuming below the recommended two portions/week. Iodine intake from fish was 24 μg/day (IQR 13-41) out of a total of 122 μg/day (IQR 79-186), which is below the WHO recommendation for sufficient intake. The TPB constructs explained 16% (Nagelkerke $R^2$) of the variance on whether the recommendation for fish would be achieved. "High" fish consumers (≥2 servings/week, 47%, n=711) had significantly higher knowledge (13%), intentions (24%), attitudes (18%) and perceived behavioural control (18%) towards fish consumption compared to "low" fish consumers (53%, n=797). The main factors influencing fish intake included taste, with 85% (n=1281) of the participants selecting 4 ("agree") and 5 ("strongly agree") in a 5-point Likert scale, freshness (65%, n=976), cost (61%, n=918) and convenience of preparation (54%, n=813). Related health risks, confusing recommendations and environmental practices also emerged as potential barriers from a 5-point Likert scale (not at all-very much). Availability as ready or take-away meals and marketing strategies were the lowest influential factors of fish and seafood choice.

Fish is an iodine-rich food, and increased consumption could potentially contribute to the elimination of iodine insufficiency in pregnant and lactating women in the UK. More than half of the UK population consumes less than 2 portions of fish weekly. Apart from the sensory attributes, factors that influence choice towards seafood products are associated with low self-control (e.g. cost). Exploring perceptions and barriers in the increase of fish in the

diet could inform the design of future interventions that would aim to increase iodine intake of the population.

## 6.1 Introduction

Fish and seafood products are excellent sources of protein, omega-3 fatty acids, vitamin D and minerals, such as iodine, iron and magnesium (Burger and Gochfeld, 2009). Due to their high nutritional value, fish and seafood intake has been related to health benefits, including reducing cholesterol levels and cardiovascular disease, pre-term delivery risk and enchasing cognitive development (Bouzan et al., 2005, Kris-Etherton et al., 2002, McMichael and Butler, 2005, Burger and Gochfeld, 2009, Willett, 2005). At the same time, some fish species (e.g. shark, swordfish, tilefish, or king mackerel) are high in contaminants and heavy metals, such as mercury and polychlorinated biphenyls (PCBs), posing a potential health risk for regular eaters (more than four weekly servings of 85 grams for women who are, or may become pregnant). Blood mercury levels have been found to be seven times higher in women with self-reported nine or more fish serving in the previous month compared to non-consumers (Institute of Medicine, 2006).

Fish is also a rich source of dietary iodine, and is the main contributor of dietary iodine intake in the UK population following dairy products, contributing towards 11% of the intake in non-pregnant adults (Henderson et al., 2003, Bates et al., 2016), and 24% during pregnancy (Combet et al., 2015). The UK population was found to be iodine insufficient (Vanderpump et al., 2011), until the latest data of the National Diet and Nutrition Survey (NDNS) which re-categorised the UK population as iodine sufficient, but lacking data for pregnancy and lactation (Roberts et al., 2018). Iodine insufficiency is a public health concern, mainly for women in childbearing age, since iodine is crucial in the production of thyroid hormones and fetal neurodevelopment during pregnancy.

In the UK, the recommendation for fish and seafood includes eating two portions of fish per week (2 x 140g), one of which should be from oily fish such as salmon, trout, mackerel and fresh tuna (Public Health England, 2016). According to the NDNS, oily fish intake remains lower than the recommended one portion of 140 grams per week without any changes over time (54 to 87 grams per week) (Bates et al., 2016). White fish is consumed more frequently compared to oil-rich fish, mainly after the classification of canned tuna in the white fish category (Whitton et al., 2011). During pregnancy, the recommendations for fish intake suggest eating “at least” two portions of fish per week, again with the one being from oil-rich fish. However, at the same time, pregnant women are advised to avoid “some types of fish” due to potentially harmful levels of mercury, as well as “raw shellfish” due to harmful bacteria and risk of poisoning, which creates confusion over the recommendations, as shown in Chapter 4. Due to the important role of iodine, but also omega 3, protein and other micronutrients that fish contains, its consumption should be promoted to achieve an increase both in pregnancy and the general population.

The theory of planned behaviour (TPB) was applied in the context of intention and frequency of fish consumption in Iran, using a self-administered questionnaire with various numbers of items and scales for each TPB construct. The study concluded that the *perceived behavioural control* and the *intention* to eat fish predicts the frequency of fish consumption ($R^2$=0.58, F=223.1, p<0.001) (Aghamolaei et al., 2012). Whether people include fish in their diet depends on drivers of food choice. There is a gap between the scientific evidence of risks and benefits related to fish and seafood consumption and actual beliefs and perceptions of consumers (Verbeke et al., 2005). In interviews with women in the perinatal period (Chapter 4), taste and heartburn have been described as the main drivers for inclusion or exclusion of fish, seafood and dairy products in the diet. Fish consumption is perceived as hard to increase or maintain during pregnancy, with taste and smell being the main barriers (Chapter 4) (Bouga et al., 2016). Most believe that eating fish is beneficial for health (94%; survey of 329 people, the United States (US)) with benefits attributable to omega-3 oils (according to 45%). A substantial proportion also perceived consumption to be "risky" (70%), with mercury content as the main risk (according to 24%) (Burger and Gochfeld, 2009). In five European countries, fish consumption was associated with country-related traditions and habits, which outweighed perceptions of risks and benefits (Jacobs et al., 2015). Ethical factors also feature in the choice to consume fish, with half Danish respondents (48%) willing to pay more for welfare fish than farmed fish (Solgaard and Yang, 2011).

In the UK, the factors that influence the choice of fish and seafood products, as well as the level of knowledge on the nutritional value, recommendations, risk and benefits have not been explored. The aim of this study is to investigate the i) behaviour, ii) perception (knowledge and awareness) and iii) practice towards fish and seafood products of UK residents.

The research questions were:

1. What is the contribution of fish and seafood products in the daily iodine intake of the UK population?

2. What are the main perceived barriers and influential factors in the consumption of fish and seafood?
3. Can behaviour towards fish and seafood products consumption be predicted through the constructs of the TPB and sociodemographic characteristics?

## 6.2 Methods

### 6.2.1 Questionnaire design

A cross-sectional survey was carried out using a validated questionnaire. The questionnaire designed for this study was based on the previously designed questionnaire on ‘Dairy products and health’ (Chapter 5), with some modifications to enable coverage of all theory of planned behaviour (TPB) constructs in more detail, with more questions and modifications due to the different targeting food category. Apart from the constructs of the TPB (*attitudes towards behaviour*, *perceived behavioural control*, *subjective norms*, *intention* and *behaviour*) that were included in the questionnaire, three new sections with i) knowledge and awareness, ii) questions on fish and seafood choices and relevant influential factors and iii) sociodemographic characteristics were developed.

Behaviour (weekly portions of fish intake) was determined by the FFQ. Questions regarding participants’ cooking habits, preferred fish and seafood types, health status, special diets, use of supplements, access to kitchen equipment and sociodemographic characteristics, with pre-specified options were also part of the questionnaire. The drivers of fish and seafood products choice were explored. Several factors were listed on the questionnaire (e.g. cost, sensory attributes, product origin, availability, convenience, shopping offers) asking participants to rate in a 5-point Likert scale (agreement: 1: not at all, 5: very much) how much each factor influenced their choice of fish and seafood products (what they buy or order).

All study documents are presented in Appendix 5. The present study is separate to the “Dairy Survey” presented on Chapter 5, using a different questionnaire and surveying a different population.

### 6.2.2 Questionnaire validation

A face and content validation of the questionnaire was performed before the initiation of recruitment. A total of 21 volunteers filled in the questionnaire to identify any questions with mistakes, missing options or that were vague or unclear. All comments were taken into consideration and were incorporated in the final version of the questionnaire, by correcting all identified mistakes or unclear questions and adding extra requested options to the response menus. The first 19 participants who completed the final version of the questionnaire online also fed-back on timing (an extra field for time had been added and was removed afterward) to provide an approximation of time required for completion.

### 6.2.3 Recruitment and participants

As described in Chapter 5 for the 'Dairy products and health' survey, eligible participants were UK residents, older than 14 years, and able to read and write in English fluently. Recruitment took place by the researcher at selected private and public locations in the Greater Glasgow area and online between November 2016 and May 2017. Face-to-face recruitment occurred in libraries, cafes, museums, canteens and door to door. For online recruitment, the study was advertised through social-networking sites (Facebook, Instagram, Twitter etc.), forums and websites targeting the general population across the UK. The study was also posted in the crowdsourcing platform 'Prolific academic' and the 'Call for participants' website.

All potential participants, both online and face-to-face, were provided with information about the study. Consent was implied, as agreement to complete the questionnaire was considered to indicate consent.

The proposed sample size of this study was 1537, based on the total UK population taken from the 2011 data (Office for National Statistics, 2012), and using a 95% confidence level and 2.5% error.

### 6.2.4 Data cleaning

After completion of the study, data were cleaned to detect and exclude duplicate and inaccurate entries, based on set criteria. Implausibility criteria included:

[1] Maximum milk, and/or other dairy, and/or fish intake: People who reported higher milk and/or other dairy and/or fish intake more than the maximum intake (milk, other dairy and fish) NDNS Years 5-6 (2013/14) reported values (2450 g/day of milk, 770 g/day of other dairy, 986 g/day of fish) were excluded (n=8 with fish range 1040-2340 g/day, n=12 with milk range 2510-3510 g/day, n=29 other dairy range 780-1723 g/day).

[2] Age and education: People who reported being 19 years or younger and having a University degree equal to or higher than a Bachelor's degree and people being 21 years or younger and having a University degree equal to or higher than a Master's degree were excluded (n=13).

[3] Vegetarians consuming dairy: People who reported being vegans (avoiding meat, fish, all other types of seafood and all dairy products including eggs) or ovo-vegetarians (avoiding all meat, fish, seafood and all dairy products except eggs) and reported any quantity of dairy intake were excluded.

[4] Vegetarians consuming fish: people who reported being vegans or any other type of vegetarians (apart from pescetarians) and reported any quantity of fish intake were excluded (n=28 in total for fish and dairy).

Definitions of the different types of vegetarians were provided on the questionnaire.

### 6.2.5 TPB constructs scoring

The TPB consists of five variables; (*attitudes towards behaviour, perceived behavioural control, subjective norms*) which predict *intention* and this affects the performed *behaviour*. The questions which consisted each section of the questionnaire were scored, and a score was created for each variable, according to Francis et al. (2004). All scores (apart from behaviour) were normalised to the same scale (0-100), as a percentage of the maximum points of each scale.

The explored behaviour was fish and seafood products' consumption (weekly fish servings). The *behaviour* variable was informed by the self-reported fish intake in the FFQ section. Iodine content of fish and seafood was also calculated from the FFQ. Due to the high variability of fish and seafood iodine concentration, fish was categorised in the FFQ as "oil-rich fish", "white sea-fish" and "other seafood" and an average portion and iodine concentration per portion was derived from a search of all relevant foods in Windiets 2005 database (Robert Gordon University, Aberdeen, UK) (Combet and Lean, 2014).

The *attitudes towards behaviour* construct included fifteen questions; four questions with three possible answers (agree / disagree / not sure (scored 4 points for positive attitudes towards increasing / including fish and seafood products answer, 0 points for negative attitude/ not sure answer), one question with possible answer on a 7-point Likert scale (from 0 to 6) and ten questions with possible answers on a 5-point Likert scale (from 0 to 4). The total score for this construct was the percentage of the maximum of all the responses (natural range 0 to 64 points).

The *subjective norms* construct included fourteen questions, of which one was in a 7-point Likert scale and the rest thirteen in 5-point Likert scale. Answers from the 7-point Likert scale were transformed from 1 to 7 points to 0 to 1.2 points and the answers from the 5-point Likert scale were transformed from 1 to 5 points to 0 to 1 points. The total score for each participant was the percentage of the maximum of all the responses (natural range 0 to 14.2 points).

The *perceived behavioural control* construct included four questions with answers on a 7-point Likert scale (from 0 to 6 points). The sum score of all questions was calculated for each participant and the *perceived behavioural control* score was the percentage of the maximum score (natural range 0 to 24 points).

The *intention* construct included three questions; two 7-point Likert scale questions scored from 0 to 6 points, depending on whether intentions were negative (minimum 0 points) or positive (maximum 6 points) and a question with two possible answers. This question was a scenario in which participants were asked to answer with a "yes" or "no", so these were scored as 6 and 0 respectively, as they favour or do not favour the behaviour, as above. All responses were allocated points and the percentage of the maximum points was the section's score for each participant (natural range 0 to 18 points).

The *knowledge* was also assessed via fourteen questions or sub questions and a score was calculated and normalised for this section, as an external to the TPB model construct. The answers to these questions were rated as correct (given 1 point) or wrong (included "not sure" answers, given 0 points) to create a knowledge score for each participant. The percentage of the maximum score was calculated for each participant (natural range 0 to 13 points).

For all the TPB constructs (including knowledge), the median (interquartile range (IQR)) score was calculated. Scores were compared between "low" (consuming less than 2 portions of fish and seafood per week) and "high" (consuming at least 2 portions of fish and seafood per week) fish consumers.

### 6.2.6 Statistics

Data analysis was performed with the statistical software SPSS version 21.0 (IBM Corporation). Normality was tested with Shapiro-Wilk normality test. Descriptive statistics were expressed as median and IQR for continuous non-parametric data and as frequencies (n) and percentages (%) for categorical data. Iodine intake was calculated from the FFQ as described by Combet and Lean (2014). Servings of fish were transformed into grams, considering as a serving 140 g of oily or white fish and 80 g of seafood. Participants who did not achieve an intake of 2 portions of fish per week, the minimum recommended by the "Eatwell Guide" (Public Health England, 2016), were classified as "low" fish consumers. Those meeting or being above the recommended weekly intake were classified as "high" fish consumers.

Group differences for continuous non-parametric variables were tested with Independent samples Mann-Whitney U test and for categorical data with Pearson Chi-Square test. Binominal logistic regression was also performed to predict a dichotomous dependant variable (*behaviour* as "low" or "high" consumers) by the constructs of the TPB. Scores were handled both as continuous variables, to find the differences between the "low" and "high" consumers, and as interval variables, in quartiles, for the purposes of the regression.

## 6.3 Results

### 6.3.1 Participants' characteristics

Between November 2016 and May 2017, 1644 responses were gathered. However, after cleaning the database for duplicate entries (n=51) and implausible responses (n=82), the final sample that was included in the analysis was n=1511 participants (Table 6.1).

In the final sample, the online questionnaire was completed by 91% (n=1379) of the participants and the paper form by 9% (n=132). Sixty percent (n=909) were females and 40% (n=602) were males. The median age of the respondents was 31 years (IQR 21-37) with the youngest participant being 14 and the oldest 82 years old. Participants were living with their partner (23%, n=342), with friends (20%, n=300), with their family (20%, n=295), in a student accommodation (13%, n=196), with their parents (11%, n=173), or alone (11%, n=165). Three percent (n=39) reported other form of living status, without specifying. In each household, there was a median of 2 adults (IQR 2-3) and no children (IQR 0), although 22% (n=326) of households had at least one child. There was no participant that reported not having access to kitchen equipment.

Table 6.1 Participants' characteristics

| Demographic data | n | % |
|---|---|---|
| Age groups | | |
| 16-29 years | 858 | 57 |
| 30-49 years | 506 | 33 |
| ≥50 years | 145 | 10 |
| Ethnicity | | |
| British | 904 | *60* |
| Other European | 434 | *29* |
| Other ethnic groups | 172 | *11* |
| Education | | |
| School level | 72 | *5* |
| College level | 581 | *39* |
| Undergraduate degree | 478 | *32* |
| Postgraduate degree | 378 | *25* |
| Educational background | | |
| Nutrition | 124 | *8* |
| Food Sciences | 46 | *3* |
| Health Sciences | 189 | *13* |
| Annual household income | | |
| <£15,000 | 500 | *33* |
| £15,001 - £30,000 | 329 | *22* |
| £30,001 - £50,000 | 248 | *16* |
| >50,000 | 185 | *12* |
| Prefer not to say | 248 | *16* |
| Main grocery shoppers | | |
| Yes | 875 | *58* |
| Sometimes | 380 | *25* |
| No | 255 | *17* |
| Main cook | | |
| Yes | 852 | *56* |
| Sometimes | 372 | *25* |
| No | 286 | *19* |
| Supplements users | 472 | *31* |

### 6.3.2 Dietary habits, seafood products preferences and health status

Three percent (n=49) of the participants were following a vegetarian diet (lacto-ovo-vegetarian, lacto- vegetarian or ovo-vegetarian) and 2% (n=26) were following a vegan diet. Another 7% (n=98) reported being pescetarians (avoiding red meat and poultry only).

Three percent (n=39) of the total study sample reported having an allergy to fish or seafood products, but only 43% of those (n=15) or 1% of the total population were diagnosed with an allergy by a healthcare professional. Furthermore, 18% (n=271) were following a weight loss diet, and 2% (n=27) were pregnant or breastfeeding when completing the survey. About half the population (51%, n=773) also reported increasing fish and seafood intake when they want to lose weight.

Participants reported having anaemia (6%, n=93), high cholesterol (4%, n=66), high blood pressure (3%, n=47), thyroid disease (3%, n=46), diabetes (1%, n=17) and other health conditions (6%, n=86), which included Inflammatory Bowel Syndrome, Crohn’s disease, Coeliac disease, asthma and fibromyalgia.

Most reported liking fish and seafood products, including white fish (81%, n=1245), oily fish (76%, n=1148), shellfish (66%, n=998) and seaweed (40%, n=599). A minority reported not liking fish and excluding it from the diet; for white fish by 4% (n=56), for oily fish by 6% (n=85), for shellfish by 3% (n=47) and for seaweed by 3% (n=43). Not liking fish but trying to include in the diet was reported for white fish by 7% (n=107), for oily fish by 14% (n=318), for shellfish by 24% (n=362) and for seaweed by 25% (n=382). Finally, 7% (n=103), 4% (n=60), 7% (n=103) and 32% (n=487) reported not having any particular feeling about those foods.

### 6.3.3 Fish and seafood consumption

The median fish and seafood servings per week calculated from the FFQ were 1.9 (IQR 0.9-3.7). Oil-rich fish consumption was 0.9 (IQR 0.5-0.9) servings per week with white fish and other seafood being consumed also a median of 0.9 (IQR 0.5-1.9) servings per week. Translating servings into amount of fish, total fish and seafood consumption in grams was calculated as a median of 233 g (IQR 131-485) per week. There was no difference in fish consumption between men and women (p=0.214).

Fifty-three percent of the participants (n=797) were “low” fish consumers. The remaining 47% (n=711) who were meeting the minimum 2 portions recommendation were categorised as “high” fish consumers. “Low” and “high” consumers differ significantly in age (25 years; IQR 21-34 vs 30 years; IQR 23-40 respectively, p<0.001).

Fresh fish (53%, n=797), followed by sushi dishes (45%, n=677) and canned fish (43%, n=648) were the types of fish most often reported to be consumed by the participants (Table 6.2).

Table 6.2 Frequency of consumption of different fish and seafood types

| | **Often** | | **Sometimes** | | **Never** | |
|---|---|---|---|---|---|---|
| | **n** | *%* | **n** | *%* | **n** | *%* |
| Fish & chips (from canteen/take away) | 127 | *8* | 820 | *54* | 546 | *36* |
| Sandwiches with fish filling | 256 | *17* | 535 | *35* | 697 | *46* |
| Fresh fish | 797 | *53* | 438 | *29* | 258 | *17* |
| Fresh seafood | 498 | *33* | 477 | *32* | 507 | *34* |
| Canned fish | 648 | *43* | 459 | *30* | 385 | *26* |
| Canned seafood | 107 | *7* | 254 | *17* | 1114 | *74* |
| Frozen fish | 474 | *31* | 518 | *34* | 491 | *33* |
| Frozen seafood | 307 | *20* | 434 | *29* | 737 | *49* |
| Ready cooked seafood dishes / meals | 118 | *8* | 364 | *24* | 996 | *66* |
| Smoked fish | 370 | *25* | 582 | *39* | 529 | *35* |
| Sushi dishes containing seafood / seaweed | 677 | *45* | 526 | *35* | 277 | *18* |

Percentages are based on the total population. Option "I don't know" (rarely selected) is not included in the table.

The cooking and eating habits were also explored by asking participants how often they cook / eat homemade food, ready meals and sandwiches. The mode for cooking and for eating homemade food made by themselves or a family member or friend was 1-2 times per day. For eating ready meals at home, eating in a restaurant or canteen and eating from shops selling sandwiches or take away food the mode was 1-2 days per month.

### 6.3.4 Iodine intake

Median total daily iodine intake from fish and seafood products was 24 µg/day (IQR 13-41). Iodine intake from dairy products was a median of 79 µg/day (IQR 62-89). The total iodine intake of the population was 122 µg/day (IQR 79-186), lower than the 150 µg/ day iodine intake recommended for adults by the WHO. "High" fish consumers had significantly higher iodine intake compared to "low" fish consumers (149 µg/day; IQR 104-222 vs 102 µg/day; IQR 60-149, $p<0.01$). Men had also higher daily iodine intake compared to women (129 µg/day; IQR 80-200 vs 118 µg/day; IQR 79-180, $p=0.05$).

### 6.3.5 Drivers of choice

Taste was reported as the main driver, with 85% (n=1281) of the participants selecting "very much" (4 & 5 in the 5-point Likert scale), followed by freshness (65%, n=976), cost (61%, n=918) and convenience of preparation (54%, n=813). Recommendation by healthcare professionals (GP, nutritionist, dietician, other) was rated as high influential factor (scores 4 and 5) by 40% (n=605), but when this advice comes from a health expert in the media the percentage drops at 21% (n=322) (Figure 6.1).

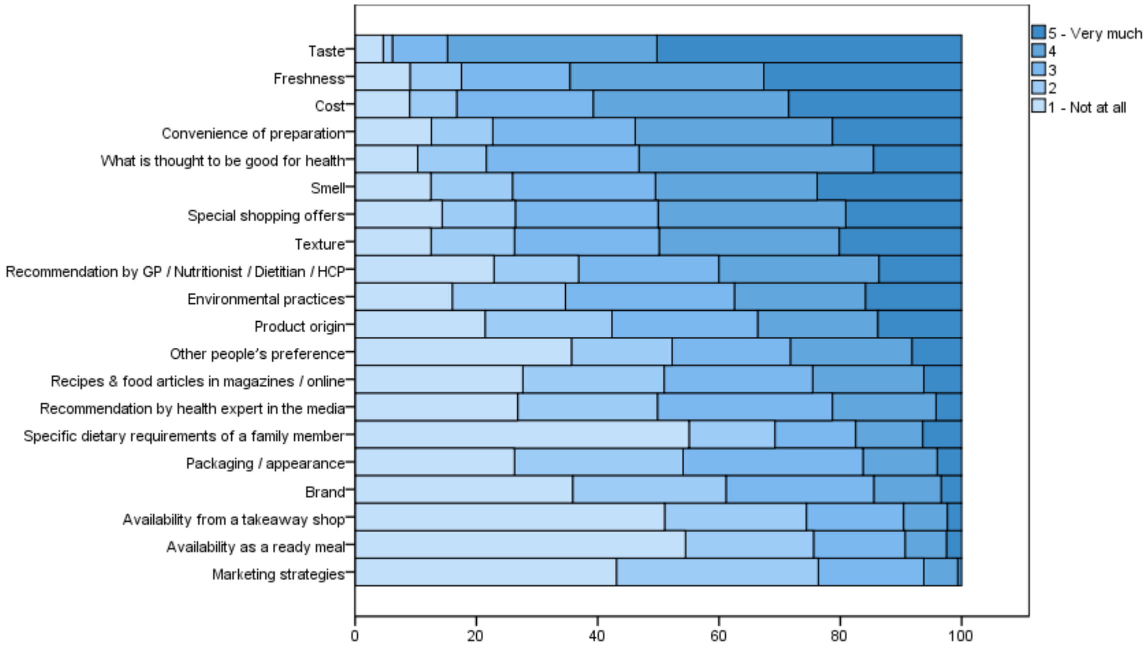


Figure 6.1 Factors influencing choice of fish and seafood products.

Participants that had experienced a pregnancy (themselves or their partner) were asked about their understanding of the provided recommendations on fish and seafood consumption in pregnancy. In a 7-point Likert scale that represented understanding, 33% (n=115) reported understanding well the recommendations (6 or 7 points).

### 6.3.6 TPB constructs scores

For all the TPB constructs (including knowledge) the median (IQR) score was calculated. Scores were compared between “low” and “high” fish consumers and are shown in Table 3. Independent samples Mann-Whitney U test was performed to compare the scores between those two groups and knowledge, *attitudes towards behaviour*, *perceived behavioural control* and *intention* were found to be significantly higher in the high consumers group of the population. Figure 6.2 shows the difference in median scores of the TPB constructs between the “low” and “high” consumers. Within the total sample, women had significantly higher knowledge and *intention* scores compared to men ($p<0.001$ and $p=0.002$ respectively).

Table 6.3 TPB constructs’ scores in the “low” and “high” fish and seafood consumers’ groups

| | **“Low” consumers n=797** | | **“High” consumers n=711** | | |
|---|---|---|---|---|---|
| | **Median** | ***IQR*** | **Median** | ***IQR*** | **p** |
| Knowledge | 55 | *41-66* | 62 | *52-72* | *<0.01* |
| ATB | 40 | *31-53* | 47 | *37-56* | *<0.01* |
| PBC | 67 | *54-79* | 79 | *67-88* | *<0.01* |
| SN | 35 | *28-41* | 36 | *29-42* | *0.077* |
| INT | 72 | *50-94* | 89 | *67-100* | *<0.01* |
| Behaviour (serv/week) | 0.9 | *0.5-1.9* | 3.7 | *2.8-6.1* | *<0.01* |

Knowledge, ATB, PBC, SN and INT scales are 0-100. ATB: Attitudes towards behaviour, PBC: Perceived behavioural control; SN: Subjective norms; INT: Intention

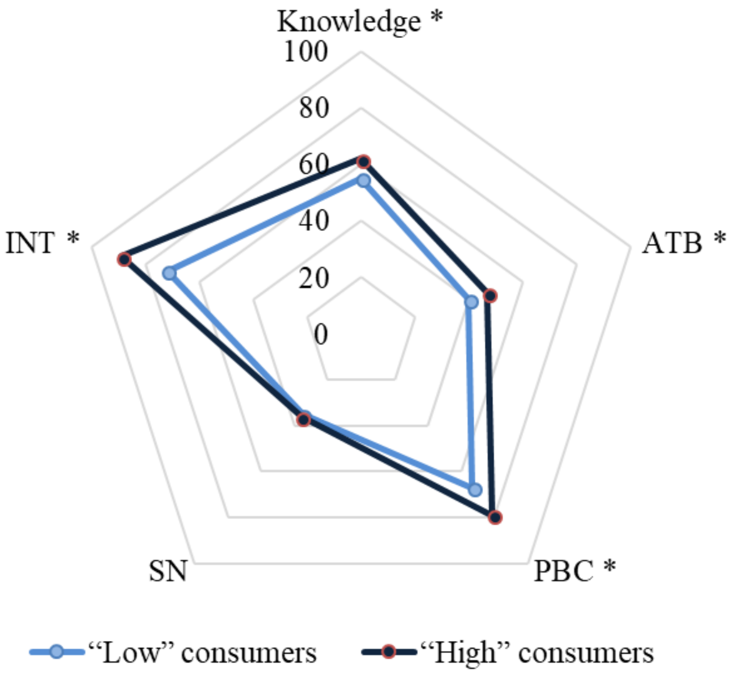


Figure 6.2 Spider graph of TPB constructs' scores for "low" and "high" consumers of fish and seafood products.
Constructs with * are significantly different between the "low" and "high" consumers ($p<0.01$); ATB: Attitudes towards behaviour, PBC: Perceived behavioural control; SN: Subjective norms; INT: Intention

A binomial logistic regression was performed to ascertain the effects of *attitudes towards behaviour*, *perceived behavioural control*, *subjective norms*, *intention* and *knowledge* on the likelihood that participants reach the recommendation for fish intake. The logistic regression model was statistically significant, $\chi^2(15)=215{,}919$, $p<0.0005$. The model explained 16% (Nagelkerke $R^2$) of the variance in meeting the recommended fish intake and correctly classified 66% of cases. Sensitivity was 65%, specificity was 68%, positive predictive value was 64% and negative predictive value was 68%. Of the five predictor variables only four were statistically significant: *attitudes towards behaviour*, *perceived behavioural control*, *intention* and *knowledge* (as shown in Table 6.4). Increasing those scores (falling to a higher quartile) was associated with an increased likelihood of meeting the recommended fish intake. The model did not control for any other variables (e.g. income, education).

Table 6.4 Binary logistic regression on TPB constructs' effect on the likelihood to achieve the recommended 2 portions of fish per week.

| | **B** | **SE** | **Wald** | **df** | ***p*** | **Odds ratio** | **95% CI for odds ratio** | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | **Lower** | **Upper** |
| **Knowledge Quartile 1 (ref)** | | | 24.337 | 3 | 0.000 | | | |
| Knowledge Quartile 2 | 0.382 | 0.16 | 5.658 | 1 | 0.017 | 1.47 | 1.07 | 2.01 |
| Knowledge Quartile 3 | 0.731 | 0.16 | 20.624 | 1 | 0.000 | 2.08 | 1.52 | 2.85 |
| Knowledge Quartile 4 | 0.649 | 0.17 | 15.486 | 1 | 0.000 | 1.91 | 1.39 | 2.65 |
| **ATB Quartile 1 (ref)** | | | 19.961 | 3 | 0.000 | | | |
| ATB Quartile 2 | 0.544 | 0.16 | 11.363 | 1 | 0.001 | 1.72 | 1.26 | 2.37 |
| ATB Quartile 3 | 0.595 | 0.16 | 13.462 | 1 | 0.000 | 1.81 | 1.32 | 2.49 |
| ATB Quartile 4 | 0.662 | 0.17 | 16.026 | 1 | 0.000 | 1.94 | 1.40 | 2.68 |
| **SN Quartile 1 (ref)** | | | 34.535 | 3 | 0.000 | | | |
| SN Quartile 2 | 0.374 | 0.16 | 5.471 | 1 | 0.019 | 1.45 | 1.06 | 1.99 |
| SN Quartile 3 | 0.551 | 0.16 | 11.796 | 1 | 0.001 | 1.74 | 1.27 | 2.38 |
| SN Quartile 4 | 0.987 | 0.17 | 33.558 | 1 | 0.000 | 2.68 | 1.92 | 3.75 |
| **PBC Quartile 1 (ref)** | | | 1.707 | 3 | 0.635 | | | |
| PBC Quartile 2 | -0.023 | 0.16 | 0.021 | 1 | 0.884 | 0.98 | 0.71 | 1.34 |
| PBC Quartile 3 | 0.158 | 0.16 | 0.948 | 1 | 0.330 | 1.17 | 0.85 | 1.61 |
| PBC Quartile 4 | -0.005 | 0.16 | 0.001 | 1 | 0.977 | 1.00 | 0.73 | 1.37 |
| **INT Quartile 1 (ref)** | | | 39.882 | 3 | 0.000 | | | |
| INT Quartile 2 | 0.642 | 0.17 | 15.060 | 1 | 0.000 | 1.90 | 1.37 | 2.63 |
| INT Quartile 3 | 0.790 | 0.17 | 22.524 | 1 | 0.000 | 2.20 | 1.59 | 3.05 |
| INT Quartile 4 | 1.067 | 0.17 | 37.402 | 1 | 0.000 | 2.91 | 2.07 | 4.09 |
| Constant | -2.172 | 0.21 | 104.751 | 1 | 0.000 | 0.11 | | |

ATB: Attitudes towards behaviour, PBC: Perceived behavioural control; SN: Subjective norms; INT: Intention

## 6.4 Discussion

### 6.4.1 Main findings and barriers' exploration

This study explored the perceptions of the general UK population on fish and seafood products. Fish is recommended as part of a healthy balanced diet, to be consumed twice a week, with one portion being oily fish (Public Health England, 2016). However, 53% (n=797) of the population in this study was not meeting this recommendation, in agreement with the NDNS data that show an inadequate intake of fish in the UK population (average of 147 grams per week) (Bates et al., 2016).

The TPB, in accordance to a previous study in Iran (Aghamolaei et al., 2012), was found to be predictive of whether people would achieve the recommended intake of fish in their diet, explaining 16% of the variance. More factors should be examined as predictors of fish consumption in the population, as a high proportion of the variance remains unexplained from the TPB model. Similar to the findings from the “Dairy and Health Survey” (Chapter 5), knowledge of recommendations and nutritional value of seafood products is a significant contributor in the prediction of fish consumption. Knowledge and awareness are indicated to be important in dietary choices and interventions aiming to alter dietary habits should target their increase via education. Similarly, *intention* and *attitude towards behaviour* significantly add to the model and differ between “low” and “high” fish consumers. Behavioural interventions should therefore target changing attitudes to more positive in regards to seafood products. In contrast to the “Dairy and Health Survey” though, PBC is also a significant contributor in this case. This can be linked to the barriers and facilitators (not being part of the TPB dimensions) explored in the survey. Taste and freshness are the main influential factors in the choice of fish and seafood in this study, in agreement with findings on the “Dairy and Health Survey” (Chapter 5). However, cost and convenience of preparation follow, which are factors that can be perceived as being beyond a person’s direct control, and can be considered as barriers for increased fish consumption. The only dimension of the TPB which did not differ between “high” and “low” fish consumers and did not contribute to predicting behaviour was *subjective norms*. In Chapter 4, women in the perinatal period reported an influence from their partner, children or family in their choices. However, this might have to do more with difficulties in cooking several different meals in a household when a family member excludes fish from the diet, rather than what the beliefs of other people are. Many studies omit subjective norms from the predictive factors of dietary choices, due to low involvement of decision and higher involvement of preferences and nutritional needs (Mahon et al., 2006).

Perception of healthiness of a product has also been found to influence the choice to include or exclude fish and seafood in the diet, being the fifth top factor of influence. The American Heart Association, reports the cardiovascular health benefits of fish and omega 3 fatty acids, and recommends eating fish at least twice weekly, focussing on oil-rich fish consumption (Lichtenstein et al., 2006). However, there are potential risks due to exposure to environmental contaminants (i.e. PCBs, polybrominated diphenylethers (PBDEs), organochlorine pesticides (OPs), polycyclic aromatic hydrocarbons (PAHs), mercury, cadmium, arsenic, lead) (Domingo, 2007). Risks versus benefits of fish consumption are in the centre of public health attention and have caused debates around that issue, clearly concluding that a dose-harm and dose-benefit are needed to shape recommendations (Gochfeld and Burger, 2005). In the UK, a risk assessment conducted in 2007 found that 140 g of shark, swordfish or merlin, if consumed once a week, could lead to 40-90% intakes of methyl mercury higher than the guideline (3.3 mg per kg of body weight) in adults. In addition, farmed salmon has been found to contain higher environmental contaminants levels (PCBs, polybrominated diphenyl ethers, organochlorine pesticides) compared to wild salmon, raising a concern for regular consumers (more than 1-3 portions/week) (Easton et al., 2002). However, depending on the stage of life, potential risks might differ. Neurotoxicity during neurodevelopment can be critical, and for this reason guidelines are different for pregnancy, lactation, preconception and young children (Maycock and Benford, 2007). During pregnancy however, recommendations about fish and seafood consumption become confusing for women. As a result, women exclude seafood products from their diet due to the uncertainty and worry caused by the confusing recommendations (Chapter 4). In this study, only 33% of the population that had experienced a pregnancy found the fish recommendations clear, agreeing with the perceived confusion that fish recommendations cause during this stage of life, highlighting the need of clarification in order to avoid total exclusion of seafood from the diet.

Around 38% of the study sample reported being influenced in their choice by environmental practices, highlighting this factor as important for more than a third of the population. Welfare and environmental risks remain controversial topics. Concerns over the impact on the environment is one of the factors that influence the dietary choices of the rising vegetarian and vegan populations (de Backer and Hudders, 2015) Vegetarians and vegans score higher in animal welfare questions compared to omnivorous populations. Welfare issues related to aquaculture are complex and currently a topic of research investigation (Ashley, 2007). In an online Danish survey, 48% of the population showed willingness to pay extra for farmed fish welfare (Hans Stubbe and Yingkui, 2011). However, this would potentially increase the cost barrier for a significant part of the population, as mentioned earlier.

### 6.4.2 Iodine in fish and seafood

Fish and seafood products are a naturally rich source of iodine. The variety of available fish and seafood products also creates a wide spectrum of food choices with a range of iodine content. White fish, such as haddock and cod, contains more iodine (approximately 48 μg/ 100 g in oily fish versus 105 μg/ 100 g in white fish) than oil-rich fish based on the McCance and Widdowson's composition of foods data (McCance and Widdowson, 2002). Iodine has been also found to vary even within the same species of fish and to decrease from the skin to the inner part of the fish fillets, being up to 20 times higher is skin in marine species such as cod (Karl et al., 2001). Marine fish contains the higher amounts of iodine, ranging from 40 to 69 μg/100 g, which is also approximately 6-fold higher compared with freshwater fish (Haldimann et al., 2005). Cooking can affect the iodine content of fish, with losses varying in average from 20% in fried fish, to 23% in grilled fish and 58% in boiled fish (Harrison et al., 1965). Other seafood (including prawns, crab, and lobster) have an average iodine content of 92 μg/ 100 g and are also a good source of iodine. In this study, the most frequently reported fish type consumed was fresh fish, followed by canned fish, although cooking methods were not explored. Fish and chips from canteen or take-away shops, although being a traditional UK meal, was reported to be consumed more than twice a month by 8%, and sometimes (less than twice per month) by 54% of the population. Fish contributed only towards 16% of the WHO recommended adult intake of 150 μg/day (median daily intake 24 μg/day; IQR 13-41). Due to fish intake remaining low in the UK, there is a potential to increase and contribute to all groups of the population achieving a sufficient iodine intake.

Seaweed is also a rich source of iodine, suitable for vegan and vegetarian populations, consumed (grouped with sushi) more than twice monthly by 45% of the population. While sushi dishes have been reported to be consumed at least once per year by 45% of the population (Brunstrom et al., 2010), less frequently in comparison to this study, they mostly contain Nori seaweed, with a lower iodine content of 16 μg of iodine per gram (an average sheet of Nori being approximately 3 grams) (Teas et al., 2004). In the present survey, the type of seaweed consumed was not assessed, which is important due to the very broad iodine level in seaweed products (range 11-6118 μg/g of dried seaweed). This could lead to an iodine excess beyond the European Tolerable Upper Limit (TUL) of 600 μg daily. Labelling of seaweed-containing products is generally poor, with limited information on iodine content or seaweed species on the product packages (Bouga and Combet, 2015). Only 10% of the seaweed-containing products stated information regarding iodine content, whilst 18% enabled its estimation. A total of 26 products could lead to an intake above the adult TUL if consumed (Bouga and Combet, 2015).

### 6.4.3 Strengths and limitations

This study was a cross-sectional survey designed to explore people's perceptions of fish and seafood products. The sample size of more than 1500 people living in the UK, of different ethnicities, educational and socio-demographic backgrounds allowed a representative picture of the UK population's fish intake and perceptions. The questionnaire was administered both online and in hard copy, in order to reach people of all ages and backgrounds, although more younger people filled in the survey, as online recruitment reached a wider population of the younger group. In addition, the use of a validated FFQ (Combet and Lean, 2014) allowed the quantification both of the behaviour of consuming fish and seafood products and the iodine intake from this food group, as one of the best ways to capture habitual intake of foods and nutrients. Through the TPB cognition model, the perceptions of the consumption of fish and seafood products were explored for the first time in the UK population.

Surveys available online can often attract only a sample with specific characteristics (Wright, 2005). However, our sample included a representative for the UK vegetarian population of 5%, including the vegan population, as well as a range of sociodemographic characteristics, which can be considered as a strength.

The online questionnaire was designed in a way that disallowed participants to leave questions unanswered, or to give multiple answers in a question, in an attempt to minimise the amount of missing data. However, in the paper copy, although all questionnaires were checked by the researcher, mistakes in the completion of the questionnaires could not be avoided and missing data occurred. The dataset was cleaned based on implausible combination of responses, aiming to exclude any questionnaires with randomly answered questions.

Finally, perceptions were captured in a quantitative way, which does not allow deep exploration of all the angles of people's beliefs and thoughts on a topic. However, a qualitative design would not allow the recruitment of a big sample size and the study would not be representative for the UK population.

## 6.5 Conclusion

Fish and seafood products are related to health benefits, as a rich source of protein, omega 3, vitamins and minerals, including iodine. However, fish intake does not reach the recommended 2 portions per week in the UK population, leaving more than half of the population below the recommendation and resulting in a low contribution to the required iodine intake. Based on the TPB, consumers that achieve the recommendations have higher *knowledge*, *perceived behavioural control*, *intention* and more positive *attitudes* towards fish consumption. Barriers and facilitators explored indicated that apart from the sensory attributes of those foods, factors associated with lower self-control, such as cost and convenience, influence the choice of seafood. Furthermore, health related risks, welfare and environmental practices are issues that are debated and impact on the decision of consumers on whether to consume fish or not. Clear recommendations, specific for each life stage, and related to portions and frequency of the species that the population should limit, would potentially help people make the right dietary choices and increase fish consumption, and consequently iodine intake.

# Chapter 7 - Food choices in early pregnancy – an interim analysis of the Pregnancy Iodine Choices (PICk) nutrition education intervention

## Abstract

Insufficient iodine intake is a contemporary challenge for pregnant and lactating populations, due to the irreversible neurological consequences it may cause to the fetus and infant. Public health strategies have focused on legislation around salt and food fortification and more rarely supplementation, with limited results for pregnant women. Low awareness about iodine has been associated with low iodine intake, and women in the UK lack both awareness and updated legislation. The aim of this study is to assess the feasibility of an intervention which would aim to increase iodine status of pregnant women and women trying to conceive, through an educational intervention targeting iodine related knowledge and awareness.

A single-blind randomised controlled trial is taking place in Glasgow, UK. Eligible women are either trying to conceive, or up to 14 weeks pregnant. The duration of the study is 12-weeks and involves three meetings (baseline, after 6 and after 12-weeks) in which participants fill in demographic, dietary and knowledge and awareness questionnaires, provide 10 spot urine samples and a dried blood spot sample at each meeting. Women are randomly allocated to the control or intervention group. The intervention includes receiving periodical text messages on the importance of iodine during pregnancy, iodine-rich food sources and advice on ways to include them in the diet. Iodine intake and urinary iodine concentration (UIC) will be the primary study outcomes and iodine knowledge and awareness will be secondary outcomes of the intervention, while for the present internal pilot, feasibility and acceptability of the intervention are examined.

A total of 33 women were included in the present analysis, of which 18 participants were in the control group and 15 in the intervention group. Dropout rate of the study was 24%, higher than the 15% initially calculated. The two groups did not differ in their demographic characteristics. The educational intervention was overall feasible, well received, and burden was reported as low for participants, and led to an increase in iodine related knowledge and confidence levels. The intervention group increased in confidence in achieving an adequate iodine intake for pregnancy, which was higher at 6-weeks compared to the control group. The median of individual differences in knowledge of iodine sources was positive and by 2 points higher compared to the control group. Women in the intervention group self-reported making dietary changes which would favour iodine intake at 6-weeks compared to the control group, but these changes were not detectable in the dietary intake from the FFQ or the UIC.

The present feasibility study has indicated that a larger intervention is promising in contributing to the increase of iodine status of women in pre-conception and early pregnancy, due to its acceptability. However, more participants are needed to explore whether the intervention can significantly increase knowledge and awareness and cause a respective increase in iodine status of the participants.

## 7.1 Introduction

Iodine insufficiency, during pregnancy or infancy, is the most preventable cause of brain retardation for the infant and consequences range from loss of IQ to cretinism, depending on the severity of deficiency. Women in the UK have an insufficient iodine status during pregnancy, which also persists postnatally for lactating mothers (Chapter 2) (Bath et al., 2013, Bath et al., 2014c, Barnett et al., 2002, Pearce et al., 2010). In Norway, pregnant women and vegans have been recently described as the groups of the population with the higher probability of being iodine insufficient (Brantsæter et al., 2018). Both countries have voluntary salt iodisation programs in place, and milk is the main source of iodine, which is due to the iodine fortification of cow fodder (Nyström et al., 2016). Availability of iodised table salt for household use is also very low in both countries (21.5% weighed availability in the UK) (Bath et al., 2014a).

In the UK, 60% of women in pregnancy do not meet the 250 μg/day World Health Organisation (WHO) recommendation of intake (Combet et al., 2015). A number of studies have emphasised the lack of knowledge and awareness of the importance and role of iodine in the general population (Combet et al., 2015, Charlton et al., 2010b, Kim and Jeong, 2014, Nithiananthan et al., 2013, Buxton and Baguune, 2012, Bouga et al., 2018a). This lack of knowledge has been associated with low dietary iodine intake amongst 520 females residing in the UK, posing knowledge and awareness as important aspects of iodine insufficiency, and the relevance of educating women in pregnancy has been highlighted (O'Kane et al., 2016). Over half of mothers (55%) were unable to identify correct sources of iodine, commonly mistaking salt (21%) and vegetables (54%) as iodine-rich foods (Combet et al., 2015). Chapter 4 examined the perceived quality and content of received dietary guidance in pregnancy and focussed on points pertinent to iodine nutrition. The guidance that was received was perceived to be unclear and confusing, focussing on following a healthy balanced diet and taking supplements. However, most women (87%) reported willingness to modify dietary behaviour if information related to the importance of iodine in pregnancy was delivered to them, so that they also have the “know-how” apart from the awareness and knowledge on a topic. For this purpose, women proposed desirable ways and characteristics of received guidance during pregnancy (Bouga et al., 2018a).

There is a lack of iodine interventions in pregnancy which do not focus on supplementation or salt fortification (Chapter 3). The study by Amiri et al. (2017) in Iranian pregnant women found increased knowledge, awareness and practice (KAP) scores on iodine questions (on low iodine intake consequences and use of iodised salt) after two face-to-face educational sessions with leaflets and follow-up phone calls, mainly to address participants' questions. There was no difference in urinary iodine concentration (UIC) between the intervention and control groups at follow up (121 μg/l; IQR 36-156 vs 78 μg/l; IQR 50-190, p=0.30). The single spot samples collected to assess iodine status could potentially be the reason for which differences in UIC were not detected. Furthermore, the main focus of this study was the use of iodised salt, rather than the increase of iodine through the consumption of other iodine-rich food sources. In countries with legislation on iodine supplementation, ethical implications are associated with placebo-controlled studies in pregnancy. In the UK, concerns over the conflicting message that salt iodisation would convey may have discouraged policymakers from changing the legislation to mandate salt iodisation, and no guidelines on supplementation exist either. The absence of prophylaxis in the UK provides an ideal ecological terrain to study the impact of a food-based intervention to tackle iodine insufficiency and its endocrine and neurodevelopmental consequences.

The increased use of mobile devices has led to the development of mobile health (mHealth), the medical and public health use of mobile technology (Kay et al., 2011). In the UK, 95% of households own a mobile phone (Office for National Statistics, 2017). By using this means to educate women of childbearing age there are no minority groups that are unable to reach this information. Strategies based on mHealth are implemented worldwide and pregnant women embrace the use of technology for effective delivery of antenatal care information (Willcox et al., 2015). Mobile messaging has been shown to be effective in improving pregnancy related behaviours, such as HIV outcomes in HIV positive pregnant women (10% increased chance of a normal vaginal delivery, 86% lower chance of delivering a low-birth weight infant) (Coleman et al., 2017) and antiretroviral treatment adherence (relative risk for non-adherence 0.81, 95% CI 0.69–0.94; p=0.006) (Lester et al., 2010). A systematic review of mHealth interventions concluded that mobile messaging can have positive impact on HIV testing, and potential facilitators include low-cost, confidentiality and motivational communication (Conserve et al., 2017). Lately, a two-way text-based intervention has been also developed in South Africa for pregnant women and new mothers, including advice on diet, which also allows women to respond to texts and ask questions, with high acceptability (Skinner et al., 2018). In adults, mHealth interventions on weight management have favoured weight loss (-2.56 kg (95% CI= -3.46 to -1.65); $I^2$=88.9%, p for heterogeneity <0.0001) (Siopis et al., 2015).

Based on the results of Chapters 4, 5 and 6, an educational intervention with information on iodine and its importance in pregnancy was designed, aiming to guide women in making food choices favouring iodine intake and increasing their iodine status. The intervention is designed with participants' involvement and considers their views on what the desirable way of getting information would be, informed by an in depth qualitative work (Chapter 4). It also considered the factors (barriers and facilitators) which influence the choice of iodine rich foods identified by two extensive surveys on dairy and seafood products (Chapters 5 and 6).

A common problem in behaviour change interventions is the lack of reproducibility. Effectiveness can not be assessed in meta-analyses due to use of poorly defined behaviour change techniques. To address the difficulty of unstandardised interventions (approaching targeting behaviour in different ways), a taxonomy of behaviour change techniques (BCTs) was developed, linked to the theory (Abraham and Michie, 2008). A systematic review by Duff et al. (2017) identified all the electronic Health (eHealth) interventions that aimed to increase physical activity in adults with cardiovascular disease that have used BCTs. The most common technique was providing information about health consequences (78% of studies), followed by goal setting (74% of studies). The authors highlighted the importance of use of BCTs in health-related interventions, to be able to assess the effectiveness of different techniques and inform healthcare policy (Duff et al., 2017). In the present study, techniques from the BCTs were implemented in the design of the intervention, to ensure optimal effectiveness and comparability with similar interventions.

The aim of this study is to test whether an educational intervention in women in preconception and early pregnancy stages is acceptable and effective. As knowledge and awareness have been associated with iodine status, the hypothesis is that increasing those elements (importance, sources, and requirements of iodine during pregnancy) will lead to changing practice and increased iodine intake. If the intervention succeeds in increasing knowledge and awareness, the proposed expected effect is a decreased proportion of pregnant women not meeting the iodine recommended 250 μg iodine per day.

Research question was:
Is an intervention with simple dietary guidance on iodine feasible, acceptable, and effective in pregnancy?

This study will inform a larger intervention study, which will increase the sample size. The research question of the larger study will be:

Does increased knowledge and awareness on iodine in pregnancy lead to a better iodine status?

## 7.2 Methods

### 7.2.1 Study design and participants

The study is a single-blinded, randomised controlled trial (RCT) with a duration of 12-weeks. Recruitment for this study is still ongoing. Women, in preconception and up to 14 weeks pregnant, are recruited and randomised either to the control or to the intervention group.

The study is advertised using posters targeted at trying to conceive and pregnant women, in public and private locations (libraries, cafes, shopping centres, community centres, pharmacies) after seeking permission. The study is also advertised on social websites (e.g. Facebook, Gumtree, Netmums, Mumsnet), targeted to women either pregnant or trying to conceive. Participants are also recruited face-to-face in antenatal classes, cafes, libraries, shopping centres, community centres, and pharmacies, after obtaining permission for access.

During face-to-face recruitment, participants are informed about the study by the researcher (verbally) and are given the information sheet to read in detail. Participants can decide to opt-in once they have read the information sheet and are satisfied that their questions have been answered, or can have a cooling period to decide to participate. The researcher ensures that all prospective participants meet the inclusion criteria and goes through the participant information sheet and consent form. Participants are officially recruited once they have signed the consent form during a face-to-face meeting. Contact details are also obtained at the same time with consent.

Inclusion criteria include actively trying to conceive, or being pregnant (first trimester, 0 to 14 weeks gestational age), speaking English fluently, and being a self-reported healthy adult woman. Exclusion criteria include abnormal pregnancies, mothers with known thyroid disorders, renal disease, multiple pregnancies, development of gestational diabetes, participation in another trial, not owning a mobile phone, being followed by a dietitian during the study period and women with existing or past eating disorders.

Participants are assigned either to the intervention or to the control group. Stratified randomisation is performed to control for two covariates; education (university degree / non-university education) (Combet et al., 2015) and pregnancy status (pregnant / trying to conceive) (due to potential higher motivation for dietary changes in pregnancy, as shown in Chapter 4). Within these four blocks, women are randomly allocated to control or intervention group by selecting a paper with the group from a concealed envelope. Both groups (control and intervention) are informed that the main aim of the study is to assess the impact of food guidance on the micronutrient intake during and prior to pregnancy. The intervention group receives texts with detailed information focussing on nutrition and iodine-rich foods specifically. The information sheet has information on all the study procedures but the focus on iodine remains discreet, to avoid unintended bias in response from participants.

### 7.2.2 Intervention and study procedures

The intervention includes weekly text messages during the study period, designed by the candidate, and focusses on pregnancy nutrition and iodine-rich foods. The choice of mHealth relies on the analysis of the interviews of Chapter 4, in which stakeholders (women in the perinatal period of life) proposed preferred characteristics and ways of delivery of dietary guidance. The texts were based on the taxonomy of behaviour change techniques (BCTs) used in interventions (e.g. prompt intention formation, provide information on consequences, provide information about behaviour health link, time management) (Abraham and Michie, 2008), the nudge theory and covered themes identified in Chapters 4, 5 and 6 (i.e. confusing recommendations in pregnancy (Combet et al., 2015) and targeting barriers in avoiding iodine rich foods) (appendix 6). The wording of the text messages was decided by the candidate to be simple, comprehensive and motivating and was reviewed by the candidate's supervisor. Choice of words and content of messages was performed with caution not to motivate any unwanted behaviour changes, not to cause confusion and not to be in contrast with any recommendations for pregnancy. The control group receives no intervention, and only text reminders regarding the study, planned visits and study logistics to limit dropouts. All texts are scheduled at specific dates and times to be consistent between participants. The software TextMagic (TextMagic LTD, Cambridge, UK) is used for all scheduled texts.

The study involves three meetings with the participants, at baseline, after 6-weeks and after 12-weeks. In each meeting, participants are asked to fill in questionnaires (demographic characteristics (visit 1), a food frequency questionnaire (FFQ) (visits 1, 2 and 3), a knowledge and awareness questionnaire (visits 1, 2 and 3), a dietary changes questionnaire (visits 2 and 3), a study assessment questionnaire (visits 2 and 3) and a study debrief questionnaire (visit 3). They also provide 10 spot urine samples and a dried blood spot sample.

All study documents are presented in appendix 6.

### 7.2.3 Outcome measures

Due to PICk study still ongoing, The main aim of the present analysis, is to assess the feasibility and acceptability of the intervention and of randomisation.

However, the design of the larger intervention and its outcomes are also presented in the present Chapter. The primary outcome measure of the PICk study will be maternal iodine status, measured as:

1) UIC measured by colorimetry
2) Dietary iodine intake, measured with a validated food frequency questionnaire (FFQ)

The two measurements, in combination, provide information on the iodine status of the women. Iodine awareness and knowledge, measured by a questionnaire, will also be secondary outcome measures.

### 7.2.4 Dietary assessment

Iodine intake is calculated from a previously validated FFQ (Combet and Lean, 2014). The questionnaire was previously described in Chapters 2 and 4. The FFQ is completed at all timepoints. Dietary changes are also assessed via a questionnaire in which different foods are self-assessed for changes (Combet et al., 2015). Participants are asked whether they increased, maintained, decreased, completely stopped or never eat certain foods since their previous study meeting (6 previous weeks).

### 7.2.5 Knowledge and awareness assessment

A questionnaire was designed to assess participants' knowledge and awareness of pregnancy recommendations and iodine nutrition. The questionnaire was based on previous knowledge and awareness questionnaires, described by Combet et al. (2015) and in Chapter 4. However, as the focus on iodine is not revealed to participants until the end of the study, questions also focus on other nutrients (mainly iron and folic acid). Specifically, the questionnaire (presented in Appendix 6) includes:

[1] A question on knowledge of relating nutrients' recommendations with food choices (yes/ no/ sometimes); a question on interest on pregnancy nutrition (7-point Likert scale);

[2] A self-assessment of awareness of dietary and lifestyle guidelines specific to pregnancy (7-point Likert scale);

[3] A question which includes dietary and lifestyle recommendations for pregnancy to select if participants are aware of;

[4] A question on whether participants have been informed (or have heard of) on healthy eating in pregnancy and several nutrients (folic acid, iron, iodine, calcium, vitamin A and vitamin D);

[5] A question on whether participants are aware that during pregnancy iodine / iron / folic acid are important for healthy development of the unborn baby (yes / no / don't know);

[6] A question on confidence on how to achieve an adequate intake in pregnancy for iodine / iron / folic acid;

[7] A question on food sources of iodine / iron / folic acid. A score is created for knowledge of sources, which is a sum of the correct chosen foods subtracting the sum of the wrongly chosen foods, to correct for the impact of chance.

### 7.2.6 Samples collection and measurements

Participants are given 10 pots for spot urine samples collection at each visit and are asked to collect 10 urine samples over 3-4 days. For each sample date and time of collection is noted. Samples are collected by the researcher 3-4 days after recruitment, and on the second and third study appointments.

UIC is measured in all urine samples. UIC is determined with the ammonium persulfate digestion on microplate colorimetric method (APDM) based on the Sandell-Kolthoff reaction (Ohashi et al., 2000) (described in Chapter 2, paragraph 2.2.3). The mean value of the 10 spot samples in each time point is calculated and represents the UIC of each participant.

A finger prick dried blood spot sample is taken from each participant in each visit by the researcher. Thyroglobulin is to be measured at each timepoint to assess differences in levels between the three visits (results not included in this thesis).

### 7.2.7 Study assessment

The study burden for the participants, the quality of the intervention (text messages and overall study communication) and the usefulness of text messages in the provision of dietary guidance are examined. The study is assessed with two similar questionnaires, one for the control and one for the intervention group. This is the only study questionnaire which differs slightly between the two study groups, due to questions that would allow participants to become unblinded. The questions are in the form of 7-point Likert scales and focus on: how the study enables positive dietary changes; whether the received messages aid the better understanding of pregnancy recommendations; whether the use of mobile technology is an appropriate means of getting information; rating the quality of the text messages and facts provided; rating the helpfulness and motivation driven by the text messages to make dietary changes; and rating the overall burden created by the study requirements (meetings, samples collection, questionnaires). Two more questions ask the participants about the frequency of reading the text messages and clicking the included links (only applicable in intervention group) (described in Appendix 6).

After completion of the last study meeting, a study debrief questionnaire is offered to all participants. The aim of this questionnaire is to explore whether participants knew to which study group they were allocated (control or intervention) and whether they understood the main aim of the study. A 7-point Likert scale also rates the overall burden of the study for the participants.

### 7.2.8 Statistics and presentation of results

In this Chapter data were used to assess acceptability and feasibility of the larger intervention. Data related to iodine intake and excretion, knowledge and awareness were also explored and are presented as preliminary results of the larger intervention. Descriptive statistics were reported using median and interquartile range (IQR) for non-parametric data and mean and standard deviation (SD) for parametric data in continuous variables, and in frequencies and percentages in categorical data. Results from 7-point Likert scale questions were calculated as medians (IQR).

Results of recruitment, dropout rate and study assessment from participants were presented with descriptive statistics. Actual clicks to the links included in the text messages were examined, in relation to reported clicks from the participants.

The data were not powered to detect differences in the main and secondary outcomes of the larger intervention, but the plan of the future analysis is described in this Chapter.

The primary aim of the larger study is to decrease the proportion of women not meeting the recommended intake for iodine. Based on a proportion of 60% of women currently not meeting the 250 μg/day recommended intake (Combet et al., 2015), a sample size of n=84 in total (42 per group) would allow to detect a decrease in proportion down to 30%. This is achievable based on the percentage of women with an intake of 150-249 μg/day, who could increase consumption by 100 μg/day (equivalent to a 200 ml portion of milk and a 125 g portion of yoghurt per day) and therefore meet the threshold. Adjusting for 15% dropout, a sample of 50 per group would be sufficient.

Normality of data will be tested using the Shapiro-Wilk test. Differences between groups at baseline, 6 and 12-weeks will be explored for categorical variables with Pearson Chi-Square test or Fisher's exact test (when more than two categories existed), for continuous parametric variables with independent samples t-test and for continuous non-parametric variables with Mann-Whitney U test. The effect size of the intervention on the main and secondary outcomes will be tested by comparing the delta difference between baseline and 12-weeks.

Differences between the three time-points within each group will be tested with Friedman's test for continuous non-parametric data, Cochran's Q test for differences in proportions for dichotomous variables and Friedman test for differences in proportions of multinomial variables. The Wilcoxon signed rank test will be used to compare baseline and follow-up measures within each group for continuous data, when comparing two timepoints. The statistical software to be used for the analysis will be SPSS version 20 (IBM Corp., Armonk, NY).

The above mentioned analysis has been performed in this part of the study population as well in order to present the large study's outcomes and variables in detail, although the limitations of the sample size are appreciated and results should be interpreted with caution.

## 7.3 Results

### 7.3.1 Recruitment and participants characteristics

Between March 2017 and April 2018, 50 participants were recruited in the study (50% of calculated sample size). As the study is ongoing, an analysis was performed only on participants who have completed the study and for whom iodine data (including FFQ and UIC) have been measured. Figure 7.1 shows the status of all study participants up to date.

A total of 33 participants have completed the study, 18 of which are in the control group and 15 in the intervention group. There were no differences in the demographic characteristics between the two groups (Table 7.1). Most participants in both groups were British. Only a few had studied health sciences (11%, n=2) in control group and 27% (n=11) in intervention group, p=0.249) and household income varied from £<15,000 (17%, n=3 in the control group and 20%, n=3 in the intervention group) to £>50,000 (11%, n=2 in the control group to 20%, n=3 in the intervention group). No participants reported lactose intolerance or being vegan. For both groups, most women reported being the main grocery shoppers in their household.

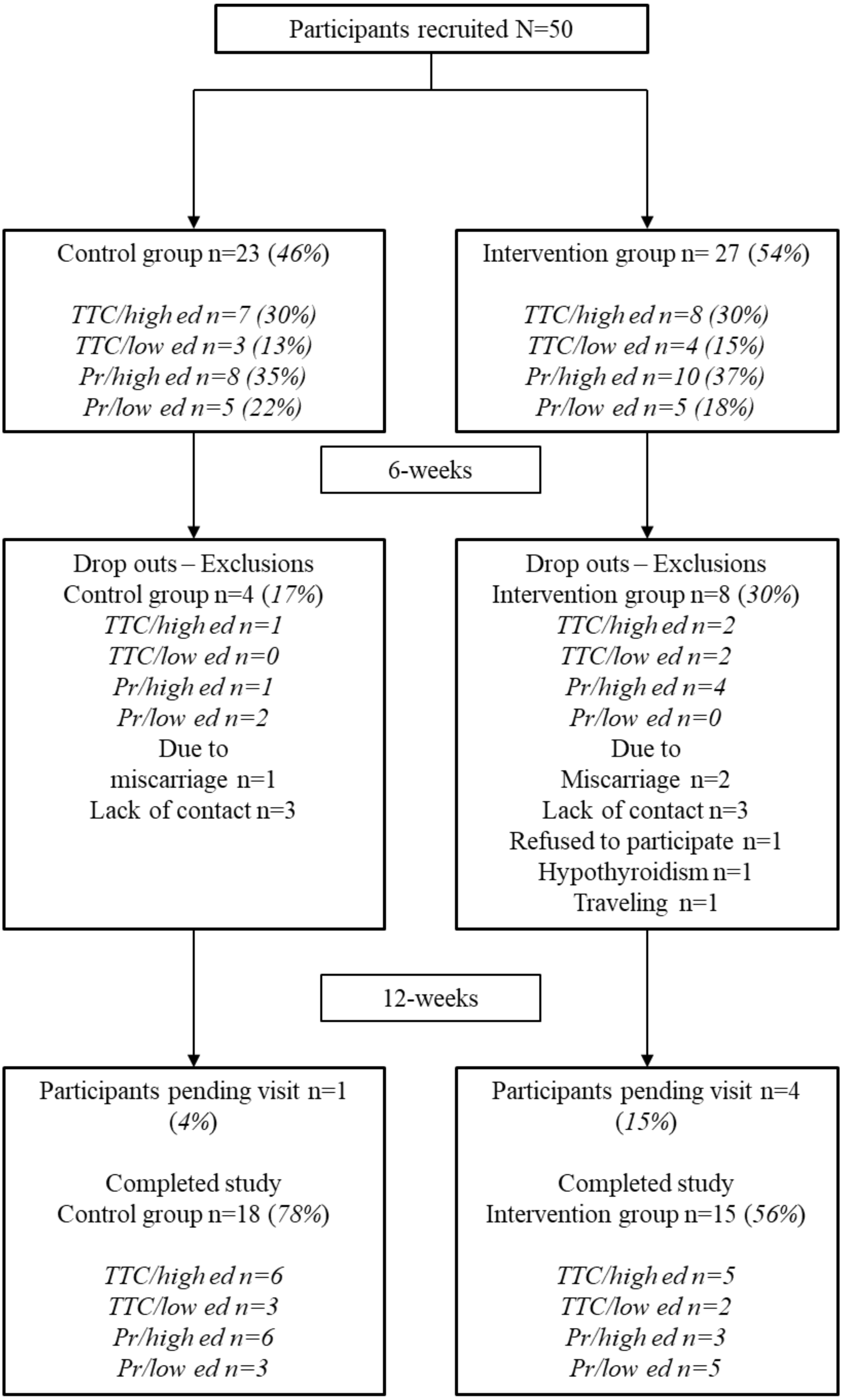


Figure 7.1 Flow chart of participants sampling and participation (n=50)
TTC: trying to conceive; Pr: pregnant; low ed: low education – not having a University degree; high ed: high education – having a BSc or higher University degree

Table 7.1 Baseline characteristics of the study population and differences between the intervention and control groups.

| **Demographic data** | **Control group n=18** | | **Intervention group n=15** | | |
|---|---|---|---|---|---|
| | **Median** | **IQR** | **Median** | **IQR** | ***p*-value** |
| Pre-pregnancy BMI (kg/m$^2$) | 23.4 | 21.0-27.4 | 24.0 | 22.7-29.4 | 0.203 |
| | **Mean** | **SD** | **Mean** | **SD** | |
| Age (years) | 29.5 | 5.0 | 32.7 | 5.7 | 0.700 |
| | **n** | **%** | **n** | **%** | |
| Ethnicity | | | | | 0.214 |
| British | 15 | 83 | 12 | 80 | |
| Other European | 2 | 11 | 0 | 0 | |
| Other ethnic groups | 1 | 6 | 3 | 20 | |
| Education level | | | | | 0.485 |
| School/College | 6 | 33 | 7 | 47 | |
| BSc | 7 | 39 | 5 | 33 | |
| MSc | 5 | 28 | 2 | 13 | |
| PhD | 0 | 0 | 1 | 7 | |
| Field of studies | | | | | 0.249 |
| Nutrition/dietetics | 0 | 0 | 0 | 0 | |
| Food Sciences | 0 | 0 | 0 | 0 | |
| Health Sciences | 2 | 11 | 4 | 27 | |
| Annual income | | | | | |
| £<15,000 | 3 | 17 | 3 | 20 | 0.673 |
| £15,001-£30,000 | 6 | 33 | 6 | 40 | |
| £30,001-£50,000 | 7 | 39 | 3 | 20 | |
| £>50,000 | 2 | 11 | 3 | 20 | |
| Status | | | | | 0.849 |
| Pregnant | 9 | 50 | 8 | 53 | |
| Trying to conceive | 9 | 50 | 7 | 47 | |
| Number of children | | | | | 0.407 |
| 0 or expecting first | 11 | 61 | 7 | 47 | |
| 1 or more | 7 | 39 | 8 | 53 | |
| Taking medication | 2 | 11 | 3 | 20 | 0.478 |
| Following specific diet | | | | | 0.530 |
| Pescetarian | 1 | 6 | 1 | 7 | |
| Lacto-ovo-vegetarian | 0 | 0 | 1 | 7 | |
| Main grocery shoppers | 15 | 83 | 13 | 87 | 0.790 |
| Smokers | 3 | 17 | 1 | 7 | 0.381 |
| Access to IT equipment | | | | | |
| Tablet | 9 | 50 | 9 | 60 | 0.566 |
| Smartphone | 17 | 94 | 14 | 93 | 0.894 |
| Laptop | 16 | 89 | 14 | 93 | 0.658 |
| Desktop | 4 | 22 | 6 | 40 | 0.269 |
| Wi-Fi at home | 18 | 100 | 14 | 93 | 0.266 |
| Mobile data | 16 | 89 | 13 | 87 | 0.846 |
| Number of IT devices* | | | | | 0.611 |
| 1 | 1 | 6 | 1 | 7 | |
| 2 | 8 | 44 | 4 | 27 | |
| 3 | 7 | 39 | 6 | 40 | |
| 4 | 2 | 11 | 4 | 27 | |

* IT devices include smartphone, tablet, laptop, desktop

### 7.3.2 Study acceptability and feasibility

The main purpose of the present analysis was to assess the study acceptability and feasibility. Out of the 50 recruited participants, presented in Figure 7.1, five participants were still in the study at the time of this analysis. From the 50 recruited women, there was a dropout (including exclusion) rate of 24% (n=12), from which 4 were in the control group (17% dropout rate) and 8 in the intervention group (30% dropout rate).

There were no significant differences between groups on all the aspects of the study assessment (Table 7.2). The control group reported that the study made them think about their diet and make positive changes at week 12 more in comparison to week 6, based on the results of the Likert scale.

Three participants (20%) allocated in the intervention group and one participant (6%) allocated in the control group guessed that iodine was the focus of the study, and filled it in an open-ending question. Overall, all 33 participants (100%) noticed the word "iodine" during the study. Out of the 33 participants 79% (n=26) were willing to learn more about iodine after the end of the study, 6% (n=2) did not want to learn more and 15% (n=5) replied that they would maybe be interested to learn more. The study was rated as being burdensome with a median of 1 point (IQR 1-2) in a 7-point Likert scale.

It is notable that nine participants (60%) of the intervention group reported always following the links that were included in the text messages at 6-weeks and 10 participants (67%) at 12-weeks. However, the links were tracked online for number of clicks, and the total clicks they had were 5, 5 and 6 (3 different links). These clicks included clicks from women that are still in the study and are not included in the present analysis.

Table 7.2 Study assessment

| | Control group | | | | | Intervention group | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 6-weeks | | 12-weeks | | | 6-weeks | | 12-weeks | | |
| | n | % | n | % | p* | n | % | n | % | p* |
| Frequency of reading messages | | | | | 1.000 | | | | | 1.000 |
| Always when I receive them, once or more. | 15 | 94 | 17 | 94 | | 14 | 93 | 15 | 100 | |
| I was following them initially, but now I ignore them. | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | |
| Sometimes, but not all of them. | 1 | 6 | 1 | 6 | | 1 | 7 | 0 | 0 | |
| I never read them. | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | |
| Frequency of following links | N/A | | N/A | | | | | | | 0.625 |
| Always when I receive them, once or more. | | | | | | 9 | 60 | 10 | 67 | |
| I was following them initially, but now I ignore them. | | | | | | 0 | 0 | 0 | 0 | |
| Sometimes, but not all of them. | | | | | | 3 | 20 | 3 | 20 | |
| I never follow them. | | | | | | 3 | 20 | 2 | 13 | |
| | **Median** | **IQR** | **Median** | **IQR** | | **Median** | **IQR** | **Median** | **IQR** | |
| Study helped positive changes[¥] | 4.5 | 3.3-5.0 | 5.5 | 4.8-6.0 | 0.040 | 6.0 | 4.0-6.0 | 6.0 | 5.0-6.0 | 0.096 |
| Messages helped understand recommendations[¥] | | | | | | 6.0 | 5.0-6.0 | 6.0 | 5.0-6.0 | 0.366 |
| Mobile technology useful/easy[¥] | 7.0 | 6.0-7.0 | 7.0 | 6.0-7.0 | 0.132 | 7.0 | 6.0-7.0 | 7.0 | 6.0-7.0 | 1.000 |
| Quality of messages[¥] | 6.0 | 5.0-7.0 | 7.0 | 6.0-7.0 | 0.258 | 6.0 | 5.0-7.0 | 6.0 | 6.0-7.0 | 1.000 |
| Study motivated think about diet/ Messages motivated changes[¥] | 6.0 | 5.0-7.0 | 6.5 | 5.8-7.0 | 0.038 | 6.0 | 5.0-6.0 | 6.0 | 5.0-6.0 | 0.166 |
| Rate burden of study requirements | 1.0 | 1.0-2.0 | 1.0 | 1.0-2.5 | 0.666 | 2.5 | 1.0-3.8 | 1.0 | 1.0-3.0 | 0.705 |

*Wilcoxon signed rank test for differences within groups for continuous variables and Friedman test for differences in proportions; [¥]7-point Likert scale: 1: not at all – 7: very much/ 1: low/ inadequate – 7: high/ adequate

### 7.3.3 Effect of intervention on diet and iodine intake

The baseline total iodine intake (from foods and supplements) was 87% higher in the intervention group compared to the control (p=0.036) (Table 7.3). There were no other differences between the two groups at baseline, 6 and 12-weeks. There was no effect of the intervention for the intervention group (no differences between baseline and 6 or 12-weeks), but the control group showed a significant increase in grams of milk intake (79 grams, p=0017). This led to significant increase in iodine intake from milk and total dairy (22 μg/day, p=0.017 and 41 μg/day, p=0.042 respectively). Specifically, over the 12-weeks the control group showed a positive delta difference in increase of 31 μg/day (IQR -14-101) in dietary and total (food & supplements) iodine intake, in contrast to the intervention group (Table 7.7). However, the difference was not significant and can be interpreted as both groups maintaining an iodine intake similar to the baseline levels. There was also an increase in the proportion of participants meeting the WHO iodine recommendation (150 μg/day for women trying to conceive and 250 μg/day for pregnant women) from baseline to 6 and 12-weeks. The increase was significant only for the control group (33% more in the control group vs 7% more in the intervention group, p=0.011).

Supplements, both iodised and non-iodised, were used by women in both groups. In the intervention group, 60% (n=9) of women were using supplements at baseline, 73% (n=11) after 6 weeks and 67% (n=10) after 12 weeks. However, supplements containing iodine were used at baseline by 27% (n=4), at 6-weeks by 20% (n=3) and at 12-weeks by 27% (n=4). In the control group, use of supplements / iodised supplements was 67% (n=12) / 17% (n=3) at baseline, 78% (n=14) / 22% (n=4) at 6-weeks and 83% (n=15) / 22% (n=4) at 12-weeks.

Based on the questionnaire assessing dietary changes, more women from the intervention group reported performing changes favouring iodine nutrition (increased dairy or milk, fish, seafood, decreased milk alternatives) compared to the control group. There was a statistically significant difference in proportions of women who performed iodine-related positive changes at 6-weeks (73% in the intervention group vs 28% in the control group, p=0.018) (Table 7.4).

Table 7.3 Iodine-rich foods intake, iodine intake from food and supplements and differences between the control and intervention groups over the study duration.

| | Control group n=18 | | | | | | | Intervention group n=15 | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | | 6-weeks | | 12-weeks | | | Baseline | | 6-weeks | | 12-weeks | | |
| | Median | IQR | Median | IQR | Median | IQR | p* | Median | IQR | Median | IQR | Median | IQR | p* |
| Milk (g/day) | 140 | 6-231 | 200 | 92-304 | 219 | 118-362 | 0.017 | 213 | 40-320 | 140 | 40-240 | 140 | 93-367 | 0.938 |
| Other dairy (g/day) | 85 | 37-133 | 82 | 38-137 | 114 | 42-138 | 0.642 | 68 | 35-168 | 76 | 46-140 | 82 | 35-123 | 0.859 |
| Fish (g/day) | 21 | 0-65 | 29 | 7-68 | 24 | 0-75 | 0.096 | 28 | 0-117 | 39 | 24-80 | 65 | 0-85 | 0.869 |
| Total iodine from dairy (µg/day) | 68 | 46-128 | 104 | 52-129 | 109 | 46-182 | 0.042 | 83 | 55-118 | 85 | 55-167 | 90 | 50-230 | 0.936 |
| Total iodine from milk (µg/day) | 38 | 2-63 | 54 | 25-83 | 60 | 32-98 | 0.017 | 58 | 11-87 | 38 | 11-65 | 38 | 25-100 | 0.938 |
| Total iodine from fish (µg/day) | 15 | 0-32 | 19 | 3-34 | 17 | 0-40 | 0.096 | 16 | 0-78 | 26 | 17-50 | 31 | 0-50 | 0.252 |
| % daily iodine from dairy | 89 | 68-98 | 85 | 68-97 | 86 | 74-99 | 0.211 | 86 | 44-99 | 73 | 33-94 | 79 | 52-99 | 0.766 |
| % daily iodine from milk | 36 | 7-51 | 47 | 26-54 | 45 | 36-58 | 0.824 | 43 | 8-53 | 41 | 6-51 | 40 | 19-61 | 0.584 |
| % daily iodine from fish | 11 | 0-31 | 14 | 3-31 | 13 | 0-25 | 0.642 | 14 | 0-55 | 27 | 6-67 | 20 | 0-47 | 0.699 |
| Total iodine from food (µg/day) | 88 | 72-137 | 115 | 83-166 | 140 | 62-208 | 0.115 | 163 | 78-221 | 154 | 74-232 | 140 | 78-260 | 0.936 |
| Total iodine with supplements (µg/day) | 97[a] | 72-191 | 139 | 94-208 | 176 | 85-243 | 0.115 | 181[a] | 89-293 | 188 | 110-260 | 192 | 84-280 | 0.936 |
| | % | n | % | n | % | n | | % | n | % | n | % | n | |
| % meeting WHO recommendation | 6[a] | 1 | 22 | 4 | 39 | 7 | 0.011 | 47[a] | 7 | 54 | 8 | 54 | 8 | 0.819 |

a. difference in baseline median values between control and intervention group ($p<0.05$) – Mann Whitney U test for differences in medians and Fisher's exact test for differences in proportions

*Related samples Friedman's two-way analysis of variance for differences within groups for continuous variables and Cochran's Q test for differences in proportions

Table 7.4 Dietary changes in relation to iodine nutrition

| | Control group | | Intervention | | |
|---|---|---|---|---|---|
| | **n** | **%** | **n** | **%** | **p** |
| **6-weeks** | | | | | 0.018 |
| Favoring iodine intake | 5 | 28 | 11 | 73 | |
| Disfavoring iodine intake | 5 | 28 | 3 | 20 | |
| No change | 8 | 44 | 1 | 7 | |
| **12-weeks** | | | | | 0.974 |
| Favoring iodine intake | 12 | 67 | 10 | 67 | |
| Disfavoring iodine intake | 4 | 22 | 3 | 20 | |
| No change | 2 | 11 | 2 | 13 | |
| **p** | 0.117 | | 0.110 | | |

Chi-square test for differences between groups; Fisher's exact test for differences in proportions between timepoints; Changes favouring iodine intake included one or more from: increased dairy or milk, fish, seafood, decreased milk alternatives; Changes disfavouring iodine intake included one or more from: decreased dairy or milk, fish, seafood, increased milk alternatives

### 7.3.4 Effect of intervention on UIC

UIC was measured in the 10 spot urine samples in each time point and the average was calculated for each participant. There was no significant effect of the intervention on UIC (Table 7.7). At baseline, all pregnant women were below the set cut-off point for sufficiency (150 μg/l) in the control group (median 91.7 μg/l, IQR 43.7-97.9). This remained unchanged after 6 (median 87.9 μg/l, IQR 70.1-102.6) and 12-weeks (median 83.0 μg/l, IQR 56.0-148.7). In the intervention group, 88% at baseline were below the cut-off (median 103.4 μg/l, IQR 50.5-115.2), which again remained unchanged. Similarly, women trying to conceive were below the set cut-off point for sufficiency (100 μg/l): 78% in the control group (median 63.4 μg/l, IQR 31.4-103.1) and 71% in the intervention group (median 78.0 μg/l, IQR 43.2-141.7) at baseline, which also remained unchanged over the study duration.

### 7.3.5 Effect of intervention on knowledge and awareness

The effect of the intervention on iodine knowledge and awareness is the secondary outcome of the study. General knowledge and awareness of diet and recommendations related to pregnancy did not differ between groups at any timepoint and was high, as women scored at baseline a median of 5 points (IQR 5-6) in the control group and 6 points (IQR 4-7) in the intervention group on their self-reported awareness (out of a maximum of 7 points) (Table

7.5). However, the control group showed a significant increase in the number of known pregnancy recommendations during the study, from 8 to 9 recommendations (p=0.002).

Women were asked knowledge–related questions on specific nutrients, including iodine (Table 7.5). All participants in both groups had heard about folic acid and healthy eating in pregnancy and lactation. Other nutrients (vitamin D, calcium) also scored high in both groups, but iodine was the nutrient that people had heard or had been informed about the least (22% in control group and 33% in intervention group at baseline). At 12-weeks, 45% of the control group and 87% of the intervention group answered positively that they had heard about iodine. The increase in proportions during the study was significant for both groups (34% more, p=0.019 for the control group and 54% more, p=0.001 for the intervention group). Women in the intervention group also showed a significant difference on iron awareness (33% more women had heard about iron at 12-weeks, p=0.012). In both groups, women who reported being aware that iodine from the diet is important during pregnancy for healthy development of the unborn baby, significantly increased (50% more, p=0.001 for the control group, 66%, p=0.007 for the intervention group).

Confidence in achieving a sufficient intake of iron and folic acid scored higher than iodine in both groups, without any differences between the two groups at any timepoint. Confidence on how to achieve the recommended iodine intake was 3 points higher at 6-weeks in the intervention group, compared to the control group (p=0.007), although this difference did not remain at 12-weeks (p=0.401). The median of individual differences on iodine was positive for both groups, with no significant difference at 12-weeks (Table 7.7).

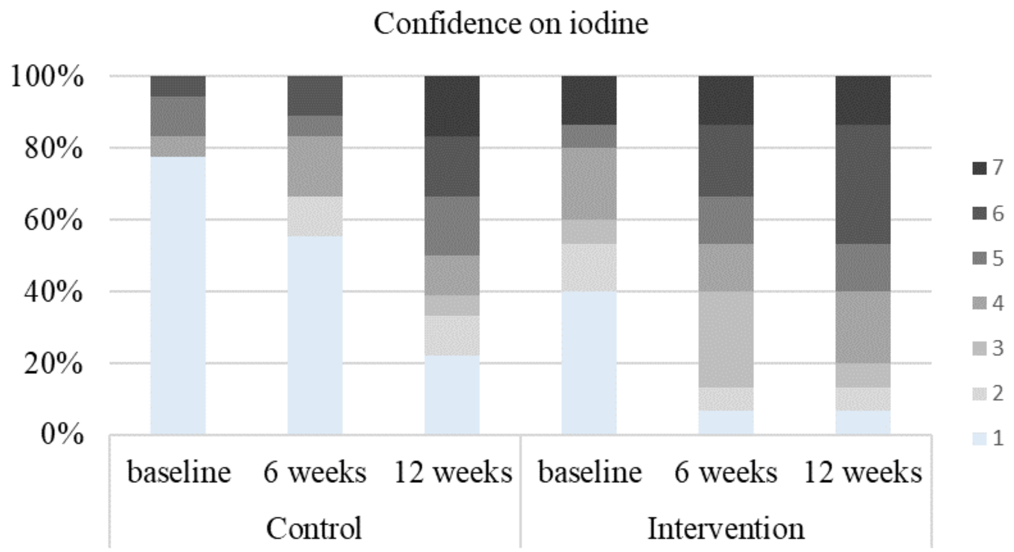


Figure 7.2 Confidence in achieving an adequate iodine intake for the control and intervention groups during the study.
Assessed by a 7-point Likert scale; 1: not at all – 7: very much

At baseline, women in the control group scored 2 points (out of a total of 9 points) higher on their knowledge of iodine food sources compared to the intervention group (p=0.001) (Table 7.6). After 12-weeks of intervention, the median of individual differences of known iodine sources was higher (p=0.002) for the intervention group (Table 7.7).

Table 7.5 General nutrition and pregnancy interest, knowledge and awareness.

| | Control group | | | | | | p* | Intervention group | | | | | | p* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Baseline** | | **6-weeks** | | **12-weeks** | | | **Baseline** | | **6-weeks** | | **12-weeks** | | |
| | **n** | **%** | **n** | **%** | **n** | **%** | | **n** | **%** | **n** | **%** | **n** | **%** | |
| Know how to relate nutrients to diet | | | | | | | 0.204 | | | | | | | 0.590 |
| Always | 4 | 22 | 4 | 22 | 6 | 33 | | 3 | 20 | 5 | 33 | 6 | 40 | |
| Sometimes | 10 | 56 | 14 | 78 | 11 | 61 | | 11 | 73 | 10 | 67 | 8 | 53 | |
| Never | 4 | 22 | 0 | 0 | 0 | 0 | | 1 | 7 | 0 | 0 | 1 | 7 | |
| | **Median** | **IQR** | **Median** | **IQR** | **Median** | **IQR** | | **Median** | **IQR** | **Median** | **IQR** | **Median** | **IQR** | |
| Interest in nutrition¥ | 7.0 | 6.8-7.0 | 7.0 | 6.0-7.0 | 7.0 | 5.8-7.0 | 0.292 | 7.0 | 6.0-7.0 | 7.0 | 6.0-7.0 | 7.0 | 6.0-7.0 | 0.468 |
| Pregnancy guidelines awareness¥ | 5.0 | 5.0-6.0 | 6.0 | 5.0-6.0 | 6.0 | 5.0-7.0 | 0.070 | 6.0 | 4.0-7.0 | 6.0 | 5.0-7.0 | 6.0 | 6.0-6.0 | 0.924 |
| Known pregnancy recommendations (max 9) | 8.0 | 6.0-9.0 | 8.0 | 7.0-9.0 | 9.0 | 8.0-9.0 | 0.002 | 8.0 | 6.0-9.0 | 8.0 | 7.0-9.0 | 8.0 | 7.0-9.0 | 0.549 |

*Related samples Friedman's two-way analysis of variance for differences within groups for continuous variables and Friedman test for differences in proportions; ¥7-point Likert scale: 1: not at all – 7: very much

Table 7.6 Iodine knowledge, awareness and confidence in relation to other micronutrients.

| | Control group | | | | | | p | Intervention group | | | | | | p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Baseline | | 6-weeks | | 12-weeks | | | Baseline | | 6-weeks | | 12-weeks | | |
| | n | % | n | % | n | % | | n | % | n | % | n | % | |
| Heard about | | | | | | | | | | | | | | |
| Folic acid | 18 | 100 | 18 | 100 | 18 | 100 | 1.000 | 15 | 100 | 15 | 100 | 15 | 100 | 1.000 |
| Iron | 15 | 83 | 17 | 94 | 17 | 94 | 0.333 | 10 | 67 | 15 | 100 | 15 | 100 | 0.012 |
| Iodine | 4 | 22 | 7 | 40 | 10 | 56 | 0.019 | 5 | 33 | 12 | 80 | 13 | 87 | 0.001 |
| Calcium | 11 | 61 | 15 | 83 | 14 | 78 | 0.074 | 12 | 80 | 14 | 93 | 15 | 100 | 0.222 |
| Vitamin D | 14 | 78 | 15 | 83 | 14 | 78 | 1.000 | 12 | 80 | 13 | 87 | 14 | 93 | 0.852 |
| Vitamin A | 9 | 50 | 12 | 67 | 12 | 67 | 0.527 | 8 | 53 | 11 | 73 | 13 | 87 | 0.049 |
| Knowledge on healthy development | | | | | | | | | | | | | | |
| Iodine | 4 | 22 | 6 | 33 | 13 | 72 | 0.001 | 4 | 27 | 11 | 73 | 14 | 93 | 0.074 |
| Iron | 11 | 61 | 17 | 94 | 18 | 100 | 0.093 | 11 | 73 | 14 | 93 | 14 | 93 | 0.719 |
| Folic acid | 16 | 89 | 18 | 100 | 18 | 100 | 0.333 | 15 | 100 | 15 | 100 | 15 | 100 | 1.000 |
| | **Median** | **IQR** | **Median** | **IQR** | **Median** | **IQR** | | **Median** | **IQR** | **Media** | **IQR** | **Media** | **IQR** | |
| Confidence on achieving intake of: | | | | | | | | | | | | | | |
| Iodine (1.0-7.0 points) | 1.0 | 1.0-1.8 | 1.0[b] | 1.0-4.0 | 4.5 | 1.8-6.0 | <0.001 | 2.0 | 1.0-4.0 | 4.0[b] | 3.0-6.0 | 5.0 | 4.0-6.0 | 0.007 |
| Iron (1.0-7.0 points) | 5.0 | 4.0-6.3 | 6.0 | 5.0-7.0 | 6.0 | 5.0-7.0 | 0.007 | 6.0 | 4.0-7.0 | 6.0 | 4.0-7.0 | 6.0 | 5.0-7.0 | 0.180 |
| Folic Acid (1.0-7.0 points) | 7.0 | 6.0-7.0 | 7.0 | 6.0-7.0 | 6.0 | 6.0-7.0 | 0.507 | 7.0 | 5.0.7.0 | 6.0 | 5.0-7.0 | 6.0 | 3.0-7.0 | 0.179 |
| Knowledge of foods | | | | | | | | | | | | | | |
| Iodine-rich (-7.0 to 2.0 points) | 0.0[a] | -0.3-0.0 | -0.25 | -2.0-0.0 | -1.0 | -2.3-0.0 | 0.008 | -2.0[a] | -2.0- -1.0 | 0.0 | -1.0-0.0 | 0.0 | -1.0-1.0 | 0.113 |
| Iron-rich (-4.0 to 5.0 points) | 2.0 | 2.0-3.0 | 2.0 | 2.0-3.0 | 2.0 | 2.0-3.0 | 0.794 | 2.0 | 1.0-2.0 | 2.0 | 1.0-2.0 | 2.0 | 1.0-3.0 | 0.486 |
| Folic acid-rich (-5.0 to 4.0 points) | 0.0 | 0.0-1.0 | 0.5 | -0.3-1.0 | 1.0 | 0.0-2.0 | 0.504 | 1.0 | -1.0-1.0 | 1.0 | 0.0-1.0 | 0.0 | -1.0-1.0 | 0.531 |

a. significant difference in baseline median values between control and intervention group (p<0.05); b. significant difference in 6-weeks median values between control and intervention group (p<0.05) – Mann Whitney U test for differences in medians and Fisher's exact test for differences in proportions; *Related samples Friedman's two-way analysis of variance for differences within groups for continuous variables and Cochran's Q test for differences in proportions for dichotomous variables and Friedman test for differences in proportions of multinomial variables.

Table 7.7 Effect of 12 weeks intervention on study primary and secondary outcomes

| | Control group | | Intervention group | | |
|---|---|---|---|---|---|
| | **Median** | **IQR** | **Median** | **IQR** | **p** |
| Δ UIC (μg/l) | 7.6 | -19.1–18.4 | 11.0 | -36.2– 2.0 | 0.704 |
| Δ iodine intake (food) (μg/day) | 30.7 | -13.9–101.1 | -0.5 | -42.7–45.2 | 0.148 |
| Δ iodine intake (total) (μg/day) | 30.7 | -13.9–148.8 | -5.1 | -79.1–62.2 | 0.129 |
| Δ iodine confidence (points) | 1.5 | 0.0–4.0 | 1.0 | 0.0–4.0 | 0.783 |
| Δ iodine sources knowledge (points) | -1.0 | -2.0–0.0 | 1.0 | -1.0–2.0 | 0.002* |

* Mann Whitney U test for differences in median individual Δ values between groups

## 7.4 Discussion

### 7.4.1 Main findings

Iodine insufficiency in women of childbearing age (mainly during pregnancy and lactation) is a concern for the UK, which re-emerged in 2011, after a long period with no national data on the iodine status of the UK population (Vanderpump et al., 2011). No actions are in place for its elimination (i.e. salt fortification, supplementation). The present study is a feasibility analysis of one of the very first interventions which aims to addressing iodine insufficiency in early pregnancy and preconception. These stages are critical for the neurodevelopment of the fetus and infant and depend on iodine availability. The findings of the study indicate that an educational intervention in women trying to conceive and early pregnant is feasible. Due to the early stages of pregnancy, dropout rates have been higher than expected (24% versus the calculated 15%), which is explained by the increased risk of miscarriages in the first trimester (Wilcox et al., 1988). All women who stayed in the study and did not experience a pregnancy loss by the second meeting, completed the intervention and rated the study requirements as being of low burden. Overall, early findings indicate an educational intervention being feasible and acceptable.

Women, who find the use of mobile technology (texting) an easy and useful way in getting information, approve an educational intervention in pregnancy (Head et al., 2013, Wei et al., 2011). In Chapter 4 women during the perinatal period of life, had proposed similar solutions for receipt of dietary information for pregnancy, such as mobile applications, emails and text messaging. Healthcare professionals are more sceptical of the use of mHealth in antenatal care, raising concerns on credibility of content and highlighting risks of non-trusted, nonevidence-based information in face-to-face interviews (Willcox et al., 2015). The limited knowledge on the effective frequency of texting has been highlighted as a barrier on interventions in a systematic review of reviews, which included interventions for health improvement (Hall et al., 2015). Interventions sending text messages less frequently than daily were found to be more effective. In the present study, the frequency of texting every 3-4 days, as well as the frequency and content of control group texts, were based on one of the most successful mHealth interventions on smoking cessation. Success could potentially be due to the large sample size and to personalisation of text messages (e.g. including participants' names) based on an algorithm (Rodgers et al., 2005).

Educational interventions for iodine nutrition have started taking take place lately in non-pregnant populations, with encouraging results (Amiri et al., 2017, Watutantrige-Fernando et al., 2018). A study in Iranian non-pregnant women aimed to increase knowledge, attitudes and practice towards iodine deficiency, mainly focusing on iodised salt. An increase in knowledge of iodine sources, awareness and confidence on how to achieve the recommended iodine intake for pregnancy is shown by the present analysis, although results should be interpreted with caution. Results agree with the present findings, as knowledge and attitudes increased in the intervention group, but practice remained unchanged (Mehran et al., 2012). More recently, Italian school-aged children increased the use of iodised salt after a face-to-face educative program from their teachers, which was the first to show an increase in UIC (from 70 μg/l to 91 μg/l) (Watutantrige-Fernando et al., 2018). The teachers, who were trained from the Food Hygiene and Nutrition Services medical staff on iodine prophylaxis and conscious salt usage, taught their pupils with the aid of a leaflet and an oral presentation.

Women lack knowledge on the role of iodine in the healthy development of the fetus and are rarely informed about iodine. Consequently, the sources of iodine remain unknown for most women, who have low confidence on achieving the recommended intake, in opposition to other nutrients, such as iron and folic acid. Knowledge, awareness and confidence of those nutrients are higher compared to iodine in the study. However, although confidence in achieving an adequate intake of iron and folic acid appeared to be high, actual knowledge of their sources was low. The public health campaigns for folic acid have succeeded in making the population aware of the nutrient and its importance (Rofail et al., 2012), but women depend mostly on supplements for covering their needs and remain unaware of its dietary sources.

Knowledge, confidence and awareness increased not only for the intervention group, but also for the control group. However, confidence on how to achieve an adequate iodine intake at 6-weeks was 3 points higher for the intervention group. There were no differences in knowledge on the role of iodine in healthy fetal development during pregnancy within or between groups, although the proportions increased (intervention group showed a 66% increase, p=0.074). Similarly, women in the intervention group who reported having been informed about iodine increased by 54% during the study (p=0.001), but at the same time there was a 34% increase in the control group (p=0.019). The intervention group also improved knowledge on iodine food sources by 2 points, in comparison to a 1-point score decrease of the control group, with no difference in the score at 12 weeks. A possible reason could be the significantly lower score of the intervention group at baseline. The number of follow-ups should be considered as a potential stimulus for self-research, which might occur from the awareness questionnaires for the control group, in which iodine and other nutrients were mentioned.

Although the intervention group showed improvement in all knowledge, awareness and confidence questions on iodine, changes in UIC or dietary intake did not occur. However, as the power was not enough to detect those differences, the data of all the participants will be analysed upon completion of the study. Amiri et al. (2017) did not find any significant differences in UIC of pregnant women after an educational intervention, but limitations, previously discussed in Chapter 3, were considered during the design of this intervention to enable the detection of differences, if those occur.

### 7.4.2 Strengths and limitations

The present study is one of the very first studies that aims to increase dietary iodine and improve iodine status of women before and during early pregnancy. Only two studies have been previously identified via a systematic review (Chapter 3) (Amiri et al., 2017, Dodd et al., 2014) which educated pregnant women to improve their diet and iodine status. Of the two studies, iodine was the main outcome for only one; the study by Amiri et al. (2017). A third study had also been designed with this aim, but other unknown reasons led to the study not starting (Prieto et al., 2011), highlighting potential difficulties faced by randomised controlled trials in pregnancy (e.g. ethical, financial) (Zhou et al., 2015).

Pregnancy and the healthy development of the fetus act as motivations for women, who are willing to change their habits for the benefit of their children (Chapter 4). Women trying to conceive need to be iodine-replete to start a healthy pregnancy, to ensure iodine availability in the first critical weeks (Velasco et al., 2018). A recent study showed an association between iodine in preconception and child's IQ (Robinson et al., 2018). However, dietary guidance for women in preconception is usually overseen in research and recommendations, compared to pregnant and lactating women, and their inclusion in the present study is a strength. However, in the UK, almost half of pregnancies remain unplanned or semi-planned (Wellings et al., 2013). Educational strategies on the importance of iodine and other micronutrients should target women of childbearing age, no matter whether they actively try for a pregnancy or not. For the purposes of coherence in our analysis, we only included women actively trying to conceive or in the first pregnancy trimester, due to the critical role of these life-stages in future health and the irreversible consequences that iodine deficiency during these periods can cause (Velasco et al., 2018, Stephenson et al., 2018).

Determination of the iodine status of individuals is a challenge, as UIC of spot urine samples is only a representative way to measure the iodine status of populations (World Health Organisation, 2007, Wainwright and Cook, 2018). To have an accurate measurement of individuals' iodine status via measurement of UIC, multiple 24-h urine samples or a minimum of 10 spot samples spread over few days are needed. If 10 spot urine samples are collected, precision of measured UIC is 24%, while with 56 spot samples precision improves (10%), while consists the collection of samples impractical (Konig et al., 2011). As such, our study included the collection of 10 spot samples at each timepoint, to ensure a robust and representative measurement of UIC. It would be more representative if the sample collection were to happen over the course of a period that covers seasonality changes, but this would not be possible due to the need for iodine status assessment in specific timepoints. The study did not consider hydration status of women as creatinine, which is the most widely-used method to correct for hydration, is not accepted by the WHO and might introduce an extra error due to false measurements (World Health Organisation, 2007). Measuring creatinine is a common practice though in studies to correct for hydration, and would be useful for comparative purposes. In pregnancy, due to increased clearance of iodine, UIC might overestimate iodine intake, but there is no other proposed method to substitute (Wainwright and Cook, 2018). Samples were not instructed to be non-fasting, which might lead to the underestimation of UIC (Konig et al., 2011).

The present feasibility study has been successful in informing of the high acceptability and feasibility of an intervention. Preliminary results of the intervention were also presented as well as an early statistical analysis, in order for all outcomes and variables to be presented rather than detect differences occurring via the intervention. However, changes in knowledge, awareness and confidence are evident and allow the study to continue, expecting results that might inform future practice (Kumar and Chakraborty, 2016). However, the study is still ongoing, and the calculated sample size will be achieved, and data will be re-analysed for the total sample. This approach of analysing results of the intervention during a feasibility analysis is controversial as it might cause Type I or Type II errors. In cases where the feasibility study is to inform the design of a future intervention, performing statistical analysis in an underpowered population might lead to false significant results. This risks the intervention to focus on outcomes which might be less important than others, leading to an unsuccessful intervention. In the present study, the RCT has been designed and is ongoing. As a result, the feasibility analysis is to ensure the study is acceptable and feasible, creating low burden for the participants, and any other results will not affect the design or the future data analysis. For this reason it has been considered as a safe approach to present early results, appreciating any limitations.

The difficulty of measuring actual changes in knowledge and awareness is also evident from the results. Although women in the control group never received information from the research team on iodine and other micronutrients, an increased knowledge, awareness and confidence was observed in this group as well. This makes the assessment of the intervention's efficacy difficult and underlines the need of multiple, parallel methods of perception assessment (including knowledge and awareness). Even though the study questionnaires might have motivated participants to engage in self-research, it is evident from the question on iodine sources, that the magnitude of self-reported increase in confidence and awareness might be over-rated. Although participants reported higher iodine confidence and awareness, there was no improvement on the actual knowledge on iodine-rich foods in the control group.

## 7.5 Conclusion

An intervention, which aims to increase iodine status before and during pregnancy, is feasible, and text messages have been an easy, acceptable and useful way to provide information to this group of the population. An increase in confidence after 6-weeks of intervention was shown, as well as a positive difference in knowledge of iodine-rich sources and iodine awareness. However, these changes did not affect the reported iodine intake and the UIC excreted. As this is a feasibility study, more participants will enable testing of whether the changes in confidence, knowledge and awareness can cause positive changes in the iodine status of pregnant women.

# Chapter 8 - General discussion

At the start of this PhD, in 2014, iodine deficiency (ID) in the UK was a recently re-emerged concern, after decades with no iodine monitoring in the British population (de Benoist et al., 2008). Studies focussed on the assessment of iodine status of different groups of the population, which was initially considered iodine-replete, until findings suggested that pregnant women and their infants were now vulnerable to ID (Bath et al., 2013, Pearce et al., 2010, Barnett et al., 2002, Bath et al., 2014c, Vanderpump et al., 2011, Bath et al., 2008, Bath et al., 2015). ID has been described, globally, as a public health concern prioritised by the WHO due to its irreversible consequences (World Health Organisation, 2007). The global improvement of iodine status has been mainly a result of the universal salt iodisation (USI) program, which was adopted in many European countries, but not by the UK. The elimination of ID in the UK in the 1980s was characterised as an "accidental public health triumph" (Phillips, 1997). Goiter was visible in 50% of school-children and adult women (Phillips, 1997). Symptoms decreased dramatically thanks to changes in farming practices, which increased iodine content of milk, in parallel with the campaigns for increase in milk consumption by school-children (Phillips, 1997). The Scientific Advisory Committee on Nutrition (SACN) had published a few months earlier (2014) a report with the evidence on iodine nutrition (Scientific Advisory Committee on Nutrition, 2014), without drawing conclusions leading to an update of the iodine guidance and recommendations for the UK population (Committee on Medical Aspects of Food Policy, 1991).

## 8.1 Rationale of overall approach and summary of findings

Public health strategies, based on salt and food fortification, supplementation and recommendations from public health authorities are in place worldwide (Lazarus, 2017). The UK, although an industrialised country, has no prophylactic measures in place for high-risk groups in the population (Bath and Rayman, 2013). However, diet, via iodine-rich foods (dairy and seafood products) is another way to ensure adequate iodine intake both in preconception and pregnancy, provided that women have competent knowledge and awareness to drive dietary changes. There is no available evidence on the effectiveness of diet to improving iodine status of women in the perinatal period of life. The hypothesis of this thesis was that iodine insufficiency could be eliminated based on simple dietary guidance. This hypothesis was tested using a systematic methodology to answer the research questions, incorporating skills across the full span of Human Nutrition, with both observational and experimental designs, as described by Margetts and Nelson (1997). Research questions, which emerged from the literature and evidence existing in 2014, were answered through the choice of the appropriate study design in each case.

*RQ1. What is the iodine status of pregnant women and their newborns in the UK?*
*RQ2. Can neonatal iodine status be associated with maternal iodine intake or urinary iodine excretion in pregnancy or postnatally?*

To answer these research questions, in Chapter 2, a longitudinal cohort study assessed the iodine status of pregnant women in the UK, and the status of mothers and their infants postnatally. The Mothers and Babies at Yorkhill (MABY) study showed that that UK pregnant women remain iodine insufficient, with 67% entering the last pregnancy trimester without achieving the iodine intake recommended by WHO (250 μg/day) (World Health Organisation, 2007). This is also evident from the measurement of UIC, which classified only 42% as having sufficient iodine status (UIC>150 μg/l). Neonates had a sufficient iodine intake based on UIC (118 μg/l; IQR 71–201), which was higher in breastfed infants compared to formula-fed (UIC 125 μg/l; IQR 75–232 vs 91 μg/l; IQR 67–137, p=0.002). However, lactating women had lower UIC compared to women who did not breastfeed (UIC 71 μg/l; IQR 30–160 vs 108 μg/l; IQR 51–192, p=0.002), indicating that lactation might have a protective effect in newborns at the expense of their mothers. British lactating women also had low iodine status in a study conducted in 168 breastfeeding mothers in 2013, with a UIC of 79 μg/l (IQR 43–120) (Bouga et al., 2015b). Feeding mode, maternal iodine status and use of supplements at the beginning of the last pregnancy trimester might affect the iodine status of newborns.

The MABY study is the most recent study, which assessed the iodine status of pregnant women in the UK, and the first to associate it with newborn infants' iodine status. The robust data collection and management of samples and data enable the conclusion to be drawn that pregnant women still have an iodine intake lower than the WHO recommendation, although ID is not a "new" public health concern anymore for the UK. More studies are needed to examine the factors that might influence the iodine status of the fetus and infants, aiming to prevent the irreversible consequences of ID. ID disorders (IDD) are not limited to the peri-conception and pregnancy periods, since the effects are often lifelong and irreversible, thereby impacting on society, with decreased productivity and increased costs (Monahan et al., 2015).

*RQ3. Are there any intervention studies in pregnant women, which aim to increase iodine intake through dietary guidance or iodine-rich foods provision?*

A systematic review of the literature from 1990 to 2016, presented in Chapter 3, identified a lack of intervention studies focusing on foods (rather than supplements and fortification) or educational programs to increase iodine intake in pregnancy. The RCT from Amiri et al. (2017) in Iranian pregnant women, the only piece of evidence directly linked to iodine, concluded that the intervention (a 4-month educational program using face-to-face educational sessions, a leaflet in the second and the third trimesters, as well as telephone) increased knowledge, attitude and practice, but not iodine status. Iodine status was however reported as median UIC of the groups, measured from a single spot urine sample, and may not be the most appropriate tool to evaluate changes in status in this small group.

This is the only systematic review that has looked to identify intervention studies in pregnancy that involved diet and education as the main aspects of testing. There is very limited evidence on the effectiveness of educational programs and food-based interventions in increasing iodine intake and improving iodine status of pregnant women, as studies tend to focus on the success, harm and benefits of supplementation and salt fortification. Prophylaxis via salt fortification is relatively cheap (0.2-0.3 US cents/kg, <5% of salt retail price) but may not be a sufficient measure during pregnancy and lactation (World Health Organization, 2006). Meanwhile, evidence of the benefits of supplementation is still unclear, and potentially affects recommendations made by HCPs. Including food guidance as a dimension of any future intervention is a realistic, vital step before the implementation of policy and public health campaigns, which would also be socially and politically acceptable. The UK offers a great opportunity for further research, as it is an ideal terrain for interventions, lacking prophylaxis such as salt fortification and supplementation. Randomised controlled trials are urgently needed to examine the effectiveness of different approaches as well as the long-term health, neurocognitive and economic effects on the population.

*RQ4. What is the current perceived level and quality of dietary guidance received by expectant mothers and new mothers?*

*RQ5. What are the perceived barriers to increasing or maintaining an adequate intake of dairy and seafood pre-conception and during pregnancy / lactation?*

*RQ6. What would be the most effective delivery of dietary guidance to expectant and new mothers?*

A mixed-methods cross-sectional study in women at the perinatal period of life explored the level of antenatal dietary guidance in the UK, the iodine-related information women receive and the barriers to iodine-rich foods consumption, and suggested ways of effective delivery of dietary guidance for pregnancy. Iodine-rich sources in the diet are varied and Chapter 4 has shown that women of childbearing age are receptive to dietary and lifestyle changes as long as guidance and support is provided, inviting strategies in this area. This is important, as it highlights that ID is a diet-related challenge, and the approach to tackle this challenge must include public health and policy strategies, without ignoring the role of foods, dietary recommendations, knowledge and awareness. Attitudes towards dairy products were positive as women found it easy to include them in their diet. Fish and seafood products were considered more difficult to consume in pregnancy, and main barriers included taste and smell, as well as confusion over the recommendations and potential risks.

Dietary guidance during antenatal care is perceived to be insufficient and confusing, driving women to use other sources of information, which are often less credible. Knowledge and awareness on iodine importance, role and sources remain low, in accordance to our previous study on iodine knowledge and awareness of UK mothers (Combet et al., 2015). Only 25% of women are aware of the role of iodine in the development of fetus and confidence on achieving an adequate iodine intake is low. Interviewed participants agreed that the role of the healthcare services in the delivery of pregnancy-related dietary information is important, as a highly trustful source. However, negative feelings, including disappointment and worry emerged when women realised that there might be important information that is missing from their antenatal guidance. The lack of involvement of diet and nutrition professionals as part of the common practice of dietary advice in pregnancy, and the incompetent nutrition content of most curriculums for the health profession likely blunt the effectiveness of any given strategy and should be re-evaluated.

Public Health strategies and educational programs could influence the improvement of nutritional status in the perinatal period and increase the iodine status of the population. A clear need for empowerment in pregnancy emerged from this study, as women are willing to follow specific and comprehensive dietary advice in pregnancy. A majority of women (87%) prefer dietary information to focus both on foods and specific nutrition elements and to be more comprehensive, clear and with a focus on portion sizes. This is the first study in the UK, which explored the needs and perceptions of women in childbearing age on the pregnancy and iodine related guidance received and the preferred ways for effective delivery of dietary advice. Suggestions regarding the preferred ways of information delivery focused on technology (e.g. mobile applications and emails), though without discouraging a short explanatory discussion with healthcare professionals.

*RQ7. What is the contribution of dairy and seafood products in the daily iodine intake of the UK population?*
*RQ8. What are the main perceived barriers and influential factors in the consumption of dairy and seafood products?*
*RQ9. Can behaviour towards dairy and seafood products consumption be predicted through the constructs of the Theory of Planned behaviour and sociodemographic characteristics?*

The two UK-wide cross-sectional questionnaire surveys on dairy (Chapter 5) and seafood products (Chapter 6) depicted attitudes and practices of the UK population towards iodine-rich foods consumption and explored factors which influence dairy and seafood intake. Findings indicated that the intake of dairy (2.2 servings/day, IQR 1.2-3.5), as well as fish and seafood (1.9 servings/week, IQR 0.9-3.7) remain low. Eating patterns have changed in the last 20 years, with a decrease in milk intake (Whitton et al., 2011), potentially driven by commercial pressures and marketing (e.g. promotion and increasing popularity of milk alternatives) (Sethi et al., 2016). Simultaneously, changes have occurred in farming practices, due to thyrotoxicosis (excess of thyroid hormones) from the high levels of iodine in milk as a result of the addition of iodine in cattle feed and use of iodophor disinfectants in sanitisation (Bath et al., 2012, Wheeler et al., 1982). The surveys presented in Chapter 5 and 6 are the first UK-wide surveys exploring the level of iodine-rich foods intake in the population, the factors influencing this intake and the differences between “high” and “low” consumers.

Sensory attributes both of dairy and seafood products were rated as the main influential factors of consumers’ choice. “High” and “low” consumers of iodine-rich foods differ not only on iodine intake levels, but also on the constructs of the Theory of Planned Behaviour, which was hypothesised to influence their behaviour on iodine-rich foods consumption. Increased consumption was associated with increased knowledge, positive attitudes towards dairy and seafood products, and intention to consume them. Fish and seafood intake was also associated with perceived behavioural control of the consumers. Exploring the attitudes of the general UK population is considered important due to the influence of family, friends and social norms on food choices of women, which was also evident in the interviews of women on Chapter 4. However, *subjective norms* were not associated with iodine-rich foods consumption in the two surveys. Social approval or disapproval of a behaviour might be a strong influential factor of *subjective norms* in the actual performance of the bevaviour (Mark, 2009). The fact that the surveys did not detect any influence of the social norms on the choice of iodine-rich foods agrees with previous findings on healthy eating and might be due to faulty measurements of the construct and limited theoretical illustration (Øygard and Rise, 1996). Lately, the negative impact of food (meat, fish, dairy) consumption on the environment has received attention, which might affect the amount of iodine-rich foods consumed by the population (Poore and Nemecek, 2018, Behrens et al., 2017). Education and marketing (which is only influencing the population subconsciously) might encourage the population to make positive dietary choices, not only for increasing iodine intake, but also for general health improvement. As such, the role of industry might be also critical for the food choices of the population, as in the area of healthy eating, governmental health policy is not strong, and the population is expected to act individually (Donovan, 2011). Positive campaigns for dairy consumption might enhance the elimination of existing misconceptions and potentially reposition milk and dairy in the UK diet.

*RQ10. Is an intervention with simple dietary guidance on iodine feasible, acceptable and effective in pregnancy?*

The different study designs allowed a thorough approach of the topic, which also led to the design of the RCT. Results from Chapters 2 to 6, the literature, and the identified needs of the UK perinatal population informed the design of the RCT (described in Chapter 7). The Pregnancy Iodine Choices (PICk) study is an educational study, designed to assess the effectiveness of an intervention based on diet and awareness for women before and during pregnancy, and the potential to improve iodine status. The PICk study is the first RCT in the UK, which educates and guides women towards dietary choices that sustain iodine needs. The feasibility analysis, presented in Chapter 7, indicate that educational interventions in preconception and early pregnancy are feasible, acceptable and have a low burden for the participants.

The PICk study pilot data showed an effect of dietary guidance on increasing confidence of achieving the recommended iodine intake. Scores on knowledge and awareness also showed an increase, however, since this was an interim analysis and the study is still ongoing, there is scope for (re)assessment of results in the future. Although iodine status did not change during the study, agreeing with previous results in pregnant women (Amiri et al., 2017) and non-pregnant females (Mehran et al., 2012), the interim analysis was not powered to detect such differences. Indeed, iodine status assessment is challenging in individuals, which might also influence the study results. Lack of a hydration biomarker (e.g. creatinine) might play a role in the result (Li et al., 2016, Knudsen et al., 2000). The collection of 24-hour urine samples would have been another way of assessment, in which case hydration would not influence the total daily excretion of iodine, but compliance in the study would have potentially been decreased, due to the burden on participants. Assessment of iodine status with thyroglobulin (Tg) is a promising approach, as it changes within 12 weeks of iodine status improvement (Monika et al., 2018, Ma and Skeaff, 2014), and should be taken into consideration to explore further whether educating women has impacted on their choices and iodine intake.

An intervention which can improve health and nutrition by sending information to women via text messages, can cover most of the population, due to the wide use of mobile phones in the UK (more than 80% in all socioeconomic groups) (Free et al., 2011). In such way, health inequalities can be (partly) tackled, with improved access to information and health promotion. However, "healthier" diets are more expensive in comparison to "unhealthier" diets. Food choices, mainly for fish and seafood, sufficient to cover the recommendation of iodine intake in pregnancy, can be expensive for women of low socioeconomic status (Darmon and Drewnowski, 2015). In the UK, based on NDNS data, low socioeconomic groups are 2.4-4.0 times less likely to consume oily fish compared to higher socioeconomic groups (Maguire and Monsivais, 2015). Both the healthcare system and society should consider supporting and offering the most vulnerable women solutions to achieve sufficient iodine intake, as a high-risk group of the population (e.g. by providing iodine supplements during pregnancy, or subsidising iodine-rich foods). Sufficient iodine intake is also beneficial in preconception (Robinson et al., 2018), but half of all pregnancies remain unplanned (Wellings et al., 2013).

As this PhD ends, in 2018, iodine insufficiency remains a concern in the UK, for women of childbearing age especially. There has been no change in the recommended daily iodine intake for pregnancy and lactation, no change from voluntary to mandatory salt iodisation and no addition of iodine to the pregnancy supplements provided by the healthcare system. Iodine-related knowledge has been established to affect iodine status (O'Kane et al., 2016).

Recent studies now focus on iodine-rich food sources, mainly milk. These studies advocate for the role and use of diet for the elimination of ID (Bath et al., 2012, O'Kane et al., 2018, O'Kane et al., 2016). However, SACN has not updated the report published in 2014 (Scientific Advisory Committee on Nutrition, 2014) and further research is needed to strengthen the available evidence on ID and stimulate Public Health policy changes.

## 8.2 Directions for future prevention

ID has been described as "the low-hanging fruit of public health" in the UK (The Lancet Diabetes, 2016). This agrees with the hypothesis of this thesis, which assumes that the elimination of the problem in women of childbearing age could emerge through the right dietary choices rather than complex public health actions. The challenge could be tackled through a range of strategies, including policy implementation (salt and staple foods iodisation, supplementation), educational campaigns for increased awareness in women and HCPs, and development of comprehensive food-based guidance for the general population, pregnancy and lactation. However, none of those potential solutions is currently in place in the UK, and the problem of insufficiency has been consistently overlooked.

### 8.2.1 The role of salt fortification

Salt fortification with iodine remains optional in many countries for reasons such as the conflicting public health message that it may deliver, opposing the salt reduction campaigns. However, it achieves health gain without conscious action by individuals: by "stealth" through addition of salt during food manufacture. Processed food contributes more to salt intake than added table salt, which contributes only 23% of sodium intake in the UK (Ni Mhurchu et al., 2011). There is also still a gap in the literature regarding iodine supplementation strategies (through salt or supplements) and their effect on prenatal or postnatal somatic child growth outcomes (Farebrother et al., 2015). Salt fortification with iodine is moderately effective as a single preventive method of insufficiency in pregnancy, when iodine requirements are higher (Fumarola et al., 2008). However, if salt becomes the main source of iodine, the current salt recommendation (maximum 5g of salt per day) is insufficient to achieve iodine recommendations, at the current recommended level of fortification. In order for a healthy non-pregnant adult who consumes 5g of salt per day to reach their iodine intake, salt would need to be fortified with 39 mg of iodine/ kg of salt. However, the current guidelines suggest that the level of iodine fortification is based on the median salt intake of the population (World Health Organisation, 2014). As a result, for countries with high salt intake, including the UK, this level of fortification will not meet iodine needs through the recommended 5g of daily salt intake, where pregnant and breastfeeding mothers are at particular risk of not meeting current iodine guidelines via this mode. Many people who seek better personal health have already reduced salt consumption below this level (He et al., 2013). Differences in USI legislation between countries were illustrated in a study which apportioned the UIC of spot samples of women. Sodium correlated with iodine in urine samples, and the study concluded that diet only would not cover a sufficient iodine status of the population (van der Haar et al., 2018).

### 8.2.2 The role of food reformulation and fortification

In countries where salt iodisation is mandatory, despite iodine sufficiency in the general population, pregnant mothers still remain iodine insufficient as reported in Denmark, Iran, New Zealand and Turkey, indicating that salt iodisation may not eliminate this problem (Iodine Global Network, 2016). Reformulation and fortification of other foods with iodine, such as bread (Edmonds et al., 2015) and vegetables (Tonacchera et al., 2013) is clearly necessary, and has already been implemented with limited success. If other foods are to be fortified with iodine, the need to add it to salt is then removed. In Scotland, a nutritionally balanced pizza was developed, which was reformulated with added seaweed in the dough, to provide iodine in the consumers, among other nutrients, and was highly acceptable (Combet et al., 2014).

In less developed countries, focus on an increased household coverage with iodised salt, and addition of iodine to condiments, soybean paste and sauce is driven by the Iodine Global Network / IGN strategy on global elimination of iodine deficiency (Codling, 2017, IDD Newsletter, 2017b). In Uganda, positive appreciation and acceptance of biofortification of crops with iodine was recently expressed, as a strategy to control IDD. Strengths and opportunities outweigh threats and weaknesses based on a performed SWAT analysis (Olum et al., 2018).

### 8.2.3 The role of supplementation

Iodine supplementation is strongly suggested for pregnant women (150 μg/day) but the evidence around its safety and efficacy is poor. Despite iodine supplementation being fruitful in increasing UIC, it has been less successful in countries with severe and mild to moderate iodine deficiency (Zhou et al., 2013). There has only been limited studies published showing a negative effect of maternal iodine supplementation in pregnancy. With more than 100 μg/day, infants at 1 year of age had a 2-points decrease of psychomotor development index, compared to women supplemented with less than 100 μg/day, which should be considered when recommending iodine supplementation in pregnancy (Murcia et al., 2011). In a Norwegian cohort of 1036 families lower gross motor skills in infants were associated with maternal use of iodine-containing supplements (b= -0.18, 95% CI -0.33- -0.03, p=0.02) (Markhus et al., 2018). A negative effect of short-term use of supplements in children at the age of 8 years born in Norway from mothers recruited between 1999-2008 (Norwegian Mother and Child Cohort (MoBa) Cohort) has been also shown (29% increased risk of ADHD diagnosis, 95% CI, p=0.053) in the first pregnancy trimester (Abel et al., 2017). However, most studies have not shown any negative effects of iodine supplementation, although evidence remains unclear on the long-term effects (Taylor et al., 2014, Zimmermann, 2009b, Nohr et al., 2000), warranting future investigation. Similarly, there is no evidence on the safety of food products, which could be the focus of public health strategies to eliminate iodine insufficiency in the UK and globally.

### 8.2.4 The role of education

Awareness and knowledge remain low when it comes to iodine nutrition in pregnancy and lactation (Combet et al., 2015) and this low knowledge, measured from a questionnaire, has been linked to lower iodine status (O'Kane et al., 2015). As such, increasing awareness and knowledge would potentially be a simpler and more cost-effective way of increasing iodine intake and solving the public health concern of iodine insufficiency and its consequences, compared to changing the legislation regarding fortification and supplementation. Randomised controlled trials would be the most appropriate way to examine this hypothesis and provide the evidence on the level of education and information required to detect a significant increase of iodine intake from the diet. Policy makers could examine the potential of solving such a public health problem with a simple informative intervention, where if there is enough evidence indicating that behaviour change is possible this could be met through simple, cost-effective techniques, such as line text messaging, emails, group education, prompts to use electronic applications etc. However, outcome measures (iodine status, iodine intake, thyroid function, fetus somatic growth and neurodevelopment etc.) and dose or exposure (exact description of level of provided knowledge) are important in these studies that present difficulties in objective measures, to be possible to be assessed and replicated.

### 8.2.5 The role of diet and nutritional status

Different diet cultures and beliefs might influence iodine nutrition. Vegan and vegetarian diets, which exclude dairy products, eggs, fish and seafood (depending on the specific diet characteristics) limit the iodine-rich dietary sources. Such dietary restriction can render the recommended intake difficult to reach, without intakes of fortified food products and use of iodised supplements (Abdulla et al., 1981, Davidsson, 1999). These cases, when seaweed could remain as the only dietary source of iodine, highlight the upmost importance of increased level of public knowledge and awareness, as well as specific dietary recommendations and their importance in decisions related to food choices, in order to avoid toxicity from very rich iodine sources (Bouga and Combet, 2015).

Co-existing deficiencies, such as iron, zinc and selenium should also be taken into consideration (World Health Organisation, 2018). These nutrients are important for thyroid function, improvement of the efficacy of iodine supplementation, and prevention of myxedematous cretinism (Zimmermann and Kohrle, 2002). In the UK, 44% of girls 11-18 years and 46% of women 19-64 years have a selenium intake below the LRNI, much lower than the acceptable 2.5% of the population (Bates et al., 2016). For the same populations, iron intake is below the LRNI of selenium for 48% and 27%, and zinc for 22% and 6%, respectively. The WHO is targeting micronutrient deficiencies globally by proposing a balanced and diversified diet, micronutrient supplementation and fortification of foods (i.e. sugar, salt, maize, oil, rice, wheat) with micronutrients (folic acid, iron, calcium, vitamin A, B12, zinc) (World Health Organisation, 2018).

Changing dietary patterns is challenging, considering the unregulated commercial marketing of foods. The UK diet is still low in fruits and vegetables, high in fat and sugar content and changes are needed to improve health of the population. The main dietary sources of iodine in the UK are dairy, and fish and seafood, which together make up 13% of energy intake in adult women (Bates et al., 2016). Oily fish consumption also remains lower than the recommended minimum of 2 portions per week (Bates et al., 2014). There is scope for better adherence with the "*Eatwell guide*" recommendations, for improvement both of the diet quality and the iodine (and general nutritional) status of the UK population (Public Health England, 2016).

## 8.3 Implications for Public Health and policy makers

Lack of high quality and sufficient research studies in the UK, as well as the varied and often inconsistent methods of iodine status assessment do not allow policy changes. The SACN report on iodine, with no recommendations to revise the reference intake values (Scientific Advisory Committee on Nutrition, 2014), indicates that the existing evidence might not be sufficient for a policy revision. Governmental actions are required, and the UK should follow the example of other countries, such as the US, Australia and New Zealand in policy for fortification and supplementation according to the WHO (World Health Organisation, 2014). The cases of cessation of water fluoridation (in Scotland) and absence of mandatory fortification for folate are two similar examples of potential missed-opportunities to positively impact on population health, possibly through a more rigid policy-making framework compared to other Western nations.

To address ID effectively, solutions should work synergistically. Changing dietary patterns is challenging, considering the unregulated commercial marketing of foods. The example of fruits and vegetables provides the evidence that dietary changes can happen, and interventions designed to increase a dietary component can be successful, although slow (Ammerman et al., 2002). Dietary change is, however, mostly effective in subgroups of the populations, leaving the lower socioeconomic groups and those with the greatest need (e.g. low income, homeless, socially deprived, urban migrant groups) untargeted (Pomerleau et al., 2005b, Pomerleau et al., 2005a). This in itself calls for a multipronged approach to tackle ID, in the UK and globally, depending on the needs and iodine status of each population.

## 8.4 Recommendations for Practice

Dietary information is abundant, but the main difficulty is identifying trusted sources of information. Healthcare professionals are the most trustful source of information for women of childbearing age. As such, ensuring adequate nutrition education of healthcare professionals could enhance the improvement of nutrient status of this population group, including iodine status. Policy changes should occur at the same time, as UK healthcare professionals are expected to provide dietary advice and guidelines recommended by the UK Department of Health. Once these guidelines are not in line with the WHO, confusion might occur, and healthcare professionals should not be expected to make personal decisions on the recommendations to provide.

Advice provided to the UK population should also be more practical and easy to understand by everyone. Clear portion sizes should be set for all foods, and information should focus more on foods rather than nutrients, as very few people can relate them. Nutrition can be discussed more at school, following the example of folic acid, resulting at the awareness of its importance being very high. Other innovative ways of informing the population should be considered as useful and successful, such as the use of social media, influencers and mobile technology, as the upcoming generations will be more familiar with these ways of receiving advice and getting influenced in their choices. Research should focus more on the ways and means of behaviour change, which may prove to be effective.

Supplementation and fortification should also be considered as potential means of action, and policy makers should consider the addition of iodine in staple foods and/or pregnancy supplements. Women of childbearing potential should be the focus of nutrition and nutrient status improvements, as they will contribute to improved future health through healthier pregnancy outcomes and the influence they might have as future parents to shaping the preferences and dietary choices of the next generations.

## 8.5 Implications for the future

Based on the present work, research questions arise for future studies, aiming to explore unanswered questions and confirm results of previous studies, to strengthen the existing evidence. Answering these research questions, will enhance the further investigation of iodine insufficiency and will provide data to inform policy-makers.

1. Is breastmilk iodine concentration a better marker for lactating women iodine status and can it be used to identify neonates at risk of deficiency?

2. Is neonatal TSH correlated with maternal UIC and Tg during pregnancy? Can the combination of Tg and UIC be used as an early biomarker for the risk of neonatal iodine insufficiency and related consequences?

3. Is maternal UIC and Tg during pregnancy associated with infant's neurodevelopmental outcomes assessed at 1 year of age?

4. Can a public health educational programme on iodine nutrition improve the iodine status of women in reproductive age and during pregnancy?

5. Can an educational intervention in HCPs improve the iodine status of pregnant women?

6. Can a combination of different public health strategies (education of women/ education of HCPs/ mandatory salt fortification or increase of iodised salt availability/ update of UK iodine recommendations) enhance the achievement of a sufficient iodine status?

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# Appendices

## Appendix 1 – MABY study documents

### Participant Introduction letter

## Participant information sheet

Human Nutrition, School of Medicine,
New Lister Building, University of Glasgow,
Glasgow Royal Infirmary campus, Glasgow G31 2ER
Tel: 0141 211 8725

NHS Greater Glasgow and Clyde

### Thyroid Health Cohort - Mothers and Babies at Yorkhill (MABY)

**Information Leaflet for Mothers**

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information.

**Who is conducting the research?**

The research is being carried out by Drs Combet and Cizmecioglu from the Department of Human Nutrition and Dr Donaldson and Mr Jones, from the Department of Child Health, School of Medicine, University of Glasgow. It is funded by the Yorkhill Children's Charity and Yorkhill Endocrine Growth Fund and sponsored by NHS Greater Glasgow and Clyde.

**What is the purpose of the study?**

During pregnancy the baby relies on the mother for thyroid hormones, which are essential for his/her development. Certain dietary components are important for the thyroid; including the mineral iodine, as well as iron, and selenium. We want to find out how a mothers' habitual diet is linked to the working of their babies thyroid glands shortly after birth.

This study aims to collect information about your habitual diet using a questionnaire, and via measurements of iodine, iron and selenium and thyroid hormones in urine/blood. This information will be compared to clinical data available about your baby's thyroid function collected during the Newborn screening test, which happens between days 4 and 7.

**Why have I been invited?**

You have been invited to take part in this study as you are half way through a normal pregnancy, and have never suffered from any thyroid disease.

**Do I have to take part?**

It is up to you to decide. We have sent this information sheet ahead of your next appointment at the antenatal clinic to give you the opportunity to think about the study and maybe discuss it with others (family, your GP or the study team) if you want to. A researcher will be present at the clinic for your next appointment and will ask whether you would like to take part. They will present the study again, this information sheet and will be available for any questions that you may have.

If you decide to take part you will be asked to sign a consent form to show your agreement, and we will inform your GP of your participation. Taking part (or not) will not affect the standard of care you receive during pregnancy or your future treatment, and you will still receive all the usual tests and standard of care regardless of your decision. You are free to withdraw from the study at any time, without giving reason.

**What does taking part involve?**

This study involves three contact points: today at the week 28 antenatal clinic, at the week 38 antenatal clinic, and once your baby is born, when the midwife comes to visit to perform the routine Newborn Screening test.

1) At the week 28 antenatal clinic, if you decide to take part after reading this information sheet and discussing the study with the researcher, we will ask you to fill a consent form. We will take your contact details and also seek permission to access clinical data stored on the computer system, related to your pregnancy and your

baby's birth and measurements. We will ask you to fill a short questionnaire about your diet. As urine and blood are routinely collected at this antenatal visit, we will ask permission to keep some of the urine, and collect an extra small tube of blood.

2) At the week 38 antenatal clinic, as urine and blood are routinely collected, we will ask permission to keep some of the urine, and collect an extra small tube of blood.
3) In the first week after birth (between day 4 and 7), we will accompany the midwife visiting you at home. When the midwife performs the Newborn Screening test, she will collect an extra "blood spot" from the baby's heel. With your help, we will attempt to "catch" some urine from the baby, either directly, or by placing cotton wool balls in the nappy. If this does not succeed, we will give you a special collection pack and a pre-paid envelope. We will ask you for a urine sample, and a "blood spot", collected by pricking the tip of the little finger. We are also collecting optional milk and hair samples. Finally, we will ask you to fill the food frequency questionnaire again.

   We will ask for permission to keep your details in order to contact you in the future, to invite you for a follow-up study. You will not have to accept this future invitation.

**What happens to the information?**

Your identity and personal information will be completely confidential and known only to the researcher. The information obtained will remain confidential and stored within a locked filing cabinet. The data are held in accordance with the Data Protection Act. Personal results may be communicated to participants as they become available, upon request. In addition, if we detect abnormal thyroid results, we will inform your doctor and you will be excused from the study. The study results will be analysed and summarised, and published in an appropriate scientific journal. No participant will be identifiable in any of the study presentations.

**What are the possible benefits of taking part?**

It is hoped that by taking part in this research, you will be providing valuable information regarding the role of diet in thyroid health for mother and baby. You will not receive any personal health benefits as a result of your participation in this research study but other women and babies may benefit in the future.

**Who has reviewed the study?**

This study has been reviewed by the Sponsor and NHS Ethics

**If you have any further questions?**

We will give you a copy of the information sheet and signed consent form to keep. If you would like more information about the study itself, please contact Dr Emilie Combet (Emilie.CombetAspray@glasgow.ac.uk, 0141 201 8527). If you wish to speak to someone not closely linked to the study, please contact Ms Janis Hickey, at the British Thyroid Foundation (0142 370 9707).

**If you have a complaint about any aspect of the study?**

If you are unhappy about any aspect of the study and wish to make a complaint, please contact the researcher in the first instance but the normal NHS complaint mechanisms is also available to you.

Thank-you for your time and co-operation.

## Consent form

Human Nutrition, School of Medicine,
New Lister Building, University of Glasgow,
Glasgow Royal Infirmary campus, Glasgow G31 2ER
Tel: 0141 211 8725

NHS Greater Glasgow and Clyde

**Subject number:**

### Thyroid Health Cohort - Mothers and Babies at Yorkhill (MABY)

**CONSENT FORM**

**Please initial the BOX**

1. I confirm that I have read and understood the leaflet entitled "Participant Information Sheet - Thyroid Health Cohort - Mothers and Babies at Yorkhill (MABY)" dated 15/12/2014 (version 2.1) and have had the chance to ask questions about the study. ☐
2. I understand that participation is voluntary and that I am free to withdraw at any time without giving any reason. My withdrawal will not affect my medical care or legal rights in any way. ☐
3. I understand that I will receive no results from the study, unless I specifically request them, and that I will obtain no benefit from taking part, although other women and babies may benefit from the study in the future. ☐
4. I authorise the study team to access my medical records and my baby's record, to specifically gather clinical data regarding the pregnancy, birth, baby's measurements, results of routine blood analysis, and my baby newborn screening test. ☐
5. I authorise the study team to inform my family doctor (GP) regarding my participation in this study. ☐
6. I agree to the use of part of my routine blood and urine samples taken during and after pregnancy as well as study samples (blood, urine, and optional hair and optional breastmilk samples) taken after giving birth for further laboratory measurements, relative to nutritional status and thyroid function. ☐
7. I agree to the study team obtaining a portion of my baby's newborn screening sample for later testing. ☐
8. I agree for my contact details to be kept by the research team, for the sole purpose of inviting me to a follow-up study (I am free to reject or ignore this invitation). ☐
9. I agree to take part in the study named above. ☐

| ............................................. | .................................. | ........................................... |
|---|---|---|
| **Name (print)** | **Date** | **Signature** |

| ............................................. | .................................. | ........................................... |
|---|---|---|
| **Witness (print)** | **Date** | **Signature** |

Version 2.1 15/12/2014

## Food frequency questionnaire

**Date:** **Participant Number:** ____________

**Thyroid Health Cohort - Mothers and Babies at Yorkhill (MABY)**

**Lifestyle and health:**

Do you smoke? ○ No, never. ○ No, I stopped ___ months/years ago ○ Yes, ____ cigarettes/day

Do you take a pregnancy supplement? ○ No ○ Yes

If yes, which brand? ________________________________ how often? ____________________

Do you follow a specific diet (e.g. vegan, vegetarian, etc)? ○ No ○ Yes, ______________________

Is there a history of thyroid disease in your family? ○ No ○ Yes, my _______ had _______________

**If you drink milk, how often and how do you drink it?**

Tick <u>one</u> column for each food (per day, per week or per month)

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | **6+** | **4-5** | **2-3** | **once** | **5-6** | **2-4** | **once** | **1-3** | **Less than once** |
| With tea / coffee | | | | | | | | | |
| In breakfast cereals | | | | | | | | | |
| In chocolate, cappuccino, horlick drinks | | | | | | | | | |
| Just as it is (i.e. glass/cup of milk) | | | | | | | | | |

**How often are you consuming organic milk?**

○ Never ○ Sometimes ○ Often ○ Always

**How often do you eat these foods?** Tick <u>one</u> column for each food (per day, per week or per month)

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | **6+** | **4-5** | **2-3** | **once** | **5-6** | **2-4** | **once** | **1-3** | **Less than once** |
| Oil-rich fish (eg salmon, mackerel, sardine, tuna, herring) | | | | | | | | | |
| White sea-fish | | | | | | | | | |
| Seafood other than fish (inc. prawns, shellfish, seaweed) | | | | | | | | | |
| Cheese (hard or soft) | | | | | | | | | |
| Cheese-based dishes (i.e. pizza, sandwich, cauliflower cheese...) | | | | | | | | | |
| Yoghurts | | | | | | | | | |
| Milk or cream-based puddings (eg custard, ice cream) | | | | | | | | | |

**At the table do you:**

| | YES | NO |
|---|---|---|
| - generally add salt to food without tasting first | | |
| - taste food and then generally add salt | | |
| - taste food but only occasionally add salt | | |
| - rarely or never add salt at table | | |

Which salt brand do you use most often? ________________________________

## Appendix 2 – Systematic Review keywords

### Keywords

[1] search regarding the exposure of the intervention and the exclusion of animal studies: *recommend* OR guideline* OR advice* OR advise* OR consult* OR provision* OR provid* OR supply* OR supplied OR increase* OR improv* OR enrich* OR fortif* NOT rabbit* NOT mice NOT rat NOT rats NOT rodent* NOT pig NOT pigs NOT sheep* NOT mouse NOT monkey* NOT hamster**

[2] search regarding the outcome: *FFQ OR "food frequency questionnaire" OR "food diar*" OR "food recall" OR urin* OR "diet* history" OR "dietary assessment"*

[3] search regarding the study design: *intervention* OR trial* OR RCT OR Prospective OR Controlled OR Cross$over OR Blind**

[4] search regarding iodine nutrition: *milk OR fish OR food* OR nutrition* OR diet* OR dairy OR iod* OR seafood* OR seaweed* OR nutrient* OR nutrition OR micronutrient* OR diet OR iodine NOT radioisotope* NOT "radio$iodine" NOT radioactive NOT radiation NOT radiotherapy NOT "iodine$131" NOT "I$131" NOT "131$I"*

[5] search regarding gestational period: *pregnan* OR gestation* OR concepti* OR pre$concepti* OR matern* OR prenatal* OR antenatal* OR perinatal*.*

## Appendix 3 – Mixed-methods study documents

### Study advertisement

# Participant information sheet

University of Glasgow | College of Medical, Veterinary & Life Sciences

## Participant Information Sheet

***Dietary guidance, iodine and food choices of women before, during and after pregnancy.***

*You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*

1. ***What is the purpose of the study?***

Iodine is an important nutrient found mainly in dairy products and seafood. It is required for the formation of thyroid hormones, which influence a wide range of organs and their functions, such as baby's brain development in the womb and childhood.

This study is part of a doctoral thesis. We aim to involve women (pregnant, planning a pregnancy or breastfeeding) to evaluate the dietary guidance received regarding pregnancy. Our aim is to develop a dietary tool to guide food choices in and around pregnancy.

2. ***Why have I been chosen?***

You are a healthy woman aged 18 to 45, pregnant, lactating or trying to conceive. You live in Scotland, and speak English fluently.

3. ***Do I have to take part?***

It is up to you whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason.

4. ***What will happen to me if I take part?***

You will meet a member of the Research Team from Glasgow University who will explain the study at a time and location convenient to you. As a token of gratitude, all participants taking part in the study will receive a £5 shopping voucher.

5. ***What do I have to do?***

If you decide to take part in this study, you will be asked to fill in a questionnaire about your habitual food consumption and your awareness of the dietary guidelines specific for pregnancy.

After that, you will be asked to take part in a small focus group with 6-8 other women, discussing the topic of *"Dietary choices in pregnancy"* with a facilitator. The conversation will take place in the Human Nutrition department of the University of Glasgow (based at Glasgow Royal Infirmary) or in the main campus of the university (Glasgow West end). They will be recorded, and will last approximately 1 hour.

6. ***What are the possible disadvantages and risks of taking part?***

The main disadvantage is loss of time.

January 2015 Version 1.3

7. ***What are the possible benefits of taking part?***

There are no direct benefits to you associated with taking part. However this study will provide us with a better understanding of the current level and quality of the dietary guidance received by women in pregnancy and lactation.

8. ***Will my taking part in this study be kept confidential?***

All information which is collected about you, or responses that you provide, during the course of the research will be kept strictly confidential. You will be identified by an ID number, and any information about you will have your name and address removed so that you cannot be recognised from it. Recordings will be transcribed in full and analysed for themes. The audio recordings destroyed thereafter and all data will be stored on university computer server for 10 years after the end of the study. Please note that assurances on confidentiality will be strictly adhered to unless evidence of wrongdoing is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies, including the Police.

9. ***What will happen to the results of the research study?***

The results will be published in a doctoral thesis, as well as presented at conferences and scientific journals. All participants who wish to hear about the study findings will be invited to leave contact details, and will be provided with the study report, and any subsequent publication. We will not provide individual transcripts or data.

10. ***Who is organising and funding the research?***

The project is being funded by the Yorkhill Research Support Scheme (R&E project ref: 67707/1).

11. ***Who has reviewed the study?***

This project has been reviewed by the ethics committee of the University of Glasgow, College of Medical, Veterinary and Life Sciences.

12. ***Contact for further information***

If you require further information please contact Dr Emilie Combet by telephone at 0141 201 8527 or via email at emilie.combetaspray@glasgow.ac.uk or Miss Maira Bouga by telephone at 0141 201 8693 or via email at m.bouga.1@research.gla.ac.uk.

***Thank you for reading this information sheet!***

## Consent form

Centre Number:
Project Number: 67707/1
Subject Identification Number for this trial:

### CONSENT FORM

**Title of Project:** ***Dietary guidance, iodine and food choices of women before, during and after pregnancy.***

**Name of Researcher(s):**

**Please initial box**

I confirm that I have read and understand the information sheet dated January 2015 (version 1.3 ) for the above study and have had the opportunity to ask questions. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐

I consent to the discussion during the focus group being recorded. ☐

I agree to take part in the above study. ☐

| | | |
|---|---|---|
| Name of subject | Date | Signature |
| Researcher | Date | Signature |

(1 copy for subject; 1 copy for researcher)

## Questionnaire

University of Glasgow | College of Medical, Veterinary & Life Sciences

**Date:** **Participant Number:** ____________________

**Researcher:**

***Evaluating a new practical tool to support dietary choices during pregnancy***

*Please answer this questionnaire based on your most recent (or current) pregnancy!*

**About you**

**Your age:** ______________ **years**

**Postcode:** ____________________

**Ethnicity:**

○ White Scottish ○ White Irish ○ Other White British ○ Other White European ○ Other White
○ Chinese ○ Indian ○ Pakistani ○ Bangladeshi ○ Other Asian
○ Black African ○ Black Caribbean ○ Other Black ○ Mixed ○ Other ethnic group

**Please specify the highest level of education <u>completed</u> by you to date:**

○ School certificate ○ Standard grade / GCSE ○ Highers / A levels ○ HND / HNC ○ NVQs
○ Other higher education diploma ○ Bachelor degree ○ Master's degree ○ PhD ○ N/A

**Annual Income:** *Please tick the appropriate box corresponding to your annual* ***household net income*** *if living in a family setting, or your* ***personal income****, if living in a shared accommodation setting (with non-family housemates):*

○ <£5,000 ○ £5,001-£10,000 ○ £10,001-£15,000 ○ £15,001-20,000 ○ £20,001-£25,000
○ £25,001-£30,000 ○ £30,001-£35,000 ○ £35,001-£40,000 ○ £40,001-£50,000 ○ > £50,000

**Are you currently a smoker?** ○ YES ○ NO
If yes, how many cigarettes per day? ________________________________________

**Are you taking any medication at the moment?** ○ YES ○ NO
If yes, what medication? __________________________________________________

**Are you currently:** ○ Pregnant — If yes, what is your due date? ____/____/______
○ Breastfeeding — Date you gave birth: ____/____/______
○ Trying to conceive
○ None of the above

Do you already have children? ○ NO ○ YES _____ child(ren)

**Your measurements:**
Height Current weight If pregnant, pre-pregnancy weight

## About your diet

**If you drink milk, how often and how do you drink it?**

Tick **one** column for each food (per day, per week **or** per month)

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | once | 5-6 | 2-4 | once | 1-3 | Less than once |
| With tea / coffee | | | | | | | | | |
| In breakfast cereals | | | | | | | | | |
| Milk for chocolate / horlicks drink | | | | | | | | | |
| Just as it is (i.e. glass/cup of milk) | | | | | | | | | |

**Is this cows milk?** ○ YES ○ NO

**If no**, what alternative do you use? ________________________________

**Is this organic milk?** ○ YES ○ SOMETIMES ○ NO

**At the table do you:**

| | YES | NO |
|---|---|---|
| - generally add salt to food without tasting first | | |
| - taste food and then generally add salt | | |
| - taste food but only occasionally add salt | | |
| - rarely or never add salt at table | | |

Which salt brand do you use most often? _________________________

**How often do you eat these foods?**

Tick **one** column for each food (per day. per week or per month)

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | once | 5-6 | 2-4 | once | 1-3 | Less than once |
| Oil-rich fish (eg salmon, mackerel, sardine, tuna, herring) | | | | | | | | | |
| White sea-fish | | | | | | | | | |
| Seafood other than fish (inc. prawns, shellfish, seaweed) | | | | | | | | | |
| Cheese (hard or soft) | | | | | | | | | |
| Cheese-based dishes (i.e. pizza, sandwich, cauliflower cheese) | | | | | | | | | |
| Yoghurts | | | | | | | | | |
| Milk or cream-based puddings (eg custard, ice cream) | | | | | | | | | |
| Broccoli | | | | | | | | | |
| Cabbage, Brussels sprouts, cauliflower, kale | | | | | | | | | |
| Turnip, pak choi, swede | | | | | | | | | |
| Beansprouts, sweet potatoes | | | | | | | | | |
| Soya products (i.e. tofu, soya milk, veggie burgers) | | | | | | | | | |

**Are you following a vegetarian or vegan diet?** ○ YES ○ NO

*If yes, please indicate which diet you follow:*

○ *Lacto-ovo-vegetarian* (avoiding meat, fish and all other types of seafood only)

○ *Lacto-vegetarian* (avoiding meat, fish, all other types of seafood and eggs only)

○ *Ovo-vegetarian* (avoiding all meat, fish, seafood and all dairy products **except** eggs)

○ *Vegan* (avoiding meat, fish, all other types of seafood and all dairy products **including** eggs)

**Do you take herbal/vitamin supplements?** ○ YES ○ NO

**If yes**, which ones?______________________________ How often? _________________________

## The dietary guidance you have received

**Are / were you generally interested in getting any information about nutrition during pregnancy and lactation?** ○YES ○NO

**Are you aware of dietary and lifestyle guidelines specific for pregnancy/lactation?**

Not at all ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Yes, very aware

**Select any recommendations for pregnant women that you are aware of:** *(Select all that apply)*

○ Stop smoking

○ Stop or limit alcohol

○ Limit caffeine

○ Limit vitamin A intake

○ Avoid certain foods due to bacterial infection risk

○ Avoid certain fish due to toxins

○ Limit oily fish to two portions per week

○ Avoid raw meat, fish or poultry

○ Wash all fruit and vegetables before consumption

**If yes, how did you find out about these guidelines?** *(Select all that apply)*

○ Written information from Doctor, Nurse or Midwife

○ Talking to Doctor, Nurse or Midwife

○ Family or friends

○ Books or magazines

○ Internet

○ Antenatal classes

○ Other *Please Specify:*

**When it comes to healthy eating in pregnancy and lactation, have you heard of, or were you informed about, the following dietary nutrients?**

| | YES | NO | **If yes, where from?** *(Select all that apply)* | | | | |
|---|---|---|---|---|---|---|---|
| | | | Doctor, Nurse or Midwife | Family or friends | Books or magazines | Internet | Antenatal classes |
| Folic Acid | | | | | | | |
| Iron | | | | | | | |
| Iodine | | | | | | | |
| Calcium | | | | | | | |
| Vitamin D | | | | | | | |
| Vitamin A | | | | | | | |

**Thinking about guidelines and recommendations for nutrition and diet during pregnancy / breastfeeding:**

| | | | |
|---|---|---|---|
| Do you find them easy to understand? | ○ YES | ○ NO | ○ N/A |
| Do you find them easy to follow? | ○ YES | ○ NO | ○ N/A |

**Are you aware of the role of the nutrient iodine in the development of the unborn baby?**

○ NO ○ YES, it is important for________________________________________

**Which foods do you think are rich in iodine in the UK?** *(Select all that apply)*

○ Potatoes ○ Oily fish ○ Milk

○ Yoghurts ○ Eggs ○ Table salt

○ Wheat ○ White fish ○ Bread

○ Dark green vegetables

**Your choices during pregnancy (only fill if you are or have been pregnant)**

**How much do you feel that you changed your dietary habits during your pregnancy?** ○ N/A

Not at all ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 Very much

**As part of your current diet, have you changed your consumption of the following foods?**

| | Reduced | Maintained | Increased |
|---|---|---|---|
| Yoghurts | | | |
| Milk (in beverages, cereals) | | | |
| Cheese and spreads | | | |
| Cheese-based dishes (i.e. pizza, sandwich, cauliflower cheese) | | | |
| Milk or cream based puddings (e.g. rice pudding, custard, ice cream) | | | |
| White fish | | | |
| Oil-rich fish (e.g. salmon, mackerel, sardine, tuna, herring) | | | |
| Seafood other than fish (prawns, seaweed, shellfish) | | | |
| Eggs | | | |
| Meat | | | |
| Bread, rice, cereals, pasta | | | |
| Soya products (i.e. tofu, soya milk) | | | |
| Brassicas (cabbages, Brussels sprouts, cauliflower, kale, broccoli) | | | |
| Other vegetables | | | |
| Fruits | | | |

**If you stopped/eat less of any of these foods, was this due to:** *(Select all that apply)*

○ Specific recommendations ○ Morning sickness ○ Heartburn

○ Uncertainty of being harmful ○ Taste / smell ○ Cost/ money

○ Time ○ Other *Please Specify:* ______________________

**Which of the following recommendations do/did you follow during conception/ pregnancy/ lactation?** *(Select all that apply)* ○ N/A

○ Stop smoking / Not smoking ○ Stop or limit alcohol / Not drinking alcohol ○ Limit / not consuming caffeine

○ Limit vitamin A intake ○ Avoid certain foods due to bacterial infection risk ○ Avoid certain fish due to toxins

○ Limit oily fish to two portions per week ○ Avoid raw meat, fish or poultry ○ Wash all fruit and vegetables before consumption

**Who/what influenced your dietary choices during conception/ pregnancy/ lactation?** *(Select all that apply)* ○ N/A

○ Written information from Doctor, Nurse or Midwife ○ Talking to Doctor, Nurse or Midwife ○ Family or friends

○ Books or magazines ○ Internet ○ Antenatal classes

○ Other *Please Specify:*

**Are you confident on how to achieve an adequate iodine intake in pregnancy and lactation?**

Not at all ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○7 Very much

**Do/did you use any resource in particular to gain information regarding diet around the time of conception, pregnancy and breastfeeding?**

○ NO ○ YES, I used ______________________________

**When reading / receiving information about diet and nutrition, do you prefer information focusing on**

○ foods only ○ specific elements (eg. vitamins, fat, proteins etc.) ○ Both

**If you receive information focussing on specific food elements (e.g. vitamins, minerals) do you know how to relate this to foods and how to modify your diet?**

○ YES ○ SOMETIMES ○ NO

**In your opinion, what would be the best way to offer understandable, practical guidance to women regarding diet around the time of conception, pregnancy and breastfeeding?**

**Would you like to participate in any future studies, relevant to the topic?** ○ YES ○ NO

## Interviews topic guide

***Questions***

1. *Are you interested in nutrition and the role it plays to health?*
2. *Think back to when you were pregnant /* ***thinking about your pregnancy*** */ thinking about pregnancy, what information were you given about food and diet for pregnancy and in what form?*
3. *Who spoke to you about food and diet for pregnancy and what did you do with this information?*
4. *a. What do you know about the importance of iodine in the diet and particularly during pregnancy? b. How do you know this?*
5. *Iodine is a nutrient important for fetus and infant development and women during pregnancy and lactation have increased demands. Do you know which of these foods the sources of iodine are?* ***(photos)***
6. *Dairy products, fish and seafood are the richest sources of iodine. How much do you think a pregnant / breastfeeding woman should eat of those foods so that she reaches the recommended intake?* ***(photos)***
7. *A pregnant woman should eat* ***2 portions of white fish and 1 portion of oily fish per week plus 1 glass of milk, 3 portions of milk in coffee or tea, 2 yoghurts, 1 cheese based dish and 2 cheese portions per day*** *to reach the recommended iodine intake! Do you find it difficult to increase the intake of dairy products, fish and seafood or even to maintain it? Which do you think these barriers are?*
8. *What do you think is the best way of getting information about a specific nutrient (e.g. iodine, folic acid, iron, vitamin D)?*
9. *What do you think would help you,* ***practically****, increase your iodine intake? For example, think of a gadget, an electronic application, advice from someone, a leaflet, a website etc.*
10. *If you had to think innovatively, what would you design to deliver this information? Can you think of a tool that would help people understand nutritional advice and change their diet accordingly?*

## Photos provided to participants during the interview

*To select iodine-rich foods*

Salt

Dairy

Red meat

Sushi

Milk

Vegetables

Fish and Seafood

*To select combination of portions to reach WHO recommended iodine intake*

Cheese

Glass of milk

Yoghurt

Oil-rich fish

Cheese based dish

White fish

Milk in drinks

## Appendix 4 – Dairy products survey documents

### Study advertisement

## Participant information sheet

University of Glasgow | College of Medical, Veterinary & Life Sciences

### Participant Information Sheet

***Consumer's perceptions on dairy products and health***

*'You are being invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.'*

1. **What is the purpose of the study?**

Nutrition is an important part of health, however, dietary recommendations and guidelines are often misunderstood, perceived as confusing, or not communicated effectively. This study is designed to investigate UK residents' behaviour and perception towards milk and other dairy products. The results of the study will inform future work on nutrition communication and the improvement of nutritional recommendations for the UK population.

2. **Why have I been chosen?**

You have been approached at a recruitment venue or you have come across the questionnaire online; you are living in the UK and speak English fluently.

3. **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep. If you decide to take part your consent is implied by filling in the questionnaire but you are still free to withdraw at any time and without giving a reason. If you are a student of the University of Glasgow or any other institution a decision not to participate will not affect your grades in any way.

4. **What will happen to me if I take part?**

You will be asked to fill in a short questionnaire, and will have the chance to enter a free prize draw to win a £50 worth shopping voucher at the end of the study.

5. **What do I have to do?**

If you agree to take part in this study you will be asked to fill in a questionnaire that takes approximately 15 minutes. You will also have the opportunity to provide us with a contact number should you be willing to take part in a phone interview on the same subject in the future. There are no lifestyle or other restrictions for you during the study.

6. **What are the possible disadvantages and risks of taking part?**

There are no disadvantages or risks to taking part in this study. The questionnaire is short and should take approximately 15 minutes to complete.

7. **What are the possible benefits of taking part?**

You will receive no direct benefit from taking part in this study. The information that is collected will give us a better understanding of UK residents' perceptions of milk and dairy products and permit us evaluate their impact on the UK diet.'

version 1.0 February 2015

8. **Will my taking part in this study be kept confidential?**

All information which is collected about you, and the responses you provide, during the course of the research will be kept strictly confidential. You will be identified by an ID number and any information about you will have your name and address removed so that you cannot be recognised from it. Please note that assurances on confidentiality will be strictly adhered to unless evidence of serious harm, or risk of serious harm, is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

9. **What will happen to the results of the research study?**

Results will be presented at meetings of learned societies and published in scientific journals. Results will also be included in student project reports, when applicable.

10. **Who is organising and funding the research?**

This study is organised by the Human Nutrition Section of the University of Glasgow.

11. **Who has reviewed the study?**

This project has been reviewed by the ethics committee of the University of Glasgow, College of Medical, Veterinary and Life Sciences.

12. **Contact for Further Information**

If you require further information please contact Dr Emilie Combet by telephone at 0141 201 8527 or via email at emilie.combetaspray@glasgow.ac.uk or Miss Maira Bouga by telephone at 0141 201 8693 or via email at m.bouga.1@research.gla.ac.uk.

***Thank you for reading this information sheet!***

## Consent form

University of Glasgow | College of Medical, Veterinary & Life Sciences

Centre Number:
Project Number:
Subject Identification Number for this trial:

### CONSENT FORM

**Title of Project:** ***Consumer's perceptions on dairy products and health***

**Name of Researcher(s):**

**Please initial box**

I confirm that I have read and understand the information sheet dated February 2015 (version 1.0 ) for the above study and have had the opportunity to ask questions. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. ☐

I agree to take part in the above study. ☐

| Name of subject | Date | Signature |
|---|---|---|

| Researcher | Date | Signature |
|---|---|---|

(1 copy for subject; 1 copy for researcher)

College of MVLS
Ethics Committee

v1.2

# Questionnaire

University of Glasgow

## Consumer's perceptions of dairy products and health

This questionnaire is designed to explore consumers' perceptions of dairy products and health. A ***dairy product*** or ***milk product*** is food produced from the milk of mammals, including milk, cheese, yogurt, butter, ice cream and crème fraiche. Chocolates, cheese-based dishes and dairy-based sweets are **not** included in the dairy products in this survey.

| ***Section 1*** |
|---|

**1. Please provide UP TO 2 words or groups of words that come to mind when thinking about the foods below and health/ nutrition:**

**a. milk:**

| |
|---|
| **1.** |
| **2.** |

**b. yogurt:**

| |
|---|
| **1.** |
| **2.** |

**c. cheese:**

| |
|---|
| **1.** |
| **2.** |

**2. Please complete the sentence with a number:**

| |
|---|
| *A balanced diet for a healthy adult should include _____ servings of dairy products per day.* |

**3a. Have you heard about the associations between dairy / dairy products and any of the following?** (*Please tick all that apply*)

☐ Calcium and bone health

☐ Iodine and thyroid function

☐ Protein-rich diets

☐ Vitamin D and bone health

**b. If yes, which did you understand well?**

☐ Calcium and bone health

☐ Iodine and thyroid function

☐ Protein-rich diets

☐ Vitamin D and bone health

**4a. Have you heard about dairy products and the diet in the news during the past few months?**

☐ No

☐ Yes, about the new "Eatwell plate" (Eatwell guide)

☐ Yes, general discussions/ news about dairy products in the media

**b. If yes, please give more detail:**

| |
|---|
| |

**c. As a result, are you considering to…**

☐ Increase your dairy products intake

☐ Decrease your dairy products intake

☐ Keep your dairy products intake same as before

**5. Do you consider soya milk and other milk alternatives as dairy products?**

○ Yes ○ No

**Section 2**

**6. Rate from 1 to 5 how much these factors influence your choice of dairy products (what you buy or order).**

*(1: not at all, 5: very much)*

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1. Other people's preference (e.g. partner, children) | | | | | |
| 2. What is thought to be healthy | | | | | |
| 3. Convenience of preparation | | | | | |
| 4. Special shopping offers | | | | | |
| 5. Dietary requirements of a family member | | | | | |
| 6. Articles about food/recipes | | | | | |
| 7. Marketing strategies (advertisements etc.) | | | | | |
| 8. Cost | | | | | |
| 9. Taste | | | | | |
| 10. Smell | | | | | |
| 11. Texture | | | | | |
| 12. Packaging / appearance | | | | | |
| 13. Brand | | | | | |
| 14. Freshness (sell by date information etc.) | | | | | |
| 15. Environmental practices (organic etc.) | | | | | |
| 16. Product origin (local, country of production etc.) | | | | | |
| 17. Recommendation by health expert in media | | | | | |
| 18. Recommendation by GP/ Nutritionist/ Dietitian/ other health care professional | | | | | |

**7. Rate from 1 to 5 how much you agree with the statements below.**

*(1: strongly disagree, 5: strongly agree)*

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1. I buy fortified products (e.g. with iron, vitamin D etc). | | | | | |
| 2. I am allergic to dairy products. | | | | | |
| 3. I choose low fat products when I want to lose weight. | | | | | |
| 4. I choose milk alternatives because they are popular (e.g. soya milk etc.). | | | | | |
| 5. I do not like trying new dairy products that I have not tasted before. | | | | | |

**8. Select which of the statements is true for you regarding…**

| | I like it. | I do not like it, so I do not drink / eat it. | I do not like it but I am trying to include it in my diet. |
|---|---|---|---|
| a. **Milk** | | | |
| b. **Yoghurt** | | | |
| c. **Cheese** | | | |

9. Choose what you think is the correct answer regarding:

| **a. Dairy products in general** | **True** | **False** | **Not sure** |
|---|---|---|---|
| 1. Only some dairy products are healthy. | | | |
| 2. Promoting dairy consumption may have negative effects on health. | | | |
| 3. Dairy products are not good for the environment. | | | |
| 4. Dairy products are the main source of iodine in the diet. | | | |
| 5. Dairy products should be avoided in order to limit saturated fats intake. | | | |

| **b. Milk** | **True** | **False** | **Not sure** |
|---|---|---|---|
| 1. Milk consumption is associated with weight gain. | | | |
| 2. Milk consumption is associated with digestive problems. | | | |
| 3. Milk alternatives (e.g. soya milk, almond milk etc.) are healthier than cow's milk. | | | |
| 4. Elderly people should increase their milk consumption. | | | |
| 5. Children should drink more milk than adults. | | | |
| 6. Women should drink more milk than men. | | | |
| 7. Milk is rich in saturated fat and is linked to heart disease. | | | |
| 8. Milk is rich in calcium. | | | |
| 9. Milk is high in protein. | | | |
| 10. Milk is rich in vitamins and minerals. | | | |
| 11. Milk consumption can prevent osteoporosis. | | | |

| **c. Yogurt** | **True** | **False** | **Not sure** |
|---|---|---|---|
| 1. Full fat yogurt consumption is associated with weight gain. | | | |
| 2. Low fat yogurt consumption helps weight loss. | | | |
| 3. Yogurt consumption is associated with digestive problems. | | | |
| 4. Women should eat more yogurt than men. | | | |
| 5. Yogurt is rich in saturated fat and its consumption is linked to heart disease. | | | |
| 6. Yogurt is rich in calcium. | | | |
| 7. Yogurt is high in protein. | | | |
| 8. Yogurt is rich in vitamins and minerals. | | | |
| 9. Yogurt consumption can prevent osteoporosis. | | | |

| d. Cheese | True | False | Not sure |
|---|---|---|---|
| 1. Full fat cheese consumption is associated with weight gain. | | | |
| 2. Cheese is high in salt. | | | |
| 3. Cheese is rich in saturated fat and its consumption is linked to heart disease. | | | |
| 4. Cheese is rich in calcium. | | | |
| 5. White cheese contains more calcium. | | | |
| 6. Cheese is high in protein. | | | |
| 7. Cheese is rich in vitamins and minerals. | | | |
| 8. Cheese consumption can prevent osteoporosis. | | | |

**10. In your opinion, what are the 3 main reasons to limit dairy consumption?**

| |
|---|
| **1.** |
| **2.** |
| **3.** |

## *Section 3*

*Circle your answer*

**11. The experts contradict each other over what foods are good / bad for health.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**12. Diet is one way of effectively reducing the risk of developing some diseases.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**13. I hope to change my dairy intake within the next month so that I follow better the guidelines of a balanced healthy diet.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**14. I understand the information available to me about diet and foods (media including TV, radio, print, internet, health professionals) and I am able to use this information to make decisions about my diet and health**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

## *Section 4*

**15. Are you following a vegetarian or vegan diet?**

○ *No*

○ *Yes, pescetarian* (avoiding meat only)
○ *Yes, lacto-ovo-vegetarian* (avoiding meat, fish and other types of seafood only)
○ *Yes, lacto-vegetarian* (avoiding meat, fish, other types of seafood and eggs only)
○ *Yes, ovo-vegetarian* (avoiding all meat, fish, seafood and all dairy products **except** eggs)
○ *Yes, vegan* (avoiding meat, fish, all other types of seafood and all dairy products **including** eggs)

**16. If you drink COW's milk, how often and how do you drink it?**

*Tick <u>one</u> column for each food (per day, per week or per month)*

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | 1 | 5-6 | 2-4 | 1 | 1-3 | <1 |
| With tea / coffee (other than cappuccino/ latte) | | | | | | | | | |
| On breakfast cereals | | | | | | | | | |
| Milk for chocolate/ horlicks drink/ cappuccino/ latte | | | | | | | | | |
| Just as it is (i.e. glass / cup of milk) | | | | | | | | | |

**17. What type(s) of milk do you use?**

| | **Never** | **Sometimes** | **Often** | **Always** | **I don't know** |
|---|---|---|---|---|---|
| Cow's pasteurised milk | | | | | |
| Cow's UHT milk | | | | | |
| Evaporated milk | | | | | |
| Organic milk | | | | | |
| Goat's milk | | | | | |
| Soya milk | | | | | |
| Other plant milks (ie. almond, rice, coconut etc.) | | | | | |
| Flavoured milk (ie. strawberry, chocolate etc.) | | | | | |
| Milk powder | | | | | |
| Lacto-free milk | | | | | |
| Other *(please specify):* | | | | | |

**18. In your typical diet, how often do you eat these foods?**

*Tick **<u>one</u>** column for each food (per day. per week or per month)*

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | 1 | 5-6 | 2-4 | 1 | 1-3 | <1 |
| Cheese (hard or soft) | | | | | | | | | |
| Cheese-based dishes (i.e. pizza, sandwich, cauliflower cheese) | | | | | | | | | |
| Yoghurts | | | | | | | | | |
| Milk or cream-based puddings (e.g. custard, ice cream) | | | | | | | | | |

**19. Are you replacing “full fat” dairy products with the following “low fat” or “fat free” dairy alternatives?**

| | Never | Sometimes | Often | Always |
|---|---|---|---|---|
| Low fat / fat free yoghurts | | | | |
| Skimmed milk | | | | |
| Semi-skimmed milk | | | | |
| Low fat cheese & spreads | | | | |

**20. How often do you:**

| | Never | 1-2 days/month | 1-3 days/week | 4-6 days/week | 1-2 times/day |
|---|---|---|---|---|---|
| Cook | | | | | |
| Eat homemade food, made by a family member / friend | | | | | |
| Eat ready meals | | | | | |
| Eat in a restaurant / canteen | | | | | |
| Eat fast food / sandwiches | | | | | |

**21a. Are you lactose intolerant?** ○ Yes ○ No

**b. If yes, was this diagnosed by a GP/ doctor?** ○ Yes ○ No

**22. Please add any comments that you have on the topic of dairy products and health.**

| Section 5 |
|---|

**23. Gender:** ○ Male ○ Female

**24. Age:** ____________ years

**25. Ethnic background?**
○ British ○ Other European ○ Mixed or Multiple ethnic groups ○ Asian
○ African ○ Caribbean or Black ○ Other ethnic group

**26. Please specify the highest level of education completed by you to date:**
○ Current pupil / School leaver / certificate / standard Grade / GCSE ○ Highers / A levels ○ HND / HNC / NVQs / Other higher education diploma
○ Bachelor degree ○ Master's degree ○ PhD

**27. Please select if you have studied any of the following:**
○ Nutrition / Dietetics ○ Food sciences ○ Health Sciences

**28. Annual Income:** *Please tick the appropriate box corresponding to your annual **household net income** if living in a family setting, or your **personal income**, if living in a shared accommodation setting (with non-family housemates):*
○ <£15,000 ○ £15,001 - £30,000 ○ £30,001 - £50,000 ○ >50,000

**29. How many adults including yourself (18 and over) live in your household?** _____

**30. How many children including yourself (under 18) live in your household?** _____

**31. Do you live…**
○ With parents ○ With friends ○ Student accommodation
○ With family ○ With partner ○ Alone

**32. Are you the main grocery shopper in your household?** ○ Yes ○ No

**33. Have you been told by your GP / doctor that you have any of the following?**
*Please select all that apply.*

☐ Diabetes ☐ High blood pressure
☐ Heart disease ☐ High Cholesterol
☐ Osteoporosis ☐ High Triglyceride
☐ Metabolic syndrome ☐ Amemia (due to iron deficiency)
☐ Osteomalacia (due to vitamin D deficiency) ☐ Other: ______________________

**34. Please select anything that applies to your current status:**

☐ Pregnant
☐ Breastfeeding
☐ Following a weight loss diet

**35. If you were told that milk is a key source of iodine in the UK diet, a nutrient essential for pregnancy, the fetus and the children, would you increase provision of milk in the house/ for your children/ your own consumption?**

○ Yes ○ No

***Please explain why:***

**Please supply contact details overleaf if you are interested in taking part in a phone interview or wold like to enter the prize draw. The final page will be detached on receipt of your filled questionnaire to anonymise your data.**

## Appendix 5 – Fish & seafood products survey documents

### Study advertisement

University of Glasgow

**Fish, seafood & health**
**Online Survey**

***#FishHabits***


If you
- live in the UK
- are older than 14 years

fill in our survey for a chance to win a £50 shopping voucher!

Questionnaire Link: bit.ly/fishhabits

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OR scan the QR code
*OR*

Find us on: facebook. Human Nutrition Research – Glasgow

*OR*
*Contact mairabouga@gmail.com for a paper version*

# Participant information sheet

University of Glasgow | College of Medical, Veterinary & Life Sciences

## Participant Information Sheet

***Consumer's perceptions on fish/ seafood and health***

*'You are being invited to take part in a research study. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.'*

1. **What is the purpose of the study?**

Nutrition is an important part of health, however, dietary recommendations and guidelines are often misunderstood, perceived as confusing, or not communicated effectively. This study is designed to investigate UK residents' behaviour and perception towards fish and seafood. The results of the study will inform future work on nutrition communication and the improvement of nutritional recommendations for the UK population.

2. **Why have I been chosen?**

You have been approached at a recruitment venue or you have come across the questionnaire online; you are living in the UK and speak English fluently.

3. **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep. If you decide to take part your consent is implied by filling in the questionnaire but you are still free to withdraw at any time and without giving a reason. If you are a student of the University of Glasgow or any other institution a decision not to participate will not affect your grades in any way.

4. **What will happen to me if I take part?**

You will be asked to fill in a short questionnaire, and will have the chance to enter a free prize draw to win a £50 worth shopping voucher every 200 entries at the end of the study.

5. **What do I have to do?**

If you agree to take part in this study you will be asked to fill in a questionnaire that takes approximately 15 minutes. You will also have the opportunity to provide us with a contact number should you be willing to take part in a phone interview on the same subject in the future. There are no lifestyle or other restrictions for you during the study.

6. **What are the possible disadvantages and risks of taking part?**

There are no disadvantages or risks to taking part in this study. The questionnaire is short and should take approximately 15 minutes to complete.

7. **What are the possible benefits of taking part?**

You will receive no direct benefit from taking part in this study. The information that is collected will give us a better understanding of UK residents' perceptions of fish and seafood and permit us evaluate their impact on the UK diet.'

version 1.0 September 2016

**8. Will my taking part in this study be kept confidential?**

All information which is collected about you, and the responses you provide, during the course of the research will be kept strictly confidential. You will be identified by an ID number and any information about you will have your name and address removed so that you cannot be recognised from it. Please note that assurances on confidentiality will be strictly adhered to unless evidence of serious harm, or risk of serious harm, is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

**9. What will happen to the results of the research study?**

Results will be presented at meetings of learned societies and published in scientific journals. Results will also be included in student project reports, when applicable.

**10. Who is organising and funding the research?**

This study is organised by the Human Nutrition Section of the University of Glasgow.

**11. Who has reviewed the study?**

This project has been reviewed by the ethics committee of the University of Glasgow, College of Medical, Veterinary and Life Sciences.

**12. Contact for Further Information**

If you require further information please contact Dr Emilie Combet by telephone at 0141 201 8527 or via email at emilie.combetaspray@glasgow.ac.uk or Miss Maira Bouga by telephone at 0141 201 8693 or via email at m.bouga.1@research.gla.ac.uk.

***Thank you for reading this information sheet!***

# Questionnaire

University of Glasgow

## Consumer's perceptions on fish & seafood and health

This questionnaire is designed to explore consumers' perceptions of fish, seafood and health.

| Section 1 |
|---|

**1. Please provide UP TO 3 words or groups of words that come to mind when thinking about fish & seafood in relation to nutrition & health:**

| |
|---|
| **1.** |
| **2.** |
| **3.** |

**2. Please complete the sentence with a number:**

*A balanced diet for a healthy adult should include _____ servings (portions) of fish / seafood per week.*

**3. Which of the following have you heard about?** (*Please tick all that apply*)

☐ Fish / seafood and muscle mass maintainance

☐ Fish / seafood and heart health

☐ Fish / seafood and vision

☐ Fish / seafood and brain / cognition

☐ Fish / seafood and anemia

☐ Fish / seafood and thyroid function

☐ Other relevant to fish / seafood consumption

**4. Have you heard / seen news stories about fish & seafood products and the diet in the media during the past few months?**

☐ No

☐ Yes, about the new "Eatwell plate" (Eatwell guide)

☐ Yes, general discussions / news in the media

**5. Fish oil supplements can be a substitute for fish and seafood consumption.**

☐ Agree ☐ Disagree ☐ Not sure

**6. Fish & seafood can be a good source of:** *(Please tick all that apply)*

- ☐ Protein
- ☐ Calcium
- ☐ Folic acid
- ☐ Vitamin D
- ☐ Iron
- ☐ Iodine
- ☐ Omega 3 fatty acids
- ☐ Sodium (salt)
- ☐ Vitamin A
- ☐ Vitamin C

***Section 2***

**7. Consider the statements regarding fish & seafood products:**

| | Agree | Disagree | Not sure |
|---|---|---|---|
| 1. Only some fish / seafood products are good for health. Some others might have negative health effects. | | | |
| 2. Promoting fish consumption may have negative effects on health. | | | |
| 3. Fish & seafood fishing / production are not good for the environment. | | | |
| 4. I increase my fish / seafood intake when I want to lose weight. | | | |
| 5. I like trying new fish / seafood products that I have not tasted before. | | | |

**8. Please rate how much you agree with the statements below:**

**a. I believe that there is a HEALTH RISK arising from fish & seafood consumption due to:**

*(1: not at all, 5: very much)*

| | 1 | 2 | 3 | 4 | 5 | I don't know |
|---|---|---|---|---|---|---|
| 1. toxins in polluted oceans | | | | | | |
| 2. antibiotics and colourings used in fish farming | | | | | | |
| 3. heavy metals | | | | | | |
| 4. food poisoning (bacteria) and parasites in fish | | | | | | |

**b. I believe that there is an ENVIRONMENTAL RISK arising from fish & seafood consumption due to:**

*(1: not at all, 5: very much)*

| | 1 | 2 | 3 | 4 | 5 | I don't know |
|---|---|---|---|---|---|---|
| 1. overfishing and risk to biodiversity | | | | | | |
| 2. ethical implications of intensive fishing and fish farming | | | | | | |
| 3. harm to other animals or to ecosystems eg. dolphins | | | | | | |

**c. I believe that there are ECONOMIC ISSUES arising from fish & seafood consumption due to:**

*(1: not at all, 5: very much)*

| | 1 | 2 | 3 | 4 | 5 | I don't know |
|---|---|---|---|---|---|---|
| 1. intensive fishing and farming is not sustainable and will cost the environment | | | | | | |
| 2. fish production costs (via farming) driving quality down | | | | | | |
| 3. the cost of fish & seafood being high for the consumer | | | | | | |

**9. Select which of the statements is true for you regarding…**

| | I like it. | I do not like it, so I do not eat it. | I do not like it but I am trying to include it in my diet. |
|---|---|---|---|
| a. **White fish** (e.g. cod, haddock, plaice, pollock) | | | |
| b. **Oily fish** (e.g. salmon, mackerel, sardines, herring) | | | |
| c. **Shellfish** (e.g. prawns, mussels, scallops, squid) | | | |
| d. **Seaweed** (e.g. kelp, nori) | | | |

**10. Diet is one way to effectively reduce the risk of developing some diseases.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**11. I know that 'fish is good for you', but I don't know why.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**12. In your opinion, what are the 3 main reasons why you do include or exclude fish from your diet?**

| |
|---|
| **1.** |
| **2.** |
| **3.** |

***Section 3***

*Please circle your answer*

**13. The experts contradict each other over what foods are good / bad for health.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**14. Rate from 1 to 5 how much these factors influence your choice of fish & seafood (what you buy or order).** *(1: not at all, 5: very much)*

| | **1** | **2** | **3** | **4** | **5** |
|---|---|---|---|---|---|
| 1. Other people's preference (e.g. partner, children) | | | | | |
| 2. Specific dietary requirements of a family member | | | | | |
| 3. What is thought to be good for health | | | | | |
| 4. Marketing strategies (advertisements etc.) | | | | | |
| 5. Recommendation by health expert in the media | | | | | |
| 6. Recommendation by GP / Nutritionist / Dietitian / other health care professional | | | | | |

**15. How much do you trust the following bodies, in terms of health recommendations for fish, seafood and production standards:** *(1: not at all, 5: very much)*

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1. the food industry | | | | | |
| 2. the government public health department | | | | | |
| 3. supermarkets and large retailers | | | | | |
| 4. scientists, researchers | | | | | |
| 5. local producers and fishermen | | | | | |
| 6. the media, journalists | | | | | |

**16. Who are the main persons / groups who have influenced your current level of consumption and choices of fish & seafood?** *- Please select up to 3*

- ☐ Parental figure (mother, father, grandparent)
- ☐ Current family (child, partner)
- ☐ Dietician, nutritionist or other healthcare professional
- ☐ Peers, friends, colleagues
- ☐ Media (TV, radio, press)
- ☐ Yourself, via education and self-study
- ☐ Scientists, researchers
- ☐ Associations (e.g. vegans / vegetarians)
- ☐ Nutritional therapist, herbalist, naturopath, alternative doctor
- ☐ Social media (Twitter, Facebook, Pinterest, Instagram, web forums etc.)
- ☐ Hometown food culture / traditions
- ☐ Other :________________________________________________

***Section 4***

*Please circle your answer*

**17. I understand the information available to me about diet and foods (media including TV, radio, print, internet, health professionals) and I am able to use this information to make decisions about my diet and health**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |

**18. The decisions I make about my fish consumption are informed by my knowledge of the related benefits and risks.**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |

**19. I have the skills / knowledge required to cook fish & seafood based meals.**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |

**20. I can find places in my neighbourhood that sell fresh fish & seafood.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

## *Section 5*

*Please circle your answer*

**21. I am willing to include fish & seafood products in my diet to meet the recommendations of a healthy balanced diet.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**22. I aim to avoid eating fish & seafood.**

| Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|---|---|---|---|---|---|---|---|

**23. If you were told that 'fish is a key source of iodine', a nutrient essential for pregnancy, the baby and the children, would you increase the provision of fish & seafood in the house / for your partner / children / your own consumption?**

☐ Yes ☐ No

***Please explain why:***

## *Section 6*

**24. Are you following a vegetarian or vegan diet?**

☐ *No*

☐ *Yes, pescetarian* (avoiding meat only)
☐ *Yes, lacto-ovo-vegetarian* (avoiding meat, fish and other types of seafood only)
☐ *Yes, lacto-vegetarian* (avoiding meat, fish, other types of seafood and eggs only)
☐ *Yes, ovo-vegetarian* (avoiding all meat, fish, seafood and all dairy products **except** eggs)
☐ *Yes, vegan* (avoiding meat, fish, all other types of seafood and all dairy products **including** eggs)

**25. How often do you:**
*Please remember to consider all meals taken throughout the day.*

| | Never | 1-2 days / month | 1-3 days / week | 4-6 days / week | 1 or more times / day |
|---|---|---|---|---|---|
| Cook for yourself / family | | | | | |
| Eat homemade food, made by a family member / friend | | | | | |
| Eat ready meals at home | | | | | |
| Eat in a restaurant / canteen (food bought and served at the table or from a buffet) | | | | | |
| Eat from shops selling sandwiches / take away food | | | | | |

**26. As far as I remember, I have never tried fish.** ☐ Agree ☐ Disagree

**27. In your typical diet, how often do you eat / drink these foods?**

*Tick one column for each food (per day or per week or per month)*

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | 1 | 5-6 | 2-4 | 1 | 1-3 | <1 or never |
| Oil-rich fish (e.g. salmon, mackerel, sardine, tuna, herring) | | | | | | | | | |
| White sea-fish (e.g. cod, haddock) | | | | | | | | | |
| Other seafood (e.g. prawns, shellfish, mussels, seaweed) | | | | | | | | | |
| Cheese-based dishes (e.g. pizza, sandwich, cauliflower cheese) | | | | | | | | | |
| Cheese (hard or soft) | | | | | | | | | |
| Yoghurts | | | | | | | | | |
| Milk or cream-based puddings (e.g. custard, ice cream) | | | | | | | | | |
| Milk in breakfast cereals | | | | | | | | | |
| Milk in chocolate / horlicks drink / cappuccino / latte | | | | | | | | | |
| Milk with tea / coffee | | | | | | | | | |
| Milk just as it is (i.e. glass / cup of milk) | | | | | | | | | |

**28. How often do you buy / eat:**

| | Never | Sometimes | Often | I don't know |
|---|---|---|---|---|
| Fish & chips (from canteen / take away etc.) | | | | |
| Sandwiches with fish filling | | | | |
| Fresh fish (cod, salmon etc.) | | | | |
| Fresh seafood (prawns, calamari etc.) | | | | |
| Canned fish (sardine, tuna, mackerel etc.) | | | | |
| Canned seafood (cockles, calamari etc.) | | | | |
| Frozen fish | | | | |
| Frozen seafood | | | | |
| Ready cooked seafood dishes / Ready meals | | | | |
| Smoked fish | | | | |
| Sushi dishes containing seafood / seaweed | | | | |

**29a. Do you take herbal/vitamin supplements?** ☐ Yes ☐ No

**b. If yes, which ones?**______________________ **c. How often?** ____________________

### *Section 7*

**30. Rate from 1 to 5 how much these factors influence your choice of fish & seafood (what you buy or order).** *(1: not at all, 5: very much)*

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 1. Convenience of preparation (how much effort) | | | | | |
| 2. Special shopping offers | | | | | |
| 3. Recipes and food articles in magazines / online | | | | | |
| 4. Cost | | | | | |
| 5. Taste | | | | | |
| 6. Smell | | | | | |
| 7. Texture | | | | | |
| 8. Packaging / appearance | | | | | |
| 9. Brand (eg. John West, Young) | | | | | |
| 10. Freshness (sell by date etc.) and storage requitements (refrigeration, freezing) | | | | | |
| 11. Environmental practices (fish farming, organic etc.) | | | | | |
| 12. Product origin (local, country of production etc.) | | | | | |
| 13. Availability as a ready meal | | | | | |
| 14. Availability from a takeaway shop | | | | | |

**31. If you or your partner are / have been pregnant, how well do / did you understand the recommendations regarding fish & seafood consumption in pregnancy?**

☐ Neither myself nor my partner have been pregnant.

| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |
|---|---|---|---|---|---|---|---|---|

**32. Please add any other comments or observations that you have on the topic of fish, seafood, diet and health.**

### *Section 8*

**33. Gender:** ☐ Male ☐ Female

**34. Age:** ____________ years

**35. Ethnic background?**

☐ British ☐ Other European ☐ Mixed or Multiple ethnic groups ☐ Asian

☐ African ☐ Caribbean or Black ☐ Other ethnic group

**36. Please specify the highest level of education <u>completed</u> by you to date:**

☐ Current pupil / School leaver / Certificate / standard Grade / GCSE ☐ Highers / A levels ☐ HND / HNC / NVQs / Other higher education diploma

☐ Bachelor degree ☐ Master's degree ☐ PhD

**37. Please select if you have studied any of the following:**

☐ Nutrition / Dietetics ☐ Food sciences ☐ Health Sciences

**38. Annual Income:** *Please tick the appropriate box corresponding to your annual* ***household net income*** *if living in a family setting, or your* ***personal income****, if living in a shared accommodation setting (with non-family housemates):*

☐ <£15,000 ☐ £15,001 - £30,000 ☐ £30,001 - £50,000 ☐ >50,000

☐ Prefer not to say

**39. How many adults including yourself (18 and over) live in your household?** _____

**40. How many children including yourself (under 18) live in your household?** _____

**41. Do you live…**

☐ With parents ☐ With friends ☐ Student accommodation

☐ With partner only ☐ Alone ☐ With family (children and / or partner) ☐ Other

**42. Are you the main grocery shopper in your household?**

☐ Yes ☐ Sometimes / occasionally ☐ No

**43. Are you the main cook in your household?**

☐ Yes ☐ Sometimes / occasionally ☐ No

**44. Please select anything that applies to your current status:**

☐ Pregnant ☐ Breastfeeding ☐ Following a weight loss diet

**45. Have you been told by your GP / doctor that you have any of the following?**

*Please tick all that apply.*

- ☐ Diabetes
- ☐ Heart disease
- ☐ Osteoporosis
- ☐ Thyroid disease
- ☐ Osteomalacia (due to vitamin D deficiency)
- ☐ High blood pressure
- ☐ High cholesterol
- ☐ High triglyceride
- ☐ Anemia
- ☐ Other: ____________________

*Details on thyroid disease:*______________________________________________

**46a. Are you allergic to any fish or seafood product?** ☐ Yes ☐ No

**b. If yes, was this diagnosed by a GP / doctor?** ☐ Yes ☐ No

**47. What kind of kitchen equipment do you have access to?** *Please tick all that apply*

- ☐ Kettle
- ☐ Toaster
- ☐ Equipment: cutlery, crockery, kitchen utensils
- ☐ Fridge
- ☐ Freezer
- ☐ Microwave oven
- ☐ Hob
- ☐ Oven
- ☐ No kitchen access

**Please supply contact details overleaf if you are interested in taking part in a phone interview or would like to enter the prize draw. The final page will be detached on receipt of your filled questionnaire to anonymise your data.**

## Appendix 6 – PICk study documents

### PICk advertisement

# PICk participants information sheet

University of Glasgow | College of Medical, Veterinary & Life Sciences

PICk

## Participant Information Sheet

***Nutrition and food choices in early pregnancy***

*You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.*

1. **What is the purpose of the study?**

Nutrition in pregnancy is important for mother's and baby's health. Although some of the pregnancy guidelines are well known amongst women in the UK, dietary guidelines are perceived to be confusing, and nutritional knowledge remains low. The purpose of this study is to study food choices and nutrition in and around pregnancy.

2. **Why have I been chosen?**

You are a healthy woman (without known thyroid disorders, renal disease or gestational diabetes) aged 18 to 45, pregnant (single pregnancy) or trying to conceive. You live in Glasgow, and speak English fluently. You own a mobile phone and you do not take part in any other trial.

3. **Do I have to take part?**

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason.

4. **What will happen to me if I take part?**

You will meet a member of the Research Team from Glasgow University who will explain the study at a time and location convenient to you.

If you decide to take part in this study, the study team will allocate you to one of two groups – each receiving a different set of information. The study lasts 12 weeks altogether, and you will be receiving text messages at regular intervals.

5. **What do I have to do?**

In the first visit, you will fill in questionnaires about your diet, as well as demographic details. The researcher will provide you with containers to collect urine samples (similar to those taken at the GP) over three days. The researcher will also collect a small dried blood spot sample (pin-prick at the finger tip).

You will return to the unit (or an alternative agreed location) at least twice more, to carry out the same steps – after 6 weeks, and after 12 weeks. If you were recruited while trying to conceive and have become pregnant in the meantime, you will return for a fourth visit around your 12th week gestation. We will send you a follow-up email once you have completed the study, to seek your feedback.

6. **What are the possible disadvantages and risks of taking part?**

There are no risks associated with this study; however short term discomfort and mild bruising may occur during finger prick blood sampling.

7. **What are the possible benefits of taking part?**

You will receive no direct benefit from taking part in this study. However your participation will help us test and evaluate dietary guidance in and around pregnancy, with a view to improve them in the future. As a token of gratitude, all participants taking part in the study will receive a £50 shopping voucher on completion (and an extra £10 worth of vouchers if your return for the fourth visit).

8. **Will my taking part in this study be kept confidential?**

All information collected about you, or responses that you provide, will be kept strictly confidential. You will be identified by an ID number, and any information about you will have your name and address removed so that you cannot be recognised from it. Please note that assurances on confidentiality will be strictly adhered to unless evidence of wrongdoing is uncovered. In such cases the University may be obliged to contact relevant statutory bodies/agencies.

9. **What will happen to the results of the research study?**

Results will be presented at meetings of learned societies and published in scientific journals. This work will contribute towards a PhD student qualification and the results will be published in the relevant thesis.

10. **Who is organising and funding the research?**

The project is being funded by the Yorkhill Research Support Scheme.

11. **Who has reviewed the study?**

This project has been reviewed by the ethics committee of the University of Glasgow, College of Medical, Veterinary and Life Sciences.

12. **Contact for Further Information**

If you require further information please contact Dr Emilie Combet by telephone at 0141 201 8527 or via email at emilie.combetaspray@glasgow.ac.uk or Miss Maira Bouga by telephone at 0141 201 8693 or via email at m.bouga.1@research.gla.ac.uk.

***Thank you for reading this information sheet!***

## PICk consent form

University of Glasgow | College of Medical, Veterinary & Life Sciences

PICk

Centre Number:
Project Number:
Subject Identification Number for this trial:

### CONSENT FORM

**Title of Project: Nutrition and food choices in early pregnancy**
**Name of Principal Researcher – Maira Bouga [supervisor: Dr Combet]**

**Please initial box**

| | |
|---|---|
| I confirm that I have read and understand the information sheet dated 16th Mar 2017 (version 1.2) for the above study and have had the opportunity to ask questions. | ☐ |
| I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected. | ☐ |
| I agree to my samples (blood, urine) being stored and used for further analysis to look at biochemical compounds, as new techniques are being available. | ☐ |
| I agree for my contact details to be kept by the research team, for the sole purpose of inviting me to a follow-up study (I am free to reject or ignore this future invitation). | ☐ |
| I agree to take part in the above study. | ☐ |

| | | |
|---|---|---|
| Name of subject | Date | Signature |
| Researcher | Date | Signature |

(1 copy for subject; 1 copy for researcher)

College of MVLS
Ethics Committee

v1.2
16/03/2017

## PICk text messages

| Order | Control | Technique (Theoretical Framework) | General theme from awareness, fish & dairy | Intervention |
|---|---|---|---|---|
| 1 | It was nice meeting you! Your ‘Ready, Steady, Baby’ book & webpage covers pregnancy diet! We will be in touch to remind you of the various stages of this study. | Use follow up prompts | | It was nice meeting you! ‘Ready, Steady, Baby’ book & web page covers pregnancy diet. We will keep in touch via texts! |
| 2 | | Prompt intention formation (TRA, TPB, SCogT, IMB) | Supplements | Nutrition resolution? Do you take your supplements? Folic acid, iron, iodine & vit D are important, but not all multivitamins contain them.. Check the labels! |
| 3 | | Provide information on consequences (TRA, TPB, SCogT, IMB) | Knowledge on consequence of insufficiency | Not enough iodine-rich foods (dairy,fish) in/around pregnancy is linked with lower IQ & learning score in children! It could also influence your thyroid health. |
| 4 | | Provide information about behavior health link (IMB) | Knowledge on consequence of insufficiency | Fish & dairy provide nutrients important for baby’s brain development (iodine & omega3 fats).UK women of childbearing age don’t get enough of these in the diet! |
| 5 | | Prompt self-monitoring of behavior (CT) | Portion/ foods to limit | At least 3 portions (140g) of cooked fish/seafood per week are recommended in / around pregnancy. Maximum 2 of them should be oily fish (e.g. salmon, fresh tuna). A fish portion is as big as the palm of your hand! Do you reach the target? |

| | | | | |
|---|---|---|---|---|
| **6** | | | General dislike / exclusion of iodine rich foods | Do you struggle with fish and dairy? Iodine can be also found in seaweed and supplements. Always check the labels – some seaweed species are not safe! |
| **7** | | Time management | Knowledge on healthy foods / time / portion / cost | A pot of yogurt (125g) (low-fat, lower-sugar) can be a quick & healthy snack, will count toward you daily dairy (aim for 3 portions) – and provides calcium, iodine and protein. Read more about diet around pregnancy: http://bit.ly/2nYNchw |
| **8** | | Prompt specific goal setting (CT) | Portion | Setting goals today? Two glasses of milk (drinks or in cereals), a yoghurt & a serving of cheese (match-box size) daily, plus 3 servings of fish weekly, will provide you with the iodine you need, as well as calcium, protein and vitamins. Worth a try! |
| **9** | | Prompt practice (OC) | Knowledge on fortified foods UK / Knowledge on iodine rich foods | There is iron in fortified breakfast cereals & bread, and vitamin D in fortified margarine, breakfast cereals & some yogurts – but iodine is not added in salt in the UK! Make sure you get it from food (dairy/fish) or a pregnancy supplement! |
| **A** | Hello – this is a reminder that your next appointment for the PICk study is coming up. Remember to collect your urine samples.. | | | Hello – this is a reminder that your next appointment for the PICk study is coming up. Remember to collect your urine samples.. |

| | | | | |
|---|---|---|---|---|
| **10** | It was nice seeing you again! We will meet again in 6 weeks for your final visit! | Use follow up prompts | | It was nice seeing you again! You will be receiving more texts from us. We will meet again in 6 weeks for your final visit! |
| **11** | | Prompt barrier identification (SCogT) | Taste | Struggling with milk? If you choose milk alternatives (e.g. soya, almond milk) check their labels to make sure that they are fortified in calcium, vitamins and iodine. There is also a great variety of different dairy products (yogurt, cheese) you can choose! |
| **12** | | Provide information on consequences (TRA, TPB, SCogT, IMB) | Bacterial risk / foods to avoid | Most cheeses are safe for pregnant women (matchbox-size portion) and are a source of protein, calcium and iodine. Some (camembert, brie, blue cheese), however, should be avoided as they can contain listeria, a bacteria harmful to your baby. Read more: *http://bit.ly/2oqTKSK* |
| **13** | | Prompt review of behavioral goals (CT) | Knowledge on healthy foods | Have you got a diet goal? 3x dairy, 5x fruit & veggies and 3x fish per week. Limit caffeine and switch to wholegrains! |
| **14** | | Provide information about others' approval (TRA, TPB, IMB) | Bacterial risk | Meat and fish that aren't cooked well can contain bacteria. The NHS advises to cook your food well. Avoid raw shellfish but eat properly cooked fish and shellfish (e.g. prawns) as they provide you with iodine, protein and omega 3 fats. |

| | | | | |
|---|---|---|---|---|
| **15** | | Time management | Time | Save time during the week: Make a shopping list which includes foods that can go towards your 3 weekly fish portions & your everyday dairy, fruits and veggies. |
| **16** | | Provide instruction (SCogT) | Cooking / skills | Not sure what to do with fish? Find some quick and simple cooking tips here: *http://bit.ly/2nan8fz* |
| **17** | | Prompt practice (OC) | Trust | Do you have a question regarding your diet? Speak to a dietitian or an accredited nutritionist; ask your GP or midwife. Do not trust unreliable sources of info! |
| **18** | | Prompt barrier identification (SCogT) | Cost | Fish too expensive? Canned and frozen fish is often cheaper than fresh, and packed with the same omega 3, iodine, protein and vitamins. |
| **B** | Hello – this is a reminder that your next appointment for the PICk study is coming up. Remember to collect your urine samples.. | | | Hello – this is a reminder that your next appointment for the PICk study is coming up. Remember to collect your urine samples.. |

# PICk questionnaires

University of Glasgow | College of Medical, Veterinary & Life Sciences

PICk

**Visit** | 1 |

**Date:** ________________ **Participant Number** [ ]

***Nutrition and food choices in early pregnancy***

**About you**

**1. Age:** ________ years

**2. Ethnic background?**

☐ British ☐ Other European ☐ Mixed or Multiple ethnic groups ☐ Asian

☐ African ☐ Caribbean or Black ☐ Other ethnic group

**3. Please specify the highest level of education <u>completed</u> by you to date:**

☐ Current pupil / School leaver / certificate / standard Grade / GCSE ☐ Highers / A levels ☐ HND / HNC / NVQs / Other higher education diploma

☐ Bachelor degree ☐ Master's degree ☐ PhD

**4. Please select if you have studied any of the following:**

☐ Nutrition / Dietetics ☐ Food sciences ☐ Health Sciences

**5. Annual Income:** *Please tick the appropriate box corresponding to your annual **household net income** if living in a family setting, or your **personal income**, if living in a shared accommodation setting (with non-family housemates):*

☐ <£15,000 ☐ £15,001 - £30,000 ☐ £30,001 - £50,000 ☐ >50,000

**6. Are you currently:**

☐ Pregnant Due date: ____/____/______

☐ Trying to conceive

**7. Do you already have children?** ☐ NO ☐ YES _____ child(ren)

**8.Your measurements:**

Height _____________ Pre-pregnancy weight __________ Current weight__________

**9. Are you currently a smoker?** ☐ NO ☐ YES

If yes, how many cigarettes per day? ________

**10. Are you taking any medication at the moment?** ☐ NO ☐ YES

If yes, what medication? ______________________________

**11. a. Are you lactose intolerant?** ☐ NO ☐ YES

**b. If yes, was this diagnosed by a GP/ doctor?** ☐ NO ☐ YES

**12. Have you been told by your GP / doctor that you have any of the following?**

*Please select all that apply.*

☐ Renal disease
☐ High blood pressure
☐ Heart disease
☐ High Cholesterol
☐ Osteoporosis
☐ High Triglyceride
☐ Osteomalacia (due to vitamin D deficiency)
☐ Anemia (due to iron deficiency)
☐ Other: ______________________

**13. Are you following a vegetarian or vegan diet?**

☐ *No*
☐ *Yes, pescetarian* (avoiding meat only)
☐ *Yes, lacto-ovo-vegetarian* (avoiding meat, fish and other types of seafood only)
☐ *Yes, lacto-vegetarian* (avoiding meat, fish, other types of seafood and eggs only)
☐ *Yes, ovo-vegetarian* (avoiding all meat, fish, seafood and all dairy products **except** eggs)
☐ *Yes, vegan* (avoiding meat, fish, all other types of seafood and all dairy products **including** eggs)

**14. Are you the main grocery shopper in your household?** ☐ NO ☐ YES

**15. Please select any IT equipment you currently have access to:**

*Please select all that apply.*

☐ Tablet
☐ Smartphone
☐ Laptop
☐ Desktop
☐ Wi-Fi at home
☐ Mobile data
☐ Other: ______________________

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**Visit** [1] [2] [3]

**Date:** ____________________  **Participant Number** [ ]

***Nutrition and food choices in early pregnancy***

## Food Frequency Questionnaire

***<u>Please answer this questionnaire based on the last 6 weeks</u>***

**Do you currently take any herbal / vitamin supplements?** ☐ YES ☐ NO

**If yes**, which brand? ________________________________

How often? ________ *times per* day **or** week **or** month

**If you drink milk, how often and how do you drink it?**
Tick <u>one</u> column for each food (per day **or** per week **or** per month)

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | 1 | 5-6 | 2-4 | 1 | 1-3 | <1 |
| With tea / coffee (other than cappuccino/ latte) | | | | | | | | | |
| On breakfast cereals | | | | | | | | | |
| Milk for chocolate/ horlicks drink/ cappuccino/ latte | | | | | | | | | |
| Just as it is (i.e. glass / cup of milk) | | | | | | | | | |

**Is this cow's milk?** ☐ YES ☐ NO
**If no**, what alternative do you use? ________________________________

**Is this organic milk?** ☐ YES ☐ SOMETIMES ☐ NO

**At the table do you:**

| | **YES** | **NO** |
|---|---|---|
| - generally add salt to food without tasting first | | |
| - taste food and then generally add salt | | |
| - taste food but only occasionally add salt | | |
| - rarely or never add salt at table | | |

Which salt brand do you use most often? ________________________

**How often do you eat these foods?**

Tick **one** column for each food (per day **or** per week **or** per month)

| | **Per day** (servings) | | | | **Per week** | | | **Per month** | |
|---|---|---|---|---|---|---|---|---|---|
| | 6+ | 4-5 | 2-3 | 1 | 5-6 | 2-4 | 1 | 1-3 | <1 |
| Cheese-based dishes (i.e. pizza, sandwich, cauliflower cheese) | | | | | | | | | |
| Cheese (hard or soft) | | | | | | | | | |
| Yoghurts | | | | | | | | | |
| Milk or cream-based puddings (e.g. custard, ice cream) | | | | | | | | | |
| Oil-rich fish (eg salmon, mackerel, sardine, tuna, herring) | | | | | | | | | |
| White sea-fish | | | | | | | | | |
| Seafood other than fish (inc. prawns, shellfish, seaweed) | | | | | | | | | |
| Broccoli | | | | | | | | | |
| Cabbage, Brussels sprouts, cauliflower, kale | | | | | | | | | |
| Turnip, pak choi, swede | | | | | | | | | |
| Beansprouts, sweet potatoes | | | | | | | | | |
| Soya products (i.e. tofu, soya milk, veggie burgers) | | | | | | | | | |

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PICk

Visit [1] [2] [3]

Date: ______________ Participant Number [ ]

*Nutrition and food choices in early pregnancy*

## Pregnancy diet Questionnaire

**1. When you receive information about specific nutrients (like iron, calcium), do you know how to relate this information to food choices and how to modify your diet accordingly?**

☐ YES, ALWAYS ☐ SOMETIMES ☐ NO

**2. Is getting information on nutrition for pregnancy something that interests you?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**3. Are you aware of dietary and lifestyle guidelines specific to pregnancy?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**4. Select the recommendation(s) for pregnant women that you are aware of:** *(Select all that apply)*

☐ Stop smoking

☐ Stop or limit alcohol

☐ Limit caffeine

☐ Limit vitamin A intake

☐ Avoid certain foods due to bacterial infection risk

☐ Avoid certain fish due to toxins / heavy metals

☐ Limit oily fish to two portions per week

☐ Avoid raw meat, fish or poultry

☐ Wash all fruit and vegetables before consumption

**5. <u>If yes</u>, how did you find out about these guidelines?** *(Select all that apply)*

☐ Written information from Doctor, Nurse or Midwife

☐ Talking to Doctor, Nurse or Midwife

☐ Family or friends

☐ Books or magazines

☐ Internet

☐ Antenatal classes

☐ Other *Please Specify:*____________________________________

**6. When it comes to healthy eating in pregnancy and lactation, have you heard of )or were you informed about) the following nutrients?**

| | NO | YES, from... *(Select all that apply)* | | | | | |
|---|---|---|---|---|---|---|---|
| | | Doctor, Nurse or Midwife | Family or friends | Books or magazines | Internet | Antenatal classes | Other* |
| Folic Acid | | | | | | | |
| Iron | | | | | | | |
| Iodine | | | | | | | |
| Calcium | | | | | | | |
| Vitamin D | | | | | | | |
| Vitamin A | | | | | | | |

**If other, please specify:*

**7a. Are you aware that during pregnancy, iodine from the diet is important for healthy development of the unborn baby?**

☐ YES, I am ☐ NO, I am not ☐ I don't know

**7b. Are you aware that during pregnancy, iron from the diet is important for healthy development of the unborn baby?**

☐ YES, I am ☐ NO, I am not ☐ I don't know

**7c. Are you aware that during pregnancy, folic acid from the diet is important for healthy development of the unborn baby?**

☐ YES, I am ☐ NO, I am not ☐ I don't know

**8. Are you confident on how to achieve an adequate intake in pregnancy for:**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **a. Iodine** | Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |
| **b. Iron** | Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |
| **a. Folic acid** | Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**9a. Which foods do you think are rich in iodine in the UK?** *(Select all that apply)*

☐ Potatoes ☐ Fish / seafood ☐ Milk / dairy products

☐ Dark green vegetables ☐ Pulses ☐ Salt

☐ Wheat based products (inc. bread, pasta) ☐ Fruits ☐ Red meat

**9b. Which foods do you think are rich in iron in the UK?** *(Select all that apply)*

| | | |
|---|---|---|
| ☐ Potatoes | ☐ Fish / seafood | ☐ Milk / dairy products |
| ☐ Dark green vegetables | ☐ Pulses | ☐ Salt |
| ☐ Wheat based products (inc. bread, pasta) | ☐ Fruits | ☐ Red meat |

**9c. Which foods do you think are rich in folic acid in the UK?** *(Select all that apply)*

| | | |
|---|---|---|
| ☐ Potatoes | ☐ Fish / seafood | ☐ Milk / dairy products |
| ☐ Dark green vegetables | ☐ Pulses | ☐ Salt |
| ☐ Wheat based products (inc. bread, pasta) | ☐ Fruits | ☐ Red meat |

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Visit 2 3 Participant Number

PICk

*Nutrition and food choices in early pregnancy*

**'Changes to the diet' questionnaire**

**As part of your current diet, have you changed your consumption of the following?**

| | This is not something I usually eat at all | Increased | Maintained | Decreased | Stopped completely |
|---|---|---|---|---|---|
| Yoghurts | | | | | |
| Dairy milk (i.e not soya, almond etc.) | | | | | |
| Milk alternatives (i.e. soya, almond etc.) | | | | | |
| Cheese-based dishes (i.e. pizza, sandwich, cauliflower cheese) | | | | | |
| Cheese and spreads | | | | | |
| Milk or cream based puddings (e.g. rice pudding, custard, ice cream) | | | | | |
| White fish | | | | | |
| Oil-rich fish (e.g. salmon, mackerel, sardine, tuna, herring) | | | | | |
| Seafood other than fish (prawns, seaweed, shellfish) | | | | | |
| Eggs | | | | | |
| Poultry | | | | | |
| Meat | | | | | |
| Bread, rice, cereals, pasta, pulses | | | | | |
| Soya products (i.e. tofu, soya milk) | | | | | |
| Brassicas (cabbages, Brussels sprouts, cauliflower, kale, broccoli) | | | | | |
| Green vegetables, other vegetables | | | | | |
| Fruits | | | | | |

**If you stopped/eat less of any of these foods, was this due to: (Select all that apply)**

☐ Specific recommendations ☐ Morning sickness ☐ Heartburn

☐ Uncertainty of being harmful ☐ Taste / smell ☐ Cost/ money

☐ Lack of time to prepare ☐ Other Please Specify: ___________________________

**If you eat more any of these foods, was this due to: (Select all that apply)**

☐ Specific recommendations ☐ Cravings ☐ Time (lack of)

☐ Following a healthier diet ☐ Other Please Specify: ___________________________

**How much have your dietary habits changed during the last 6 weeks?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Less healthy | 1 | 2 | 3 | 4 - no change | 5 | 6 | 7 | Healthier |

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Visit 2 3 Participant Number

*Nutrition and food choices in early pregnancy*

## Intervention assessment

When refering to the intervention, we are speaking of your interactions with the researcher, as well as any messages / documentation you may have received during the course of this study.

**1. Did the study help you make positive changes in your diet?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**2. Was the use of mobile technology a useful and easy way in getting information to you?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not useful at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very useful |

**3. How would you rate the quality of the received messages and facts provided?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low / inadequate | 1 | 2 | 3 | 4 | 5 | 6 | 7 | High / adequate |

**4. How much do you think the study has made you think about your diet?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**5. Do you read the messages…**

- ☐ Always when I receive them, once or more.
- ☐ I was reading them initially, but now I ignore them.
- ☐ Sometimes, but not all of them.
- ☐ I never read them.

**6. How would you rate the study requirements (samples collection/ questionnaires completion/ meetings etc.) in terms of difficulty?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Extremely easy | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Extremely difficult |

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PICk

Visit | 2 | 3 |        Participant Number | |

***Nutrition and food choices in early pregnancy***

**Intervention assessment**

When refering to the intervention, we are speaking of your interactions with the researcher, as well as any messages / documentation you may have received during the course of this study.

**1. Did the study help you make positive changes in your diet?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**2. Did the received messages help you understand better the pregnancy recommendations?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not useful at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very useful |

**3. Was the use of mobile technology a useful and easy way in getting information to you?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not useful at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very useful |

**4. How would you rate the quality of the received messages and facts provided?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Low / inadequate | 1 | 2 | 3 | 4 | 5 | 6 | 7 | High / adequate |

**5. How much do you think the messages have helped and motivated you to make changes in your diet?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

**6. Do you read the messages…**

- ☐ Always when I receive them, once or more.
- ☐ Sometimes, but not all of them.
- ☐ I was reading them initially, but now I ignore them.
- ☐ I never read them.

**7. Do you follow the links included in the messages…**

- ☐ Always when I receive them.
- ☐ Sometimes, but not all of them.
- ☐ I was following them initially, but now I ignore them.
- ☐ I never follow them.

**8. How would you rate the study requirements (samples collection/ questionnaires completion/ meetings etc.) in terms of difficulty?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Extremely easy | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Extremely difficult |

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PICk

Visit 3

Date: ________________ Participant Number

*Nutrition and food choices in early pregnancy*

## End of study questionnaire and discussion

**We had two groups in this study – each receiving different types of messages.**

**Can you tell which group you were allocated to?**

☐ YES, absolutely ☐ MAYBE ☐ NO

My group was ____________________________

**Throughout this study, you will have seen a lot of paperwork (questionnaires) and received text messages.**

**Did you guess what is the main interest of the researchers in this study?**

☐ YES, absolutely ☐ MAYBE ☐ NO

The focus was on ____________________________

**How burdensome was the study for you (everuthing, from attending meetings, to collecting samples, and filling questionnaires)?**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Not at all | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Very much |

*Please turn over*

**We are particularly interested in one specific compoenent in the diet – named iodine – which most often people are unaware of.**

**From you experience in this study, did you notice the word "iodine"?**

☐ YES, absolutely ☐ MAYBE ☐ NO

**Would you like to learn more about "iodine"?**

☐ YES, absolutely ☐ MAYBE ☐ NO

**If so, we can send you further information about the nutrient**

*Confirm your email address:* ________________________________