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ARE OVO-LACTO-PESCO-VEGETARIANS AND VEGANS RISK GROUPS FOR SUBOPTIMAL IODINE INTAKE?

Iodine intake and status in a group of Norwegian vegetarians

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Abstract

BACKGROUND: Iodine is a trace mineral of vital importance for brain development and function. Vegetarians generally avoid or limit their consumption of animal foods. Salt iodization in Norway is exceptionally low, and approximately 80% of dietary iodine derives from animal foods, with milk, seafood and eggs as the main sources. The iodine status in Norwegian vegetarians is unknown.

OBJECTIVE: The main objective was to evaluate iodine intake and status of a group of Norwegian vegetarians.

METHOD: Two day food diaries and morning spot urine samples for analysis of iodine concentration (UIC) were obtained from 52 vegetarians (including 18 vegans and 34 ovo-lacto-pesco-(OLP-) vegetarians) and 67 non-vegetarians (control group). Use of iodine containing supplements was reported, and evaluated in addition to the contribution of iodine from food.

RESULTS: None of the vegans and 24% of OLP-vegetarians reached the recommended iodine intake of 150 µg/day with diet as the only source of iodine.

Use of iodine-containing supplements was reported by 18% and 28% of OLP-vegetarians and vegans, respectively. When including iodine from supplements, 17% of vegans and 38% of OLP-vegetarians reached the recommended intake of 150 µg/day. According to WHOs criteria for evaluating iodine status based on spot urine samples only 12% of vegans and 21% of OLP-vegetarians had adequate iodine intake.

In the total vegetarian group, the median urinary iodine concentration was 52 µg/L in non-iodine-supplement and 102 µg/L in supplement users. High UIC (>700 µg/L) was found in three vegetarians using kelp supplements. Total iodine intake (food and supplements) did not differ between vegetarians and controls.

CONCLUSION: This study showed that suboptimal iodine intake was prevalent in vegans, OLP-vegetarians and non-vegetarians. Although the participants are not representative groups of all vegetarians in the Norwegian population, the results highlight the need to focus on iodine nutrition in subgroups of the population.

KEYWORDS: Iodine, Vegetarians, Vegans, Iodine nutrition, iodine status, iodine deficiency, mild-to-moderate iodine deficiency, plant based diet

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Abbreviations

ALSPAC	The Avon Longitudinal Study of Parents and Children
ADHD	Attention Deficit Hyperactivity Disorder
Donexpo	Experimental study of DeOxyNivalenol biomarkers in urine
FAO	Food and Agriculture Organization of the United Nations
FHI	Folkehelseinstituttet (Norwegian Institute of Public Health)
HiOA	Oslo and Akershus University College of Applied Sciences
ICCIDD	International Council for Control of Iodine Deficiency Disorders
IDD	Iodine deficiency disorder
IGN	Iodine Global Network
IOM	Institute of Medicine (United States)
Lacto-vegetarian	a vegetarian whose diet includes dairy products
Lacto-ovo vegetarian	a vegetarian whose diet includes dairy products and eggs
MID	Mild to moderate iodine deficiency
MoBa	Norwegian Mother and Child Cohort Study
n	number
NIS	The Sodium Iodide Symporter
NNR	Nordic Nutrition Recommendations
OLP-vegetarian	Ovo-lacto-pesco (OLP), a vegetarian whose diet includes dairy products, eggs and fish
Pesco	Fish
rT3	Reverse T3 (triiodothyronine)
SIFO	National Institute for Consumers Research
SPSS	Statistical Package for the Social Sciences
T4	Thyroxin
Tg	Thyroglobulin
TSH	Thyroid stimulating hormone
UIC	Urinary iodine concentration
UIE	Urinary iodine excretion
UL	Upper intake level
UNICEF	United Nations Children’s Fund
US	United States of America
WHO	World Health Organization
µg	Micrograms (millionths of a gram)
µg/g	Microgram/gram
µg/L	Mikrogram/Litre
24 h	24 hours

1 INTRODUCTION

Vegetarians are persons who base their diet primarily on plant food and do not eat meat and fowl. Fish/seafood and food derived from animals such as milk, cheese or eggs, may or may not be included in the wide range of vegetarian dietary patterns. Those who confine their diet strictly to plant food; such as vegetables, fruits, legumes, nuts and grains are categorized as vegans (Orlich et al., 2014).

Even though the global iodine status continues to improve, primarily due to iodine fortification of salt, nearly 400 million of the European population is still mildly to moderate iodine deficient, and concerns have been raised that subgroups may not get enough iodine in countries considered iodine sufficient (Lazarus, 2014; Zimmermann & Andersson, 2012).

Norwegian vegetarians constitute a probable risk group for iodine deficiency. The Norwegian soil is iodine depleted, drinking water contains negligible concentration of iodine, iodine fortification of salt is among the lowest in Europe, and there are few dietary iodine sources (Dahl, Johansson, Julshamn, & Meltzer, 2004b). Due to iodine fortification of fodder for dairy cows and high iodine concentration in seawater, dairy products and marine fish are the main iodine sources, and contributes up to 80 % of iodine in the Norwegian diet (Dahl et al., 2004b).

Data on iodine status in vegetarians is limited and estimates of iodine intake and analysis of urinary iodine has not previously been evaluated in Norwegian vegetarians. However, previous studies have revealed low iodine intake among Norwegians who have a low intake of milk and fish (Brantsæter, Abel, Haugen, & Meltzer, 2013; Dahl et al., 2004b). A group of Norwegians (n=44) with restricted intake of fish and dairy intake had a lower median urinary iodine concentration (UIC) (85 µg/L) than a group (n=63) with normal intake of fish and dairy (117 µg/L.) (Dahl, Margrete Meltzer, et al., 2003) Likewise, other literature on this topic suggests that lower intakes of animal food can contribute to inadequate iodine intakes (Kraj et al., 2003; Rasmussen et al., 2002). A recent Danish study, found that dietary intake of iodine differed significantly between a group of vegans and the general Danish population (Kristensen et al., 2015). The iodine intake (including supplements) did not reach the Nordic Nutrition Recommendations (NNR) for the vegan group.

The number of vegetarians and vegans worldwide has yet to be established, but studies suggests that the amount of people adopting a vegetarian diet is increasing rapidly (Leitzmann, 2014; Phillips, 2005). According to a survey conducted by National Institute for Consumers Research (SIFO) there was around 100-200 000 vegetarians in Norway in 2004[1] (Norsk Vegetar Forening, 2016). This constitutes about 2-4% of the population. A more recent survey conducted by Demoskop in Sweden in 2014, suggested a 4% increase of vegetarians from 6 to 10%, in the last 5 years[2] (Nilsson, 2016). Considering the suggested rapid increase in the Swedish population and other European countries, the present number could be higher in Norway as well.

Various groups, including the Norwegian Directorate of Health highlight the benefits associated with replacing animal based foods with plant foods in all stages of the life cycle, including during pregnancy, lactation, infancy, childhood, and adolescence (Dietitians of Canada, 2016; Phillips, 2005; The American Dietetic Association, 2003; The Norwegian Directorate of Health, 2015a). A vegetarian diet can meet current dietary recommendations if well planned. However although all vegetarian diets exclude meat, they may diverge considerably from eating no animal products at all, to including fish, dairy and/or eggs. The risk of iodine deficiency in vegetarians depends on the extent to which iodine-containing foods are excluded from their diets.

Iodine intake and status of pregnant, lactation women and children are of special importance and of great concern, because iodine is essential for normal brain development and growth in foetuses and children (Skeaff, 2011; Zimmermann, 2012). Iodine intake in pregnant women was previously found to be suboptimal in Norway (Brantsæter et al., 2013). Women of childbearing age and young children that follows an iodine depleted diet, which includes the vegetarian diet, may therefore be at particular risk. The potential adverse effects of mild to moderate iodine deficiency during pregnancy are not fully known (Zimmermann, Jooste, & Pandav, 2008), but may be associated with decreased cognitive functions of the child (Bath, Steer, Golding, Emmett, & Rayman, 2013). Iodine status in a group of pregnant non-vegetarian women has been evaluated separately in another master project parallel to this study *Iodine intake and status in a group of pregnant women in Norway* (Nyheim, 2016).

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[1] Cited by Norsk Vegetar Forening

[2] Cited by Peter Nilsson, Djurens Rett

As a vegetarian for many years I was intrigued by the opportunity to evaluate iodine nutrition in vegetarians, when offered the chance to do this for my master thesis. A study initiated to examine dietary exposure to mycotoxins in subgroups of Norwegians (Donexpo) was also approved for evaluation of iodine nutrition. The study population included vegetarians and was therefore an opportunity to investigate iodine nutrition in this group. In order to get a better understanding of the scientific process involved in human studies it was decided to ask the Regional Committee for Ethics in Medical Research for approval to recruit more vegetarians. The approval was granted and I was able to be involved in all stages of this study, starting with recruitment, data collection, and preparation of urine samples, coding and calculation of iodine intakes as well as description of results, statistical analyses and discussion.

This study investigated the iodine nutrition of Norwegian vegetarians and may provide new insight regarding the iodine status and iodine containing food sources of this subgroup of the Norwegian population.

2 TEORETICAL BACKGROUND

In the following sections I will describe some of the subcategories of vegetarians, characteristics associated with choosing a vegetarian diet, possible health benefits and how following a vegetarian diet may pose nutritional concerns, including limited sources if iodine. I will also give an outline of the role of iodine in human nutrition, including recommendations, how iodine status is evaluated, and various factors affecting iodine status. Furthermore, I will give a description of vulnerable groups for iodine deficiency.

2.1 Vegetarians

There are different reasons for choosing a vegetarian diet. Concerns about animal welfare, global warming and sustainable food production are in addition to health considerations, the main motivations for vegetarianism in the western world (Radnitz, Beezhold, & DiMatteo, 2015).

The term “vegetarian” is believed to derived from the words; “(veget) able” + “arian” which denote a person who supports or practice a theory or a set of principles associated with “vegetables”(Dictionary.com, 2016a, 2016b). The first known use of the word” vegetarian” in print was in 1842 (John Davis, 2011). It should be noted that in the early 19th century the word “vegetable” had a slightly different meaning than today, and denoted any kind of plant food, including fruits, grains, and beans, not just certain kinds of plants (John Davis, 2011).

The number of vegetarians globally is uncertain, but estimates suggest that there are approximately one and half billion, which represents roughly 22% of the global population. Of these, only about 75 million are vegetarians by choice and 1.450 million abstains from animal products out of necessity and are expected to eat meat as soon as they can afford it (Leahy, Lyons, & Tol, 2010).

2.1.1 Definitions and sub-categories of vegetarian practices

There are several vegetarian categories, all of which avoid meat and some of which in addition also avoid fish and/or the animal products milk/dairy products and eggs (Table 2.1-1).

Table 2.1-1 Different types if vegetarian diets

Types of diet	Included foods	Excluded food
Lacto-vegetarian	Plant food + milk/dairy	Meat[1], fish[2], egg
Lacto- Ovo-vegetarian	Plant food + dairy + egg	Meat[1], fish[2]
Pesco- vegetarian	Plant food + fish (dairy,egg)	Meat[1]
OLP-Vegetarians	Include all the above groups i.e. may include milk/dairy and/or egg and/or fish	Meat[1]
Vegan	Plant food	Meat[1], fish[2], egg, dairy

[1]Including poultry, [2]Includes all sea animals

In this study the dietary terms and definitions outlined in Table 2.1-1 are used.
The lacto- vegetarian diet consists of plant food with the addition of milk and dairy products, while the lacto-ovo vegetarian diet additionally includes eggs. Pesco-vegetarians were defined as a vegetarian who do not eat any meat, but who may or may not include eggs and dairy in addition to fish. OLP- vegetarians were used as a term for those who do not eat any meat but may include eggs and /or dairy-products and/or fish. Vegans were defined as those eating only plant food. The term vegetarian refers to all forms of this diet. Whenever one of the two vegetarian diets (OLP- vegetarians or vegans) are implied this is explicitly mentioned.

Even if these categories have been defined by vegetarian societies, dietetic associations and others (Davey et al., 2003; The American Dietetic Association, 2009) research studies sometimes use different definitions. One study defined lacto-ovo vegetarians as those who consume unlimited amounts of dairy and eggs and allow meat, poultry and fish less than once a month (Rizzo, Jaceldo-Siegl, Sabate, & Fraser, 2013). Other studies generalized vegetarians as those who eat meat or fish less than once a week (Cade, Burley, & Greenwood, 2004) or red meat less than once a month and chicken or fish no more than once a week (Ball & Bartlett, 1999). Pesco-vegetarians may or may not be included to the vegetarians' spectrum. One large cohort study that included a high proportion of vegetarians, defined pesco- vegetarians as individuals who consume fish one or more times per month, and also eats red meat and poultry less than one time per month (Rizzo et al., 2013). Thus, the descriptions of the different vegetarian diets seem to lack appropriate definitions as they are sometimes overlapping and often inconsistent.

It is estimated that about 10 % of vegetarians are vegans, but the number of vegans is growing more rapidly than those of other vegetarians (Leitzmann, 2014). The British Vegan Society defines veganism like this:

> *A philosophy and way of living which seeks to exclude – as far as possible and practicable- all forms of exploitation of, and cruelty to, animals for food, clothing or any other purpose; and by extension, promotes the development and use of animal-free alternatives for the benefit of humans, animals and the environment. In dietary terms it denotes the practice of dispensing with all products derived wholly or partly from animal* (The Vegan Society, Undated).

2.1.2 Characteristics associated with choosing a vegetarian diet

The two most common motivations for becoming vegetarians are health concerns and the concerns about animal welfare (Hoffman, Stallings, Bessinger, & Brooks, 2013; Ruby, 2012). The reasons giving for following a vegetarian diet have been the same over the past 2.5 millennia. Pythagoras (570–500 BC), the Greek philosopher, is considered to be the father of ethical vegetarianism (Leitzmann, 2014). The ancient Greeks believed that animals were related to humans thus killing them meant injustice and harm. According to sources cited by Leitzmann (2014), they were also of the opinion that eating meat was not as healthy as other options at the time.

It appears that the process of becoming a vegetarian develops differently, depending on one's motivations. Health vegetarians are more focused on benefits of the diet out of concern for personal health. They eliminated meat more gradually from their diets, and were relatively less likely to transition toward veganism. In contrast, ethical vegetarians adopted their vegetarian diet out of moral considerations related to animal welfare. They tended to adopt their diets more abruptly and had a greater likelihood of transitioning toward veganism (Ruby, 2012). There are generally more female vegetarians than male vegetarians (Larsson, Klock, Nordrehaug Åstrøm, Haugejorden, & Johansson, 2002; Ruby, 2012) and vegans tend to be younger compared to other vegetarians (Davey et al., 2003).

2.1.3 Benefits of a vegetarian diet

In the 21st century there has been a paradigm shift regarding the health aspects of the vegetarian nutrition supported by scientific evidence. Opposed to former prejudices of vegetarianism leading to malnutrition, there has been a growing international acceptance of the health benefits of such diets (Leitzmann, 2014). Vegetarian diets can be suitable in the prevention and treatment of certain diseases, and is considered appropriate for all stages of the life cycle, including during pregnancy, lactation, infancy, childhood, and adolescence (Craig & Mangels, 2009; The Norwegian Directorate of Health, 2015a). Plant based diets tends to be lower in saturated fat, cholesterol and animal protein, and higher in fibre, magnesium, potassium, folate, vitamin C and E, carotenoids and phytochemicals (The American Dietetic Association, 2003). There is evidence of lower rates of ischemic heart disease and lower LDL cholesterol levels among vegetarians (Dinu, Abbate, Gensini, Casini, & Sofi, 2016; Fraser, 2009). Vegetarian diets were associated with reduction in type-2 diabetes incidence (Tonstad, Butler, Yan, & Fraser, 2009; Tonstad et al., 2013) and a lower Body Mass Index (Dinu, Abbate, Gensini, Casini, & Sofi, 2016).Studies further suggests that vegetarian diets are associated with an overall lower incidence of some forms of cancers (Dinu et al., 2016; Key et al., 2014; Orlich et al., 2015).Compared to lacto-ovo-vegetarian diets, vegan diets seem to offer additional protection for obesity, hypertension, type-2 diabetes, and cardiovascular mortality (Le & Sabaté, 2014)

2.1.4 Concerns related to vegetarian diets

The habitual eating patterns of vegetarians vary considerably depending on diet choices. The extent of nutrient deficiencies tends to be higher in persons who become vegetarians for ethical, religious, economic or political reasons compared with those who turn to vegetarianism for health reasons (Waldmann, Koschizke, Leitzmann, & Hahn, 2003).

There are some key nutrients that vegetarians should pay attention to; essential amino acids, iron, zinc, calcium, vitamin D, riboflavin, vitamin B6, vitamin B12, vitamin A, n-3 fatty acids, selenium and iodine (Craig & Mangels, 2009; The Norwegian Directorate of Health, 2015b).

There is limited knowledge about nutrition status in Norwegian vegetarians, but some studies from other Nordic countries found that the dietary intake in vegans was in lack of certain nutrients. At the micro nutrient level, considering both diet and supplements, the intake did not reach the NNR for vitamin D, iodine and selenium in a group of Danish vegans. Among vegan women, vitamin A intake also failed to reach the recommendations with reference to the NNR (Kristensen et al., 2015). The study of Food and Nutrient Intake and Nutritional Status of Finnish Vegans and Non-Vegetarians (2016) found lower intake of B12, selenium and vitamin D in vegans compared to the reference group. The median concentration of iodine in urine was below the recommended levels in both groups (Elorinne et al., 2016).

Norway is in an extraordinary position when it comes to iodine, because the iodine supply derives almost exclusively from the drinking of milk and eating fish. Neither table salt nor industrial iodisation of salt is mandatory in Norway (Dahl et al., 2004b). Some brands of table salt have added iodine, but only 5 µg per gram of NaCl, which is among the lowest in Europe (WHO, 2007b). Because the soil, salt and drinking water contains insignificant amount of iodine, iodine containing supplements and seaweed is an important source of iodine for vegans. The amount of iodine in the diet of OLP- vegetarians depends on the extent to which the animal based iodine-containing (milk, egg and fish) foods are included in their diet(Kraj et al., 2003).

2.2 Iodine in human nutrition

Iodine is an essential micronutrient. At present, the only known physiological role of iodine in humans is in the synthesis of the thyroid hormones (thyroxine and triiodothyronine) (WHO, 2004). Thyroid hormones regulate and control embryonic development and coordinate physiology within and between cells and tissues via dose-dependent regulatory effect on essential genes. A certain level of thyroid hormones is needed for optimal metabolic rate, mental and physical development, and to sustain a normal function of the central nervous system (Crockford, 2009; Delange, 2000).

2.2.1 Iodine and thyroid metabolism

The thyroid is a large gland located in the front of the neck below the larynx. The thyroid gland traps and uses iodide in the synthesis and storage of the two thyroid hormones; thyroxine (T_4)

and triiodothyronine (T_3). A healthy adult human body contains up to 20 mg of iodine, whereas about 70-80 percent of iodine resides in the thyroid gland. After entering into the body from dietary sources, the absorption occurs in the stomach and duodenum and is nearly complete (> 90 percent) (Küpper et al., 2011; Rohner et al., 2014; Zimmermann et al., 2008). Iodine is converted into iodide before it is absorbed, and enters the circulation as plasma inorganic iodide (WHO, 2004).Under normal circumstances, plasma iodide has a half-life of approximately 10 hours, and generally the clearance is done by the thyroid gland and kidney. The thyroid uses iodide for synthesis of thyroid hormones and the kidney excretes the excess iodine with urine.

The renal clearance is quite constant, whereas the thyroid clearance varies in accordance with the iodine supply. When there is an adequate supply, ≤ 10 percent of absorbed iodide is taken up by the thyroid gland to balance losses and maintain synthesis of thyroid hormones. However if there is an iodine deficiency this fraction can go above 80 percent (Küpper et al., 2011; Zimmermann, 2009). The Sodium Iodide Symporter (NIS) – a transmembrane protein- transfers iodide into the thyroid follicles by active transport.

After iodide is transported into the cell it diffuses to the apical surface of the thyrocyte and into the follicular lumen, where it is used in the synthesis of thyroid hormones.

An enzyme (thyroid peroxidase) integrates iodine into two hormones: triiodothyronine - containing three iodine atoms and is also known as T3, and levothyroxine - containing four iodine atoms and is also known as thyroxine or T4. T3 and T4 are accumulated as thyroglobulin in the colloid of the thyroid follicles (Küpper et al., 2011; Zimmermann et al., 2008). In healthy adults there is normally about 6 µg of T3 and 90 µg of T4 produced daily (Daniels & Dayan, 2006).

When thyroid stimulating hormone (TSH) is released from the pituitary gland, it activates the release of the thyroid hormones. The major hormone secreted by thyroid gland is T4. T4 are taken up by peripheral tissues, de-iodinated and converted into T3, mainly by liver and kidney. T3 is the more active of the two. There is also a conversion of T4 into an inactive form of T3 - called reverse T3 or rT3. More than 99% of T3 and T4 are bound to protein in the circulation. When the concentration of these binding proteins decrease or increase, the serum concentration of T3 and T4 will decrease or increase as well. However, the portion of the free hormone remains the same (Daniels & Dayan, 2006; Zimmermann, 2011).

Thyroid hormones affect all cells in the body and provide a number of physiological effects. It regulates the basal metabolism and has major effects on the metabolism of carbohydrates, proteins and lipids (Sand, Sjaastad, & Haug, 2010) Thyroid hormones affect the heart rate and pulmonary ventilation and are also responsible for normal growth physically and mentally. Normal production of thyroid hormones is also important for normal gonad function in both women and men, and an insufficient thyroid hormone production can lead to loss of menstruation, reduced sperm production and infertility (Sand et al., 2010)
Hypothyroidism may occur if the thyroid gland is not able to make enough thyroid hormone to meet the body's needs, and the metabolism slows down. Hyperthyroidism is a condition due to increased production of thyroid hormones, leading to an increased metabolic condition. Symptoms related to these conditions are variable according to the severity of the condition (Sand et al., 2010).

2.2.2 Dietary sources of iodine

Opposed to many other essential dietary nutrients, iodine status is not as related to socioeconomic development, as to geographical conditions and dietary habits.

Dietary iodine is obtainable from both animal and plant based sources. The food sources of marine origin, such as sea fish, shellfish and seaweeds are naturally iodine- rich and reflect the abundant concentration of iodine in seawater (Johnson; Fordyce & Stewart, 2003).The water cycling brings small amounts of iodine from the sea to soils were it binds with organic material. The concentration of iodine in food and drinking water are highly dependent on the soil, which has a broad variation of iodine, determined by geographical circumstances (from <0.1 to 150 mg/kg) (Johnson; Fordyce & Stewart, 2003). The soil in inland regions, particularly mountainous areas, is commonly deficient in iodine.

On the other hand, there are areas in the world that have excessive iodine concentrations, which could lead to adverse health effect (Shen et al., 2011; Zimmermann, Ito, Hess, Fujieda, & Molinari, 2005) In fact in 34 countries iodine intake tends to be more than adequate or excessive, (Zimmermann et al., 2008). In Algeria, for example, endemic goitre[3] was found in Saharawi children due to excessive iodine concentration in the local water and milk (Henjum, Barikmo, et al., 2010). In some countries like China, there is a coexistence of iodine deficiency and excessive intake (Du et al., 2014).

Customised to the nutritional habits of populations in industrialized countries, the fodder of farm animals is supplied with iodine, which significantly influences cow milk and egg content of iodine (Dahl, Opsahl, Meltzer, & Julshamn, 2003; Yalçin, Kahraman, Yalçin, Yalçin, & Dedeoğlu, 2004). Iodine content in plant food thus reflects the iodine in the environment in which they grow, and iodine content of animal products reflects both natural occurring iodine and iodine originating from supplementation of animal fodder (Dahl et al., 2004b; Phillips, 1997). Cow milk contains iodine mainly because the cow fodder is fortified with minerals, including iodine. Eggs contain some iodine because a kind of “soup” of fish waste is added in small amounts in the fodder of laying hens (L. Nordang, personal communication, April 21, 2016).

A large proportion of the world`s populations lives in areas where natural sources of iodine are low and rely on iodine-supplying interventions. The World Health Organization (WHO) recommends mandatory salt iodization as the preferred strategy for prevention and control of iodine deficiency disorders. Salt has been the vehicle of choice for iodine fortification as it is relatively inexpensive, easy to monitor and is consumed by most people in a population (WHO, 2014). More than 70 percent of all households worldwide have access to iodized salt, as a result of the Universal Salt Iodization Project (The United Nations Children`s Fund, 2008). Iodine-fortified salt has been used for more than 70 years and has extensively influenced iodine status internationally (Food and Agriculture Organization of the United Nations, 1996). The amount of iodine added to salt differs widely. WHO recommends iodine levels of 20-40 µg/g salt and most countries add 10-40µg/g of iodide to the salt (WHO, 2014).

Iodine may also be obtained from supplements like multi-mineral tablets or from seaweed like kelp, but these can in varying degree contribute to the daily iodine intake (Leung, Pearce, & Braverman, 2009). These issues will be discussed in more detail later.

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[3] Endemic goitre is a term used for enlargement of the thyroid gland in more than 5% of the population in a given geographic area (Hughes & Eastman, 2012)

Milk and dairy products was found to be the primary source of iodine in the Norwegian diet with a contribution of approximately 60% of the iodine supply in adults. For the Norwegian children (4-13 years), milk and dairy contributed with 64-71 % of the iodine in the diet. Fish intake was found to contribute with approximately 20-25% of daily iodine intake in adults, and 12-14% in children. Eggs contributed with around 5 % of the daily intake of iodine. These data are based on the mean food intake data from a nationwide food consumption survey among 2672 men and women aged 16-79 years (Norkost 1997) and 4 years olds- and students in 4-8th grade (n=391) (Ungkost 2000) (Dahl, Johansson, Julshamn, & Meltzer, 2004a)

Worldwide, the most important dietary factors influencing iodine status are the iodine concentration in drinking water, the amount of iodine added to salt, to what extent iodized salt is consumed, as well as the consumption of milk from cows raised on iodine fortified fodder, sea animals, seaweeds and iodine containing supplements.

2.2.3 Iodine requirement and recommended intake

Due to the limited storing capability of iodine, a regular supply is required. The daily recommended intake of iodine is 150 µg for adults, whereas the recommendation is lower for children and higher for pregnant and lactation women (Nordic Council of Ministers, 2014; WHO, 2007a). Table 2.2-1 shows the recommended intake for different age groups and population by WHO and the NNR (2012) correspondingly. The recommendations by WHO were based on the intake estimated to cover the needs of "nearly all" healthy individuals according to specific life phase (WHO & FAO, 2006). And the recommendations from NNR were based on the amount of iodine required to prevent goitre and maintenance of the normal function of the thyroid in adults (Nordic Council of Ministers, 2014). The references for children were based on urine iodine excretion, goitre preventions and requirements of iodine related to growth and energy needs. For pregnant and lactating women there was considered an extra supply to cover the needs of the foetus and to provide an ideal composition of the breastmilk (Nordic Council of Ministers, 2014).

Table 2.2-1 Recommended daily iodine intake (μg/ d) by WHO, and NNR for different age groups and populations (Nordic Council of Ministers, 2014; WHO, 2007a)

Age/ population groups	**Recommended intake, μg/day** ***According to WHO et al***
Children 0-59 months	90
Children 6 – 12 years	120
Children > 12 years	150
Adults	150
Pregnant women	250
Lactating women	250
	Recommended intake, μg/day According to NNR[1]
Children 2-5 years	90
Children 6-9 years	150
Children 6-9 years	120
Adults	150
Pregnant women	175
Lactating women	175

[1] The recommendations in Norway is in compliance with those of NNR(The Norwegian Directorate of Health, 2014)

Although a proper physiological amount of iodine is essential for a normal thyroid function, overconsumption of iodine should be avoided as well (Leung & Braverman, 2014). The therapeutic range for iodine is rather narrow and both insufficient and too high iodine intake is associated with thyroid diseases (Laurberg et al., 2010). Therefore, regulatory bodies have established an upper intake level (Table 2.2-2). The tolerable upper intake level (UL) is the highest average daily nutrient intake level likely to pose no risk of adverse effects to nearly all individuals in the general population (Institute of Medicine (US), 2001). In addition to too high levels of iodine naturally occurring thru drinking water, excessive intake of iodine can occur through intake of food naturally rich in iodine like seaweed or through iodine – containing dietary supplements (Leung & Braverman, 2014). The upper limit is set due to the range of individual variation. Individuals who have been exposed to iodine deficiency for a prolonged period or have a thyroid disorder, might be more sensitive to excess iodine exposure (Leung & Braverman, 2014). The Scientific Committee of the European Food Safety Authority (EFSA) concluded in their opinion on the tolerable upper intake level of iodine that an intake up to 600 μg/day in adults are acceptable, and that this also include pregnant and lactating women.

(European Food Safety Authority, 2006). The Institute of Medicine of the National Academies (IOM) in the US set the tolerable upper limit of daily iodine intakes to 1100 µg/day for adults, pregnant and lactating women, and lower for children (Table 2.2-2)(Institute of Medicine (US), 2001).

Table 2.2-2 Upper intake level (UL) of iodine (µg/day) according to EFSA and IOM

Age/ population groups	**Upper Level of intake, µg/day** ***according to EFSA***[1]
Adults	600
Pregnant/lactating women	600
	Upper Level of intake, µg/day ***according to IOM***
Children 1-3 years	200
Children 4-8 years	300
Adults	1100
Pregnant/lactating women	1100

[11] The recommendations in Norway is in compliance with those of EFSA (NNR, 12)

2.3 Iodine deficiency disorder

When physiological requirement of iodine is not met, it may lead to thyroid dysfunction and a range of developmental and functional abnormalities due to insufficient production of thyroid hormones (Delange, 1994). Thyroid dysfunctions caused by inadequate iodine intake are collectively called Iodine Deficiency Disorders. It has been estimated that iodine deficiency affects 1.88 billion people worldwide (WHO, 2014), and constitutes the most common cause of brain damage worldwide although it is easy preventable (Benoist, McLean, & Andersson, 2009). Several European countries are still suffering from moderate or mild iodine deficiency (WHO, 2007b).

2.3.1 Consequences of severe iodine deficiency

Worldwide, iodine deficiency disorder remains a great threat to human health and development. The main impact of iodine deficiency disorder is on pregnant, lactating women and young infants (Skeaff, 2011; Zimmermann, 2012).As iodine deficiency in pregnancy results in lowering maternal circulation of thyroid hormone concentration, this leads to reduction in placental transfer of thyroxine and it may affect the brain and nervous system development of the foetus (Zimmermann, 2012). Cretinism, a condition characterized by various degrees of short stature, impaired motor development, deaf- mutism and irreversible mental retardation is the most extreme consequence of iodine deficiency disorder. Other consequences are goitre, miscarriages and stillbirths, poor growth and cognitive impairment (Zimmermann, 2012).

The most well-known consequence of iodine deficiency is goitre. The term goitre originates from the Latin word ”guttur," meaning the throat, and was formerly used to denote swelling of any kind in the front of the neck (Berry, 1901). Today the term is used to describe enlargement of the thyroid gland. Common causes for goitre besides iodine deficiency are autoimmune disease and thyroid nodules (Hughes & Eastman, 2012). When the iodine intake is insufficient, an increased secretion of TSH from the pituitary gland follows as an attempt to optimize uptake of the available iodine (Hughes & Eastman, 2012). Because of a continuously reduced ability by the thyroid to synthesize adequate amount of thyroid hormones, thyroid growth is stimulated as a compensatory mechanism. In mild iodine deficiency, this adaptation response can be satisfactory in order to provide the body with sufficient thyroid hormone. However in more severe cases this can result in hypothyroidism. Patients with goitre may be asymptomatic, or might experience various symptoms due to pressure on the trachea and oesophagus with associated discomfort like breathing difficulties, dysphagia, cough and hoarseness. There may be additionally symptoms associated with hypothyroidism or hyperthyroidism. The term “endemic goitre” is used when the disorder affects > 5% of the population in a given geographic area (Hughes & Eastman, 2012).

2.3.2 Consequences of mild to moderate iodine deficiency

The consequences of mild to moderate iodine deficiency are less recognized than those of severe iodine deficiency. However, it is the most feasible variety of iodine deficiency to occur in

Western countries, and there is especially high occurrence of mild to moderate iodine deficiency in European countries (WHO, 2007b).

In adults, mild to moderate iodine deficiency increases the risk of thyroid abnormalities as well as secondary neurologic impairment with reduced physical and cognitive capacity (Rohner et al., 2014). The Danish investigation on iodine intake and thyroid disease, DanThyr found that even small differences in iodine intake gave profound effect on the prevalence of goitre and thyroid nodules (Laurberg et al., 2006). Mild to moderate iodine deficiency was also highly associated with hyperthyroidism in elderly individuals, especially women, with an additionally risk of cardiac arrhythmias, osteoporosis and muscle wasting (Laurberg et al., 2000). Available evidence further suggests that iodine deficiency might be a risk factor for thyroid cancer, which is an increasing type of cancer particularly affecting women (Rahib et al., 2014; Zimmermann & Galetti, 2015).

Pregnant and lactating women are vulnerable for iodine deficiency, even the mild to moderate variety (Bath et al., 2013). Most of the development of the foetus brain takes place during the pregnancy and the first two to three years of postnatal life. Pregnant women have a higher daily iodine requirement due to changes in the thyroid function.These changes, predominately in the first and second half of gestation; represent a profound hormonal change and a subsequent increased demand for hormones during pregnancy. If the pregnant woman is iodine deficient, the neonate is at high risk of irreversible mental impairment (Zimmermann, 2011). Another susceptible group for iodine deficiency is women breastfeeding their children, as this may be the only source of iodine during the first 6 months of life (Glinoer, 2007). The evidence suggests that insufficient iodine intake during early pregnancy associates adversely with the child's cognitive development (Bath et al., 2013). Studies found that populations in countries with moderate to severe iodine deficiency scores lower on IQ than those of iodine-sufficient countries (Qian et al., 2005).The Avon Longitudinal Study of Parents and Children (ALSPAC) and other studies found a higher risk of low IQ and reduction of academic skills in children born to mothers who were iodine- deficient during pregnancy, in spite of being raised in a iodine sufficient environment (Bath et al., 2013; Hynes, Otahal, Hay, & Burgess, 2013; van Mil et al., 2012). A causal relationship between mild to moderate iodine deficiency and attention deficit and hyperactivity disorder (ADHD) in children as a consequence of maternal hypothyroxinaemia has also been suggested (Vermiglio et al., 2004). However the fully effect on mild to moderate iodine deficiency in pregnant women remains uncertain (Zimmermann, 2011).

Even if iodine deficiency disorder first and foremost is caused by insufficient iodine intake, some foods contain substances that interfere with iodine utilization or thyroid hormone production. These substances are collectively referred to as goitrogens and can become an additional problem when the iodine intake is already marginal (Messina & Redmond, 2006). Certain food items such as soy, cassava and cruciferous vegetables are goitrogenic, but the impact is considered modest. Smoking is also known to be affection the utilization of iodine (Cho et al., 2010).

2.3.3 The prevalence of iodine deficiency worldwide, in Europe and in Norway

Even though 1.88 billion people worldwide still suffers from iodine deficiency, the global iodine status continues to improve (WHO, 2014). Many countries worldwide have successfully eliminated iodine deficiency disorders or made significant progress in their control, mainly as a consequence of salt iodization (WHO, 2014). In 2015, only 25 countries remained mild to moderate iodine deficient compared to 32 in 2011. Currently no country is in the severely deficient category and severe endemic goitre has mainly disappeared (Iodine Global Network, 2015).

Many of the remaining countries with mild to moderate iodine deficiency are in the industrialized world. Europe has the greatest proportions of children with inadequate iodine intake (WHO, 2007b). The Universal Salt Iodization Project promote that all salt used for human consumption, including salt used in agriculture, food processing and households should be iodized (WHO, 2014). In European countries in particular, this is often not the case. Iodized salt reach only 27 percent of households in Europe compared to 70 percent worldwide (WHO, 2007b). Approximately 393 million individuals in Europe have insufficient iodine intake and the greatest proportion of children with inadequate iodine intake are in Europeans (43.9%) (Zimmermann & Andersson, 2012). Furthermore inadequate iodine supply in pregnancy was found in nearly 30 percent of the European countries. 400 million people from 20 countries have no or limited access to iodised salt (Lazarus, 2014). Recently, a European project called EUthyriod was initiated to ensure adequate iodine intakes in Europe. A total of 24 member states from the European Union and 6 other countries, including Norway will be participants in this project (EUthyroid, 2015).

Iodine deficiency was once endemic in in Norway. In 1934 there was an extensively investigation for goitre conducted in all school children in Modum, an inland region southeast in Norway. As many as 1570 individuals were examined and the prevalence of goitre was found in 80 percent of these children. Forty three years later, in 1977, the same area was reinvestigated for goitre prevalence. Again all children was examined (n= 1480), but this time only 1.5 percent of the examined children had goitre by palpation. This change in goitre incidence was directly related with the findings of trace minerals deficiencies in the Norwegian cattle in the 1950s. The department of agriculture then required minerals, including iodine to be added to the cattle fodder. Thus the mandatory fortification of cow`s fodder initiated to improve the animal health, unintendedly also resulted in eradication of goitre in Norway (Frey, Rosenlund, Try, & Theodorsen, 1993). Fortification of cow`s fodder is still controlled by legislation in Norway[4] (Dahl, Opsahl, et al., 2003). Combined with a more widespread use of saltwater fish and seafood, the Norwegian population has been considered to be iodine sufficient since the 1950s. Some studies have since been conducted during the 1970s and 1980s, primarily of small groups from different geographically districts in Norway, showing an adequate iodine excretion in urine (Frey et al., 1993)

More recent studies in Norway have mostly focused on iodine nutrition in pregnant women and low fish eaters (Brantsæter et al., 2013; Dahl, Margrete Meltzer, et al., 2003). In general the most susceptible and vulnerable groups for iodine deficiency are women of reproductive age and small children. Iodine intake was estimated in a large population of pregnant women recruited to the Norwegian Mother and Child Cohort study (MoBa). Only 21.7 % of 61 904 women reached the WHO recommendation for iodine intake of 250 µg/day. This insufficient iodine intake was confirmed in a sub-study of MoBa where a suboptimal UIC (69µg/L) was measured in 119 pregnant participants (Brantsæter et al., 2013). I addition to pregnant and lactating women, Norwegians adolescents and individuals with low intake of dairy, fish and eggs are groups at risk for insufficient intake of iodine according to findings of previous studies, (Dahl, 2004, Brantsæter, et al. 2013).

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[4] Cited by Dahl, et al., 2003

2.4 Assessment of iodine status

Several methods are used to assess iodine status in populations. Iodine status was traditionally evaluated by palpation of the thyroid gland and reported as prevalence of goitre (Zimmermann & Andersson, 2012). Evaluation of thyroid size by thyroid ultrasonography and testing for abnormal levels of TSH, T3, T4 and thyroglobulin, can also reflect iodine deficiency (Henjum, Strand, Torheim, Oshaug, & Parr, 2010; Rohner et al., 2014; Vejbjerg, Knudsen, Perrild, Laurberg, Carle, et al., 2009). The recommended reference group for measuring iodine status in a population is school age children (6-12 years) (WHO, 2007a).The body has low storage capacity of iodine and the amount excreted in urine reflects the ingested intake. More than 90% of ingested iodine is excreted in the urine within the next 24 hours (Zimmermann, 2009).The currently recommended method for assessing dietary iodine intake of populations, is to measure the concentration of iodine in urine and comparing the median UIC to UIC cut-offs established by WHO in order to categorize the iodine status of the population. Calculating iodine intake from dietary assessment is another method that is useful for assessing iodine status, especially in populations where the contribution of iodine from salt is limited, as in Norway (Rohner et al., 2014). Table 2.4-1 describes some of the advantages and disadvantages of the different methods, of which only the two first are described in more detail in this chapter.

Table 2.4-1 Different methods and biomarkers for iodine assessment (Rohner et al., 2014; Zimmermann & Andersson, 2012)

Methods/Biomarker	Description	Advantages	Disadvantages
UIC/UIE	UI can be expressed as a 24-h excretion (UIE; µg/day), as a concentration (UIC; µg/L), or in relation to creatinine excretion (mg iodine/g creatinine).	Spot urines are easy to collect. Useful for measuring resent iodine intake	Needs sufficiently large sample size to even out individual variations.
Dietary assessment	FFQ, food diaries, or 24-h food intake recall and weighed food records, duplicate portion technique	Can identify the most important food sources, which is useful for planning of intervention strategies	Time-consuming Wide variation of iodine in food relative to soil, seasons etc
TSH	TSH can be used as an indicator of iodine nutrition.	TSH is a sensitive indicator of iodine status in the new born period.	A relatively insensitive indicator of iodine nutrition in school aged children and adults. May be within the normal range even if iodine deficiency is present.
Thyroglobulin	Serum thyroglobulin increases due to greater thyroid cell mass and TSH stimulation in areas of iodine deficiency and endemic goitre,	A more sensitive indicator of iodine repletion than TSH or T4.	There are no cut offs for thyroglobulin to distinguish severity of iodine deficiency
T3/T4	Serum T3 increases or remains unchanged, and serum T4 usually decreases in iodine-deficient populations,	Gives a direct reflection of thyroid function.	Poor indicator of iodine status except in areas of severe iodine deficiency. Changes in T3/T4 are often within the normal range even if there is iodine deficiency.

2.4.1 Urinary iodine concentration and excretion

Urinary iodine concentration is the main indicator for epidemiological assessment of iodine status and a good marker of the recent dietary intake. The body has low storage capacity of iodine and the amount excreted in urine reflects the ingested intake. More than 90% of ingested iodine is excreted in the urine within the next 24 hours (Gibson, 2005; Zimmermann, 2009).

Urine iodine can be measured in spot urine samples and expressed as the iodine concentration (µg/L), as UIC adjusted for creatinine excretion (µg iodine/g creatinine) to take into a hydration level into account, or used as an equation that estimates 24-hour iodine intake taking age, sex expected creatinine excretion into account (Knudsen, Christiansen, Brandt-Christensen, Nygaard, & Perrild, 2000). Urinary iodine can also be measured in 24-hour urine samples and expressed as 24-hour excretion (UIE µg/24 h) (König, Andersson, Hotz, Aeberli, & Zimmermann, 2011). The concentration of iodine in urine can be also be back-transformed to estimate iodine intake by using the following equation: Iodine intake (µg/day) = UIC (µg/L) *0.0235 x weight (kg)(Institute of Medicine (US), 2001).

In individuals, urinary iodine excretion varies from day to day and within a given day, depending on fluid and iodine intake. Higher fluid intake leads to increased volume of urine and dilution of the urinary iodine concentration. Thus a single spot urine sample may be misleading in the interpretation of an individual’s iodine status. However, in sufficient large number of samples (ideally > 500) this variation tends to even out (WHO, 2007a). 24-hour collection of all urine produced throughout the day (UIE µg/day) is considered the “reference- standard” for describing iodine intake in a population and thus often used for validation of other methods (Vejbjerg, Knudsen, Perrild, Laurberg, Andersen, et al., 2009). The disadvantage of this method is that it is a lot more demanding for participants to carry out, especially for more than one day. A major advantage of urinary iodine analysis in general, is that it represents the total iodine intake from all dietary sources, including supplements.

The degree of iodine deficiency in a population is categorized according to the median urinary iodine concentration (UIC) in school age children as mild (UIC 50–99 µg/l), moderate (UIC 20–49 µg/l) or severe (UIC <20 µg/l)(WHO, 2007a). These categories are used as epidemiological criteria for assessing iodine nutrition not only in school children, but also in other population groups. For pregnant women, median UIC<150 is considered to reflect insufficient iodine intake (Table 2.4-2).

Table 2.4-2 Epidemiological criteria for assessing iodine nutrition based on median iodine concentration of school-age children and pregnant women (WHO, 2007a)

Median UIC (μg/L)	Iodine intake	Iodine Status
School aged children		
<20	Insufficient	Severe iodine deficiency
20-49	Insufficient	Moderate iodine deficiency
50-99	Insufficient	Mild iodine deficiency
100-199	Adequate	Adequate iodine nutrition
200-299	Above requirements	Likely to provide adequate intake for pregnant/lactating women, but may pose a slight risk of more than adequate intake in the overall population
≥300	Excessive[1]	Risk of adverse health consequences
Pregnant women:		
<150	Insufficient	
150-249	Adequate	
250-499	Above requirements	
≥500	Excessive[1]	

[1] The term “excessive” means in excess of the amount required to prevent and control iodine deficiency.

2.4.2 Calculating dietary iodine intake

When quantifying the dietary intake of a nutrient, food consumption data are combined with data on concentration of the nutrient of concern in different food items. The measured and estimated dietary intake of the relevant nutrient is then compared with recommendations for nutritional intake based on currently available scientific knowledge.

There are several methods for measuring the dietary intake. The weighed food record and 24-hour recall methods are considered the most accurate method for precise assessment of nutritional intake.(Gibson, 2005) These methods require participants to record prospectively (food record) or recall retrospectively (24-h recall) all food consumed over a given time period (Gibson, 2005; Hjartåker & Veierød, 2013)

The weighted food record method require that all food and beverages that are consumed for a certain period (usually three to seven days) are weighted and recorded as accurate as possible. Generally, a large number of days are required to obtain the habitual diet of individuals, while fewer days are needed to obtain a population average (Hjartåker & Veierød, 2013; Thompson & Subar, 2013).

Only few food groups are found to contain substantial amounts of iodine (Dahl et al., 2004b). The variation in iodine intake between and within individuals is primarily explained by the choice of food and dietary habits (Brantsæter et al., 2013). The iodine concentration in foods and diets can also vary to some extent depending on environment and seasonal variables, which may lead to some inaccuracies for food items with large variation in iodine content (Dahl et al., 2004b).

Some decades ago, the milk produced in the summer had lower iodine than winter-milk due to cows grazing outside in the summer and eating less fodder and mineral salt (Dahl, Opsahl, et al., 2003). However, in recent years, the seasonal variation in iodine content of milk is largely subdued. This is explained by more use of fortified fodder also in the summer, which is now currently just about 10% lower than in winter and mineral concentrate is now provided to cows also during summer season (L. Nordang, personal communication April 19, 2016). The iodine values for milk and dairy products in the updated Norwegian Food Composition Table, are based on a number of analysed samples and the values represent the weighted mean of a range of analytical values (G, Waage, personal communication, April 19, 2016). According to the references given in the Norwegian Food Composition Table, these values have been provided by the dairy industry (The Norwegian Food Safety Authority, The Norwegian Directorate of Health, & University of Oslo, Undated)

The data on iodine concentrations in the Norwegian food composition table has been limited, but the number of data has increased in the last few years, and the latest update on data on iodine in the table was in November 2015 (The Norwegian Food Safety Authority, The Norwegian Directorate of Health, & University of Oslo, 2015). Given the relatively limited number of food items with reasonable high concentrations of iodine, estimating iodine intake based on food consumption data has been found to be relatively valid in Norway (Brantsater, Haugen, Julshamn, Alexander, & Meltzer, 2007).

It should be noted that the use of nutrient databases to calculate nutrient intake from food can be less precise for certain groups, like vegetarians, who often consume unconventional food items (Lightowler, 2009). The database may not contain complete information on the nutritional content of all foods likely to be consumed by this group, for example seaweeds.

Iodine contributed by dietary supplements and/or seaweed

For many decades, seaweeds were the primary source of iodine for medicinal purposes, and it is likely that seaweeds have been part of traditional diets of coastal dwelling peoples worldwide (Teas, Pino, Critchley, & Braverman, 2004a). However, despite being a cheap and natural source of iodine, seaweeds have been rather neglected in Europe and Norway (Duinker, 2014). Consequently limited data is available on the current seaweed products in Europe (Combet, Ma, Cousins, Thompson, & Lean, 2014).

The iodine content varies greatly both between and within seaweed species (Table 2.4-3) due to geographic location, season, preparation and storage conditions (Lightowler, 2009). A study in Norway, measuring the iodine level in some Norwegian seaweed (Duinker, 2014) found that particularly brown alga and sugar kelp had a high content of iodine with values ranged from 2000 to more than 4000 µg / g dry weight and correspondingly from about 300 to about 800 µg / g on the wet weight. Consequently, calculating the amount of iodine from dietary supplements and seaweeds in different forms is challenging.

It seems that the availability of iodine from kelp is far below 100%, which also makes it problematic to recommend how much one should eat for an adequate intake (Duinker, 2014). Previous analysis has also reported great variability of content of iodine in different supplements (Leung et al., 2009). Some kelp supplements and multivitamins/ minerals have been proven to contain very high doses of iodine with sometimes higher iodine content than reported by the product labelling (Leung et al., 2009).

In Norway there is regulations relating to food supplements, and the maximum iodine content pr. recommended daily dose in multivitamin/mineral tablets is up to 225 µg (Forskrift om kosttilskudd, 2004). However tablets and products with higher iodine content can be purchased on the internet.

There are no known benefits deriving of taking doses of iodine above the recommendations (150 µg/day) and “excessive” assumption should be discouraged, since it may cause adverse health effects (Prete, Paragliola, & Corsello, 2015). To the best of my knowledge, the use of iodine containing supplements among vegetarians in Norway has not previously been described.

Table 2.4-3 Iodine concentration in common edible seaweeds (Teas et al., 2004a) and seaweed collected in Norway in 2013 (Duinker, 2014)

Common edible seaweeds[5]	**Iodine (mg/kg) dry weight**
Arame (Eisenia bicyclis)	586
Dulse (Palmaria palmate)	72
Hijiki Sargassum fusiforme)	629
Kelp whole (Phaeophyceae)	1820
Kelp products-capsules, powder	3283
Kombu (Saccharina japonica)	1350
Nori (Pyropia)	16
Wakame (Undaria pinnatifida)	66
Iodine concentration in seaweed collected from Lindesnes, Norway 2013	
Brown alga (Laminaria digitate) [Norwegian: fingertare/brunalge]	2136 - 4375
Thin flat green alga, also called sea lettuce (Ulva lactuca) [Norwegian: grønnalge, havsalat]	60 - 288
Sugar kelp (Saccharina latissima), in Norwegian: sukkertare/brunalge	2103 - 3960
Red alga (Palmaria palmate) [Norwegian: søl/rødalge]	57 - 414

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[5] Provided samples from Canada, Tasmania, and Namibia

2.5 Rationale for the study

As outlined in the background section, in the scientific literature there is limited knowledge about iodine intake and status in Norwegian vegetarians. In this perspective, we conducted the present study with the objectives outlined in the next section.

3 OBJECTIVES

The overall objective of this study was to investigate iodine status in a group of Norwegian vegetarians by evaluating the calculated iodine intake and urinary iodine concentration. The data on iodine nutrition (intake and urinary concentrations) were examined in subgroups of vegetarians and compared with established national and international reference values for recommended intake. Due to vegetarians being more likely to have fewer sources of iodine in the diet, I specifically wanted to study to what extent vegetarians use supplements with iodine and how this contribute to total intake of iodine. The data on iodine nutrition, including iodine supplement use, in the vegetarian groups was also compared with a group of non – vegetarians.

The specific objectives of this thesis are:

1. To describe the calculated iodine intake from food in vegetarians, including the subgroups OPL-vegetarians and vegans, based on two days food records and compare the intake to established recommendations for iodine intake
2. To examine the contribution of different food sources to the iodine intake in vegetarians
3. To examine to what extent vegetarians use iodine containing supplements and how this contribute to total iodine intake and urinary iodine concentrations in vegetarians
4. To describe the urinary iodine concentrations in the vegetarians based on two morning urine samples and compare to WHO recommendations.
5. To examine the agreement between the calculated iodine intake and urinary iodine concentration by exploring the correlation
6. To compare the calculated iodine intake and urinary iodine concentration in vegetarians (total group) with a control group of non-vegetarians, including a comparison of iodine sources.

4 MATERIALS AND METHODS

4.1 Population and study design

The current master thesis is based on data from a cross-sectional study denoted Donexpo (experimental study of DeOxyNivalenol biomarkers in urine”). This is a collaborative study between partners in the United Kingdom, Italy and Norway initiated to provide data on dietary exposure and urinary metabolites of deoxinivalenol, a mycotoxin originating from cereals (Brera C et al., 2015). The Norwegian Institute of Public Health (FHI) and Norwegian Veterinary Institute were responsible for the Norwegian part of this study. Participants for Donexpo were recruited among employees of these two institutes. Information about the study, including contact information of internal project workers was posted on the internal intranet system within each institution. In order to include all subgroups, including vegetarians, potential participants were asked to extend the information to family and friends, and to pass on an information leaflet with the contact details on how to contact the project workers. A simplified information leaflet was developed and given to children. Donexpo was primarily conducted to investigate the levels of mycotoxins in urine, but the consent declaration specifically asked for permission to use the data for studies of other substances, including iodine.

A total of 257 participants were recruited to Donexpo. The study population included children (3-9 years), adolescents (10-17 years), adults (18-64 years), elderly (65+ years), pregnant women and vegetarians. The vegetarian group in Donexpo comprised 38 men and women. For the study of iodine we obtained permission from the Regional Committee for Medical and Health Research Ethics (REC South-East) to further recruit pregnant women and vegetarians from Oslo and Akershus University College of Applied Sciences (HiOA). The recruitment strategy at HiOA was similar to the strategy used for Donexpo and aimed to recruit students and employees (or members of their family) through information posted on the internal web site. Participants in Donexpo were recruited from late March 2013 to December 2014, and the participants from HiOA were recruited from August to September 2015. The second wave of recruitment resulted in the inclusion of 14 additional vegetarians, resulting in a final study population of n=52 vegetarians.

The participants were to be healthy, but other that this there were no exclusion criteria.

All participants were assigned a project participant number and all data have been handled anonymously.

The 52 vegetarians (age range 6-70 years) were identified based on their answers to the question about dietary practices and restrictions during the baseline interview (Appendix 1). Vegetarians were defined as those not consuming meat or poultry. They were further categorized as OLP-vegetarians (n=34) if milk/dairy and/or eggs and/or fish were included in the diet. Vegans (n=18) were defined as those omitting all animal products.

The reference group (n=67) was selected from among non-vegetarian, non-pregnant participants in Donexpo. All adults in the age group 18 to 49 years were used as controls (n=49). Of the remaining, 8 controls in the age group < 18 years and 10 controls in the age group 50 years or above were selected randomly (by SPSS) in order to obtain as comparable age distribution as possible between vegetarians and controls. No pregnant women were included in the control group as iodine status in the pregnant group was evaluated in another master project, while some of the same female controls were used in both this and the other master project. The final dataset in this project included 119 participants, i.e. 52 vegetarians and 67 controls (Table 4.1-1).

Table 4.1-1 Overview of the selection of participants

		All	Vegetarians	Controls
Sample	n	n	n	n
Participants recruited to Donexpo	257		38	
Additional participants recruited at (HiOA)	19		14	
Total participants recruited		**276**	**52**	**184**
Included all non-pregnant omnivores 18-49 years				49
Included (age –matched)[1]				18
Excluded pregnant group[2]		40		
Excluded (age –matched)[1]		117		
Final selection		**119**	**52**	**67**

[1] Selected by random sampling in youngest and oldest age group (by SPSS)
[2] Participants to be described in another master thesis

4.2 Data collection

During an initial meeting, those interested in the study were given a leaflet and oral information about the aim of the study and the specific tasks they had to carry out if they consented to participate. A separate information leaflet for children were given to parents to use when talking to the children they were willing to include in the study. All participants were informed about the right to withdraw from the study at any time. After signing the informed consent (Appendix 2), each participant was asked to answer some basic questions about food habits. These questions were asked as a structured interview (Appendix 1). The information included age, gender, smoking habits, food restrictions, physical activity, and self-reported weight and height. Body mass index (BMI) was calculated from weight and height as kg/m^2. Participation recruited to the study were asked to record all food, beverages and dietary supplements for two whole days in an open diary, and to provide a fasting morning spot urine on the day following each recorded day (i.e. 2 morning urine samples). They were also asked to provide information about demographic and lifestyle variables. The data collection could be carried out either on consecutive days or non-consecutive days, and the majority of participants did so on consecutive days.

Most participants possessed a digital kitchen scale and were asked if they could weigh all food items when possible, and when not possible (e.g. eating out of the house) to describe each consumed item or food portion in terms of household measures. The few participants who did not possess kitchen scales were asked to report all in terms of household measures (e.g. one medium slice of bread, two large slices of cheese etc).

Pregnant participants were asked about which gestational week they were in and vegetarians were asked how long they had followed a vegetarian diet. Each participant signed a consent declaration (see Appendix 2). Parents signed for their children, while adolescents were asked to sign in addition to a parent. All participants were then given detailed description of what the data collection entailed and they were giving an open food diary and equipment (0.5 L wide neck bottles) for collecting the urine samples (bottles depicted in Figure 4.2-1).

4.2.1 Assessment of dietary iodine intake

All participants were given an open food diary and information on how to record all food and drink items (see Appendix 3). They were also required to report the intake of all dietary supplements by name and manufacturer (if possible). The diary was self –administrated and the food items were to be quantified in grams (or ml). When a kitchen scale was not available, participants were asked to report in household measures (cups, glasses, etc.) and to give an estimate of the portion size (big, small etc). For mixed dishes, the name of the dish and a list of single ingredients were to be recorded in addition to the total weight or household measure.All completed food diaries were returned to the Norwegian Institute of Public Health.

Every food and drink items in all food diaries were manually coded by two master students. One by one, the food item were assigned the food number used in the Norwegian Food Composition Table “Matvaretabellen” (version 2015), which is a database containing 1543 food items (The Norwegian Food Safety Authority et al., 2015). If the food item described by the participants was not present in the Food Composition Table, it was substituted by a similar food item in consultation with a qualified person. The data regarding iodine concentrations in Norwegian food items has been corrected and expanded in recent years. The last update was done in October 2015 and used for calculating iodine intake from food. For food items with missing information on iodine concentration in Food Composition Table, data for comparable items were used, and a protocol created for this purpose (Appendix 4). Likewise, data was imputed for mixed dishes containing iodine.-rich food items such as pancakes, dairy-desserts and mixed fish dishes using standard recipes.

For one participant at the time, all food numbers and the amount of food consumed (in grams) were entered into an Excel-file. A diet planner calculation program, developed by the Norwegian Directorate of Health and the Norwegian Food Safety Authority was used (Kostholdsplanleggeren, 2014) for conversion into gram when only household measures or portion sizes were reported. The final calculation of nutrients, including iodine was done using the free online nutrient calculation program FoodCalc (Lauritsen, 2010) to combine food consumption amounts with nutrient concentrations in the Food Composition Table (The Norwegian Food Safety Authority et al., 2015).

4.2.2 Assessment of iodine from supplements and seaweed

The amount of iodine from dietary supplements reported in the food diaries were coded based on brand name and dose. For some brands of seaweed, e.g. wakame and some of the kelp, information about iodine concentration was not available and we searched for information on web-sites. Nori is listed in the Food Composition Table and was therefore coded as a food item and not a supplement.

For obtaining the total iodine intake we summed iodine contributed by food with iodine contributed by iodine-containing dietary supplements.

4.2.3 Assessment of urinary iodine concentration (UIC)

Participants were given two 0.5 L plastic bottles with wide opening and screw capped double lids for collecting morning spot urine samples (Figure 4.2-1). Urine samples were fasting spot morning urines and taken in the mornings following a full day of diet recording. The bottles with the urine samples were stored in a refrigerator (4°C) by participants until they were brought back to the respective work place or collected by a project worker who distributed the sample into vials for storage at -20 °C until analysis. All urine samples were returned to the Norwegian Institute of Public Health, Oslo.

Vials containing urine from each sampling day (two samples per participant) were packed in dry ice and shipped by courier to the National Institute for Health and Welfare, Helsinki, Finland for iodine analysis. The method for analysing urinary iodine concentrations was a microplate method based on the Sandell-Kolthoff reaction. In brief, ammonium persulfate digestion was performed in a polypropylene microplate in an oven at 91 ^{o}C for 90 min. After the digestion, part of the mixture was transferred to a transparent polyethene microplate and the Sandell-Kolthoff reaction was performed for 40 min. Urinary iodine was measured by a Thermo Scientific Varioskan flash microplate reader at 405 nm. The limit of quantification (LOQ) is 20 µg/l. The result is expressed as µg/l.

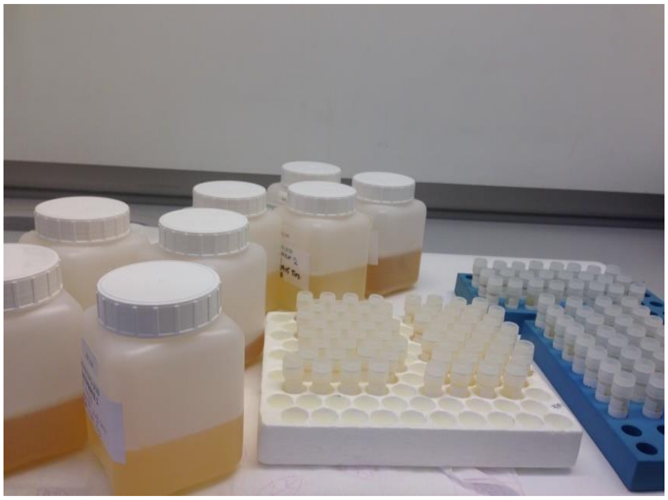

Figure 4.2-1 *Urine samples were returned to the Norwegian Institute of Public Health. Each large bottle (representing one morning urine) was distributed into smaller vials in preparation for storage and later shipment to other laboratories of analysis of iodine and creatinine.*

In order to evaluate urinary iodine while taking hydration status into account, the urine samples were also analysed for creatinine. Creatinine is a metabolic product from muscle tissue creatinine (Puri., 2014). In healthy individuals, the rate of creatinine clearance is relatively constant and iodine is often corrected for creatinine by expressing the concentration of iodine as µg/g of (Soldin, 2002).

Urine creatinine concentration was analysed at the Department of drug analysis (Norwegian Institute of Public Health) according to an accredited method using a colorimetric assay (modified kinetic Jaffe method) on a Beckman Coulter AU680 analyser (Thermo Fisher Scientific, Undated). The limit of quantification was 0.2 mml/L. In brief, the method is based on a reaction with alkaline picrate forming a red-orange complex. The colour intensity is directly proportional to the creatinine concentration and is measured spectrophotometrically at 505nm.

The result for creatinine concentration is expressed as mmol (mmol/L). Molecular weight is 113.12 g/mmol corresponding to 0.11312 g/mmol. To have creatinine expressed as g/L, the concentrations must therefore be multiplied with 0.11312 g/mmol.

4.3 Ethical considerations

Application for approval of the project and for recruiting additional participants in 2015 were sent to and approved by the Regional Committee for Medical and Health Research Ethics (REC South East) (see Appendix 5 and 6). The main reason for extending the recruitment was to include more vegetarians and pregnant women in order to obtain larger sample size for these special groups, which would strengthen the scientific value of the data. It was pointed out in the application that this is considered prudent because this data collection involves a relatively small burden for participants.

Like participants recruited for Donexpo, the participants recruited at HiOA signed an informed consent and received the information leaflet in Norwegian, and was made aware of their right to withdraw from the study at any time if desired. All data was treated in a non- identifiable way. Sensitive information has been stored in locked cabinets. For the children participating in the study, consent was provided by the parent of the child taking part in the study. Examples of documents (Ethics Approval and Informed Consent) are reported in Appendix 6 and 2

Research participants will not receive financial compensation.

4.4 Data processing and statistical analyses

Processing of the data was done in the calculation program Excel (Microsoft Office Excel 2010) and the statistical programme SPSS 21 (SPSS Inc, IBM Company, Chicago, Illinois, USA). The variables reflecting iodine intake and urinary concentrations were examined for normal distribution using visual plots. While iodine intake from food was approximately normally distributed, the urinary concentrations were not and consequently non-parametic test were used in all the analysis. This is considered safer also in term of comparison between small groups.The data was presented as median and 25th and 75th percentiles and proportions as percentages. However due to the incapability of summarizing median values, mean values were given when the contribution of the different food sources were described. For analysis of continuous values, the Mann Whitney *U* test was used for two- group comparison. Wilcoxon Signed Rank test was applied to check if there was a difference between the two days regarding calculated dietary intake and urinary iodine concentration. The test showed that there was no statistical difference between the days/ urine samples and thus the mean of the two days where used in all tests.

To investigate the correlation between urinary iodine concentration and dietary analysis, the Spearman`s rank correlation coefficients was chosen. To compare the categorical values, the Chi Square test was used. All *p* values were two- sided and a 5% significance level was used.

5 RESULTS

5.1 Description of study participants

Background characteristics of the participants are presented in Table 5.1-1. Those participants in the source population who reported that they considered themselves vegetarians were included in the present study. This was true for 52 persons of which 34 (65%) included eggs (n=13) and/or dairy-products (n=30) and/or seafood (n=5) and were denoted ovo-lacto-pesco- (OLP) vegetarians, while 18 excluded all animal products and were denoted vegans. Of the OPL-vegetarians, 16 included only dairy products, two included only eggs, and two included only seafood, while 16 had combinations. None of the OPL vegetarians included all; dairy, eggs and fish. As described in the methods section, a total of 67 participants were selected from the study populations as a control group. The control group comprised non-vegetarian males and women (denoted omnivores) selected as far as possible to be of comparable age as the vegetarians. Comparison of background characteristics of the study participants showed that the vegetarian group included a larger proportion of women and a larger proportion of iodine supplement users, while other characteristics did not differ (Table 5.1-1).

Table 5.1-1 Distribution of background characteristics of the vegetarian participants (including both OLP-vegetarians and vegans) and a non-vegetarian control group (omnivores)

Characteristics of participants	**Vegetarians n (%)**	**Omnivores n (%)**	***P* value**
Subjects: n (%)	52 (44)	67 (56)	
Sex:			*0.024*
Female	37 (71)	34 (51)	
Male	15 (29)	33 (49)	
Age (years)			*0.084*
<18	4 (7.7)	8 (12)	
18-34	25 (48)	17 (25)	
35-49	18 (35)	32 (48)	
50+	5 (9.6)	10 (15)	
BMI (kg/m2)[a]			*0.996*
<18,5	6 (12)	8 (12)	
18,5-24.9	33 (64)	42 (63)	
25+	13 (25)	17 (25)	
Smoking n (%)			*0.267*
No	47 (90)	64 (96)	
Yes	5 (9.6)	3 (4.5)	
Iodine supplement use			
No	41 (79)	65 (97)	*<0.001*
Yes	11 (21)	2 (3)	
Physical activity			
Very low	2 (3.8)	2 (3.0)	*0.987*
Low	18 (35)	22 (33)	
Moderate	25 (48)	34 (52)	
High	7 (14)	9 (13)	

[a] BMI calculations are based on WHOs BMI classifications for adults (WHO, 2006)

Characteristics of the two vegetarian subgroups

Comparison of participant characteristics within the vegetarian group showed that OLP-vegetarians were older than the vegans (mean age 37 versus 30 years, *p*=0.010), and the OLP vegetarians included a larger proportion of males (38% vs 11%, *p*=0.04). There were no differences between the groups with regard to iodine supplement use, BMI or smoking (p>0.05) (Table 5.1-2).

Table 5.1-2 Background characteristics of the two vegetarian subgroups

Characteristics	**OLP- vegetarians n (%)**	**Vegans n (%)**	*P* value
All	34 (65)	18 (35)	
Sex:			*0.040*
Female	21 (62)	16 (89)	
Male	13 (38)	2 (11)	
Age (years)			*0.002*
<18	4 (12)	0 (0)	
18-34	10 (29)	15(83)	
35-49	15 (44)	3 (17)	
50+	5 (15)	0 (0)	
BMI (kg/m^2)[a]			*0.935*
<18.5	4 (12)	2 (11)	
18.5-24.9	21(62)	12 (67)	
25+	9 (27)	4 (22)	
Smoking			*0.576*
No	30 (88)	17 (94)	
Yes	4 (12)	1 (6)	
Supplements[b]			*0.395*
No	28 (82)	13 (72)	
Yes	6 (18)	5 (28)	

[a] BMI calculations are based on WHOs BMI classifications for adults (WHO, 2006)
[b] Iodine containing supplements use

5.2 Estimated intake of iodine from food and iodine-containing supplements

The calculated intake of iodine from food did not differ significantly between day 1 and day 2 in either OLP-vegetarians [median day 1: 82 µg, median day 2: 82 µg (*p*= 0.68)] or vegans [median day 1: 25 µg, median day 2: 20 µg (*p* = 0.33)]. Spearman correlation coefficient for calculated iodine intakes on the two days was 0.5 in both groups. Therefore the mean iodine intake for the two days was used in all further analyses.

In order to distinguish between food and supplements as iodine sources, we examined the OLP-vegetarians and vegans separately and found that the iodine intake from food was particularly low in vegans, and was significantly lower in this group than in OLP–vegetarians (Table 5.2-1).

Table 5.2-1 Iodine status according to calculated iodine intake from food, total intake (diet and supplements) and iodine intake estimated from UIC in the two groups of vegetarians (OLP–vegetarians and vegans)

Iodine status	OLP– vegetarians (n=34)			Vegans (n=18)			Difference OPL-vegetarians and vegans
	Median	P25[1]	P75[1]	Median	P25[1]	P75[1]	*p-value*
Intake from diet (µg/day)	89	48	144	24	15	46	<0.001
Total iodine intake[2] (µg/day)	124	81	195	50	15	97	0.003
Iodine intake estimated from UIC[3] (µg/day)	108	57	170	52	43	139	0.102

[1] 25th and75th percentile

[2] Iodine from food and iodine containing supplements

[3] Estimated from the equation: daily iodine intake =UIC (µg/L) x 0.0235 x bw (kg) (Institute of Medicine (US), 2001)

The median calculated iodine intake from food differed significantly between the OLP–vegetarians and vegans (*p<0.001)* (Table 5.2-1). Likewise, when the calculated amount of iodine from iodine containing supplements was included, the vegan group still had a statistically significant lower intake than the OLP–vegetarians (*p*=0.003) (Table 5.2-1). However, when iodine intake was estimated from urinary iodine concentration [UIC*0.0235 x weight (kg)(Institute of Medicine, 2001)] the estimated median intakes were 108 µg/day and 52 µg/day in OLP–vegetarians and vegans respectively (Table 5.2-1), and this difference was not significantly different.

Distribution of the calculated iodine intake from food in the vegetarians

The distribution of calculated iodine intake from food sources showed that in total 78 % of the vegans had intake <50 µg/day, and none the vegans reached the WHO/NNR recommendations for iodine intake based on calculated food intake (Figure 5.2-1). In the OLP- vegetarians, only 24% reached the 150 µg/day recommendation for iodine intake from WHO and NNR.

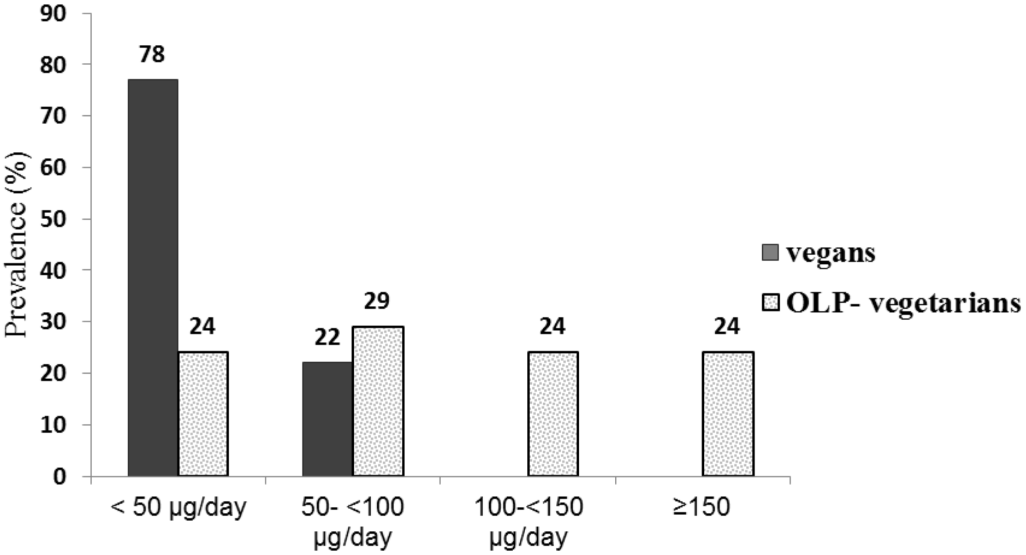

Figure 5.2-1 *Frequency of distribution of iodine intake (µg/day) from diet in the two vegetarian groups given in percentage.*

5.2.1 *The contribution from different food groups*

The mean contribution from different food groups to the calculated iodine intake is shown in Figure 5.2-2. Milk and dairy products is the main dietary source of iodine in the OLP-vegetarians (61%). In the vegan group, iodine from food were from three sources primarily; dishes and ready products (38 %), vegetables, fruit and berries (27%) and cereals and nuts (23%). It should be noted that the mean total intake (100%) differed and was 106 µg/day in the OLP-vegetarian group and 32 µg/day in the vegan group.

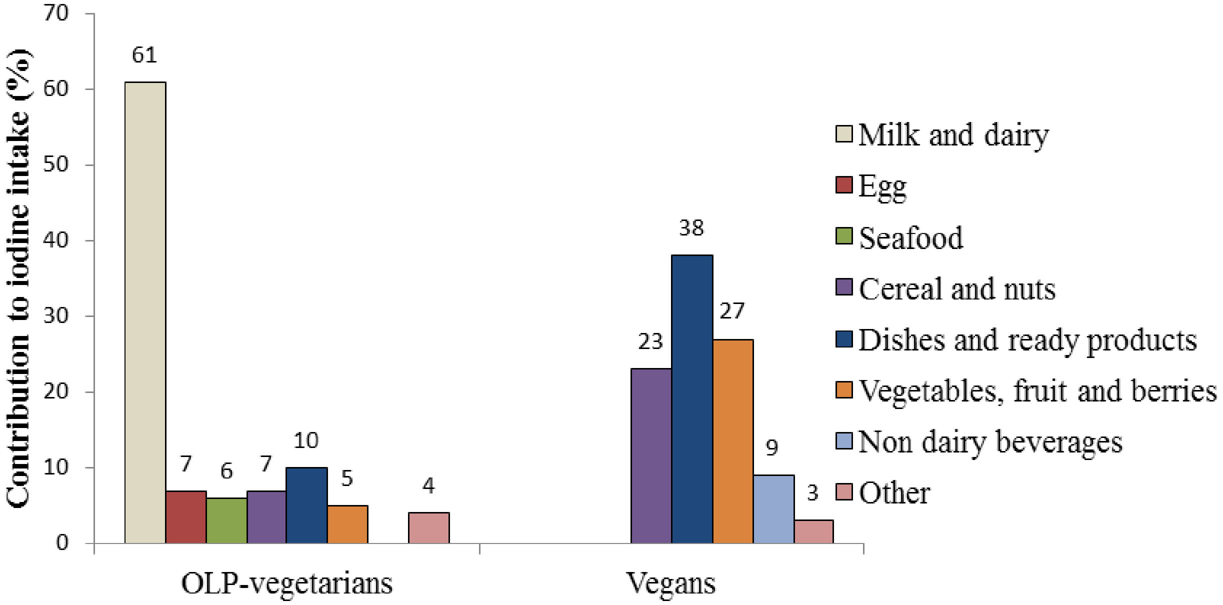

Figure 5.2-2 *Mean contribution of iodine from different food groups in OLP-vegetarians (n=34) and vegans (n=18) based on the two days of food records.*

5.2.2 *Calculated iodine intake from supplements*

In the group of OLP-vegetarians, 18% of the participants used iodine containing supplements (n=6). The median intake of iodine in the OLP vegetarians increased by 39% when adding the amount of iodine from supplements (up from 89 µg/day to 124 µg/day) (Table 5.2-1). When iodine from supplements was added, the proportion of participants that reached the recommendation by WHO/NNR increased from 24% to 38% (Figure 5.2-3). However, 62% still had an intake lower than150 µg/day (38% ≥ 150 µg/day).

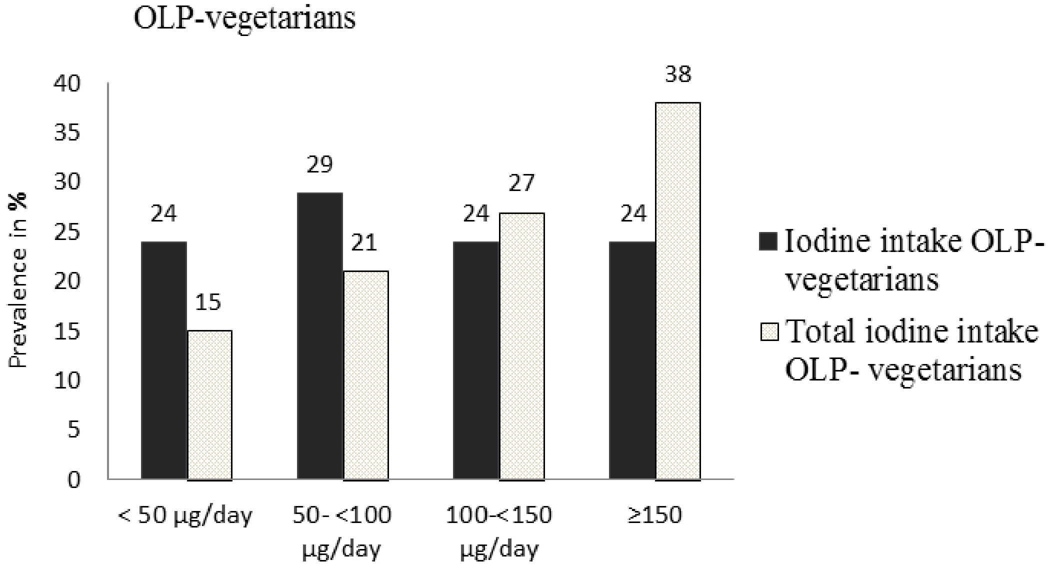

Figure 5.2-3 *Frequency of distribution of iodine intake from food alone and total iodine intake from diet and iodine containing supplements) (µg/day) in the OLP-vegetarians. Prevalence is presented as percentage.*

In the vegan group 28% (n=5) reported use of iodine containing supplements. Based on the calculated iodine intake, the median intake in the vegans increased by 108% from 24 µg/day to 50 µg/day (Table 5.2-1) when iodine from supplements where added.

The most commonly used supplements among the vegetarians were multivitamin/mineral supplements, and various kelp supplements. One person used wakame. Mineral supplements used by participants in this current study were one of the two following products: Veg 1 (a product designed specifically for vegans) or Nycomed Multi. Both these products specified on the bottle to contain 150 µg of iodine.

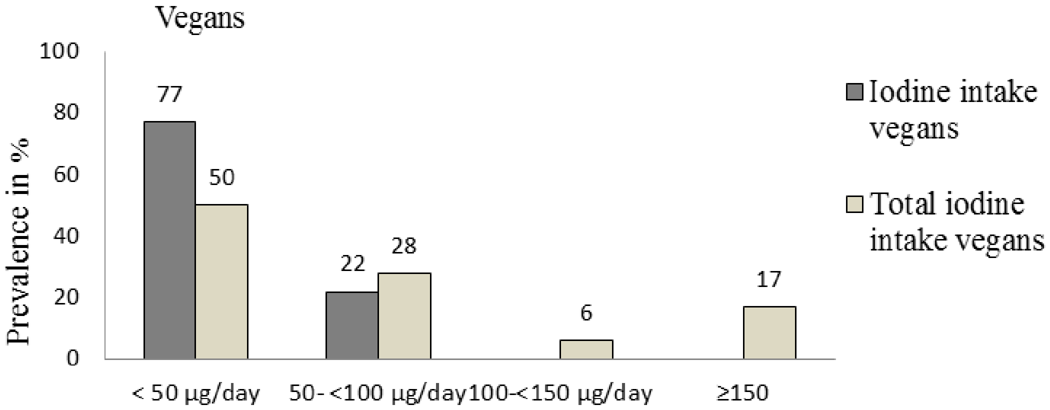

Figure 5.2-4 *Frequency of distribution of iodine intake from food alone and total iodine intake from diet and iodine containing supplements) (µg/day) in the vegan group. Prevalence is presented as percentage.*

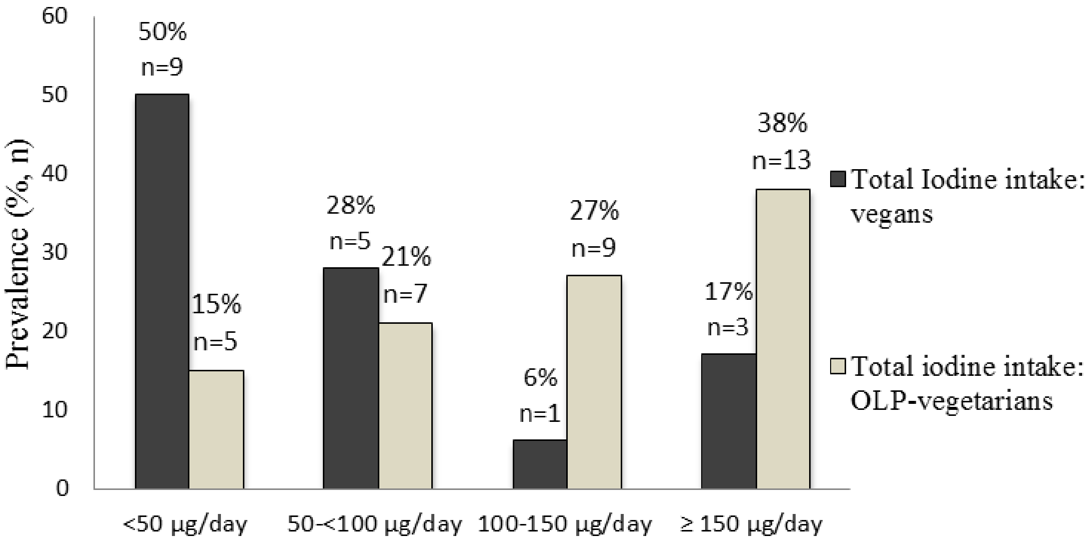

Figure 5.2-5 *Frequency of distribution of total iodine intake (µg/day) (from diet and iodine containing supplements) in the two vegetarian groups. Prevalence is presented as percentage and number of participants in each group.*

The iodine sources in Figure 5.2-2 included only foods. Including iodine supplements among the sources (Figure 5.2-6) showed that milk and dairy products were still the predominant iodine source in the OLP-vegetarians (on average contributing 48 % of the iodine supply). In this group, iodine containing supplements contributed with 23% to the total intake. In the vegan group, the supplements contributed with more than half of the daily iodine intake (58%) (Figure5.2-6). Again it should be noted that the mean total intake (100%) differed. The mean total iodine intake (100%) from food and supplements was 135 µg/day in the OLP- vegetarian group and 77 µg/day in the vegan group.

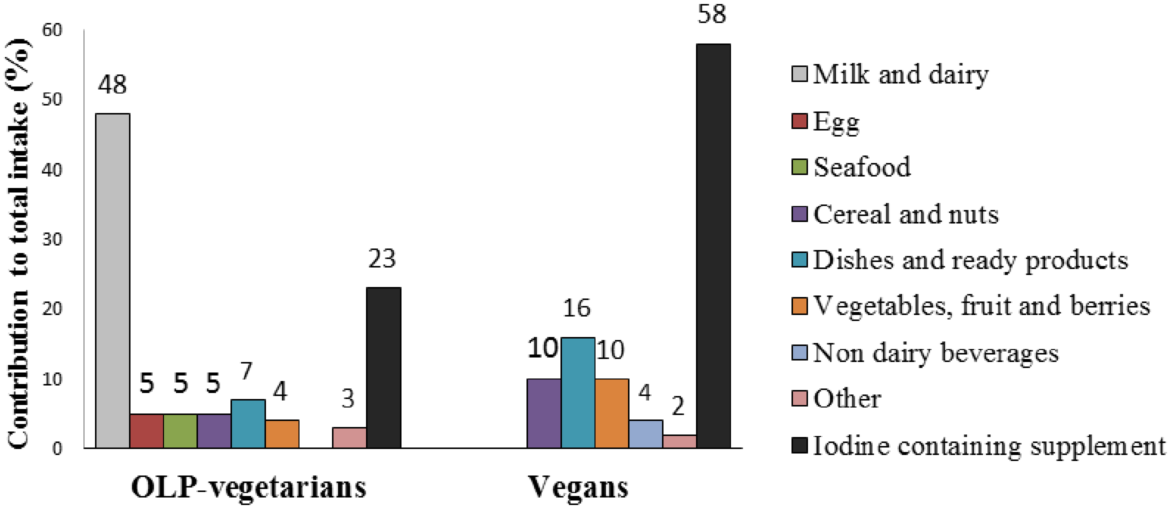

Figure 5.2-6 *Mean iodine intake from different food sources and supplements in OLP-vegetarians and vegans relative to the total intake in the two groups.*

Taking iodine from supplements into account (Figure 5.2-7), 11 % of the vegans, and 35% of the OLP-vegetarians reached the recommended intake of iodine, and 6% of vegans and 3% of OLP-vegetarians had higher than recommended intake (≥300 µg/day).

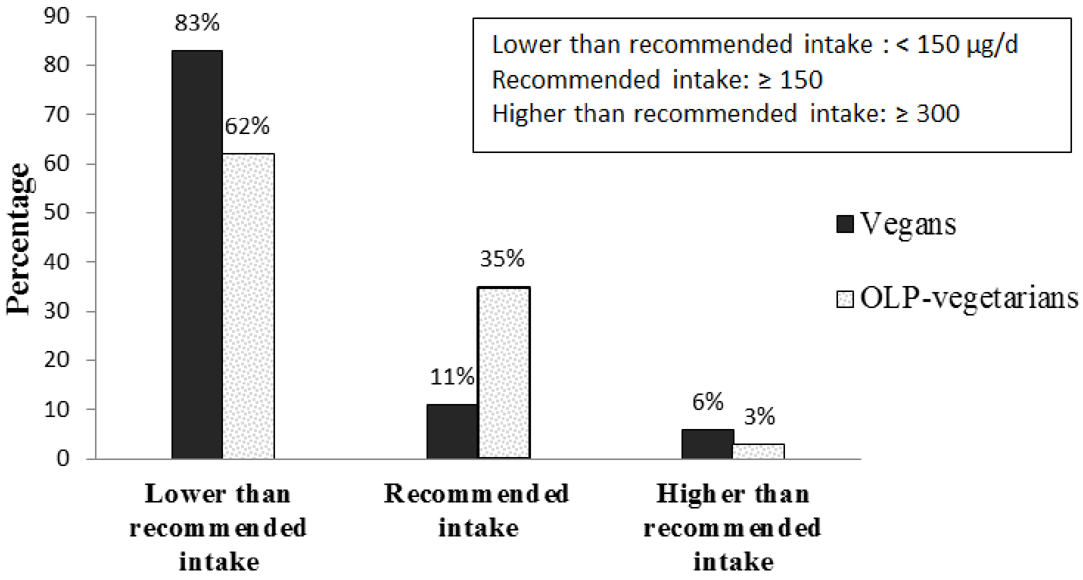

Figure 5.2-7 *Total iodine intake (from food and supplements) categorized according toWHOs classifications in the two groups.*

In the vegetarians as a whole there were 11 supplement- users and 73% of these reached the recommended intake for iodine. For the 41 vegetarians who did not use iodine containing supplements, only 20% had intakes ≥ 150µg/day (Figure 5.2-8).

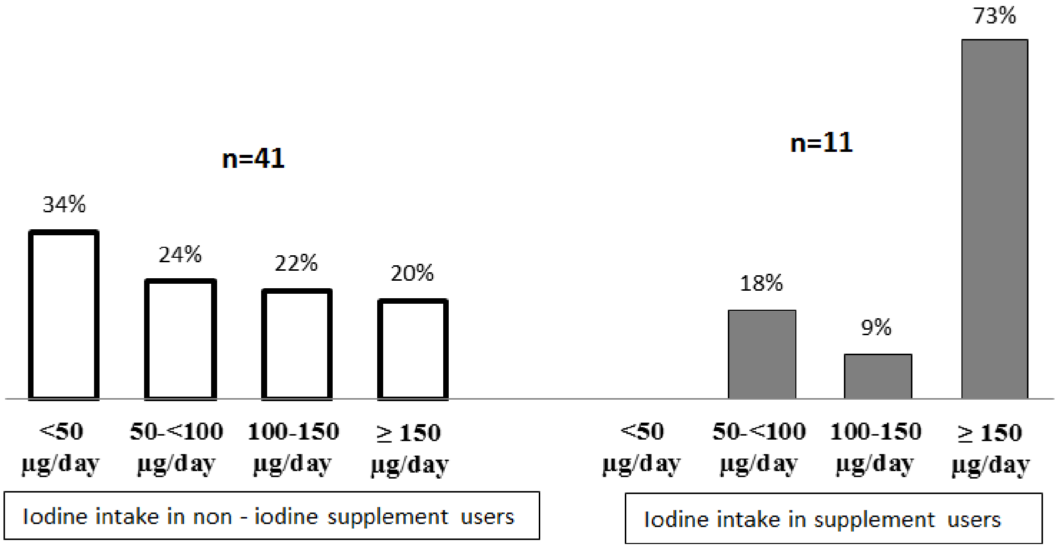

Figure 5.2-8 *Non- supplement users versus supplement- users of all the vegetarians.*

5.3 Urinary iodine concentration

The median urinary iodine concentration in the morning spot urines did not differ significantly between day 1 and day 2 in either OLP vegetarians [median day 1: 62 µg/L, median day 2: 69 µg (*p*= 0.57)] or vegans [median day 1: 39 µg/L, median day 2: 34 µg/L (*p*= 0.15)] and the mean UIC for the two days was used in all further analyses.

The median urinary iodine concentration (µg/L) was 73 µg/L in the OLP- vegetarians and 39 µg/L in the vegans. The difference was not statistically different (*p*= 0.098). The distribution is shown in Table 5.3-1. After adjusting for creatinine the median UIC value in the OLP-vegetarians decreased 62 µg L/g cre, and in the vegan group increased to 45 µg L/g cre. The difference was still not statistical significant *(p*= 0.155).

Table 5.3-1 Iodine status based on UIC (µg/L) and iodine/creatinine ratio (µg L/g creatinine)

Iodine	**OLP-vegetarians (n=34)**			**Vegans (n=18)**		
status	Median (min,max)	P25[1]	P75[1]	Median (min,max)	P25[1]	P75[1]
UIC µg/L[a]	73 (10, 1348)	36	101	39 (10, 784)	25	68
µg I/g cre[b]	62 (8, 3097)	49	94	45 (14, 2877)	34	83

[1] 25th , 75th percentile

[a] Mean UIC from the two morning spot urine samples

[b] iodine/creatinine ratio (µg I/g creatinine)

According to WHOs criteria for assessing iodine nutrition based on UIC, 72% of the vegans and 74% of the OLP-vegetarians have mild to moderate iodine deficiency, and 12% of the vegans and 21% of OLP-vegetarians have adequate iodine intake (Figure 5.3-1).

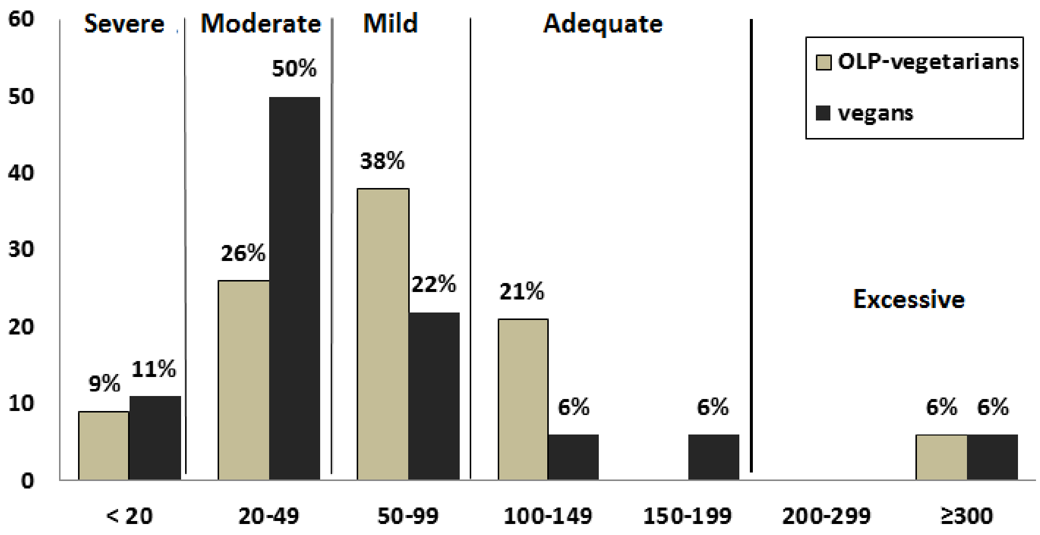

Figure 5.3-1 *Urinary iodine concentration (µg/L) and prevalence of iodine deficiency in OLP-vegetarians and vegans categorized according to WHOs criteria for assessing iodine nutrition (WHO, 2007.*

Use of iodine-containing supplements contributed significantly to UIC in vegetarians group, with median UIC of 52 µg/L in non-supplement and 102 µg/L in supplement users (*p*=0.016). When looking at the vegetarian subgroups, the difference in UIC between non-supplement and supplement users was statistically significant in OLP-vegetarians, with median UIC being 65 µg/L and 111 µg/L, respectively (*p*=0.047). In vegans, the median UIC was 37 µg/L in non-supplement users and 101 µg/L in iodine supplement users, but the difference was not statistically different (*p*=0.173)

The distribution of UIC was skewed and surprisingly high concentrations were observed in some of the supplement users (Figure 5.3-2).

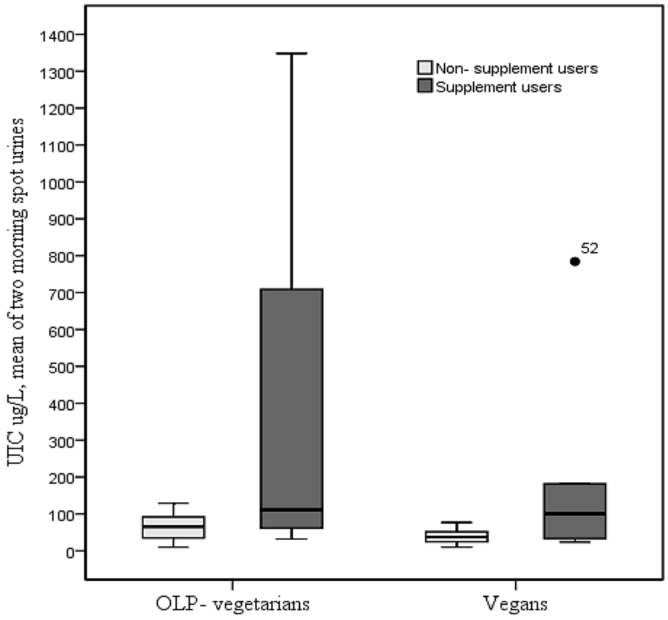

Figure 5.3-2 *Box plot showing the median UICµg/L (the horizontal line) in vegans and OLP-vegetarians, users and no-users of iodine containing supplements. The box indicates the interquartile range (IQR) of 25th to 75th percentile; the whiskers represent observations within 1.5 times the IQR. The dot represents the observations more than 1.5 times the IQR away from the box (outliners)*

A total of 7 participants had UIC > 300 µg/L, four omnivores and three vegetarians. More details of foods and supplements intake in these participants are presented in Table 5.3-2.

Table 5.3-2 Details of the seven participants with UIC >300 µg/L

Participant ID, sex and age	**Dietary practice**	**Iodine from food, µg/day**	**Iodine from supplements, µg/day**	**Urinary iodine, µg/L**	**Comments**
13, female 27 years	Omnivore	212	----[1]	317	High urinary creatinine (2.0 g/L)
22, female 16 years	Omnivore	83	150	363	1 Nycoplus Multi both days
29, male 35 years	Omnivore	76	300	487	4 Nycoplus Multi on day 2
149, female 16 years	Omnivore	36	----[1]	473	High urinary creatinine (1. 9 g/L)
301, female 47 years	OLP-veg	50	250[2]	1348	Liquid Kelp
302, male 11 years	OLP-veg	37	235[2]	708	Liquid Kelp
313, female 41 years	Vegan	29	200[2]	784	Kelp

[1] Did not report use of iodine containing supplements

[2] Based on information on the product label

The distribution of UIC in the 112 participants with UIC<300 confirmed low iodine intakes in the majority of both vegetarians and omnivores (Figure 5.3-3).

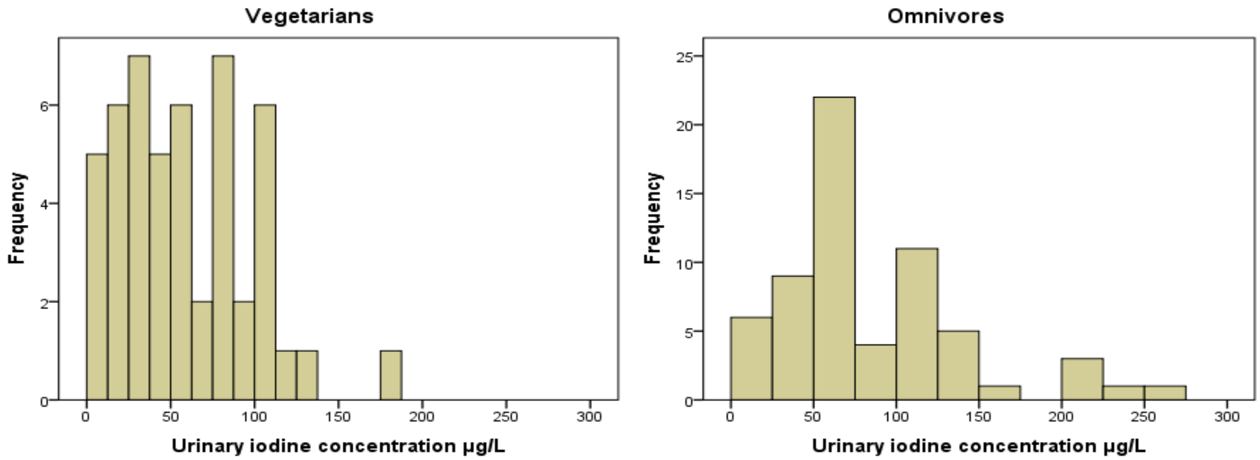

Figure 5.3-3 *Histograms illustrating the urinary iodine concentrations (mean of two morning urines) in the groups of vegetarians (n=49) and omnivores (n=63) after exclusion of 7 subjects with UIC> 300 µg/L.*

5.4 Exploration of correlation between iodine intake and UIC

We did not find a significant correlation between calculated iodine intake from food and urinary iodine concentration in either of the groups (OLP-vegetarians Spearman rho: 0.29 (p= 0.098), vegans Spearman rho: 0.27 (p=0.274)).

However, when including the amount of calculated iodine from the iodine containing supplements to the calculated iodine intake from food, the Spearmans rho was 0.67 (*p*= <0.001) for the OLP- vegetarians (Figure. 5.4-1). The correlation was borderline significant in the vegan group, with Spearmans rho 0.45 (*p*= 0.07) (Figure 5.4-2).

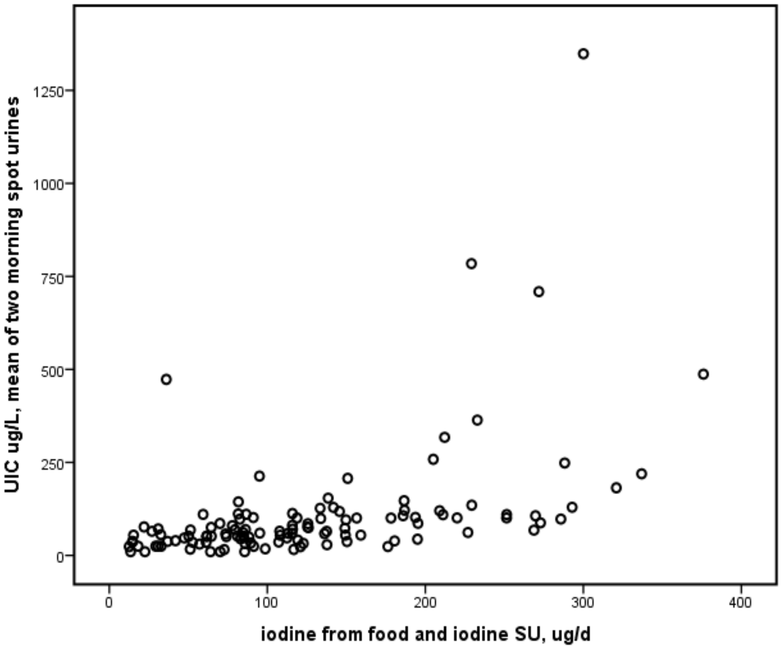

Figure 5.4-1 *Scatter plot illustrating the correlation between urinary iodine concentration (µg/L)(y axis) and total iodine intake (food and supplements)(µg/day) in OLP- vegetarians (n=34).*

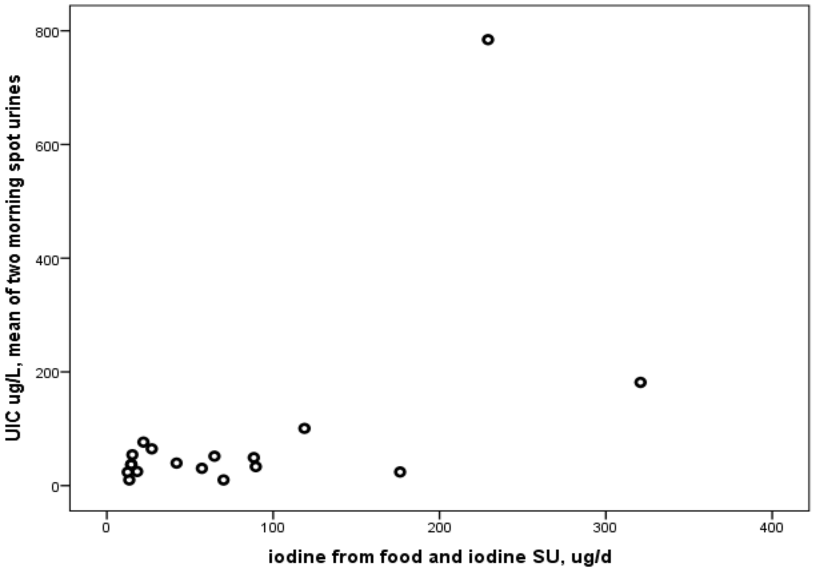

Figure 5.4-2 *Scatterplot illustrating the correlation between and urinary iodine concentration (µg/L) (y axis) and total iodine intake (food and supplements) (µg/day) in vegans (n=18).*

Adjusting UIC for creatinine concentration resulted in comparable correlations as for unadjusted UIC in both groups (Scatter plot not shown for creatinine adjustment) (Table 5.4-1). The strongest correlation was observed for total iodine intake with unadjusted UIC in the OPL-vegetarians (rho=0.67; 95%CI: 0.43-0.82).

Table 5.4-1 Correlation between intake from food, total iodine intake (food and supplements combined) and UIC with and without creatinine adjustment in OLP-vegetarians and vegans

Correlations Spearman's rho	**UIC µg/L**[a] (OLP-vegetarians)	**UIC µg/L**[a] (vegans)	**µg L/g cre**[b] (OLP-vegetarians)	**µg L/g cre**[b] (vegans)
Iodine intake from food, µg/day, mean of the two days	r = 0.29 (*p*= 0.090)	r = 0.27 (*p*= 0.270)	r = 0.19 (*p*=0.274)	r = 0.32 (*p*= 0.194)
Iodine from food and iodine - containing supplements, µg /d mean of the two days	r = 0.67 (*p*<0.001)	r = 0.44 (*p*= 0.071)	r = 0.54 (*p*=0.001)	r =0.42 (*p*= 0.081)

[a] Mean UIC from the two morning spot urine samples
[b] iodine/creatinine ratio (µg L/g creatinine).

5.5 Comparisons between vegetarians and omnivores

5.5.1 Calculated iodine intake in vegetarians and omnivores

The control group comprised 67 omnivores men and women described in Table 5.1-1 (page 37). The calculated median iodine intake from food was 64 µg/day in vegetarians (OLP-vegetarians and vegans combined) and 113 µg/day in the control group (omnivores). The calculated iodine intake from food was statistically higher in omnivores than in vegetarians (*p*< 0.001). The distribution of iodine intake from food in the two groups is shown in Figure 5.5-2 (page 54).

The median total iodine intake (food and supplements combined) was 90 µg/day in vegetarians and 113 µg/day in omnivores. Contrary to iodine from food only, the difference in total iodine intake did not differ between vegetarians and omnivores (*p*=0.208).

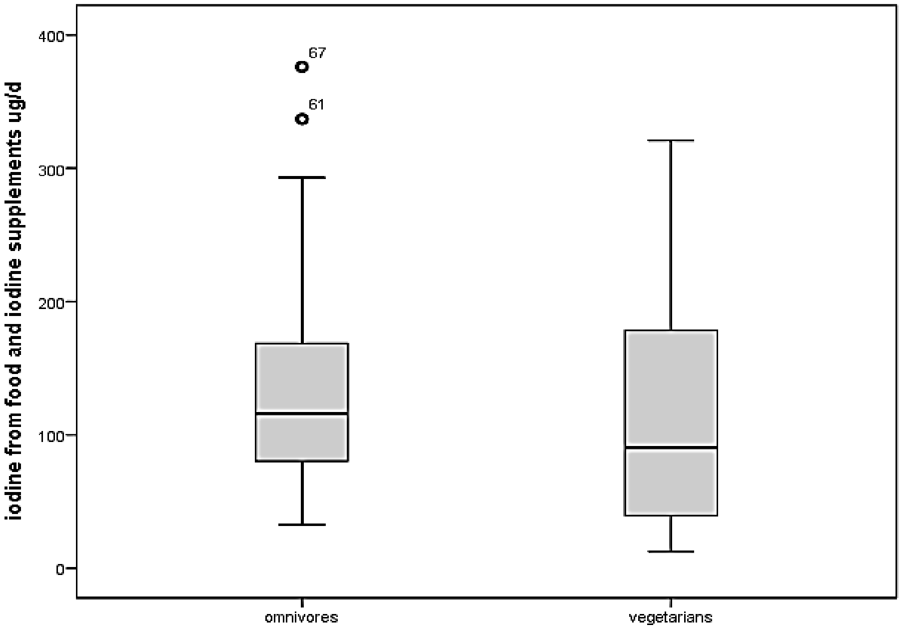

Figure 5.5-1 *Total iodine intake (food and supplements combined) in omnivores and vegetarians. The box indicates the interquartile range (IQR) of 25th to 75th percentile; the whiskers represent observations within 1.5 times the IQR. The dot represents the observations more than 1.5 times the IQR away from the box (outliners)*

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Food groups contribution to iodine intake in vegetarians and omnivores

Comparison of food groups as sources of iodine in vegetarians (OLP-vegetarians and vegans combined) and omnivores shows that 'milk and dairy products' is the major contributor in both groups (Figure 5.5-2).

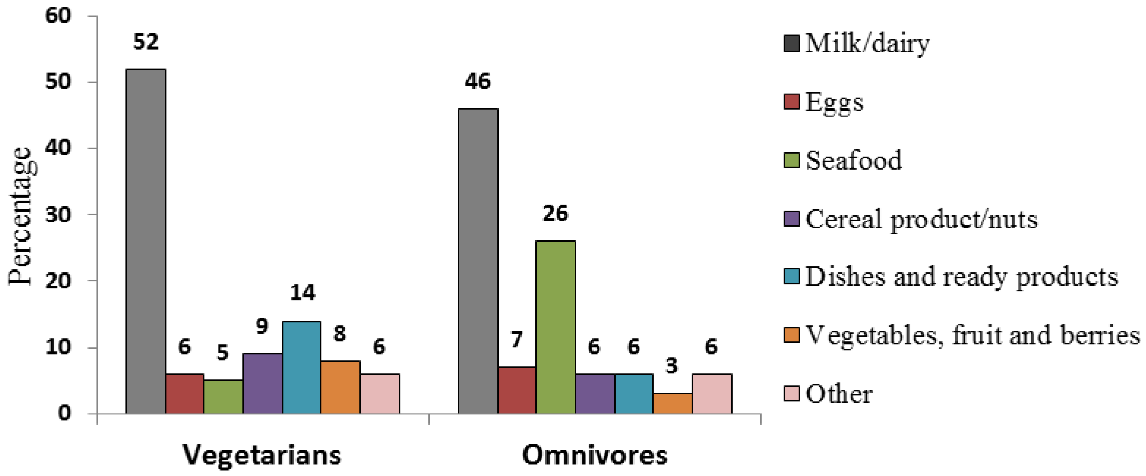

Figure 5.5-2 *Mean contribution to iodine intake from different food sources in vegetarians (n=52) and omnivores (n=67).*

The average quantitative contribution to iodine intake from milk and dairy products was 42 µg/day in vegetarians and 59 µg/day in omnivores. Fish and other seafood contributed on average 4 µg/day in vegetarians (5 consumers) and 33 µg/day in omnivores. In Figure 5.2-2 (see page 41) we showed the contribution of food groups to iodine intake from food in OLP-vegetarians and vegans separately (the mean intake (100%) was 106 µg/day in OLP-vegetarians and 32 µg/day in vegans). In Figure 5.5-2 the mean intake (100%) was 81 µg/day in OLP-vegetarians and 127 µg/day in omnivores.

Iodine containing supplements comprised 30% of the daily iodine supply in vegetarians and 5% in in omnivores (Figure 5.5-3).

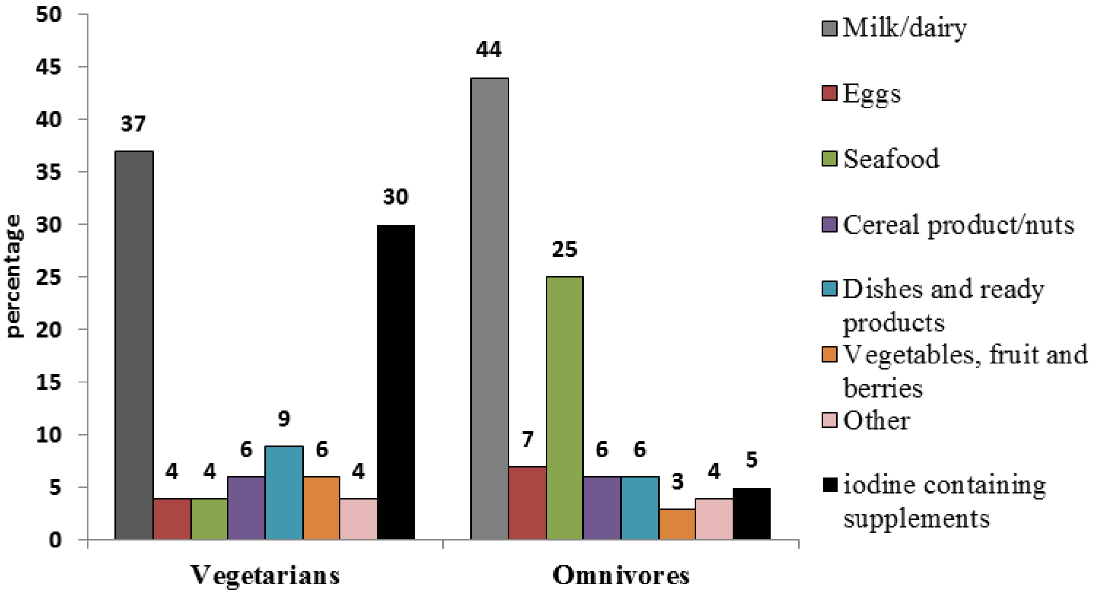

Figure 5.5-3 *Mean contribution to iodine intake from food sources and iodine containing supplements in vegetarians and omnivores*

5.5.2 Urinary iodine concentration in vegetarians and omnivores

The median UIC was significantly higher in omnivores than vegetarians (*p*= 0.020), while UIC adjusted for creatinine did not differ significally between the two groups (*p*= 0.692) (Table 5.5-1).

Table 5.5-1 Iodine status based on UIC (µg/L), iodine/creatinine ratio (µg L/g creatinine).

Iodine status	**Vegetarians (n=52)**			**Omnivores (n=67)**		
	Median (min,max)	P25[1]	P75[1]	Median (min,max)	P25[1]	P75[1]
UIC µg/L[a]	54 (10, 1348)	32	99	70 (16, 487)	51	118
µg L/g cre[b]	58 (8, 3097)	36	89	61 (14, 402)	43	98

[1] 25th, 75th percentile

[a] Mean UIC from the two morning spot urine samples

[b] iodine/creatinine ratio (µg L/g creatinine)

Figure 5.5-4 shows the distribution of UIC for all vegetarians (OLP-vegetarians and vegans) in comparison with omnivores. In total, 68% of the vegetarians and 55% of the omnivores are classified as having moderate to mild iodine deficiency according to WHOs criteria for assessing iodine nutrition in children above the age of 6 and adults. Only 17% of the vegetarians and 26% of the omnivores are classified as having adequate iodine intake based on UIC.

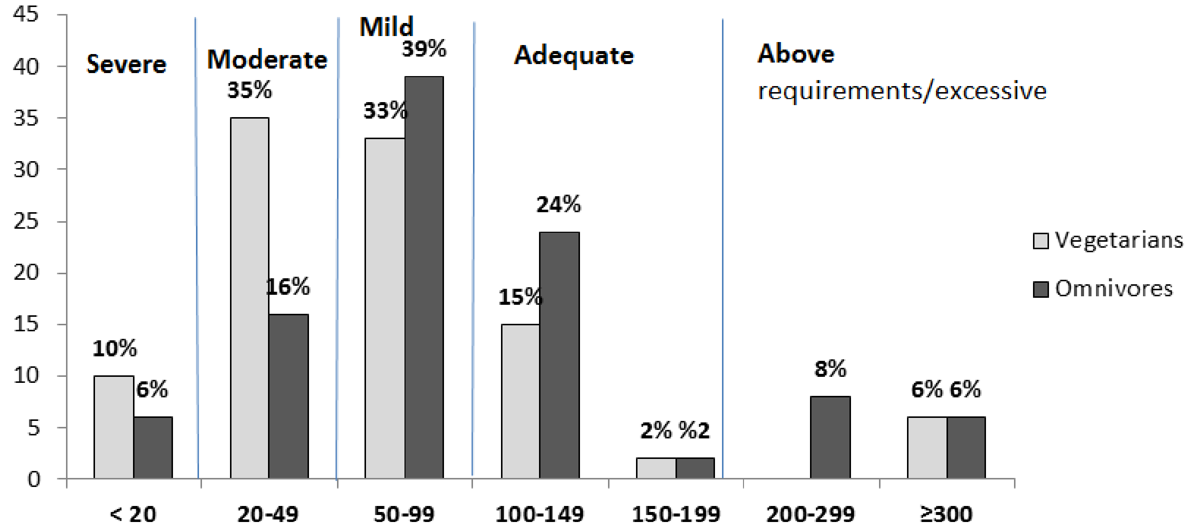

Figure 5.5-4 *Prevalence of iodine deficiency in vegetarians and omnivores categorized according to WHOs criteria for assessing iodine nutrition (WHO, 2007a)*

5.5.3 Comparison of iodine nutrition in vegetarian subgroups and omnivores

In chapters 5.5.1 and 5.5.2 we compared iodine intake and UIC in vegetarians and non-vegetarians (omnivores) for OLP-vegetarians and vegans combined. Comparing iodine intake and UIC in vegetarian subgroups with omnivores, shows that the vegan group had the lowest iodine intake and lowest UIC (Table 5.5-2)

Table 5.5-2 Iodine status according to estimated iodine intake from food, total intake (diet and supplements) and urinary iodine concentration (UIC) in the two groups of vegetarians (OLP-vegetarians and vegans)

Iodine status	OLP vegetarians (n=34)	Vegans (n=18)	Omnivores (n=67)	Difference OLP-veg Omnivores	Difference Vegans Omnivores
	Median	Median	Median	*p-value* [a]	*p-value* [a]
Intake from diet (µg/day)	89	24	112	*0.051*	*<0.001*
Total intake (µg/day)[1]	124	50	113	*0.620*	*0.001*
UIC (µg/L)	73	39	70	*0.209*	*0.006*

Figure 5.5-5 shows the total iodine intake (food and iodine supplements) for the three groups (Omnivores, OLP-vegetarians and vegans) separately.

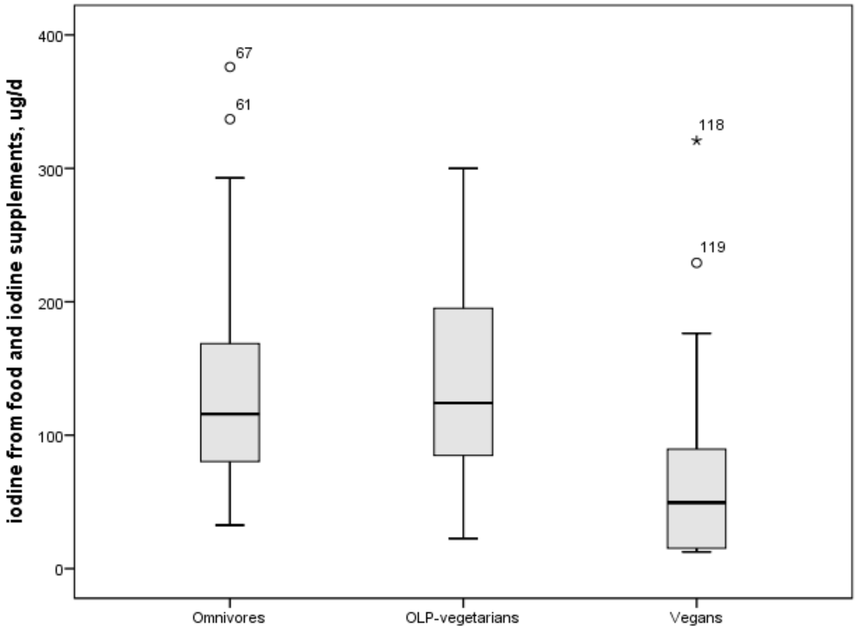

Figure 5.5-5 *Total iodine intake (food and supplements combined) in omnivores, OLP vegetarians and vegans. The box indicates the interquartile range (IQR) of 25th to 75th percentile; the whiskers represent observations within 1.5 times the IQR. The dot represents the observations more than 1.5 times the IQR away from the box (outliners)*

5.5.4 Comparison of iodine intake and status in vegetarian and non-vegetarian pregnant women

Five of the vegetarians (all in the OLP-vegetarian group) included in this thesis were pregnant. They were treated as non-pregnant in this thesis due the low number. However, both dietary recommendations and criteria for evaluation of UIC are different for pregnant and non-pregnant women. Iodine nutrition in pregnancy was investigated separately in a group of 40 pregnant non-vegetarian women in another master thesis (Nyheim, 2016).The calculated median iodine intake from food in the 40 pregnant non-vegetarian women was 124 µg/day, and the total intake (food and supplements) was 170 µg/day. In the five pregnant vegetarians the corresponding intakes were 108 µg/day (food only) and 123 µg/day (total intake). Median UIC was 80 µg/L in pregnant non-vegetarians and 54 µg/L in pregnant vegetarians (n=5). Milk and dairy products were a larger contributor (on average 75 µg/day) in the non-vegetarian pregnant women than in the pregnant vegetarians (on average 54 µg/day). No statistical comparison was done due to the low number of pregnant vegetarians. The rationale for this comparison is to highlight the special vulnerability of pregnant vegetarians.

6 DISCUSSION

6.1 Results and findings

To the best of my knowledge, this is the first study describing iodine intake and status in Norwegian vegetarians. The main findings suggest that Norwegian vegetarians, particularly vegans are in risk of suboptimal iodine intake, and that ensuring optimal iodine nutrition should be of concern for this group.

6.1.1 Iodine nutrition in vegetarians, with main focus on vegans

The calculated iodine intake was lower than the recommended intake of 150 µg/day in both subgroups of vegetarians, albeit more so in the vegan group.

In general, there are limited data on iodine status of vegetarians and vegans. Some previous studies have shown that iodine nutrition was compromised in vegans when evaluated according to established recommendations for iodine intake and/ or urinary iodine concentration. The references and a brief description of the published studies are summarized in Table 6.1-1.

In the present study, we calculated dietary iodine intake by a two-day weighed food record; we also included data on iodine intake from supplements and had access to iodine concentration measured in morning spot urine samples. Some of the other studies (Draper, Lewis, Malhotra, & Wheeler, 1993; Kristensen et al., 2015) assessed the iodine status by weighed food records only, whilst others assessed the UIC / UIE in addition to the dietary intake (Elorinne et al., 2016; Kraj et al., 2003; Leung, Lamar, He, Braverman, & Pearce, 2011; Lightowler & Davies, 1998; Schupbach, Wegmuller, Berguerand, Bui, & Herter-Aeberli, 2015). The various approaches for investing iodine status in vegetarians in previous studies are displayed in Table 6.1-1.

Most of the studies are based on relatively small study samples in Europe (n=15-70 vegans) and one study conducted in the USA with 62 vegans (Leung et al., 2011). The results of all the studies, independent of sample size, corroborate insufficient iodine intake or status in vegans (Table 6.1-1). The iodine nutrition among Norwegian vegans (median total intake 50 µg/day, median UIC: 39 µg/L) was in the lower range when compared with the majority of findings in the studies presented in Table 6.1-1. Some possible explanations for this could be the methodological differences among the present study and the earlier studies, furthermore -

geographical variations and the fortification practice in each country. There is a clear trend towards the same result in all these studies, and in agreement with our study all available studies show inadequate iodine intake and status in vegans.

Table 6.1-1 Other studies assessing iodine nutrition in vegans and/or vegetarians (and omnivores).

Study/year/population	Study group (n)	Iodine assessment[1]	Results
Draper et al.1993 UK	Vegans (38) Vegetarians (52) Meat-avoiders (38)	Three- days WFR[2]. No urine samples	Mean intake Vegans: M/F[6]: 98/66 µg/day Vegetarians: M/F 216/167 µg/day Meat-avoiders:M/F 253/172 µg/day
Lightowler & Davies, 1998, UK	Vegans (30)	Four– days WFR[2] + direct analysis of duplicate diets + UIE (4-days)	Mean UIE Males : 49 µg/L Females: 72 µg/L
Kraj. et al , 2003 Slovakia	Vegans (15) Vegetarians(31) Omnivores (35)	FFQ[4], 24-h UIE/ creatinine adjust.	Median UIC Vegan: 71 µg/L Vegetarians: 177µg/L Omnivores. 210 µg/L
Leung, et al 2011 USA	Vegans (62) Vegetarians (78)	UIC spot urine samples + TSH	Median UIC Vegans: 78.5 µg/L Vegetarians: 147 µg/L
Kristensen et al, 2015 Denmark	Vegans (70) Omnivores (1257)	Four-days WFR[2] No urine samples	Median intake[3] in vegans: Males: 107 µg/day Females: 79 µg/day
Elorinne et al, 2015 Finland	Vegans (22) Omnivores (19)	Three-days WFR[2] Urine samples UIE	Median (P25, P75)[5] UIE Vegans:15 (4.6, 21.8) µg/L Omniv. 37.4 (17.7, 86.5) µg/L
Schupbach et al., 2015 Switzerland	Vegans (53) Vegetarians (53) Omnivores (100)	3 days WFR[2] + UIC(4 samples)	Median UIC Vegan: 56 µg/L Vegetarians: 75 µg/L Omnivores 83 µg/L

[1] Method applied for iodine assessment,

[2] WFR= weighed food record

[3] Total intakes (Food and iodine containing supplements)

[4] Food Frequency Questionnaires

[5] P25=25th percentile, P75=75th percentile

[6] M/F = Males/ Females

6.1.2 Iodine nutrition in vegetarians, with main focus on the OLP- vegetarians

The low iodine intake in vegans, with a diet based on plants, was more or less what we expected to find, considering the small number of supplement users, the iodine depleted soil, and salt iodization practice in Norway. The average iodine intakes of the Norwegian OPL-vegetarians and omnivores, living under the same conditions regarding iodine in salt and soil, were significantly higher than in the vegan group. Certainly, this was not unexpected, as the iodine supply in Norway almost exclusively derives from animal sources, specifically drinking milk, fish and products including these items. It was somewhat surprising; however, that the median UIC in both OPL- vegetarians and omnivores both were equally low and lower than the recommended values (Table 5.5-2 page 57).

Even though all vegetarians have meat avoidance in common, they may differ immensely in what takes the meat`s place in the diet. Some vegetarians do eat dairy, eggs and even fish on a regular basis. Others eat animal food rarely, and in very small amount. Iodine intake from food ranged between 23-286 µg/day (mean intake of the two days) in the OLP- vegetarian group.

The median calculated intake among the OLP vegetarians was 89 µg per day from food (not including iodine from supplementation) which indicates that not only vegans, but also other vegetarians in Norway are in risk of getting insufficient iodine from food sources. This was confirmed by a suboptimal UIC in the OLP- vegetarian group (median:73 µg/L).

In contrast to our findings of total intake (food and supplements) of 124 µg iodine/d, which indicated a suboptimal intake, other studies (Table 6.1) found that iodine intake in vegetarians (reflected in the median urine iodine concentration) were within; (Draper et al., 1993; Kraj et al., 2003) or borderline (Leung et al., 2011) with the recommendation of the WHO (150µg/day). However, in accordance with the present study, a Swiss study found that 66% of vegetarians were below the recommended intake of iodine. It should be noted that the participants in that study were restricted to use any supplements 14 days prior to the measurements (Schupbach et al., 2015).

The only thing that actually separates OLP – vegetarians and omnivores regarding dietary iodine is meat consumption. Because meat is not a significant source of iodine, one can argue that these two groups are more interrelated than vegans and OLP- vegetarians; groups commonly categorized together. Theoretically an OLP- vegetarian can get the same amount of iodine in their diet as an omnivore.

Nonetheless, there appear to be some differences in the amount of animal products consumed by the two groups. The three animal sources (milk, fish and eggs) contributed in the OLP-vegetarian diet with on average 58% of the daily iodine supply (Figure 5.5-2), whereas in the omnivores these food items contributed with an average of 79 % of the daily intake (Figure 5.2-6).

The amount of iodine from milk and dairy, the main food source of iodine, was on average 42 µg/day in OLP-vegetarians, and 59 µg/day in omnivores. It might be expected that lacto-ovo vegetarians would have consumed higher amounts of dairy and eggs to compensate for the lack of meat in the diet. Conversely, and in line with our findings, a study of food consumption patterns among 89 455 vegetarians and non-vegetarians in USA showed that all categories of vegetarians consumed less dairy and eggs and more plant foods compared to mixed eaters. Basically, the consumption of dairy products and eggs tended to correlate with that of meat (Orlich et al., 2014).

We had five pesco- vegetarians in the OLP vegetarians group. As our study was not designed to investigate each of the different categories within the OLP- vegetarian group specifically, little is known about the iodine intake in Norwegian pesco- vegetarians. Studies conducted elsewhere found that pesco- vegetarians consumed fatty fish and other fish in amounts similar to those consumed by non-vegetarians. However, they tended to consume less amount of the other iodine containing animal products (i.e dairy and eggs) compared to non-vegetarians (Orlich et al., 2014).

Another study found that consumption of milk, dairy and cheese was not significantly different between groups of vegetarians and non-vegetarians and that vegetarians consumed nearly twice as much fish as non - vegetarians (Haddad & Tanzman, 2003).

These patterns may not simply be generalizable to Norwegian pesco-vegetarians. Further studies with appropriate sample size and methodology might help to identify different eating patterns among Norwegian vegetarians. Some might argue that fish consumers should not be included in the vegetarian group in the first place. Either way, fish is a food item which is normally *not* eaten every day, which makes it difficult to get a true picture of habitual intake in a two day food diary. The Norwegian Health Directorate recommendation regarding iodine intake in the Norwegian populations in general is 150 µg/day in non-pregnant, non-lactating adults (Table 2.2-1). The food based dietary recommendation is to eat fish 2-3 times a week, besides daily consumption of milk and dairy. However, the intake of milk is not quantitative, and given an average iodine concentration in milk of 20µg/100 mL, an adult needs to consume 0.75 L milk/yoghurt per day if this is the only source. This is a rather large amount of milk and illustrates that having few sources of iodine in the diet make those who omit these sources very vulnerable to inadequate intake.

6.1.3 Pregnant vegetarians

There were five pregnant vegetarians included in the OLP vegetarian group. As this current study was designed to investigate vegetarians, this small group was included because of their dietary practice (vegetarians), and not investigated in light of their pregnancy. It should be noted that iodine intake recommendations and UIC cut- of values are different during pregnancy, something we did not take into account in the current results. Pregnant women are particularly vulnerable to insufficient iodine intake, as even mild iodine deficiency may have potential adverse effects during pregnancy (and lactation) (Bath et al., 2013; Brantsaeter, Abel, Haugen, & Meltzer, 2013). The Norwegian Health Authorities recommend that pregnant vegetarians use an iodine containing supplement (The Norwegian Directorate of Health, 2015c) Iodine status in a group of pregnant non-vegetarian women has been evaluated separately in another master project parallel to this study *Iodine intake and status in a group of pregnant women in Norway* (Nyheim, 2016).

6.1.4 Supplements

We found that omnivores had a slightly lower UIC (70 µg/L) compared with the OLP-vegetarians (73 µg/L) which is most likely the consequence of a higher proportion of the vegetarians using iodine containing supplements (18%) compared to the omnivores (3%).
We found no difference in use of iodine supplements between vegans and OLP-vegetarians. Still, only five of the eighteen vegan participants reported using an iodine supplement. Interestingly, a study in US vegans found a difference in supplement use among those choosing veganism for

ethical reasons and those choosing it for health reasons. Those choosing a vegan diet due to ethical reasons were more likely to take vitamin supplements, but not algae-supplements, than those being vegan for health reasons (Radnitz et al., 2015).

In our study sample, 28% of vegans, 18% of OLP- vegetarians and 3% of the omnivores reported use of an iodine-containing supplement during one or both days of food intake recording. The median intake of iodine in vegans was still significantly lower than in OLP- vegetarians and omnivores, even when adding in the iodine from supplements. Among the vegetarians using iodine containing supplements (11 of 52), 73% reached the recommended iodine intake of 150µg/day. In contrast, of the 41 of 52 vegetarians who did not use iodine- supplements, only 20% reached the recommended intake of 150 µg/day.

Even though high doses of iodine are well tolerated in most cases, it may cause thyroid abnormalities in susceptible individuals. A dysfunction of the self-regulatory mechanisms of thyroid hormone synthesis may occur, even in patients with no history of thyroid disease (Prete et al., 2015).

Five of the eleven supplement-using vegetarians were using seaweed supplements, such as various kelp products and wakame. A surprisingly high proportion of the seaweed consumers; three (of five) had a high UIC ≥ 300 µg/L. A phenomenon also reported in other studies (Kristensen et al., 2015; Leung et al., 2011). On the other hand, 100% (2 of 2) of the omnivores reported to have used a mineral-supplements had a high UIC as well. One of these two reported taking 4 tablets one of the recording days, which can explain the high urinary iodine concentration. None of the omnivores reported use of seaweeds. There were four omnivores with high UIC, whereas only two reported using a mineral supplement. The other two had high creatinine level, but this cannot alone explain the high iodine concentration in urine. It is possible that these participants may have used a supplement (or ate something with high iodine content) without recording this in the diary.

Although the iodine content of dietary supplements was not analysed in this study, previous research has shown that there is uncertainty and variability in the iodine content of dietary supplements. In fact, some kelp supplements and multivitamins/ minerals have been proven to contain very high doses of iodine (Leung et al., 2009) and iodine content can be higher than reported by the product labelling, also demonstrated in this present study.

Some of the seaweed- products were purchased through internet. Although there is not a specific national regulation regarding such supplements, the Norwegian Health Authorities warns specifically against purchasing supplements on internet, because product labelling on such products can be misleading (The Norwegian Food Safety Authority & The Norwegian Directorate of Health, 2013; The Norwegian Medicines Agency, 2016).
The Norwegian Health Directorate updated their recommendation for vegans in February 2015 and suggested that vegans should use a pinch of kelp or iodine containing mineral supplement to secure the intake of iodine. However, our study found that less than one third of the Norwegian vegan participants followed this advice. The use of supplements was therefore not contributing to iodine intake in a way that secured an adequate intake in this group, and the use of kelp-supplements in OLP-vegetarians resulted in UIC values reflecting excessive iodine intake with risk of adverse health consequences (Table 5.3-2).

6.2 Methodological considerations

6.2.1 Study design and selection of participants

The present study was cross-sectional, which is a commonly used study design for assessing iodine status in a population, as it is relatively inexpensive, easy to conduct and at the same time suitable for health surveillance purposes (Gibson, 2005). Cross sectional studies give "snapshots" of current situations, as data is collected at one single point in time, and the association between a potential risk factor and an outcome in that particular point of time is measured (Veierod & Thelle, 2013). Cross sectional studies are useful for assessing status and prevalence, but have very limited scientific value in studies examining potential causal associations as the direction of the association cannot be established. Cross-sectional studies are also limited by different kinds of bias and confounding factors (Pandis, 2014; Veierod & Thelle, 2013).

The selection of participants in a study should preferably be implemented by a random sampling, which would give the same probability for each individual to be included and thus constitute a representative sample from the study population (Pandis, 2014). However, the current study was conducted to assess iodine status in subgroups of the population and to examine the agreement between calculated iodine intake and UIC, but not to examine exposure outcome associations.

The study population was recruited using convenience sampling and do not comprise representative samples of the studied population groups. This is a major limitation which affects the generalizability of our results.

Participants were recruited among employees (and family) of the Norwegian Institute of Public Health, the Norwegian Veterinary Institute, and among students and employees (and family) at HiOA. Preferably the assessment of socioeconomic status of the participants should have been included in the questionnaires, as this may affect participant's dietary behaviour and composition of their diet. Still, since these institutions relates to health and higher education, it is likely that the majority of participants in this study consisted of persons relatively more health conscious and/ or with a higher education than the general population. A higher education is associated with overall higher health literacy (Feinberg et al., 2016). Besides, dietary supplement usage tends to be influenced by educational level (Bailey et al., 2011; Dickinson & MacKay, 2014).

Furthermore, the vegan group comprised 16 women and two males. Even if studies indicate that there are more female vegetarians in general (Beardsworth et al., 2002; Larsson et al., 2002; Ruby, 2012), still it is not very likely that this gender distribution is representative for Norwegian vegans. This female domination may have affected the result in various ways. Females have been found to eat healthier than men, besides the use of supplements is higher among women (Dickinson & MacKay, 2014; Naughton, McCarthy, & McCarthy, 2015). Due to time limitations, the present study did not aim to find associations between demographic variables (e.g. age, sex, physical activity) and iodine intake in Norwegian vegetarians. However studies have suggested that women tend to have lower iodine status compare to men (Rasmussen et al., 2002).

It is possible that the vegans selected for this study may have been systematically different in some of their characteristics (i.e. education level and gender distribution) compared with other vegans not selected. The OLP- vegetarians may consist of persons with relatively higher education compared to the average vegetarian. This may have altered the outcome of the study and limited the generalizability of the findings to the target population.

The significant higher distribution of females (89%), and significantly lower average age among the vegans compared to the other subgroup of vegetarians may be confounders affecting the internal validity as well. As already mentioned; healthier diets and supplement usage tends to be more prevalent among women than among men (Johansson, 1999). Age has also been found to be a determinant for supplement usage. Evidence suggests that prevalence of dietary supplement usage increases with age in both males and females (Bailey et al., 2011; Dickinson & MacKay, 2014). OLP- vegetarians were in average seven years older than the vegans.

Other potential sources of inaccuracy and bias in this study arise from the fact that the 38 vegetarians sourced from the Donexpo study were mainly and originally requited to measure mycotoxin, originating from cereals, in diet and urine. Whereas the second wave of recruited vegetarians (n=14) were foretold that iodine were to be measured. These two different perspectives for the purpose of their participation in the study might have affected the outcome. It is possible that their food choice, intentionally or unintentionally were affected by the knowing of being evaluated for a certain dietary substance. The first group may have been more careful when recording bread, grain products etc., whilst the second group more conscious regarding iodine containing food items. This may have led to a social desirability bias, where subjects will try to provide the right and what they believe to be the desirable answers, thus leading to possible inaccuracy in the information given. The knowledge of being evaluated for iodine intake may also have led to more attention regarding iodine supplementing and seaweed consumption among the latest recruited participants, comprised of nine vegans and five OLP- vegetarians.
Regarding generalisability, it could be speculated that suboptimal iodine nutrition is likely to be even more prevalent in the general population of vegans and vegetarians than in our selected group.

6.2.2 Dietary assessment

The intention of dietary assessment in general is to measure the average habitual intake, i.e., food choices, amounts consumed, and frequency of consumption, and thereby to estimate the level of nutrients, for instance iodine in the diet (Hjartåker & Veierød, 2013). Food composition databases rely on nutritional and toxicological analyses conducted by government, academia and the food industry to determine the potential contributions of foods to the diet (Greenfield & Southgate, 2003). The Norwegian Food Composition Table declares an average of the analysed samples of each food, and is recently presented in an updated version (2015).

In this present study, a two-day recorded weighed food diary was applied, and the mean iodine of these two days was used in all analyses. The iodine intake did not differ significantly between these two days in our study group; however it is still possible that subjects may regularly consume iodine-rich foods not ingested during the two days of recording. Because individual iodine intake can vary substantially from day to day, depending on the types of iodine-containing foods consumed and their iodine content, it can be difficult to quantify the usual iodine intake accurately without covering several more days for each individual.

Yet, the dietary data from studies like this can still be used to identify the most significant food sources of iodine, and the results can be useful for adapting iodine intervention strategies (Zimmermann & Andersson, 2012).

The advantage of using an open diary approach is that information can be recorded without restrictions, which is considered suitable for measuring populations with a wide range of eating habits, like vegetarians (Shim, Oh, & Kim, 2014). Because the eating and recording occurs almost concurrently the subjects will be less likely to forget what they have eaten in contrast to retrospect recall approaches like dietary recall interviews or food frequency questionnaires which ask about average intake over a specified time window in the past.

On the other hand there are some limitations to the open diary method. As a considerable burden is placed at the participants, a relatively high level of motivation is necessary to participate (Hjartåker & Veierød, 2013). Furthermore, in order to obtain precise data, a thorough instruction is needed before partaking (Hjartåker & Veierød, 2013). This method is therefore more suitable for a few days recording thus mainly focusing on short-term intake (Shim et al., 2014).

In the course of measurements and recording, consumption and coding of dietary intakes, errors may have occurred, of which some will be discussed here. Firstly; the accuracy in weighing and recording the food items varied noticeably among the participants. Some weighed each ingredient in a precise accurate manner, specified in grams or ml, whereas others gave more imprecise approximations like “a cup of” or “a big plate of...”etc. Estimations of portion sizes can be rather subjective as “a small plate, “big bowl” and such can have different value for different people. Moreover, the quantity of food consumed was to be converted to its actual weights in grams or ml, which may be a potential source of error. Furthermore, uncertainties may arise regarding the actual quantity of the food consumed, as there was no instruction of weighing the leftover food on the plate. Consuming shared serving dishes could be another potential source of error (Gibson, 2005). Even if the participants were encouraged to register every single ingredient in such dishes it is still demanding to quantify the exact amount eaten by each person after mixing it together. It is therefore possible that the subjects may have, intentionally or unintentionally adjusted their intake by under/ overestimate their eating pattern by mistake, to better suit their self-image, or simply to avoid the burden of writing down everything (Gibson, 2005; Shim et al., 2014).

In addition, all foods and mixed dishes consumed according to the more or less detailed descriptions of the respondents were to be matched and coded with the most appropriate food listed in the food composition database.The use of a food diary to assess iodine intake in vegetarian and vegans may be imprecise due to lack of some of the foods used by this group in the Food Composition Table. To minimize the source of error in the coding process, food and drink items in all food diaries were cautiously given the most suitable food number from the updated version of Norwegian Food Composition Table (Matvaretabellen, version 2015). If the food item described by the participants was not present in the Food Composition Table, it was substituted by a similar food item in consultation with an experienced person. A protocol was made to be able to consequently use comparable alternatives for unregistered food items (Appendix 4). It is unlikely that this would have altered the iodine intake considerably as these are mostly plant food, and thus equally low in iodine.

The coding process is, therefore, despite some potential errors, considered to have been performed with the most achievable accuracy as possible within the context in which the study has been conducted.

6.2.3 Assessment of supplements and identification of iodine containing supplements

Seaweeds have the unique capability to concentrate iodine from the sea, with certain types of brown seaweed accumulating over 30,000 times the iodine concentration of seawater (Küpper et al., 1998).

The estimation of iodine from supplements might have been afflicted with potential errors. All seaweeds, except Nori (the only seaweed listed in the Food Composition Table), were categorized as supplements. We used alternative sources on internet, as an attempt to estimate the amount of iodine in different brands of seaweed; however this is certainly infested with great uncertainties. The amount eaten was often not clearly stated and the iodine content in seaweed is highly variable, not only depending on the different species, but even on harvest location and preparation. Dried iodine contents range from 16 µg/g in Nori to over 8,000 µg/g in kelp flakes (Teas, Pino, Critchley, & Braverman, 2004b).

This may have led to inaccuracy. Additionally measurement is further complicated by the fact that the seaweed can be applied through tablets and drops or like food in the dried or fresh form, and the accurate amount of iodine may not be applied on the product. When multivitamin/mineral tablets were used, the amount listed on the product was used as a source of iodine content. Accuracy of iodine intake from supplements is particularly important as this is an important source of iodine for vegetarians, particularly vegans. There were seaweed users in both subgroups of vegetarians, but not in the control group.

6.2.4 Urinary iodine concentration

At this present study morning, spot urine samples (UIC) are used and presented as median µg/L Urinary iodine concentration is currently the recommended biochemical marker for epidemiological iodine assessment (WHO, 2007a). Taking into account that 90% of the iodine is excreted in urine, a UIC of minimum 100 µg/L indicates iodine sufficiency (WHO, 2007a; Zimmermann, 2009). The urinary iodine excretion displays very wide variation between individuals, within individuals and in groups compared with most other biological analysts (Andersen et al 2003). A variable amount of iodine excreted in urine is unavoidable and normal due to the relatively few sources of iodine in the diet. This variation first and foremost displays the variation in resent iodine intake (Andersen, Karmisholt, & Laurberg, 2009).

To limit the intra-individual variation introduced by random spot samples, fasting, morning spot urine samples were used in this study. This time point is considered the time with the less variation due to recent food intake (Ovesen & Boeing, 2002).

However the time of measurement may also be a limited factor. Reflections of the ingested iodine will appear in the urine around 4-5 hours after the meal (Als et al., 2000). Iodine concentration in the urine is at the lowest in the morning due to the overnight fast (Als et al., 2000; Soldin, 2002). Fasting, morning spot urine samples are therefore not considered to be a representative measure of the average iodine intake in individuals nor in a population and interpretation of morning spot urines must take this into account (Andersen, Karmisholt, Pedersen, & Laurberg, 2008).

There may be some other limitations as well. While most of the overnight spot samples in our analysis may have been fasting samples, as we specifically encouraged a fasting first morning sample, we cannot know for sure if all participants were in fact fasting at the time of taking the urine sample. It should also be noted that the laboratory in Finland informed about concerns regarding a possible contamination of the instrument used for measuring urinary iodine concentration in our study which may have resulted in slightly lower values of iodine.

Ideally, the spot urine values should be compared to 24h UIE in the same population, due to the uncertainties linked to spot urine samples in general. However, collection of 24h urine samples is a much larger burden for participants and may severely restrict the participation rate (Vejbjerg, Knudsen, Perrild, Laurberg, Andersen, et al., 2009)

To regard the low UIC in this study as iodine deficiency might be a misinterpretation. Two single urinary iodine measurements per person are not representative of an individual's nutritional iodine status (Soldin, 2002). The measurement of urinary iodine excretion may be used as an indicator of the resent iodine intake, although obtaining urinary iodine that truly reflects iodine status is difficult (Lightowler & Davies, 1998).

It is possible that the UIC are underestimates of the actually iodine status in our participants. However, the difference will not be of a magnitude that will change the main conclusion that the results from the food diaries as well as UIC indicate suboptimal iodine intake and status in vegans and OLP-vegetarians. Furthermore, the UIC is also a useful tool to validate the calculated iodine intake (Brantsaeter et al., 2007).

Creatinine adjustment

Another method to assess the iodine nutrition is to use the adjusted iodine: creatinine ratio to estimate the daily urine iodine excretion from spot urine samples (Andersen et al., 2008; Soldin, 2002). For the spot urine samples to be comparable with the 24-hours UIE the volume of urine per day should be taken into account. Urinary iodine spot urine and 24-h UIE are interchangeable only if of the volume of urine passed in 24-hours is one liter (Laurberg et al., 2007). However in adults, this volume is usually closer to 1.5 liter/day which mean that median UIE given as µg /24-hours will be 50% higher than the median UIC given as µg/L (Laurberg et al., 2007). Adjustment with creatinine is used to reduce the variation in UIE caused by dilution. However this should ideally be stratified for gender, age and ethnicity (Haddow, McClain, Palomaki, & Hollowell, 2007).

Our data were adjusted for creatinine, however we did not stratified for gender and age, as sex and age iodine/Creatinine ratio: values only include participants >/= 25 years. We chose to not apply this stratified ratio analyze, as this would have resulted in that part of our study group would have to be excluded due to lack of reference value for those aged <25. The non- stratified creatinine adjustment gave a lower correlation coefficient than non- adjusted UIC.

Both UIC and I/cr are considered to be underestimates compared to 24h UIE (Als et al., 2003).

6.2.5 Association between iodine intake and urinary iodine concentration

We found a relatively high correlation between total iodine intake (food and supplements combined) and UIC in vegetarians (r= 0.67), and a somewhat lower correlation coefficients (r= 0.45) in vegans. The correlation coefficients show that the calculated intakes may quite accurately describe the subjects' iodine nutrition at the time of measurement and therefore strengthen the validity and reliability of iodine intake calculated from the food diaries.

Methods relying on self-reported food intake are associated with possible errors as previously discussed. Therefore, complementing the assessment with biochemical measurements (biomarkers), like substances contributed by diet that can be measured in urine or blood samples serves as valuable reference measures for evaluating the quality of the self-reported data. Biomarkers are objective measures that cannot be influenced by recall subjective recall errors. However, biomarkers are influenced by metabolic and homeostatic processes (Hjartåker & Veierød, 2013) and the correlation between a biomarker and calculated dietary intake can be considered an estimate of the lower limit of validity of the dietary method (Brantsaeter et al., 2007).

6.3 Overall remarks

The main findings in this thesis are that both the calculated iodine intake and the measured urinary iodine concentration suggest that Norwegian vegetarians, particularly vegans are at risk of suboptimal iodine intake. Interestingly, suboptimal iodine status was also indicated in the control group of non-vegetarians.

The main strengths of the study are the relatively large study population, the detailed dietary assessment and the supplementary measurement of UIC taken in the morning to limit the intra-individual variation. The main limitations of the study are that participants are not representative of the general population, the inherent errors in dietary assessment and the uncertainty related to use of morning spot urine samples.

The low iodine intake in vegans, with a diet based on plants, was more or less what we expected to find, and is in line with studies of iodine nutrition in vegans in other western countries. Although OLP-vegetarians and omnivores had significantly higher iodine intakes than the vegans, a large proportion of both the omnivores and vegetarians did not reach the recommended intake levels. Suboptimal iodine status was supported by a large percentage of participants having low urinary iodine concentrations in all groups. It is important to keep in mind that not reaching the recommended intake does not necessarily lead to deficiency because the recommendations aim to meet the physiological needs in 97.5% of the population (Institute of Medicine (US), 2001). The fact that large groups of the population does not reach recommended intake levels imply increased risk of deficiency in vulnerable individuals. Furthermore, the long-term implications of mild- to moderate iodine deficiency is not well known and ensuring optimal iodine nutrition in all population groups, including vegetarians is of public health concern.

7 CONCLUSIONS

This thesis had several aim and I will first present the conclusion to each of the specific objectives before reflecting on the implication and future perspectives of the findings.

Objective 1: To describe the calculated iodine intake from food in vegetarians, including the subgroups OPL-vegetarians and vegans, based on two days food records and compare the intake to established recommendations for iodine intake.

The median calculated iodine intake from food in all vegetarians (n=52) was 116 µg/day. When vegetarians were examined by the subgroups i) vegans (no animal products) and ii) OLP-vegetarians (no meat but could include eggs, milk and/or fish), the median iodine intake from food sources was 24 µg/day in vegans and 89 µg/day in OLP-vegetarians. None of the vegans and 24% of OLP-vegetarians reached the recommended iodine intake of 150 µg/day with food (including beverages) as the only source of iodine.

Objective 2: To examine the role of different food sources to iodine intake in vegetarians.

The main food source of iodine in OLP vegetarians were “milk and dairy”, which contributed on average 61% of all iodine, while minor sources were “eggs” (7%) and “mixed dishes” (some of which contain milk and eggs) (10%). Only five (15%) of the OLP-vegetarians consumed “fish” and the contribution from fish was 6%. The main sources of iodine in vegans were “mixed dishes” (38%), “vegetables, fruit and berries” (27%) and cereals and nuts (23%). It should be noted that the mean iodine intake (100%) from food was higher (106 µg/day) in OLP-vegetarians than in vegans (32 µg/day).

Objective 3: To examine to what extent vegetarians use iodine containing supplements and how this contribute to total iodine intake and urinary iodine concentrations in vegetarians.

Use of iodine containing dietary supplements was reported by 6 (18%) OLP-vegetarians and by 5 (28%) vegans. The median total intake from food and iodine supplements was 50 µg/day in vegans and 124 µg/day in OLP-vegetarians. Only 17% of the vegans and 38% of OLP-vegetarians reached the recommended iodine intake of 150 µg/day.

When including iodine from supplements in dietary sources, “milk and dairy” was still the main contributor to iodine in the OLP-vegetarians (contributing on average 48%), while iodine-supplements contributed on average 23%. Iodine from supplements increased the median intake in OLP-vegetarians from 89 to 124 µg/day (the corresponding mean intake increased from 106 to 135 µg/day. In the vegan group, iodine supplements contributed on average 58% to the total iodine intake, and increased the median intake from 24 µg/day to 50 µg/day (the corresponding mean intake increased from 32 µg/day to 77 µg/day).

Use of iodine containing supplements resulted in higher median urinary iodine concentrations in in supplement users than in non-iodine supplement users. In the OLP-vegetarian group, median urinary iodine concentration was 65 µg/L in non-supplement and 111 µg/L in supplement users (*p*=0.047), while in the vegans, median urinary iodine concentration was 37 µg/L in non-supplement and 101 µg/L in iodine supplement users (*p*=0.173)

Another important finding related to iodine supplement use was the extremely high urinary iodine concentrations (>700 µg/L) measured in three vegetarians using kelp supplements.

Objective 4: To describe the urinary iodine concentrations in the vegetarians based on two morning urine samples and compare to WHO recommendations.

Median urinary iodine concentrations did not differ between the two morning spot urines and the mean of the two days were used in all analyses. In the total vegetarian group, the median urinary iodine concentration was 52 µg/L in non-supplement and 102 µg/L in supplement users (*p*=0.016). According to WHO criteria for evaluating iodine status based on spot urine samples, 11% of vegans and 9% of OLP-vegetarians are classified as ‘severe iodine deficiency’, 72% of vegans and 74% of OLP-vegetarians are classified as ‘mild to moderate iodine deficiency’, 12% of vegans and 21% of OLP-vegetarians are classified as ‘adequate iodine intake’, while 6% in both groups are classified as ‘excessive iodine intake’ (Figure 5.9).

Objective 5: To examine the agreement between the calculated iodine intake and urinary iodine concentration by exploring the correlation.

The correlation between calculated iodine intake from food and supplements showed fairly strong agreement with urinary iodine concentrations, with Spearman rho being 0.67 (p<0.001) in OLP-vegetarians and 0.45 (p=0.070) in vegans.

Objective 6: To compare the calculated iodine intake and urinary iodine concentration in vegetarians (total group) with a control group of non-vegetarians, including a comparison of iodine sources.

The calculated iodine intake from food was lower in vegetarians than in the control group (omnivores), whereas the calculated total iodine intake (food and supplements) did not differ between vegetarians and omnivores (median 124 µg/day in vegetarians and 113 µg/day in omnivores, *p*=0.208). The main differences in iodine intake, food sources and urinary iodine concentrations seen for vegans and OLP-vegetarians were even more pronounced when comparing vegans and omnivores, whereas there were no significant differences between OLP-vegetarians and omnivores. Inadequate iodine status is of special concern for pregnant women and young children.

It should be noted that results from this study must be interpreted with caution, especially the WHO criteria applied to urinary iodine concentration. The WHO criteria are intended to be applied in population groups of several hundred individual using random spot urine samples, while in the current study we apply the criteria to small groups and iodine measured in morning spot urine samples. The results are likely an underestimate of the “true” but unknown status of these groups.

Future perspectives and implications

Considering the findings of this study there are few sources of iodine for those who omits or limits animal based food in Norway. The population sample in the current study is likely to be overrepresented by highly educated and health conscientious subjects which may actually have higher iodine intakes than the general population. Suggestions for future research could therefore include further studies of Norwegian vegetarians composed with larger and more representative sample of each subgroup.

Studies have implied that vegetarianism in general, and veganism in particular, is rising and if the current trends continue, a predominant group for adopting this lifestyle might be young people and especially females. To ensure the iodine intake, especially in women of childbearing age, there is need for updated information and suitable nutritional strategies in order to meet such dietary patterns among the population. These should include strategies on how to better inform vegetarians and vegans about the alternative sources of iodine, which currently means supplementation with mineral tablets or seaweed. There is also need for more precise information regarding the use of kelp, and seaweed consumption to hinder excessive intake. There is limited knowledge about the iodine content in the seaweed supplements available in Norway, and of how many who uses these products.

At time being it is important that pregnant, lactating vegetarians and vegans continues to be informed about the necessity to use iodine containing supplements as recommended by the Norwegian Health Authorities. Further studies with appropriate sample size and methodology implemented to identify different eating patterns among Norwegian vegetarians are needed to secure adequate intake of iodine in this group.

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APPENDICES

Appendix 1 Baseline interview

BAKGRUNN OG KOSTVANER

ID KODE: limes i høyre hjørne
Intervju dato:

PERSONLIG INFORMASJON:
Navn:
Født: (dag/mnd/år):
Kjønn: Mann Kvinne
Høyde (cm):
Vekt (kg):

Røykevaner
Røyker ikke: [ ]
Av og til: [ ]
Daglig: [ ]

Aktivitetsnivå Velg det som best beskriver ditt nåværende daglige aktivitetsnivå**:**
- **[ ] Stillesittende/Veldig lavt**
- **[ ] Lett**
- **[ ] Moderat**
- **[ ] Høyt**
- **[ ] Eksepsjonelt høyt**

FORKLARING TIL AKTIVITITETSNIVÅ:
STILLESITTENDE/VELDIG LAVT: veldig lite eller ingen aktivitet (sittende og stående aktivitet, lett husarbeid (stryke, lage mat, feie gulv), bilkjøring, arbeid ved datamaskin eller på laboratorium, spille musikkinstrument.
LETT: Lett aktivitet eller sport 1 til 3 ganger per uke (Rolig gange uten motbakker, mekanisk arbeid, lett dans, snekkerarbeid, stående og gående arbeid, servering, rengjøring, barnepass, golf, seiling og bordtennis)
MODERAT: Moderat aktivitet eller sport 3 til 5 ganger per uke (Rask gange, hagearbeid, tunge løft, sykling, tennis, dansing, slalåm)
HØYT: Hard aktivitet eller sport 6 til 7 ganger per uke (hoppe tau, tungt fysisk arbeid, ballspill, fotball, jogging, langrenn)
EKSEPSJONELT HØYT: Virkelig hard daglig aktivitet eller sport tilsvarende to harde treningsøkter daglig (idrett på toppnivå)

Har du spesielle restriksjoner i kostholdet ditt?
Nei:
Ja: Hvis ja, vennligst spesifiser____ _

Bare for vegetarianere:
Hvor lenge har du praktisert et vegetarisk kosthold? (antall år) ________________

Bare for gravide:
Svangerskapsuke nå ved datainnsamling: ____________

Antall tidligere svangerskap (sett kryss):
- **[ ] 0 (ikke vært gravid tidligere)**
- **[ ] 1 (ett tidligere svangerskap før dette)**
- **[ ] 2-3**
- **[ ] 4 eller mer**

Bruker du noen gang økologisk mat?

Økologisk matvare	**Sjelden/aldri**	**Noen ganger**	**Ofte**	**For det meste**
Melk, melkeprodukter, ost	☐	☐	☐	☐
Brød og kornprodukter, f eks mel, müsli	☐	☐	☐	☐
Egg	☐	☐	☐	☐
Grønnsaker	☐	☐	☐	☐
Frukt	☐	☐	☐	☐
Kjøtt	☐	☐	☐	☐

1

Appendix 2 Information about the study and consent declaration

UNDERSØKELSE AV JODKONSENTRASJON I URIN

Oslo august 2015

Forespørsel om deltakelse i forskningsprosjektet:

”Undersøkelse av jodkonsentrasjon i urin hos gravide og vegetarianere”

Bakgrunn og hensikt

Jod er et viktig sporstoff for produksjonen av stoffskiftehormoner, som er nødvendig for at skjoldbruskkjertelen fungerer. Det finnes få studier her i Norge om jodinntak hos vegetarianere og gravide. Derfor ønsker vi å undersøke dette nærmere i våre masteroppgaver. Dette er en forespørsel til deg om å delta i en studie hvor vi ønsker å finne ut hvor mye jod gravide og vegetarianere får i seg gjennom kostholdet. Dette kan undersøkes ved å analysere mengden jod i prøver av urin. Studien vil også framskaffe data om matvarers betydning for mengde jod i urinen. Studien inngår i en del av en større undersøkelse ved Folkehelseinstituttet. Kunnskapen er nyttig i videre arbeid for å kartlegge inntak av jod hos vegetarianere og gravide.

Hva innebærer studien for deg?

Deltakelse i denne studien innebærer at du kan levere to urinprøver og svare på et bakgrunnsskjema. De to urinprøvene skal tas om morgenen på to ulike dager. I tillegg ber vi deg registrere fortløpende maten du spiser de to dagene *før* du tar urinprøve i en kostholdsdagbok.

Mulige fordeler og ulemper

Studien vil kunne gi deg informasjon om ditt jodinntak. Deltakelse innebærer å avgi urinprøver og å bruke tid til å rapportere kostvaner, hvilket kan oppleves noe belastende.

Hva skjer med prøvene og informasjonen om deg?

Prøvene du gir fra deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene og prøvene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Det er kun prosjektledere som har adgang til navnelisten og som kan finne tilbake til deg.

Personvern

All informasjon om deg vil behandles konfidensielt, og kodenøkkelen som kan identifisere deg med de innsamlede opplysningene vil bli slettet når prosjektperioden er avsluttet. Etter dette vil opplysninger og analysesvar kun foreligge anonymisert.

Frivillig deltakelse

Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. **Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side.**
Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke. Dersom du senere ønsker å trekke deg eller har spørsmål til studien kan du kontakte prosjektleder Kristine Nyheim (41452222) eller Nina Johansen (90638258).

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver

Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre kodenøkkelen er slettet eller opplysningene brukt i vitenskapelige sammenheng.

Nærmere opplysninger om undersøkelsen kan fås ved henvendelse til prosjektledere Kristine Nyheim og Nina Johansen, tlf 41452222 eller 90638258, e-post: kristinen91@hotmail.com eller nina_c_johansen@hotmail.com.

Vennlig hilsen
Kristine Nyheim og Nina Johansen
Høgskolen i Oslo og Akershus
Postboks 4 St. Olavs plass

Samtykke til deltakelse i studien

Jeg har mottatt skriftlig informasjon om studien «**Undersøkelse av jodkonsentrasjon i urin hos gravide og vegetarianere**» og er villig til å delta i studien

----
(Signert av prosjektdeltaker, dato)

NAVN: ____

ADRESSE:____

E-postadresse:____

Mobiltelefon:____

Dersom deltakelsen gjelder ditt barn (for barn< 12 år):
Stedfortredende samtykke dersom barnet er innforstått med å delta

----
(Signert av foreldre, dato)

Dersom deltakelsen gjelder ditt barn (for barn 12-16 år):
Stedfortredende samtykke i tillegg til barnet selv, dersom barnet ønsker å delta

----
(Signert av barnet selv, dato)

Jeg bekrefter å ha gitt informasjon om studien

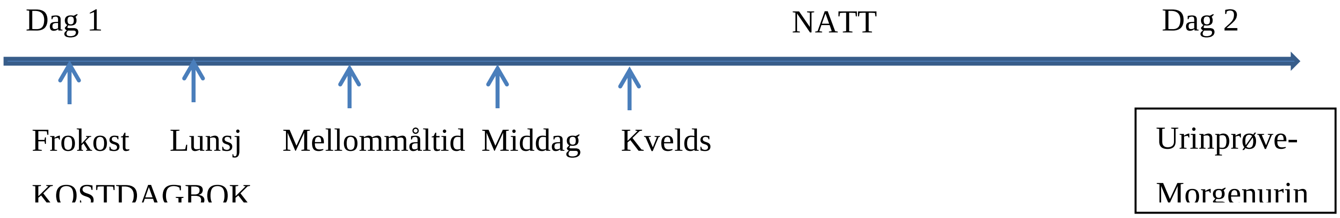
(Signert, rolle i studien, dato)

Appendix 3 Instruction for food recording and food diary

INSTRUKSJON

Denne kostdagboken skal brukes til å registrere all mat fra du står opp om morgen til du legger deg om kvelden. Dette gjelder for begge dagene før du samler morgenurinprøve. Denne studien handler ikke om hvorvidt du spiser sunt eller ikke, men at du spiser mest mulig slik du vanligvis gjør.

PLAN FOR DATAINNSAMLINGEN: Må gjennomføres to påfølgende dager



Tilsvarende neste dag.

I dagboken ber vi deg skrive dag og dato og deretter å notere alt du spiser og drikker i løpet av dagen før du samler morgenurin-prøven. Det er spesielt viktig å angi *type brød*, frokostkorn og andre kornvarer, spesielt type korn og hvor grovt/finmalt mel som er brukt. Les gjerne på pakningen og skriv andel finmalt/siktet mel (lyst) og/eller sammalt/fullkorn (Se evt innholdsfortegnelse). Det er best om mengde kan angis i vekt, men hvis du ikke har vekt kan du angi enhet (f eks en skive, ett glass). Skriv også opp kosttilskudd som tran, vitamintilskudd, mineraltilskudd etc.

For brød, middagsporsjoner og drikke ber vi deg angi om du anser mengde spist som en liten, middels eller stor porsjon. For sammensatte retter kan du gjerne bruke flere linjer.

For urinprøvene: samle urinen om morgenen med en gang du våkner. Om du må tisse før du trenger å stå opp er det den første urinen du skal samle. Benytt en ny flaske til hver prøve og noter dato og klokkeslett. Flaskene er merket med Prøve 1 og Prøve 2.

Detaljer for hvordan urinprøven skal samles:

1. Vask hendene med såpe og vann, og tørk dem.
2. Skru av lokket på flasken og ta ut den ekstra forseglingen.
3. Avgi urinen direkte i plastflasken. Pass på at du ikke fyller flasken mer enn halvfull.
4. Legg tilbake forseglingen og skru lokket på flasken, sjekk at lokket er skrudd godt til.
5. Noter dato på etiketten utenpå flasken.
6. Oppbevar flasken(e) i kjøleskapet til du skal levere den til.

På neste side er et eksempel på registrering:

Dag og dato: ____________________________

Tid	**Matvare**	**Detaljer**	**Mengde, angi om det er liten, middels eller stor porsjon**		**Økologisk**
7.30	Appelsinjuice	Fra kartong, Synnøve	1 lite glass (1,2 dl)	Liten	
	Havregrøt av 1,5 dl havre gryn og 3 dl lettmelk	Store havregryn, Axa	1 stor tallerken	Stor porsjon	
	Sukker på grøten	Vanlig hvitt	1 ts		
	Kaffe	Filterkaffe	1 krus (2 dl)	Middels	
	Melk, ekstra lett lettmelk		1 stort glass (2 dl)	Middels	
	Tran	Møllers	1 spiseskje		
10.30	Knekkebrød	Husmann, rug fullkorn	2 stk	Middels	
	Smør, bremykt	Tynt lag	3 gram		
	Brunost	G35	To skiver, 20 gram totalt	Middels	
12.00	Brødskiver	Kornbrød grovt brød, mest hvetemel	2 tykke skiver, ca 40 gram totalt	Middels	X (=Ja)
	Smør, bremykt	Tynt lag på begge	6 gram		
	Jarlsberg ost		To tykke skiver		
	Servelat		1 skive		
	Agurk	Rå	2 skiver		
	Te	Vanlig tepose	2 dl vann, 1 pose	Middels	
15.30	Eple	Grønt, med skall	1 middels stort	Middels	

16.30	Middag: To poteter	Skrelt og kokt	2 middels	Middels
	Lakseskiver	Fra frysedisk, 2 stk pakket individuelt	Vekt før tilbereding: 100 g per stykke	Middels
	Rømmesaus	Rømme, løk og urter	3 spiseskjeer	
	Salat	Salat laget av issalat, agurk, og rocculasalat	1 stor porsjon	
	Vann	Fra springen	2 glass, 4 dl	
19.00	Kaffe	Filterkaffe	1 kopp, 1,5 dl	
	Bolle	Gjærbakst, bakt med hvetemel, siktet	2 stk	
22.00	Brødskive	Flerkorn brød Bakers, Grovhet: 45%. Ingredienser: hvetemel, sammalt hvete (12,7 %), rug (10,0 %), havre helkorn (3,6 %), havremel (3,6 %)	1 tykk skive	
	Brie ost		2 tykke skiver	

Det er satt av tre sider til hver dag. Har du spørsmål underveis kan du ringe Anne Lise på telefon nummer: 21036326 eller 91303207

Dag og dato: _______________

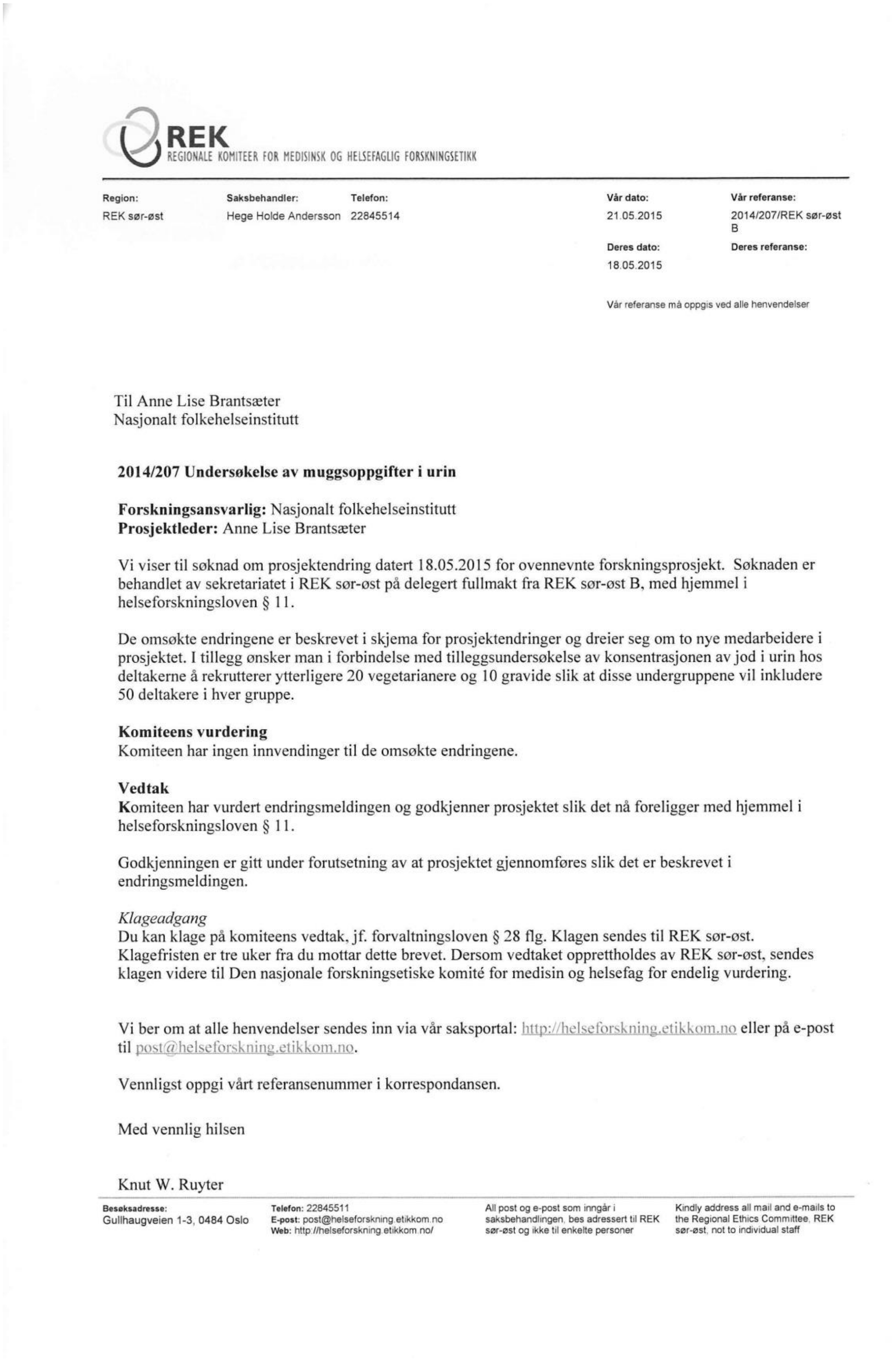
Tid	Matvare	Detaljer	Mengde. Angi også om det er liten, middels eller stor porsjon		Økologisk

Appendix 4 Protocol for food items not listed in Food Composition Table

The food item given	**Coded as**	**Food code**
Soy flakes	Soy protein	6737
Soymilk, unspecified	Soy beverage, sweetened	13066
Soy ice cream	Soy beverage, sweetened	13066
Oat milk, unspecified	Oat beverage with calcium and vitamins	13068
Almond milk	Soy beverage, sweetened	13066
Chickpea flour	Dried chickpeas	6091
Cocos cream , Cocos water	Coconut milk, canned	6701
Chia seeds	Quinoa	6615
Falafel	Chickpeas	6128
Hemp seeds	Linseed	5012
Maple syrup	Syrup	9015
Goji berries	Black chokeberry, raw	6764
Vegetarian burgers	Soy protein, textured	6737
Bean burgers	Burger, vegetarian with beans	6705
Linseed oil	Linseed, crushed	5012
Hummus chips	Tortilla chips	12017
Vegetar patè	Vegetarian spread, Tartex	6713
Vegetarian soup	Casserole, with beans, no meat	6708
Vegetarian stews, unspecified	Vegetable stew	6706
Vegetarian schnitzel	Soy protein, textured	6737
Vegetarian pizza	Pizza with tomato sauce and cheese	6734
Hummus	Chick beans and tahini	6091/6702
Vegetarian spread (for bread)	Soy protein, textured	6737
Spring roll	Croissant, plain (with vegetables)	5312
Samosa	Wheat flour	5006
Vegan “cheese”	Coconut fat (some contains other fats)	8001
Cocos cake with buckwheat	Buck wheat flour and coconut fat	5132/8001
Coconut meal	Coconut fat	8001
Sesame pate	Vegetarian spread, Tartex	6713
Vegan sausage	Soy protein, textured	6737
Sting nettles	Spinach, raw	6064
Pesto without cheese	Pesto, green, homemade	6143
Nut oil, unspecified	Walnut oil	8250
Vegetarian “meatballs”	Soy protein, textured	6737

Bread, not specified	Bread, semi-coarse (25-50 %), unspecified, industrially made	5341
Oil not specified	Olive oil	8019
Butter not specified	Butter	8005
Milk not specified	Milk, semi-skimmed, 1,2 % fat	1002

Appendix 5 Project approval



REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	**Saksbehandler:**	**Telefon:**	**Vår dato:**	**Vår referanse:**
REK sør-øst	Hege Holde Andersson	22845514	21.05.2015	2014/207/REK sør-øst B
			Deres dato:	**Deres referanse:**
			18.05.2015	

Vår referanse må oppgis ved alle henvendelser

Til Anne Lise Brantsæter
Nasjonalt folkehelseinstitutt

2014/207 Undersøkelse av muggsoppgifter i urin

Forskningsansvarlig: Nasjonalt folkehelseinstitutt
Prosjektleder: Anne Lise Brantsæter

Vi viser til søknad om prosjektendring datert 18.05.2015 for ovennevnte forskningsprosjekt. Søknaden er behandlet av sekretariatet i REK sør-øst på delegert fullmakt fra REK sør-øst B, med hjemmel i helseforskningsloven § 11.

De omsøkte endringene er beskrevet i skjema for prosjektendringer og dreier seg om to nye medarbeidere i prosjektet. I tillegg ønsker man i forbindelse med tilleggsundersøkelse av konsentrasjonen av jod i urin hos deltakerne å rekrutterer ytterligere 20 vegetarianere og 10 gravide slik at disse undergruppene vil inkludere 50 deltakere i hver gruppe.

Komiteens vurdering
Komiteen har ingen innvendinger til de omsøkte endringene.

Vedtak
Komiteen har vurdert endringsmeldingen og godkjenner prosjektet slik det nå foreligger med hjemmel i helseforskningsloven § 11.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i endringsmeldingen.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningsloven § 28 flg. Klagen sendes til REK sør-øst. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn via vår saksportal: http://helseforskning.etikkom.no eller på e-post til post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Knut W. Ruyter

Besøksadresse:
Gullhaugveien 1-3, 0484 Oslo

Telefon: 22845511
E-post: post@helseforskning.etikkom.no
Web: http://helseforskning.etikkom.no/

All post og e-post som inngår i saksbehandlingen, bes adressert til REK sør-øst og ikke til enkelte personer

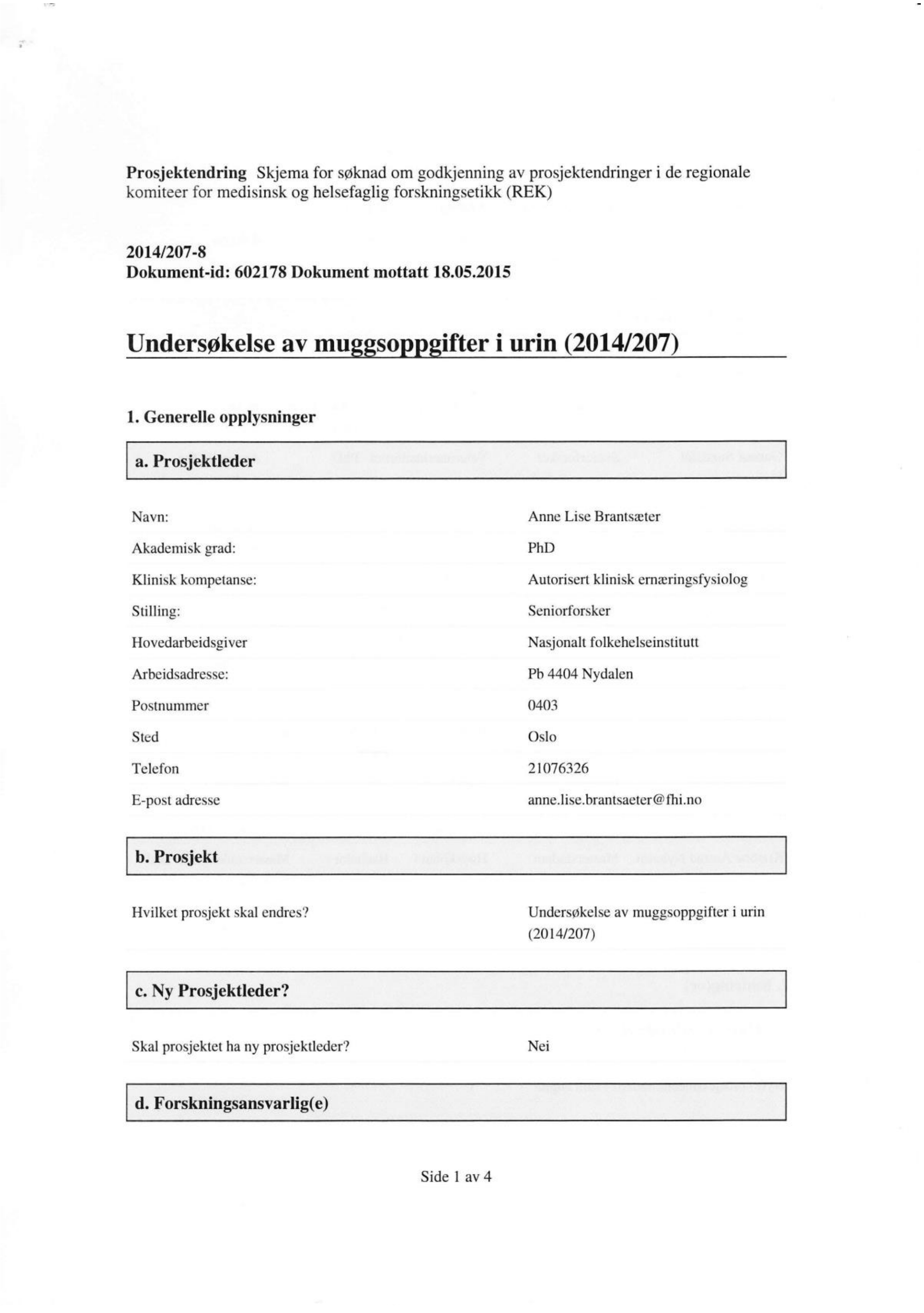
Kindly address all mail and e-mails to the Regional Ethics Committee, REK sør-øst, not to individual staff

avdelingsdirektør
REK sør-øst

Hege Holde Andersson
komitésekretær

Kopi til: Nasjonalt folkehelseinstitutt ved øverste administrative ledelse: reksoknad@fhi.no

Appendix 6 Approval for recruiting additional participants



Prosjektendring Skjema for søknad om godkjenning av prosjektendringer i de regionale komiteer for medisinsk og helsefaglig forskningsetikk (REK)

2014/207-8
Dokument-id: 602178 Dokument mottatt 18.05.2015

Undersøkelse av muggsoppgifter i urin (2014/207)

1. Generelle opplysninger

a. Prosjektleder

Navn:	Anne Lise Brantsæter
Akademisk grad:	PhD
Klinisk kompetanse:	Autorisert klinisk ernæringsfysiolog
Stilling:	Seniorforsker
Hovedarbeidsgiver	Nasjonalt folkehelseinstitutt
Arbeidsadresse:	Pb 4404 Nydalen
Postnummer	0403
Sted	Oslo
Telefon	21076326
E-post adresse	anne.lise.brantsaeter@fhi.no

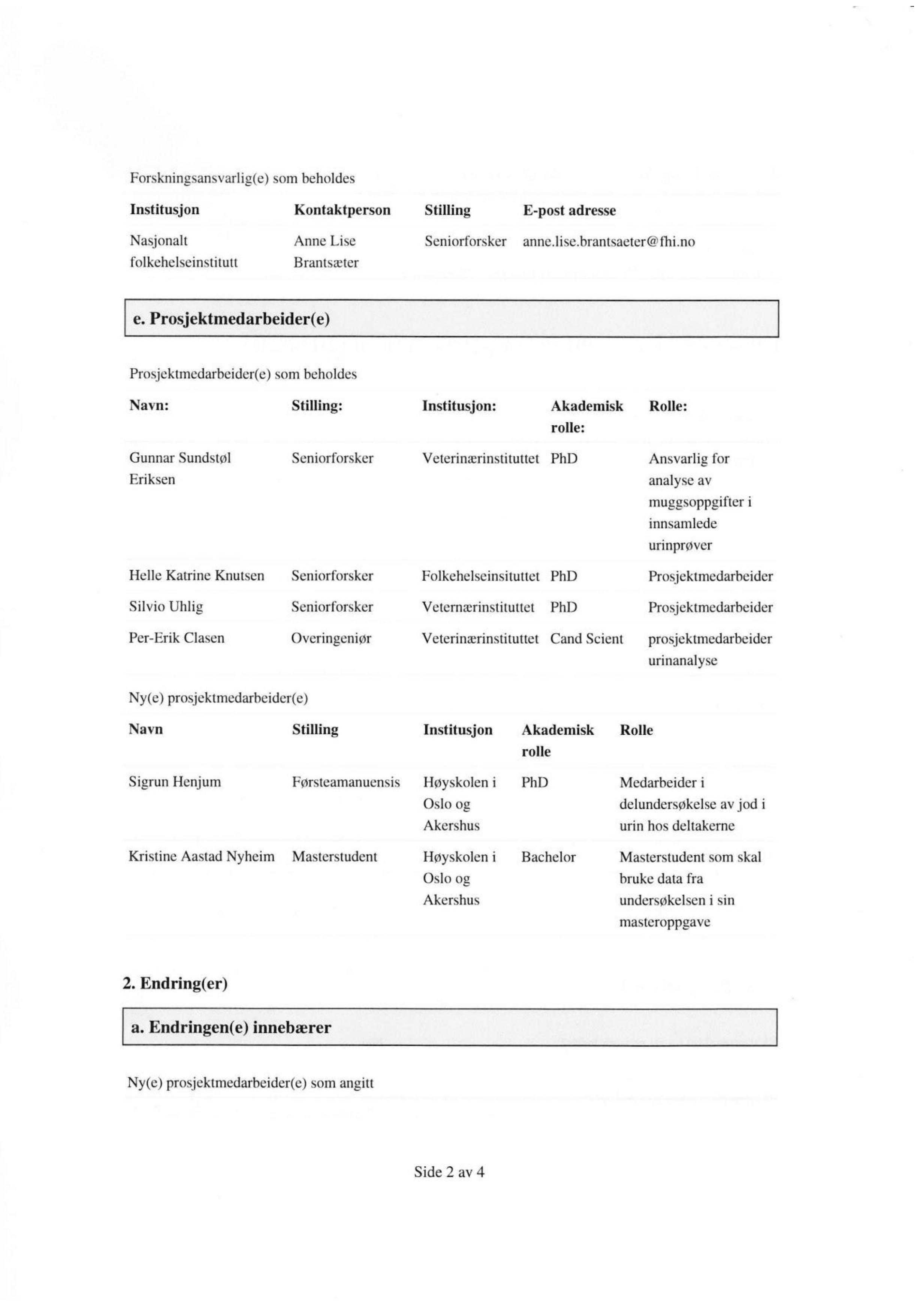
b. Prosjekt

Hvilket prosjekt skal endres?	Undersøkelse av muggsoppgifter i urin (2014/207)

c. Ny Prosjektleder?

Skal prosjektet ha ny prosjektleder?	Nei

d. Forskningsansvarlig(e)



Forskningsansvarlig(e) som beholdes

Institusjon	Kontaktperson	Stilling	E-post adresse
Nasjonalt folkehelseinstitutt	Anne Lise Brantsæter	Seniorforsker	anne.lise.brantsaeter@fhi.no

e. Prosjektmedarbeider(e)

Prosjektmedarbeider(e) som beholdes

Navn:	Stilling:	Institusjon:	Akademisk rolle:	Rolle:
Gunnar Sundstøl Eriksen	Seniorforsker	Veterinærinstituttet	PhD	Ansvarlig for analyse av muggsoppgifter i innsamlede urinprøver
Helle Katrine Knutsen	Seniorforsker	Folkehelseinsituttet	PhD	Prosjektmedarbeider
Silvio Uhlig	Seniorforsker	Veternærinstituttet	PhD	Prosjektmedarbeider
Per-Erik Clasen	Overingeniør	Veterinærinstituttet	Cand Scient	prosjektmedarbeider urinanalyse

Ny(e) prosjektmedarbeider(e)

Navn	Stilling	Institusjon	Akademisk rolle	Rolle
Sigrun Henjum	Førsteamanuensis	Høyskolen i Oslo og Akershus	PhD	Medarbeider i delundersøkelse av jod i urin hos deltakerne
Kristine Aastad Nyheim	Masterstudent	Høyskolen i Oslo og Akershus	Bachelor	Masterstudent som skal bruke data fra undersøkelsen i sin masteroppgave

2. Endring(er)

a. Endringen(e) innebærer

Ny(e) prosjektmedarbeider(e) som angitt

Økning i antall forskningsdeltakere

Antall nye deltakere relatert til prosjektets utvalgsgrupper

I forbindelse med tilleggsundersøkelse av konsentrasjonen av jod i urin hos deltakerne i dette prosjektet ønsker vi å rekrutterere ytterligere 20 vegetarianere og 10 gravide slik at disse undergruppene vil inkludere 50 deltakere i hver gruppe.

Hovedprosjektets mål er undersøkelse av muggsoppgifter i urin, men tilleggsundersøkelse av jod og eventuelt andre stoffer i urin var allerede inkludert i opprinnelig forsøksprotokoll, informasjonsmateriell til deltakerne og samtykke-erklæring.

Endring i rekrutteringsprosedyre(r)

Redegjør nærmere for ny(e) rekrutteringsprosedyre(r)

Dersom prosjektet gis tillatelse til rekruttere flere deltakere ønsker vi å rekruttere disse blant studenter og ansatte ved Høyskolen i Oslo og Akershus. Rekruttering vil foregå viaintranett og gjennom oppslag på samme måte som opprinnelig rekruttering ble gjort via intranett og oppslag på Folkehelseinstituttet og Veterinærinstituttet

b. Begrunnelse for endringen(e)

Praktisk, faglig og vitenskapelig begrunnelse for endringen(e)

Dersom deltakerantallet i gruppen "Vegetarianere" og gruppen "Gravide" økes til 50 vil det vil styrke muligheten til å gjøre statistiske sammenlikninger og vitenskapelig publisering.

3. Avveining av nytte og risiko ved prosjektendringene

Hvorfor er det forsvarlig å gjennomføre endringene? Gi en begrunnet avveining av fordelene og ulempene ved prosjektendringene.

Det er forsvarlig å gjennomføre endringene fordi denne studien innbærer liten belastning for deltakerne. Fordelen er at flere deltakere gir økt mulighet til å gjøre statistiske analyser og vil gi ny masterstudenten innsikt og erfaring i rekruttering og gjennomføring av datainnsamlingen.

4. Vedlegg

Ingen vedlegg

5. Ansvarserklæring

Jeg erklærer at prosjektet vil bli gjennomført

i henhold til gjeldende lover, forskrifter og retningslinjer

i samsvar med opplysninger gitt i denne søknaden

i samsvar med eventuelle vilkår for godkjenning gitt av REK