Urinary iodine concentration and iodine intake in pregnant Norwegian women

Results from the "Little in Norway" Study (LiN)

Perla Vanessa Roldan Sanchez

Master Thesis in Clinical Nutrition

May 2015

University of Bergen (UiB)

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ACKNOWLEDGEMENTS

I want to start to thank Anders Bjørnsen Kulseng Higher Executive Officer Department of Physics and Technology at UiB for their support during my time as a student in the Master in Clinical Nutrition, as well as Liv Breisten, my classmate, who not only supported me studing, she encouraged me to continue with my professional and personal goals and be always there when I needed.

My thesis was developed in The National Institute of Nutrition and Seafood Research (NIFES), and therefore I wish to thank to all the people who support me in this long process: Stig Hollund, Tonja Lill Eidsvik and Berit Solli for technical assistance and guidance. Thank to Dr. Scient Marian K. for her interest in invite me on integrate the team work and for showing me the right way to work on my thesis.

I also have an infinite gratitude to my Dr. Scient Lisbeth Dahl for their patience, support and understanding within and outside the project. Thanks to her, I learned a lot about iodine and I hope that in a near future put the knowledge in practice!. Also I want to thank Dr. Scient Pedro Araujo for his unselfish support, for the many talks in Spanish, the laughs and good times while we were discussing the goals of my project and see my mistakes in an opened and positive way...gracias!!!

On the other hand, I would like to thank to my friends, for their unconditional support and helping me to keep going on, even in the most difficult moment that I lived: Patricia Lopez, Anita Lagos, Veronica Delgado, Melva Valderrama, Gisella Mauricio, Lesli Llacsa, Wilmer Fuentes, Ellen Bryne, Maribel Blanco…. A special thanks to my parents in law for lending me their internet and having a cup of coffee on my desk when I wrote my thesis

Finally, I want to thanks my dear husband Øystein Mo *"i gode og onde dager"* you have been with me... I am proud of you and hope you are also proud of me... I finished my thesis!!! I love you and I hope this is the beginning of a new stage in our lives together. Thanks from the bottom of my heart!!!

With love,
Vanessa

To my family in Peru:

Gracias!!! Mama Lety, papa Cesar, Junior, Brenda, Ubin, ruffi... son todo para mí y todo lo que hago día a día es pensando en Uds. A pesar de la distancia, sé que siempre están conmigo apoyándome... juntos siempre!!!

Agradezco a Dios por tener una familia como Uds. y haber vivido lo que he vivido me ha hecho más fuerte. Gracias mi Divino Nino Jesús por cambiar mi vida para bien. Gracias Matty por esos adorables sueños contigo.

Con amor,
Vanessa.

ABSTRACT

Background

Iodine is an essential nutrient for the synthesis of thyroid hormones. Inadequate iodine intake is especially critical during pregnancy, lactation and early childhood. Iodine deficiency early in life impairs the developing brain. Iodine deficiency is defined as a median urine concentration less than 150 µg/ L in pregnant women. Seafood, milk-and dairy products, eggs and iodine-containing supplements are dietary iodine sources in Norway. Recently studies indicate that iodine status in pregnant women could be suboptimal.

Aims

The aims of the study were: [1] to determinate the iodine status of the pregnant women based on urinary iodine concentration from a spot urine sample using the World Health Organization (WHO). [2] to estimate the iodine intake from selected food groups and iodine-containing supplements using a food frequency questionnaire (FFQ) to evaluate whether or not it is in accordance with the Norwegian recommendation. [3] to assess influence of some factors (e.g. weeks of gestation, timing and season of spot urine collection) on the urinary iodine concentration (UIC) during pregnancy.

Methods

A total of 1036 pregnant women included in the study were recruited within the period 2011 – 2012 from nine well-baby clinics across the Norwegian Health Regions. A spot urine sample (to measure UIC) was collected from 1008 participants at the first meeting in the clinic. UIC were determined using inductively couple plasma spectrometry (ICP-MS). A self-administrative, semi quantitative FFQ (to estimate iodine intake) were filled in at home from 833 participants.

Results

Median UIC was 82 µg/ L and 80% of the urine samples were below 150 µg/ L. Data from the FFQ revealed that 30% ate seafood 2 – 3 times per week at dinner, 68% ate milk-and dairy products 2 – 3 times per day and 39% ate egg 2 – 3 times per week. Iodine-containing supplements were reported by 14% of the women. The total median iodine intake from foods and supplements was 153 µg/ day. Intake of milk-and dairy products and gestational age correlated significantly with median UIC.

Conclusions

Findings in the present study from median UIC classify the pregnant women as iodine deficient. Estimated dietary iodine intake also shows inadequate iodine intake among the women. In conclusion, this study shows that the diet of the pregnant women does not secure a sufficient iodine intake and one strategy to increase the iodine intake could be to increase the seafood intake.

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ABBREVIATIONS

ALSPAC	Avon Longitudinal Study of Parents and Children
BMI	Body Mass Index
EFSA	European Food Safety Authority
FFQ	Food Frequency Questionnaire
I	Iodine
ID	Iodine Deficiency
IDD	Iodine Deficiency Disorders
IGN	Iodine Global Network[i]
IOM	Institute of the United States
L	Liter
LiN	Little in Norway
MoBa	Norwegian Mother and Child Cohort Study
MUIC	Median Urinary Iodine Concentration
NIFES	National Institute of Nutrition and Seafood Research
NNR5	Nordic Nutrition Recommendations
Norkost	Nationwide Food Consumption Survey Conducted in Norway
SAC	School Age Children
SRM	Standard Reference Material
T_3	Triiodothyronine
T_4	Thyroxine
Tg	Thyroglobulin
TH(s)	Thyroid Hormone(s)
TSH	Thyroid Stimulating Hormone
UI	Urinary Iodine
UIC	Urinary Iodine Concentration

[i] Formerly ICCIDD Global Network

UK	United Kingdom
UN	United Nations
UNICEF	United Nations Found for Children
USA	United States of America
VKM	Norwegian Scientific Committee for Food Safety
WHO	World Health Organization
µg	Microgram

1. INTRODUCTION

1.1 Background

Iodine is an essential trace element for the production of thyroid hormone (TH). Inadequate iodine intake is a challenge on a population level in several countries and iodine deficiency (ID) is recognized as the most important cause of mental retardation. The severity of the damage in the central nervous system is not only related to nutritional deficiency of iodine, but also with the stage of development during which it occurs. The intake of iodine should be sufficient to meet the nutritional needs and an adequate supply of iodine is especially important in pregnancy and lactation and during the early childhood. In some countries like Norway, national representative survey data on iodine intake and iodine status, especially during pregnancy are limited (Li and Eastman 2012).

The iodine intake of a population is often assessed by determination of iodine concentration in a casual sample of urine and it is classified as adequate with median values above 150 µg/ L given by the World Health Organization (WHO) for pregnant women.

The main source of iodine in humans is the food. In Norway, seafood, milk-and dairy products and eggs have the highest iodine content. Other food groups such as meat and meat products, bread and cereals, fruits and vegetables have low levels of iodine. Iodized salt is the most important source of iodine worldwide. Although iodized salt is available in Norway, the level of iodization is very low. Supplement could also be an important source of iodine.

Several surveys in previously iodine-sufficient countries such as Australia, UK, USA, New Zealand, Switzerland, Ireland, France, Spain, Hong Kong and Belgium (Zimmermann 2011, Li and Eastman 2012) have shown that mild-to-moderate ID has re-emerged in vulnerable groups such as pregnant women (Stagnaro-Green and Pearce 2013, WHOa 2014).

A recently performed study in Norway “The Fjell Study” including 64 pregnant women found that the median urinary iodine concentration (MUIC) was 127 µg/ L (Seldal 2012). Results from 119 pregnant women in the Norwegian Mother and Child Cohort study (MoBa) found a MUIC of 69 µg/ L (Brantsæter, Abel et al. 2013). Both studies indicate that iodine status of pregnant women in Norway could be suboptimal (Brantsæter, Abel et al. 2013) regardless of the population size. Moreover, MoBa study showed by using a frequency food questionnaire (FFQ) that 54.3% of pregnant women had an insufficient iodine intake (Brantsæter, Abel et al. 2013).

Based on findings in those two Norwegian studies; the present thesis will evaluate the iodine status of 1036 pregnant women who were recruited to the “Little in Norway” study by measuring MUIC and by estimation of dietary iodine intake.

1.2 Global iodine nutrition

Although ID is often considered to be a primarily challenge of developing countries, industrialized countries are not immune (Zimmermann 2010, Li and Eastman 2012, Bath, Steer et al. 2013, Stagnaro-Green and Pearce 2013). Among the WHO Regions, Europe has the highest prevalence of ID with a 44 % of the population remaining mildly iodine deficient (Andersson, Karumbunathan et al. 2012, Ristic-Medic, Novakovic et al. 2013).

Iodine Global Network (IGN) estimates that nearly 29.8 % (241 million) of the world's population continue to have insufficient iodine intake and the situation is still affecting 30 countries (Andersson, Karumbunathan et al. 2012, Pearce, Andersson et al. 2013, IGN 2014), distributed as moderately deficient (9 countries), mildly deficient (21 countries) and fortunately none are currently severe iodine deficient **(Fig. 1)**.

Further, it is critical that there are insufficient data from nearly all countries to estimate the prevalence of ID in pregnant women (Zimmermann 2010), but just in developing countries, there are 38 million newborn babies per year are at risk of ID (Li and Eastman 2012) despite ongoing and concerned efforts by WHO, the United Nations (UN) and IGN (Stagnaro-Green and Pearce 2013) to avoid that it may become a public health problem (Brantsæter, Abel et al. 2013) with a national and international interest.

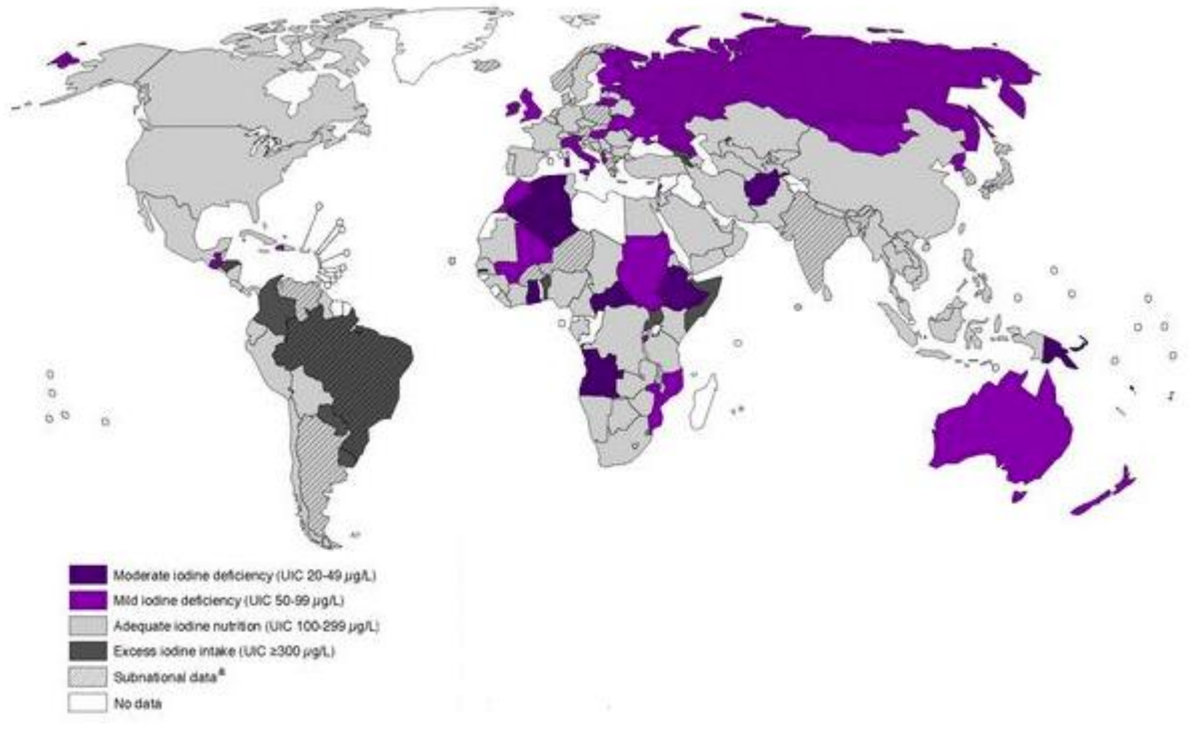

Figure 1. ***National iodine status[ii] elaborated by Pearce, Andersson et al. 2013***

[ii] Figure based on median urinary iodine concentrations in school-age children

1.3 Biological function of iodine

Iodine (atomic symbol I) is an essential component of thyroid hormones (THs). In humans, iodine is present in the thyroid gland which is responsible for its synthesis, storage and secretion in the body (Zimmermann, Jooste et al. 2008, Erdman, MacDonald et al. 2012, Bath and Rayman 2013).

The tyrosine-based hormones are T_4 (Thyroxine) and T_3 (Triiodothyronine) **(Fig. 2)**. It is believed that both T_4 and T_3 are active hormones, having the last one, the highest biological activity in the body (Mari Nes 2006).

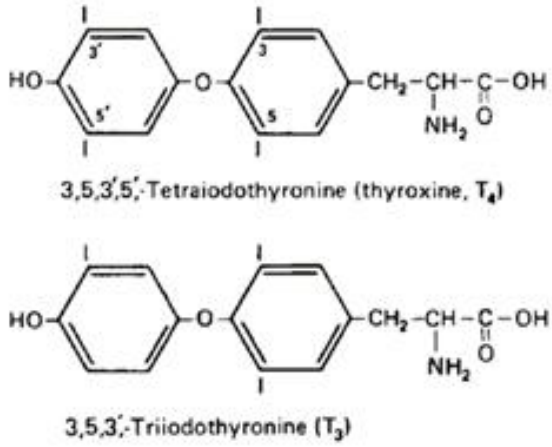

Figure 2. ***Thyroid hormones***

THs are needed for adequate growth and development of tissues and metabolism of the body and for adequate neuronal migration and myelination of the fetal and neonatal brain (Zimmermann 2012). This maintains the body temperature, increase the absorption of glucose in the intestine and break down fat and glycogen. It must be mentioned that the regulation mechanism during pregnancy is not completely understood (Zimmermann 2009), however the hormones are necessary to development of hearing and vision and maturation of most organs like brain, muscle, hearth, pituitary, reproductive system and bones (IOM 2001).

1.4 Iodine metabolism during pregnancy

Normally, the body of a healthy adult contains up to 15 – 20 mg of iodine. The ingested inorganic iodine and iodate (extensively used in salt iodization) are nearly completely absorbed from the gastrointestinal tract (Zimmermann 2010, Erdman, MacDonald et al. 2012, Li and Eastman 2012) **(Fig. 3)**. It has been estimated that more than 90% of ingested iodine is ultimately excreted in the urine, being the kidney the main route of excretion; about 20% are excreted in the feces, 5% appear in the sweat, saliva and the bile. Lactating women excretes 10 – 15% of the daily iodine intake into breast milk (SCF 2002, IOM 2001).

Hormonal and metabolic changes during normal pregnancy occur due to the hormone requirements and bioavailability of iodine (Glinoer 1997, Glinoer and Delange 2000) **(Fig. 4)**. In pregnancy, iodine intake should be increased ≥ 50% (Zimmermann 2012) due to the:

Increased production of TH, elevate renal clearance of iodine and transfer of maternal iodine and TH to the fetus.

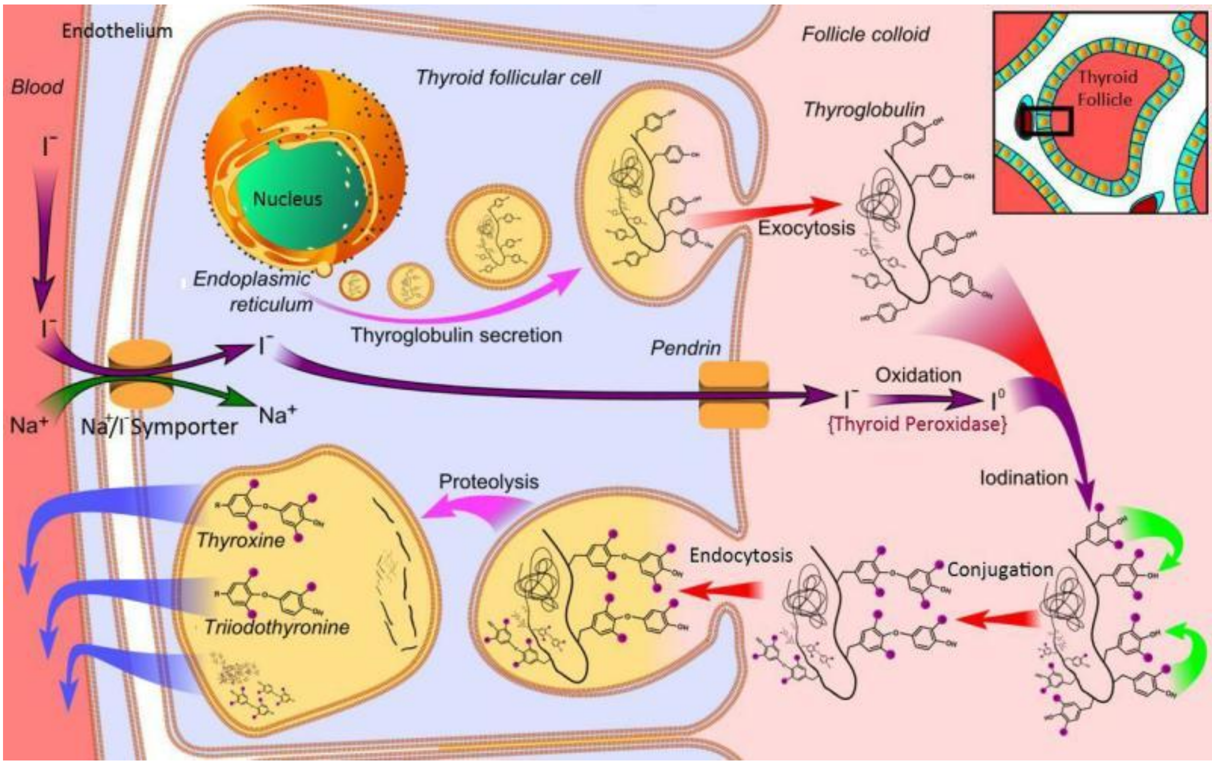

Figure 3. ***Thyroid hormone synthesis*** *(thyroMend 2013)*

[1] **Increased production of thyroid hormone:** During the first half of pregnancy, elevated levels of THs are needed to control maternal euthyroidism[iii] (Trumpff, De Schepper et al. 2013). At the beginning of the second trimester TH concentrations are 30 – 100% higher than before conception (Fantz, Dagogo-Jack et al. 1999).

[2] **Elevate renal clearance of iodine:** During normal pregnancy, higher iodine losses occurs due to the increase in renal iodine clearance (RIC) due to abundance of oestrogen (Eltom, Eltom et al. 2000) and the increase of glomerular filtration rate (GFR) (Trumpff, De Schepper et al. 2013). GFR begins to rise during pregnancy, becoming a mandatory renal iodine "leakage" (Glinoer 1997 highlighting conferred).

Later, during the second half of pregnancy, an iodine loss takes place from the passage of a part of the available iodine from the mother to the fetus, which starts to produce TH in order to keep a normal fetal brain development. Therefore, when iodine needs exist during the first half of gestation, it tends to become more severe in the second half of gestation (Glinoer 1997).

[3] **Transfer of maternal iodine and thyroid hormone to the fetus:** Thyroid development of the fetus starts at 10 – 12 weeks of gestation and from the 18 – 20th weeks T_4 is secreted by

[iii] The state of having normal thyroid function.

the fetal thyroid gland. Iodine is transferred through the placenta from the mother to the fetal thyroid gland and the fetus starts to produce its own TH (Trumpff, De Schepper et al. 2013)

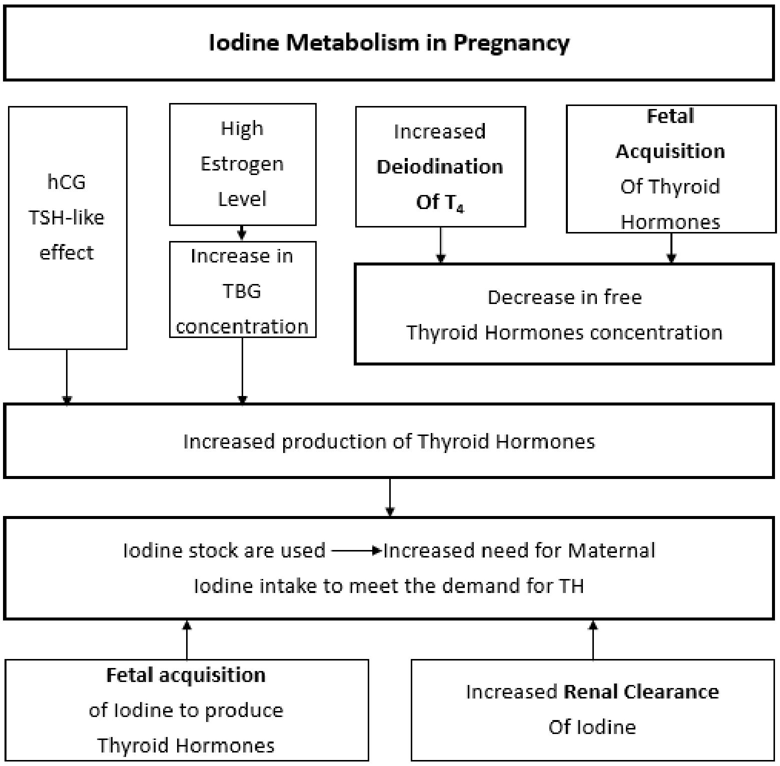

Figure 4. ***Iodine metabolism in pregnancy elaborated by Glinoer and Delange 2000***

1.5 Health consequences of deficiency and excess of iodine

1.5.1 Iodine deficiency disorders (IDD)

ID leads to severe clinical effects on the development and growth of animal and humans (Zimmermann 2010, Andersson, Karumbunathan et al. 2012, Erdman, MacDonald et al. 2012, Zimmermann 2012). These clinical effects are considered as iodine deficiency disorders (IDD) (Hetzel 1983, WHOa 2014) due to the inadequate TH production. The main impact of ID is on pregnancy, lactating women and during the first two years of life (Andersson, de Benoist et al. 2007).

ID cause mental impairment, motor and physical deficits in utero and childhood (Pardede, Hardjowasito et al. 1998, Bhutto, Hurrell et al. 2012, Bath, Steer et al. 2013, Hynes, Otahal et al. 2013). Conversely, early and adequate iodine in the mother improve head growth, reduce the prevalence of microcephaly (Cao, Jiang et al. 1994), increase birthweight, weight-for-age (WFA), mid-upper-arm circumference (MUAC) (Chaouki and Benmiloud 1994, Mason, Deitchler et al. 2002) and may reduce the infant mortality rate (IMR) by $\geq$ 50% (Cobra, Rusmil et al. 1997) in the infant. Moreover, two controlled trials in school age children (SAC) affirm that iodine repletion contribute to a positive cognitive function and information processing, fine motor skills and improve visual problem in mild and moderately iodine deficient children (Zimmermann, Connolly et al. 2006, Gordon, Rose et al. 2009). However, the cognitive deficit may not be associated only with infant and children whose mother was iodine deficient because in children without IDD but residing in areas of ID, a neuro -psychomotor retardation occur (Boyages, Collins et al. 1989, Azizi, Kalani et al. 1995).

The effects of ID become more evident during pregnancy (Trumpff, De Schepper et al. 2013) with increased incidence of intrauterine fetal death, infant mortality, preterm delivery, frequency of caesarian section and congenital abnormalities like cretinism which is considered as extreme expression of the abnormalities (Delange, de Benoist et al. 2001, UNICEFc 2008). Severe ID and hypothyroidism during pregnancy leads to impaired neurological development in the children (Li and Eastman 2012).

Adequate iodine intake is important during pregnancy, but there is no evidence about whether the mother or the child who has the most damage in mild ID (Laurberg, Andersen et al. 2007). Therefore, an iodine supplementation before, and during pregnancy is recommended on both mother and fetus.

IDD is the most common cause of goiter in all ages (IGN/UNICEF/WHO 2007). Glinoer, Lemone et al. 1992, Rotondi, Amato et al. 2000 and Knudsen, Bulow et al. 2002 referred to by Braverman and Cooper 2012 suggest that: “goiters formed during pregnancy may only partially regress after parturition”.

1.5.2 Iodine excess

It has been reported that ten countries had national MUIC in SAC > 300 μg/ L in 2011 (Andersson, Karumbunathan et al. 2012, Pearce, Andersson et al. 2013). The reported ten countries were classified as excessive according to the WHO. In pregnant women, a MUIC between 250 and 499 μg/ L is considered more than adequate, whereas a MUIC ≥ 500 μg / L is considered excessive (IGN/UNICEF/WHO 2007). Few studies have associated excessive iodine intake with adverse effects in pregnant women (Sang, Wei et al. 2012). However, it is undeniable that either excessive or deficient, iodine intake can cause alterations in thyroid function (Pearce, Andersson et al. 2013).

It has been reported cases of hypothyroidism, hyperthyroidism, thyroiditis, Grave`s disease (Laurberg., Andersen. et al. 2007, Erdman, MacDonald et al. 2012, IOM 2001) and thyroid papillary cancer in some individuals with excess iodine intake (IOM 2001). The exact dose/ response association between higher iodine intake and hypothyroidism is unknown at present (Laurberg., Andersen. et al. 2007)

Acute iodine poisoning is associated with burning of the mouth, throat, gastrointestinal irritation, abdominal pain, fever, nausea, vomiting, diarrhea, weak pulse, cardiovascular symptoms, cyanosis and even coma (Erdman, MacDonald et al. 2012, IOM 2001).

1.6 Assessment of iodine status

Several methods to assess iodine status depend of their performance, available resources, the age or life stage of the subjects, dietary partners, the iodine status of the study group and the study objectives to be used (Ristic-Medic, Piskackova et al. 2009). In some studied groups, urinary iodine (UI), newborn thyroid-stimulating hormone (TSH) and blood concentrations of thyroglobulin (Tg), T_4 and $T_{3,}$ are useful biomarkers of iodine status indicating the recent iodine intake in days (UI), weeks to months (Tg), months to years (changes in the goiter rate reflecting long term iodine nutrition) (Zimmermann 2008, Erdman, MacDonald et al. 2012).

Elevated TSH levels have been used to assess the severity of ID in neonates (Trumpff, De Schepper et al. 2013). Iodine levels are lower in neonates than in adults, but has higher rates of iodine turnover therefore a TSH stimulation is increased when the iodine supply is low (Erdman, MacDonald et al. 2012).

Serum Tg is a hopeful biomarker for monitoring thyroid function and abnormalities in populations studies which seems to correlate with UIC (Hambidge 2003, Ristic-Medic, Piskackova et al. 2009). However, a high serum concentration of Tg is not a specific sign of ID (Laurberg, Andersen et al. 2007, Ristic-Medic, Piskackova et al. 2009).

TH concentrations are generally less sensitive indicators of iodine status (Erdman, MacDonald et al. 2012), unless iodine deficiency is severe (Zimmermann 2010). A moderate fall in the concentration of serum free T4 during pregnancy is insufficiently sensitive to be used as indicator of maternal ID (Laurberg, Andersen et al. 2007).

Size of thyroid gland increases during ID (including during pregnancy) (IOM 2001).Thyroid size is recommended by WHO/UNICEF/IGN and classified goiter by palpation: grade 0 (no goiter), grade I (a goiter palpable but not visible when the neck is in normal position) and grade II (visible goiter). However when the thyroid is small, a ultrasounds is indicated (Delange, de Benoist et al. 2001).

1.6.1 Urinary iodine (UI)

Considering that > 90% of dietary iodine eventually appears in the urine (Travers, Guttikonda et al. 2006, Erdman, MacDonald et al. 2012, Li and Eastman 2012, Zimmermann 2012), the UI is widely use as biochemical marker of iodine status in the absence of other more – stable practical biomarker and because it reflects a recent dietary iodine intake (a few days) (Hambidge 2003, Ristic-Medic, Piskackova et al. 2009). The WHO recommendations for using the MUIC from spot – urine samples are established as cut offs to indicate iodine sufficiency in populations and are shown in **Table 1**.

UI can be expressed as a concentration (µg/ L) or as a 24-hour excretion (µg/ day), in relationship to creatinine excretion (µg iodine/ g creatinine) (Busnardo, Nacamulli et al. 2006, Konig, Andersson et al. 2011). A 24- hour collections of urine is also used, however the collection of urine is more inconvenient for the subjects, by using a larger sample of spot urines, the variation in hydration among the individuals and day to day variation in the iodine intake generally even out, so that the MUIC is suitable marker of iodine intake (Zimmermann and Andersson 2012). To determinate reliability of surveys with a certain number of urine samples 100 – 500 spot urine samples are required (Hurrell 1997).

It has been reported that a single spot UIC is not suitable indicator for individual assessment (Konig, Andersson et al. 2011) due to the values are not normally distributed and only the median, in µg / L can be used to classify iodine intake of the entire group (Laurberg., Andersen. et al. 2007).

Table 1. Epidemiological criteria from the World Health Organization for Assessment of Iodine Nutrition in a Population based on median or range of Urinary Iodine Concentrations†

Population group	Iodine intake	Iodine nutrition
School- age children		
< 20 µg/L	Insufficient	Severe iodine deficiency
20 – 49 µg/L	Insufficient	Moderate iodine deficiency
50 – 99 µg/L	Insufficient	Mild iodine deficiency
100 – 199 µg/L	Adequate	Optimum
200 – 299 µg/L	More than adequate	Risk of iodine – induced hyperthyroidism in susceptible groups
>300 µg/L	Excessive	Risk of adverse health consequences (iodine induced hyperthyroidism, autoimmune thyroid disease)
Pregnant women		
<150 µg/L	Insufficient	
150 – 249 µg/L	Adequate	
250 – 499 µg/L	More than adequate	
≥500 µg/L	Excessive	
Lactating women		
<100 µg/L	Insufficient	
≥100 µg/L	Adequate	
Children less than 2 years of age		
<100 µg/L	Insufficient	
≥100 µg/L	Adequate	

†**Adapted table from** IGN/UNICEF/WHO 2007 by Erdman, MacDonald et al. 2012

1.7 Assessment of food intake

The iodine status refers to the median casual UIC as a reflection of iodine intake (van den Briel, West et al. 2001, Wong, Sullivan et al. 2011); therefore, another method to assess iodine is to calculate the iodine intake direct from the diet.

In epidemiological studies, self-report methods may give information about diet and other factors related to live style and health without being invasive; therefore the questions asked should be easy to administer and less time-consuming, but still give useful information (NOO 2011).

The choice of a dietary method depends on many factors as the purpose of the study, the number of subjects to be surveyed, the food and nutrient of interest, short or long term intake, dietary habits and nutrient intakes with respect to the dietary recommendations, characteristics of the population and the resources (Seldal 2012). A FFQ meets these demands (Rasmussen, Ovesen et al. 2001) and can be used to classify low and high iodine intake groups (Brantsaeter, Haugen et al. 2008). In order to assess the dietary intake of iodine in a population and in sub groups of the population, accurate data are needed regarding the iodine content of the different food groups, as well as food consumption data (personal communication Lisbeth Dahl).

A comparison between FFQ and other methods of dietary assessment as food diaries or 24-h food intake recalls and weighed food records indicate that a FFQ give more precise information of a long-term intake (usually 1 year) (Ortiz-Andrellucchi, Doreste-Alonso et al. 2009, Seldal 2012).

A FFQ is a retrospective review of intake frequency (i.e. food consumed per day, per week, or per month) useful in epidemiological studies (Ortiz-Andrellucchi, Doreste-Alonso et al. 2009). FFQs assess the frequency and portion sizes of iodine-containing foods and/or food groups consumed and captures iodine-rich sources that are irregularly consumed and accounts due to the day-to-day variation of the major dietary patterns (Zimmermann and Andersson 2012). Because the aim of the FFQ is the frequency on consumption of food groups rather than of specific, for certain nutrients; the level of nutrient intake estimated by FFQ should be regarded as approximations (Brantsaeter 2007).

Short FFQs may be used to measure the relationship between consumption of several specific foods or nutrients (Eysteinsdottir, Thorsdottir et al. 2012), while long FFQs pretend to give a comprehensive assessment of the whole diet (Seldal 2012).

1.8 Dietary sources of iodine

Iodine is obtained primarily through the diet (Brantsæter, Abel et al. 2013). The main source of iodine in the Norwegian diet is milk-and dairy products due to its frequent intake. Higher milk/ yogurt intake than 200 – 300 ml/ day (1 – 2 serving) is needed to obtain 150 µg iodine daily (Brantsæter, Abel et al. 2013).

Marine fish and other seafood contribute also with iodine (Bhutto, Hurrell et al. 2012) with a range of 5 – 380 µg (NorwegianFoodSafetyAuthority 2014). Lean fish contains twice as much iodine, as oily fish, although there are very large variations e.g. cod, haddock and saithe (86 µg I/ 100 g) have higher levels of iodine in the fillet than typical fatty fish species such as farmed salmon, herring, mackerel (40 µg I/ 100 g) (Preedy, Burrow et al. 2009). Marine sources contain more iodine than terrestrial vegetables (TheNorwegianDirectorateofHealth 2011).

Eggs provides 45 µg I/ 100 g (Dahl, Johansson et al. 2004), dependent on the chicken feed (Vanderpump and reply. 2011). According to the new version of Norwegian Food Composition Database 2014, raw egg, raw egg whites and raw egg yolk contains 49 µg, 3 µg and 120 µg iodine respectively per 100 g.

Other foodstuffs e.g. meat and meat products, bread and cereals, vegetables, potatoes, fruits and berries, and fats and oils contain 2 – 3 µg I/ 100 g providing a limited amount of iodine to the total iodine intake (Dahl, Johansson et al. 2004).

In Norway, a study showed that multi- or single- vitamin preparations and mineral supplements were the most frequently used supplements (Brantsaeter, Haugen et al. 2007). Pregnant women should receive once-daily iodine-containing supplement (150 µg) (Zimmermann and Delange 2004). One prenatal vitamin should contain between 150 and 200 µg iodine/ table (Dinc, Cakar et al. 2013) although other interventional studies which include supplementation, recommends lower, similar or higher doses (Brucker-Davis, Panaia-Ferrari et al. 2013).

One major dietary source of iodine is iodised table. Actually, 76% of the world is estimated to be covered by iodized salt (UNICEFa 2014). In Norway, voluntary iodized salt is not extensively used due to the low contribution of iodine from some brands of table salt (5 µg I/g Na Cl) compared to other sources of iodine (Opsahl 2002). In industrialized countries, the average amount of reported salt use per capita is 10 g/ day and only 1 g of household salt is consume daily. The intake of 3 g table salt /day contributes with 15 µg I if used (Dahl, Opsahl et al. 2003). Therefore, the use of iodised salt in the food industry will supplant the deficiency of iodine in the most part of the population (Zimmermann 2010, Zimmermann 2011).

1.9 Dietary recommendations of iodine

In the Nordic countries, the recommendations of iodine has been set at 150 µg/ day for children 10 years and older, 175 µg/ day for pregnant and 200 µg/ day for lactating, according to the Nordic Nutrition Recommendations (NNR5 2012) (TheNodicCouncilofMinisters 2013, TheNorwegianDirectorateofHealth 2014). The lowest and the maximum intakes per day are 70 µg and 1 mg iodine, respectively. WHO, the United Fund for Children (UNICEF) and the IGN established a recommend intake of 250 µg/ day for pregnant and lactating women.

The European Food Safety Authority (EFSA) and The Institute of the United States (IOM) have established Upper levels (UL) of iodine at 600 µg /d and 1100 µg/d respectively (SCF 2002, IOM 2001). These levels are considered safe for healthy adults including pregnant and lactating women according to EFSA (Flynn, Hirvonen et al. 2009). However, although most individuals tolerate high dietary intakes remarkably well (Pearce, Andersson et al. 2013) and no altered susceptibility has been noted, a higher daily intake of 500 µg during pregnancy is excessive (Andersson, de Benoist et al. 2007).

Table 2. Recommended iodine intake (µg per day)[†]

Age or Population Group	Recommended Iodine Intake (µg per day)
1 – 2 y	70
3 – 5 y	90
6 – 9 y	120
10 – >75 y	150
Pregnant	175
Lactating	200

[†]Modified from the table of Norwegian nutrient recommendations 2014

1.10 Aims of the study

The overall aim of the present thesis is to assess the iodine status of pregnant women which participated in the “Little in Norway” (Liten i Norge-LiN) study.

The specific objectives of the thesis were:

[1] To determinate the iodine status of the pregnant women based on urinary iodine concentration (UIC) from a spot urine sample using the epidemiological criteria from World Health Organization (WHO).

[2] To estimate the iodine intake from selected food groups and iodine-containing supplements using a food frequency questionnaire (FFQ) to evaluate whether or not it is in accordance with the Norwegian recommendation.

[3] To assess influence of some factors (e.g. weeks of gestation, timing and season of spot urine collection) on the urinary iodine concentration during pregnancy.

2. MATERIALS AND METHODS

This thesis is part of LiN study, which is a population prospective cohort study aiming at generating new knowledge about infant and early childhood mental health and development from pregnancy to age 18 months.

LiN project is a collaboration between the National Network for Infant Mental Health in Norway, at the Regional Center for Child and Adolescent Mental Health East and South. National Institute of Nutrition and Seafood Research (NIFES) is responsible for the nutritional part of the project. The Regional Committees for Medical Research Ethics has approved the study. LiN is not registered in clinical trials because this study qualifies as non-interventional.

2.1 Participants and recruitment

The participants were pregnant women recruited between September 2011 and mid-October 2012 from nine well-baby clinics across the Norwegian Health Regions. The data collection consisted of five phases namely: t_1 (enrolment, week 8 - 34), t_2 (week 20 - 25), t_3 (week 26 - 31), t_4 (week 32 – 34) and t_5 (week 36) and time of birth. The phases were based on the time of the gestational age the mother at the moment of enrolment. Data collection up to age 18 months ended in November 2014.

At the first meeting in the clinic, the mothers filled in several questionnaire (i.e. sociodemographic questionnaires) (t_1) and were asked to provide a urine sample (t_1 and t_3). The FFQ was within one week send to the mothers by e-mail and filled in at home (t_1-t_5). **Figure 5** shows an overview of the data collection at inclusion (different "*t*") and during pregnancy. In the present master thesis, results from t_1 are presented.

The questionnaires were answered electronically using a program called "Confirmit". The answers were transferred and recorded directly in an SPSS file. The FFQ and sociodemographic's file contained a raw data and therefore data clean and data conversion efforts were needed. The files were merged into a single file after that.

2.2 Determination of iodine in the diet

2.2.1 Data collection

Iodine in the diet was assessed using a part of a self – administrate, semi quantitative FFQ for dietary intake (t_1 and t_4) as well as a very short FFQ (3 questions only) with focus only in oily - lean fish consumption during dinner and the use of supplements ($t_{2,}t_3$ and t_5). The FFQ was in Norwegian and based on the validated seafood FFQ (Dahl, Maeland et al. 2011) and the seafood index (Markhus, Graff et al. 2013).

All questions from FFQ have variable names starting with "Sjo" and it's followed by the letter "T" and a number which stands for the data collection phase. Then the number corresponding to each question in the questionnaire comes e.g. "SjoT4_1". Some questions have sub-questions and come with the corresponding number, e.g. "SjoT4_1_1" (see Appendix). The variable name from sociodemographic questionnaire is according to the question. This system allows that each question has a variable and the data of multiple phases are recorded in the same file.

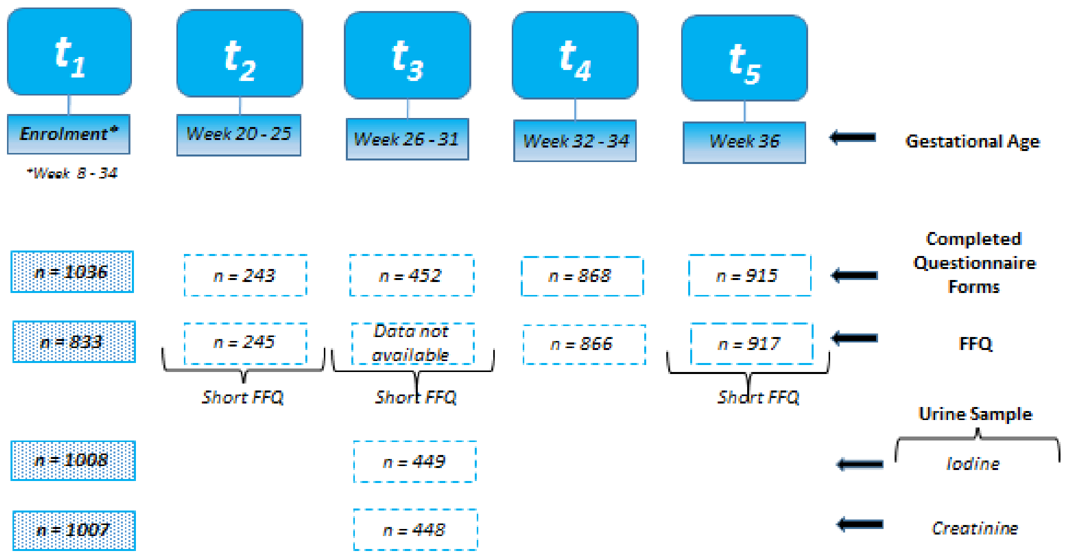

Figure 5. ***Flow chart describing Little in Norway study***

2.2.2. Frequency food questionnaire: Seafood

The FFQ asked for dietary habits of the seafood consumption for the last three months. For the purposes of this thesis, there were considered only those questions related to seafood consumption of seafood as dinner, spread salads or as snack meal divided in main and item questions, and the use of supplements containing iodine. It was also possible to register other seafood species and supplement brands not given in the questionnaire (“other seafood” and “other supplements”).

Frequency of consumption of seafood was recorded in six options: “never”, “less than once per month”, “one to three times per month”, “one time per week”, “two to three times per week”, “four times or more per week” in the main question for dinner and “never”, “rarely”, “one to three times per month”, “one to two times per week”, “three to five times per week”, ”more than five times per week” in the main question for spread.

Frequency intake of seafood as dinner and spread in the item questions was also recorded in five options: “never”, “less than once per month”, “one to three times per month”, “one to two times per week”, “three or more per week”.

The portions size was recorded in five options: “half a portion or les”, “one portion”, “one a half portion”, “two portions”, and "three portions” [iv]

[iv] 1 portion = 150 g

Seafood categories

Seafood was grouped into six categories: “oily fish”, “lean fish”, “freshwater fish”, “shellfish”, “sushi” and “processed fish”. It must be emphasized that to elaborate the categories it was considered the definitions of the Norwegian Scientific Committee for Food Safety 2007 (VKM), this mean; oily and lean fish (including half oily fish) if a fish contains > 5 g fat/100 g and < 5 g fat/100 g respectively; processed fish which does not include spread and typically consist of 40 – 60% oily fish filled. Within the category "freshwater fish", perch/ pike and char/powan were nominated in two different items. The first and the second item include lean fish and oily fish respectively. The reason why these fish were not re grouped within their respective categories was because it would not have been able to identify the frequency of consumption individually. However, these were re-grouped to make a calculation of the contribution of each seafood category.

2.2.3. Frequency food questionnaire: Milk-and dairy products

Milk and dairy products (milk, yogurts, and cheese) were reported as follows: “yes” (the person consumes) or “not”. If the mother indicates “yes”, the next option was to indicate the daily frequency of consumption as: “one time per day”, “two to three times per day”, “four to five times per day”, “seven to nine times per day” and “ten or more times per day”. Consumption of different products fortified with vitamin D was not considered in this thesis.

2.2.4. Frequency food questionnaire: Eggs

Weekly consumption of eggs as fried, boiled, scrambled eggs and omelet was recorded as: “less than one egg per week”, “one egg per week”, “two to three eggs per week”, “four to five eggs per week”, “six to seven eggs per week” and “eight or more eggs per week”.

2.2.5. Frequency food questionnaire: Multivitamin and mineral supplements

The use of multivitamin and mineral supplements was entered as: “never use”, “one to three times per month”, “one to three times per week”, “four to six times per week” and “daily”.

2.2.6. The seafood index

Recently in Norway, it was established and validated a seafood index from seafood FFQ to capture seafood consumption in pregnant women and since seafood is a good source of iodine, the present study used the seafood index to assess iodine intake.

[1] For estimation of frequency of consumption, ordinal data from seafood FFQ were transformed to numerical data using the seafood-index system which has been explained by Markhus, Graff et al. 2013 .

[2] To avoid double reporting on sushi consumption and to specify the amount of fish that contains, it was decided to weigh the amount of fish in a portion of sushi (between 6 – 10 bits) composed of nigiri and sushi rolls (maki) from three different seafood processing companies (Tradisjonell Sushi, Sushi Premium and Lerøy). The results showed that a portion of sushi can contain up to 25% of fish and this result was used in the seafood index.

[3] Simultaneously, it was developed a weekly index for milk-and dairy products and eggs consumption (**Table 3-4)**.

Table 3. Milk and dairy products index – conversion of frequencies to numerical values

Reported Frequency	Numerical interval per week	Index
one time per day	7	7
two to three times per day	14 – 21	14
four to five times per day	28 – 42	35
seven to nine times per day	49 – 63	56
ten or more times per day	70	70

Table 4. Eggs index – conversion of frequencies to numerical values

Reported Frequency	Numerical interval per week	Index
less than one egg per week	0 – 0.25	0.15
one egg per week	1	1
two to three eggs per week	2 – 3	2.5
four to five eggs per week	4 – 5	4.5
six to seven eggs per week	6 – 7	6.5
eight or more eggs per week	8	8

[4] In addition, it was elaborate a list of equivalent weights and measures (kostholdsplanleggeren, NorwegianFoodSafetyAuthority et al. 2014) of the named food products in the FFQ to calculate iodine contain. The iodine content in supplements was calculated from the nutrition facts labels and personal communication with the distribution companies.

The daily iodine intake from milk-and dairy products, eggs and supplements were calculate first by using the corresponding product index (milk and dairy products, eggs and supplements) divided by seven (the number of days in a week) and the results was multiplied by the equivalent weight of the food product and then, the results were multiplied by the amount of iodine contained in the food and divided by 100. The iodine intake from seafood was calculated by multiplying the reported portion size by the equivalent weight of the food product and the results were multiplied by the amount of iodine contained in the food and divided by 100. The total iodine intake is the sum of the all results from each food product which were calculated. **(Fig. 6)**.

[6] The total weekly intake of Seafood for dinner was calculated multiplying the seafood index for the main question for dinner by the equivalent weight of the food product.

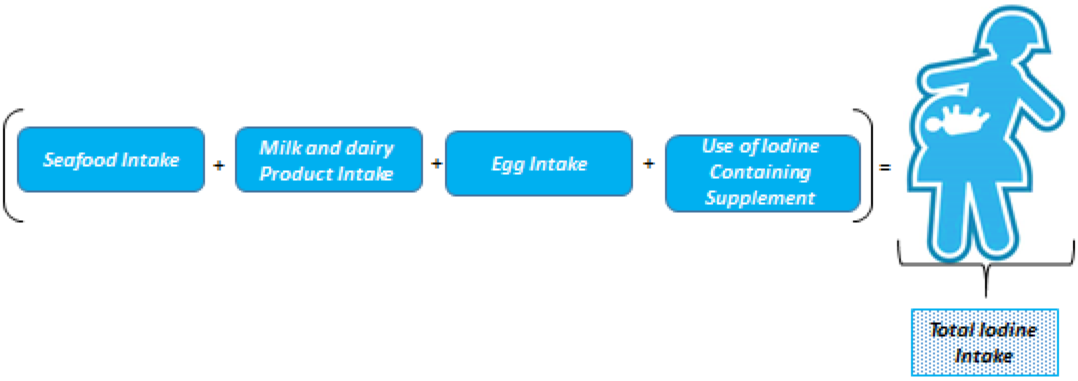

Figure 6. ***Assessment of the total iodine intake***

2.3 Determination of iodine in human urine spot samples

2.3.1. Collection of Sample

Pregnant women provided a non-fasting spot urine sample. The urine samples were collected from 1008 women. The nine well-baby clinics were Fjell, Frogner, Høylandet, Lørenskog, Namsos, Strindheim, Tromsø, Ulset and Østensjø. Laboratory results were fully delivered in September 2014.

Urine samples were stored in cryo tubes and then, stored for each baby clinic in the same box in the freezer at minus 20˚C. Cryo tubes were labeled with the mother's identity, date, time (hour) of sample collection and gestational age (week). Not all tubes were labeled or had completed information. Gestational age was reported in 929 tubes, time was reported in 612 tubes and the date was reported in 987 tubes.

Gestational age was re-grouped into weeks 1 – 16, 17 – 29, and 30 to delivery, corresponding to the first, second and third trimesters, respectively (Bauch, Meng et al. 1986, Glinoer, Nayer et al. 1990, Smyth, Hetherton et al. 1997, Brander, Als et al. 2003).

To see the variation by timing of collection (Wang, Cogswell et al. 2013) the urine samples were re-grouped in concordance to the time when urine sample were collected **(Table 5)**.

Table. 5 Timing of spot urine collection

Timing	Hours
Morning sample	08:30 and 12:30
Afternoon sample	12:31 and 17:30
Evening sample	17:31 and 23:59
Overnight sample	04:00 and 12:00

Urine samples were also re-grouped according to the season of the year they were taken: Spring (5 Feb – 6 May), Summer (7 May – 6 Aug), Autumn (7 Aug – 16 Nov) and Winter (17 Nov – 5 Feb).

A laboratory technician performed all analyses. The master student was responsible for sample preparation after a theoretical and practical introduction.

2.3.2. Procedure for determination of iodine in urine sample

All sample preparation and analysis of iodine in human urine was performed according to the method under development by the staff at NIFES. Iodine was determined using inductively coupled mass spectrometry ICP-MS (Agilent Technologies [Inc.] , Tokyo, Japan) (Julshamn, Dahl et al. 2001).

Prior to analysis, the urine samples were defrosted in a refrigerator the day before. The sample preparation was as follow: 500 µl of urine were diluted in 4.5 ml 1% TMAH tetramethylammonium hydroxide (10 ml 25% TMAH diluted in 1 l of distilled water from Millipore) and filtered by using a sterile syringe filter with a 0.45 mm pore size and a 10 ml syringe. Blank samples were prepared at the same time by using distilled water instead of urine.

Approximately, three to four standard solutions were made by mixing small amounts from a random selection of the sample solutions of the same matrix (mixed sample). These solutions were prepared to elaborate a urine calibration curve to against the measured ^{127} I by taken out 05-10-20-50-100-200 µl of 5 ml/ L standard iodine Spectrascan 998 ± 4µg/ L, Teknolab AS (50 µl of standard iodine diluted in 10 ml distilled water) diluted with urine mixture (thoroughly mixed samples) up to a total of 5 ml. Blank samples was always run together with the standard curve.

The accuracy of the results was verified with the certified Standard Reference Material (SRM) -Seronorm ™ Trace Elements Urine L-1 and L-2, SRM 2670a Toxic Elements in Urine **(Table 6)**. The SRM bottle was reconstituted with 5 ml for Seronorm L-1, 2 and 20 ml for SRM 2670a.

Table 6. List of the standard reference material and their values

Standard Reference Material	Analytical Value	Acceptable Range
Seronorm ™ Trace Elements Urine L-1	84 µg/ L	72 – 96 µg/ L
Seronorm ™ Trace Elements Urine L-2	304 µg/ L	260 – 348 µg/ L
SRM 2670a Toxic Elements in Urine	88,2 µg/ L	87,1 – 89,3 µg/ L

2.3.4. Procedure to determination of creatinine in urine Sample

The procedure was performed by technicians at NIFES. For the urinary creatinine determination, the urine samples prior to analysis were defrosted at room temperature and centrifuged (15 min, 2000 g). All sample treatment was automatic in the Maxmat carousel; samples (200 µL urine) were diluted 1:20 with distilled water and reagents added. Determination of creatinine was performed by a colorimetric enzymatic principle using MAXMAT PL II multidisciplinary diagnostic platform (Maxmat S.A., Montpellier, France) using the creatinine PAP kit (personal communication Lisbeth Dahl).

2.4 Measurement of iodine status

Three measurements of iodine status were calculated from casual urine samples **(Table 7)**.

Table 7. Methods for assessment iodine status

Measurements	Expression	Reference
Iodine concentration	µg/ L	referred in several articles
Iodine/ creatinine ratio	µg I/ g creatinine	Barr, Wilder et al. 2005
Age- and sex-adjusted Iodine/ creatinine ratio	Estimated I µg/ day	Knudsen, Christiansen et al. 2000, Garde, Hansen et al. 2004

The UIC was assessed on casual urinary samples and expressed as median value. The correction of the urinary volume in the mothers was calculated by using a sample iodine to creatinine ratio (Andersen 2008) **(Formula 1)**.

$$\textbf{Iodine/ creatinine ratio} = \frac{\textit{Iodine } (\mu g/\ L)}{\textit{Creatinine } (g/\ L)}$$

Considering that there was only one spot – urine sample available, it was decided to adjusted age and sex to creatinine ratio to estimate daily UIE and reduce the intra individual coefficient of variation in daily urine volume. The method seems to be better compared to non-adjusted iodine concentration and iodine/ creatinine ratio (Ovesen and Boeing 2002, Konig, Andersson et al. 2011). (**Formula 2)**

$$\textbf{Age- and sex-adjusted Iodine/ creatinine ratio} = \frac{\textit{Iodine } (\mu g/\ L)}{\textit{Creatinine } (g/\ L)} \ast \textit{Expected creatinine } (g/\ day)$$

The expected creatinine excretion for pregnant women according to the literature was 1.09 g/ day (Pedersen, Borlum et al. 1988, Andersen, Moller et al. 2014).

2.5 Sociodemographic questionnaire

The general questionnaire collected details on participant age, smoking habits, self-reported anthropometric measures (weight prior to the pregnancy and current weight) to calculate the body mass index (BMI) **(Formula 3),** education, pregnancy-related concerns, uses medication and economic income and employment and marital status.

$$\textbf{Body Mass Index (BMI)} = \frac{\textit{Weight } (Kg)}{\textit{Height } (m^{2})}$$

2.6 Statistical analysis

The present thesis is based on descriptive statistics. For quantitative variables, means, median, min and max values, standard deviations, percentiles and percentage were calculated. Qualitative variables were presented in contingency tables. All statistical analyses were performed using IBM SPSS Statistics 22 (originally Statistical Package for the Social Sciences). The various figures were made using SPSS and Microsoft Excel 2010. Due to the characteristics of the gathered data Pearson's Correlation Coefficient was employed. The level of significance was set at $p < 0.05$ and $p < 0.01$.

3. RESULTS

3.1 Descriptive characteristics of the study population

A total of 1041 pregnant mothers were recruited to the study. **Table 8** shows descriptive characteristics of the 1036 included pregnant women in the LiN study.

Table 8. Socio-economic, behavioral characteristics and anthropometric measurements of study participants in LiN• (n= 1036)

Characteristics	Mean ± SD (min, max)	Count (n)	Percent (%)
		n = 828	
Age (years)	29 ± 5 (17, 43)		
Height (m)	1.67 ± 0.06 (1.30, 1.84)		
Current weight (kg)	72.92 ± 13 (50, 185)		
Prior weight (kg)	66.26 ± 12 (42, 158)		
Current BMI (kg/ m^2)	26 ± 4.5 (17.30, 65.62)		
Prior BMI~ (kg/ m^2)	23 ± 4.2 (16.80, 48.77)		
BMI Category (current)		***n = 828***	
Underweight (< 18.5)		2	1
Normal (18.5 – 24.9)		375	45
Overweight (25 – 29.9)		325	39
Obese Class I (30 – 34.9)		92	11
Obese Class II (35 – 39.9)		25	3
Obese Class III (> 40)		9	1
BMI Category (prior)		***n = 828***	
Underweight (< 18.5)		33	4
Normal (18.5 – 24.9)		567	68
Overweight (25 – 29.9)		154	19
Obese Class I (30 – 34.9)		50	6
Obese Class II (35 – 39.9)		16	2
Obese Class III (> 40)		8	1
Education		***n = 884***	
Lower secondary school		42	5
Higher secondary school		249	28
< 4 years of university education†		265	30
≥ 4 years of university education†		328	37
Employment		***n = 1036***	
Full-time (80 – 100%)		801	77
Part-time (50 – 79%)		60	6
Part-time (< 50%)		17	2
Student		60	6
Student and employee		60	6
Other		38	4
Marital Status		***n = 1036***	
Married		375	36
Cohabiting		619	59
Single		26	3
Other		16	2
Own Income in NOK‡		***n = 1036***	
< 1,50,000		122	12
1,50,000 – 2,99,999		201	19
3,00,000 – 4,49,999		460	44
4,50,000 – 5,99,999		177	17
≥ 6,00,000		76	7
Self-reported smoking/ using of snuff during pregnancy		***n = 245***	
Non-smoker/ non-user		238	97
Current smoker/ current user		7	3
Focus on Healthy Diet		***n = 245***	
Very small		2	0.2
Small		17	2
Medium		355	43
High		375	45
Very high		78	9

†University or University College
‡1,00,000 NOK 14,000 EUR
~Before pregnancy
*Little I Norway

3.2 Urinary creatinine

At $t_{1,}$ gestational age was registered in 944 when the spot urine samples were collected. Gestational age was then grouped into three trimesters. Level of creatinine by trimesters I given in **Figure 7**. Mean level ± SD of creatinine were 1.3 ± 0.7, 1.2 ± 0.8 and 1.1 ± 0.6 g/ L for the first, second and third trimester respectively. Mean creatinine level from all samples was 1.24 ± 0.7 g/ L (median 1.1).

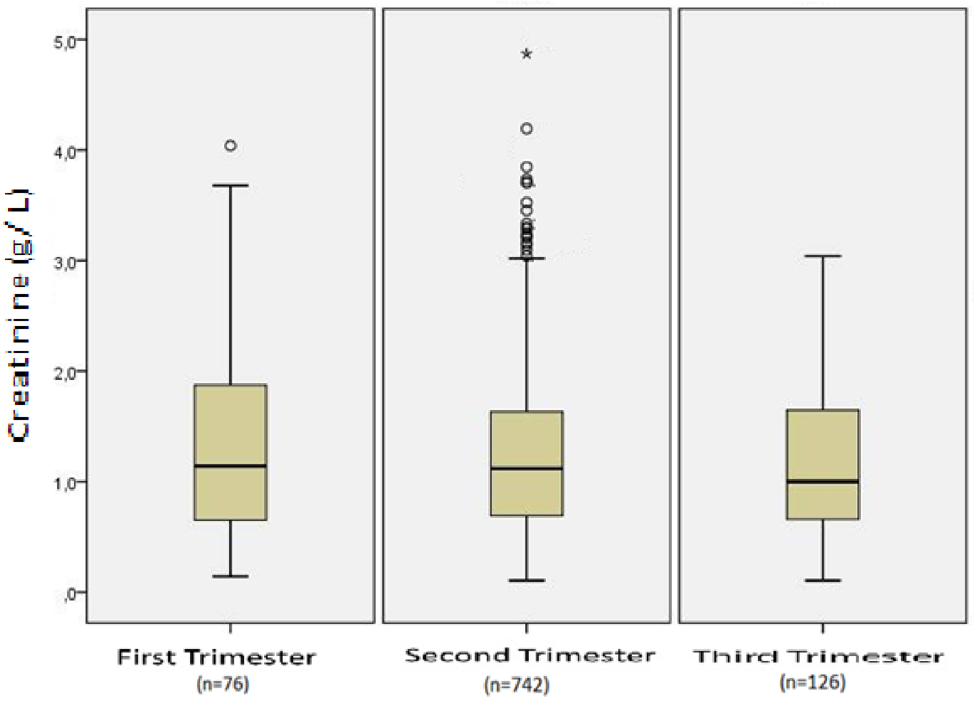

Figure 7. ***Creatinine (g/ L) in spot urine samples in pregnant Norwegian women distributed by trimesters (n = 944)***

Box plot details: the horizontal line indicates the median; the box indicates the interquartile range (IQR) (IQR: 25th percentile to 75th percentile); the whiskers indicates observations within 1.5-times the IQR; the circles indicate observations more than 1.5-times the IQR away from the box, considered as outliers and the star indicate a score greater than the upper quartile plus 3 times the IQR which is labeled as extreme case (Field 2013).

3.3 Urinary iodine and iodine status

Table 9 shows Median urinary iodine concentration (MUIC) for pregnant women.

Table 9. Urinary iodine concentration in pregnant Norwegian women

	n=	Median (min, max)			P25†	P75†	Mean ± SD	
PREGNANCY SAMPLES								
-Iodine µg/ L	1008	82	4	774	48	135	105	90
-µg I/ g cre	1006	75	5	1784	49	114	98	89
-Estimated I µg/ day	1006	82	5	1944	53	123	106	97

†P25 = 25th percentile, P75 = 75th percentile.

µg/ L = microgram per liter; g = gram; cre = creatinine; SD = Standard Deviation

According with the cut off values for pregnant women established by WHO/UNICEF/IGN **(Table 1)** approximately 80% of pregnant women had an insufficient iodine level, 20% had an adequate iodine level and 1% had excess **(Fig. 8)**. **Figure 9** shows the same prevalence based on severity of iodine deficiency (mild: 50 – 99 µg/ day, moderate: 20 – 49 µg/ day, and severe: < 20 µg/ day) (Travers, Guttikonda et al. 2006)

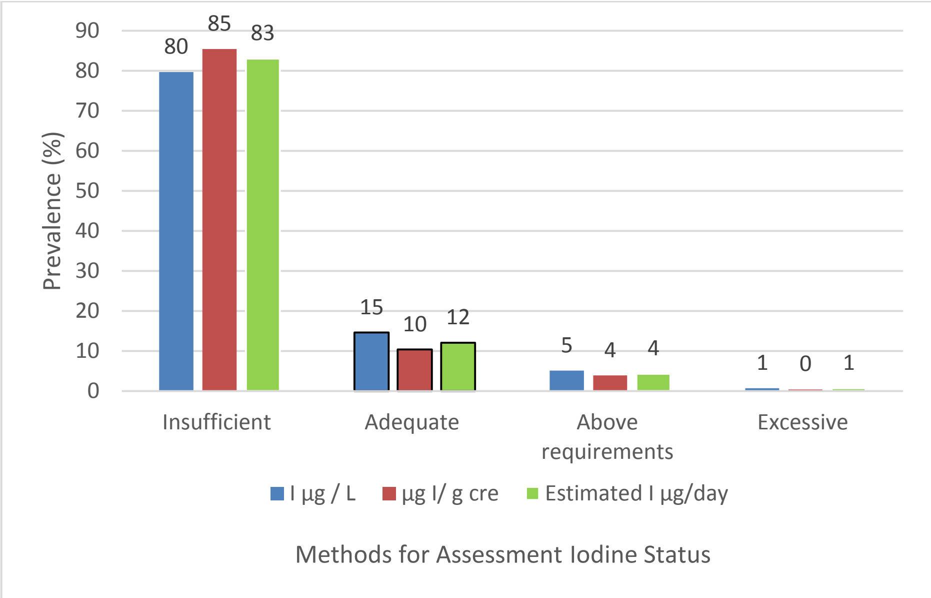

Figure 8. ***Prevalence of iodine status in pregnant Norwegian women given as: iodine concentration (µg/ L) (n = 1008), iodine/ creatinine ratio (µg I/ g creatinine) (n = 1006) and age- and sex-adjusted iodine/ creatinine ratio (estimated I µg/ day) (n = 1006)***

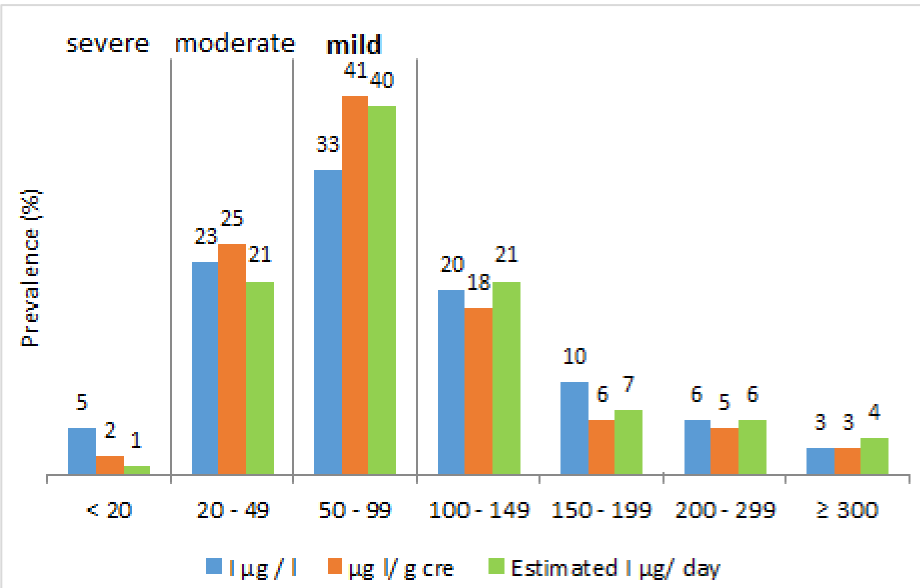

Figure 9. ***Prevalence of severity of iodine deficiency in pregnant Norwegian women given as: iodine concentration (µg/ L) (n = 1008), iodine/ creatinine ratio (µg I/ g creatinine) (n = 1006) and age- and sex-adjusted iodine/ creatinine ratio (estimated I µg/ day) (n = 1006)***

3.4 Frequency food questionnaire

At t_1 833 women filled out the FFQ which revealed that almost every pregnant women included seafood, milk-and dairy products and eggs in the diet. Although the iodine rich food groups were included in their diet, frequency of consumption varied. Only 118 pregnant women reported to use iodine-containing supplements.

3.4.1 Seafood intake

At t_1, 833 women reported the frequency of seafood intake for dinner. The estimated mean seafood intake was 1.3 ± 0.9 times per week (median 1.0). **Figure 10** shows the frequency of seafood consumption as dinner. The median and mean seafood intake for dinner was 150 g per week and 29 g/ day (median 21), respectively. A total of 824 pregnant women reported the most preferred portion size at dinner: half portion is preferred for the 2% of the women, 54% preferred 1 portion, 20% preferred one and a half portion and 3% preferred two or more than two portions.

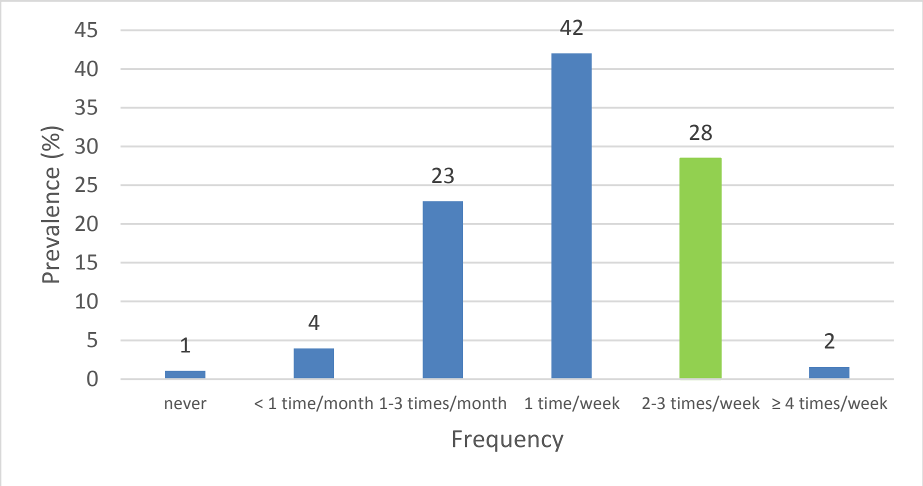

Figure 10. ***Frequency of intake of Seafood for Dinner given as percent of total numbers of pregnant Norwegian women (n = 833)***

Details about the type of seafood for dinner were reported in 822 pregnant women **(Fig. 11)**. Oily fish represent the 37% of the fish consumption for dinner with an estimated mean of 0.5 ± 0.6 times per week (median 0.4). Lean fish was consumed by 27% of the pregnant women with an estimated mean intake of 0.4 ± 0.5 times per week (median 0.3). Processed fish was consumed at dinner by 26% of the pregnant women with an estimated mean of 0.4 ± 0.4 (median 0.4). Freshwater, shellfish and sushi was consumed at dinner for 10% of the women.

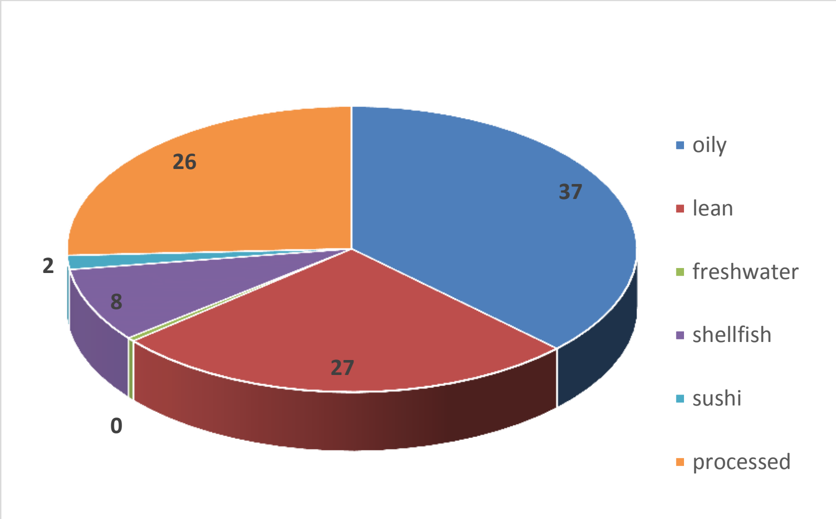

Figure 11. ***Distribution (%) of consumption of seafood for dinner in pregnant Norwegian women (n = 822)***

Consumption of seafood as spread was also evaluated in 833 pregnant women **(Fig. 12)** and it showed that 59% ate < 1 – 3 times per month or never, 39% ate 1 – 5 times per week and only 1% ate > 5 times per week. The estimated mean seafood intake as spread was 1 ± 1.2 times per week (median 0.5).

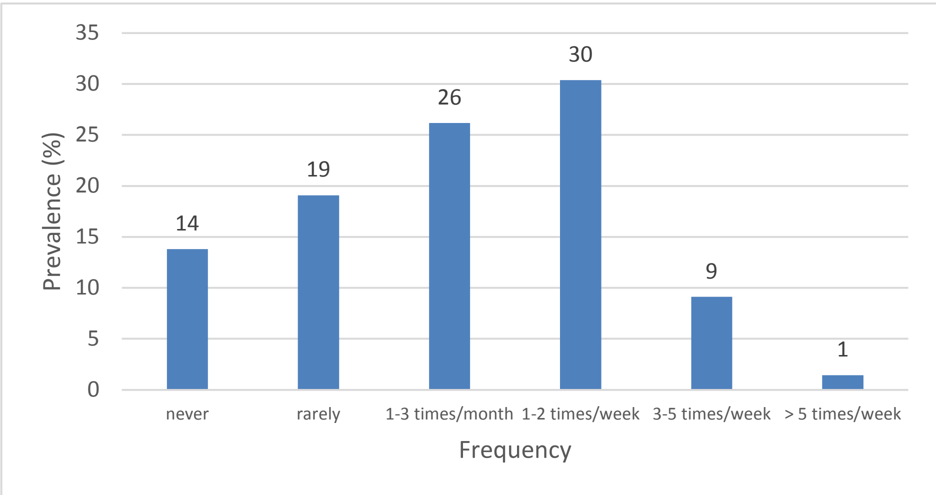

Figure 12. ***Frequency of seafood as spread given as percent of total numbers of pregnant Norwegian women (n = 833)***

Frequency of consumption of seafood for dinner and as spread is detailed in **Table 10** (n = 831)**.** The most frequently reported intake of seafood for dinner was salmon/ trout in the oily fish group; cod in the lean fish group; shrimp in the shellfish group and fish cake in the processed group in a frequency of 1 – 3 times per month. In the same frequency per month, sushi was consumed by 20% of the women. Freshwater fish was consumed < 1 time per month. More than 90% of the participants chose not to consume herring, redfish, perch/ pike, char/ powan or lobster.

Seafood as spread listed in the FFQ is primarily oily fish. 88% of pregnant women preferred oily seafood as spread while 12% preferred lean seafood. The estimated mean intake for oily and lean seafood as spread were 1.3 ± 1.5 times per week (median 1) and 0.2 ± 0.3 times per week (median 0.1) respectively. **Figure 13** shows the type of oily seafood products which were most consumed between the participants and the prevalence of lean seafood products as spread.

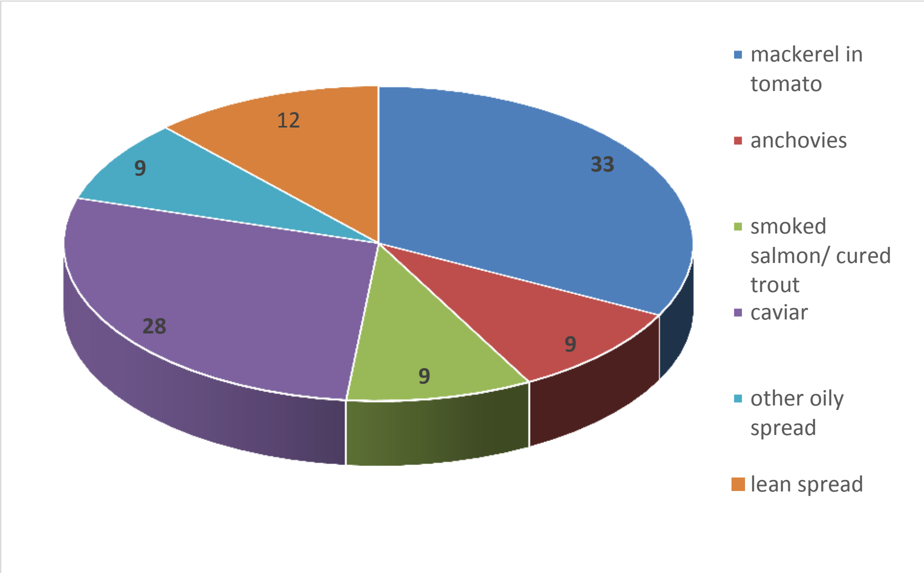

Figure 13. ***Distribution (%) of seafood consumption as spread (oily and lean) in pregnant Norwegian women (n = 716)***

Table 10. Frequency of seafood intake in pregnant Norwegian women (*n = 831*)

Count (*n*) and percent (%) is shown†

	never		< 1 time/ month		1-3 times/ month		1-2 times/week		≥ 3 times/week	
SEAFOOD FOR DINNER										
OILY (> 5%)	*n*	%	*n*	%	*n*	%	n	%	n	%
-Salmon/ Trout	86	10	127	15	403	48	206	24	9	1
-Mackerel	603	72	96	11	90	10	34	4	8	1
-Herring	771	92	45	5	13	1	2	0.2	0	0
-Halibut	573	69	195	23	58	7	5	0.6	0	0
LEAN (< 5%)										
-Redfish	762	91	55	6	14	1	0	0	0	0
-Catfish	666	80	122	14	40	4	3	0.4	0	0
-Flounder/Plaice	694	83	92	11	42	5	3	0.4	0	0
-Cod	202	24	220	26	330	39	78	9	1	0.1
-Saithe	469	56	185	22	143	17	34	4	0	0
-Haddock	754	90	53	6	18	2	6	0.7	0	0
FRESHWATER										
-Perch/ Pike	817	98	14	2	0	0	0	0	0	0
-Char/ Powan	797	95	29	4	5	1	0	0	0	0
SHELLFISH										
-Shrimp	317	38	245	29	236	28	31	3	2	0.2
-Crab	692	83	108	13	29	3	2	0.2	0	0
-Lobster	769	92	56	6	5	0	1	0.1	0	0
-Blue Mussel	720	86	86	10	22	2	3	0.4	0	0
-Scallop	699	84	102	12	29	3	1	0.1	0	0
SUSHI	510	61	125	15	168	20	28	3	0	0
PROCESSED										
-Fish Cakes	223	26	203	24	337	40	65	7	3	0.4
-Fish Ball	367	44	191	23	235	28	36	4	2	0.2
-Fish Pudding	554	66	140	16	114	13	23	2	0	0
-Fish au gratin	309	37	204	24	281	33	36	4	1	0.1
-Fish Sticks	478	57	176	21	151	18	26	3	0	0
-Fish Soup	414	49	231	27	172	20	12	1	2	0.2
-Clip Fish	741	89	73	9	17	2	0	0	0	0
SEAFOOD AS SPREAD										
OILY (> 5%)										
-Mackerel in tomato	315	37	101	12	182	21	175	21	58	6
-Canned Sardine	795	95	19	2	13	1	2	0.2	2	0.2
-Canned Salmon	771	92	30	4	21	2	7	0.8	2	0.2
-Brisling	825	99	4	1	1	0	1	0.1	0	0
-Anchovies	784	94	29	3	13	1	5	0.6	0	0
-Smoked Salmon/ cured Trout	503	60	123	14	150	18	48	5	7	0.8
-Marinated Salmon/ Cured Trout	774	93	30	3	23	2	3	0.3	1	0.1
-Herring	733	88	50	6	29	3	16	2	3	0.3
-Caviar	435	52	58	6	149	17	131	15	58	6
-Patty ("svolværpostei")	822	98	8	1	0	0	1	0.1	0	0
-Patty ("lofotpostei")	828	99	3	0.3	0	0	0	0	0	0
LEAN (< 5%)										
-Shrimp	376	45	177	21	211	2	61	7	6	0.7
-Tuna‡	650	78	93	11	70	8	16	1	2	0.2
-Crabsticks	747	89	46	5	28	3	9	1	1	0.1

†Answers from the question "other seafood" were not included in this table.

‡Tuna in water

In the question "other seafood" the participants were asked to fill in the name of the seafood they had eaten. The following seafood was given: stock fish, pepper smoked mackerel (vacuum packing), scampi, liver pate, crayfish, octopus, pangasius (n = 14). Some other participants named a seafood product which was already listed in the FFQ (n = 46).

3.4.2 Milk-and dairy products intake

The majority of pregnant women who completed the FFQ consumed milk-and dairy products 2 – 3 times per day (68%) **(Fig. 14).** No one consume milk ≥ 10 times per day. The estimated mean milk-and dairy products frequency intake was 2 ± 0.6 times daily (median 2.0).

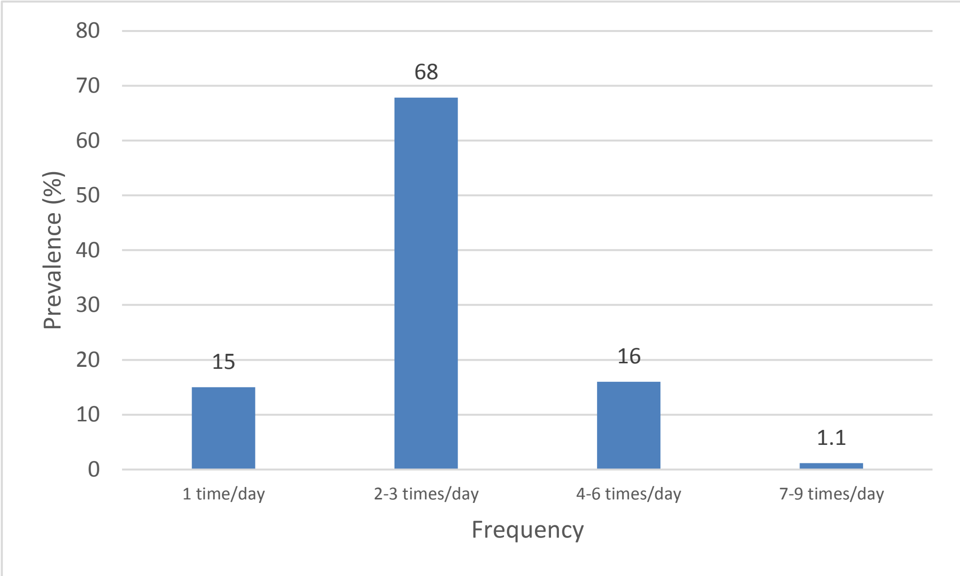

Figure 14. ***Frequency of milk-and dairy products intake given in percent of total numbers of pregnant Norwegian women (n = 793)***

3.4.3 Egg intake

The frequency of egg intake was mainly 2 – 3 eggs per week (39%) **(Fig. 15)**. The estimated mean egg intake was 2.6 ± 0.1 times per week (median 3.0).

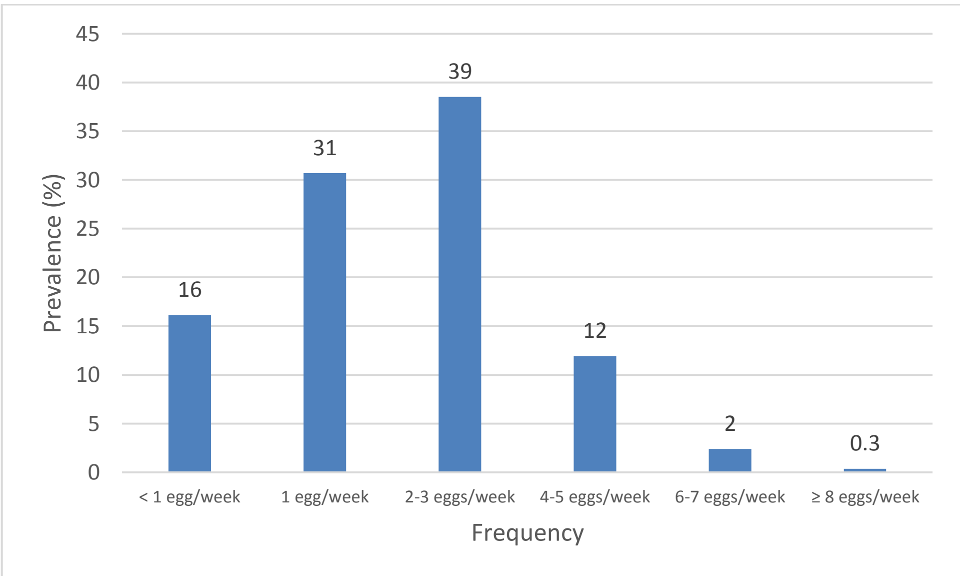

Figure 15. ***Frequency of egg intake given in percent of total numbers of pregnant Norwegian women (n = 831)***

3.4.4 Multivitamin and mineral supplement:

The frequency of multivitamin and mineral supplement intake is showed in **Table 11**. At inclusion of 343 of the 1036 women answered the question about the use of supplements. The list of supplements was re-grouped in this thesis into non-iodine-containing and iodine-containing supplement. Most of the participants did not use the supplements given in the questionnaire. A total of 118 participants used iodine-containing supplement.

Table 11. Frequency of multivitamin and mineral supplement intake in pregnant Norwegian women (*n = 343*)
Count (*n*) and percent (%) is shown†

	never		1-3 times/ month		1-3 times/ week		4-6 times/ week		daily	
NON IODINE-CONTAINING SUPPLEMENT										
	n	**%**	***n***	**%**	***n***	**%**	n	%	n	%
-Møllers Tran	172	50	20	6	26	8	31	9	94	27
-Møllers Dobell	316	92	8	2	4	1	2	1	13	4
-Krillolje	343	100	0	0	0	0	0	0	0	0
-Selolje	342	100	0	0	0	0	1	0	0	0
-Complete Folat og Omega-3	342	100	1	0	0	0	0	0	0	0
-Møllers Omega-3 + Folat	340	99	1	0.5	0	0	0	0	1	0.5
-Gevita Omega-3 med Kalsium, vitamin D og K	342	100	0	0	0	0	0	0	1	0
-Trippel Omega-3	339	98	2	1	1	0.5	0	0	1	0.5
-Multi-tabs GraviOmega	342	100	0	0	1	0	0	0	0	0
IODINE-CONTAINING SUPPLEMENT										
-Lifeline Gravid	326	95	3	1	3	1	3	1	8	2
-Lifeline Ammende	335	98	0	0	1	0	3	1	4	1
-Nycomed Gravid	340	99.5	1	0.5	1	0.5	0	0	1	0.5
-Nycopluss Omega-3	335	98	1	0	1	0	2	1	4	1
Other Supplement	322	94	3	1	2	1	0	0	16	4

†Answers from the question "other supplement" were included in this table and will be explained below.

In the question "other supplement" the participants were asked to fill in the name of the supplement they had used. The following supplements were given for 19 mothers: arctic cod liver oil, «linfrøolje», «sanasol», «lofot tran» - capsules, efanatal – capsules, okinawa omega 3,6,7,9, udo's choice omega 3,6, eye q liquid, «naturlig omega 3», «nycoplus tran», «multivitaminer med mineraler», omega cure, super food omega 3,6,9, «havfruenes tran», «jomfrueolje».

The FFQ had also another open ended question "other supplement – vitamins and mineral". The following non-iodine-containing supplements were given for 35 mothers: «pluss multivitaminer», «floradix», pregnant care multivitamin, «berocca», «biovit», life multivitamin, «sanasol», «collett kostpluss multivitamintilskudd», «collet multivitaminbjørner», spectra vitaminer, «vitaminbjørner», «nycoplus aktiv med magnesium», cederroth multivitamin. In the other hand; iodine-containing supplements were given for 114 mothers: «gravitamin», prenatal nutrients, «gevita», «kelp», «møllers total», «nycoplus omega 3 multi», «nycoplus multi uten vit A og D», «lifeline care gravide og ammende», «vitaplex», «nycoplus», «lifeline care for gravide», «nycoplus multi».

It was also considered to show the MUIC using the first estimate: Iodine Concentration (µg/ L) in consumers and non-consumers of seafood and milk-and dairy products according to the frequency of consumption **(Figs. 16, 17)** and users and non-users of iodine-containing supplement **(Fig. 18)**. The following **Figs. 16-18** show the cut-off value for insufficient iodine status during pregnancy (< 150 µg/ L) modified from Bath, Walter et al. 2014 .

MUIC was 82 µg/ L and 78 µg/ L for seafood consumers (n = 824) and non-seafood consumers (n = 9) respectively **(Fig. 16)**.

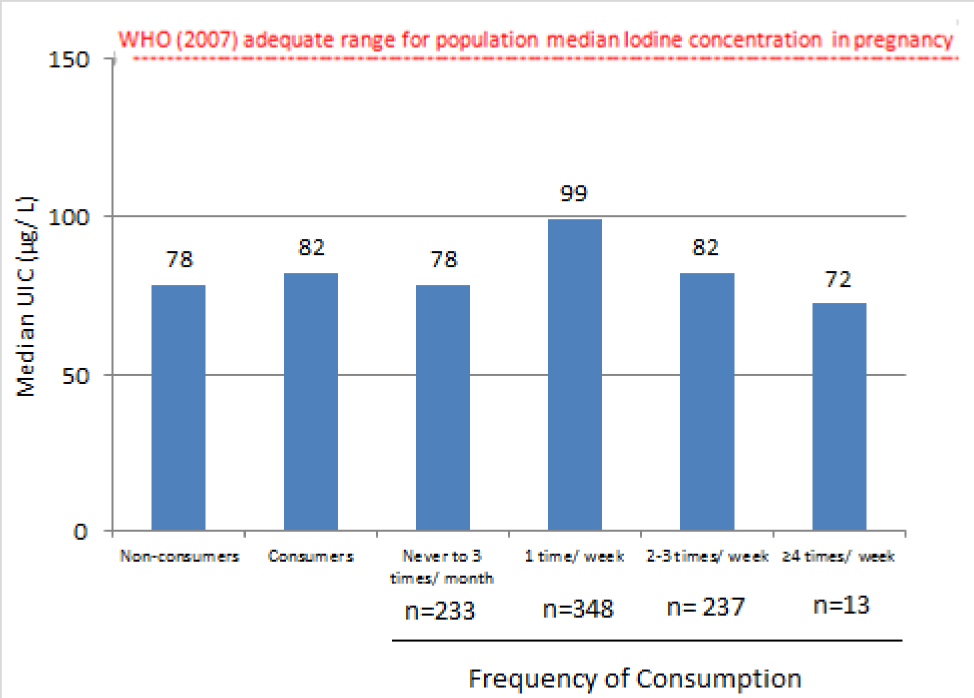

Figure 16. ***Median urinary iodine concentrations of non-seafood consumers (n = 9) and seafood consumers (n = 824) according to frequency of seafood intake***

MUIC was 87 µg/ L and 49 µg/ L for milk-and dairy product (n = 793) and non-milk-and dairy product (n = 38) consumers respectively **(Fig. 17).**

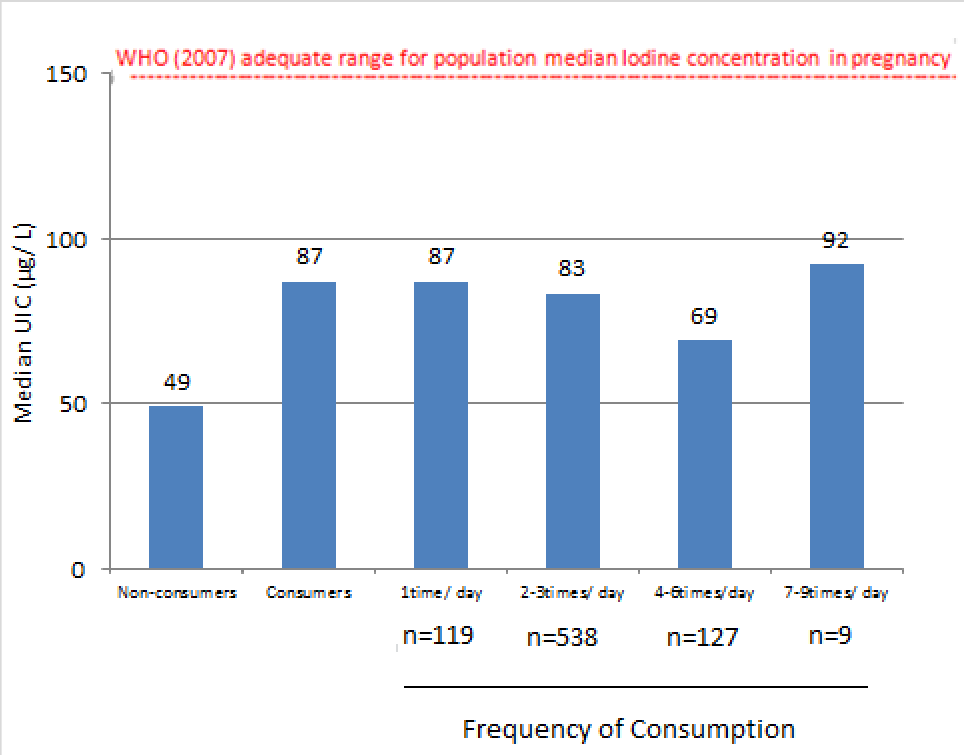

Figure 17. ***Median urinary iodine concentration of non-milk-and dairy product consumers (n=38) and milk-and dairy product consumers (n= 793) according to frequency of milk-and dairy product intake***

MUIC was 101 µg/ L and 79 µg/ L for iodine-containing supplement users (n = 118) and non-user of iodine-containing supplement (n = 687) respectively **(Fig. 18).**

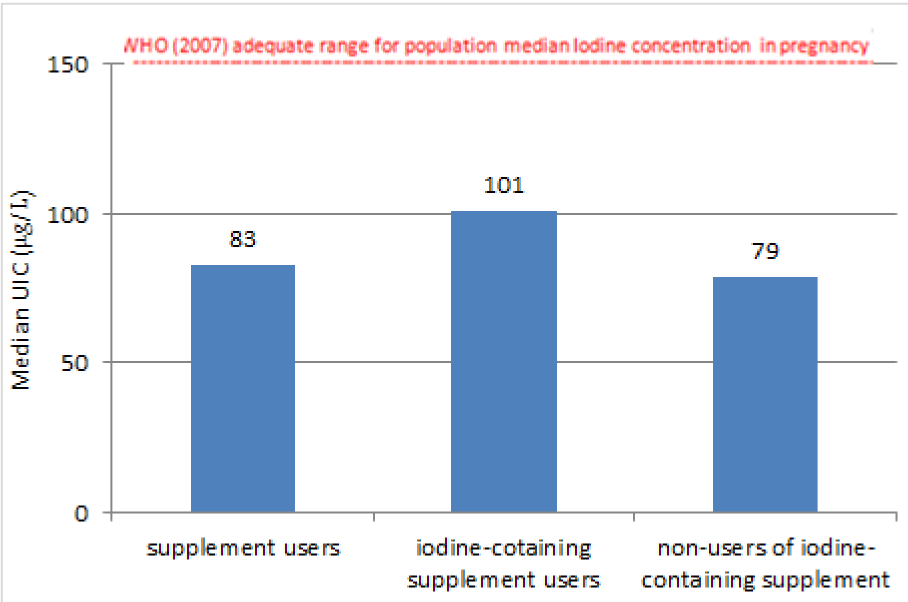

Figure 18. ***Median urinary iodine concentration of supplement users (n=805); iodine-containing supplement users (n= 118) and non-user of iodine-containing supplement (n= 687)***

3.5 Total iodine intake

The total iodine intake is the sum of the intake of seafood, milk-and dairy product, egg and the use of iodine-containing supplements. The mothers who reported iodine-containing supplement in the question: "other supplement – vitamins and mineral" were not considered in this calculation due to the lack of information on the frequency of intake. The total median iodine intake from food and supplements was calculated to be 153 µg/ day (n= 833). The estimated median iodine intake of 800 non-users of iodine-containing supplement was 153 µg/ day (range: 4 - 383 µg); whereas the median iodine intake of 33 iodine-containing supplement users was 268 µg/ day (range: 70 - 595 µg). Iodine intake < 150 µg/ day were found in the 36% (n=297) of the pregnant women. Intake less than 100 µg I/ day was found in 5% (n = 42) of participants. A higher intake more than 300 µg I/ day was revealed in 3% (n = 21) of pregnant women including one woman with an intake over 500 µg I/ day. Furthermore, the study showed that none of the participants had an intake of iodine above 1 mg/ day **(Fig. 19)**

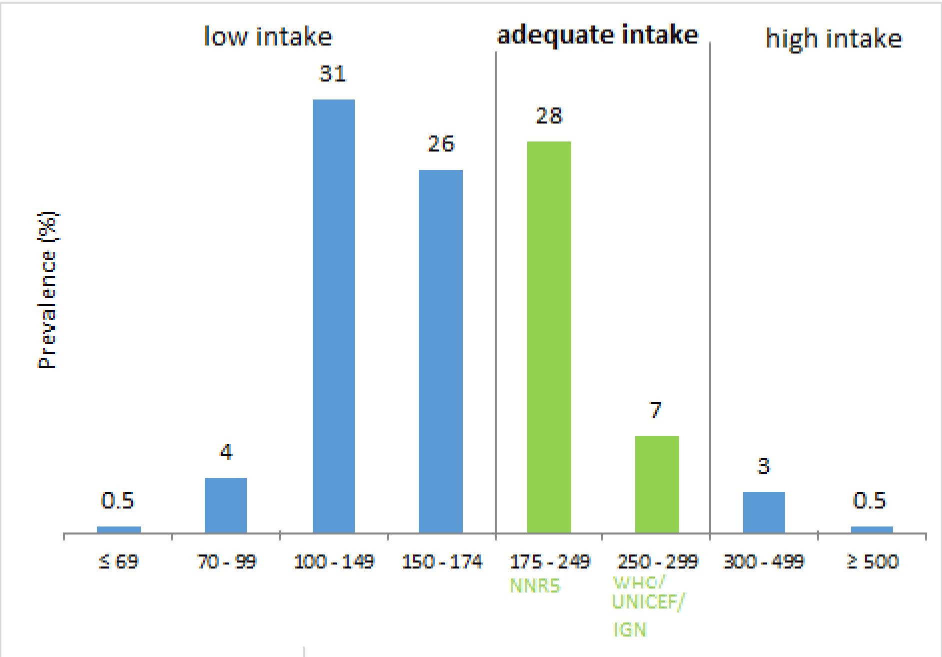

Figure 19. ***Total iodine intake of pregnant Norwegian women from foods and supplements given as percent in each category (n= 833)***

The participants were grouped by trimesters, timing and season the spot urine sample was taken and distributed by the three different estimates in order to estimate the MUIC for each group. The following **Figs. 20-22** show the WHO cut-off value for iodine status during pregnancy (< 150 µg/ L).

Gestational age was registered at inclusion in 929 of the 1008 spot samples collected registered gestational age (92%). A total of 6%, 79% and 14% gave a urine sample at the first, second and third trimester, respectively **(Fig. 20)**.

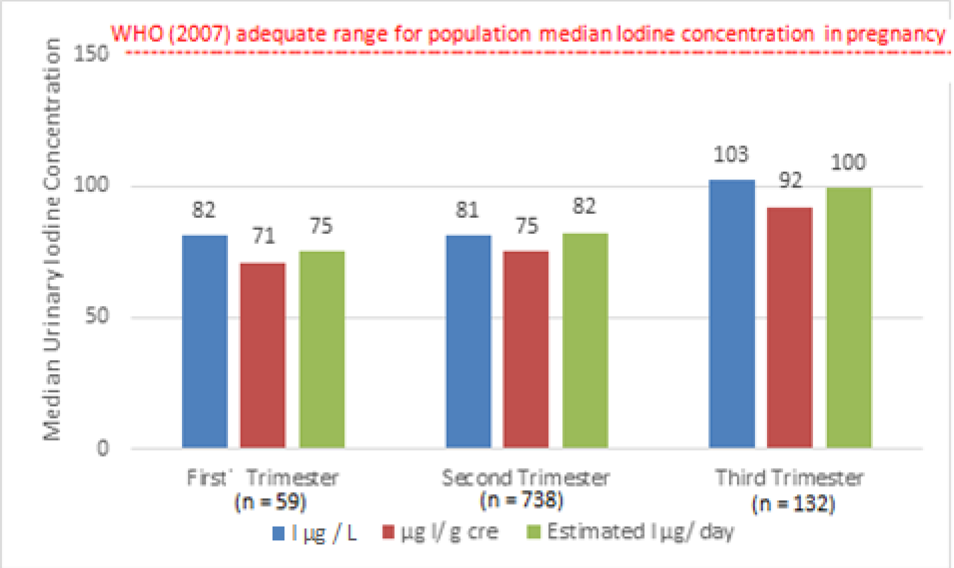

Figure 20. ***Median urinary iodine concentration by trimesters given as: iodine concentration (µg/ L), iodine/ creatinine ratio (µg I/ g creatinine) and age- and sex-adjusted iodine/ creatinine ratio (estimated I µg/ day) in pregnant Norwegian women (n = 929)***

The time of collection of the spot urine was registered in 60% of the 1008 samples collected (n = 612). A spot urine sample from pregnant women was collected for 38% in the morning, 36% in the afternoon, 11% in the evening and 15% in the overnight **(Fig. 21)**.

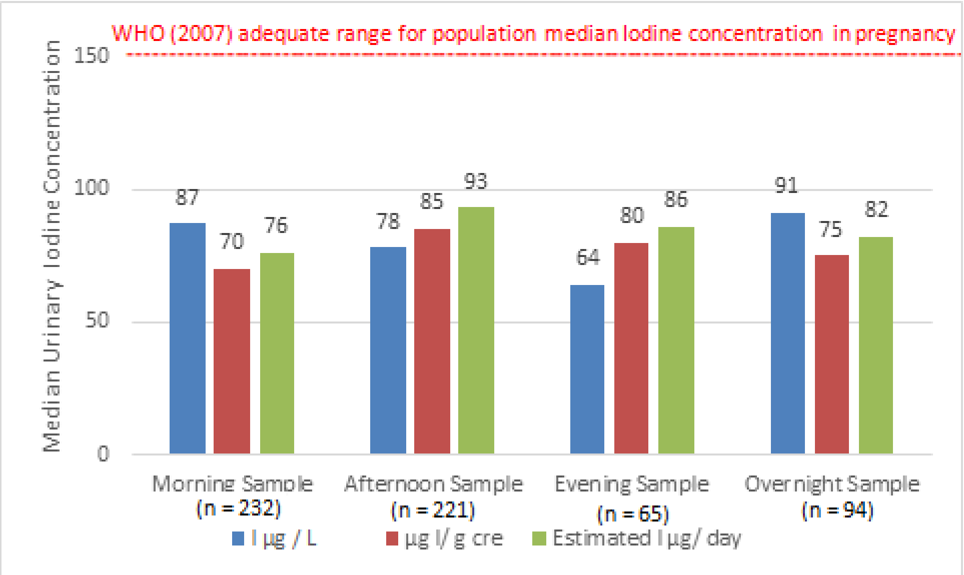

Figure 21. ***Median urinary iodine concentration by sampling time given as: iodine concentration (µg/ L), iodine/ creatinine ratio (µg I/ g creatinine) and age- and sex-adjusted iodine/ creatinine ratio (estimated I µg/ day) in pregnant Norwegian women (n =612)***

The date of the spot sample collection was registered in the 98% (n = 987) of the 1008 pregnant women which gave a spot sample. According to the distribution, 25% of the women gave a spot sample in winter, 26% in spring, 19% in summer and 30% in winter **(Fig. 22)**.

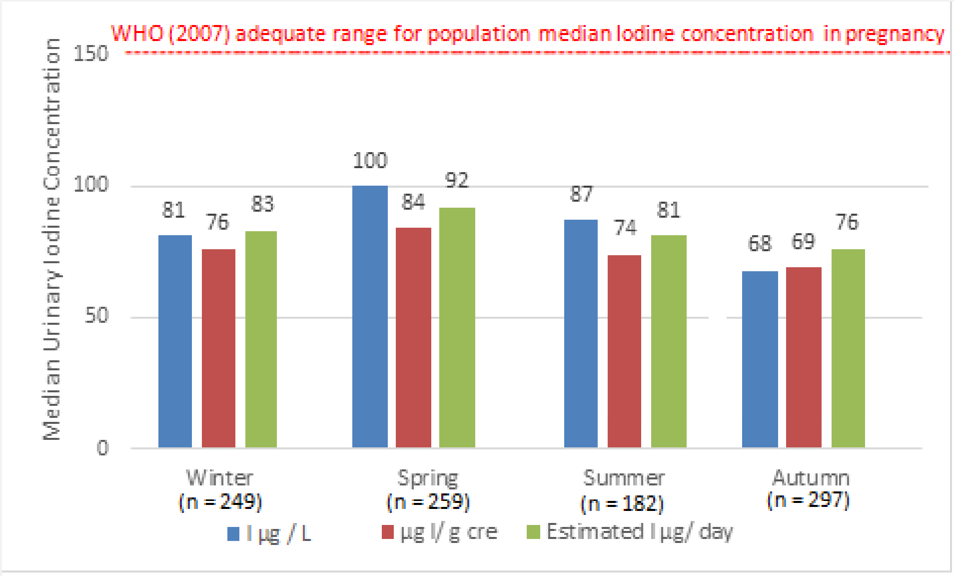

Figure 22. ***Median urinary iodine concentration by sampling season given as: iodine concentration (µg/ L), iodine/ creatinine ratio (µg I/ g creatinine) and age- and sex-adjusted Iodine/ creatinine ratio (estimated I µg/ day) in pregnant Norwegian women (n = 987)***

3.6 Statistical correlations

For statistical analysis, only quantitative variables were considered. There was a significant correlation ($p < 0.05$) between MUIC and milk-and dairy products intake (R Pearson: 0.079 and 0.075 for the 1st and 2nd estimate, respectively).

There was a significant correlation ($p < 0.01$) between MUIC and gestational age (R Pearson: 0.072 and 0.097 for the 2nd and 3rd estimate, respectively).

Table 12. Pearson's correlation between selected variables[€] and the three different estimates iodine concentration (µg/ L), iodine/ creatinine ratio (µg I/ g creatinine) and age- and sex-adjusted iodine/ creatinine ratio (estimated I µg/ day)

	1st. Estimate *µg/ L*			2nd. Estimate *µg I/ g creatinine*			3rd. Estimate *Estimated I µg/ day*		
	R Pearson	**P value**	***n***	**R Pearson**	**P value**	***n***	**R Pearson**	**P value**	***n***
FFQ-variables									
1.Seafood for dinner									
Oily	0.024	0.504	794	0.010	0.779	767	-0.002	0.954	792
Lean	0.039	0.271	794	0.048	0.185	767	0.010	0.775	792
Freshwater	-0.019	0.585	794	-0.031	0.393	767	-0.025	0.488	792
Shellfish	-0.002	0.955	821	-0.012	0.740	801	-0.007	0.850	824
Sushi	-0.009	0.811	794	-0.003	0.932	767	0.010	0.777	792
Processed	0.020	0.582	794	-0.004	0.918	767	-0.055	0.122	792
2. Seafood as Spread									
Oily	0.039	0.300	692	0.047	0.222	668	0.006	0.881	689
Lean	0.029	0.446	692	-0.036	0.355	668	-0.019	0.610	689
3.Milk-and dairy products	0.079*	0.028	766	0.075*	0.043	739	-0.006	0.862	763
4.Egg	0.003	0.938	803	0.023	0.528	776	-0.036	0.306	801
5.Multivitamin and Mineral Supplement	0.068	0.354	188	-0.052	0.483	181	0.114	0.117	190
6. Total Seafood Index (1. +2.)	0.073	0.320	188	0.099	0.185	181	0.034	0.643	190
7.Combined variables									
Combined 6. +3.	0.073	0.330	180	0.094	0.221	173	0.020	0.791	181
Combined 6. +4.	0.054	0.462	188	0.119	0.112	181	-0.038	0.603	190
Combined 6. +5.	0.091	0.111	310	0.050	0.386	299	-0.029	0.616	309
Another variable									
Gestational Week	0.010	0.775	899	0.072*	0.031	895	0.097**	0.003	928

*$p < 0.05$ (2 tailed)
**$p < 0.01$ (2 tailed)
[€]FFQ variables and Gestational week variable

4. DISCUSSION

4.1 Methodological considerations

4.1.1 Recruitment

A total of 1041 mothers were enrolled in LiN study, but 1036 (99%) of them gave consent to keep the information and use the present results. The study had the collaboration of local health clinics which it is favorable in regard to the sampling of subjects used in the study (Lande, Andersen et al. 2000). The objective of LiN study was to have population-level results and not to link the mother with her survey results. This methodology may encourage respondents to be more sincere in their reply and have few concerns about exposure of the results (Kiesler and Sproull 1986).

4.1.2 Exclusion criteria

Exclusion criteria were not considered in this thesis. All women were included in this study. Reviewing the literature, some studies had excluded women who reported taking TH drugs (e.g., thyroxine) (Opsahl 2002, Travers, Guttikonda et al. 2006, Dorey and Zimmermann 2008, Bath, Steer et al. 2013) or had any diseases related to the thyroid (Cobin, Gharib et al. 2001, Sawka, Ibrahim-Zada et al. 2010). In healthy adults, the absorption of iodine is greater than 90% (IOM 2001) but if the mother has low levels of TH and therefore hypothyroidism, it could be assumed that the mother has already low iodine levels due to hypothyroidism is a disorder induced by ID (Delange 1994) and when thyroxine is orally administered, the iodine bioavailability is approximately 75% (IOM 2001). There was only one mother who reported taking levaxin which is used to treatment of hypothyroidism. Undiagnosed hypothyroidism in pregnant women is probably more prevalent than usually considered (Glinoer 1997) and it is possible that some women with thyroid disease were unrecognized. This mother was not excluded because one case will not affect the final results and the preexisting thyroid diseases do not influence UIC (Brander, Als et al. 2003). Further, the highest values in the spot urine sample were not excluded in this study as in The Avon Longitudinal Study of Parents and Children (ALSPAC) (UIC > 500 µg/ L). Although levels of iodine higher than 500 µg/ L could be statistical outliers it is not unusual to find such levels in the urine samples.

4.1.3 Urinary creatinine

Creatinine is normally excreted daily in urine in a relatively constant rate (Soldin 2002, Price, Newall et al. 2005). The study used urinary creatinine concentration to correct UIC for intra-individual variation within the mothers and closely approximate iodine status in the whole group using the age-and sex-adjusted iodine/ creatinine ratio **(Formula 2)**. The daily creatinine excretion was estimated to be 1.09 g/ day for the studied pregnant women aged from 17 to 43 years. The results **(Table 9)** showed no differences between iodine concentration (µg/ I) and the age-and sex-adjusted iodine/ creatinine ratio (estimated I µg/ day) as was expected and obtained in previous studies: 127 vs. 167 (Seldal 2012) and 85 vs. 151 (Bath, Walter et al. 2014) for µg/ I and estimated I µg/ day respectively. One possible reason why these studies got higher values is because the expected daily creatinine excretion used was 1.23 g/ day (Knudsen, Christiansen et al. 2000) but for non-pregnant women.

Although some studies affirm that creatinine excretion values from non-pregnant women can be used as unaltered in pregnancy (Mojtahedi, de Groot et al. 2002), it was decided to use in this study, a creatinine excretion value from pregnant women used recently in Denmark (1.09 g) which is also in accordance with a studied conducted in Switzerland (1.0 g) (Brander, Als et al. 2003).

Creatinine concentrations are also used to determine whether the spot urinary sample is valid. According to WHO, if a sample has a creatinine concentration < 30 mg/ dl or > 300 mg/dl, another urine void should be collected (Barr, Wilder et al. 2005). One limitation of this study is that all creatinine spot samples from the phase t_1 were used without first determining the creatinine concentration. This determination was done, after creatinine samples were analyzed and there were 78 (25 too diluted and 53 too concentrated) samples which should have been discarded (data not shown).

This study also shows the mean urinary creatinine concentration (g/ L) by trimesters **(Fig. 7)**. To our knowledge, no study has shown this type of results in urine for comparison purposes. The values from a spot sample may vary from 0.4 to 1.4 g/ L in non-pregnant women (Surgery 2001).

4.1.4 Seafood-FFQ

The FFQ was completed for the 80% of participants which means that even if the participation in LiN study was voluntary, the response rate was very good (Baruch and Holtom 2008). The measurement of dietary habits during pregnancy are difficult due to metabolic and physiological changes in appetite, eating patterns, myths and beliefs on some type foods (Meltzer et al. 2008, Pinto, Severo et al. 2010, Brantsæter, Abel et al. 2013). However, this FFQ does not intend to measure the whole diet (Seldal 2012).

An association between maternal diet and health outcomes require a valid tool to accurately measure the diet (Pinto, Severo et al. 2010). This study used a short semi-quantitative FFQ (portion size of a list of food items is included) to measure diet in pregnant women and it is adequate to estimate long-term iodine intake (Willett, Sampson et al. 1988, Ortiz-Andrellucchi, Doreste-Alonso et al. 2009). The FFQ collected the information for the last three months, which must be the most trusted in this kind of studies (Rasmussen, Ovesen et al. 2001). A FFQ is easy to administer in large and geographically widespread samples (Cade, Thompson et al. 2002, Willett 2013) and is less time-consuming in comparison with other dietary methods (Brantsaeter 2007).

The women were asked to fill in the self-administered FFQ using a web access sent by e-mail address. The data were transformed of raw data into computer-readable form (Kiesler and Sproull 1986). Electronic questionnaires are more complete with fewer mistakes (Kiesler and Sproull 1986) within a few days (Sheehan 2001). The mothers had to fill in all questions before they were allowed to finish the FFQ. Although there is not interviewer to ask in the case of any misunderstanding and the women may not be motivated enough to complete the whole questionnaire (Reja, Manfreda et al. 2003); the FFQ do not require trained personnel and can be self-administered (Barrat, Aubineau et al. 2012). Moreover, the time used to complete the FFQ was not measured, but it is supposed to be 15 minutes. Questionnaire length could or not influence response in the whole questionnaire or any questions (Herzog and Bachman 1981, Sheehan 2001).

The FFQ had multiple choice questions (e.g. Appendix: SjoT1_5, SjoT1_6). These kind of questions often are easier to answer, require less of the respondents' time, permit direct quantification of answers (Johnson, Sieveking et al. 1974) and reduce errors compared to open-ended questions (Subar, Thompson et al. 1995). However, multiple choice questions are often supplemented with open-ended questions in order to obtain clear answers (Johnson, Sieveking et al. 1974). The question “other seafood” (Appendix: SjoT1_6a) was not specified but the intention was to obtain the consumption of fish as a spread. It would have been better to place an open-question after each multiple choice question to reinforce the results.

Increasingly detailed questionnaires decrease the information obtained (Willett 2013) as shown in **Table 10** and **Table 11** where many of the women choose “never”. Many reasons can justify this result (i.e. mothers decrease fish consumption during pregnancy, mothers did not find the fish consumed in the list or they just chose this option (Herzog and Bachman 1981)). However, the result shown in that table is due to an error in the electronic questionnaire which made that the participants could not answer the questions (personal communication, Marian K. Malde).

Open-ended questions are useful to explore given responses in the close-ended questions. A drawback is the use of an extensive coding before the actual analysis can take place (Reja, Manfreda et al. 2003). The total number of iodine-containing supplement users was calculated using the open-ended question “other supplement – vitamins and mineral” (Appendix: SjoT1_9e3). However, the amount of iodine coming from those supplements was not possible to calculate in some mothers from this open-ended question because the frequency of intake was not reported. Open-ended question produce more missing data than close-ended question (Reja, Manfreda et al. 2003).

The present study calculated total iodine intake (μg) from the FFQ based on frequency, portion size (Appendix: SjoT1_2) and iodine content in the food and in the supplement. Only the amount of iodine intake from fish as dinner was taken into account to achieve this calculation. The amount of iodine from seafood as spread was not calculated due to several factors: [1] The FFQ contains 15 specific items on seafood consumption as a spread (Appendix: SjoT1_6). Extensive detailed interrogation is susceptible to overestimation (Tjonneland, Overvad et al. 1991) and could be over reported (Willett and Lenart 1990). [2] The FFQ does not give information about the portion size of the spread. In theory a portion size of seafood as spread is 25 g (TheNorwegianDirectorateofHealth 2011) but the correct amount the women chose to eat lunch was difficult to estimate. [3] The FFQ does not include the daily frequency of seafood consumed as a spread.

A challenge was to calculate the iodine intake from milk-and dairy products. The FFQ had only one general question about the daily frequency of intake of milk-and dairy products (Appendix: SjoT1_8b1) given as one glass of milk, one cup of yogurt or a portion of cheese. Therefore, it was not possible to determinate what type which had been consumed. However, according to the nationwide food consumption survey conducted in Norway - Norkost 3 (Totland 2012) women with high education level have a higher consumption of milk than cheese and therefore; the author of this thesis assumed that the answers given in the questionnaire refer principally to the frequency of milk consumption. The limited information obtained from this question leads the author to conclude that the question should be improved and more explicit about the frequency and the portion size for each dairy product. This limitation may have underestimate the results of total iodine intake (e.g. one portion milk contains ~16 μg I but one portion whey cheese contains ~26 μg I (Dahl, Johansson et al. 2004)). Inaccurate portion sizes and food specification limit the quantity of intake (Biro, Hulshof et al. 2002).

Traditionally a FFQ is combined with food composition tables to calculate intake of specific nutrients (Wild, Andersson et al. 2001, Combet and Lean 2014) since the iodine content of food is varied and the values are not always available (Bath, Jolly et al. 2013). To calculate the total iodine intake; the food weights (gram per day) were multiplied by the nutrient value per 100 g of food using the amount of iodine in food, estimated in previous studies developed at NIFES (Dahl, Johansson et al. 2004) which are in accordance with the new version of the food composition table 2014 in Norway.

The FFQ did not include any question about the use of table salt or use of iodine fortified salt. The consume of drinking water was not considered possible because it's non-significant amounts of iodine (~2 μg/ L) in Norway (Dahl, Johansson et al. 2004).

4.2 Discussion of results

4.2.1 Descriptive characteristics

The average age was 29 ± 5 years **(Table 8)** and is within the range of the national average age (30.5) of women giving birth to children (Statistics and NorwayA 2013). The mean age reported in other Norwegian studies (Brantsaeter, Haugen et al. 2007, Haugen, Brantsaeter et al. 2008, Brantsaeter, Haugen et al. 2009, Brantsaeter, Haugen et al. 2010, Seldal 2012, Markhus, Graff et al. 2013) and in studies in other European countries (Limbert, Prazeres et al. 2010, Bath, Steer et al. 2013, Hynes, Otahal et al. 2013, Bath, Walter et al. 2014, Rydbeck, Bottai et al. 2014) also includes women within the same age range.

It is known that iodine has an influence on both physical and mental development (Merkiel and Chalcarz 2011). Current BMI showed also that 39% of the women were overweighted and 15% were obese. Overweight and morbid maternal obesity is a risk factor for thyroid dysfunction in pregnant women in iodine-deficient areas (Gowachirapant, Melse-Boonstra et al. 2014).

The education level was in accordance with MoBa study and higher than in the general female population of Norway (statistics and NorwayB 2013) and Norkost 3 (Totland 2012). Maternal education is positively associated with maternal iodine status (Bath, Steer et al. 2013) and higher seafood intake (Gallo, Jean-Philippe et al. 2010). It was not made any association between educational level and UIC in this thesis.

The percent of women working full-time was higher than in MoBa study (Meltzer, Brantsæter et al. 2008) and in accordance with the results showed by Markhus, Graff et al. 2013 .

4.2.2 Urinary iodine

The MUIC (82 µg/ L) **(Table 11)** classifies the pregnant women as iodine deficient. The median creatinine: ratio value is also low and the median age-and sex-adjusted iodine/ creatinine ratio value is not what was expected (i.e. 158 - 225 µg) (Bath, Walter et al. 2014). Taking into account that 90% of iodine is excreted in urine, a UIC of minimum 150 µg/ day indicates iodine sufficiency (Seldal 2012). However, only 17% have a UIC above this minimum value. Furthermore, even when the MUIC is adjusted by creatinine, age and sex; the results are still below the WHO criteria **(Table 1)** and a mild iodine deficiency is shown in almost half part of the group with a MUIC between 50 and 99 µg/ L **(Fig. 9)**. The UIC is not valuable for individual assessment (IGN/UNICEF/WHO 2007) and therefore this degree of deficiency found in the study, should be interpreted with caution.

The MUIC obtained in the present study are according to other studies reporting a high prevalence of borderline iodine deficiency in pregnant women worldwide with a UIC close to or below 150 µg/ L like the recent ALSPAC study in the UK (91 µg/ L), Australia, Spain, Australia, Portugal, Italy and Israel (Benbassat, Tsvetov et al. 2004, Travers, Guttikonda et al. 2006, Marchioni, Fumarola et al. 2008, Alvarez-Pedrerol, Ribas-Fitó et al. 2010, Charlton, Gemming et al. 2010, Limbert, Prazeres et al. 2010, Murcia, Rebagliato et al. 2010, Fisher, Tran et al. 2011, Bath, Steer et al. 2013, Hynes, Otahal et al. 2013). The iodine status in pregnant women in Norway is in contrast with Nederland (median UIC 229.6 µg/ L) (Ghassabian, Steenweg-de Graaff et al. 2014) and other countries like Japan and Switzerland (Brander, Als et al. 2003, Fuse, Ohashi et al. 2011) where the iodine status is adequate. The comparison of the results between these studies and our study indicate that Norway is a part of the European countries with inadequate iodine supply during pregnancy (Lazarus 2014).

The IGN published the Global Iodine Nutrition Scorecard for 2014 and assume that Norway is an iodine sufficient country (IGN 2014). The results from this study, “The Fjell Study” and MoBa study; indicate that even if the general population have an adequate iodine intake, there is an inadequate iodine status in some sub-groups like pregnant women in Norway (Lazarus 2014). The consequences of ID in this particular group should be more investigated to update our knowledge and thereby identify, optimize and maintain the optimal iodine status in the pregnant population (Andersson, de Benoist et al. 2007).

4.2.3 Seafood intake

According with the FFQ, only 30% of pregnant women met the Norwegian recommendation of 2 – 3 meals weekly **(Fig. 10)**. Intake of fish 2-3 times a week, covers the normal need for iodine (TheNorwegianDirectorateofHealth 2011). Furthermore, the median seafood intake for dinner was 150 g per week and it is below the Norwegians Recommendations of eating 300-450 g of fish weekly (TheNorwegianDirectorateofHealth 2011).

A mother who eats fish 3 times a week, eats 347 g fish per week (~50 g/ day) (Hibbeln, Davis et al. 2007). Maternal seafood intake lower than 340 g per week is associated with an increased risk of low verbal IQ score (Bath, Steer et al. 2013) and suboptimum neurodevelopment outcomes in the child (Hibbeln, Davis et al. 2007, Malde, Alvheim et al. 2012). Almost the 70% of the participants who eat fish had a weekly intake lower than 375 g.

The estimated mean intake of maternal seafood for dinner was 29 g/ day. This average is lower than in other Norwegian studies in pregnant women e.g. 42 g/ day (Brantsaeter, Haugen et al. 2010), 36 g/ day (Brantsaeter, Birgisdottir et al. 2012), a median of 32 g/ day (Markhus, Graff et al. 2013) and in other international studies e.g. 32 g/ day in Mexico (Parra, Schnaas et al. 2002), 47 g/ day in Iceland (Thorsdottir, Birgisdottir et al. 2004) and 34 g/ day in UK (Hibbeln, Davis et al. 2007). On the other hand, the estimated average in this study is higher than the 16 and 27 g/ day reported in pregnant women in Denmark (Olsen and Secher 2002, Halldorsson, Meltzer et al. 2007) or 21 g/ day in Boston, USA (Oken, Guthrie et al. 2013). The average seafood intake (g/ day) from all these studies appointed is the combined seafood intake for dinner and as a spread, while the result in this thesis only represents dinner.

It was not possible to estimate quantitative intake (g) of seafood as a spread. Therefore, the total seafood intake (g/ week) is probably higher than 150 g weekly. However, it is still unlikely that these women reach the Norwegian recommendations even when including a spread, since the average frequency of seafood as a spread was one portion per week. Approximately six portions (25 g each) of spread are needed to replace one dinner portion (150 g) (TheNorwegianDirectorateofHealth 2011).

According to Norkost 3, a Norwegian women aged from 18 to 79 years eat 56 g fish/ day (Totland 2012). Although this information; it is clear that Norwegian women have been shown to have lower consumption of seafood over the past decades (Johansson and Solvoll 1999) and this increases during maternity. The reason is unclear. One possible reason is the geographical location.The seafood consumption is relatively high in coastal areas (Johansson and Solvoll 1999, Welch, Lund et al. 2002). A second possibility is the avoidance of certain fish species due to mercury exposure which decrease the total seafood consumption in ~1.4 servings/ month (Oken, Kleinman et al. 2003). The Norwegian recommendations to pregnant women advise to limit the intake of large perch, wild trout and halibut and to not eat pike liver or exotic predatory fish like fresh tuna (TheNorwegianDirectorateofHealth 2009). Furthermore, the avoidance of certain fish in fear for damage the child is reported in 53% of the mothers (data not shown).A third possible reason is called the morning sickness (Kramer, Bowen et al. 2013). However, a Canadian study showed that most pregnant women feel relief by week 22 and the period lasts a month (Lacroix, Eason et al. 2000). In this study 70% and 33% pregnant women reported nausea and vomiting respectively, before week 22 (data not shown). Additionally to these possible reasons; a study conducted in Belgium affirm that the seafood intake among women increases with increasing age but decreases in the maternity (Verbeke and Vackier 2005).

Despite these possibilities; the seafood intake in pregnant women should be increased; not only due to the nutritional benefics, but also for the risk of preterm delivery and low birth weight (Leventakou, Roumeliotaki et al. 2014) increased with a daily intake below 15 g fish (Olsen and Secher 2002). The lowest weekly intake in this study was 22.5 g fish.

The Norwegian recommendations during pregnancy suggest to eat small portions, more often during the day (TheNorwegianDirectorateofHealth 2009). A possibility to increase the total seafood intake without affecting the dietary habits within the family is to increase the seafood consumption as a spread (Seldal 2012). In theory, if this group of women had increased the seafood intake as a spread, they would have reached the Norwegian recommendations. However, this theory may not be feasible in the whole group, due to physical and psychological factors, the fact that some women eat maximum three meals daily during pregnancy (Siega-Riz, Herrmann et al. 2001) and that the seafood intake as spread decrease (Malde, Alvheim et al. 2012). The possibility to increase seafood intake as spread is important, but it is even more important to promote and increase the frequency of seafood at dinner in pregnant women.

Total oily and lean fish intake

The total oily fish intake in the present study was higher compared to the Norkost 1997, the "Fish and Game Study[v]" and the Norkost 3 (Johansson and Solvoll 1999, NorwegianScientificCommitteeforFoodSafety 2007, Totland 2012). However, these studies include participants in a broader age range.

Assuming that the greatest consumption comes from oily fish, the median seafood intake for dinner was 150 g weekly and the median oily fish intake was once per week; it could be possible that the women have been reached the recommended 200 g of oily fish per week (TheNorwegianDirectorateofHealth 2011). However, it is a lean fish and processed fish (primarily of lean fish) (NorwegianScientificCommitteeforFoodSafety 2007) which contains more iodine than oily fish and in this study, total lean fish intake represents the third part of the total seafood intake.

Oily fish intake delay spontaneous delivery and premature labor (Olsen and Secher 2002), but, lean fish have a greater benefit than fatty fish such as fetal growth during pregnancy (Oken, Guthrie et al. 2013). Lean fish intake has a positive association between infant birth weight and head circumference (Brantsaeter, Birgisdottir et al. 2012) and increases the iodine intake in the body.

4.2.4 Milk-and dairy products intake

Most women had a milk-and dairy products intake 2 – 3 times daily with a significant correlation with the MUIC. The MUIC among pregnant women varied with the frequency of the food, but the women who do not consume milk-and dairy products have lower MUIC than frequently consumers **(Fig. 17)**. This result is in agreement with a recent study from UK among pregnant women also using a spot urine sample (Bath, Walter et al. 2014). On the other hand, a woman with more than 7 servings per day, have higher MUIC than the others. Higher milk and yogurt intake is needed to obtain 150 μg iodine daily (Brantsæter, Abel et al.

[v] Fisk- og viltundersøkelsen 1999

2013). These women with highest milk- dairy products intake had a median iodine intake of 374 µg / day.

Milk- and dairy products are an important source of iodine in Norway due to relative high consumption of them. Although it is assumed that the iodine requirements are covered in the Norwegian population due to the high dairy products intake; national studies have pointed out that the iodine content in these products is lower in summer than in winter months (Dahl, Opsahl et al. 2003) but without variations within the same season for the different types of milk (15 µg/ 100 g) (Dahl, Johansson et al. 2004). Despite this fact, it should note that a recent study in Norway found that the iodine content in milk from the winter season has been reduced to nearly the half during the last decade (Haug, Taugbøl et al. 2012). The iodine content in these food products must be analyzed and the information should be updated to supply an adequate iodine intake in the population and have an appropriate choice of foods which contain iodine.

4.2.5 Egg intake

A significant correlation between egg intake and MUIC was not found in this study. However, studies suggest a positive association between egg consumption and iodine status in pregnant women (Alvarez-Pedrerol, Ribas-Fitó et al. 2010, Bath, Steer et al. 2013, Bath, Walter et al. 2014) despite the small amount eaten (Dahl, Johansson et al. 2004).

4.2.6 Multivitamin and mineral supplement

This study showed that only 14% of mothers were using a prenatal vitamin and mineral supplement contained iodine. The percent is lower than in a sub group of 119 women (19%) and in the total group of 61, 904 women (31.6%) in MoBa study (Brantsaeter, Haugen et al. 2007, Brantsæter, Abel et al. 2013) and a study conducted in the UK (42%) with 100 women enrolled (Bath, Walter et al. 2014). All these studies used also a FFQ. Many reasons can justify this result.

Studies suggest that only 13 – 50% of pregnant women in Europe receive an iodine-containing supplement (Zimmermann and Delange 2004), and in Norway, the Norwegian Recommendations during pregnancy do not include use of iodine supplementation (Brantsæter, Abel et al. 2013). Adequate iodine through prenatal vitamins (Stagnaro-Green and Pearce 2013) among pregnant (no later than 4 – 6 weeks of gestation) (Leung, Pearce et al. 2013) and breastfeeding women is important due to the positive effects in the mother and fetus (Hynes, Otahal et al. 2013). Further, clinicians in European countries has pointed out a daily supplementation with ≥ 150 µg I/ day for a long period before conception to ensure plenty intrathyroidal iodine stores.

Although there are no published data about iodine content in supplements in Norway, the author of the present thesis made some calculations based on the available supplements containing iodine in the Norwegian market and concluded that the most used supplements contain iodine in the range of 25 to 175 µg I/ tablet (median 150) unlike the stated by Seldal 2012 of 150 to 175 µg I/ tablet and by Dahl 2003 of 50 to 200 µg I/ tablet. The range of iodine in the supplements reported by the participants in this study was lower than the range reported in a recently study in UK (75 – 150 µg I/ tablet) maybe because the most consumed UK prenatal supplements brand does contain iodine (Bath, Walter et al. 2014). According to Zimmermann 2010 most multivitamin/ mineral preparation contain iodine but that was not found in this study. On the contrary, it seems like the minimum amount of iodine in a tablet, has been declining over the years.

This study showed that the MUIC in women taking iodine-containing supplements was higher than in non-users of iodine-containing supplement **(Fig. 18)** and this is in agreement with previous studies reported in Europe (Zimmermann and Delange 2004, Bath, Walter et al. 2014) and within the country (Brantsaeter, Haugen et al. 2007). The use of iodine-containing supplements is important to supply adequate iodine for those who do not eat or have low intakes of seafood and/ or milk-and dairy products in their diet (Brantsæter, Abel et al. 2013).

4.2.7 Total iodine intake

In this study, the total median iodine intake from foods and supplements was 153 µg/ day and 62% and 90% of pregnant women have a daily iodine intake below the Nordic Recommendations **(Table 2)** and the WHO/UNICEF/IGN recommendation of 250 µg/ day, respectively. These results showed that only a third part of this group has an adequate iodine intake and the WHO recommendation is difficult to achieve in Norway.

An iodine intake < 150 µg/ day was shown in 35% of the women and the percentage was lower than in a sub group from MoBa study (Brantsæter, Abel et al. 2013). However, even if our group is still not in a risk for sub optimal intake like the mothers in MoBa study, it does not mean that the iodine intake is inadequate for the majority of pregnant women in this study.

Fortunately, no one had the minimum intake of iodine of 70 µg/ day and an iodine excess was showed only in one woman who take 2 iodine-containing supplements 4 – 6 times per week. The use of supplements with iodine increases the total iodine intake in the person which is reflected in the highest values of MUIC in this study.

Between users and non-users of iodine-containing supplement, the total median iodine intake was higher in the first group than in the another and above the Nordic recommendation. The non-users group did not reach the national recommendation and the total median intake is the same than in the whole group.

4.2.8 Median urinary iodine concentration by trimesters

The MUIC increased from the first to the third trimester of pregnancy through the three different estimates **(Fig. 20)** although there is a slight tendency for lower value in the second trimester (with median creatinine: ratio). A similar pattern was observed in other recently studies (Vila, Serra-Prat et al. 2011, Rydbeck, Bottai et al. 2014) but it should emphasize that the studies did not use the same criteria to define the trimesters. Otherwise, studies on UIC values through gestational weeks are not consensual (Brander, Als et al. 2003, Ainy, Ordookhani et al. 2007, Limbert, Prazeres et al. 2010). Moreover, MUIC observed in the third trimester is higher than the other, which is contradictory with the idea that during the first trimester, the increases in renal iodine excretion elevate the UIC levels while the iodine excretion decrease with advancing gestation (Hynes, Otahal et al. 2013). These differences are probably due to the amount of iodine ingested, the initial thyroidal iodine store, degree of iodine deficiency or difference in the sample size (Fuse, Ohashi et al. 2011). Despite this result, a significant correlation between gestational week and MUIC was found in the study **(Table 12)**.

4.2.9 Median urinary iodine concentration by sampling time

The MUIC varies with the time of day the spot sample was taken **(Fig. 21)**. The urine sample was taken throughout the day and in non-fasting conditions. Some studies affirm that the iodine excreted during the day it is ingested, have peaks following the three main meals by 4 – 5 hours (Soldin 2002, Busnardo, Nacamulli et al. 2006). The time since last meal was not recorded by the health care personnel and could be a disadvantage to complete the objective of this thesis, but variability among MUIC and timing could have been avoided if the urine samples had been collected in fasting conditions (Thomson, Packer et al. 2001, Busnardo, Nacamulli et al. 2006).

4.2.10 Median urinary iodine concentration by sampling season

Season at urine collection **(Fig. 22)** showed that MUIC increase during spring and not on winter as was expected (on the basis that iodine concentration in milk-and dairy products which is the major source of iodine is higher on winter). A similar result was found in a study carried out in Denmark among adults (Rasmussen, Ovesen et al. 2002). It is known that UIC in spot samples can vary between seasons (Konig, Andersson et al. 2011, Amouzegar and Azizi 2013). However; there are few studies concerning the seasonal fluctuations of UIC values during pregnancy to explain and compare the results.

4.3 Summary and conclusions

In certain European countries such as Norway, the high seafood intake and milk-and dairy products have secured on the iodine status of the general population. However, there is increasing evidence that an inadequate iodine intake has re-emerged in some subgroups such as pregnant women. Adequate iodine supply from foods and supplements is required to avoid damage in the developing brain in the fetus and related thyroid diseases in the mother. The assessment of the iodine status either by measuring urinary iodine concentration or by estimating dietary intake is suitable methods which can be used for the general population. A maternal iodine deficiency has public health implications and therefore more studies are needed in order to establish a strategy against the consequences of ID in the mother and especially in the fetus.

The results from this thesis show that:

[1] The MUIC is 82 µg/ L and 80% of the women had an inadequate iodine status below the WHO criteria of 150 µg/ L.

[2] The total median iodine intake from foods and supplements (153 µg/ day) was below the Norwegian recommendations of 175 µg/ day.

[3] Intake of milk-and dairy products and gestational age correlated significantly with MUIC.

Findings in the present study from median UIC classify the pregnant women as iodine deficient. Estimated dietary iodine intake also shows inadequate iodine intake among the women. In conclusion, this study shows that the diet of the pregnant women does not secure a sufficient iodine intake and one strategy to increase the iodine intake could be to increase the seafood intake.

4.4 Future perspectives

The results from this thesis indicate that this group of women has an inadequate iodine intake. The possibility to further investigate the importance of the deficiency and how it will affect the growth and intellectual development of children is a point that should be considered in future studies.

To assess the iodine intake, accurate and sensitive tools are needed. The new version of the Norwegian food composition table 2014 includes iodine levels from different food products. However, since the food on the markets may change or new products could be available, a regular collection of foods for determination of iodine is of importance. This monitoring of the food will contribute to make appropriate choice of foods high in iodine if iodine supply is needed.

Furthermore, published data about the iodine content in supplements in Norway and the promotion of its use among women is required. When there is a low intake of dietary sources of iodine, an iodine-containing supplement may secure the iodine intake needed. Especially in pregnancy, an adequate supplementation even before pregnancy is advisable. Specifics dietary recommendations about iodine intake should be included in Norwegian food and diet recommendations.

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6. Appendix - FFQ

LIN WEB MOR

Sendes inn hjemmefra

Denne kommer til å gjøres om til hovedundersøkelsen som foreldrene via epostutsendelse sendes inn i ulike deler av på ulike tidspunkt.

login_velkommen

webskjema - Velkommen til Liten i Norge studien.

Hvilken undersøkelse vil du åpne?

- ❍ Spørreskjemaer (3)
- ❍ Svangerskapsuke 20 (SPM20u)
- ❍ Svangerskapsuke 32 (SPM32u)
- ❍ Svangerskapsuke 36 (SPM36u)
- ❍ Kostholdsskjema (6)
- ❍ Svangerskapsuke 16 (M16uSjo)
- ❍ Svangerskapsuke 32 (M32uSjo)
- ❍ Barn 6 uker gammel (M6uSjo)
- ❍ Barn 6 måneder gammel (M6mSjo)
- ❍ Barn 12 måneder gammel (M12mSjo)
- ❍ Barn 18 måneder gammel (M18mSjo)
- ❍ Temperamentsskjema (8)
- ❍ Barn 6 måneder gammel (M6mTemp)
- ❍ Barn 12 måneder gammel (M12mTemp)
- ❍ Barnets kosthold (1)
- ❍ Barn 6 uker gammel (B6uKost)
- ❍ Barn 6 måneder gammel (B6mKost)
- ❍ Barn 12 måneder gammel (B12mKost)
- ❍ Barn 18 måneder gammel (B18mKost)

start_M16uSjo - Velkommen til Liten i Norge studien

Takk for at du deltar og bidrar med viktig kunnskap om hva som påvirker barns utvikling.

Denne gangen spør vi hovedsakelig om hva du spiser.

Innsendingen av skjemaet blir kryptert. Opplysningene kan ikke knyttes til deg under overføringen.

Start spørreskjemaet ved å klikke på " >> "-knappen neders på siden.

iSjo_infot1 - Her vil vi gjerne få informasjon om sjømatinntaket ditt.

Ha de 3 siste månedene i bakhodet når du fyller ut skjemaet.

Med sjømat mener vi fisk, fiskeprodukter og andre sjømatprodukter som for eksempel skjell og skalldyr. Vi er klar over at kostholdet varierer fra dag til dag. Prøv likevel så godt du kan å gi et "gjennomsnitt" av ditt sjømatinntak spist til middag, som pålegg, i salat og eller spist som mellommåltid.

SjoDatet1 -

Dato for utfylling:

Hvis skjemaet ble fylt ut på en annen dato, må feltet oppdaters til denne datoen (dd.mm.åååå)

SjoT1_1 - Hvor ofte har du spist fisk, fiskeprodukter eller annen sjømat som middagsmat de siste 3 mnd?

❍ Aldri (1)
❍ Sjeldnere enn 1 gang/måned (2)
❍ 1-3 ganger/ måned (3)
❍ 1 gang/uke (4)
❍ 2-3 ganger/ uke (5)
❍ 4 ganger eller mer/uke (6)

SjoT1_2 - Når du spiser fisk, fiskeprodukter eller annen sjømat til middag, hvor mye spiser du vanligvis?
(1 porsjon = 150 gram, tilsvarer for eksempel 1 laksekotelett eller 3 fiskekaker eller 2 dl reker u/skall)

❍ ½ porsjon eller mindre (1)
❍ 1 porsjon (2)
❍ 1 ½ porsjon (3)
❍ 2 porsjoner (4)
❍ 3 porsjoner (5)

SjoT1_3 - Hvor ofte har du spist sjømat som pålegg, i salat, mellommåltid, snacks eller lignende de siste 3 mnd?

❍ Aldri (1)
❍ Sjelden (2)
❍ 1-3 ganger/ måned (3)
❍ 1-2 ganger / uke (4)
❍ 3-5 ganger / uke (5)
❍ Mer enn 5 ganger / uke (6)

SjoT1_5 - Hvor ofte har du spist følgende sjømat som middag siste 3 mnd?

	Aldri (1)	Sjeldnere enn 1 gang/måned (2)	1-3 ganger /måned (3)	1-2 ganger/uke (4)	3 ganger eller mer/uke (5)
Laks, ørret (1)	❍	❍	❍	❍	❍
Makrell (2)	❍	❍	❍	❍	❍
Sild (3)	❍	❍	❍	❍	❍
Kveite (4)	❍	❍	❍	❍	❍
Uer (5)	❍	❍	❍	❍	❍
Steinbit (6)	❍	❍	❍	❍	❍
Flyndre, rødspette (7)	❍	❍	❍	❍	❍
Torsk (8)	❍	❍	❍	❍	❍
Sei (9)	❍	❍	❍	❍	❍
Hyse (10)	❍	❍	❍	❍	❍

	Aldri (1)	Sjeldnere enn 1 gang/måned (2)	1-3 ganger /måned (3)	1-2 ganger/uke (4)	3 ganger eller mer/uke (5)
Abbor, gjedde (ferskvann) (11)	❍	❍	❍	❍	❍
Røye, sik (ferskvann) (12)	❍	❍	❍	❍	❍
Reker (13)	❍	❍	❍	❍	❍
Krabbe (14)	❍	❍	❍	❍	❍
Hummer (15)	❍	❍	❍	❍	❍
Blåskjell (16)	❍	❍	❍	❍	❍
Kamskjell (17)	❍	❍	❍	❍	❍
Sushi (18)	❍	❍	❍	❍	❍
Fiskekaker (19)	❍	❍	❍	❍	❍
Fiskeboller (20)	❍	❍	❍	❍	❍
Fiskepudding (21)	❍	❍	❍	❍	❍
Fiskegrateng (22)	❍	❍	❍	❍	❍
Fiskepinner (23)	❍	❍	❍	❍	❍
Fiskesuppe (24)	❍	❍	❍	❍	❍
Klippfisk (25)	❍	❍	❍	❍	❍

SjoT1_6 - Hvor ofte har du spist følgende sjømat som pålegg siste 3 mnd?

	Aldri (1)	Sjeldnere enn 1 gang/måned (2)	1-3 ganger /måned (3)	1-2 ganger/uke (4)	3 ganger eller mer/uke (5)
Makrell på boks (1)	❍	❍	❍	❍	❍
Sardin på boks (2)	❍	❍	❍	❍	❍
Laks på boks (3)	❍	❍	❍	❍	❍
Brisling (4)	❍	❍	❍	❍	❍
Ansjos (5)	❍	❍	❍	❍	❍
Røkt laks, ørret (6)	❍	❍	❍	❍	❍
Gravet laks, ørret (7)	❍	❍	❍	❍	❍
Reker (8)	❍	❍	❍	❍	❍
Tunfisk på boks (9)	❍	❍	❍	❍	❍
Sild (sursild, rømmesild, kryddersild el.lign.) (10)	❍	❍	❍	❍	❍
Kaviar (11)	❍	❍	❍	❍	❍
Crabsticks (12)	❍	❍	❍	❍	❍
Svolværpostei (13)	❍	❍	❍	❍	❍
Lofotpostei (14)	❍	❍	❍	❍	❍
Annet sjømat (15)	❍	❍	❍	❍	❍

SjoT1_6a - Annen sjømat

Vennligst spesifiser:

SjoT1_7 - Spiser du fiskerogn eller fiskelever?

❍ Ja (1)

❍ Nei (0)

SjoT1_7a - Hvor mange ganger per år spiser du fiskeinnmat?

	Aldri (0)	1-3 ganger/år (1)	4-6 ganger/år (2)	7-9 ganger/år (3)	10 ganger eller mer/år (4)
Fiskerogn (1)	❍	❍	❍	❍	❍
Fiskelever (2)	❍	❍	❍	❍	❍

SjoT1_8a - Andre generelle spørsmål om kostholdet ditt:

Hvor ofte spiser du frukt og grønnsaker?

	Sjeldnere enn 1 gang/uke (1)	1-3 ganger/uke (2)	4-6 ganger/uke (3)	1 gang/dag (4)	2-3 ganger/dag (5)	4 ganger eller mer/dag (6)
Frukt (inkludert juice og smoothie) (1)	❍	❍	❍	❍	❍	❍

	Sjeldnere enn 1 gang/uke (1)	1-3 ganger/uke (2)	4-6 ganger/uke (3)	1 gang/dag (4)	2-3 ganger/dag (5)	4 ganger eller mer/dag (6)
Grønnsaker (2)	❍	❍	❍	❍	❍	❍

SjoT1_8b - Spiser du meieriprodukter (melk, yoghurt, ost) daglig?

❍ Ja (1)
❍ Nei (0)

SjoT1_8b1 - Hvor mange ganger per dag spiser du meieriprodukter?

En gang er for eksempel ett glass melk eller en yoghurt eller ost til en skive brød

❍ 1 gang/dag (1)
❍ 2-3 ganger/dag (2)
❍ 4-6 ganger/dag (3)
❍ 7-9 ganger/dag (4)
❍ 10 ganger eller mer/dag (5)

SjoT1_8b2 - Når det finnes vitamin D berikete varianter av de ulike meieriproduktene (for eksempel melk, yoghurt, ost), hvor ofte velger du da disse?

❍ Aldri (1)
❍ Sjelden (2)
❍ Noen ganger (3)
❍ Som oftest (4)
❍ Alltid (5)
❍ Vet ikke (6)

SjoT1_8c - Hvor mange egg spiser du per uke? (stekt, kokt, eggerøre, omlett)?

❍ Mindre enn 1 egg/uke (1)
❍ 1 egg/uke (2)
❍ 2-3 egg/uke (3)
❍ 4-5 egg /uke (4)
❍ 6-7 egg/uke (5)
❍ 8 eller flere egg/uke (6)

SjoT1_8d - Bruker du smør eller margarin på skiven/knekkebrødet?

❍ Ja (1)
❍ Nei (0)

SjoT1_8d1 - Fyll inn til hvor mange brødskiver/knekkebrød/rundstykker du vanligvis bruker smør/margarin per uke

Margarin (1) ________________________________
Lettmargarin (2) ________________________________
Smør (3) ________________________________

SjoT1_8d2 - Hvor mye smører du pr. brødskive/knekkebrød/rundstykke?

En porsjonspakning på 10-12 gram rekker til antall skiver/knekkebrød/rundstykke:

❍ 1 brødskive/knekkebrød/rundstykke (1)
❍ 2 brødskiver/knekkebrød/rundstykker (2)
❍ 3 brødskiver/knekkebrød/rundstykker (3)
❍ 4 brødskiver/knekkebrød/rundstykker (4)
❍ 5 brødskiver/knekkebrød/rundstykker (5)

SjoT1_8e - Angi hvilken type fett du vanligvis bruker til matlaging

	Aldri (1)	Sjelden (2)	Månedlig (3)	Ukentlig (4)	Daglig (5)
Margarin (1)	❍	❍	❍	❍	❍

	Aldri (1)	Sjelden (2)	Månedlig (3)	Ukentlig (4)	Daglig (5)
Lettmargarin (2)	❍	❍	❍	❍	❍
Smør (3)	❍	❍	❍	❍	❍
Olivenolje (4)	❍	❍	❍	❍	❍
Soyaolje (5)	❍	❍	❍	❍	❍
Rapsolje (6)	❍	❍	❍	❍	❍
Solsikkeolje (7)	❍	❍	❍	❍	❍
Maisolje (8)	❍	❍	❍	❍	❍
Annen olje (9)	❍	❍	❍	❍	❍

SjoT1_8e1 - Vennligst spesifiser Annen olje

SjoT1_8f - Når det finnes vitamin D berikete varianter av oljer, hvor ofte velger du da disse

❍ Aldri (1)
❍ Sjelden (2)
❍ Noen ganger (3)
❍ Som oftest (4)
❍ Alltid (5)
❍ Vet ikke (6)

SjoT1_9a - Kosttilskudd:
Har du tatt tran, fiskeolje- eller omega-3 tilskudd (flytende eller som kapsler) de siste 3 mnd?

	Ja (1)	Nei (0)
Flytende (1)	❍	❍
Kapsler (2)	❍	❍

SjoT1_9b - Hvor mye flytende tran, fiskeolje eller omega-3 tar du per gang?

❍ 1 teskje (1)
❍ 1 barneskje (2)
❍ 1 spiseskje (3)

SjoT1_9c - Hvor mange tran-, fiskeolje- eller omega-3 kapsler tar du per gang?

❍ 1-2 kapsler (1)
❍ 3-4 kapsler (2)
❍ 5 eller flere kapsler (3)

SjoT1_9d - Hvilken type tran- eller fiskeolje/omega-3 tilskudd pleier du å bruke?

	Bruker ikke (1)	1-3 ganger/måned (2)	1-3 ganger/uke (3)	4-6 ganger/uke (4)	Daglig (5)
Møllers tran (1)	❍	❍	❍	❍	❍
Møllers dobbel (2)	❍	❍	❍	❍	❍
Krillolje (3)	❍	❍	❍	❍	❍
Selolje (4)	❍	❍	❍	❍	❍
Complete folat og omega-3 (5)	❍	❍	❍	❍	❍
Møllers omega-3 + folat (6)	❍	❍	❍	❍	❍
Gevita omega-3 med kalsium, vitamin D og K (7)	❍	❍	❍	❍	❍
Trippel Omega-3 (8)	❍	❍	❍	❍	❍
Lifeline gravid (9)	❍	❍	❍	❍	❍
Lifeline ammende (10)	❍	❍	❍	❍	❍
Nycomed gravid (11)	❍	❍	❍	❍	❍
Nycopluss omega-3 (12)	❍	❍	❍	❍	❍
Mulit-tabs GraviOmega (13)	❍	❍	❍	❍	❍
Annen (14)	❍	❍	❍	❍	❍

SjoT1_9d1 - Vennligst spesifiser hvilken annen type tran- eller fiskeolje/omega-3 tilskudd du bruker:

SjoT1_9e - Bruker du annet kosttilskudd (vitaminer og mineraler)?

❍ Ja (1)

❍ Nei (0)

SjoT1_9e1 - Hvilke type kosttilskudd bruker du og hvor ofte

	SjoT1_9e2 -					SjoT1_9e3 - Vennligst spesifiser hvilke(t) merke på kosttilskudd og hvor mye du tar hver gang
	Bruker ikke (0)	1-3 ganger/ mnd (1)	1-3 ganger/ uke (2)	4-6 ganger/ uke (3)	Daglig (4)	
Multivitaminer og mineral (1)	❍	❍	❍	❍	❍	______
Jern (2)	❍	❍	❍	❍	❍	______
B-vitaminer (inkl folsyre) (3)	❍	❍	❍	❍	❍	______
Kalsium og vitamin D (4)	❍	❍	❍	❍	❍	______
Annet (5)	❍	❍	❍	❍	❍	______

SjoT1_10 - Kryss av for feltene under som ev. gjelder for deg:

❑ Er vegetarianer (1)

❑ Har diabetes (sukkersyke) (2)

❑ Er gravid/ammer (3)

❑ Har matvareallergi/intoleranse (4)

❑ Spiser ikke melprodukter (5)

❑ Spiser ikke melkeprodukter (6)

❑ Spiser ikke kjøttprodukter (7)

❑ Spiser ikke grønnsaker (8)

SjoT1_11a - Svangerskapskvalme

Har du vært plaget med svangerskapskvalme?

❍ Nei (0)

❍ Ja, men bare deler av svangerskapet (1)

❍ Ja, hele tiden (2)

SjoT1_11b - Hvilken svangerskapsuke opphørte svangerskapsrelatert kvalme?

SjoT1_11c - Har du kastet opp?

❍ Nei (0)

❍ Ja, men bare deler av svangerskapet (1)

❍ Ja, hele tiden (2)

SjoT1_11d - Hvilken svangerskapsuke opphørte svangerskapsrelatert oppkast?

SjoT1_11e - Er det matvarer (mat, drikke, annet) du har spist/drukket spesielt mye av i svangerskapet (”cravings”)?

❍ Nei (0)

❍ Ja, men bare deler av svangerskapet (1)

❍ Ja, hele tiden (2)

SjoT1_11f - Spesifiser:

SjoT1_11g - Er det matvarer du har unngått å spise i svangerskapet på grunn av aversjon?

- ❍ Nei (0)
- ❍ Ja, men bare deler av svangerskapet (1)
- ❍ Ja, hele tiden (2)

SjoT1_11h - Spesifiser:

SjoT1_11i - Er det matvarer du har unngått å spise av frykt for å skade barnet?

- ❍ Nei (0)
- ❍ Ja (1)

SjoT1_11j - Spesifiser:

SjoT1_11k - Er det matvarer du har begynt å spise fordi det kan være gunstig for barnet?

- ❍ Nei (0)
- ❍ Ja (1)

SjoT1_11l - Spesifiser:

SjoT1_12a - Solvaner

Hvor ofte de siste 3 månedene har du brukt solarium?

- ❍ Aldri (1)
- ❍ Sjeldnere enn 1gang/måned (2)
- ❍ 1 gang/måned (3)
- ❍ 2-3 ganger/måned (4)
- ❍ 1-2 ganger/uke (5)

SjoT1_12b - Hvor mange uker de siste tre månedene har du vært på badeferie (Norge eller Syden)?

- ❍ Har ikke vært på badeferie (1)
- ❍ 1 uke (2)
- ❍ 2-3 uker (3)
- ❍ 4-6 uker (4)
- ❍ 7 uker eller mer (5)

SjoT1_12c - Hvor mange dager/uker de siste tre månedene har du vært på fjellet i snø?

- ❍ Har ikke vært på fjellet i snø (1)
- ❍ 1-6 dager (2)
- ❍ 7-13 dager (3)
- ❍ 2-3 uker (4)
- ❍ 4 uker eller mer (5)

SjoT1_12d - Hvor mye utendørsaktivitet har du om sommeren (turer, hagearbeid, jobb)?

- ❍ Lite (1)
- ❍ Middels (2)
- ❍ Ganske mye (3)
- ❍ Ute nesten hele tiden (4)

SjoT1_13a - Andre spørsmål

Alder, år (1) ________________________

Høyde, cm (2) ________________________

Vekt nå, kg (3) ________________________

SjoT1_13b1 - Hvor mye veide du før du ble gravid (dette svangerskapet)?

SjoT1_13c - Hvor ofte har du mosjonert sammenhengende i minst 30 minutter den siste måneden?

	Aldri (1)	Sjeldnere enn 1 gang/uke (2)	1 gang/uke (3)	2-3 ganger/uke (4)	4-6 ganger /uke (5)	Hver dag (6)
Går (1)	❍	❍	❍	❍	❍	❍
Jogger (2)	❍	❍	❍	❍	❍	❍
Sykler (3)	❍	❍	❍	❍	❍	❍
Svømmer (4)	❍	❍	❍	❍	❍	❍
Sal (aerobic eller lingende) (5)	❍	❍	❍	❍	❍	❍
Styrketrening (6)	❍	❍	❍	❍	❍	❍
Annet (7)	❍	❍	❍	❍	❍	❍

SjoT1_13c1 - Vennligst spesifiser hvilken annen form for mosjon

SjoT1_13d - Hvor stor vekt legger du på å ha et sunt kosthold?

❍ Svært liten (1)

❍ Liten (2)

❍ Middels (3)

❍ Stor (4)

❍ Svært stor (5)

SjoT1_13f - Spiser du vanligvis ett eller flere måltider om dagen sammen med resten av familien?

❍ Ja (1)

❍ Nei (0)

❍ Ikke relevant (2)

SjoT1_kommentar - Eventuelle kommentarer til undersøkelsen: