Iodine status in Norwegian preschool children and significance of dietary sources of iodine and parental socio-economic factors
- A cross-sectional study

Master Thesis in Clinical Nutrition

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ABSTRACT

Introduction: Iodine is an essential trace element with important physiological effects in the human body. Iodine is necessary for thyroid hormone synthesis. The hormones are needed for tissue development in the central nervous system, growth and brain development in children, and regulation of basal metabolic rate and macronutrient metabolism. Iodine deficiency is still a global threat despite international efforts to eliminate the condition. In recent years, major progress have been made towards elimination of iodine deficiency due to introduction of universal salt iodization programs. However, iodine deficiency is still the number one cause of preventable mental retardation in children. In Norway, goiter prevalence was high prior to introduction of fortification of cow fodder in 1950. Since then, iodine status of the Norwegian population have gradually improved. However, several studies have suggested that subgroups of the Norwegian population may be susceptible to iodine deficiency due to low intake of iodine-rich food sources including seafood and dairy products. Studies on iodine status in Norwegian preschool children (aged 4-6 years) are old and lacking.

Study aims: Main aim of the present thesis was to determine and evaluate the iodine status of preschool children living in Bergen. Specific aims included investigations of possible associations between urinary iodine concentration and iodine-rich food sources and parental socio-economic factors. Associations between parental socio-economic factors and the children's intake of iodine-containing foods were also examined.

Methods and materials: The present thesis is part of a larger intervention study. Habitual dietary intake was assessed by a semi-quantitative food frequency questionnaire. Iodine concentration was determined by inductively coupled plasma-mass spectrometry in non-fasting, spot urine samples.

Results: Approximately 50% of the children consumed fish and other seafood less frequently than current Norwegian recommendations of two to three servings per week. Nearly all children consumed dairy products daily. The iodine status of the preschool children was adequate (133 µg/L). Intake of fatty fish (OR = 1.95, 95% CI = 1.01-3.77, p = 0.048) and sweet milk (OR = 2.17, 95% CI = 1.07-4.38, p = 0.031) were associated with sufficient iodine status. Weak correlations were observed between iodine status and intake of iodine-rich food sources and between iodine status and parental socio-economic factors. In addition, unadjusted logistic regression models found higher socio-economic status to be associated with increased likelihood of a higher intake of seafood for dinner and dairy products among the children.

Conclusions: The preschool children in this study had adequate iodine status, and intake of sweet milk and fatty fish were significant predictors of sufficient iodine status. Parental socio-economic status seemed to be associated with the children's intake of seafood and dairy products.

SAMMENDRAG

Introduksjon: Jod er et essensielt sporstoff med viktige fysiologiske funksjoner i menneskekroppen. Jod er nødvendig for syntese av thyreoideahormoner. Hormonene er nødvendig for vevssyntese i sentralnervesystemet, vekst og hjerneutvikling hos barn, samt regulering av basal metabolsk rate og metabolisme av makronæringsstoffer. Jodmangel er fortsatt en omfattende global utfordring til tross for internasjonale tiltak for å eliminere tilstanden. I senere år har man sett stor framgang i retning av eliminering av jodmangel på bakgrunn av introduksjon av universelle programmer for bruk av jodisert salt. Men, jodmangel er fortsatt nummer én årsak til mental retardasjon hos barn som kan forebygges. I Norge var forekomsten av struma høy før beriking av kraftfôret til kyr i 1950. Siden den gang har jodstatus gradvis bedret seg i den norske befolkningen. Nylig har flere studier foreslått at undergrupper i den norske befolkningen kan være utsatt for jodmangel på grunn av lave inntak av jodholdige matvaregrupper som sjømat og meieriprodukter. Studier på jodstatus hos norske førskolebarn i alderen 4-6 år er få og de fleste er av eldre årgang.

Studiens mål: Hovedmålet med masteroppgaven var å bestemme og evaluere jodstatus hos førskolebarn i Bergen. Spesifikke målsetninger inkluderte å undersøke mulige assosiasjoner mellom jodstatus og inntak av jodholdige matvaregrupper samt mellom jodstatus og foreldrenes sosioøkonomiske status. Assosiasjoner mellom foreldrenes sosioøkonomiske status og barnas inntak av jodholdige matvaregrupper ble også undersøkt.

Metoder og materialer: Masteroppgaven er del av en større intervensjonsstudie. Barnas vanlige kosthold ble undersøkt ved hjelp av et semi-kvantitativt matfrekvensskjema. Jodkonsentrasjon ble bestemt ved hjelp av induktivt koblet plasma-massespektrometri i ikke-fastende, spot urinprøver.

Resultater: Omtrent 50% av barna spiste fisk og annen sjømat sjeldnere enn det som anbefales av norske myndigheter, altså å innta fisk to til tre ganger per uke. Nesten alle barna inntok meieriprodukter daglig. Jodstatus hos førskolebarna var adekvat (133 µg/L). Inntak av fet fisk (OR = 1.95, 95% CI = 1.01-3.77, $p = 0.048$) og søt melk (OR = 2.17, 95% CI = 1.07-4.38, $p = 0.031$) var assosiert med å ha tilstrekkelig jodstatus. Svake korrelasjoner ble observert mellom jodstatus og inntak av jodholdig mat og mellom jodstatus og foreldrenes sosioøkonomiske status. I tillegg viste ujusterte logistiske regresjonsmodeller at høyere sosioøkonomisk status så ut til å øke sannsynligheten for et høyere inntak av sjømat til middag og meieriprodukter blant barna.

Konklusjoner: Førskolebarna i denne studien hadde adekvat jodstatus, og inntak av søt melk og fet fisk var signifikante prediktorer for tilfredsstillende jodstatus. Foreldrenes sosioøkonomiske status så ut til å være assosiert med barnas inntak av sjømat og meieriprodukter.

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FORMULAS

ABBREVIATIONS

µg	Microgram
µm	Micrometer
µl	Microliter
µg/L	Microgram/liter
µmol	Micromole
BMI	Body Mass Index (kg/m^2)
CI	Confidence interval
EAR	Estimated average requirement
FFQ	Food frequency questionnaire
FINS	Fish Intervention Studies
ICCIDD	International Council for Control of Iodine Deficiency Disorders
ICP-MS	Inductively coupled plasma-mass spectrometry
IDD	Iodine deficiency disorders
IDF	International Dairy Federation
IQ	Intelligence quotient
IQR	Interquartile range
KI	Potassium iodine
LMU	Ludwig-Maximillians University
LOD	Limit of detection
LOQ	Limit of quantification
mmol	Millimole
MS	Mass spectrometer
NIFES	National Institute of Nutrition and Seafood Research
nmol/L	Nanomole/liter
NNR	Nordic Nutrition Recommendations
NOK	Norwegian kroner
NSD	Norwegian Social Science Data Service
OR	Odds ratio
REC North	Regional Committees for Medical Health Research Ethics
RKBU West	Regional Knowledge Center for Children and Youth Vest
RNI	Recommended nutrient intake

rpm	Revolutions per minute
SCF	Scientific Committee on Food
SD	Standard Deviation
SEQ	Socio-economic questionnaire
SPSS	Statistical Product and Service Solutions (IBM SPSS Statistics)
SRM	Standard reference material
T_4	Thyroxine
T_3	Triiodothyronine
TMAH	Tetramethylammonium hydroxide
TPO	Thyroid peroxidase
TSH	Thyroid-stimulating hormone
UiB	University of Bergen
UIC	Urinary iodine concentration
UIE	Urinary iodine excretion
USI	Universal salt iodization
VKM	Norwegian Scientific Committee for Food Safety
WHO	World Health Organization
WP5	Work package 5

1. INTRODUCTION

1.1 Background

Iodine is a trace element located mainly in the thyroid gland (70-80%) and is essential for thyroid hormone production (1, 2).

Worldwide, iodine deficiency is still a major threat even though salt iodization programs have had a large impact on global iodine nutrition (3). Globally, approximately two billion people, including 246 million school-age children, are estimated to have inadequate iodine intakes, despite national and international efforts to increase the dietary iodine intake. Europe is still the continent with highest prevalence of iodine deficiency (43.9% of schoolchildren) (4).

When iodine intakes are inadequate, the body may respond with impaired thyroid hormone synthesis, which can result in several functional and developmental abnormalities (5). Clinical signs and conditions related to severe iodine deficiency include goiter, stillbirth, hypothyroidism, inadequate growth, and impaired mental development. The latter is regarded as the most devastating consequence of iodine deficiency, leading to brain damage in children (6). Mild-to-moderate iodine deficiency may also induce adverse health effects during childhood, including weakened intellectual function and lower intelligence quotients (IQ-scores) (7, 8). In recent years, mild iodine deficiency has re-emerged in developed countries previously recognized as iodine sufficient. Studies performed in New Zealand, Australia and the United Kingdom have shown reoccurrence of mild iodine deficiency in subgroups of the population (e.g. children and adolescents) (9-11).

In Norway, Brantsaeter et al. (2013) found that vulnerable groups, including pregnant and lactating women and infants, are especially at risk of insufficient iodine intake due to low maternal intake of dairy products, seafood and eggs, in addition to inadequate use of iodinated supplements (12).

Regular consumption of iodine-rich food sources including seafood (primarily lean fish and shellfish), in addition to milk and dairy products, is important for optimal iodine intakes through all age groups in the Norwegian population (13). Norwegian dietary surveys show that consumption of milk has decreased in recent years (14). According to the International Dairy Federation (IDF), the Norwegian consumption of milk decreased by 2% in 2012, while intake of cheese and butter increased by 2 and 34%, respectively (15). In spite of this minor reduction in milk intake, Norway is still one of the countries with the highest milk consumption per capita in the world (15, 16).

Studies focusing on iodine status (measured in urinary iodine concentration) in Norwegian preschool children are outdated and lacking. Dahl et al. (2004) conducted a study on the iodine content of Norwegian foods, along with assessment of iodine intakes in subgroups of the Norwegian population. In their study, the iodine intakes among 4-year-old girls and boys were calculated to 98 µg/day and 101 µg/day, respectively. This indicates iodine intakes slightly above the recommended intake level for this age group (90 µg/day) (13).

Studies from other parts of the world, including New Zealand, United States, Australia and Korea have examined iodine nutrition (intake and/or status) in preschool children. Results indicate that preschool children might be a susceptible group in relation to both iodine deficiency and excessive iodine intakes (9, 17-19). Sufficient iodine status in preschool children is important due to iodine's role in thyroid hormone synthesis, and secondly growth and mental development (5, 20).

The present master thesis is a cross-sectional study examining the iodine status among 4-6 year old children living in Bergen, Norway. This master project is part of a larger intervention study (work package 5) in the "Fish Intervention studies" (FINS-project). The intervention study (WP5) investigates the significance of diet on learning abilities in preschool children.

1.2 Iodine

1.2.1 Definition and functions

Iodine is an indispensable component of the thyroid hormones, thyroxine (T_4) and triiodothyronine (T_3) (**Fig. 1.1**), and is therefore necessary for hormone synthesis in the thyroid gland. Approximately 65% and 58% of T_4's and T_3's molecular weight is comprised of iodine. The hormones are the only iodine-containing compounds with known physiological importance in humans, and the potentially harmful effects resulting from iodine deficiency are related to a decrease in hormone production (21). The thyroid hormones are essential for normal tissue development in the central nervous system. The hormones also play an important role in regulation of the basal metabolic rate and macronutrient metabolism (22).

There are also evidence of hormonal effects on development of the fetal and neonatal brain. A study by Pharoah et al. (1984), showed a significant correlation between serum levels of T_4

in women during pregnancy in an iodine deficient region, and intellectual ability and motor competence of their children at age 10-12 years. The study depicts that maternal levels of T_4 may be essential for normal neurological maturation of the fetus (23).

Thyroid hormones have several crucial effects in the developing brain, and by binding to specific nuclear receptors in the brain, T_3 controls the expression of genes involved in myelination, cell differentiation, migration, maturation and signaling (5, 24). The impact of iodine on cognition and IQ in children seems to be associated with thyroid hormones effect on the macrostructure (e.g. differentiation) and microstructure (e.g. myelination) of the developing brain (24). Iodine may also influence the functions of specific neurotransmitters, which eventually can result in reduced processing speed and deteriorated memory. Myelination is a process starting in the second trimester of gestation and remains active until 40 years of age. Thus, iodine deficiency has the potential to induce adverse effects on cognition and mental health from childhood and well into adult life (25).

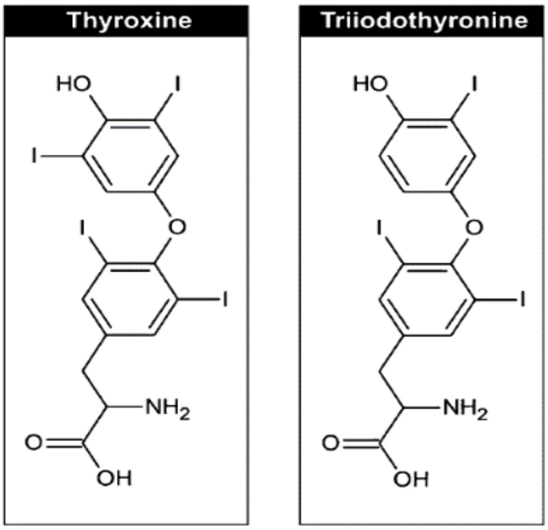


Figure 1.1: The thyroid hormones thyroxine (T_4) and triiodothyronine (T_3).
Retrieved from MB Zimmermann (2012) (26).

1.2.2 Hormone synthesis and regulation

The hormones are synthesized from thyroglobulin, which is an iodine-containing glycoprotein. Thyroglobulin is recognized as the storage form of the thyroid hormones (27). The synthesis and storage of hormones takes place in the follicular cells and the colloid of the thyroid gland. When iodide is positioned in the follicular cells, an oxidation process happens and yields active iodine. The reaction is dependent upon hydrogen peroxide and the enzyme thyroid peroxidase (TPO). Active iodine is then transported across the apical surface of the follicular cell, and here iodine is incorporated into tyrosine residues of thyroglobulin. Iodinated thyroglobulin is taken up by the colloid of the follicle. The following step is a coupling process between pairs of iodinated tyrosine molecules (28).

The amount of thyroid hormones produced is regulated by the concentration of thyroid-stimulating hormone (TSH), released from the anterior pituitary gland. Ultimately, TSH controls the endocrine function of the thyroid gland. Negative feedback regulation will control the levels of thyroid hormones in the body. If the levels of circulating T_4 is adequate, signals will tell the pituitary gland to reduce the release of TSH. In cases where mild iodine deficiency is present, the pituitary gland will increase the secretion of TSH (22, 28).

1.2.3 Absorption and metabolism

Iodine from the diet will almost completely be absorbed in the stomach and duodenum. The absorbed amount of iodine depends on the amount of iodine in the diet. There are different forms of ingested iodine (22). Dietary iodine is absorbed and transported in the circulation as iodide (21). In addition, iodate is reduced to iodide in the gut. Absorption of iodide happens rapidly from the upper small intestine or the stomach (22, 29). Secondly, iodide will immediately be taken up and put to use by the thyroid gland. Iodide is incorporated into a series of reactions, which eventually leads to the production of the thyroid hormones (22).

The healthy adult human body contains between 15-20 mg iodine (1). Approximately 8-12 mg is present in the thyroid gland (30). The remaining iodine is present in skeletal muscle (1) and the blood stream (31). The iodine concentration in the gland will vary in relation to age, dietary iodine intake and gland activity (27). The half-life of T_4 and T_3 is around 5 and 1.5-3 days, respectively. When iodine is released into the plasma it either gets trapped by the thyroid gland, or excreted by the kidneys (32). Urine is the main excretion pathway for iodine, and reflects recent dietary iodine intakes. Approximately 90% of iodine is excreted through urine due to complete reabsorption of iodide from the gastrointestinal tract (1, 33-35). In addition, small amounts of iodine can be excreted through sweat, feces and breast milk (1).

1.3 Iodine food sources and intake in Norway

Iodine is present in food mainly as inorganic iodide. Different food items and drinking water contains variable amounts of iodine, and the level reflects the iodine content of soils in a particular region and use of fertilizer (amount and type) (27). Seafood including fish, shellfish, seaweed and kelp are rich in iodide (36, 37). Even though seafood is considered the best natural source of dietary iodine, milk and dairy products are the main source of iodine in several countries because of higher total consumption in the population (13). Since 1950 the cow fodder in Norway has been fortified with iodine (2 mg KI/kg fodder), for protecting the health of humans and animals (38). The addition of iodine to cow fodder in Norway has resulted in higher iodine content of milk and dairy products, and thus higher total iodine intake in the Norwegian population. Dairy products is the largest contributor to iodine intake in the Norwegian population (**Fig. 1.2**), and about 50-60% (in adults) and 70% (in children) of the total iodine intake stems from milk and dairy products. Fish and fish products contributes with 12-14 % of iodine intake in children (13). Other food groups including bread and cereals, meat and meat products, eggs, fruit and vegetables, oils and fats, and beverages will also contribute to the overall Norwegian dietary iodine intake (~20%) (39).

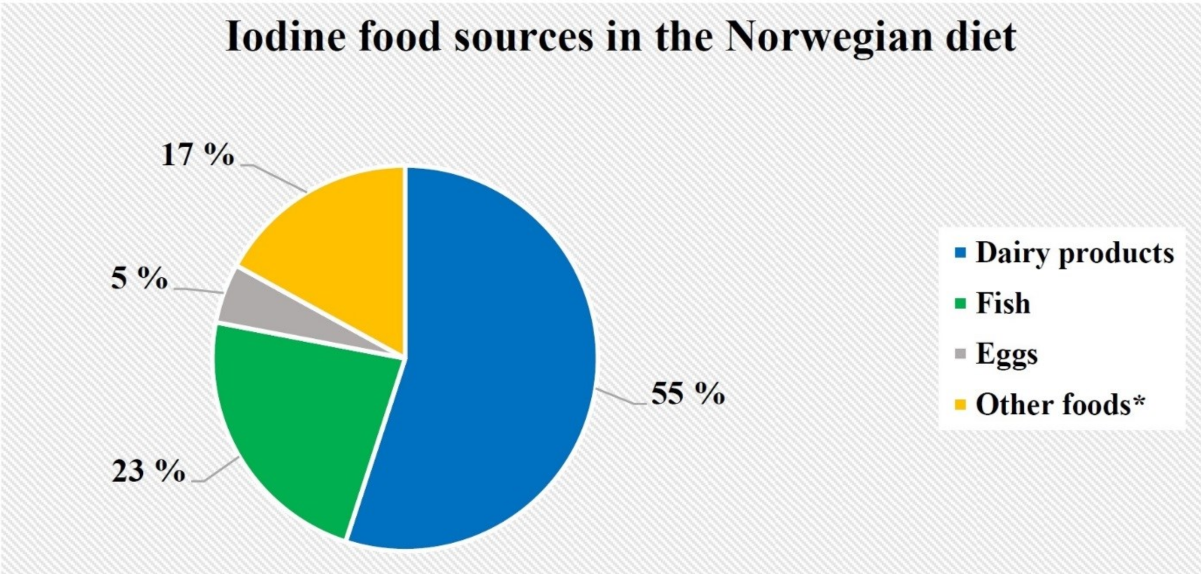


Figure 1.2: Food sources of iodine in the Norwegian diet. Estimated from food intake data in “Norkost 1997” by Dahl et al. (2004) (13, 40).
*Other foods include meat and meat products, bread and cereals, vegetables and potatoes, beverages, fats and oils, fruit, berries and juice

For years, the intake of sweet milk has decreased in the Norwegian population. However, the intake seems to be stabilizing at approximately 87-89 L per person a year (41). According to Dahl et al. (2003), the iodine content of milk varies significantly through different seasons. In their study, the iodine content in low-fat milk was highest during the winter and lowest during the summer. The average iodine concentration in low-fat milk during summer and winter were 88 and 232 µg/L, respectively (42).

The iodine content of different fish species varies considerably. Dahl et al. (2004) found that, on average, the iodine content of lean fish is more than twice that of fatty fish (13). The Norwegian Scientific Committee for Food Safety (VKM) presents similar findings in a report from 2014. Here, the iodine content of lean fish species including cod, saithe and haddock were significantly higher than the iodine content of fatty fish like mackerel, salmon and herring (43). **Table 1.1** shows the iodine content of different fish- and seafood items together with other iodine-rich food sources (dairy products and eggs).

Table 1.1: Overview of the iodine content in selected food groups (44).

Food groups	Iodine content (µg/100g)
Fatty fish[a,b]	5-63
Lean fish[c,d]	93-320
Shellfish[e]	10-218
Processed fish products[f]	36-56
Other seafood items[g]	8-234
Milk[h]	14-20
Cheeses[i]	18-166
Eggs	49

[a]Salmon, trout, mackerel and herring. Values are based on raw fish
[b]Fatty fish with > 5% fat content (43)
[c]Lean fish with < 5% fat content (43)
[d]Cod, saithe, pollack and haddock. Values for cod are based on wild, raw fish and unspecified, raw fish
[e]Shrimps, crab and mussels. Values for shrimps in brine and boiled crab
[f]Fish cakes, fish sticks and fish gratin (frozen)
[g]Sushi, mackerel in tomato sauce (canned), tuna (canned), caviar, "Svolvaer- and Lofotpostei"
[h]Sweet milk, cultured milk and yogurt
[i]White cheeses ("Norvegia", "Jarlsberg" and cream cheeses) and brown cheese

1.3.1 Iodized salt

Iodized salt is by far the most important source of dietary iodine in countries where salt iodization is common (45). Universal salt iodization (USI) is the main strategy for ensuring adequate iodine intakes in populations. The USI programs involves iodization of all human and livestock salt, including salt used in the food industry (46). In Norway, the food industry is not allowed to use iodized salt (47). Only one brand of table salt is fortified with iodine, and the added amount of iodine is five µg/g salt. Due to the low amount of iodine added to table salt and the simultaneous public efforts in order to reduce the salt intake in the general population, the intake and use of iodized salt is not considered to be relevant for iodine status in Norway (48, 49). The plan for salt reduction is related to the association between salt intake, hypertension and risk of cardiovascular disease (50). To accomplish the goal of salt reduction, the government has established a "Salt partnership", which is a collaboration between Norwegian central authorities and key participants in the food industry (49). Hence, the contribution of iodized salt to the overall Norwegian dietary iodine intake will most likely not increase in the future.

1.3.2 Intake challenges

There are different challenges related to iodine intake in individuals. Iodine is unevenly distributed in the environment, and climatic changes like flooding and erosion may create iodine deficient soils. Consequently, foods and crops grown in such areas will be low in iodine (5). In addition, iodine intake from foods will be affected by different cooking methods. Iodine losses depends on temperature, food type and length of cooking (51). Also, freezing and freeze drying will negatively affect the iodine level of different food items, and can reduce iodine content by up to 20-25% (22, 36). Goindi et al. (1995) examined the iodine losses during different cooking methods of typical Indian food courses. They found that mean iodine losses ranged from 6% (roasting) to 37% (boiling). The high loss of iodine during boiling may be related to the fact that added salt will absorb water, while iodine leaks out (52). Another study found similar results. Boiling decreased the iodine content of prawn and kelp by 23% and 91%, respectively (53). In addition, goitrogens (substances in food that can interrupt absorption and/or utilization of iodine) can reduce the uptake of iodine to the thyroid gland. Cabbage, broccoli, cauliflower and soy are examples of common goitrogens in the diet (22, 54). Exposure to dietary goitrogens will not usually cause goiter unless simultaneously low iodine intakes (55). Thus, in healthy individuals, consumption of goitrogens are not likely to result in compromised iodine status and related adverse health effects.

1.4 Iodine requirements and recommendations

Iodine storage in the body is limited, with half-life in plasma of ~10 hours. In iodine sufficient adult individuals, the thyroid gland retains 60-80 µg iodine/day in order to maintain adequate thyroid hormone synthesis (26). Iodine requirements are dependent upon several factors including thyroidal radioiodine accumulation and turnover, iodine balance, urinary excretion, hormone production and thyroid volume (31). Iodine balance is likely achieved with intakes between 40 and 100 µg/day (31, 56).
The recommended daily intake of iodine in children aged 4-6 years is 90-120 µg per day (57). Recommended nutrient intakes (RNI) for iodine are based on the amount of iodine needed to prevent goiter. Approximately 1-2 µg iodine/kg body weight plus a 100% safety margin is required (58).

Adults with normal thyroid function may tolerate sustained consumption of iodine up to 1 mg/day. Others have indicated that subgroups of the population may develop adverse effects (goiter, hypothyroidism/hyperthyroidism) at intake levels of 300-1000 µg/day (59). The Scientific Committee on Food (SCF) has set the tolerable upper intake level of iodine for adults at 600 µg/day. According to SCF, the tolerable upper intake level for children was derived by adjustment of the adult level according to body surface area. The tolerable upper intake level of preschool children (4-6 years old) is 250 µg/day (60). **Table 1.2** shows the iodine recommendations stratified by age or population group, set by the World Health Organization (WHO) and the Norwegian Directorate of Health/Nordic Nutrition Recommendations 2012 (NNR 2012).

In 2007, WHO, the United Nations Children's Fund (UNICEF) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) increased the recommended iodine intake for pregnant and lactating women, because of increasing evidence that these groups and their infants are especially vulnerable towards iodine deficiency. The recommended iodine level for pregnant and lactating women was set at 250 µg/day (46). The recommended iodine intake level among pregnant and lactating women were not altered in the NNR 2012 (61). In Norway, the recommended iodine intake for pregnant and lactating women are set at 175 µg/day and 200 µg/day, respectively (57, 62).

Table 1.2: Recommendations for iodine intake (µg/day) by age or population group (46, 57).

Age or population group[a]	Iodine intake (µg/day)
Children 0-5 years	90
Children 6-12 years	120
Adults > 12 years	150
Pregnancy	250
Lactation	250

[a]WHO/UNICEF/ICCIDD (46)

Age or population group[b]	Iodine intake (µg/day)
Children 2-5 years	90
Children 6-9 years	120
Children 10-13 years	150
Adults >13 years	150
Pregnancy	175
Lactation	200

[b]Norwegian guidelines on diet, nutrition and physical activity (57)

1.5 Iodine nutrition

1.5.1 Global iodine status

According to Pearce et al. (2013), global iodine status has improved substantially since 1990 due to introduction of USI-programs recommended by WHO and UNICEF (63, 64). Surveys conducted between 2006 and 2010 found that approximately 70% of all households worldwide had access to iodized salt (65), and in 2014, 116 countries were recognized as iodine sufficient (3).

Over the past 10 years, improvements in iodine nutrition have been made in several regions worldwide. However, little progress is seen in Africa. (63, 65). According to the Global Iodine Nutrition Scorecard released in 2015, 25 countries around the world still have an insufficient iodine status (**Fig. 1.3**). Both developed and developing countries are affected by iodine deficiency, but none of the countries have a severely deficient population (UIC < 20 µg/L) (3). In 2014, 12 countries had populations with excessive iodine status which corresponds to a median UIC ≥ 300 µg/L (3).

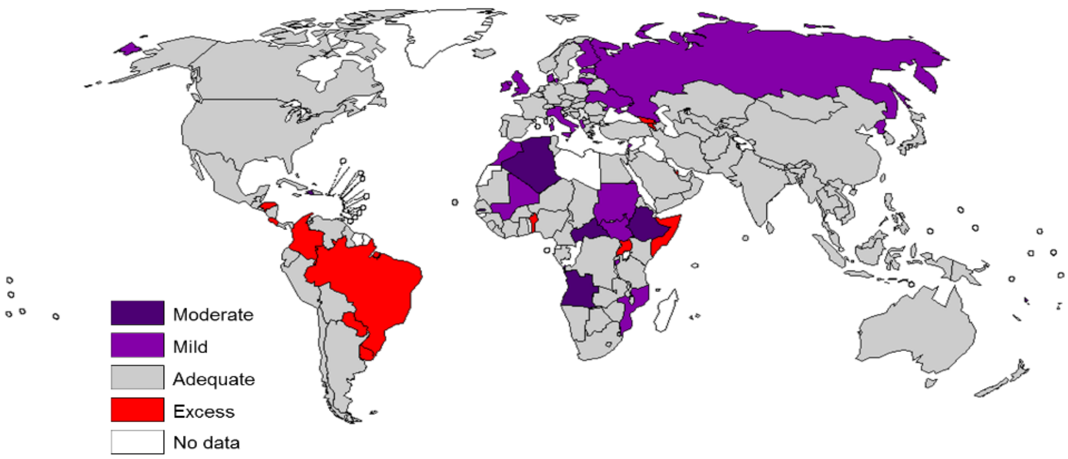


Figure 1.3: Global map of iodine nutrition 2014-2015. Iodine nutrition is measured in median UIC and assessed according to WHO/UNICEF/ICCIDD criteria: moderate deficiency (20-49 µg/L), mild deficiency (50-99 µg/L), adequate (100-199 µg/L) and excessive (≥ 300 µg/L). Retrieved from Iodine Global Network (2015) (66).

1.5.2 Iodine status in Norway

Before World War II, endemic goiter due to iodine deficiency was prevalent in specific areas of Norway. A study by Carl Schiøtz (1917) examined the goiter prevalence in Norwegian schoolchildren (age 6-14 years old). According to his results, goiter prevalence increased by poorer living conditions, and the prevalence was highest among children of workers and crofters (67). In addition, Devold et al. (1937) showed that inland areas far from the coast had high goiter prevalence among school-aged children (7-15 years old), and low fish intakes were correlated with higher goiter incidence (68). Introduction of mandatory iodization of cow fodder in 1950 resulting in higher iodine content in milk, along with higher intake of lean fish, resulted in rapid improvement in Norwegian iodine status and a large decline in the goiter rate among children (69-71). Today, Norway is considered to have an overall adequate iodine status (median UIC = 104 µg/L), but only sub-national data are available[1] (3). In Norway, large national surveys of iodine nutrition in the total population, and studies on iodine status (UIC/UIE) in preschool children are old and lacking. However, iodine status in Norway has previously been measured in specific regions and among different age groups (**Table 1.3**). Recent studies indicate that subgroups within the Norwegian population, including pregnant women and adolescent girls, may suffer from mild iodine deficiency due to inadequate intake of dietary iodine (12, 13).

[1] According to Iodine global Network, the reported iodine sufficiency in Norway is based on one single study in adults (21-64 years) conducted in Tromsø and Bergen (76).

Table 1.3: Overview of studies on iodine status among different subgroups of the Norwegian population.

Region, year	Methods	Number of subjects and gender	Age range (years)	Results	Reference
Kristiania/Opplandene, 1917	-	Children (unknown n)	6-14	Goiter prevalence: 5-25%	(67)
Modum, 1934-35	Palpation of the thyroid[a]	106 boys and 106 girls	3-6	Goiter prevalence: 51.9% (boys) and 59.4% (girls)	(68)
	24h urine	29 men (with goiter)	19-71	22.5 µg iodine/24h[b]	
		20 men (no goiter)	37-64	24.6 µg iodine/24h[b]	
	24h urine	9 controls	17-31	35.1 µg iodine/24h[b]	
Vågå, Florø, Karasjok and Vadsø, 1971-72[e]	24h urine (winter)	116 men	19-57	199 µg iodine/24h[c]	(72)
	Casual urine (summer)	82 men	19-57	215 µg iodine/24h[c,f]	
Oslo, 1971-72	Casual urine	213 men	20-70	248 µg iodine/24h[e]	(73)
		76 women	20-70	173 µg iodine/24h[e]	
Modum, Gjøvik, Forsand, Valldal and Herøy, 1972	Casual urine	171 men	20-70	260 µg iodine/24h[c]	
Oslo, Kjeller, Lillestrøm, 1974-75	24h urine (for 7 consecutive days)	2 children	3.5-5.5	74 µg iodine/ 24h	(70)
		13 men	20-49	256 µg iodine/ 24h	
		8 women	24-33	154 µg iodine/24h	
Modum, 1977	Palpation of the thyroid, serum TSH, T_4 and T_3	1418 children[g]	7-15	Goiter prevalence: 1.5% TSH: 0.4 ± 0.09 µg/L T_4: 107 ± 12.3 nmol/L T_3: 2.3 ± 0.2 nmol/L 133 µg iodine/g creatinine	(69)
	Casual urine[d]	243 children (controls)	7-15	129 µg iodine/g creatinine	
Oslo, Modum, Gjøvik, Forsand, Herøy and Valldal, 1985	Casual urine	252 men	-	207 µg iodine/24h[c,f]	(48, 74, 75)
Tromsø (T), Bergen (B), 1999	Casual urine	35 men, 28 women (T)	23-64 (T)	Median UIC: 117µg/L	(76)
	24h urine	9 men, 35 women (B)	21-49 (B)	Median UIE: 96 µg/24h	
Norway, 2013	24h urine	119 pregnant women	<25-≥35	Median UIC: 69 µg/L Median UIE: 130 µg/24h	(12)

[a]The age group 3-6 years is shown due to highest relevance for the present thesis
[b]Mean iodine concentration in urine
[c]Mean iodine concentration in urine from all locations
[d]Urinary iodine concentration from casual urine samples expressed as µg iodine per g creatinine
[e]24h urine samples: winter 1971-72, casual urine samples: summer 1972
[f]Estimated 24h UIE
[g]Results are given for 22 participants. Spot urine samples were expressed in relation to creatinine concentration
B: Bergen, T: Tromsø, TSH: Thyroid-stimulating hormone, UIC: Urinary iodine concentration,
UIE: Urinary iodine excretion, 24h: 24 hours

1.6 Iodine deficiency

Iodine deficiency is the greatest cause of preventable mental retardation in childhood (77). Iodine deficiency has multiple adverse effects on growth and development in humans, and they are collectively termed iodine deficiency disorders (IDD) (**Table 1.4**) (78, 79). IDD are common, but highly preventable and treatable conditions (80). In general, iodine deficiency is caused by inadequate dietary intake (22). The severity of health effects associated with iodine deficiency are related to timing, degree, and extent of insufficient dietary iodine intake (81).

Iodine prophylaxis (e.g. thyroxine hormones, iodized oil) in areas with severe iodine deficiency is vital for elimination of new cases of cretinism (severe mental- and growth retardation) (35, 46, 82). In a study conducted on iodine deficient schoolchildren from Albania, treatment with iodine-containing supplements significantly enhanced iodine and thyroid status after 24 weeks of supplementation. In addition, information processing, fine motor skills and visual problem solving improved in the treatment group as opposed to the control group (20).

Table 1.4: The spectrum of iodine deficiency disorders (IDD) across the lifespan.
Retrieved from WHO/UNICEF/ICCIDD (2007) (46), adapted from BS Hetzel, (1983) (79).

Physiological groups	Health consequences of iodine deficiency
All ages	Goiter Hypothyroidism Increased susceptibility to nuclear radiation
Fetus	Spontaneous abortions Stillbirths Congenital anomalies Increased perinatal mortality
Neonate	Infant mortality Endemic cretinism Mental deficiency and/or mutism, short stature, squint and spastic diplegia
Child and adolescent	Impaired mental function Delayed physical development Iodine-induced hyperthyroidism
Adult	Impaired mental function Iodine-induced hyperthyroidism

1.7 Iodine excess

Excessive iodine intake may cause adverse health effects, including hypothyroidism, hyperthyroidism and autoimmune thyroiditis. Susceptible population groups (the elderly, fetuses and neonates) with recurring thyroid disease are most at risk (83, 84). There are large inter-individual differences in relation to excessive iodine intakes. Generally, the thyroid gland is adaptable to high levels of iodine in the body, and many individuals might tolerate iodine intakes well above physiological needs (85). Rapid correction of iodine deficiency may cause iodine-induced hyperthyroidism. This is mainly a problem in elderly populations with autonomous nodules due to their inability to regulate newly available iodine. This dysregulation results in excessive thyroid hormone synthesis (86, 87). In children, adverse effects of iodine excess is not well elucidated. A study from China, showed that exposure to long-term excessive iodine intakes caused both higher TSH-concentrations and higher positivity of thyroid antibodies in children. There were also found higher prevalence of thyroid diseases (e.g. subclinical hypothyroidism) and significant correlation between increased thyroid volume and higher UIC (88).

1.8 Assessment of iodine status

There are several available biomarkers for assessing iodine status in a population (89). Biomarkers can be measured accurately and reproducibly, and is not influenced by the patient's own perceptions (90). Methods for assessment of iodine status in a population includes UIC, blood measurements of TSH, T_4, T_3 and thyroglobulin, and goiter prevalence (89). In the following, only UIC is further explained due to relevance for the present thesis.

1.8.1 Urinary iodine concentration (UIC)

UIC in casual urine samples (spot-urine) is regarded as a reliable biomarker of recent iodine intake, and is recommended by WHO, UNICEF and ICCIDD for assessing a population's iodine status (46). Reference values for UIC originates from measurements collected in school-aged children worldwide. UIC between 100-199 µg/L indicate an adequate iodine intake (**Table 1.5**). In addition, not more than 20% of the study population should have UIC below 50 µg/L, and not more than 50% should have UIC less than 100 µg/L. The current practice is to report UIC as a median concentration (µg/L), due to generally not normally distributed data (46). In order to identify the iodine status of an entire population (not subgroups), spot urine samples from ~1200 children are required (35, 46).

In individuals with a positive iodine balance, over 90% of ingested iodine will be excreted through urine within 1-2 days (34, 91). A median UIC of 100 µg/L will roughly indicate an iodine intake of 150 µg/day under steady-state conditions (46). Diurnal- and day-to-day variations in UIC occur within and between individuals, and this limits the use of UIC as a biomarker for assessing individual iodine intake and status (92). These variations tend to even out when UIC is measured in large populations (46). 24h urine collections are known to give a more reliable estimate of iodine status in individuals (92) and populations (93) due to the methods ability to account for total urine volume in subjects. However, the method is rarely used at population levels due to impractical sample collection and risk of low compliance among study participants (92).

One of the analytical methods used for determination of UIC is inductively coupled plasma-mass spectrometry (ICP-MS) (see section 2.6.3). However, the majority of iodine status studies involve the Sandell-Kolthoff reaction or modifications of this method (94, 95).

Creatinine is a breakdown product of creatine and is steadily excreted through urine in 24 hours if fluid intake is regular. High or low fluid intake may decrease or increase urinary concentrations of iodine and creatinine. However, inadequate or excessive fluid consumption will not usually affect the overall daily amount of creatinine excreted (96). Excretion of creatinine is constant at ~ 1 g/day, but can vary according to factors like gender, age and nutritional status (92, 96). Thus, the iodine concentration measured in spot urine samples can be expressed as µg iodine/g creatinine. The iodine/creatinine ratio aims to reduce the effect of hydration in urinary iodine analysis (96, 97). The method of relating urinary iodine to creatinine is known to be burdensome, expensive and unnecessary (46). Urinary iodine/creatinine ratios may be unreliable especially when protein intake is low, and loss of muscle mass will lead to reduced creatinine excretion in urine (46, 96).

Table 1.5: Epidemiological criteria from WHO/UNICEF/ICCIDD for assessment of iodine nutrition in a population. Based on median urinary iodine concentrations of school-aged children (≥ 6 years old) (46).

School-aged children	Iodine intake	Iodine nutrition
< 20 µg/L	Insufficient	Severe iodine deficiency
20-49 µg/L	Insufficient	Moderate iodine deficiency
50-99 µg/L	Insufficient	Mild iodine deficiency
100-199 µg/L	Adequate	Adequate iodine nutrition
200-299 µg/L	Above requirements	Possibly adequate for pregnant/lactating women, may pose a risk in the overall population
≥ 300 µg/L	Excessive	Risk of adverse health consequences (iodine-induced hyperthyroidism, autoimmune thyroid diseases)

1.9 Socio-economic factors in relation to iodine nutrition

Impact of socio-economic status on dietary habits (98) and health outcomes (99) have previously been investigated. Studies examining the influence of parental socio-economic factors on iodine nutrition in children are limited, and studies conducted in the adult population show conflicting results. Völzke et al (2013), found no major impact of socio-economic status on iodine excretion, nor incidence of thyroid deficiency-related disorders in an adult German population (100). In contrast, Knudsen et al. (2003), found that thyroid volume and elevated serum thyroglobulin-levels were significantly associated with lower levels of education in a Danish population. In addition, lower education levels were associated with higher goiter prevalence and lower estimated urinary iodine excretion (101).

1.10 Assessment of dietary intake

There are two main methods for examining dietary intake in a population, and these are collectively termed retrospective and prospective methods. The retrospective methods include 24-hour recall, dietary history and food frequency questionnaire (FFQ), while prospective methods include food item registration and the double portion method. Retrospective methods involve registrations of food and drinks already consumed, while prospective methods assesses ongoing food and beverage intake. Choice of method depends on the study sample, study purpose and available resources (102).

1.10.1 Food frequency questionnaire

FFQ is a well-known method for estimating long-term habitual dietary intake in a large study population (102). The aim of a FFQ is to assess the frequency of intake of different food items or food groups within a given period. The simplest form of a FFQ entails a list of foods and a related set of frequency-of-use response categories (e.g. daily, weekly, monthly) (103). In epidemiology, FFQ has become the method of choice for assessing habitual dietary intake in populations due to user-friendliness, low cost and time-efficiency (104). The length of a FFQ depends on the overall purpose. Short-FFQ's are suitable for measuring intake of specific food groups (e.g. dairy products) or single nutrients, while longer FFQ's aim to assess intake of several nutrients or give an overview of the total diet (105). There are several weaknesses related to the FFQ. Lack of detail about specific foods, semi-quantitative data and random errors contribute to uncertainty (106). In addition, behavioral patterns and memory lapses may result in biased responses (107, 108).

1.11 Study aims

The present thesis is part of one of the studies in the FINS-project that focuses on the significance of diet on cognitive outcomes in children. A semi-quantitative questionnaire and non-fasting, spot urine samples from preschool children living in the community of Bergen were used for determination and evaluation of iodine status.

Main aim of this master thesis:

- **Determine and evaluate the iodine status of Norwegian preschool children.**

Specific aims:

- Measure UIC and creatinine concentration in non-fasting, spot urine samples.
- Examine the intake frequencies of iodine-rich food sources reported in a FFQ.
- Investigate if UIC is associated with intake of iodine-rich food sources.
- Investigate if UIC is associated with parental socio-economic factors.
- Investigate if parental socio-economic factors are associated with intake of iodine-rich food sources.

2. METHODS AND MATERIALS

2.1 Design

This master thesis is a cross-sectional study assessing the iodine nutrition among Norwegian preschool children. The present thesis is part of a larger interdisciplinary intervention study (WP5), which is a collaboration between NIFES, Regional Knowledge Center for Children and Youth West (RKBU Vest), Uni Research and the Ludwig-Maximillians University (LMU) in Munich, Germany.

During winter and spring of 2015, 232 preschool children aged 4-6 years old were randomly allocated into two groups, and served study meals containing either fatty fish or meat three times per week for a total of 16 weeks. Before and after the intervention period, biological data were collected (see section 2.4).

In the present master thesis, baseline data, including a questionnaire (dietary habits, anthropometry and parental socio-economic factors) and non-fasting, spot urine samples are used in the assessment of iodine status in a sample of Norwegian preschool children.

2.2 Ethics

The participation of children and their parents in the intervention study (WP5) was voluntary. Written, informed consent was obtained from all families before inclusion of the child, and the participants were free to resign from the study without reason. Obtained data was at all times treated strictly confidentially, and the biological samples were kept in a specific research biobank. Both biological samples and other data are stored at NIFES and RKBU West until study completion in 2025, and thereafter the data are kept in the Norwegian Social Science Data Service (NSD). Data was entered into UHeads, a research server that secure optimal standards for storage of clinical data. The data obtained from the intervention study (WP5) are considered important for improvement of nutritional science, and did not put the study subjects at significant risk. Thus, the study was regarded as ethically well justified. The study was conducted according to the established regulations based on the Declaration of Helsinki and the Oviedo Convention, including the registration of clinical trials. The study was evaluated by the Regional Committees for Medical Health Research Ethics (REC North). NIFES and the University of Bergen (UiB) financed the present master thesis.

2.3 Participants and recruitment

The recruitment process took place in each of the kindergartens with help from the kindergarten staff (advertisement, handing out information to parents, logistics etc.) from November 2014 until the end of January 2015. Seventeen kindergartens from six (out of eight) districts in the Bergen area were asked to participate in the intervention study (WP5). The flow chart presented in **figure 2.1** describes the inclusion and exclusion of study participants, and gives an overview of available data used in the present thesis.

Inclusion criteria (WP5):

1) Children aged 4-6 years old (oldest age cohorts in the kindergartens).
2) Sufficient understanding and knowledge of the Norwegian language by the child to participate in the cognitive testing regime (main outcome variable in the intervention study). In addition, at least one of the parents had to know and understand the Norwegian language in order to comply with study requirements (e.g. answer the questionnaire).

Exclusion criteria (WP5):

1) Children with known food allergies.

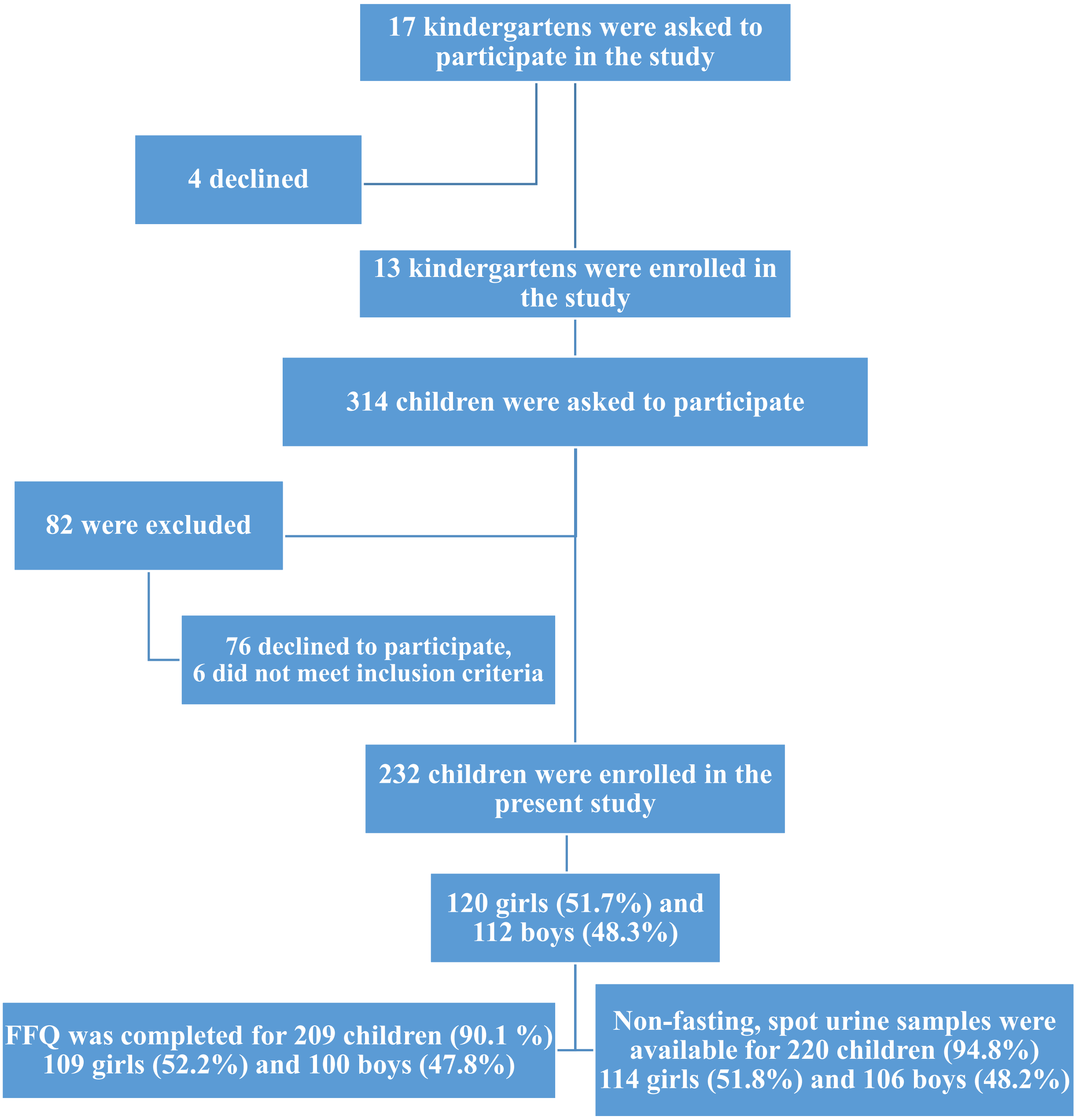


Figure 2.1: Flow chart describing the recruitment process and the data material available for the present thesis.

2.4 Data collection

Dietary data was obtained through a FFQ filled out by the children's parents. Baseline biological samples (e.g. blood, saliva and urine) were collected from the participating children during January and February 2015. All biological samples from one child were collected in the same day, except urine, which was mainly collected in the child's home and delivered to the respective kindergartens the following day, and thereafter retrieved by study personnel.

2.4.1 Questionnaire

A semi-quantitative questionnaire (**Appendix I**) containing both a socio-economic- and anthropometric part (SEQ-part) and diet-related questions (FFQ-part), was distributed electronically to the parents to acquire information on demographics, parental socio-economic status, the children's basic anthropometric measurements and habitual dietary intake.

2.4.1.1 Socio-economic variables:

The SEQ-part of the questionnaire contained questions about the child's gender, age, weight, height and birthplace. In addition, the parents had to answer questions related to their birthplace, education level, current main occupation and total household income. In the present thesis, questions regarding the child's gender, age, weight, height and calculated body mass index (BMI), along with birthplace (child + parents), parental education level and total household income were included in the descriptive results.

The question regarding both the children's and their parent's birthplace originally contained 62 answer categories (different countries of origin). Prior to statistical analysis, these questions were recoded into the following three answer categories: countries within EU/EEA (1), countries outside EU/EEA (2) and Norway (3).

Originally, parental education levels were divided into five subcategories; elementary school and lower secondary school, secondary (vocational) school, secondary (general) school, < 4 years of University education (University or University College) and > 4 years of University education (University or University College), for both maternal and paternal education levels. To shift the categories into "total years in education", the educational subgroups were converted to numerical variables (total years in education). Elementary school and lower secondary school equals 10 years, secondary (vocational + general) school equals 13 years, < 4 years of University education equals 16 years, and > 4 years of University education equals 17 years of education. Education levels for mothers and fathers were summarized and divided by two, to get the total parental education level.

Total household income was originally divided into eight different categories in the SEQ-part of the questionnaire. In the present thesis, the categories were aggregated into three main income levels, termed low income, medium income and high income. In the present thesis, low income equals an annual gross, total household income of < 200 000 – 549 999 NOK, medium income corresponds to a total household income of 550 000 – 999 999 NOK, while high income equals a household income of 1 000 000 - > 2 000 000 NOK.

2.4.1.2 Dietary variables:

Iodine nutrition was assessed by using parts of the semi-quantitative FFQ. The parents were instructed not to report the children's meals in the kindergartens. The FFQ contained four questions on habitual consumption of fish and seafood items either for dinner or as bread spread, in salads or as a snack meal (referred to as "spread" from now on). Thus, the children's total seafood consumption was described through two summary questions and two detailed item questions.

The frequency intervals ranged from never to ≥ 4 times per week for the two questions (summary and detailed item) related to seafood for dinner, and from never to > 5 times per week for the two questions concerning seafood as spread (summary and detailed item). The maximum frequency interval was higher for the latter because of relatively high consumption of bread in Norway (109). The detailed item question related to dinner had 12 different answer categories, which included both fatty fish, lean fish, sushi, shellfish and different processed fish products. The frequency intervals were the same as in the summary question mentioned above. The summary question related to seafood as spread had seven frequency intervals, and the corresponding detailed item question contained six different categories (fatty and lean spreads) and the same seven frequency intervals as the summary question.

Summary questions related to intake of dairy products and eggs (fried, boiled, scrambled, omelet) were also included in the present thesis due to their consumption frequency and iodine content. In addition, there was one detailed item question containing different sorts of dairy products. This question had 11 answer categories including different types of sweet milk, cultured milk, yogurt and cheeses. The two questions regarding intake of dairy products had six frequency intervals ranging from never/rare to ≥ 3-4 times/day. The question on total egg intake had six frequency intervals ranging from none to ≥ 8 eggs/week.

The parents also reported use of supplements in addition to type and dosage. Based on low or undeclared iodine content in cod liver oil and other fish oil- and omega-3 supplements, this question was not included in the present thesis (44, 110). The children's use of multimineral supplements were included. Each reported supplement (type) was looked up, and checked for possible iodine content.

Questions with the highest relevance for iodine status were included in the thesis. Four questions on seafood intake, two questions regarding intake of dairy products, one question on egg intake, and three questions related to use of supplements.

2.5 Data processing

2.5.1 Anthropometry

The parents reported weight and height of the children in the SEQ-part of the questionnaire. Subsequently, BMI was calculated using **formula 1**. Weight-, height- and BMI-values of boys and girls were then compared to reference values from the growth standards developed by WHO (**Table 2.1**). According to the Norwegian Directorate of Health (2010), these growth standards are recommended for use in Norwegian child health clinics for children (0-5 years) (111). Z-scores for the age group 5.2 years are shown (median age of the total study population).

Formula 1: BMI = kg/m^2

Table 2.1: WHO growth standards for boys and girls (age 5.2 years) given in z-scores (112).

Boys	-3 SD	-2 SD	-1 SD	Median	+1 SD	+2 SD	+3 SD
Weight-for-age (kg)	12.8	14.5	16.4	18.7	21.3	24.4	27.8
Height-for-age (cm)	96.9	101.6	106.2	110.8	115.4	120.0	124.7
BMI-for-age (kg/m^2)	12.1	13.0	14.1	15.3	16.6	18.3	20.2

Girls	-3 SD	-2 SD	-1 SD	Median	+1 SD	+2 SD	+3 SD
Weight-for-age (kg)	12.5	14.1	16.0	18.4	21.4	25.1	29.8
Height-for-age (cm)	95.7	100.5	105.3	110.1	114.9	119.7	124.5
BMI-for-age (kg/m^2)	11.8	12.7	13.9	15.2	16.9	18.9	21.4

SD: Standard deviation

2.5.2 Seafood index

In the present thesis, a seafood index based on a method by Markhus et al. (2013) has been used to estimate weekly intake frequencies of certain FFQ-variables (seafood (dinner and spread), dairy products, eggs and supplements). The index was originally developed to assess the seafood intake among pregnant women in Norway (109). The seafood index was established and validated from a seafood-FFQ against several blood biomarkers (the omega-3 index, the omega-3 HUFA score, and serum 25OH vitamin D). The index was utilized for conversion of ordinal frequency data from the seafood-FFQ into numerical scale data. Based on this, aggregation of different types of seafood and supplements, and the quantity of their consumption (obtained from the FFQ), were made possible. The seafood index was mainly developed because subjects tend to overestimate consumption frequencies when asked about different detailed items in a separate manner, like in the detailed item questions in the FFQ. Therefore, the index was based on the lowest possible weekly intake of seafood items eaten either for dinner or as spread (109). By using index values in this thesis, it was intended to limit potential over-reporting and make the statistical calculations more reasonable.

In the present thesis, the index values for summary questions (seafood, dairy products, eggs and supplements) were determined by calculating the average (mean) weekly intake frequency, while the indexes for detailed items questions (types of seafood and dairy products) were based on the lowest possible weekly intake.

Processed fish products for dinner usually contain about 40-60 % fish fillet (43). Based on this, the lowest possible weekly intake of processed fish products for dinner were halved when calculating the index values.

Table 2.2 shows the indexes for intake of seafood either for dinner or as spread (summary and detailed items questions), and the summary question on use of supplements. Summary questions were scored as the mean weekly frequency of intake, while the detailed item questions were scored as the lowest possible weekly intake.

Table 2.2: Indexes for summary questions and detailed item questions for seafood (dinner and spread) and supplements. Based on a method by Markhus et al. (2013) (109).

	Numerical interval per week[a]	Index value (intake/week)
Seafood for dinner (summary question)		
Never	0	0
Rarer than 1 time per month	> 0-0.25	0.15
1-3 times per month	0.25-0.75	0.5
1 time per week	1	1
2-3 times per week	2-3	2.5
≥ 4 times per week	4	4
Seafood for dinner (detailed item question)		
Never	0	0
Rarer than 1 time per month	> 0-0.25	0.1[c]
1-3 times per month	0.25-0.75	0.25
1 time per week	1	1
2-3 times per week	2-3	2
≥ 4 times per week	4	4
Processed fish products (detailed item question)[b]		
Never	0	0
Rarer than 1 time per month	> 0-0.25	0.05
1-3 times per month	0.25-0.75	0.125
1 time per week	1	0.5
2-3 times per week	2-3	1
≥ 4 times per week	4	2
Seafood as spread (summary question)		
Never	0	0
Rare	> 0-0.25	0.15
1-3 times per month	0.25-0.75	0.5
1 time per week	1	1
2 times per week	2	2
3-5 times per week	3-5	4
> 5 times per week	5	5
Seafood as spread (detailed item question)		
Never	0	0
Rare	> 0-0.25	0.1[c]
1-3 times per month	0.25-0.75	0.25
1 time per week	1	1
2 times per week	2	2
3-5 times per week	3-5	3
> 5 times per week	5	5
Use of supplements (summary question)[d]		
Never	0	0
1-3 times per month	0.25-0.75	0.5
1-3 times per week	1-3	2
4-6 times per week	4-6	5
Daily	7	7

[a]Weekly frequency based on the reported intake frequencies from the FFQ
[b]Index values for fish cakes, fish sticks and other fish products for dinner (detailed item question) were halved due to their lower fish content
[c]Index value is set to 0.1 to make it possible to distinguish between the two lowest intake frequencies
[d]Question regarding use of multiminerals

2.5.3 Indexes for other iodine-containing food groups

In addition to intake of seafood and use of supplements, index values were also used for questions related to consumption of dairy products and eggs (**Table 2.3**).

Table 2.3: Indexes for summary questions and detailed item question for dairy products and eggs Based on a method by Markhus et al. (2013) (109).

	Numerical interval per week[a]	**Index value (intake/week)**
Dairy products (summary question)		
Rare/never	0	0
1-3 times per week	1-3	2
4-6 times per week	4-6	5
Every day	7	7
2 times per day	14	14
≥ 3-4 times per day	21-28	24.5
Dairy products (detailed item question)		
Rare/never	0	0
1-3 times per week	1-3	1
4-6 times per week	4-6	4
Every day	7	7
2 times per day	14	14
≥ 3-4 times per day	21-28	21
Eggs (summary question)		
None	0	0
1 egg per week	1	1
2-3 eggs per week	2-3	2.5
4-5 eggs per week	4-5	4.5
6-7 eggs per week	6-7	6.5
≥ 8 eggs per week	8	8

[a]Weekly frequency based on the reported intake frequencies from the FFQ

2.5.4 Grouping and summarizing FFQ-variables

Multiple FFQ-variables were grouped together and summarized to create larger iodine-containing food groups, and to make it easier to distinguish between intake of different types of seafood and dairy products. Due to large variations in iodine content of different food items, the grouping of foods were to some extent based on the item's iodine content (e.g. lean fish and fatty fish species). The constructed index-variables were used when grouping and summarizing the different FFQ-variables.

In the present thesis, the different fish species included in the original detailed item question (seafood for dinner) in the FFQ were grouped together to create four categories. These were "fatty fish", "lean fish", "shellfish" and "processed fish products".

Fatty fish included salmon and trout, mackerel, herring and halibut[2]. In the group of lean fish were cod, saithe, pollack, haddock and plaice. Shellfish included shrimps, crab and mussels. The category of processed fish products included the following items: fish cakes, fish sticks, fish gratin and fish balls. The processed fish products consists of lean fish species (43).

Seafood used as spread (detailed item question) was gathered in two different categories: "fatty spreads" and "lean spreads". In the category of fatty spreads, the following items were included: mackerel in tomato sauce, canned sardines and herring, pepper mackerel, smoked or cured salmon and trout, caviar and "Svolvaerpostei" and "Lofotpostei". Tuna was the only lean spread included in the FFQ.

The detailed item question related to intake of dairy products were summed up in four categories: "sweet milk", "cultured milk and yogurt", white cheeses" and "brown cheese". This made it easier to assess the contribution of the different dairy items included in the FFQ. In the sweet milk category, included items were whole milk, low-fat milk, extra-low fat milk, skimmed milk and chocolate milk. Cultured milk and yogurt included drinking yogurt, "Biola", "Cultura" and yogurt. The category of white cheeses consisted of different types or labels e.g. "Norvegia", "Jarlsberg" and cream cheeses. The last category included brown cheese. The various types of cheeses were not included in one category due to difference in iodine content. Norwegian brown cheese contain more than twice as much iodine as various white cheeses (44).

2.6 Urinary iodine concentration (UIC)

Iodine status was assessed by measuring iodine concentration in urine. Analysis of urine samples were performed according to the method description *"424 – Arsen- og jod-bestemmelse med induktivt koblet plasma-massespektrofotometri (ICP-MS) etter basisk ekstraksjon"*, developed by NIFES (113). In the present thesis, the method was applied for analysis of human urine. Baseline and endpoint (post-intervention) urine samples were analyzed simultaneously.

The master student performed all sample preparation, and ICP-MS analysis was done in collaboration with laboratory technicians at NIFES. The analyses were performed during

[2]Halibut is often referred to as a semi-fat fish (fat content of 2.3-7.6 g/100g) (43). In the present thesis, halibut is included in the fatty fish category.

February and March 2016. Iodine concentration in urine was quantitatively determined by using Agilent 7500, with auto sampler (ICP-MS). The method is not accredited (see section 4.4.3).

2.6.1 Collection of urine samples

Data for assessment of iodine status was obtained from non-fasting, spot urine samples collected during the baseline data collection in the intervention study (WP5). The children received a urine sample glass in the kindergarten on the day of data collection. The parents or kindergarten staff were told to collect urine from the child either at home or in the kindergarten. Most of the urine samples were collected at home and delivered to the research technicians from NIFES the following day. The urine samples were stored in Cryotubes à ~ 3.5 ml and kept on dry ice before transportation to NIFES. Thereafter, the samples were stored in a freezer at -80ºC prior to analysis in February 2016.

2.6.2 Sample preparation

Prior to analysis, the urine samples were defrosted in room temperature or refrigerator the day before preparation. 15 ml sample tubes were marked with the correct identification (ID-number) before sample preparation.

The sample preparation included the following steps:

1) Dilution of urine samples by extracting 500 µl of urine and adding 4.5 ml 1% tetramethylammonium hydroxide (TMAH). The TMAH-solution was prepared by adding 10 ml of 25% TMAH to 1 liter of distilled water.

2) Filtration of the samples (500 µl urine + 4.5 ml TMAH) by using a sterile membrane filter with a 0.45 µm pore size and a 10 ml syringe (without needle).

3) Transfer of samples to tubes appropriate for the analysis by the Agilent 7500, or for further storage in refrigerator/cold rooms (4ºC) pending on analysis.

A calibration curve (standard addition curve) was prepared by extracting 10-20-50-100-200 µl of an iodine/arsenic solution (50 µl iodine standard + 50 µl arsenic standard diluted to a volume of 10 ml with distilled water). All of the five iodine/arsenic solutions were diluted to 5 ml by adding the correct amount of urine mix (4990 µl, 4980 µl, 4950 µl, 4900 µl and 4800 µl, respectively). In addition, one sample tube contained 5 ml of urine mix. The urine mix was a random mixture of urine and 1% TMAH sample solutions (prepared by mixing already analyzed urine samples). The calibration curve was developed to measure the unknown iodine concentration (^{127}I) in the collected urine samples.

In addition, three blank samples were prepared by using 5 ml 1% TMAH solution. The standard blank samples were analyzed together with the calibration curve and urine samples.

To control for systematic errors (during ICP-MS analysis) and measure the methods accuracy, a certified standard reference material (SRM) was included in each analytical run.

Four samples (2+2) Seronorm™ Trace Elements Urine L-1 and Seronorm™ Trace Elements Urine L-2 were prepared before every ICP-MS analysis run, and routinely analyzed together with the urine samples. The SRM's were made by first adding 5 ml of distilled water to the Seronorm ampules (powder) and letting it set for 15 minutes. Thereafter, we extracted 500 µl Seronorm L-1/L-2 and added 4.5 ml TMAH to 15 ml sample tubes. The certified analytical value of the SRM were 84 µg/L (L-1) and 304 µg/L (L-2), respectively. The acceptable range was 72-96 µg/L (84 ± 12) for the L-1 reference and 260-348 µg/L (304 ± 44) for the L-2 reference.

The limit of quantification (LOQ) is the lowest concentration at which the analyte can be reliably determined, and where bias and imprecisions are accounted for (114). The LOQ in the present method is calculated from standard deviation (SD) between 25 blanks analyzed over a period of five days (LOQ = 10 × SD). The LOQ for iodine is 1.47 µg/L (113).

The limit of detection (LOD) is the lowest concentration of an analyte in a sample that can be identified and distinguished from zero (115). The LOD in the present method is calculated from the SD between 25 blanks analyzed over a period of five days (LOD = 3 × SD). The LOD for iodine is 0.44 µg/L (113).

2.6.3 ICP-MS

ICP-MS is a method for analysis of multiple elements, including iodine. The elements are chromatographically separated before detection in the mass spectrometer (MS) (**Fig. 2.2**). Analysis of iodine requires an instrument with a collision cell. Samples are introduced to the ICP-MS as liquid droplets in the plasma (argon gas) (116).

A pump inserts liquid samples (e.g. urine samples) to the nebulizer and an aerosol is formed. Auxiliary and plasma gases ensures the consistency of the aerosol, and further introduction to the plasma. The ICP consists of concentric quartz tubes with argon gas. A torch is placed in the middle of a radio frequency coil, where radio frequency energy passes through. This high-energy field causes collisions between argon atoms, and subsequently form the plasma. The aerosol will rapidly decompose in the plasma due to high temperatures. Analyte atoms are made and ionized for plasma extraction, and thereafter transferred to the MS. High vacuum in the MS contributes to ion extraction. Several ion lenses focus the analyte ions into the quadrupole mass analyzer. Here, the ions are separated based on their mass/charge ratio. An electron multiplier measures the ions, and creates a mass spectrum. Peak intensity in the spectrum is directly proportional to the initial concentration of the isotope (e.g. iodine) in the sample solution (117). The Agilent 7500 ICP-MS analyzer used in the present thesis, completed iodine analysis of one urine sample in 3-3.5 minutes.

The instrument includes properties such as high speed, high sensitivity, quick sample preparation and the opportunity of multi-element analysis. Methodological limitations include high costs (lower availability) and sensitivity to salt precipitation (118).

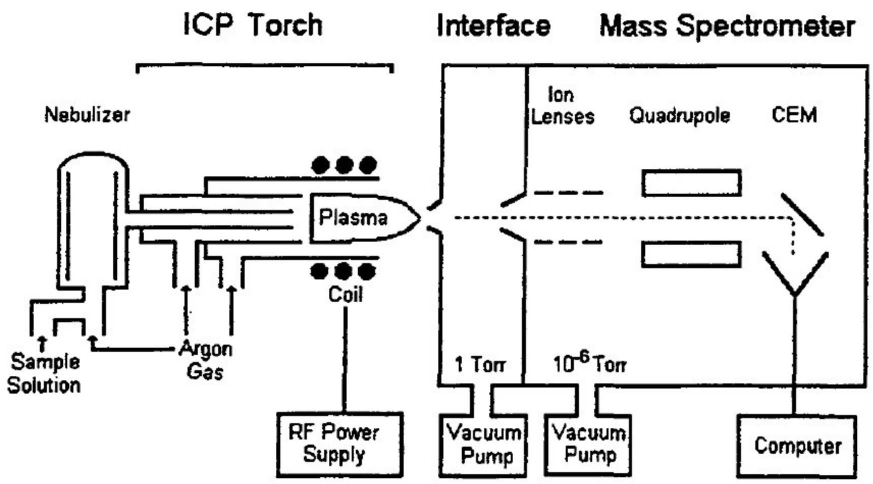


Figure 2.2: Schematic illustration of ICP-MS. Retrieved from Nuttal et al. (1995) (118).

2.7 Urinary creatinine concentration

Determination of urinary creatinine concentration is based on a colorimetric-enzymatic method with the following reactions (119):

1) Creatinine + H_2O $\xrightarrow{\textit{Creatininase}}$ Creatine

2) Creatine + H_2O $\xrightarrow{\textit{Creatinase}}$ Sarcosine + urea

3) Sarcosine + O_2 $\xrightarrow{\textit{Sarcosine oxydase}}$ Glycine + HCHO + H_2O_2

4) H_2O_2 + EHSPT[a] + amino-4-Antipyrine $\xrightarrow{\textit{Peroxydase}}$ Quinoneimine

[a]EHSPT: N-Ethyl-N-2(-Hydroxy-3-Sulfopropyl)-m-Toluidine

Urine samples were defrosted at room temperature before determination of urinary creatinine concentration. Analyses were performed using the MAXMAT PL II multidisciplinary diagnostic platform with creatinine PAP kit. First, the instrument was calibrated with a standard (value = 363 µmol/L). Thereafter, the method's accuracy was controlled with two independent controls (MaxTrol P and MaxTrol N). The target values for MaxTrol P and MaxTrol N is 361 µmol/L (325-397 µmol/L) and 76 µmol/L (67-85 µmol/L), respectively (values are set by the manufacturer). To ensure adequate instrumental control, it is suggested to use one control, which is close to normal patient values (MaxTrol N), and a second control representing pathological values (MaxTrol P). The control material is plasma (there does not exist values for urine), and therefore not directly comparable to values seen in urine samples. The control material was analyzed for every fortieth sample. The detection limit is set at 7 µmol/L (119).

The urine samples were centrifuged for 15 minutes at 2000 revolutions per minute (rpm) in order to purify the urine samples prior to analysis. All sample preparation was automatically done in the MAXMAT carousel including dilution of 200 µl urine with distilled water (1:20) and subsequent addition of reagents (Creatinine PAP R1 and R2) (119). Laboratory technicians at NIFES performed all creatinine analyses used in the present thesis. The method is not accredited (see section 4.4.3).

2.8 Calculations

In the present study, three estimates of iodine status were determined or calculated from non-fasting, spot urine samples. The different estimates were:

1) UIC (µg/L)
2) Iodine/creatinine ratio (µg iodine/g creatinine)
3) Estimated 24h urinary iodine excretion (µg iodine/day)

The UIC was expressed as a median value due to not normally distributed data.

Creatinine data was initially expressed in µmol/L. For further use in this thesis, the creatinine unit was changed to g/L by dividing the scores with a conversion factor (8.84) and thereafter dividing the scores by 1000.

The iodine/creatinine ratio was determined by the following equation:

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

Estimation of the daily urinary iodine excretion (estimated 24h UIE) was determined by using an anthropometry-based reference value for 24h urinary creatinine excretion (g/day) originally developed in German children (120). The reference value was determined according to definite height groups. Values from the German study were linked to the median height of the present study population (115 cm). The 24h urinary creatinine excretion according to the height interval 115-119.9 cm for boys (3.49 mmol/day) and girls (3.45 mmol/day) were used in the present thesis. A mean value including both genders was calculated (3.47 ≈ 3.5 mmol/day). Dividing the mean value (3.5 mmol/day) by the conversion factor (8.84) resulted in a unit change from mmol/day to g/day. The expected value for 24h urinary creatinine excretion used in the present thesis is 0.4 g/day. Subsequently, the estimated 24h UIE was calculated as follows:

$$\textbf{Estimated 24h UIE} = \frac{\text{Iodine concentration } (\mu g/L)}{\text{Creatinine concentration } (g/L)} \times \text{Expected creatinine } (g/day)$$

Population estimates of daily iodine intake can be extrapolated from UIC measured in spot urine samples by assuming a daily urine volume of approximately 0.9 ml/hour/kg (121), and an average iodine bioavailability of 92% (55). The following calculation is used:

Daily iodine intake = UIC (µg/L) ÷ 0.92 × (0.0009 L/hour/kg × 24 hour/day) × weight (kg)

2.9 Statistical analysis

All statistical analyses were performed using the Statistical Product and Service Solutions (IBM SPSS Statistics, version 23). In the present thesis, figures (bar graphs and pie charts) are made in Microsoft Excel 2013.

Normality was tested with the non-parametric Kolmogorov-Smirnov test. In addition, the distribution of data and outliers were assessed using histograms and probability plots termed "Normal Q-Q Plot". The full data set was used in all analyses.

Variables with p-values < 0.05 in the Kolmogorov-Smirnov test for normality was considered not normally distributed. None of the FFQ-variables were normally distributed. The Mann-Whitney U test was used for assessment of differences between groups (e.g. gender) for non-parametric data. Independent Samples T-Test was used in the assessment of parametric data. Results from not normally distributed data are given in median and interquartile range (IQR). Pearson chi-square test was used to investigate possible differences between genders for categorical variables (e.g. total household income). If the chi-square assumption "minimum expected cell frequency" (at least 80% of cells have expected frequencies of five or more) was not met, the likelihood ratio is presented.

Ordinal frequency data from original FFQ-questions were recoded into new numerical variables in SPSS (see section 2.5.2/2.5.3).

Spearman's rank order correlation coefficient was used to assess the association between two non-parametric variables (e.g. UIC and FFQ-variables). In addition, the Spearman's rank order correlation coefficient was used to assess the association between UIC and socio-economic-variables, and between socio-economic variables and FFQ-variables. Only statistically significant correlations are presented in the results section. The correlation's effect size (strength) is based on guidelines from Cohen (1992) (**Table 2.4)** (122). A correlation coefficient of 1.0 or -1.0 indicates a perfect positive or negative correlation between variables. A correlation of 0.0 indicates no relationship between two variables (123).

Table 2.4: Guidelines for determining the effect size (strength) of the correlation coefficient (122).

Small	r = 0.10-0.29
Medium	r = 0.30-0.49
Large	r = 0.50-1.0

Binary logistic regression was performed to assess the impact of a number of factors (predictors) on the likelihood of a median UIC ≥ 100 µg/L (indicating adequate iodine status). The UIC-variable was changed from continuous to a dichotomous, dependent variable. Median UIC < 100 µg/L was set as the reference value. This method was chosen instead of multiple linear regression due to the use of a categorical dependent variable, and not normally distributed UIC-data. In addition, the UIC-data are subject to large daily inter- and intra-individual variations. Binary logistic regression is the better method for dealing with such fluctuations.

Binary logistic regression was performed between UIC and the iodine-containing food groups (seafood, dairy products and eggs). Intake of multiminerals were excluded from the logistic regression analysis due to low reported consumption among the children. The FFQ-predictors were recoded into new independent, dichotomous variables (indicating either a low (reference value) or a high intake of the food group/item). The cut-off values for "high" or "low" intake of the different food items were based partly on current dietary recommendations (e.g. seafood intake) and/or number of subjects available in the different response categories (a minimum of 30 subjects in each group).

It was adjusted for factors known to possibly influence the UIC (gender, creatinine (g/L) and intake of iodine-containing foods). Based on significant results from the unadjusted logistic regression models, the following adjustment variables were included in the adjusted regression models: creatinine (g/L), intake of fatty fish for dinner and intake of sweet milk. Both unadjusted and adjusted models are presented in the result section 3.5. Overall analyses and analyses stratified on gender was done. It was not adjusted for other types of seafood and dairy products due to the risk of over-adjustment, and thus loss of potentially significant associations between UIC and independent predictors.

Binary logistic regression was also performed between parental socio-economic factors and FFQ-variables. Parental education level and total household income was recoded into dichotomous variables. Low parental education level (10-13 years) and high education level (16-17 years) was coded 0 (reference) and 1, respectively. Low income was coded 0 (< 200 000 -549 999 NOK) (reference) and medium/high income was coded 1 (550 000 - > 2 000 000 NOK).

P-value < 0.05 was used as statistical value of significance in all tests.

3. RESULTS

3.1 Descriptive characteristics of the study population

The different descriptive characteristics, anthropometric measurements and socio-economic variables of the children and their parents are summarized in **table 3.1**. There was a slight majority of girls included in the study. Neither the median age, weight and height of the study population, nor the calculated BMI was significantly different between genders. Both median weight-, height- and BMI-for-age for boys and girls were within (+2 SD) of international reference values set by WHO (**Table 2.1**).

Regarding ethnicity, there was almost exclusively inclusion of Norwegian children. Only few individuals originated from countries within or outside EU/EEA.

Parental education level was significantly different between boys and girls in the present study population. The boys had parents with highest education level. The median parental education level was 16 years (all participants), which corresponds to < 4 years of University education (University or University College).

Over 80% of the current study population had parents in the medium- or high-income category, ranging from 550 000 to > 2 000 000 NOK. Approximately 16% of the children had parents in the low-income category. Total household income was significantly different between boys and girls ($p = 0.001$), with boys having a higher proportion of parents in the medium- and high-income groups.

Table 3.1: Descriptive characteristics and anthropometric measurements of the children, and socio-economic characteristics of their parents. Data are given as median (IQR) if not other is indicated.

Characteristics	n (total)	All participants	n (boys)	Boys	n (girls)	Girls	p-value[a]
Gender[b]	232 (100)		112 (48.3)		120 (51.7)		
Age (years)	218	5.2 (0.9)	106	5.2 (1.1)	112	5.2 (0.8)	0.266
Weight (kg)	186	20.0 (4.0)	87	20.0 (5.0)	99	20.0 (4.0)	0.073
Height (cm)	188	115.0 (8.0)	87	116.0 (12.0)	101	113.0 (7.0)	0.182
BMI (kg/m^2)	184	15.4 (2.3)	85	15.5 (2.6)	99	15.2 (2.4)	0.204
Birth place (Norway)[c]	203						
Child		199 (98.0)	94	93 (98.9)	109	106 (97.2)	0.480[i]
Mother		184 (90.6)	94	86 (91.5)	109	98 (89.9)	0.264[i]
Father		175 (86.2)	94	80 (85.1)	109	95 (87.2)	0.848[j]
Parental education level (years)[d]	203	16.0 (2.5)	94	16.5 (2.5)	109	15.0 (3.3)	**0.007**
Household income (NOK)[e]	202		94		108		**0.001**[j]
Low[f]		33 (16.3)		6 (6.4)		27 (25.0)	
Medium[g]		81 (40.1)		39 (41.5)		42 (38.9)	
High[h]		88 (43.6)		49 (52.1)		39 (36.1)	

[a]P-value is calculated with Independent Samples Mann-Whitney U Test (non-parametric test), significance level: $p < 0.05$
[b]Gender given in count and percent (%)
[c]Birth place (Norway) given in count and percent (%)
[d]Median education level (all) = 16.00 years corresponds to < 4 years of University (University or University College), see section 2.4.1.1
[e]Total gross annual income in the household last year (in NOK) given in count and percent (%)
[f] Low income is < 200 000 – 549 999 NOK
[g]Medium income is 550 – 999 999 NOK
[h]High income is 1 000 000 - > 2 000 000 NOK
[i]Likelihood ratio
[j]Pearson chi-square test
BMI: Body Mass Index, IQR: Interquartile range, NOK: Norwegian Kroner

3.2 Food frequency questionnaire – the children's diet

Of the 232 included children, FFQ-responses were available for 209 children (90.1%).

3.2.1 Seafood

The reported frequency of seafood for dinner is presented in **figure 3.1**. According to the FFQ, approximately 85% of the children ate seafood for dinner at least once a week. The highest prevalence was found among those who ate seafood 2-3 times per week (47%). None of the children never consumed seafood for dinner. The median intake of seafood for dinner was 1.0, IQR = 1.50 (mean = 1.7 ± SD 0.9) times per week.

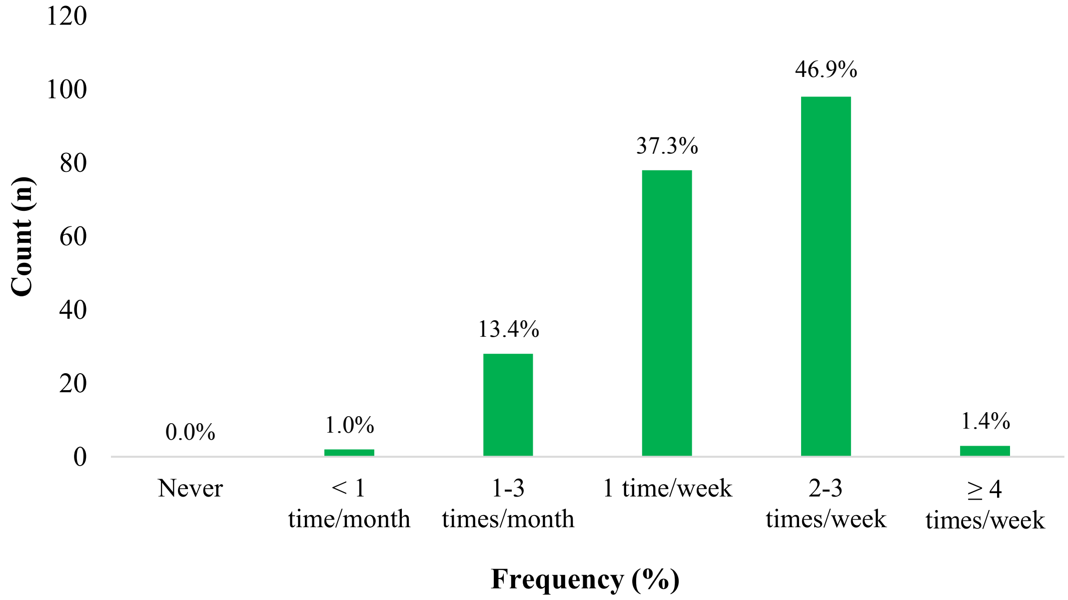


Figure 3.1: Intake frequency of seafood (fish, fish products, other seafood items) for dinner among the children given in count (n) and percent (%) of the total number of children (n = 209).

Table 3.2 gives an overview of the intake frequencies of different types of seafood consumed for dinner by the children. Salmon and/or trout was the type of fish most frequently reported for dinner in the category 1 time/week. Lean seafood and processed fish products were particularly frequently reported in the category 1-3 times/month.

Table 3.2: Intake frequencies (%) of the different fish- and seafood items consumed for dinner by the children (n = 209).

			Frequency (%)			
Seafood/fish type	**Never**	**< 1 time/month**	**1-3 times/month**	**1 time/week**	**2-3 times/week**	**≥ 4 times/week**
Fatty fish						
Salmon/trout	9.6	9.6	41.1	35.9	3.8	0.0
Mackerel	74.1	14.8	5.3	4.8	1.0	0.0
Herring	93.3	5.7	0.5	0.5	0.0	0.0
Halibut	76.6	16.7	5.7	1.0	0.0	0.0
Lean seafood						
Cod	15.3	16.3	46.9	19.6	1.9	0.0
Saithe	46.9	23.0	23.4	6.2	0.5	0.0
Other lean fish (pollack, haddock, plaice)	68.4	18.7	9.6	3.3	0.0	0.0
Shellfish (shrimps, crab, mussels)	73.2	18.2	7.2	1.4	0.0	0.0
Processed fish products						
Fish cakes	3.3	12.4	53.2	27.3	3.8	0.0
Fish sticks	23.9	24.9	35.4	14.8	1.0	0.0
Other fish products (fish gratin, fish balls)	15.8	23.0	45.9	13.4	1.9	0.0

Figure 3.2 shows the reported distribution of weekly seafood intake for dinner among the children. Intake of lean fish and processed fish products contributed with about ⅔ of the weekly seafood intake[3]. Shellfish represented only a small part of the weekly seafood intake for dinner in this population group. The weekly median intake of fatty fish for dinner were 0.4, IQR = 0.8 (mean = 0.7 ± SD 0.6) times per week, while the median reported intake of lean fish and processed fish products per week were 0.4, IQR = 0.6 (mean = 0.6 ± SD 0.6) and 0.4, IQR = 0.4 (mean = 0.5 ± SD 0.5), respectively. The median weekly intake of shellfish were 0.0, IQR = 0.1 (mean = 0.1 ± SD 0.1). There were no significant gender differences between weekly intakes of seafood for dinner (data not shown).

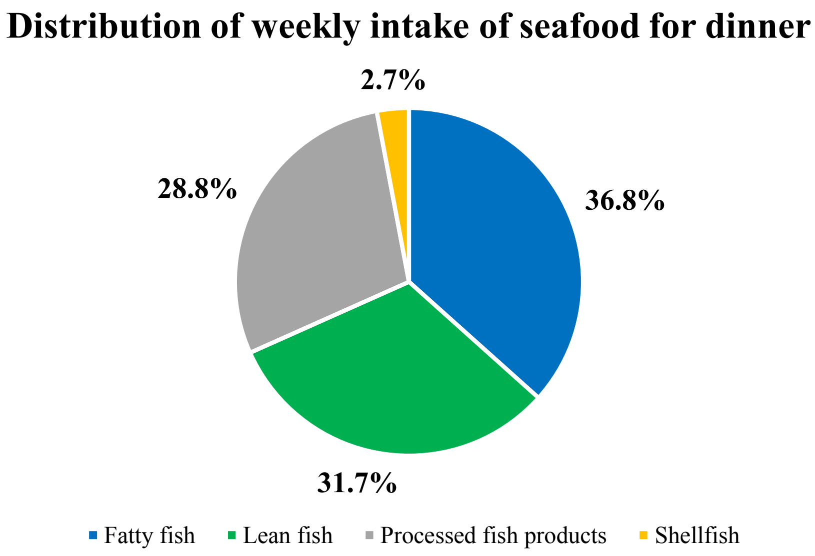


Figure 3.2: The distribution (%) of weekly intake of fatty fish (salmon/trout, mackerel, herring and halibut), lean fish (cod, saithe, pollack, haddock and plaice), processed fish products (fish cakes, fish sticks, fish gratins and fish balls) and shellfish (shrimps, crab and mussels) for dinner among the children (n = 209).

[3]Sushi was not included in the results because of low intake frequency among the children (> 80 % reported to never consume sushi for dinner) and lack of details about type of sushi consumed.

Figure 3.3 shows the intake frequencies of seafood consumed as spread. A significant proportion of children never consumed seafood as spread. Roughly, 48% consumed seafood as spread at least once a week. The median intake of seafood as spread was 0.5, IQR = 1.9 (mean = 1.3 ± SD 1.4) times per week. When using seafood as spread, almost all children (99%) ate a type of fatty spread (see section 2.4.2). Median intake of fatty spreads among the children were 1.0, IQR = 2.8 (mean = 1.7 ± SD 1.8) times per week. The median intake of tuna (lean spread) was zero times per week (median = 0.0, IQR = 0.0, mean = 0.0 ± SD 0.1). Intake of "Svolvaer- and Lofotpostei" differed by gender, with boys having the highest weekly intake (p = 0.031). No other gender differences were observed (data not shown).

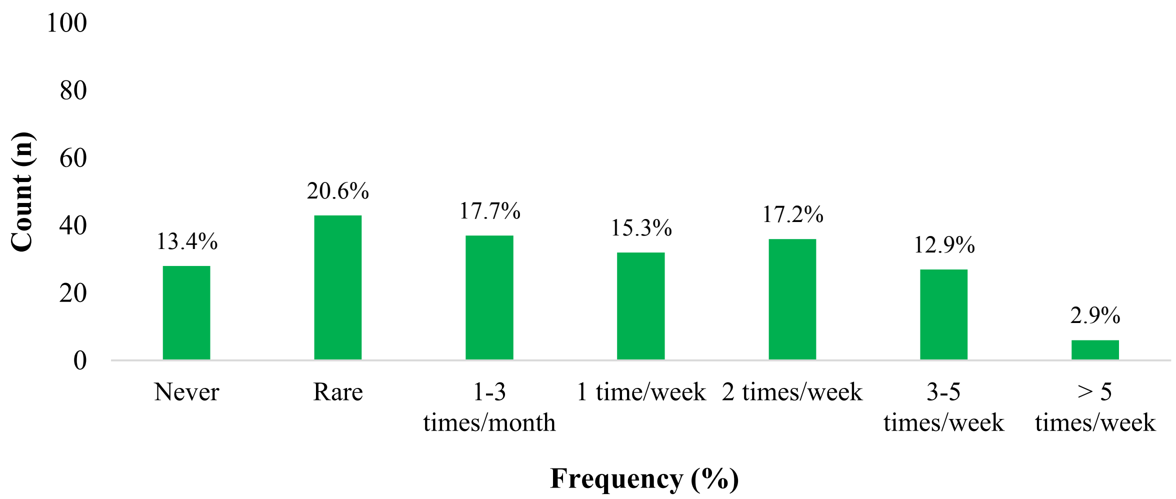


Figure 3.3: Intake frequency of seafood consumption as spread among the children, given in count (n) and percent (%) of the total number of children (n = 209).

Table 3.3 shows the intake frequencies of different types of seafood used as spread. Mackerel in tomato sauce and caviar were by far the most frequently consumed spreads. Tuna was rarely consumed among the children.

Table 3.3: Intake frequencies (%) of the different fish and seafood items consumed as spread by the children (n = 209).

				Frequency (%)			
Fish/seafood	**Never**	**Rare**	**1-3 times/month**	**1 time/week**	**2 times/week**	**3-5 times/week**	**> 5 times/week**
Fatty spreads							
Mackerel in tomato sauce	27.8	14.8	19.6	14.8	15.8	6.2	1.0
Canned sardines or herring	90.0	5.7	3.3	1.0	0.0	0.0	0.0
Other fatty spreads[a]	71.9	12.4	10.0	3.3	2.4	0.0	0.0
Caviar	37.8	17.2	15.3	8.6	9.1	9.6	2.4
"Svolvaer- and Lofotpostei"	93.7	4.3	0.5	1.0	0.5	0.0	0.0
Lean spreads							
Tuna	90.9	6.2	2.4	0.5	0.0	0.0	0.0

[a]Other fatty spreads include pepper mackerel, smoked/cured salmon or trout

3.2.2 Dairy products

The majority of children consumed dairy products on a daily basis. Approximately 90% consumed dairy products at least once a day (**Fig. 3.4**). None of the children reported to never/rare eat or drink dairy products. Median intake of different dairy products among the children were 7.0, IQR = 7.0 (mean = 12 ± SD 6.9) times per week.

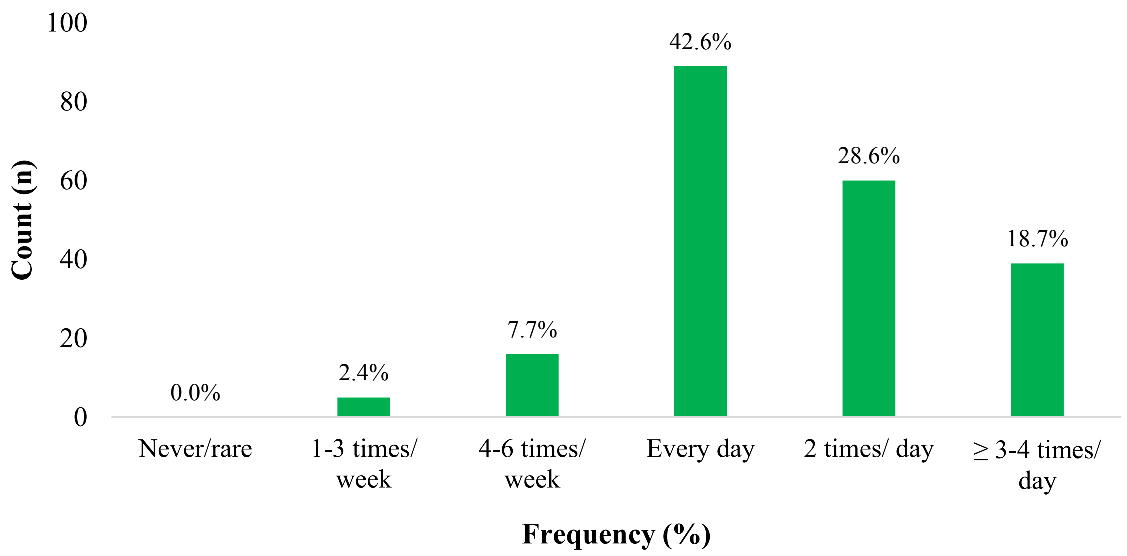


Figure 3.4: Intake frequency of dairy products (milk, yogurt and cheese) among the children, given in count (n) and percent (%) of the total number of children (n = 209).

The intake frequencies of different types of dairy products are given in **table 3.4**. On a daily basis, extra low-fat milk and low-fat milk are the types of sweet milk most frequently consumed by the children. In addition, different types of cheese and yogurt are consumed several times a week by a large proportion of the children.

Table 3.4: Intake frequencies (%) of the different dairy products consumed by the children (n = 209).

	Frequency (%)					
Dairy products	**Never/ rare**	**1-3 times/week**	**4-6 times/week**	**Every day**	**2 times/day**	**≥ 3-4 times/day**
Sweet milk						
Whole milk	90.0	5.2	1.0	2.8	0.5	0.5
Low-fat milk	33.0	15.3	14.8	17.2	14.4	5.3
Extra low-fat milk	53.6	6.6	7.2	18.7	8.6	5.3
Skimmed milk	87.2	4.3	3.8	3.3	1.4	0.0
Chocolate milk	71.3	28.7	0.0	0.0	0.0	0.0
Cultured milk and yogurt						
Drinking yogurt	75.6	21.5	1.0	1.9	0.0	0.0
"Biola"	67.5	23.9	5.3	2.8	0.5	0.0
"Cultura"	96.1	2.9	0.5	0.5	0.0	0.0
Yogurt	7.7	42.1	34.0	13.8	1.4	1.0
Cheeses						
White cheeses[a]	9.6	37.3	35.3	14.4	2.9	0.5
Brown cheese	33.5	44.0	15.8	5.7	1.0	0.0

[a]Includes "Norvegia", "Jarlsberg" and cream cheeses

The distribution of weekly intake of different dairy products are given in **figure 3.5**. Over half of the weekly dairy product intake consisted of sweet milk, while the weekly intake of cultured milk and yogurt contributed with 22%. White cheeses contributed more to the weekly dairy product intake than did brown cheese. Median intake of sweet milk was 8.0, IQR = 7.0 (mean = 10.4 ± SD 7.1) times per week, and the median intake of cultured milk and yogurt were 4.0, IQR = 5.0 (mean = 4.3 ± SD 3.9) times per week. Median consumption of white cheeses were 4.0, IQR = 3.0 (mean = 3.3 ± SD 3.2) times per week, while the median intake of brown cheese was 1.0, IQR = 1.0 (mean = 1.6 ± SD 2.3) time per week. The weekly intake of yogurt ($p = 0.010$), extra low-fat milk ($p = 0.041$) and skimmed milk ($p = 0.038$) was significantly different between gender. The boys had highest consumption of extra-low fat milk, while the girls had higher intakes of yogurt and skimmed milk. None of the other dairy products differed by gender (data not shown).

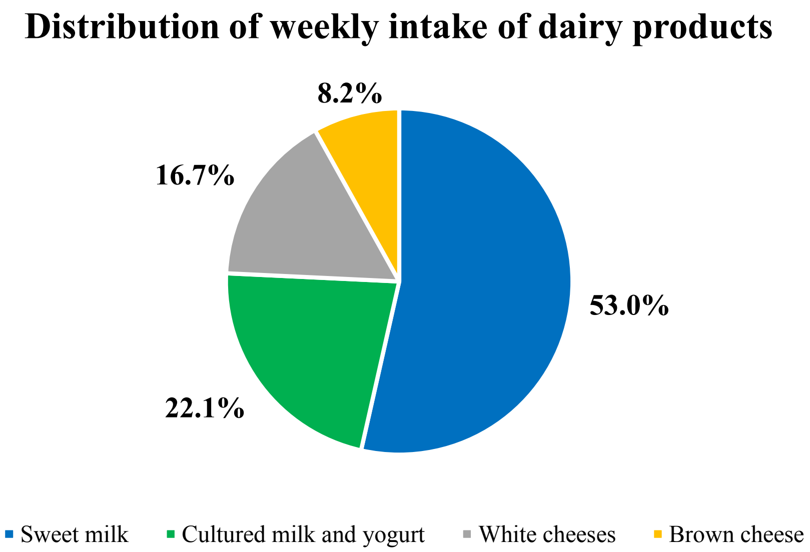
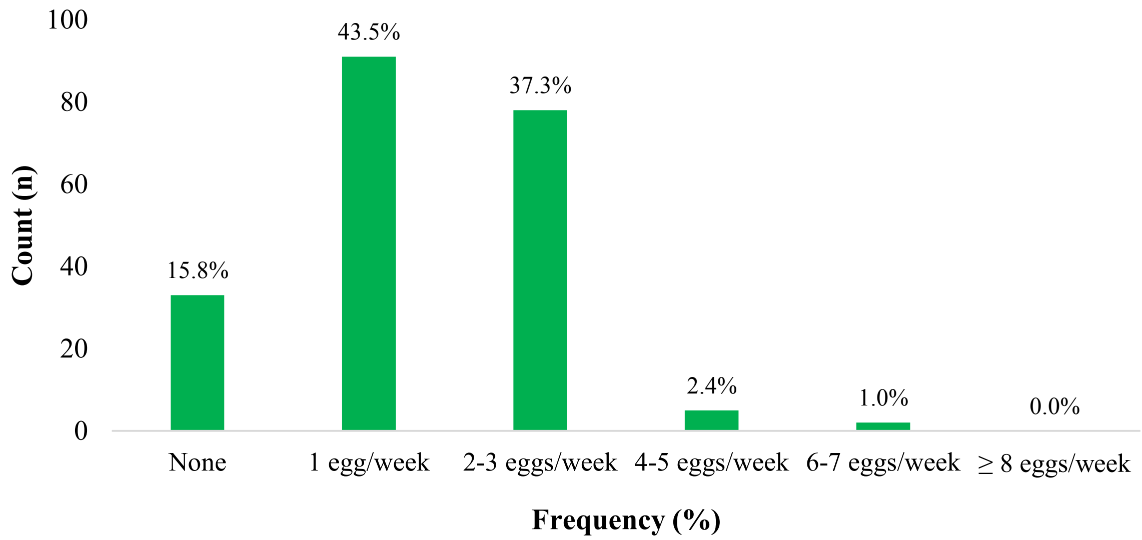


Figure 3.5: The distribution (%) of weekly intake of dairy products among the children (n = 209). Dairy products are divided into four categories; "sweet milk" (whole milk, low-fat milk, extra low-fat milk, skimmed milk and chocolate milk), "cultured milk and yogurt" (drinking yogurt, "Biola", "Cultura" and yogurt), "white cheeses" ("Norvegia", "Jarlsberg" and cream cheeses) and "brown cheese".

3.2.3 Eggs

The majority of children ate one egg per week, and 81% consumed 1-3 eggs per week (**Fig. 3.6**). Median weekly intake of eggs among the children were 1.0, IQR = 1.5 (mean = 1.5 ± SD 1.1). The weekly egg intake was not significantly different between boys and girls (p = 0.122).



<u>Figure 3.6:</u> Intake frequency of eggs among the children given as count (n) and percent (%) of the total number of children (n = 209).

3.2.4 Supplements

Approximately 40% (n = 82) of the parents answered yes when questioned about the children's use of "other supplements (vitamins and minerals)". Regarding use of multiminerals, 97% of children never used multiminerals. Only one child consumed a daily dose of multiminerals. No significant gender differences in intake of multiminerals were observed. When checking the written answers in Q21 ("Spesifiser hvilke(t) merke på kosttilskudd og hvor mye barnet tar hver gang"), five children (2.4%) took daily doses of iodine-containing supplements.

3.3 Iodine status

3.3.1 Estimates of urinary iodine and creatinine concentration

Non-fasting, spot urine samples from 220 children (94.8%) were available for analysis. Median UIC, mean creatinine concentration (g/L), along with the estimated iodine/creatinine ratio (µg/g) and estimated 24h UIE (µg/day) is presented in **table 3.5**. The boys had a slightly higher median UIC than the girls, but the difference in results were not statistically significant ($p = 0.321$). There were not observed any significant gender differences in urinary creatinine concentration ($p = 0.083$), nor the estimated iodine/creatinine ratio ($p = 0.676$) or the estimated 24h UIE ($p = 0.676$).

Estimation of the daily iodine intake (extrapolated from UIC in spot urine samples) showed a median intake of 64 µg iodine/day in the study population.

<u>**Table 3.5:**</u> Urinary iodine concentration, urinary creatinine concentration, estimated iodine/creatinine ratio and estimated 24h urinary iodine excretion in the children (n = 220).

	All participants (n = 220)			**Boys (n = 106)**	**Girls (n = 114)**	
Norwegian preschool children	**Median (IQR)**	**Min**	**Max**	**Median (IQR)**	**Median (IQR)**	**p-value**
UIC (µg/L)	133 (96)	17	782	136 (97)	131 (97)	0.321[a]
Creatinine concentration (g/L)[b]	0.9 ± 0.3[b]	0.1	2.1	0.9 ± 0.5[b]	0.8 ± 0.4[b]	0.083[c]
Iodine/creatinine ratio (µg/g)	163 (138)	28	810	163 (143)	163 (138)	0.676[a]
Estimated 24h UIE (µg/day)	65 (55)	11	324	65 (57)	65 (55)	0.676[a]

[a]P-value calculated with Mann-Whitney U Test due to not normally distributed data
[b]Value given in mean ± SD due to normally distributed data
[c]P-value calculated with Independent Samples T-test
IQR: Interquartile range, SD: Standard deviation, UIC: Urinary iodine concentration,
UIE: Urinary iodine excretion, 24h: 24 hours

UIC-results from the present study population are compared to WHO/UNICEF/ICCIDD criteria (**Fig. 3.7**). The majority of children had UIC within the optimal range (median UIC = 100-199 µg/L). In this study, 29.1 % of the sample had UIC below 100 µg/L. According to the criteria, nine children had excessive iodine intakes (median UIC ≥ 300 µg/L).

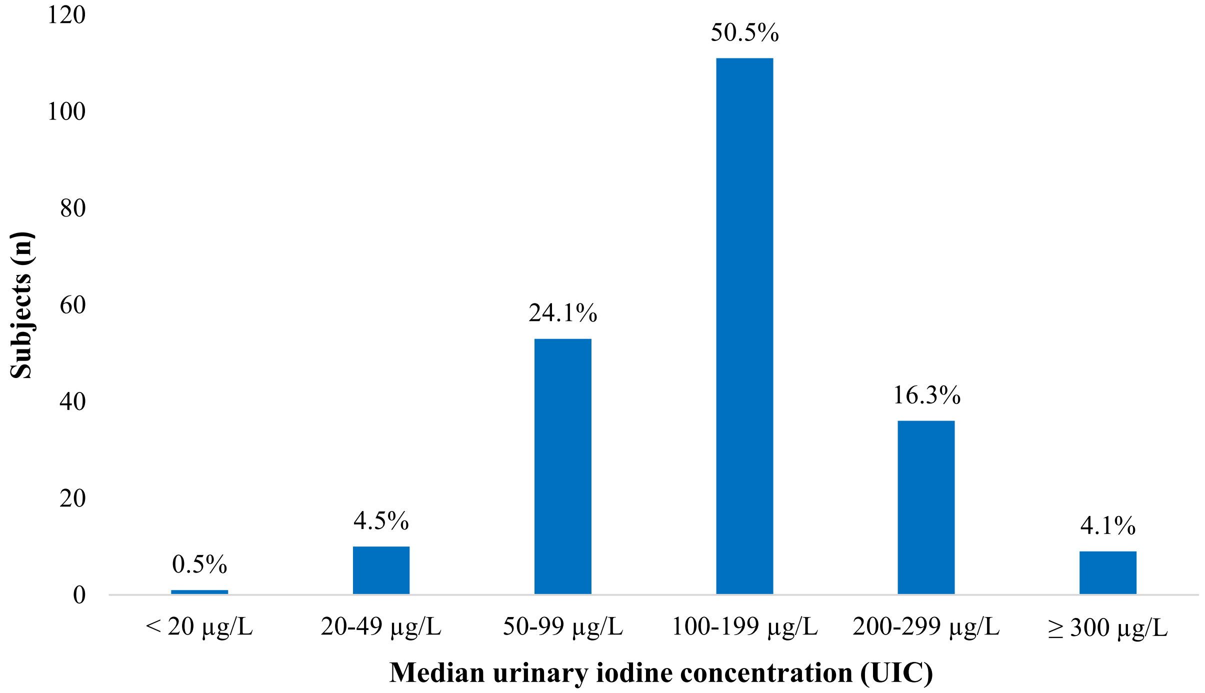


Figure 3.7: Distribution of urinary iodine concentrations (UIC) among the children (n = 220). Presented according to WHO/UNICEF/ICCIDD criteria on iodine nutrition in populations (based on surveys in school-aged children ≥ 6 years old) (46).

3.4 Correlation analyses

3.4.1 UIC and FFQ-variables

Correlations between UIC and iodine-related FFQ-variables showed four statistically significant associations ($p < 0.05$) (**Table 3.6**). The intake of fatty fish (dinner), lean fish (dinner), fatty spreads and the use of multiminerals were weakly correlated with UIC. All correlations were positive, except for intake of lean fish (dinner), which showed a weak and negative correlation with UIC. Lean fish (dinner) were only significant for the boys, while intake of fatty fish (dinner) were significant for the girls. The correlation between UIC and fatty spreads were statistically significant for the total study population and the girls. Intake of multiminerals were significantly correlated with UIC in the total population and among the boys. No other significant correlations were discovered between UIC and iodine-containing food groups (data not shown).

Table 3.6: Correlations between urinary iodine concentration (UIC) and iodine-containing dietary items from the FFQ, in Spearman's rank order correlation coefficient (rho).

Variables	All		Boys		Girls	
	n = 198		n = 94		n = 104	
	rho	**p-value[a]**	**rho**	**p-value[a]**	**rho**	**p-value[a]**
UIC (µg/L)						
Fatty fish (dinner)[b]	0.13	0.079	0.01	0.933	0.25	**0.012**
Lean fish (dinner)[c]	-0.06	0.368	-0.22	**0.032**	0.08	0.431
Fatty spreads[d]	0.17	**0.019**	0.13	0.205	0.21	**0.037**
Multiminerals	0.16	**0.026**	0.23	**0.027**	0.08	0.434

[a]2-tailed, significance level $p < 0.05$
[b]Fatty fish (dinner) include salmon/trout, mackerel, herring and halibut
[c]Lean fish (dinner) include cod, saithe, other lean fish (pollack, haddock and plaice)
[d]Fatty spreads include mackerel in tomato sauce, canned sardines/herring, other fatty spreads (pepper mackerel, smoked/cured salmon), caviar, "Svolvaer- and Lofotpostei"
UIC: Urinary iodine concentration

3.4.2 UIC and socio-economic- and anthropometric variables

A significant, weak and negative correlation was found between UIC and total household income among participating boys (rho = -0.22, p = 0.042). Parental education level was not significantly correlated with UIC. For both of these variables the correlation coefficient (rho) was negative, indicating a negative association between socio-economic factors and UIC (data not shown). In addition, no significant correlation was found between UIC and the children's gender, weight, age or BMI (data not shown).

When correlating UIC to creatinine (g/L) a medium strong association was found for the total study population (rho= 0.34, p < 0.001), as well as for the boys (rho= 0.38, p < 0.001). The girls presented a somewhat weaker correlation (rho= 0.29, p = 0.002).

3.4.3 Parental socio-economic factors and FFQ-variables

Parental education level was significantly correlated with three FFQ-variables (**Table 3.7**). Intake of seafood for dinner and dairy products showed weak, but positive correlations with the parent's education level. Only boys showed a significant and medium strong, positive correlation between parental education level and seafood for dinner (rho = 0.41, p = 0.000). In addition, parental education level and dairy products were positively correlated for both boys (rho = 0.30, p = 0.003) and girls (rho = 0.27, p = 0.005). Intake of multiminerals were significantly and negatively associated with parental education level (rho = -0.23, p = 0.023) among the boys.

When dividing seafood and dairy products into the different subcategories none of the dietary variables showed significant correlation with parental education level (data not shown).

Table 3.7: Correlations between parental education level and iodine-containing dietary items from the FFQ, in Spearman's rank order correlation coefficient (rho).

Variables	All		Boys		Girls	
	n = 203		n = 94		n = 109	
	rho	**p-value[a]**	**rho**	**p-value[a]**	**rho**	**p-value[a]**
Parental education level (years)						
Seafood (dinner)	0.24	**0.001**	0.41	**< 0.001**	0.09	0.370
Dairy products[c]	0.27	**< 0.001**	0.30	**0.003**	0.27	**0.005**
Multiminerals	-0.09	0.183	-0.23	**0.023**	0.05	0.607

[a]2-tailed, significance level $p < 0.05$
[b]Seafood (dinner) includes fish, processed fish products and other seafood items (summary question)
[c]Dairy products include milk, yogurt and cheeses (summary question)

Seafood for dinner was weakly, but positively correlated with total household income for the boys (**Table 3.8**). In addition, dairy products were positively correlated with total household income for the total study population. When correlating egg intake with total household income, a weak and negative association was observed for the overall study population and when considering gender, only the girls showed a significant negative correlation between total household income and egg intake.

Table 3.8: Correlations between total household income and iodine-containing dietary items from the FFQ, in Spearman's rank order correlation coefficient (rho).

Variables	All		Boys		Girls	
	n = 202		n = 94		n = 108	
	rho	**p-value[a]**	**rho**	**p-value[a]**	**rho**	**p-value[a]**
Total household income (NOK)						
Seafood (dinner)[b]	0.13	0.063	0.26	**0.011**	0.05	0.587
Dairy products[c]	0.23	**0.001**	0.23	**0.029**	0.26	**0.006**
Eggs	-0.19	**0.008**	-0.13	0.231	-0.19	**0.047**

[a]2-tailed, significance level $p < 0.05$
[b]Seafood (dinner) includes fish, processed fish products and other seafood items (summary question)
[c]Dairy products include milk, yogurt and cheeses (summary question)

3.5 Logistic regression models

3.5.1 UIC and seafood consumption

Table 3.9 shows the unadjusted logistic regression model between UIC and seafood intake among the children. A statistical significant association between UIC and intake of fatty fish for dinner was found (OR = 1.95, p = 0.048). Thus, children who consumed fatty fish for dinner ≥ 1 time/week were approximately two times more likely to have adequate iodine status (median UIC ≥ 100 µg/L).

Stratifying the data by gender showed that UIC was significantly associated with intake of fatty fish (dinner) for the included girls (OR = 2.85, 95% CI = 1.18-6.89, p = 0.021).

Table 3.9: Logistic regression model (unadjusted) between UIC (≥ 100 µg/L)[a] and intake of seafood[b] among the children (n = 198).

		Unadjusted model		
Variables	**Frequency interval[c]**	**OR**	**95% CI**	**p-value[d]**
Seafood dinner (all types)	< 2 times/week	1 (ref.)		
	≥ 2 times/week	1.22	0.65-2.28	0.542
Lean fish (dinner)	< 1 time/week	1 (ref.)		
	≥ 1 time/week	1.01	0.49-2.10	0.973
Fatty fish (dinner)	< 1 time/week	1 (ref.)		
	≥ 1 time/week	1.95	1.01-3.77	**0.048**
Processed fish products (dinner)	< 1 time/week	1 (ref.)		
	≥ 1 time/week	0.99	0.45-2.15	0.971
Shellfish (dinner)	< 1 time/month	1 (ref.)		
	≥ 1 time/month	1.00	0.5-2.01	1.000
Seafood spreads	< 2 times/week	1 (ref.)		
	≥ 2 times/week	1.26	0.64-2.49	0.499

[a]UIC < 100 µg/L is the reference group
[b]To see which dietary items are included in the categories lean fish (dinner), fatty fish (dinner), processed fish products (dinner), shellfish (dinner) and seafood spreads see section 2.5.4
[c]The lowest frequency interval is the reference group (OR = 1, ref.)
[d]Significance level (p < 0.05)
CI: Confidence interval, OR: Odds ratio, UIC: Urinary iodine concentration

In **table 3.10**, adjusted regression models are given between UIC and intake of seafood among the children. Intake of fatty fish for dinner remained a significant predictor for UIC after several adjustments. When adjusting for gender and creatinine (g/L) in model 1, the association between UIC and intake of fatty fish for dinner was stronger than what was found in the unadjusted model (OR = 2.44, p = 0.014). After adjusting for creatinine (g/L) and sweet milk (model 2), the association between UIC and intake of fatty fish for dinner, remained significant (OR = 2.37, p = 0.018).

No other seafood variables were associated with UIC after adjusting for other possible UIC-predictors (creatinine (g/L) and sweet milk).

In adjusted models stratified by gender, intake of fatty fish (dinner) were only significant for the girls (OR = 3.05, 95% CI = 1.21-7.70, p = 0.018). Stratifying the data according to gender did not change the results of the other seafood variables (data not shown).

Overall, the adjusted models indicated that children who consumed fatty fish for dinner ≥ 1 time/week were approximately two times more likely to have UIC ≥ 100 µg/L, controlling for other factors in the models (gender, creatinine (g/L) and intake of sweet milk).

Table 3.10: Adjusted logistic regression models between UIC (≥ 100 µg/L)[a] and intake of seafood[b] among the children (n = 198).

		Adjusted model 1[c]			Adjusted model 2[d]		
Variables	**Frequency intervals[e]**	**OR**	**95% CI**	**p-value[f]**	**OR**	**95% CI**	**p-value[f]**
Seafood dinner (all types)	< 2 times/week	1 (ref.)			1 (ref.)		
	≥ 2 times/week	1.16	0.60-2.24	0.663	1.17	0.60-2.27	0.649
Lean fish (dinner)	< 1 time/week	1 (ref.)			1 (ref.)		
	≥ 1 time/week	1.16	0.54-2.53	0.703	1.17	0.53-2.57	0.697
Fatty fish (dinner)	< 1 time/week	1 (ref.)			1 (ref.)		
	≥ 1 time/week	2.44	1.20-4.98	**0.014**	2.37	1.16-4.82	**0.018**
Processed fish products (dinner)	< 1 time/week	1 (ref.)			1 (ref.)		
	≥ 1 time/week	0.90	0.40-2.04	0.801	0.80	0.35-1.84	0.594
Shellfish (dinner)	< 1 time/month	1 (ref.)			1 (ref.)		
	≥ 1 time/month	0.962	0.46-2.01	0.918	1.02	0.48-2.15	0.968
Seafood spreads	< 2 times/week	1 (ref.)			1 (ref.)		
	≥ 2 times/week	1.21	0.60-2.46	0.596	1.19	0.58-2.42	0.633

[a]UIC < 100 µg/L is the reference group
[b]To see which dietary items are included in the categories lean fish (dinner), fatty fish (dinner), processed fish products (dinner), shellfish (dinner) and seafood spreads see section 2.5.4
[c]Model 1 is adjusted for gender and urinary creatinine concentration (g/L)
[d]Model 2 is adjusted for urinary creatinine concentration (g/L) and sweet milk
[e]The lowest frequency interval is the reference group (OR = 1, ref.)
[f]Significance level ($p < 0.05$)
CI: Confidence interval, OR: Odds ratio, UIC: Urinary iodine concentration

3.5.2 UIC and intake of dairy products and eggs

Table 3.11 shows the unadjusted logistic regression model between UIC and intake of different types of dairy products among the children. UIC was significantly and positively associated with intake of sweet milk (OR = 2.17, p = 0.031). The regression model indicates that children who consumed sweet milk once a day or more, were over two times more likely to have UIC ≥ 100 µg/L.

Stratifying the data by gender resulted in a loss of the significant association between UIC (≥ 100 µg/L) and intake of sweet milk (≥ 2 times/day). No other results changed due to gender stratification.

<u>**Table 3.11:**</u> Logistic regression model (unadjusted) between UIC (≥ 100 µg/L)[a] and intake of different dairy products[b] among the children (n = 198).

		Unadjusted model		
Variables	**Frequency interval**[c]	**OR**	**95% CI**	**p-value**[d]
Dairy products (all types)	< 2 times/day	1 (ref.)		
	≥ 2 times/day	1.39	0.74-2.60	0.311
Sweet milk	< 1 time/day	1 (ref.)		
	≥ 1 time/day	2.17	1.07-4.38	**0.031**
Cultured milk and yogurt	< 4 times/week	1 (ref.)		
	≥ 4 times/week	1.16	0.62-2.17	0.641
White cheeses	< 4 times/week	1 (ref.)		
	≥ 4 times/week	0.95	0.51-1.78	0.871
Brown cheese	< 4 times/week	1 (ref.)		
	≥ 4 times/week	1.21	0.56-2.60	0.628

[a]UIC < 100µg/L is the reference group
[b]To see which dietary items are included in the categories sweet milk, cultured milk and yogurt and white cheeses see section 2.5.4
[c]The lowest frequency interval is the reference group (OR = 1, ref.)
[d]Significance level (p < 0.05)
CI: Confidence interval, OR: Odds ratio, UIC: Urinary iodine concentration

Adjusted logistic regression models between UIC and intake of dairy products are given in **table 3.12**. When adjusting for gender and creatinine (g/L) (model 1) only sweet milk showed a significant association with UIC (OR = 2.46, p = 0.020). In model 2, sweet milk remained statistically significant after adjustments for creatinine (g/L) and intake of fatty fish for dinner (OR = 2.51, p = 0.017). None of the other dairy products were significantly associated with the measured UIC.

In adjusted models stratified by gender, the association between UIC and intake of sweet milk disappeared. The intake of sweet milk was not significantly associated with UIC for boys (OR = 3.13, 95% CI = 0.86-11.10, p = 0.077), nor girls (OR = 1.93, 95% CI = 0.72-5.17, p = 0.188).

None of the other dairy product variables were significantly changed after stratifying the data by gender (data not shown).

Looking at the whole study population, the adjusted models suggested that children who consumed a daily amount of sweet milk were approximately 2.5 times more likely to have adequate iodine status (UIC ≥ 100 µg/L).

In unadjusted analyses, no significant association between UIC and intake of eggs (≥ 2 eggs/week) was found (OR = 1.12, 95% CI = 0.59-2.13, p = 0.723). In addition, no significant association was found between UIC and intake of eggs when adjusting for gender and creatinine (g/L) (OR = 1.16, 95% CI = 0.59-2.27, p = 0.336), and additional adjustments with intake of sweet milk and fatty fish for dinner (OR = 1.09, 95% CI = 0.57-2.08, p = 0.790). Stratifying the data by gender did not change the results (data not shown).

Table 3.12: Adjusted logistic regression models between UIC (≥ 100 µg/L)[a] and intake of dairy products[b] among the children (n = 198).

		Adjusted model 1[c]			**Adjusted model 2[d]**		
Variables	**Frequency intervals[e]**	**OR**	**95% CI**	**p-value[f]**	**OR**	**95% CI**	**p-value[f]**
Dairy products (all types)	< 2 times/day	1 (ref.)					
	≥ 2 times/day	1.58	0.81-3.10	0.181	1.46	0.74-2.87	0.271
Sweet milk	< 1 time/day	1 (ref.)					
	≥ 1 time/day	2.46	1.15-5.25	**0.020**	2.51	1.18-5.35	**0.017**
Cultured milk and yogurt	< 4 times/week	1 (ref.)					
	≥ 4 times/week	1.62	0.81-3.23	0.173	1.50	0.76-2.97	0.243
White cheeses	< 4 times/week	1 (ref.)					
	≥ 4 times/week	0.99	0.52-1.92	0.984	1.00	0.51-1.93	0.989
Brown cheese	< 4 times/week	1 (ref.)					
	≥ 4 times/week	1.22	0.55-2.73	0.628	1.10	0.49-2.50	0.817

[a]UIC < 100 µg/L is the reference group
[b]To see which dietary items are included in the categories sweet milk, cultured milk and yogurt and white cheeses see section 2.5.4
[c]Model 1 is adjusted for gender and urinary creatinine concentration (g/L)
[d]Model 2 is adjusted for urinary creatinine concentration (g/L) and intake of fatty fish (dinner)
[e]The lowest frequency interval is the reference group (OR = 1, ref.)
[f]Significance level ($p < 0.05$)
CI: Confidence interval, OR: Odds ratio, UIC: Urinary iodine concentration

3.5.3 UIC and parental socio-economic factors

Neither unadjusted nor adjusted logistic regression models found significant associations between UIC and the two parental socio-economic factors (parental education level and total household income) (data not shown). Stratifying the data by gender did not change the results.

3.5.4 Parental socio-economic factors and FFQ-variables

Unadjusted logistic regression models showed positive significant associations between parental education level and intake of seafood for dinner (summary question) (OR = 2.21, 95% CI = 1.06-4.59, p = 0.034) and dairy products (summary question) (OR = 3.20, 95% CI = 1.46-6.99, p = 0.004). In addition, unadjusted models showed negative significant association between total household income and intake of shellfish (OR = 0.44, 95% CI = 0.20-0.94, p = 0.035) and positive significant association between income and intake of dairy products (summary question) (OR = 2.33, 95% CI = 1.04-5.19, p = 0.039). Thus, the results indicate that children of parents with high parental education level were over two times more likely to have a high intake of seafood (≥ 2 times/week), and over three times more likely to have a high intake of dairy products (≥ 2 times/day). In addition, children of parents with medium/high income were 0.4 times less likely to have an intake of shellfish ≥ 1 time/month, and over two times more likely to have a high intake of dairy products (≥ 2 times/day).

When stratifying by gender in unadjusted models, parental education level was significantly and positively associated with intake of dairy products among the girls (OR = 4.11, 95% CI = 1.19-14.15, p = 0.025), and seafood for dinner among the boys (OR = 4.26, 95% CI = 1.11-16.44, p = 0.035). In addition, total household income was significantly and negatively associated with intake of shellfish (OR = 0.10, 95% CI = 0.01-0.50, p = 0.010) among the boys, and positively associated with intake of dairy products (OR = 2.63, 95% CI = 1.06-6.56, p = 0.038) among the girls.

4. DISCUSSION

The aims of the present thesis were to assess and evaluate the iodine status of preschool children and investigate the significance of different dietary sources of iodine and parental socio-economic factors. The iodine status was assessed by determination of iodine in urine samples by ICP-MS, and results are given as UIC (µg/L), iodine/creatinine ratio (µg/g), and estimated 24h UIE (µg/day). In this thesis, the association between UIC and different seafood items, dairy products, eggs, and use of iodine-containing supplements were investigated. In addition, associations between UIC and parental socio-economic variables, and associations between parental socio-economic factors and the children's intake of iodine-rich food sources were examined.

The included children had an overall sufficient iodine status according to WHO/UNICEF/ICCIDD criteria (46). Expressed in relation to creatinine, the iodine status improved.

UIC was significantly correlated with several FFQ-variables, including seafood for dinner (lean and fatty fish), intake of fatty seafood spreads and the use of multiminerals. One statistical significant correlation was found between the children's UIC and total household income. In addition, several significant correlations were discovered between parental socio-economic factors and FFQ-variables.

Unadjusted logistic regression models showed that UIC was significantly associated with intake of fatty fish (dinner) and sweet milk. When adjusting for creatinine (g/L), gender and FFQ-variables, the association between UIC and intake of fatty fish for dinner and sweet milk became stronger. No other associations were found between UIC and intake of iodine-rich food sources. Logistic regression models did not find any significant associations between UIC and parental socio-economic factors. However, significant associations were found between parental socio-economic factors and intake of iodine-rich food sources.

In the following, results from the present study are discussed and thereafter methodological considerations are given. Finally, a summary with conclusions and future perspectives are provided.

4.1 Recruitment, descriptive characteristics and representativity

The recruitment process was completed in the local kindergartens by arranging information meetings and provide study material to parents. This made it easier to recruit multiple children within the same kindergarten. In the recruitment process, the size and location of the kindergartens resulted in a somewhat convenience sample of kindergartens in the Bergen area. Inclusion of 200 children (100 in each group) was considered adequate for ensuring statistical power and detection of IQ-differences in the intervention study (WP5) (124). The inclusion rate was good, and as shown, 74% of the requested children were enrolled in the present study. A good inclusion rate indicates enrollment of a representative sample of preschool children from different families with various backgrounds. In addition, inclusion of kindergartens from different city districts throughout the Bergen area contributed to representativity. School-aged children are useful for assessing iodine status because they are easily accessible and they reflect current iodine nutrition in the general population (18, 125).

In the present study, the gender distribution was slightly in favor of the girls. However, there was rarely found significant differences between genders in relation to intake frequencies of iodine-containing foods. Median weight, height and BMI for the girls were within + 1 SD (> median) in relation to WHO Child Growth Standards for the relevant age group of 5.2 years, while median weight, height and BMI for the boys were within + 2 SD (> median) relative to WHO standards (112). Previous studies involving Norwegian children have shown a tendency among the children to be taller and heavier than the reference populations used in the growth standards developed by WHO (126, 127). In accordance with our results, Júlíusson et al. (2009), found that Norwegian children in general had higher birth weight, were taller, heavier and had larger head circumference compared to international WHO Growth Standards (126). Since BMI is a ratio between weight and height, the BMI of the present study population was comparable to the median BMI of the WHO reference population for the relevant age group (5.2 years).

The median parental education level in the present thesis was 16 years. This corresponds to < 4 years of University or University College education. Forty-seven percent of mothers and thirty-five percent of fathers had ≥ 4 years of University or University College education. The current parental education level resembles what was found in “Ungkost 2000”, where approximately 50% of parents had education levels above secondary school (128).

Nearly all study subjects were born in Norway. Only three children were born in other EU/EEA-countries, while one child was born outside of EU/EEA. Regarding the parents, the majority were born in Norway, but a larger quantity were born within or outside EU/EEA. Due to lack of information about the parent's countries of origin, it was difficult to predict a potential cultural effect on the children's dietary habits. Families originating from countries other than Norway may have a diet different from what is usually found here, and thus contain either smaller or larger quantities of iodine-rich food sources.

The large sample size, the children's birthplace and the presented anthropometric measurements seems to increase the present study's overall representativity. However, lack of information about individuals declining study participation may give rise to bias. Thus, generalization of the current study results to other subgroups and/or populations in Norway or abroad may not be appropriate.

4.2 Iodine status and associated dietary predictors

4.2.1 Evaluation of iodine status

The iodine status of the included preschool children was adequate. Approximately one third of the children had UIC below WHO/UNICEF/ICCIDD cutoff-criteria of 100 μg/L. Only 4% of the children had median UIC ≥ 300 μg/L. Thus, the risk of iodine-induced adverse health effects are low in the present population. When correcting for urinary creatinine concentration, the iodine status improved. The estimated 24h UIE was lower than the measured UIC. In addition, the estimation of daily iodine intake (from UIC) was lower than the recommended daily intake of iodine in preschool children.

The present iodine status results are in accordance with a large cross-sectional study of school-age children (6-12 years old) from Sweden. Andersson et al. (2009) found a median UIC of 125 μg/L, and 30% of children had UIC below 100 μg/L. In accordance with us, no significant differences in median UIC between genders were found (129). In contrast to Norway, the largest dietary source of iodine in the Swedish diet is iodized salt, with an intake of 5-7 g/day in children (129, 130). Unlike our study, the urinary iodine analyses were performed by use of the modified Sandell-Kolthoff method. However, a strong correlation between ICP-MS and the Sandell-Kolthoff method has been suggested, and this indicates insignificant differences in measured iodine concentrations by the two analytical methods (131). However, Macours et al. (2008), found that the ICP-MS method measured significantly lower UIC compared to the Sandell-Kolthoff method (132). Thus, comparing iodine results analyzed by the two different analytical methods should be interpreted with caution.

Our results are also in accordance with a cross-sectional iodine status study performed in Australian preschool children (aged 1-5 years). Here, spot urine samples from 279 children showed a median UIC of 129 µg/L, and 35% of the children had UIC below 100 µg/L (no gender differences) (133). As in the Swedish study (129), the urinary iodine analyses were performed using the modified Sandell-Kolthoff method (133).

The values for urinary creatinine concentration found in the present thesis is in agreement with a recently published study from Denmark. Andersen et al. (2014), examined the iodine status of pregnant women, their partners and children (n= 51, median age = 6 years). Results showed that the children had a median UIC of 126 µg/L. In addition, measurements of urinary creatinine (from spot samples) showed a median creatinine concentration of 7.2 mmol/L, and an estimated 24h UIE of 63 µg/day (134), which is similar to our results. However, the analytical methods used in the Danish study were different from our study, and the results may therefore not be directly comparable.

The mean creatinine concentration from the measured spot urine samples in our study was well within published American reference ranges for urinary creatinine concentrations (from spot samples) in children aged 3-8 years (urinary creatinine concentration = 0.02-1.49 g/L) (135). This may be an indication that neither too diluted nor too concentrated urine samples were included in the present analyses. Too diluted or concentrated samples may disrupt analyses and affect iodine and creatinine results. Usually, too dilute urine samples may impair determination of low levels of the substances of interest (e.g. creatinine), while too concentrated urine samples may be associated with low fluid intake (dehydration), and cause falsely elevated substance concentrations. Thus, using too dilute or too concentrated urine samples may result in imprecise creatinine and iodine concentrations (136). Norwegian reference intervals for urinary creatinine concentration measured in spot urine samples in children (4-6 years old) are not established (137).

The three estimates for iodine status presented in our study showed quite different results. Median UIC was lower than the estimated iodine/creatinine ratio, and the estimated 24h UIE was much lower than both the median UIC and the iodine/creatinine ratio. The higher iodine/creatinine ratio is associated with the measured mean urinary creatinine concentration of 0.9 g/L. Other studies with inclusion of older study populations report conflicting results. Gunnarsdottir et al. (2010) found the estimated iodine/creatinine ratio to be lower than the UIC (138). Caldwell et al. (2005) found similar results among children ≥ 6 years old. However, in the age group 6-11 years, the iodine/creatinine ratio was higher than the UIC (139), which is in accordance with our results. Lower iodine/creatinine ratio than median UIC is most likely associated with a higher urinary creatinine concentration, e.g. 1.6 g/L, as reported by Gunnarsdottir et al. (2010) (138). In our study, the estimated daily iodine intake (extrapolated from UIC) among the children was 64 µg/day. This is below the recommended intake of 90-120 µg/day, and just below the estimated average requirement (EAR) for this age group (65 µg/day). Due to variations in daily urine volume among individuals, this extrapolation may be associated with uncertainty, and give incorrect calculations (55). Thus, we cannot exclude an overall adequate daily iodine intake in the present study population.

In the present thesis, UIC-results showed large variation in iodine excretion among the included children. The measured UIC ranged from 17-782 µg/L. This is an indication of the large inter-individual variation seen in UIC. Consequently, presenting iodine status results in median UIC provides a better reflection of results than mean UIC-levels.

4.2.2 UIC and significance of dietary sources of iodine

In our study, the iodine status (UIC) was positively associated with intake of different types of sweet milk and fatty fish species. The iodine content of sweet milk is reported to be 16-20 µg/100g. Thus, a glass of milk will provide nearly half and one third (40 µg) of the daily amount of iodine recommended in preschool children (90-120 µg/day) (44). In our study, nearly all children consumed dairy products on a daily basis. Consequently, children who consumes large amounts of dairy products may be subject to excessive iodine intakes. In the present thesis, children who consumed sweet milk on a daily basis were over two times more likely to have UIC ≥ 100 µg/L. This suggest an important role of dairy products to ensure adequate iodine status in Norwegian preschool children. The role of dairy products in relation to adequate iodine status is also in agreement with studies conducted in the adult Norwegian population (12, 76).

Recent surveys indicate a decrease in milk intake in the Norwegian population. According to the Norwegian Information Office for Dairy products (“Melk. no”), the milk consumption has decreased from 3.1 dl/day in 2000, to 2.4 dl/day in 2015 (41, 140). Milk intolerance, higher water consumption, intake of meals outside of the home and negative publicity in the press may be reasons associated with the reduction in milk consumption (140). The current Norwegian recommendation of a daily intake of low-fat dairy products is important to ensure adequate intake of several nutrients including iodine, calcium, proteins and B-vitamins (57, 141).

Studies from other countries have also found milk- and dairy products to be important predictors of iodine status in children. Johner et al. (2013) found that intake of milk, eggs and iodized salt were significantly associated with the 24h UIE in German preschool children. Intake of whey-based dairy products (sweet milk and yogurt) were found to be the second most important predictor of the children's UIE. In addition, sea fish was not significantly associated with the 24h UIE, possibly due to low intake among the included children (142). A study in U.S children (aged 6-12 years), found that median UIC increased by quartile of previous dairy product intake, and dairy products accounted for 70% of iodine intake in the included children (17). This is in accordance with results from Dahl et al. (2004), who found that dairy products constitute approximately 70% of the dietary iodine intake among Norwegian children (aged 4-13 years) (13).

In our study, UIC was also significantly associated with intake of fatty fish for dinner. Fatty fish (dinner) included the following species: salmon/trout, mackerel, herring and halibut. Weekly, just under 40% of the current study population consumed fatty fish. Overall, approximately half of the included children reported consumption of fish and other seafood items for dinner less than current Norwegian recommendations of two to three servings per week (57). Thus, our results suggest a fish intake among preschool children below Norwegian recommendations. This is in accordance with previous studies in children from Norway (43, 128). A low seafood intake among children are also present in other Scandinavian countries (130, 143). In accordance with our results, Johner et al. (2011) found a significant association between intake of salt-water fish products (fatty and lean fish species) and 24h UIE in German children (6-12 years old). However, the overall contribution of fish to the measured 24h UIE was limited (144).

In the frequency interval "one time per week", the children most often consumed salmon and/or trout. Lean fish species with higher iodine content including cod, saithe, pollack and haddock were less frequently eaten among the children in the same frequency interval. The iodine content of lean fish is approximately twice that of fatty fish (13), and intake of such seafood is therefore preferred for achieving an adequate dietary iodine intake. Processed fish products usually consists of different types of lean fish (e.g. cod and haddock) (43), and will therefore also contribute to the iodine intake despite lower fish content than fish fillets. Thus, promoting intake of seafood and especially lean seafood among preschool children may be one approach to ensure adequate iodine intakes in this particular population group.

The iodine content of seafood varies considerably, both between and within species (13, 36). Consequently, it is difficult to estimate the dietary iodine contribution from such food items. The large variations in iodine content in different foods may contribute to large variations seen in the measured UIC from spot urine samples. Thus, the iodine concentration measured in casual urine samples will be a reflection of recent dietary iodine intake. In the present thesis, children who consumed fatty fish for dinner ≥ 1 time/week were approximately two times more likely to have adequate UIC (≥ 100 µg/L). UIC was not significantly associated with intake of lean fish species, despite their higher iodine content (13, 145). The lack of association might be caused by a slightly lower reported intake of lean fish species among the included children, and the large variation in daily iodine excretion (146). Thus, we cannot exclude the possibility of associations between UIC and other iodine-rich food sources (e.g. lean fish and eggs) due to the large day-to-day variations in dietary iodine intakes among individuals.

Only 2.4% of the included children used an iodine-containing supplement on a daily basis. Consequently, it is considered irrelevant for the overall iodine status in the present study population. Outliers may be explained by use of such supplements. In accordance with our results, the dietary survey “Ungkost 2000” showed that approximately 90% of included children never used multivitamins (a question regarding use of multiminerals was not included) (128). In addition, in Sweden, there is also found insignificant use of dietary supplements in children, and as a result, the assessment of iodine status is likely to reflect the true iodine intake from food sources (129, 130). UIC was significantly correlated with intake of supplements (multiminerals), but since only a few subjects reported regular use, further statistical analysis (logistic regression) was not performed between UIC and intake of multiminerals. In studies examining larger and/or older populations and where use of supplements are more frequently reported, associations between UIC and intake of iodine-containing supplements have been suggested (17, 147).

4.3 Parental socio-economic factors

4.3.1 UIC and significance of parental socio-economic factors

Logistic regression models did not discover any associations between UIC and parental socio-economic factors, which is similar to the study by Skeaff et al. (2012) among schoolchildren (aged 5-14 years). In their study, UIC did not differ by sex, age, socio-economic status or ethnicity (9). In our study sample, the parental education level and total household income was relatively high, and it is therefore reasonable to assume that the consumption of iodine-rich food sources (e.g. dairy products, seafood and eggs) are fairly equal among the included children. Thus, associations between UIC, which reflects recent dietary iodine intake, and parental socio-economic factors were not expected, nor discovered in the present thesis.

4.3.2 Parental socio-economic factors and intake of iodine-rich food sources

No strong correlations between parental socio-economic factors and reported consumption of iodine-rich food sources were found in the present thesis. A cause may be the overall high socio-economic status among the children's parents. However, weak correlations were observed between parental socio-economic factors and several FFQ-variables. In addition, unadjusted logistic regression models found significant associations between the two socio-economic variables and intake of iodine-rich food sources. Consequently, we cannot exclude a potential association between parental socio-economic status and consumption of dietary sources of iodine among preschool children.

Several studies indicate that higher socio-economic status may be associated with healthier eating habits including higher consumption of seafood, lean meats and dairy products (148, 149). A recent study conducted in Finnish children (aged 6-8 years) showed that higher parental education (vocational high school and University) and high family income (≥ 60 000 €) was significantly associated with higher fish consumption (≥ 2 times per week). In addition, higher intake of skimmed milk was seen among children from families in the highest income category (≥ 60 000 €) (150). A study in adolescents from Norway showed similar results. Here, parental education and especially maternal education level was associated with healthier dietary habits in children. Children with the least educated mothers had higher prevalence of consuming less healthy foods (e.g. soft drinks), and lower prevalence of consuming vegetables daily. In contrast to the Finnish study, the Norwegian study did not find associations between household income and dietary habits (151). Skårdal et al. (2014) found that higher family income (> 600 000 NOK) and higher parental education level (College or University) was associated with higher weekly fish intake among 13-14 year old children (98). Thus, results from the present thesis are in accordance with previous studies from Norway (98, 151) and Finland (150).

4.4 Methodological considerations

4.4.1 Design and bias

The data used in this master thesis are cross-sectional. This design is suitable for finding the prevalence of an outcome and associated factors within a population or a subgroup of the population, at a specific time (152). The cross-sectional design is here useful for assessment of iodine status and understanding the possible relationship between iodine status and associated factors (e.g. dietary variables). An additional advantage of the cross-sectional design is that there does not exist loss to follow-up (152). However, due to the "snapshot" feature of this design, it is difficult to know if the measured iodine status is a real reflection of the current situation. UIC varies considerably from day-to-day depending on factors like dietary intake, fluid intake, disease state and use of medications (22, 146).

Different types of bias (systematic error) may appear in epidemiological studies. Bias may result from recruitment methods, measurement of the variable of interest and confounding factors. Selection bias refers to systematic errors related to the methods used for selection of study participants, and is seen when the association between the outcome and related factors differ between study participants and the general population (153).

In our study, the intention was to include children from all districts and social groups in Bergen, and thus achieve a representative sample from the source population. However, due to practical reasons, and the overall intention of efficient data collection and food distribution in the intervention study (WP5), kindergartens furthest away from NIFES were not included in the study. In addition, few immigrant families were included due to the inclusion criteria of having knowledge of the Norwegian language (the questionnaire distributed to parents was written in Norwegian). Both publicly and privately owned kindergartens were included in the present study. It was not possible to obtain information about the individuals who declined to participate, and their reasons for not wanting to be part of the study. Thus, one cannot exclude a difference between included individuals and those who declined participation in the present study. There is a possibility of inclusion of families that are more resourceful and health conscious than those who declined participation. With a non-response rate of 24%, we cannot exclude an effect of selection bias in the present thesis.

4.4.2 FFQ

The present FFQ was part of a larger questionnaire which originally was developed for use in the intervention study (WP5) in order to collect information about the children's habitual dietary intake (last three months). Consequently, the FFQ was not developed for assessing iodine status and intake alone, and did not include follow-up questions about portion sizes. To make the FFQ more suitable for assessment of iodine status and further estimation of iodine intake from different foods, the inclusion of questions regarding portion sizes are helpful. However, it is possible to estimate iodine intake from a FFQ without questions regarding portion sizes, if weight of standardized portion sizes are available. However, standardized portion sizes for young children are lacking (154). Thus, estimating the iodine intake from the present FFQ using this approach, may cause additional uncertainties and is therefore not performed.

A strength to the use of a FFQ in the present cross-sectional study is the possibility to estimate consumption frequencies of usually eaten foods, and thus rank individuals according to given answers (105). The FFQ makes it possible to differentiate between individuals with a low or high intake of iodine-rich food sources. The response rate of 90% (in the FFQ) is high, knowing that participation in the study was voluntary. Study samples with response rates > 80% are considered more valuable and generally provides more reliable results than samples with lower response rates (155, 156).

The FFQ-method largely depends on the memory and perceptions of the respondents (105). Self-reported dietary data may be subject to memory lapses, misinterpretations and modifications (modifying answers according to more socially desirable responses) (157). Ideally, the food list of a FFQ should be adapted to the population being studied (105). In this thesis, the FFQ contained questions about several food items rarely consumed by preschool children (e.g. sushi, "Svolvaer/Lofotpostei" and tuna) and this may elevate the chance of misleading results due to over-reporting. Regular consumption of foods (e.g. daily) are easier to remember than foods that are rarely consumed. Thus, it is easier to overestimate intake of infrequently eaten single food items (158, 159). In addition, over-reporting is seen when the FFQ contains many detailed questions. Our results suggest some degree of over-reporting. Questions regarding intake of different dairy products showed the highest occurrence of over-reporting between the summary question and the detailed item question. The over-reporting seen in the question regarding intake of different dairy products may be related to an actual underestimation of intake in the related summary question, due to misinterpretations. The questions related to intake of dairy products contained the category “every day”, which may impose a risk of misunderstanding. It is difficult to know if parents have answered “every day” even if their child consumed dairy products more than once a day. To avoid possible misunderstandings the category should be changed to “1 time/day”. Although there is a chance of over-reporting, it is important to include detailed questions due to the large variation in iodine content of different foods.

The FFQ did not contain a question about intake of iodized salt from fortified table salts. However, iodine contribution from iodized salt is considered non-significant in Norway (74).

4.4.3 UIC measured in non-fasting, spot urine samples

UIC from spot urine samples is the recommended biomarker for assessing iodine status in a population (46), but there is ongoing debate whether this is a good estimate for measuring iodine status, especially in individuals (96). Measured 24h UIE is considered the “reference standard” for estimation of iodine intakes in individuals. However, this method is associated with high participant burden, incomplete urine collections and loss-to-follow up (92). The relatively large sample size from the current study is recognized as a study strength in the present thesis, and according to Andersen et al. (2008), a sample size of this magnitude makes it possible to estimate (with 95% confidence) the iodine status from spot urine samples within a precision range of ± 7-10% (160).

As mentioned, UIC measured from spot urine samples reflect recent iodine intake (days), and is subject to large day-to-day inter- and intra-individual variations (91). Factors known to influence UIC includes dietary intake, fluid intake, season and circadian rhythmicity (146, 161, 162). According to König et al. (2011), at least ten spot urine samples or 24h urine samples from one individual is needed to assess individual iodine status with 20% accuracy (163). Due to collection of one spot urine sample per child, iodine status in the present study is only assessed on a population level. No further assessment of individual iodine status is performed.

In the present thesis, UIC was found to be associated with intake of sweet milk and fatty fish (dinner). However, since UIC is an estimate of current dietary iodine intake, and the FFQ assesses habitual dietary intake (past three months), these dietary factors may not be the actual contributors of the measured UIC. Which dietary items that are associated with the UIC will highly depend on dietary intake prior to urine collection, especially when UIC is measured from one single spot urine sample.

Using the estimated 24h UIE for assessment of iodine status in the present study population is challenging due to lack of reference values. Currently there is no population-based reference values for the estimated 24h UIE, like those for median UIC, established by WHO/UNICEF/ICCIDD (46, 164). Due to uncertainties related to the application of the iodine/creatinine ratio and its overall minor effect on the measured iodine status in our population, in addition to the challenging interpretation of the estimated 24h UIE, the measured UIC (< 100 and ≥ 100 μg/L) was used for further statistical analyses in this thesis.

The urine samples provided for determination of iodine status in the present study were collected in the winter season. Several studies have found seasonal differences in iodine content of milk and dairy products, with highest iodine content during the winter months (13, 42, 165). Due to higher iodine content in milk and dairy products during winter, the children's UIC may have been affected, and consequently resulted in a somewhat misleading (fake high) iodine status. In Denmark, the iodine content of milk has also shown to be different according to seasons. Larsen et al. (1999) found that the iodine content of winter milk was significantly higher than milk from the summer months. The reason for this rise in iodine content is most likely related to an increased use of iodinated cow fodder in the winter season (animals graze less during winter) (166). Seasonal effects on iodine content in milk may result in over- or underestimation of the true iodine status (147).

In our study, the non-fasting spot urine samples were collected either at home or in the kindergarten. A potential weakness in the present thesis is the unknown time of urine collection. However, it is assumed that the majority of samples were taken in the morning hours before the children were delivered in the kindergartens. Several studies have examined the effect of circadian rhythmicity on UIC and UIE. Als et al. (2000) investigated the effect of spot sampling hour on UIC in children and adults. They found that UIC was significantly influenced by season and sampling hour, and not by gender and age. For children, the lowest levels of UIC were found during morning hours (8-11 h). Thereafter, the UIC increased throughout the day. In their study, UIC was affected by food intake and digestion, and consequently the UIC peaked 4-5 hours after main meals (161). In contrast, Wang et al.

(2013), found no significant association between UIC and different timed-spot urine samples. The UIC remained consistent throughout the day (167).

Due to possibly lower UIC in fasting morning urine (146), results from the present thesis may not be directly comparable to studies measuring UIC from fasting, morning urine specimens. On the other hand, collection of spot urine samples (throughout the day) have shown to be suitable for determination of UIC in cross-sectional epidemiological studies (preferably studies with large sample sizes) (96). Determining individual iodine status and intake is more complicated than for populations due to the high daily variation in iodine intakes and seasonal variations in iodine content of foods (93). Due to a possible effect of timing and seasonal variations in iodine content of different foods, the ideal way to collect urine specimens for iodine analysis could be to collect several samples from each individual throughout the year. However, this seems both time consuming, expensive and will cause high participant burden, especially when the study subjects are young children. High dropout rate is to be expected with such an approach.

Montenegro-Bethancourt et al. (2015) showed that UIC, measured in spot urine samples from children, only reflects the true 24h UIE when expressed in relation to creatinine. The study found a stronger correlation between the estimated 24h UIE and the measured 24h UIE, than between the measured UIC and the measured 24h UIE. Furthermore, UIC was found to be affected by hydration status, not only on an individual level, but also among subgroups of growing children. Therefore, using only the unadjusted UIC may potentially influence estimation of the true iodine status (97). A low UIC may represent only a nadir value for a person, and the UIC could be considerably higher on a different day due to diverse dietary intake. In addition, a high fluid intake on the day of urine collection may result in lower UIC due to diluted urine samples (92). Thus, in our study, one cannot conclude that 24% of the sample had mild iodine deficiency (median UIC = 50-99 μg/L).

The methods used for urinary iodine and creatinine analysis, were not accredited. However, these methods still strive to follow strict quality procedures developed for all laboratory methods at NIFES. The quality procedures are based on the ISO17025 standard. All analytical methods used at NIFES follow this standard, independent of accreditation (168). Reasons for not accrediting a method includes number of samples and comprehensive method evaluation prior to accreditation (requires time commitment and resources). In addition, it is expensive to maintain a method accreditation.

4.4.4 Urinary creatinine concentration

Based on the assumption that the rate of creatinine excretion is constant during 24 hours, the creatinine concentration (g/L) is used for correction of individual differences in diuresis (urine volume) (96, 97). A fluid intake above normal may subsequently lower the urinary creatinine and iodine concentrations (96). In addition, measuring the urinary creatinine concentration made it possible to estimate the 24h UIE. The creatinine analyses performed at NIFES consistently measured the reference material (controls) to be 10% above the values set by the manufacturer. However, these values were stable throughout every analytical run, and is approved by technicians for further use in the present thesis. Due to higher values for the controls, the measured values for creatinine concentration may also be slightly elevated (169).

WHO recommends exclusion of urinary creatinine concentrations < 30 mg/dL and > 300 mg/dL (136, 170). In our study, eight individuals (3.4%) had creatinine concentrations < 30 mg/dL (0.3 g/L), none had values > 300 mg/dL (3 g/L). Ideally, urine collection from these eight individuals should be repeated because of too diluted samples. It was not possible to collect new urine samples from these individuals. Therefore, in spite of the WHO guidelines, all urine samples were included in the statistical analyses.

Use of the creatinine correction method may cause further uncertainty in iodine status results. Creatinine excretion is influenced by several factors, including gender, age, exercise, muscle mass and intake of dietary proteins (171-173). Barr et al. (2005) found creatinine concentrations to be higher in morning urine samples, and that urinary creatinine excretion significantly differed throughout the day (136). Furthermore, growing children may not be in protein balance and thereby have lower creatinine excretion than do individuals with adequate protein intake. Neubert et al. (1998) showed that creatinine excretion was correlated with total protein intake in healthy children (aged 4-13 years). Creatinine excretion was lower in children with a low dietary intake of animal protein (174). In the present thesis, the expected value for daily creatinine concentration (g/day) used in the estimation of 24h UIE, was based on anthropometric-adjusted 24h urinary creatinine reference values in healthy white children (aged 3-18 years) from Germany (120). Age, race and health status resembles the current study population. However, dietary intake among German children and children from Bergen might differ, and we cannot exclude any differences in intake of animal protein. Thus, use of the creatinine references values obtained from a sample of German children may be associated with additional uncertainty.

4.5 Summary and conclusions

The present master thesis shows that the iodine status of preschool children in Bergen is adequate. However, due to the cross-sectional design of this thesis, large day-to-day variations in dietary iodine intake and urinary concentrations of iodine, along with variations in iodine content of foods, the present results may not necessarily be valid for similar populations in other parts of Norway. No major studies on iodine status have been conducted in Norwegian preschool children for decades. Thus, our results are important for describing the current iodine status of preschool children in Norway, and may be important as part of a larger national investigation of iodine status among Norwegian children. Our results suggest that iodine status among preschool children seems to be associated with intake of dairy products (sweet milk) and seafood (fatty fish). Parental socio-economic status was positively associated with intake of seafood and dairy products among the children. Thus, higher socio-economic status may be related to a higher consumption of iodine-rich food sources.

In this thesis, the reported consumption of fish and other seafood items were lower than the recommended amount of two to three servings per week for the majority of included children. However, the reported intake of dairy products were high. Despite the findings of adequate iodine status in the present study population, it seems advisable to increase the overall consumption of seafood among Norwegian preschool children, due to seafood being an important source of other nutrients such as essential fatty acids and vitamin D (145).

4.6 Future perspectives

The adequate iodine status found among Norwegian preschool children does not warrant any immediate actions. However, due to variations in dietary iodine intakes and UIC, the current results should be interpreted with caution. In order to ensure and secure adequate iodine status in the general population and in vulnerable subgroups, regular monitoring of population-based studies are required. Performing studies on dietary iodine intake along with assessment of iodine status is necessary in future public surveillance of iodine nutrition in the Norwegian population. In addition, monitoring the iodine content of different foods will make it easier to account for the large variations seen in UIC, and help with determining the iodine intake in a population and among individuals. Regularly performing population-based studies on iodine status is also important due to the timed occurrence of changes in dietary patterns among different populations (133).

Even though the iodine status is adequate in this thesis, and in the Norwegian population, studies suggest that specific subgroups may have increased risk of inadequate iodine intakes (12, 13). New public actions are now being discussed in the Norwegian Nutrition Council to secure the iodine intake, and a national iodine report will be published in 2016.

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6. APPENDIX I – Questionnaire

FINS_WP5_Barnehagestudien

Q1 Spørreskjema om livsstil og hva barnet spiser. Ha de 3 siste månedene i bakhodet når du fyller ut skjemaet. Vi er klar over at kostholdet varierer fra dag til dag. Prøv likevel så godt du kan å gi et "gjennomsnitt" av barnets inntak. Ta IKKE med måltidene barnet har fått i barnehagen i forbindelse med dette prosjektet («Barnehagestudien»). Du skal bare sette ETT kryss på hvert spørsmål med mindre noe annet er spesifisert, og krysset skal være inne i en boks, ikke mellom boksene.

Q3 1. Hvor ofte har barnet spist fisk, fiskeprodukter eller annen sjømat som middagsmat siste 3 måneder?

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

Q5 2. Hvor ofte har barnet spist følgende sjømat som middag siste 3 måneder?

	Aldri (1)	Sjeldnere enn 1 gang/måned (2)	1-3 ganger/ måned (3)	1 gang/uke (4)	2-3 ganger/ uke (5)	4 ganger eller mer/uke (6)
Laks, ørret (1)	❍	❍	❍	❍	❍	❍
Makrell (2)	❍	❍	❍	❍	❍	❍
Sild (3)	❍	❍	❍	❍	❍	❍
Kveite (4)	❍	❍	❍	❍	❍	❍
Torsk (5)	❍	❍	❍	❍	❍	❍
Sei (6)	❍	❍	❍	❍	❍	❍
Annen mager fisk (Lyr, hyse, rødspette) (7)	❍	❍	❍	❍	❍	❍
Sushi (8)	❍	❍	❍	❍	❍	❍
Skalldyrmiddag (reker, krabbe, blåskjell) (9)	❍	❍	❍	❍	❍	❍
Fiskekaker (10)	❍	❍	❍	❍	❍	❍
Fiskepinner (11)	❍	❍	❍	❍	❍	❍
Andre fiskeprodukter (fiskegrateng, fiskeboller) (12)	❍	❍	❍	❍	❍	❍

Q4 3. Hvor ofte har barnet spist sjømat som pålegg, i salat, mellommåltid, snacks eller lignende de siste 3 måneder?

❍ Aldri (1)
❍ Sjeldent (2)
❍ 1-3 ganger/ måned (3)
❍ 1 gang/uke (4)
❍ 2 ganger/uke (5)
❍ 3-5 ganger/ uke (6)
❍ Mer enn 5 ganger/uke (7)

Q6 4. Hvor ofte har barnet spist følgende sjømat som pålegg, i salat, mellommåltid, snacks eller lignende de siste 3 måneder?

	Aldri (1)	Sjeldent (2)	1-3 ganger/ måned (3)	1 gang/uke (4)	2 ganger/uke (5)	3-5 ganger/ uke (6)	Mer enn 5 ganger/uke (7)
Makrell i tomat (1)	❍	❍	❍	❍	❍	❍	❍
Sardiner eller sild på boks (2)	❍	❍	❍	❍	❍	❍	❍
Annen fet fisk som pålegg (peppermakrell, røkt/gravet laks/ørret) (3)	❍	❍	❍	❍	❍	❍	❍
Tunfisk (4)	❍	❍	❍	❍	❍	❍	❍
Kaviar (5)	❍	❍	❍	❍	❍	❍	❍
Svolværpostei/ Lofotpostei (6)	❍	❍	❍	❍	❍	❍	❍

Q7 5. Hvilken brødtype spiser barnet vanligvis?

❍ Fint (0 -25% sammalt/hele korn) (1)
❍ Halvgrovt (25-50% sammalt/hele korn) (2)
❍ Grovt (50-75% sammalt /hele korn) (3)
❍ Ekstra grovt (75-100% sammalt/hele korn) (4)

Q8 6. Bruker barnet smør eller margarin på brødskiven/knekkebrød/rundstykke?

❍ Ja (1)
❍ Nei (2)

Q9 7. Spiser barnet meieriprodukter (melk, yoghurt, ost)?

❍ Sjelden/aldri (1)
❍ 1-3 ganger/uke (2)
❍ 4-6 ganger/uke (3)
❍ Hver dag (4)
❍ 2 ganger/dag (5)
❍ 3-4 ganger eller mer/dag (6)

Q10 Hvis ja, hvor mange ganger per uke eller dag spiser/drikker barnet følgende meieriprodukter?

	Sjelden/aldri (1)	1-3 ganger/uke (2)	4-6 ganger/uke (3)	Hver dag (4)	2 ganger/dag (5)	3-4 ganger eller mer/dag (6)
Helmelk (1)	❍	❍	❍	❍	❍	❍
Lettmelk (2)	❍	❍	❍	❍	❍	❍
Ekstra lett melk (3)	❍	❍	❍	❍	❍	❍
Skummet melk (4)	❍	❍	❍	❍	❍	❍
Sjokolademelk (5)	❍	❍	❍	❍	❍	❍
Drikkeyoghurt (6)	❍	❍	❍	❍	❍	❍
Biola (7)	❍	❍	❍	❍	❍	❍
Cultura (8)	❍	❍	❍	❍	❍	❍
Yoghurt (9)	❍	❍	❍	❍	❍	❍
Hvitost (Norvegia, Jarlsberg, smøreoster) (10)	❍	❍	❍	❍	❍	❍
Brunost (11)	❍	❍	❍	❍	❍	❍

Q11 8. Hvor ofte har barnet spist retter med rødt kjøtt (pølser, kjøttdeig, biff, koteletter fra svin, storfe, vilt og lam) som middagsmat siste 3 måneder?

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

Q12 9. Hvor ofte har barnet spist retter med kylling som middagsmat siste 3 måneder?

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

Q13 10. Hvor mange egg spiser barnet per uke (stekt, kokt, eggerøre, omelett)?

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

Q14 11. Hvor mange porsjoner grønnsaker eller frukt/bær spiser barnet i løpet av dagen? (En porsjon kan for eksempel være 1 middels stor frukt (eple, pære, banan eller annet), eller en håndfull druer, eller ett glass juice. En porsjon grønnsaker kan for eksempel være 1 gulrot eller 3 buketter brokkoli eller en porsjonsbolle med salat. Poteter regnes ikke med)

	Aldri/ sjelden (1)	1-3 porsjoner/ uke (2)	4-6 porsjoner/u ke (3)	1 porsjoner/d ag (4)	2 porsjoner/d ag (5)	3 porsjoner/ dag (6)	4 porsjoner eller mer/dag (7)
Frukt og bær (ikke juice og smoothie) (1)	❍	❍	❍	❍	❍	❍	❍
Grønnsaker (2)	❍	❍	❍	❍	❍	❍	❍
Juice (eks. eple, appelsin) (3)	❍	❍	❍	❍	❍	❍	❍
Smoothie (4)	❍	❍	❍	❍	❍	❍	❍

Q15 12. Har barnet tatt tran, fiskeolje- eller omega-3 tilskudd (flytende eller kapsler) de siste 3 måneder?

- ❍ Ja (1)
- ❍ Nei (2)

Q16 Hvis ja på spørsmål 12, hvilke type tran, fiskeolje- eller omega-3 tilskudd bruker barnet og hvor ofte?

	1-3 ganger/måned (1)	1-3 ganger/uke (2)	4-6 ganger/uke (3)	Daglig (4)	Aldri (5)
Tran/Fiskeoljer, flytende (1)	❍	❍	❍	❍	❍
Tran/ Fiskeoljer, kapsler (2)	❍	❍	❍	❍	❍

Q18 Spesifiser hvilke(t) merke på tran, fiskeolje- eller omega-3 tilskudd og hvor mye barnet tar hver gang:

Q19 13. Bruker barnet annet kosttilskudd (vitaminer og mineraler)?

- ❍ Ja (1)
- ❍ Nei (2)

If Nei Is Selected, Then Skip To 14. Hvor mange uker de siste 3 måneder...

Q20 Hvis ja på spørsmål 13, hvilke type kosttilskudd bruker barnet og hvor ofte?

	1-3 ganger/måned (1)	1-3 ganger/uke (2)	4-6 ganger/uke (3)	Daglig (4)	Aldri (5)
Multivitamin (sanasol, vitaminbjørner, biovit, tabletter) (1)	❍	❍	❍	❍	❍
Multimineral (2)	❍	❍	❍	❍	❍
Vitamin D (3)	❍	❍	❍	❍	❍
Jern (4)	❍	❍	❍	❍	❍
Annet (5)	❍	❍	❍	❍	❍

Q21 Spesifiser hvilke(t) merke på kosttilskudd og hvor mye barnet tar hver gang:

Q22 14. Hvor mange uker de siste 3 månedene har barnet vært i Syden?

- ❍ Har ikke vært i Syden (1)
- ❍ 1 uke (2)
- ❍ 2 uker (3)
- ❍ 3 uker (4)
- ❍ 4 uker eller mer (5)

Q23 15. Hvor mange timer er barnet fysisk aktiv totalt i løpet av en uke (rask gange, løping, ballsport, kampsport og lignende)?

- ❍ En halv time eller mindre/uken (1)
- ❍ 1 time/uken (2)
- ❍ 2 timer /uken (3)
- ❍ 3 timer/uken eller mer (4)
- ❍ 4 timer/uken eller mer (5)

Q24 16. Hvor stor vekt legger du på at barnet skal ha et sunt kosthold?

- ❍ Veldig liten (1)
- ❍ Liten (2)
- ❍ Middels (3)
- ❍ Stor (4)
- ❍ Veldig stor (5)

Q25 17. Spiser barnet frokost (enten hjemme eller i barnehagen)?

- ❍ Aldri (1)
- ❍ 1-2 ganger/uke (2)
- ❍ 3-4 gang/uke (3)
- ❍ 5-6 ganger/uke (4)
- ❍ hver dag (5)

Q26 18. Hvor ofte spiser barnet lunsj (enten hjemme eller i barnehagen)?

- ❍ Aldri (1)
- ❍ 1-2 ganger/uke (2)
- ❍ 3-4 gang/uke (3)
- ❍ 5-6 ganger/uke (4)
- ❍ hver dag (5)

Q27 19. Hvor ofte spiser barnet sjokolade, kaker, kjeks, snop eller lignende i barnehagen?

- ❍ Aldri (1)
- ❍ 1-2 ganger/uke (2)
- ❍ 3-4 gang/uke (3)
- ❍ hver dag (4)

Q28 20. Hvor ofte spiser barnet sjokolade, kaker, kjeks, snop eller lignende på fritiden?

- ❍ Aldri (1)
- ❍ 1-2 ganger/uke (2)
- ❍ 3-4 gang/uke (3)
- ❍ 5-6 ganger/uke (4)
- ❍ hver dag (5)

Q30 21. Hvor ofte drikker barnet følgende drikker?

	Aldri/sjelden (1)	1-3 ganger/uke (2)	4-6 ganger/uke (3)	Hver dag (4)	2 ganger/dag (5)	3-4 ganger/dag (6)	5 ganger eller mer/dag (7)
Brus/ is-te (med sukker) (1)	❍	❍	❍	❍	❍	❍	❍
Sukkerfri/ lettbrus (2)	❍	❍	❍	❍	❍	❍	❍
Vann (3)	❍	❍	❍	❍	❍	❍	❍

Q31 22. Er barnet jente eller gutt?

❍ Jente (1)
❍ Gutt (2)

Q72 Fødselsmåned

❍ Januar (1)
❍ Februar (2)
❍ Mars (3)
❍ April (4)
❍ Mai (5)
❍ Juni (6)
❍ Juli (7)
❍ August (8)
❍ September (9)
❍ Oktober (10)
❍ November (11)
❍ Desember (12)

Q73 Fødselsår

❍ 2014 (1)
❍ 2013 (2)
❍ 2012 (3)
❍ 2011 (4)
❍ 2010 (5)
❍ 2009 (6)
❍ 2008 (7)

Q72 Høyde i cm:

Q73 Vekt i kg:

Q34 Utfylt av

- ❍ Mor (1)
- ❍ Far (2)
- ❍ Annen, spesifiser (3) ____________________

Q37 I hvilket land er du/dere født?

	Norge (1)	Afghanistan (2)	Albania (3)	Algerie (4)	Andorra (5)	Angola (6)	Antigua og Barbuda (7)	Argentina (8)	Armenia (9)	Aserbajdsjan (10)	Australia (11)	Bahamas (12)	Bahrain (13)	Bangladesh (14)	Barbados (15)
Mor (1)	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
Far (2)	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
Barn (3)	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍

Belgia (16)	Belize (17)	Benin (18)	Bhutan (19)	Bolivia (20)	Bosnia-Hercegovina (21)	Botswana (22)	Brasil (23)	Brunei (24)	Bulgaria (25)	Burkina Faso (26)	Burundi (27)	Canada (28)	Chile (29)	Colombia (30)
❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍

Cookøyene (31)	Costa Rica (32)	Cuba (33)	Danmark (34)	Den dominikanske republikk (35)	Den sentralafrikanske republikk (36)	Djibouti (37)	Dominica (38)	Ecuador (39)	Egypt (40)	Ekvatorial-Guinea (41)	El Salvador (42)	Elfenbenskysten (43)	Eritrea (44)	Estland (45)
❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍

Etiopia (46)	Fiji (47)	Filippinene (48)	Finland (49)	Forente arabiske emirater (50)	Frankrike (51)	Gabon (52)	Gambia (53)	Georgia (54)	Ghana (55)	Grenada (56)	Guatemala (57)	Guinea (58)	Guinea-Bissau (59)	Guyana (60)
❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍	❍ ❍ ❍

Haiti (61)	Hellas (62)
❍ ❍ ❍	❍ ❍ ❍

Q40 Hva er den høyeste utdanningen dere har fullført?

	Grunnskole, ungdomsskole eller lign. (2)	Videregående skole med yrkesfag, yrkesskole, realskole (3)	Videregående skole med allmennfag, gymnas/artium (4)	Høyskole eller universitet, mindre enn 4 år (5)	Høyskole eller universitet, 4 år eller mer (6)
Mor (1)	❍	❍	❍	❍	❍
Far (2)	❍	❍	❍	❍	❍

Q42 Hva er deres hovedbeskjeftigelse for tiden?

	Heltidsarbeid (80-100%) (2)	Deltidsarbeid (50-79%) (3)	Deltidsarbeid (mindre enn 50%) (4)	Trygdet / attføring / arbeidsa-vklarings-penger (5)	Hjemme-værende (6)	Arbeids-søkende (7)	Under utdanning (8)
Mor (1)	❍	❍	❍	❍	❍	❍	❍
Far (2)	❍	❍	❍	❍	❍	❍	❍

Q47 Hva var den samlede inntekten i husholdningen sist år?(samlet brutto årsinntekt inkludert overføringer og bidrag før skatt og fradrag er trukket fra)

❍ Under 200 000 (1)
❍ 200 - 349 999 (2)
❍ 350 - 549 999 (3)
❍ 550 - 749 999 (4)
❍ 750 - 999 999 (5)
❍ 1 000 000 -1 250 000 (6)
❍ 1 250 000 - 2 000 000 (7)
❍ Mer enn 2 000 000 (8)

Q66 Hvor mange personer bor i husholdningen hjemme hos dere?

	1 (1)	2 (2)	3 (3)	4 (4)	5 (5)	6 (6)	7 (7)	8 (8)	9 (9)	10 (10)	11 (11)	12 (12)	13 (13)	14 (14)	15 (15)	mer enn 15 (16)
Voksne (1)	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
Barn (2)	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍

Q46 Hvordan vil du beskrive familiens økonomi?

- Svært god (1)
- God (2)
- Middels (3)
- Dårlig (4)
- Svært dårlig (5)

Q80 Søvn - Her er noen spørsmål om barnets søvn. Svar for hvordan det har vært på hverdagene de siste to ukene.

Q49 Når legger hun/han seg vanligvis?

Q51 Hverdager

- 18:00 (2)
- 18:15 (3)
- 18:30 (4)
- 18:45 (5)
- 19:00 (6)
- 19:15 (7)
- 19:30 (8)
- 19:45 (9)
- 20:00 (10)
- 20:15 (11)
- 20:30 (12)
- 20:45 (13)
- 21:00 (14)
- 21:15 (15)
- 21:30 (16)
- 21:45 (17)
- 22:00 (18)
- 22:15 (19)
- 22:30 (20)
- 22:45 (21)
- 23:00 (22)
- 23:15 (23)
- 23:30 (24)
- 23:45 (25)
- 00:00 (26)

Q55 Når står han/hun vanligvis opp?

Q72 Hverdager

- 04:00 (1)
- 04:15 (2)
- 04:30 (3)
- 04:45 (4)
- 05:00 (5)
- 05:15 (6)
- 05:30 (7)
- 05:45 (8)
- 06:00 (9)
- 06:15 (10)
- 06:30 (11)
- 06:45 (12)
- 07:00 (13)
- 07:15 (14)
- 07:30 (15)
- 07:45 (16)
- 08:00 (17)
- 08:15 (18)
- 08:30 (19)
- 08:45 (20)
- 09:00 (21)
- 09:15 (22)
- 09:30 (23)
- 09:45 (24)
- 10:00 (25)
- 10:15 (26)
- 10:30 (27)
- 10:45 (28)
- 11:00 (29)
- 11:15 (30)
- 11:30 (31)
- 11:45 (32)
- 12:00 (33)

Q68 Hvor lang tid tar det vanligvis fra barnet legger seg til det sovner om kvelden:

- ❍ 15 min (1)
- ❍ 30 min (2)
- ❍ 45 min (3)
- ❍ 1 time (4)
- ❍ 1 time og 15 min (5)
- ❍ 1 time og 30 min (6)
- ❍ 1 timer og 45 min (7)
- ❍ 2 timer (8)
- ❍ 2 timer og 15 min (9)
- ❍ 2 timer og 30 min (10)
- ❍ 2 timer og 45 min (11)
- ❍ 3 timer (12)
- ❍ 3 timer og 15 min (13)
- ❍ 3 timer og 30 min (14)
- ❍ 3 timer og 45 min (15)
- ❍ 4 timer (16)
- ❍ 4 timer og 15 min (17)
- ❍ 4 timer og 30 min (18)
- ❍ 4 t imerog 45 min (19)
- ❍ 5 timer (20)
- ❍ 5 timer og 15 min (21)
- ❍ 5 timer og 30 min (22)
- ❍ 5 timer og 45 min (23)
- ❍ 6 timer (24)
- ❍ 0 timer (25)

Q74 Hvor lenge er barnet vanligvis våkent om natten (etter at det først har sovnet)?

- 15 min (1)
- 30 min (2)
- 45 min (3)
- 1 time (4)
- 1 time og 15 min (5)
- 1 time og 30 min (6)
- 1 timer og 45 min (7)
- 2 timer (8)
- 2 timer og 15 min (9)
- 2 timer og 30 min (10)
- 2 timer og 45 min (11)
- 3 timer (12)
- 3 timer og 15 min (13)
- 3 timer og 30 min (14)
- 3 timer og 45 min (15)
- 4 timer (16)
- 4 timer og 15 min (17)
- 4 timer og 30 min (18)
- 4 t imerog 45 min (19)
- 5 timer (20)
- 5 timer og 15 min (21)
- 5 timer og 30 min (22)
- 5 timer og 45 min (23)
- 6 timer (24)
- 0 timer (25)

Q60 Synes du barnet ditt for nok søvn?

- Ikke nok (1)
- Litt lite (2)
- Passe (3)
- Litt mye (4)
- For mye (5)

Q63 Har barnet en kronisk sykdom eller funksjonshemming?

- Ja (1)
- Nei (2)

Q61 Har barnet en kronisk sykdom eller funksjonshemming? Hvis ja, kryss av for:

- ❑ Epilepsi (1)
- ❑ Diabetes (2)
- ❑ Astma (3)
- ❑ Annet (hva?) (4) ____________________

Q82 Bruker din datter/sønn medisin jevnlig?

- ❍ Ja (1)
- ❍ Nei (2)

Q86 Hvis ja: Skriv ned hva den/de heter (evt hva du bruker den for), dosering og kryss av for hvor ofte.

	Dosering	Hyppighet				
	Av medisin (1)	Ukentlig (1)	Daglig (2)	Daglig x2, eller mer (3)	Sjeldent (4)	Sesong (5)
Navn på medisin (1)		❍	❍	❍	❍	❍
Navn på medisin (2)		❍	❍	❍	❍	❍
Navn på medisin (3)		❍	❍	❍	❍	❍

Q61 Har din datter/sønn fått en diagnose for psykiske vansker? (feks. ADHD, angst, autisme)

- ❍ Ja (1)
- ❍ Nei (2)

Q63 Hvis ja: Skriv inn hvilken diagnose og om den gjelder nå eller tidligere:

Q60 Sterke og svake sider (SDQ-NOR)

Q62 Vennligst kryss av for hvert utsagn: Stemmer ikke, Stemmer delvis eller Stemmer helt. Prøv å svare på alt selv om du ikke er helt sikker eller synes utsagnet virker rart. Svar på grunnlag av barnets oppførsel de siste 6 månedene.

	Stemmer ikke (0)	Stemmer delvis (1)	Stemmer helt (2)
Omtenksom, tar hensyn til andre menneskers følelser (1)	❍	❍	❍
Rastløs, overaktiv, kan ikke være lenge i ro (2)	❍	❍	❍
Klager ofte over hodepine, vondt i magen eller kvalme (3)	❍	❍	❍
Deler gjerne med andre barn (godter, leker, andre ting) (4)	❍	❍	❍
Har ofte raserianfall eller dårlig humør (5)	❍	❍	❍
Ganske ensom, leker ofte alene (6)	❍	❍	❍
Som regel lydig, gjør vanligvis det voksne ber om (7)	❍	❍	❍
Mange bekymringer, virker ofte bekymret (8)	❍	❍	❍
Hjelpsom hvis noen er såret, lei seg eller føler seg dårlig (9)	❍	❍	❍
Stadig urolig eller i bevegelse (10)	❍	❍	❍
Har minst en god venn (11)	❍	❍	❍
Slåss ofte med andre barn eller mobber dem (12)	❍	❍	❍
Ofte lei seg, nedfor eller på gråten (13)	❍	❍	❍
Vanligvis likt av andre barn (14)	❍	❍	❍
Lett avledet, mister lett konsentrasjonen (15)	❍	❍	❍
Nervøs eller klengete i nye situasjoner, lett utrygg (16)	❍	❍	❍
Snill mot yngre barn (17)	❍	❍	❍
Lyver eller jukser ofte (18)	❍	❍	❍
Plaget eller mobbet av andre barn (19)	❍	❍	❍
Tilbyr seg ofte å hjelpe andre (foreldre, lærere, andre barn) (20)	❍	❍	❍

Tenker seg om før hun / han handler (gjør noe) (21)	❍	❍	❍
Stjeler hjemme, på skolen eller andre steder (22)	❍	❍	❍
Kommer bedre overens med voksne enn med barn (23)	❍	❍	❍
Redd for mye, lett skremt (24)	❍	❍	❍
Fullfører oppgaver, god konsentrasjonsevne (25)	❍	❍	❍

Q66 Samlet, synes du at barnet ditt har vansker på ett eller flere av følgende områder: med følelser, konsentrasjon, oppførsel eller med å komme overens med andre mennesker?

❍ Nei (1)
❍ Ja, små vansker (2)
❍ Ja, tydelige vansker (3)
❍ Ja, alvorlige vansker (4)

Q68 Hvis du har svart: Ja, vennligst svar på følgende spørsmål: Hvor lenge har disse vanskene vært tilstede?

❍ Mindre enn en måned (1)
❍ 1 - 5 måneder (2)
❍ 6 - 12 måneder (3)
❍ Mer enn ett år (4)

Q70 Blir barnet selv forstyrret eller plaget av vanskene?

❍ Ikke i det hele tatt (1)
❍ Bare litt (2)
❍ En god del (3)
❍ Mye (4)

Q72 Påvirker vanskene barnets dagligliv på noen av de følgende områdene?

	Ikke i det hele tatt (1)	Bare litt (2)	En god del (3)	Mye (4)
Hjemme/ I familien (1)	❍	❍	❍	❍
Forhold til venner (2)	❍	❍	❍	❍
Læring på skolen (3)	❍	❍	❍	❍
Fritidsaktiviteter (4)	❍	❍	❍	❍

Q74 Er vanskene en belastning for deg eller familien som helhet?

- ❍ Ikke i det hele tatt (1)
- ❍ Bare litt (2)
- ❍ En god del (3)
- ❍ Mye (4)