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VITAMIN D SECURITY IN NORTHERN NORWAY IN RELATION TO MARINE FOOD TRADITIONS

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Ja, før Gud sin ære skal forlise,
før skal hav og grummen hval ham prise,
samt og tanteien som løper leien,
stenbit og seien
og torsk og skreien
og nise.

Petter Dass (1698)

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Tromsø, November 2003
Magritt Brustad

List of papers

1. Brustad M, Sandanger T, Wilsgaard T, Aksnes L, and Lund E. Change in plasma levels of vitamin D after consumption of cod liver and fresh cod-liver oil as part of the traditional north Norwegian fish dish "Mølje". *Int. J. Circumpolar Health* 2003; 62:40-53.

2. Brustad M, Braaten T, and Lund E. Predictors for cod-liver oil supplement use – the Norwegian Women and Cancer Study. *Eur. J. Clin. Nutr.* 2004;58(1):128-36.

3. Brustad M, Alsaker E, Engelsen O, Aksnes L, and Lund E. Vitamin D status of middle-aged women at 65-71 degrees north in relation to dietary intake and exposure to ultraviolet radiation. *Public Health Nutrition.* (In press)

4. Brustad M, Sandanger T, Aksnes L, and Lund E. Vitamin D status in a rural population of northern Norway with high fish-liver consumption. *Public Health Nutrition.* (In press)

Introduction

Vitamin D, or the fourth vitamin was first identified by McCollum et al in 1922 (McCollum *et al.* 1922) as a factor present in cod-liver oil that could prevent the onset of rickets. In the 1920s, several animal and clinical studies were published that proposed that rickets could be cured not only by substances in cod-liver oil but also sunlight exposure (Hess *et al.* 1921; Hess & Unger 1921; Powers *et al.* 1921). The work by Steenbock and Black (1924) on the anti-rickets properties of foods and other substances exposed to ultraviolet (UV) radiation, led Steenbock to patent the use of food items fortified with UV-exposed provitamin D_2. Vitamin D fortification in the 1930s eradicated rickets as a severe health problem in North America and Europe. In Norway, margarine has been fortified with vitamin D since 1950, and butter and milk since 1990 and 2000 respectively.

The awarded paper by Johan Kloster "*The distribution and frequency of rickets in one of the fishery districts of Finnmark and relation of diet and the disorder*" (Kloster 1931) was based on field work conducted in Finnmark in northern Norway (70 ^{0}N) during 1928-1929. Kloster revealed a high prevalence of rickets; up to 60-70 % in some of the investigated communities. The prevalence was strongly related to season; it was highest in April and lowest in the summer months. When looking at dietary habits in relation to rickets, Kloster found that "*generous quantities of fish liver are invariable consumed along with fresh fish*" and "*liver and liver oil are the most important vitamin D source*". Thus, the prevalence of rickets depended inversely on the access to fresh fish and fish liver. He observed that rickets was more common in places without an appropriate marine harbor and where the open sea made fishing extremely difficult during the winter months due to strong winds. Rickets was less common in the innermost parts of the fjords, where the sea was much smoother, and fishing could be carried on every day of the year. Kloster stated that in these places "*every single family has a plentiful supply of fresh fish at all the times of the year*".

Other northern Norwegian dietary surveys or reports in the 1960s have also indicated that cod-liver and cod-liver oil or "mølje", which is the local Norwegian name for this combined dish, were consumed frequently especially in the coastal population (Bække *et al.* 1968). For the period 1869 –1975, the efforts by Professor Anders Forsdahl at the Institute of Community Medicine, University of Tromsø have made available the annual regional public health reports for Finnmark, the most eastern county in northern Norway (Forsdahl, 1992). These reports included information on nutrition and food access, and confirm that cod-liver and cod-liver oil were consumed in high amounts and constituted an important part of the northern diet.

Sources of vitamin D and ultraviolet radiation in northern Norway.

A limited number of food items contain vitamin D. The sources are, according to national dietary surveys (Johansson & Solvoll, 1999), fatty fish, cod-liver oil, and fortified butter and margarine. Ultraviolet light (UV-light) has long been recognized as the principal source of vitamin D for humans (Webb & Holick, 1988). Dramatic influences of seasonal and latitudinal changes of solar UV-B radiation on vitamin D synthesis in skin have been found. It has been suggested that below a certain threshold of UV-radiation (which is described in more detail in Paper 3) no photoconversion of provitamin D to previtamin D occurs in human skin (Webb *et al.,* 1988). Northern Norway is situated at 65-71 ^{0}N, which means that its population lives at some of the northernmost geographical locations of significant human settlement. Due to the warmth of the Gulf Stream the temperatures are comparable with the rest of northern Europe, but the high latitude strongly affects the amount and intensity of UV-exposure available. Figure 1 demonstrates the hours per day with UV-radiation above the stated threshold needed for vitamin D production in skin, based on local measurements conducted by Norwegian Institute for Air Research (NILU) of UV-radiation through one year at different

Norwegian latitudes. The right bar explains the colour codes given in hours per day of UV-radiation adequate for cutaneous vitamin D production (UV-hours). The length of the "vitamin D winter", is denoted by the black area in the figure, which increases with higher latitude.

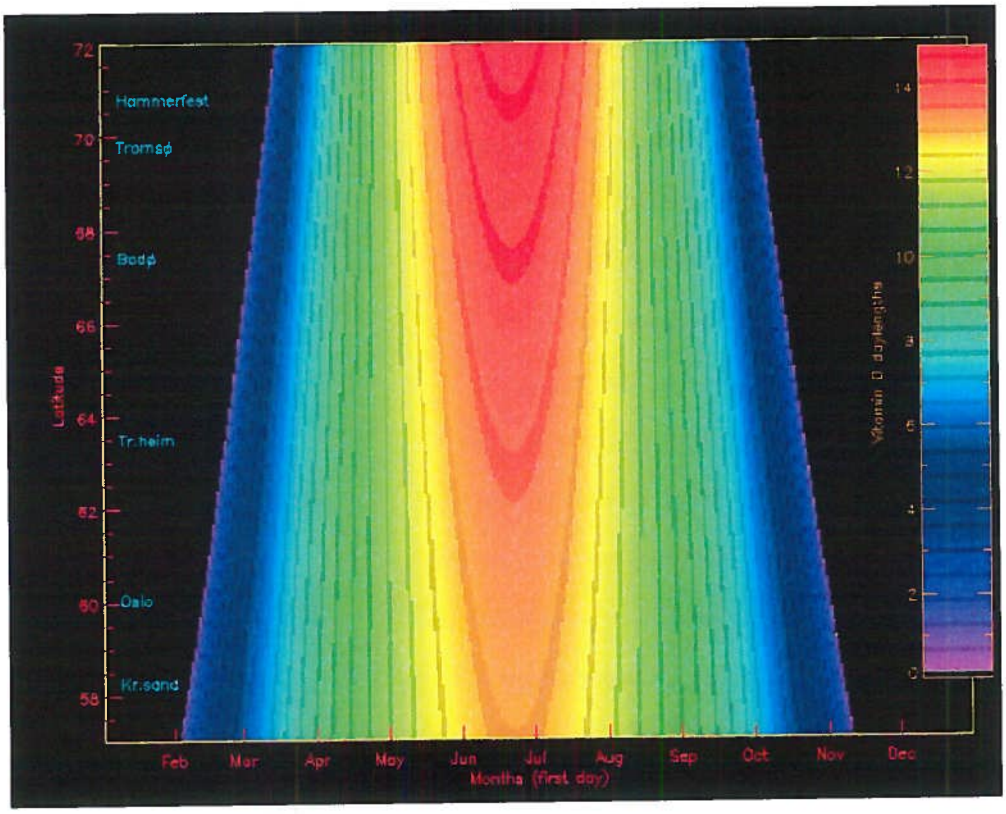

Figure 1. Hours per day with UV-radiation that gives vitamin D production in skin by latitude and month. (Clouds, altitude, and snow which impact UV-radiation available are not accounted for in the estimation)

Vitamin D metabolism

Vitamin D synthesis in skin consists of two basic stages (Holick 1994). In the first stage, initial provitamin D (7-dehydrocholesterol, 7-DHC) is converted photochemically to previtamin D by radiation of wavelengths 290-315 nanometers (Figure 2). At the second stage, the latter undergoes heat-induced isomerization to vitamin D (cholecalciferol), which is specifically translocated by the vitamin-D-binding protein into the circulation. Cholecalciferol does not have significant biological activity and is transformed to its active form in two steps. First it undergoes hydroxylation in the liver to 25-hydroxy vitamin D [25(OH)D]. Second, in the kidney 25(OH)D serves as a substrate for 1-alpha-hydroxylase, yielding 1,25-dihydroxycholecalciferol which is the biological active vitamin D metabolite. The major inducer of 1-alpha-hydroxylase is parathyroid hormone (PTH) whose concentration in blood is elevated upon reduced calcium concentrations. Since hepatic synthesis of 25(OH)D is loosely regulated, circulating 25(OH)D is considered to be the most sensitive clinical marker for determining nutritional vitamin D status (Hollis, 1996). A 25(OH)D concentration of ≤ 37.5 nmol/l in blood has been used as an indicator for moderate hypovitaminosis D (Thomas *et al.* 1998), and 25(OH)D > 50 nmol/l

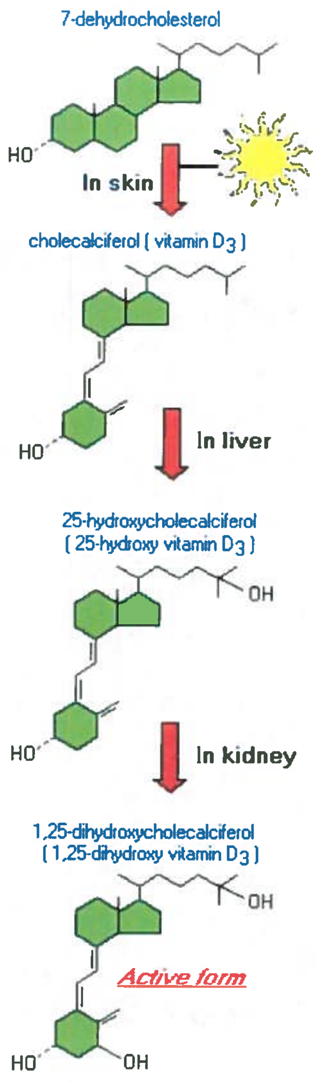

Figure 2. Vitamin D metabolism

has been suggested as the recommended level (Malabanan *et al.* 1998;Schmidt-Gayk *et al.* 1997).

Vitamin D and health

Until the late 1970s, it was believed that 1,25$(OH)_2D$ biological function was only related to calcium and phosphate regulation by activating calcium absorption in the intestine and release from bone. Studies have however, suggested that vitamin D additionally plays a role in the regulation of cellular metabolism at multiple levels (Rucker & Stites, 1994). In 1979 Strumpf and colleagues published work that suggested that many other tissues in the body had the ability to recognize 1,25$(OH)_2D$ (Stumpf *et al.,* 1979). Today it is well known that 1,25$(OH)_2D$ receptors (VDR) are present not only in the intestine and bone, but in a wide variety of other tissues e.g. the brain, heart, stomach, pancreas, gonads, skin, and activated T and B lymphocytes (Holick, 2003). In addition, it is now recognized that many tissues in the body including prostate, breast, colon, skin, and osteoblasts have the capacity to synthesize the active vitamin D metabolite 1,25$(OH)_2D$ locally (Schwartz *et al.,* 1998; Cross *et al.,* 2001; Tangpricha *et al,*. 2001) (Figure 3). The immune modulator properties of 1,25$(OH)_2D$ (Manolagas *et al.,* 1985) have lead to the hypothesis of an effect of vitamin D on autoimmune diseases like type 1 diabetes (Hypponen *et al,*. 2001), psoriasis (Pinette *et al,* 2003), and arthritis (Cantorna *et al.,* 1998).

A protective effect of vitamin D on colon, prostate, and breast cancers has been suggested based on both epidemiological (Garland *et al.,* 1989; Grant, 2002b; Grant, 2002a; John *et al.,* 1999) and experimental studies (Banwell *et al.,* 2003). It has been proposed that local production of the active vitamin D form may be for the purpose of cell growth regulation (Figure 3), which can decrease risk of cancers in these organs (Holick, 2003).

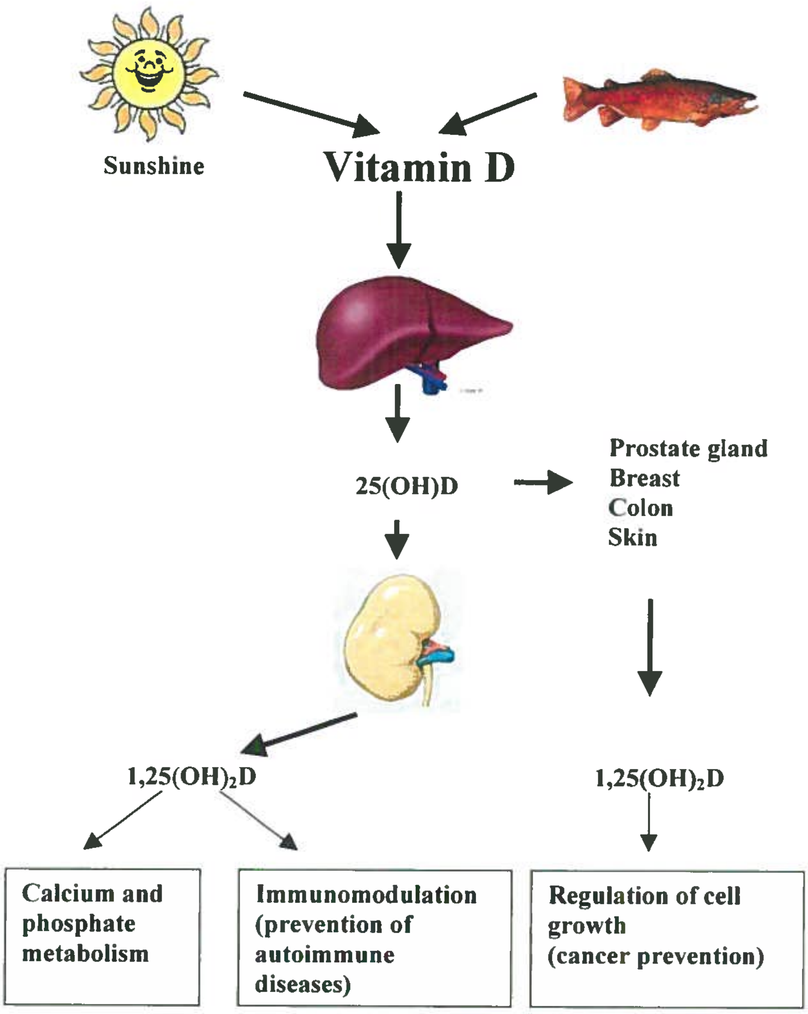

Figure 3. Sources of vitamin D and known and proposed biological functions

Food security has been defined by Oshaug (1994) and is expressed in terms of both *adequacy* and *stability* of the food supply and access (Figure 4). The major components of 'food adequacy' are *local adequacy, food safety and quality*, and *cultural acceptability*. Further the 'food stability' rests upon both *social* and *environmental sustainability*.

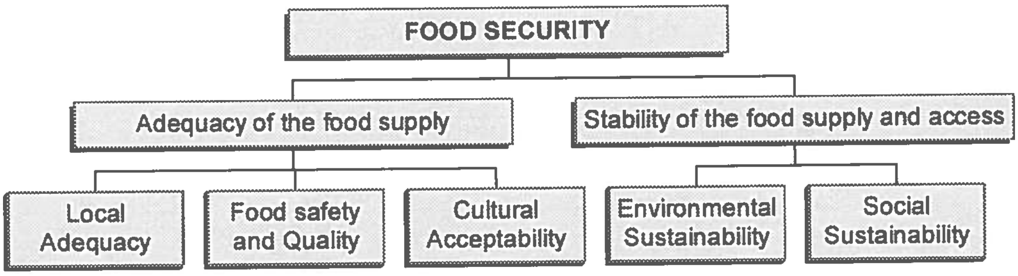

Figure 4. A definition of Food Security. Adapted from Oshaug (1994)

Due to its nature, it is likely that both the adequacy and sustainability of the vitamin D supply in northern Norway are affected by geographical location, climate and marine dietary tradition. Published studies focusing on vitamin D security in northern Norway are scarce. Based on data from The Tromsø Study, estimates of daily vitamin D intake or 25(OH)D levels in blood have been reported (Jorde *et al.*,2000; Jorde & Bønaa, 2000; Linden, 1975; Vik *et al.*, 1979). However, none of these studies have included data on sun-exposure. A recent study from Finnmark, found self-reported mean vitamin D intake below the recommended levels among both costal and inland teenagers. Around 90 % of the participants answered that they seldom or never ate fish (Brox *et al.* 2003). Only two studies conducted in northern Norway have examined determinants of vitamin D status measured as 25(OH)D, and they were both based on small sample sizes. Vik *et al.* (1980) assessed 25(OH)D levels in 17 employees at the Tromsø University Hospital from September 1977 to September 1978. Further, Markestad *et al.* (1984) investigated longitudinally the impact of breast milk on serum concentrations of vitamin D metabolites in seven infants living at 70 ^{0}N north and found that that all but one of the infants had 25(OH)D levels in the rachitic range (<20nmol/l). The purpose of the present work was to enhance our knowledge of vitamin D security among the northern Norwegian population.

Aims of the thesis

The general aim of this thesis was to assess vitamin D security in northern Norway by addressing a number of aspects relevant for populations living at high latitudes. Specifically, the impacts of a traditional marine diet, UV-radiation and cod-liver oil supplement use have been addressed.

Project aims:

1. To investigate vitamin D status among middle-aged women living in northern Norway (65-71^{0}N) by determining the 25-hydroxyvitamin D levels in plasma and its relationship to vitamin D intake and UV-exposure;
2. To assess the use of cod-liver oil supplements among Norwegian women and to examine dietary, lifestyle, demographic, and health factors associated with its use;
3. To assess changes in plasma 25-hydroxy vitamin D concentrations after ingestion of "mølje", a traditional northern Norwegian fish dish rich in vitamin D, both in a rural and an urban study sample.

Materials and methods

In this thesis, both cross-sectional and experimental designs were utilized. The methods and study samples are described in details in the individual papers. The cross-sectional studies (Paper 2 and 3) were all based on study samples from the Norwegian part of the European Prospective Investigation into Cancer and Nutrition (EPIC-study), which is a sub-sample of the nationwide Norwegian Women and Cancer Study (NOWAC). The experimental field studies (Paper 1 and 4) were based on volunteers from a rural and an urban community located in northern Norway. Table 1 summarizes the method, sample size and measurements employed in each paper.

Table 1. Summary of study designs, tools, matrices, and measurements employed and populations studied.

Paper	Study design (n)	Tool or matrix	Measurement	Study population
1	Experimental field study (n=33)	Questionnaire	Usual vitamin D intake	Tromsø (Northern Norway, urban)
		Observed weighed record	Vitamin D intake from the "mølje" meal	
	Exposition: one "mølje" meal	Blood sample	25(OH)D concentration in plasma	
		Food sample	Vitamin D content in the served "mølje" meal	
2	Cross-sectional (n=37226)	Questionnaire (NOWAC)	Cod-liver oil supplement use Usual diet and estimated usual nutrient intake Demographic and lifestyle factors	Norwegian women
3	Cross-sectional (n=300)	Questionnaire	Usual vitamin D intake UV-exposure	Northern Norwegian women
		Blood sample	25(OH)D concentration in plasma	
		FastRT* – UV simulation tool	Biological effective UV dose rate for vitamin D photo-conversion	
4	Experimental field study (n= 35)	Questionnaire (NOWAC)	Usual nutrient intake	Skjervøy (Northern Norway, rural)
		Observed weighed records	Vitamin D intake from the "mølje" meal	
	Exposition: three "Mølje"-meals	Blood sample	25(OH)D, $1,25(OH)_2D$, and PTH concentrations in plasma	
		Food sample	Vitamin D content in the served "mølje" meal	

* The abbreviation FastRT refers to the fast, but accurate UV simulation tool described in detail in Paper 3

Study populations

The study participants for the experimental field studies were recruited both from urban and rural study populations. Tromsø (Paper 1), the largest city in northern Norway, was chosen mainly for practical reasons, but also to allow the study of the impact of traditional food consumption on vitamin D levels in an urban setting. Skjervøy was chosen (Paper 4), based on dietary data from the NOWAC study, in which this rural community ranked among the places where "mølje" was consumed most frequently (unpublished data). In order to find volunteers who were willing to consume three "mølje" meals in one week, Skjervøy was thus considered an appropriate place.

The cross-sectional studies (Paper 2 and 3) were based on data from the Norwegian EPIC-cohort, which originates from the NOWAC study. For the study sample in Paper 2 on predictors for cod-liver oil use, data from the whole EPIC-cohort was used. In the examination of vitamin D status in northern Norway (Paper 3), a sub-sample from the EPIC-cohort bio bank was selected.

Dietary assessments and questionnaires

For the studies presented in the Papers 1 and 3, semi-quantitative food-frequency questionnaires were developed to estimate usual dietary intake of vitamin D. The questionnaire described in Paper 1, collected detailed information only on food items containing vitamin D (Appendix A), while the questionnaire of Paper 3, in addition, collected information on UV-exposure (Appendix B). For the remaining papers (Papers 2 and 4) the NOWAC food questionnaire (Appendix C) aimed to cover most of the diet was used. However, in the work described in Paper 4 the questions on fish liver in the NOWAC-questionnaire were replaced with more comprehensive questions regarding use of "mølje" (Appendix D). In addition we also included issues regarding sun- and UV-exposure.

The nutrient calculations were based on values from the Norwegian Food Table (Rimestad *et al.* 2001), except for the vitamin D content in "mølje" for which the data were derived from our food sample analysis as described in more detail below. In the experimental field studies (Papers 1 and 4) observed weighed records were used to quantify the amount of cod-liver and fresh cod-liver oil consumed in the served "mølje" meals.

Blood sampling and analysis

In all papers, except Paper 2, vitamin D metabolite-concentrations were measured in plasma specimens. The laboratory methods employed to determine vitamin D metabolites are described in the individual papers, and the actual analysis were done at the Department of Paediatrics, Haukeland University Hospital, Bergen, Norway.

Food sample analysis

Since data on the nutrient content in the Norwegian Food Composition Table (Rimestad *et al.* 2001) are given per 100 g of raw and not cooked food item, food analysis were needed on the vitamin D content in the boiled cod-liver and fresh cod-liver oil served to get a more valid estimation of vitamin D intake in the experimental field studies. These data were also used in the calculation of daily vitamin D intake based on the questionnaire data. The food sample analyses were carried out by the Directorate of Fisheries, Institute of Nutrition, Bergen, Norway.

Statistics

Statistical analysis were conducted employing the SAS software package, version 6.12 or 8.02 (SAS Institute Inc., 1989). Both parametric and non-parametric statistics were utilized and they are described in appropriate details in the individual papers. In the statistical analysis when dietary- and nutrient intake were compared by different characteristics, non-parametric methods were selected because the distributions of this intake data were generally skewed to the right. The parametric statistical approach was based on univariate analysis, analysis of variance, logistic regression, analysis of variance with a repeated measurement design, as well as linear regression. Levels of 25(OH)D plasma had in general a skewed distribution and were log-transformed in some of the analyses.

Ethics

The studies were all approved by the Regional Ethical Committee, University of Tromsø, Norway. All participants were asked to join the study by completing a consent form. The NOWAC study had previously been approved for the collection and compilation of identifiable personal data. The mølje-studies conducted in Skjervøy and Tromsø were reported to the Norwegian Data Inspectorate as required by regulation.

Summary of results

PAPER 1. CHANGE IN PLASMA LEVELS OF VITAMIN D AFTER CONSUMPTION OF COD-LIVER AND FRESH COD-LIVER OIL AS PART OF THE TRADITIONAL NORTH NORWEGIAN FISH DISH "MØLJE".

In this study we assessed changes in plasma 25-hydroxy vitamin D [25(OH)D] concentrations after ingestion of one "Mølje" meal consisting of cod, cod-liver and fresh cod liver oil by 33 volunteers living in the city of Tromsø. At baseline, 69.7 % of the subjects had 25(OH)D concentrations below 50 nmol/l and for one quarter they were less than 37.5 nmol/l. The participants who reported taking cod-liver oil supplements more than twice per week had significantly higher 25(OH)D plasma levels at baseline compared to those reporting not doing so ($p=0.02$). The average vitamin D intake from the "mølje" meal was 50.0 µg from the liver and 23.3µg from the fresh cod-liver oil. Changes in plasma levels after the meal relative to baseline were significantly associated with body mass index ($p<0.01$). Further, when the baseline plasma concentrations were dichotomized into 25(OH)D< 37.5 nmol/l and 25(OH)D ≥ 37.5 nmol/l, the mean deviations from the respective baseline values were significantly different between the two groups ($p=0.02$). One meal was not sufficient to change the overall vitamin D status of the study group. However, modest beneficial effects were noted for those with low baseline levels and for leaner individuals.

PAPER 2. PREDICTORS FOR COD-LIVER OIL SUPPLEMENT USE – THE NORWEGIAN WOMAN AND CANCER STUDY.

By assessing predictors for cod-liver oil supplement use among 37226 women aged 41-55 years (the Norwegian EPIC-cohort), we found that use of this supplement was associated with several dietary, lifestyle, demographic and health factors. Cod-liver oil supplement use was reported by 44.7 % of the participating women. Subjects with higher education, high physical activity level, never smokers, and body mass index in the normal range were more likely to use cod-liver oil supplements. In addition, consumption increased with age, reported consumption of fruits, vegetables, fish (both lean and fatty), and vitamin D (excluding contribution from cod-liver oil supplements). The strongest predictor for cod-liver supplement intake was that of other dietary supplements (OR=2.45, 95% CI:2.28-2.62).

These results show that consumption of cod-liver oil supplements was not matched with vitamin D needs but can be considered an indicator of healthier lifestyles. These findings raise the need for awareness of potential confounder effects when assessing the relationship between cod-liver oil use and diseases.

PAPER 3 VITAMIN D STATUS IN MIDDLE-AGED WOMEN AT 55-71 DEGREES NORTH IN RELATION TO DIETARY INTAKE AND EXPOSURE TO ULTRAVIOLET RADIATION.

When analyzing 25(OH)D concentrations in blood among the 300 randomly selected middle-aged women living in northern Norway, the prevalence of moderate hypovitaminosis D was highest in January/February when one quarter of the participants had 25(OH)D concentrations ≤ 37,5 nmol/l. Predictors for 25(OH)D levels in blood were: 'age', 'vitamin D intake', 'taking a sun holiday', 'solarium use', 'whether residing or not in northern Norway during the whole summer prior to the blood sampling', and 'time of the year when the blood sample was collected'. Vitamin D intake was significantly positively associated with 25(OH)D in plasma in all the time strata (November-February, Mach-April, and May -June) for subjects who had not been on a sun holiday or to a solarium. The variable 'UV-hours', which represented estimated time- and geographic specific hours per day with UV-radiation exposure that theoretically causes vitamin D production in skin, significantly explained 25(OH)D concentrations in plasma in the 'no solarium/no sun holiday' strata ($p<0.0001$).

These findings confirm the importance of dietary sources of vitamin D among people living at high latitudes. Further, our results suggest a long-term impact of summer UV-radiation exposure on vitamin D status throughout one year.

PAPER 4. VITAMIN D STATUS IN A RURAL POPULATION OF NORTHERN NORWAY WITH HIGH FISH-LIVER CONSUMPTION.

The main purpose of this experimental field study was to assess vitamin D status and the impact of three repeated fish meals consisting of cod-liver and fresh cod-liver oil on plasma levels of vitamin D metabolites by subjects living in a high cod-liver and cod-liver oil consumption area.

In the last part of March 2001, thirty-two volunteers from the Skjervøy (70^0N) municipality in northern Norway were recruited to consume three "mølje"-meals consisting of cod, cod-liver, fresh liver oil, and hard roe in one week.

We found that the median usually vitamin D intake, estimated from the questionnaire, was 9.9 µg/day. The proportion of the subjects with baseline 25(OH)D levels below 50 nmol/l was 15.4 % and none was below 37.5 nmol/l. Only "mølje"-consumption and "hours spent in daylight" were significantly associated with baseline log25(OH)D. The mean total intake of vitamin D though the three meals served was 271.9 (SD=93.9) µg ranging from 142.4 –434.4 µg. There was a slight decrease in 25(OH)D concentrations after the last meal. For the active vitamin D metabolite 1,25$(OH)_2$D, there was an increase from baseline to 12 hours after the last meal ($p=0.03$).

It is concluded that three repeated "mølje" meals provide on average 54 recommended daily doses of vitamin D. Subjects with food habits that include frequent "mølje"-meals during the winter can sustain satisfactory vitamin D levels in blood in spite of a long "vitamin D winter" when no UV-induced vitamin D production in skin occurs.

General Discussion

Traditional food and Norwegian minimum diet (Sikringskost)

The Norwegian Fishery Director in 1958 issued a paper (Natvig, 1958) outlining the defined *minimum diet* with a special emphasis on the importance of cod-liver oil. The guidelines for the minimum diet were, according to the paper, aimed to be *"a norm for an adequate diet…that will cover the needs for essential nutrients"*. The guidelines included the six food groups itemized in Table 2. Fish liver and cod-liver oil were both listed.

Table 2. Minimum diet ("sikringskost")

Food groups
1. Milk and milk products
2. Egg
3. Fruits, berries, vegetables, and roots
4. Meat, offal, and food made of animal blood
5. Lean and fatty fish, hard roe and liver
6. Cod-liver oil

One of the stated rationales for the minimum diet list was that the recommended diet should be based on Norwegian food customs and traditions. Based on dietary surveys a pronounced concern focused on the inadequate dietary intake of vitamin D, vitamin C, and calcium in the Norwegian population.

Nutritional benefits of traditional food

In the last decade, several investigations have been conducted aiming at assessing the impact of traditional food on nutrient intake among populations living in the arctic (Kuhnlein, 1995). *Traditional food systems* have been defined as being composed of food items from the local natural environment that are culturally acceptable. It also includes the associated sociocultural meanings, acquisition, and processing techniques, use, composition, and the nutritional consequences for the people using the food (Kuhnlein & Receveur, 1996). In particular, indigenous peoples have been the focus for this research, especially, with concerns regarding the effect of rapid dietary changes toward a decrease in use of traditional foods (Kuhnlein, 1994; Receveur *et al.,* 1997). Traditional food has been found to be an important source of essential nutrients, as well as having social and cultural benefits (Kuhnlein, 1995). Blanchets *et al.*, (2000) found that for Inuit women living in Nunavik, northern Quebec, Canada, traditional food was an important source of several essential nutrients. Although market food contributed the most to the women's energy intake, 40% of the intake of several nutrients including protein, vitamin D, phosphorus, and zinc were derived from traditional food. Moreover, traditional food supplied over 100% of the daily recommended intake of vitamin D. A higher nutrient density in traditional food compared to market food has also been reported in other studies (Kuhnlein 1995). Further, an increased risk of low intakes of some nutrients has been observed to accompany a reduction in the consumption of a traditional diet. In particular intake of vitamin D, which is found in high concentrations in a limited number of foods, has been characterized as negatively associated with dietary changes toward a more "modern" dietary pattern among arctic populations (Receveur *et al.*,1997; Specker, 1994). A recent study based on 25(OH)D measurements in blood and dietary data concluded that a change in dietary habits from a traditional to a westernized fare was associated with reduced vitamin D status in native Greenlanders (Rejnmark *et al.,* 2003). Concern has also been raised regarding health consequences of change in dietary habits among northern indigenous peoples, especially in relation to an increase rise in the prevalence of type 2 diabetes (Mamleeva *et al.,* 1998).

Northern Norwegian food traditions and nutrition

Most studies on traditional food and nutrients in the arctic areas have, as mentioned earlier, focused on native peoples mainly from Greenland or arctic regions of Canada. For generations, these communities have lived maintaining ties to subsistence economies based on the available natural resources (Durning, 1992). However, in more recent times these indigenous groups have lived alongside new settlers with more westernized lifestyles. By contrast, in northern Norway, for several generations both indigenous and non-indigenous groups have developed a successful subsistence base by using available natural resources from the local environment. This means that the findings from studies on issues regarding traditional food systems among indigenous peoples in other part of the northern regions can be of relevance for or have some common features with the situation for the northern Norwegian population.

Our findings confirm the role of traditional diets in maintaining vitamin D status. In Paper 3 we found that salmon/trout and "mølje" together contributed 40 % of the self-reported daily vitamin D intake. When including cod-liver supplements, the percentage was more than 60.

The difference in vitamin D status between the Skjervøy (Paper 4) and Tromsø (Paper 1) groups are illustrated in Table 3. These results indicate that subjects on a more traditional diet (i.e. the Skjervøy group) have satisfactory vitamin D levels as no individuals exhibited plasma 25(OH)D concentrations below the limit for moderate hypovitaminosis D [25(OH)D≤37.5 nmol/l], while 25 % did so in Tromsø. Moreover, a significant trend was observed in the Skjervøy-group between frequency of "mølje" consumption and vitamin D levels in blood (Paper 4).

Table 3. Comparison of 25(OH)D levels in blood between the study samples from Tromsø and Skjervøy.

	% of study sample	
25(OH)D levels *nmol/l*	Tromsø *(n=33)*	Skjervøy *(n=32)*
< 37.5	**24**	**0**
37.5-50	**46**	**16**
>50	**30**	**84**

Last, in our cross-sectional study (Paper 3) "mølje" consumption was predictive of vitamin D status, although with borderline significance (p=0.06).

In the food security model (Figure 3), adequacy and stability constitute its major components. From a traditional food system perspective, vitamin D security rests upon adequate marine sources to vitamin D and stability of supply of these sources. The tradition that involves a balance between sun-induced vitamin D during summer months and high consumption of marine vitamin D food items during wintertime affords stability in the vitamin D supply.

"The Arctic Dilemma" – food safety and vitamin D security

As already indicated, food safety, together with cultural acceptability and local adequacy are necessary for adequacy of the food supply. Traditional food in the arctic and food safety in relation to persistent organic pollutants (POPs) have, during the last decade, caused serious concern about possible negative health effects of chronic exposure (AMAP, 2003; Kuhnlein & Chan, 2000). Present levels of POPs in the arctic have mainly been attributed to long-range transport from lower latitudes and only to a minor extent to local pollution sources (Burkow & Kallenborn, 2000). Recently, the Norwegian Food Control Authority has recommended that all women of childbearing age, pregnant women and children should avoid eating fish liver because of the risk of long-term health impact due to POPs content above estimated tolerable limits (Norwegian Food Control Authority, 2003). Reports on pollution in the arctic and its accumulation in the food chain and the associated health risks have been criticised (Hild, 1998), especially the communication of consumption advisories and their justification. Further, criticisms have also been raised because often in communication no suitable practical solutions are provided for local communities to act on. *The Arctic Dilemma* (Nilsson & Huntington, 2002) is a term that covers issues on how to maintain a balance in providing clear and accurate information on both the benefits and risks of arctic diets and how to communicate this. It is essential to bear in mind that while the nutritional and cultural benefits of traditional food in the arctic are well known, the possible negative health effects of pollutants are not yet well demonstrated for human health (Kuhnlein, 1995; Van Oostdam *et al.,* 1999). Second, the word "risk" is a mathematical concept. The foundation of much of today's science is a statistical probability of an event occurring. On the contrary, the concept of "risk" has no reality for most communities in the mathematical context in which it is given. The same is true for the word "significant", which for the researchers is a mathematical construct, but for others it is something that is noticeable and of concern. Our results strongly support that traditional marine food habits is important for vitamin D status. Thus, dietary advices that warns against use of these food items can have an effect on vitamin D security in addition to a dilution of a cultural identity markers which traditional foods represent. Another concern in this connection is how local people respond to the statements from researchers that part of their food should be avoided; such as the fish liver. It is likely that from the holistic perspective often held by peoples who have strong ties to natural local resources, this information can lead to the conclusion that if part of the fish contains too much of a contaminant, then the entire fish is not suitable for consumption. This could hypothetically lead to a reduced intake of fish, which is well established as an undesirable outcome. A solution to the Arctic Dilemma has been proposed to foster new community-based approaches. In this approach, the identification of concerns under investigation and the communicators of the findings are done by the local residents in partnership with the researchers or public health authorities.

Vitamin D status in Europe

Vitamin D status measured as 25(OH)D concentrations in blood have been reported to be higher in Scandinavia than in the rest of Europe both for young adults and the elderly (McKenna, 1992). This has been explained by dietary factors like higher intake from natural, and fortified sources in addition to supplement use. When comparing vitamin D status between countries, the seasonal variation in 25(OH)D concentrations is a methodological challenge. Further, the cut off points used for prevalence of vitamin D deficiency varies and it is still debated what specific level should be considered as indicating deficiency or the optimal concentration (Heaney, 1999). Thus, due to the lack of standardized blood sampling procedures and clear status definition, conclusions drawn when comparing results from different countries have limitations. Elderly subjects have often been the focus in vitamin D status investigations mainly in relation to bone health. In Table 4, wintertime vitamin D levels reported in studies conducted in different European countries among younger study groups are summarized.

Table 4. Winter vitamin D status in Europe

Country	n	Mean 25(OH)D (SD) or % below specified cut off points	Subjects
France (Guillemant *et al.* 1999)	175	20.6 (6.0) nmol/l	Male adolescents 13- 17 years
Southern Finland (Lehtonen *et al.* 1999)	186	33.9 (13.9) nmol/l 67.7 % ≤ 37.5 nmol/l	Children 9-15 years
Island (Kristinsson *et al.* 1998)	259	43.9 (range 1.7-132.0) nmol/l 18 % < 25 nmol/l	Adolescent girls 16-20 years
France (Chapuy *et al.* 1997)	1569	14 % ≤ 30 nmol/l	Adults, men and women 35-65 years
Southern Finland (Lamberg-Allardt *et al.* 2001)	202	47 (34) nmol/l 26.6 % < 25 nmol/	Women 31-43 years
Denmark (Brot *et al.* 2001)	2016	7 % 25(OH)D< 25nmol/l	Women 45-58 years
Northern Norway (Brustad *et al.* 2003)	300	55.4 (range 8.1-125.4) nmol/l	Women 44-59 years

Despite the limitations associated with comparing the different studies, it appears that vitamin D status in the northern Norwegian group was not notable low compared to other countries, by contrast to what might have been expected due to residing at high latitude. Van der Wilen *et al.*, (1995) found in a study conducted among European elderly people that vitamin D status increased with increased latitude. Their investigation was based on 824 free-living elderly from 11 European countries. The strength of their study was that the 25(OH)D concentration was determined in a standardized way in that samples were analyzed in one laboratory, collected in the same period of the year in the same age category, and lastly, all participants were living in relatively small towns across Europe. Greece, Italy and Spain were the countries with the lowest mean 25(OH)D concentrations and highest prevalence of concentrations below 30 nmol/l. The groups from the northern European towns had the highest mean values and the group from Norway ranked first. Again the north-south difference was explained by food fortification and dietary intake.

Comparisons of dietary intake of vitamin D across Europe will probably not be valid because at the moment there is no standardized food composition table. Thus, difference in nutrient intake can hypothetically be attributed to differences in the databanks rather than actual intake.

Hypothesis on the relationship of vitamin D and different health outcomes have originated from a latitudinal difference of the occurrence of some diseases like cancer (Apperly, 1941), and multiple sclerosis (Hayes, 2000). These ecological studies have suggested low levels of vitamin D due to limited UV-exposure, to a be a risk factor for diseases. However, the observed north-south gradient in vitamin D levels; probably due to different dietary habits, does not fit with distribution patterns of these diseases. Dietary studies in Norway have shown a higher vitamin D intake in the north compared to the south (Johansson & Solvoll, 1999). Thus, it seems that population groups with less exposure to sunshine, have developed a diet that compensates for reduced UV-induced vitamin D production.

Methodological considerations

Epidemiological studies can in general be classified as experimental or observational studies. Broadly, these two types of investigations are distinctive in that in the experimental design exposure is controlled by the investigator, whereas in observational studies the investigator has no influence or control over the way in which subjects are exposed (Margetts & Nelson 1998).

The "mølje" investigations conducted in Tromsø (Paper 1) and Skjervøy (Paper 4) fall in the experimental category. The assessment of vitamin D status and its predictors in northern Norway (Paper 3) and the investigation on predictors for cod-liver oil supplement use (Paper 2) are both cross-sectional studies i.e. observational designs.

Validity

The validity of a study refers to whether the findings can be taken as being a reasonable representation of the true situation. In studies on human subjects, it is often separated into two components, namely internal and external validity. The former is the validity of the measures used and the conduct of the study, and the latter refers to the generalizability of the finding to groups outside the study sample. The validity of a study is affected by selection bias, information bias, and confounding (Encyclopedia of Epidemiologic Methods, 2000; Margetts & Nelson, 1998).

Selection bias

Selection bias refers to a bias that arises when the study participants are sampled or recruited so that the study sample differs systematically from the population from which it was meant to represent.

The cross-sectional studies (Papers 2 and 3) were based on the Norwegian EPIC-cohort that consists of subjects who completed a NOWAC- questionnaire both in 1991/1992 and 1998. The response rate in the Norwegian EPIC-cohort can be calculated as follows: 56.7% (crude response rate 1991/1992) x 82.3% (crude response rate 1998) =46.7%. The response rates in the NOWAC and EPIC- cohorts are similar to many other population-based cohorts (The Million Women Study, 1999; Kolonel *et al.,* 2000; Manjer *et al.,* 2001). Brøgger et al (2003) have shown that the prevalence estimate and risk factors associations were similar when the response rate varied between around 43 to 80 %. In an external validation study it was shown that the NOWAC cohort has identical cumulative age-specific all-cancers and breast cancer incidence rates compared to national figures (Lund *et al.* 2003).

Blood samples were collected from 69.8 % of the randomly selected subjects on a monthly basis in the EPIC cohort in northern Norway during November 2001- June 2002. Thus, the total response rate for the blood sampled for vitamin D status determination (Paper 3) was 46.7% x 69.8% =32.5%. The finding that usual vitamin D intake reported in the food frequency questionnaire did not differ with respect to when the subjects where recruited to the study support that the randomization was satisfactory.

The "healthy volunteer effect" (Lund *et al.,* 2003) due to higher education for responders and thereby higher socio-economic status, could potentially have affected the external validity of both the Paper 2 and 3 studies. However, there is no reason to assume that the relationship between UV-radiation and vitamin D intake from the diet, and 25(OH)D levels in blood plasma (Paper 3) differ across education- or socio-economical groups. Selection bias with respect to education was outlined in Paper 2 because there was evidence for it both when comparing selected variables in the 1991/1992 questionnaire with national register data and comparing participants in 1998 with all who participated initially in 1991/1992. In Table 5 the distribution of selected variables from the 1991/1992 questionnaire database are compared between all who answered and those who answered in 1998. For some of the variables the one-way Chi-square test was highly significant. However, the practical consequence of this is small. It can be demonstrated by calculating the difference in number of for example cod-liver oil users between the observed in 1998 (Norwegian EPIC-cohort) and the expected when applying the 1991/1992 distribution in education. In the 1991/1992 questionnaire, cod-liver oil supplement was not included, thus for this calculation exercise only the 1998 distribution of cod-liver oil supplement use was available (Table 6). Differences up to one percent for subjects in the highest and lowest educational groups (Table 5); the overall discrepancy corresponds to 59 subjects, which again is small.

Table 5. Comparison of distribution of selected variables between all who answered the 1991/1992 questionnaire and those who answered in 1998.

Characteristics	All in 1991/1992 %	Responders in 1998	p-value X^2-*test*
Geography			
East	49.7	49.6	
South	13.1	13.1	
West	16.8	17.1	
Mid	8.9	8.7	
North	11.5	11.6	0.55
Age			
40-44	29.1	28.9	
45-49	33.0	33.0	
50-54	32.7	32.8	
55-59	5.3	5.2	0.82
BMI			
<18.5	3.6	3.5	
18.5-<25	75.2	75.7	
25-<30	17.0	16.7	
30+	4.2	4.1	0.10
Education (y)			
-8	10.7	9.7	
9	13.6	12.7	
10	13.6	13.3	
11-12	22.7	23.0	
13-15	21.4	22.2	
16+	18.1	19.1	<0.001
Smoking			
Yes	36.7	35.1	
No	63.3	64.9	<0.001
Fatty fish			
1+ /week	28.3	27.7	
3 /month	71.7	72.3	0.02
Perceived health			
Very good	35.8	37.1	
Good	57.7	57.0	
Bad	5.9	5.4	<0.001
Very bad	0.6	0.5	
Marital status			
Married	77.6	78.4	
Cohabitee	8.5	8.3	
Other	13.9	13.4	0.002

The central element when considering selection bias and its impact on the validity of the study is to what extent the relationship between exposure and outcome differs between those who participated and those who should be theoretically eligible for the study but did not participate. We assume that there is no reason to believe that the pattern of cod-liver oil use with respect to other variables not included in the comparison test differed between responders and non-responders.

For both the experimental field studies (Papers 1 and 2) the generalizability to the whole population is of less importance in light of their objectives. The objective with the study in Tromsø (Paper 1) was to assess the metabolic response. This demonstrates another main view regarding external validity when it refers not to comparisons between the study sample and population from which the sample is drawn, but rather to an experience from the study that can be described as a phenomenon which is believed to apply to all subjects in the same way (Margetts & Nelson, 1998). For the study carried out in Skjervøy it is likely that the individuals who attended were the heavy "mølje"-consumers, but again we were interested in the vitamin D status and metabolic response for subjects who maintained the marine food tradition of consuming high amounts of liver during the winter.

Table 6. Expected cod-liver oil supplement users given no change in education distribution between 1991/1992 and 1998 sample.

Education (years)	Reply 1998 Observed	Reply 1998 Expected[a]	Supplement use in 1998 Observed n	Supplement use in 1998 Observed %	Supplement use in 1998 Expected[a]	**Supplement use expected - observed**
0-8	3559	3921	1461	41	1610	**149**
9	4680	4983	1826	39	1944	**118**
10	4897	4991	2010	41	2048	**38**
11-12	8436	8331	3684	44	3638	**-46**
13-15	8159	7874	3715	46	3585	**-130**
16+	7005	6636	3576	51	3388	**-188**
Total	36736	36736	16272		16213	**-59**

[a] Expected based on the education distribution in 1991/1992

Information bias

Information bias is usually separated into non-differential and differential. For the latter, the information bias on the exposure variables is associated with the outcome variable. This can bias the association in both directions and can thus be responsible for spurious associations Non-differential information bias usually dilutes the effect of the exposure (dos Santos Silva, 1999).

In the studies on vitamin D status in relation to UV-exposure and vitamin D intake (Paper 3), and "mølje" consumption (Papers 1 and 4), the subjects were unaware of their blood levels when they answered the questionnaire. This eliminates the possibility of differential information bias. For the cod-liver oil supplement study (Paper 2), the reported lifestyle factors could theoretically be affected by the reported use of the supplement. We observed that the use of cod-liver oil supplement was associated with a self-reported healthier lifestyle. This relationship could hypothetically be due to a systematic misclassification where subjects who tend to report healthier lifestyles with respect to diet, physical activity, smoking etc. also reported higher cod-liver oil supplement use than what they actually took. This example demonstrates a validity challenge in cross-sectional studies. Further, since the information on both exposure and outcome are collected simultaneously, cross-sectional studies are not the appropriate study design to investigate causal relationships. The purpose of our study was, however, not to assess causality but rather to investigate what characterized subject using cod-liver oil supplements. Due to the limitations in a cross-sectional study where all data is based on self-reported information, the impact of differential information bias or misclassification on our findings can be questioned. However, the NOWAC food-frequency questionnaire has been validated against biomarkers as has been described in detail elsewhere (Hjartaker *et al.* 1997). In short, this validation showed a significant correlation between calculated intake of n-3 fatty acids and serum phospholipids n-3 fatty acids. Further, a highly significant relationship was found between reported intake of cod-liver oil and n-3 levels in blood (r=0.46, P=<0.001). The use of biomarkers is recommended to validate self-reported dietary data (Willett, 1998). The results from the sited study by Hjartåker et al (1997) provides a strong indication that the reported cod-liver oil supplement data using the NOWAC questionnaire are valid.

Confounding

Confounding is when a variable other than the exposure of interest has influenced the outcome (Margetts & Nelson 1998). Confounders are associated with both the exposure and the outcome and can provide a true explanation of an apparent association between the exposure and the outcome. For a variable to be a confounder, it has to be associated with exposure but not causally dependent upon the exposure of interest. Typical confounders in epidemiology are gender, age, and smoking.

In Paper 2, we found that cod-liver oil supplement use was an indicator of a healthy lifestyle. Our study provides a good demonstration of challenges related to possible confounders that need to be considered when assessing the relationship between cod-liver oil supplement use and diseases.

Another example of possible confounding is illustrated by an ecological study conducted by Grant (2002a) where the relationship between UV-induced vitamin D and cancer was assessed. He found that when omitting the Scandinavian countries from the analysis, latitude did significantly predict breast carcinoma mortality. As mentioned earlier, wintertime vitamin D status in Europe measured as 25(OH)D in blood has been found to increase with latitude due to increased dietary intake (van der Wielen *et al.*, 1995). Given an association between intake and UV-induced vitamin D, dietary vitamin D intake can be considered a potential confounder in the ecological study on UV-radiation and breast cancer. This example emphasizes the importance of collecting data on both UV-induced and dietary vitamin D simultaneously when investigating vitamin D and various health outcomes.

The optimal epidemiological study where it is possible to adjust for all confounders does not exist, but the identification and provision of good measures on confounders are essential. An important advantage of the NOWAC questionnaire is its comprehensiveness that provides data on various potential confounders than can be controlled for.

Concluding remarks and further perspectives

Main conclusions

This present thesis has addressed different aspects related to vitamin D security, in particular for populations living at high latitudes. The main conclusions can be summarized as indicated below.

- Because of the long "vitamin D winter" when there is no UV-induced vitamin D production in skin, dietary sources of vitamin D seem to be of considerable importance for the population living in northern Norway.
- Northern Norwegian marine food customs constitute important vitamin D sources. The traditional fish dish "mølje" (cod, cod liver and fresh cod-liver oil) contains high levels of vitamin D. Subjects who consume frequent "mølje"-meals during winter sustain satisfactory vitamin D levels in blood when measured at the end of the "vitamin D winter".
- Variation in estimated UV-radiation during winter and spring predicted vitamin D levels in blood.
- It is essential when assessing relationships between vitamin D and different health outcomes that data on diet and UV-exposure are collected simultaneously.
- The use of cod-liver oil supplement among Norwegian middle-aged women is not matched with vitamin D needs, but is rather an indicator for a healthy lifestyle.
- Mean self-reported dietary intake of vitamin D seems to be higher than what has been reported in the south of Norway and other Nordic countries and above the recommended level. Vitamin D status measured as 25(OH)D levels in blood plasma

among adult women living in northern Norway is not lower than what has been reported in other European studies.

- Travelling to southern locations during the summer gives higher vitamin D levels in blood plasma during wintertime.

Further perspectives

Several issues regarding vitamin D status among subjects living in northern Norway and other arctic areas deserve further research.

- There is a need for more studies to investigate risks and benefits in relation to traditional food patterns in different ethnic groups and the impact of dietary change on vitamin D status.
- Further efforts must be made to create good and appropriate communications between researchers and the population regarding risks and benefits of traditional foods.
- Much is still not well understood regarding variation in UV-radiation in the arctic and its impact on vitamin D production in skin in relation to latitude, clouds, snow, and other meteorological data.
- There is a need for prospective population-based investigations to include both UV-radiation and dietary data when assessing the proposed relationship between vitamin D and different health outcomes like cancer.

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ERRATA

Paper 1

In Figure 3, the *p*-values for difference in 25(OH)D change between baseline 25(OH)D-groups and BMI-groups should be 0.02 and <0.01 respectively.

Reference in the first sentence in second paragraph in Discussion should be 15.

Paper 4

The text associated to the *y*-axis in *Figure 4* should be: Plasma concentrations [nmol/l for 25(OH)D, pmol/l for 1,25$(OH)_2$D].

Paper I

CHANGE IN PLASMA LEVELS OF VITAMIN D AFTER CONSUMPTION OF COD-LIVER AND FRESH COD-LIVER OIL AS PART OF THE TRADITIONAL NORTH NORWEGIAN FISH DISH "MØLJE".

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Torkjel Sandanger[2],
Tom Wilsgaard[1],
Lage Aksnes[3],
Eiliv Lund[1]

ABSTRACT

Objective. To assess changes in plasma 25-hydroxy vitamin D (25(OH)D) concentrations after ingestion of «Mølje», a traditional north Norwegian fish dish rich in vitamin D.

Methods. Thirty-three volunteers all living in the city of Tromsø, located in northern Norway (latitude 69°), were served a "Mølje" meal consisting of cod, hard roe, cod liver, and fresh cod-liver oil. The amounts of liver, and cod-liver oil consumed were weighed and recorded. Blood samples were collected before the meal, and at 4 hours, 12 hours and 5 days after it. The cod liver and cod-liver oil were analysed for vitamin D content and the plasma samples for the metabolite 25(OH)D. Trends in plasma 25(OH)D levels during the five-day observation period were analysed. The study was conducted at the beginning of April of 2000.

Results. Among the 33 participating subjects, 69.7% had baseline plasma 25(OH)D concentrations below 50 nmol/l and for one-quarter of the subjects, they were < 37.5 nmol/l. The participants who acknowledged taking cod-liver oil supplements had significantly higher baseline 25(OH)D plasma levels at the outset of the study compared to those reporting not doing so (p=0.02). Changes in plasma 25(OH)D levels relative to baseline concentrations were significantly associated with the body mass index (p<0.01).

Conclusion. Vitamin D status in populations living in circumpolar areas needs more research to investigate to what degree people living in the Arctic areas are at increased risk for vitamin D insufficiency and to determine the role of the traditional diet in preventing such deficiency.

Keywords. 25-hydroxy vitamin D; cod liver; cod-liver oil; traditional diet; arctic diet

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INTRODUCTION

Vitamin D is essential for normal calcium and bone metabolism in humans (1) and is synthesized in the skin on exposure to sunlight (2). Ultra-violet B (UVB) radiation, with wavelengths between 280-320 nm, is needed for cutaneous vitamin D synthesis (2). Studies have shown that seasonal changes in the UVB radiation is responsible for the absence of cutaneous vitamin D production during winter and, not surprisingly, the length of the "vitamin D winter" increases with increased latitude (3,4).

Diet is the other source of vitamin D. Vitamin D is found in only a limited number of foods, such as fat fish, cod-liver oil, eggs, mushrooms, fortified milk, margarine, and butter.

In the population in north Norway, the impact of dietary vitamin D on vitamin D status is of importance, since, at this latitude (Tromsø city 69°N), no cutaneous vitamin D synthesis is likely to occur during a considerable part of the year.

The north Norwegian fish dish "Mølje", consisting of cod, cod liver, hard roe and fresh cod-liver oil, has traditionally been an important part of the diet during the winter season among people living in the northern coastal areas of Norway. Cod liver and cod-liver oil are rich in vitamin D. According to the Norwegian Food Composition Table, 100 g of cod liver and 100 g of cod-liver oil contain 125 µg (5000 IU) and 261µg (8640 IU) vitamin D respectively. Cod muscle tissue contains only small amounts of vitamin D (1.5 µg/100 g). A dietary survey from northern Norway in 1931 did show that cod liver and fresh cod-liver oil were the most important vitamin D sources (5). According to that study, considerable amounts of both liver and oil were consumed and constituted one of the main fat sources. Today, the contribution of "Mølje" to the daily north Norwegian diet is not as pronounced as it was some time ago, but unpublished data from the nation-wide NOWAC-study (Norwegian Women and Cancer Study) (6) have shown that there are still areas where "Mølje" is consumed frequently.

The 25-hydroxy vitamin D (25(OH)D) concentration in blood has been considered the most valuable metabolite for determining the overall vitamin D status of an individual (1). A 25(OH)D concentration ≤ 37.5 nmol/l in blood has been used as an indicator of moderate hypovitaminosis D (7,8), while a 25(OH)D concentration ≥50 nmol/l has been considered as the recommended level (9,10). In the present study, changes in plasma 25(OH)D were monitored after a single meal comprising cod, liver, and hard roe, corresponding to the traditional north Norwegian fish dish, "Mølje".

MATERIAL AND METHODS

Study sample

Study subjects were recruited mainly from the Institute of Community Medicine, University of Tromsø. Thirty-three volunteers, 13 men and 20 women aged from 28 to 65 (average of 42), agreed to participate in the study. This project was approved by the Regional Committee for Research Ethics, and all subjects signed a consent form.

Study design and data collection

The participants were served the traditional north Norwegian fish dish "Mølje" with potatoes. The meal was prepared in the traditional way as follows: both the cod and the hard roe were boiled separately in water, while the liver was boiled in small amounts of water. The oil derived from this constituted the fresh cod-liver oil. Participants could eat as much as he, or she, wanted, but the amounts of liver and cod-liver oil consumed by each participant were weighed and recorded (Table III).

The study was carried out at the beginning of April of 2000. Its design and blood sample collection schedule are illustrated in Figure 1. The meal was served between 6 and 7 p.m. on day 1. Blood samples were collected just before the meal, and after 4 hours, 12 hours and 5 days. The '12-hour' and '5-day' samples were taken in the morning, before breakfast, while the '0-' and '4-hour' blood samples were taken

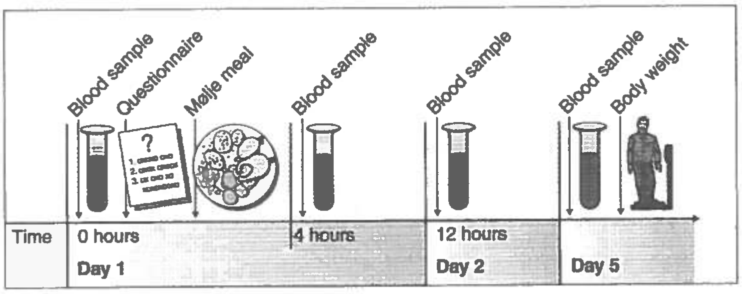

Figure 1. Study design and blood sampling schedule.

in the evening. The blood samples were collected employing EDTA-containing vacutainer tubes (BD Vacutainer Systems, Preanalytical Solutions Belliver Industrial Estate, Plymouth, UK).

Participants were asked to maintain their ordinary diet during the study period, but were instructed not to have any meals between lunch and the cod dish served on day 1. Body weight was measured on day 5.

To estimate the participants' usual daily vitamin D intake, all participants answered a semi-quantitative food-frequency questionnaire. The questionnaire explored the intake of fish and fish products rich in vitamin D, including questions on seasonal variations of consumption for each fish variety. Use of vitamin D-fortified foods, such as margarine, butter and milk were also addressed, as well as the consumption of cod-liver oil supplements, including seasonal variations and the use of other fish oil capsules and vitamin supplements. Usual daily vitamin D intake was computed using the vitamin figures from nutrient values reported in the Norwegian Food Composition Table (11), the specified content of supplements taken, and our food analysis of liver and fresh cod-liver oil as described below. The questionnaire also contained questions on the gender, age, height and weight of the respondents.

Food sample analyses

Samples from the served liver and fresh cod-liver oil were analysed for vitamin D, according to the method described by Horvli and Lie (12). In short, vitamin D was extracted using 96 % ethanol/ 60 % KOH, containing pyrogallol, ascorbic acid and an internal standard (vitamin D_2). Heating to 70°C for 20 minutes saponified the sample. After addition of water, the sample was extracted twice with hexane using a whirl-mixer and centrifuge. The combined hexane phases were extracted with water, and iso-propanol was added before evaporation. The sample was further cleaned up using a HPLC system consisting of a Spectra Physics P1000 isocratic pump, a Shimadzu SPD 6AV UV-detector, a Shimadzu C-3A integrator, fitted with a Brownlee silica column (25 cm x 4.6 mm, 5 µm). For the analytical step, a C_{18} column (25 cm x 4.6 mm, 5 µm Supelco Inc., Bellefonte, USA) was used.

For the preparative clean-up step, tetrahydrofurane : n-hexane (in the ratio 12.5:87.5 v/v) was used as the mobile phase. For the analytical step, chloroform : methanol : acetonitrile (6:12:82 v/v) was employed as eluent and the sample was dissolved in methanol. The flow rates were 1 ml/min for both columns. Vitamin D_2 (internal standard) and D_3 were detected on-line by the UV-detector at 265 nm. The food analysis was performed by the Directorate of Fisheries, Institute of Nutrition, Bergen, Norway.

The vitamin D intake from the "Mølje" meal was estimated based on the vitamin D content of the liver and the fresh cod-liver oil served, since the rest of the food items consumed (cod, potatoes and hard roe) contain little, or no, vitamin D.

Plasma levels of 25(OH)D

The blood samples were analysed for 25(OH)D. Blood plasma was collected and stored at -80°C until analysis, which was performed by a modified version of the method described by Aksnes (13,14). Briefly, 0.1 ml plasma samples were mixed with 1.4 ml 0.15 M NaCl. To estimate the 25(OH)D recovery, [^{3}H]25(OH)D_3 (1500 DPM) in 50 µl ethanol was added. The plasma dilutions were mixed with 2 ml acetonitrile, vortexed and centrifuged at 1,000 x g for 10 min to remove proteins. The supernatants were collected, 3.5 ml 0.1 M K_2HPO_4 (pH 10.5) were added, and the mixture was applied to C-18-OH vacuum columns (Varian, USA). The columns were washed with 5 ml distilled H_2O, followed by a second wash with 5 ml methanol: H_20 (70:30, v/v), after which the 25 (OH)D_3 fractions were eluted with hexane:isopropanol (95:5, v/v), and evaporated with nitrogen gas. The samples were dissolved in 250 µl hexane: isopropanol: ethanol (95:2.5:2.5, v/v) and separated on a Supelcosil silica column (15 cm x 4.6 mm, 3 µm; Supelco Inc, Bellefonte, USA) by HPLC. The fractions containing 25(OH)D were evaporated with nitrogen gas and dissolved in 400 µl ethanol. 25(OH)D was quantified by a radio-receptor assay (RRA) using human vitamin D-binding protein from blood plasma as the binding protein. The inter-assay coefficient of variation in this method was 8.5 % (estimated based on ten measurements of the same blood sample on ten different days).

Statistical Analyses

Statistical analyses and nutrient calculations were performed employing the SAS software package, version 6.12 (SAS Institute, 1996). To assess the relation between the daily vitamin D intake estimated from the questionnaire data and 25(OH)D levels in blood, the Pearson's correlation coefficient was calculated. When comparing both plasma 25(OH)D mean values and mean plasma 25(OH)D changes at 5 days as a function of age, body mass index (BMI = weight/height^2), gender and supplement use, the Student t-test was used. The Mann-Whitney test was used for analysing differences in vitamin D consumed trough the "Mølje" meal by these characteristics. Changes in plasma 25(OH)D levels over time were assessed by ANOVA with repeated measurement design. When considering the amounts consumed as predictors for the post-meal 25(OH)D levels (difference between baseline and 5-day levels), a multivariate regression model was used.

RESULTS

Some characteristics of the participating subjects are shown in Table I. The mean daily vitamin D intake for the whole group, as estimated from the questionnaire, was 7.9 µg/day (95% C.I.; 5.8, 10.0), when vitamin D contributions from supplements other than cod-liver oil supplements were excluded. Six out of the 10 subjects who reported using a cod-liver oil supplement more than twice per week, did so in addition to other vitamin supplements. The mean value at baseline for plasma 25(OH)D was 51.2 nmol/l (SD=24.0). Among the participating subjects, 69.7% had baseline plasma 25(OH)D concentrations below the recommended level of 50 nmol/l. One-quarter of the subjects had levels below 37.5 nmol/l, which has been set as a limit for moderate hypovitaminosis D.

The distribution of the plasma 25(OH)D levels at baseline is shown in Figure 2. The correlation between estimated daily vitamin D intake, based on the questionnaire and 25(OH)D levels in blood, was r=0.38 (p=0.03). The participants who reported taking a cod-liver oil supplement more than twice per week had significantly higher

Table I. Characteristics of the study sample (n=33).

Characteristics	Mean or %	SD	Range
Mean age	42	8.0	28-65
BMI[a]	24.2	2.9	19.5-29.4
Usual vitamin D intake (µg/day) (supplements other than cod-liver oil excluded)	7.9	5.9	1.3-27.0
Usual vitamin D intake (µg/day) (supplements included)	8.8	6.3	1.3-27.0
Sex, % women	60.6		
Proportion of subjects reporting taking cod liver oil supplement twice per week or more (%)	30.3		

[a] (weight / height^2)

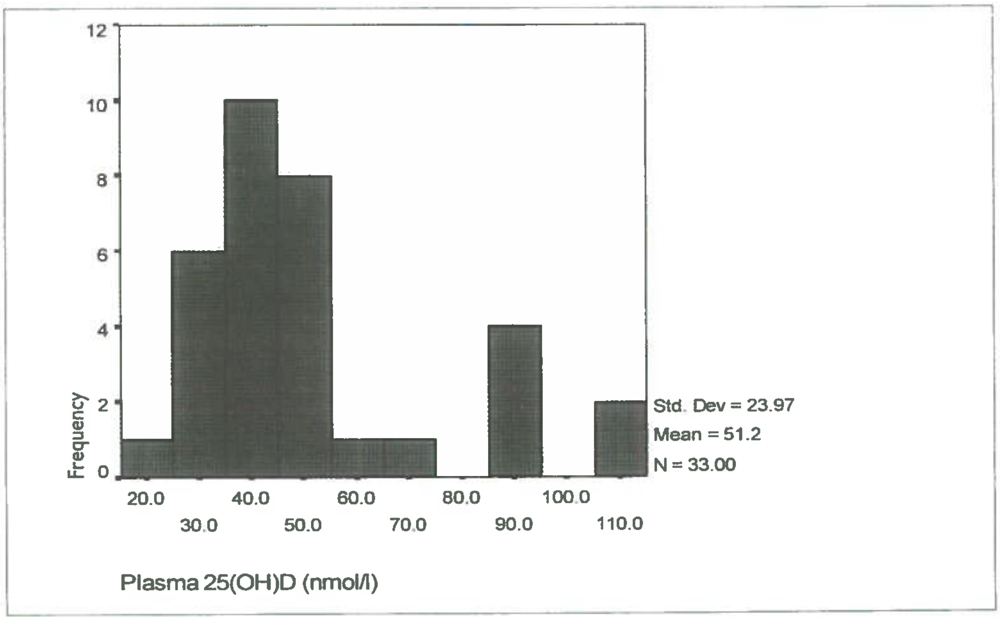

Figure 2. The distribution of 25(OH)D at baseline.

25(OH)D plasma levels at baseline compared to those reporting not using, or taking cod-liver oil twice per week or less (p=0.02), with mean values of 66.3 nmol/l (SD=25.7) and 44.7 nmol/l (SD=20.4), respectively. None of the subjects reporting not using, or consum-

Table II. Vitamin consumed through the "Mølje-meal" and plasma 25(OH)D levels by different characteristics.

Characteristic	Baseline 25(OH)D[a] Mean (SD)	% below 50 nmol/l	Mean vitamin D consumed (mg) through the "Mølje-meal"[b]	Mean plasma 25(OH)D change at 5-days (SD)[a]
Age				
< 42 (n=15)	47.5 (23.5)	80	59.6 (35.5)	-0.1 (5.0)
≥ 42 (n=18)	54.4 (24.6)	61	84.7 (63.9)	1.3 (7.2)
	n.s		n.s	n.s
BMI				
< 25 (n=23)	50.7 (24.8)	74	72.5 (58.2)	2.4 (5.9)
≥ 25 (n=10)	52.4 (23.3)	60	75.1 (44.2)	-3.3 (5.4)
	n.s		n.s	p=0.02
Gender				
Men (n=13)	57.1 (29.6)	45	67.9 (40.9)	-0.8 (6.6)
Women (n=20)	47.4 (19.4)	75	76.8 (61.3)	1.6 (5.9)
	n.s		n.s	n.s
Supplements				
Yes (n=10)	66.3 (25.7)	40	100.4 (75.0)	1.8 (6.3)
No (n=23)	44.7 (20.4)	83	61.5 (37.5)	0.1 (6.3)
	p=0.02		n.s	n.s

[a]Student t-test [b] Man-Whitney test

Table III. Mean intake of liver, fresh cod-liver oil, and vitamin D calculated from the served "Mølje-meal".

	Weight (g)	SD	Range (g)	Vit D_3(µg)	SD	Range (µg)	Vit D content/100 g boiled food item (µg)
Liver	113.6	50.5	33-281	50.0	22.2	14.5-123.6	44
Fresh cod-liver oil	20.8	31.6	0-152	23.3	35.4	0-170.2	122

ing, cod-liver oil twice per week or less, were taking other vitamin supplements more than twice per week. Baseline 25(OH)D plasma levels increased with supplement use, while gender, BMI and age had no significant effect (Table II). The mean plasma 25(OH)D change at 5 days was significantly different between BMI groups (p=0.02). Supplement users seemed to consume more vitamin D through the "Mølje" meal compared to the non-supplements users, but this difference was not significant.

The vitamin D content per 100 g cooked food item was nearly three times higher for cod-liver oil than for the liver (Table III). The amount consumed in the served meal of both liver and cod-liver oil varied considerably among the subjects, ranging from 33 to 281 g and from 0 to 152 g for the liver and the cod-liver oil, respectively. The calculated mean total vitamin D intake from the served "Mølje" meal was 73.3 µg, ranging from 14.5 to 293.8 µg.

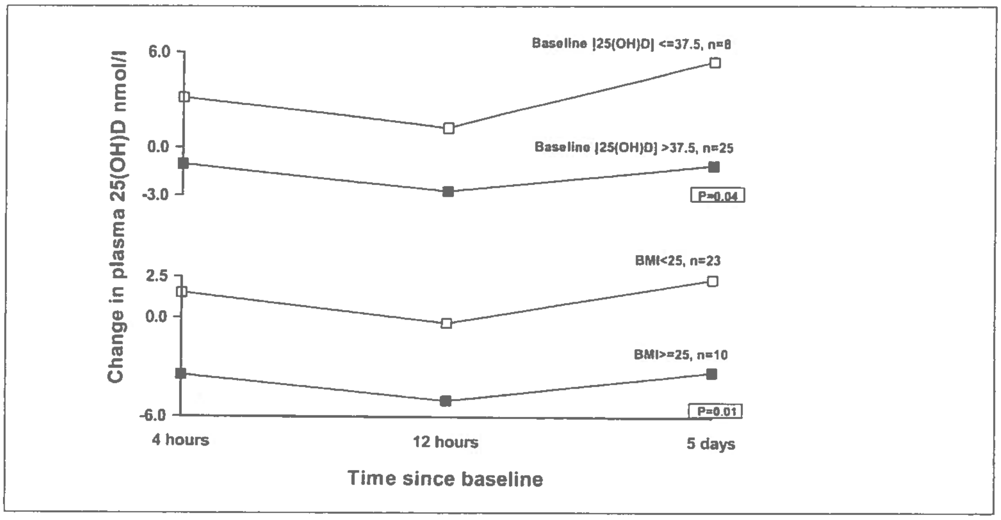

Figure 3. Relative change from baseline in 25(OH)D by BMI group or 25(OH)D baseline levels after consumption of a "Mølje" meal.

The mean plasma 25(OH)D levels after consumption of "Mølje" were 51.2 nmol/l (SD=23.2), 49.5 nmol/l (SD=23.5), and 52.2 nmol/l (SD=24.0) after 4 hours, 12 hours and 5 days, respectively. Ingested vitamin D from the meal did not predict variation in plasma 25(OH)D over time ($p=0.86$). When the response variable was alteration in plasma levels of 25(OH)D relative to baseline levels, and baseline concentrations was re-coded into a dichotomous variable ([25(OH)D]< 37.5 nmol/l and [25(OH)D] ≥ 37.5 nmol/l), the plasma level change was significantly different between the two groups ($p=0.02$). As shown in Figure 3, the group with moderate deficiency had, on average, an increase, while subjects with 25(OH)D concentrations above 37.5 nmol/l showed a decrease. Furthermore, change in plasma level relative to baseline was significantly associated with BMI ($p<0.01$) (Figure 3). Subjects with a BMI < 25 kg/m^2 showed a mean increase in 25(OH)D levels at 4 hours and 5 days; by contrast, subjects with BMI ≥ 25 kg/m^2 exhibited mean decreases at 4 hours, 12 hours and 5 days. The observed difference in plasma 25(OH)D change between the two BMI groups did not depend on time (i.e., non-significant interaction term for BMI group and time). The amount consumed did not predict the post-meal levels in plasma 25(OH)D (calculated as the difference between the 5-day and baseline levels) when adjusting for 25(OH)D baseline levels (low vs. high) and BMI in the multivariate regression model ($p=0.17$).

DISCUSSION

The main finding in this study was a high prevalence of 25(OH)D levels in blood below recommended levels, especially among those not taking supplements. Further, the BMI and baseline plasma 25(OH) D concentrations determined the change in mean 25(OH)D levels in the blood after consumption of a single fish meal with cod liver and cod-liver oil as major components.

The vitamin D concentrations found in the present study were low for the majority of the participants and, thus, contradict the anecdotal assumption that vitamin D status in north Norway is satisfactory (5). Since sunshine exposure has been considered to be the main source of vitamin D, its status is known to drop during winter and improve during summer months (16-19). Lehtonen-Veromaa *et al* (7) found a prevalence of 25(OH)D levels ≤ 37.5 nmol/L in excess of sixty percent during winter, which reduced to less than two percent during the summer among 15-year-old Finnish girls in Turku, Southwest Finland. Vitamin D production in skin has been associated not only with the season, but also with latitude (2). Webb *et al* (3) found that, in Boston, USA (42°N), vitamin D production was curtailed from November to February, while in Edmonton, Canada (52°N), the photosynthesis of vitamin D ceased in October and did not occur again until April. This seasonal-latitude dependency of vitamin D production in the skin suggests that, in Tromsø, which is located at 69° north, the sun's role as a vitamin D source is limited to a few months of the year. Our study was carried out during the last part of the "vitamin D winter" (April). Thus, one would expect to observe the lowest vitamin D levels at this time of the year and our findings would, therefore, not necessarily constitute a valid measure of the yearly mean value. However, UVB radiation levels are also affected by the weather, and there is most likely a great variation in the contribution of the north Norwegian summers to vitamin D production from one year to another. The assumption that vitamin D status in north Norway is adequate, due to sufficient dietary intake and sufficient light during the summer months, is primarily based on one study conducted by Vik *et al* (15) in 1977/1978. In the latter study, blood samples were collected every two months throughout a year from seventeen laboratory workers at the University Hospital of Tromsø. The blood samples were analysed for 25(OH)D content and for several other characteristics as well. Subjects taking supplements were not included. The mean values for 25(OH)D for March (no data for April) found by Vik *et al* (15) did not differ significantly from those found in our study, when excluding the individuals reporting the use of supplements (mean=51.5 nmol/l, SD=19.5 v.s. mean=44.7, SD=20.4, p=0.30). However, Vieth and Carter (20) have warned against presenting only mean ± S.D. values when assessing changes in 25(OH)D levels. They suggested a statistic that highlights the prevalence of insufficiency. About 50 % of the participants in Vik and colleagues' study had values below 50 nmol/l. Based on their distribution pattern of serum 25(OH)D, it is estimated that nearly 40 % of the subjects had values below 37.5 nmol/l, with two subjects having values less than 20 nmol/l; the latter concentration defines severe hypovitaminosis D (8). The Vik *et al* (15) survey is commonly referred to, despite this high prevalence of insufficient vitamin D status and the small sample size. It has been used as an argument for the of an adequate vitamin D status in the northern Norwegian population. Their conclusion might have contributed to a neglect of potential nutritional and related health problems. To our knowledge, there has been no randomised population-based survey on 25(OH)D levels in north Norway. Although the participants in the present study constituted a select group (mainly academics), the results, when considered along with the data from the study by Vik and colleagues, suggest that the population in the North is at increased risk of vitamin D deficiency, especially during winter.

We found significantly higher levels of 25(OH)D in subjects using supplements compared to non-supplement users. The association between the use of supplements and the 25(OH)D blood concentration has been reported in several studies (8,21). Cod-liver oil was the most frequently used supplement. The use of cod-liver oil in Norway has been estimated to be 36.8 % and 33.9% for men and women, respectively (22). These numbers are in agreement with the present study, as 10 out of 33 participants used cod-liver oil supplements more than twice per week.

The correlation between the estimated daily vitamin D intake and 25(OH)D blood concentrations has been shown to be significant among subjects with low sun exposure (23,24). In our study, no such data was collected. However, the significant correlation between estimated daily intake and 25(OH)D blood concentrations supports the hypothesis that diet is the main contributor to vitamin D levels among people living at northern latitudes during winter. Our work emphasises the necessity of a sufficient dietary intake of vitamin D in circumpolar areas.

We found the change in 25(OH)D levels after ingestion of the "Mølje" meal to be associated with the BMI. An inverse association between the BMI and 25(OH)D in blood has been reported in other studies (16,25-27). Obesity has been considered to be an independent predictor of vitamin D deficiency (28). The reason for an increased risk of vitamin D deficiency in obese individuals remains unknown. However, it has been postulated by Bell *et al* (29) that obesity modifies the vitamin D endocrine pathways; this is attributed to a feedback inhibition by increased serum levels of the active metabolite 1,25$(OH)_2$D produced during the hepatic synthesis of 25(OH)D. It has also been suggested that the metabolic clearance of vitamin D may increase in obesity, possibly through an enhanced uptake by adipose tissue (30) related to the larger fat mass and the consequently larger pool size in obese individuals (16). In our study, the only vitamin D metabolite measured was 25(OH)D. Thus, a reduction in 25(OH)D caused by an increase in active vitamin D could not be assessed. However, the results from our work indicate that the BMI predicts the metabolic response to a meal rich in vitamin D.

The ingested dose of vitamin D from one "Mølje" meal was not sufficient to raise the 25(OH)D level for the group. The stability of the mean 25(OH)D concentrations could also be due to the low baseline 25(OH)D values. The 25(OH)D metabolite has been considered a marker of medium-to-long-term vitamin D availability. Bates *et al* (31) have suggested that when vitamin D supplements are given to individuals with vitamin D deficiency, 1,25$(OH)_2$D will rise rapidly to normal values, whereas 25(OH)D will remain low until a reserve accumulates. This was, however, not supported by our data showing that individuals with moderate vitamin D deficiency at baseline exhibited a relative increase in plasma 25(OH)D. This must be interpreted with caution, as this analysis is based on a small number of subjects (n=8). Wortsman *et al* (27) found that, after ingestion of 1.25 mg vitamin D, 25(OH)D rose rapidly until approximately 10 hours after intake, declining slightly thereafter. According to this, one would expect the blood collected after 12 hours to have levels closer to the peak level. However, in our study, the mean 25(OH)D levels measured at 12 hours were the lowest for both normal and overweight subjects. The mean ingested dose of vitamin D from the "Mølje" meal was less than six percent of the dose in the study by Wortsman *et al* (27), which suggests that one "Mølje" meal was not sufficient to generate a peak level of plasma 25(OH)D for the group.

In conclusion, one meal was not sufficient to change the overall vitamin D status of the study group, but repeated meals over time may be anticipated to have a beneficial effect. However, modest beneficial effects were noted for those with low baseline levels and for leaner individuals. The vitamin D status and related health outcomes in populations living in circumpolar areas require more research to investigate to what degree people are at increased risk for vitamin D insufficiency during the winter, and to elucidate further the role of the traditional diet in preventing deficiency. Emphasis should also be on the intensity of different wavelengths within the UVB spectra at high latitudes and its impact on vitamin D status.

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Paper II

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ORIGINAL COMMUNICATION

Predictors for cod-liver oil supplement use — the Norwegian Women and Cancer Study

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Objective: To assess the use of cod-liver oil supplements among Norwegian women and to examine dietary, lifestyle, demographic, and health factors associated with use of this supplement.
Design: Cross-sectional study.
Setting and subjects: The study is based on data from a food frequency questionnaire from 1998 answered by 37 226 women aged 41–55 y, who in 1991/1992 participated in the Norwegian component of the European Prospective Investigation into Cancer and Nutrition (EPIC). The Norwegian EPIC cohort was based on a random nation-wide sample of Norwegian women.
Results: Cod-liver oil supplement use was reported by 44.7% of the participating women. Subjects with higher education, high physical activity level, and body mass index (BMI) in the normal range were more likely to use cod-liver oil supplements. Consumption did also increase with increased age as well as with increased reported consumption of fruits, vegetables, fatty fish, lean fish, and vitamin D (excluding the vitamin D contribution from cod-liver oil). Energy intake was higher among cod-liver oil users than nonusers. Whole-year daily users of cod-liver oil were also more likely to take other dietary supplements (OR = 2.45, 95% CI: 2.28–2.62). Never smokers were more likely to use cod-liver oil supplements than current smokers.
Conclusion: Use of cod-liver oil is associated with several sociodemographic factors, self-reported health issues, and intake of fish, fruit, and vegetables. When assessing the relationship between cod-liver oil use and occurrence of chronic diseases potential confounders need to be considered. Cod-liver oil use seemed not to be matched with vitamin D needs. Thus, emphasis on assessing vitamin D status by measuring levels in blood should be investigated further, in particular, among people living in northern latitudes.
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Keywords: cod-liver oil; vitamin D; vitamin supplements; fish intake; Norwegian Women and Cancer Study (NOWAC)

Introduction

In Norway, consumption of dietary supplements is widespread. Surveys have shown that more than half of the female population and nearly 40% of the men use vitamin or mineral supplements (Johansson & Solvoll, 1999). Cod-liver oil has traditionally been consumed as part of the diet, in particular, by people living in northern coastal areas of Norway (Kloster, 1931). Recent dietary surveys have shown that cod-liver oil supplements were used by around 35% of the population in Norway and more than half of the eldest age group of the population surveyed (Johansson *et al*, 1997; Johansson & Solvoll, 1999). One dose of cod-liver oil supplement (5 ml) contains 500 μg vitamin A, 10 μg vitamin D, and 10 mg vitamin E as well as 1.2 g of n-3 fatty acids (Rimestad *et al*, 2001) (Cod-liver oil consumed as capsules provides equal amount of nutrients as 5 ml liquid cod-liver oil, provided that the recommended numbers of capsules are ingested).

Cod-liver oil has, in particular, been considered an important source of vitamin D. However, risk of insufficient vitamin D status in populations in Scandinavia because of low levels of vitamin D intake has been reported in several studies (Andersen *et al*, 1997; Johansson *et al*, 1997; Lehtonen Veromaa *et al*, 1999). To prevent vitamin D deficiency, fortification of food items has been used for decades in Scandinavia (Pedersen *et al*, 1995). In addition, the Norwegian National Council on Nutrition and Physical

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Activity has recommended daily consumption of cod-liver oil supplements, partly because of the suspected vulnerability to vitamin D deficiency in the Norwegian population in relation to low intake in the diet and limited exposure to sunshine, which is the main source of vitamin D (Webb & Holick, 1988). However, numerous surveys on predictors for dietary supplement use have shown that subjects with the highest nutrient intake are the most likely to take dietary supplements (Koplan *et al*, 1986; Slesinski *et al*, 1996; Frank *et al*, 2000; Dwyer *et al*, 2001; Troppmann *et al*, 2002). This suggests that the most likely consumers are less likely to need it, and *vice versa*.

The possible benefits and risks of use of various dietary supplements on health have been debated (Patterson *et al*, 1997; Maxwell, 1999). An important challenge in analysing and interpreting the relationship between diet and health is adjustment for several demographic and lifestyle factors that can influence apparent associations.

Several studies have shown that supplement taking has been associated with health-related factors such as age, gender, body mass index (BMI), socioeconomic status, physical activity, alcohol consumption, smoking, education, and diet (Slesinski *et al*, 1996; Lyle *et al*, 1998). Supplement users tend to have health behaviours associated with reduced risks of chronic diseases. By using information collected from the Norwegian European Prospective Investigation into Cancer and Nutrition (EPIC) cohort, the aim of this study was to assess the use of cod-liver oil supplements among Norwegian women and to examine dietary, lifestyle, demographic, and health factors associated with the use of this supplement.

Method

Subjects

The Norwegian EPIC cohort is a subsample of the Norwegian Women and Cancer Study (NOWAC). In 1991/1992, 81 000 women in Norway, randomly selected by the Central Bureau of Statistics Norway received a questionnaire on diet and other health-related issues. The questionnaire was answered and returned by 45 962 (crude response rate = 56.7%). In 1998 these women received a similar, but extended, questionnaire. Of the original 1991/1992 study respondents, 713 women had deceased or emigrated, leaving 45 249 who received this new questionnaire; 37 231 answered, giving a crude response rate of 82.3%. Subsequently, five women withdrew their informed consent. The current study is thus based on data from the 37 226 remaining women, that is, 46.4% of the original sample from 1991/1992. To test for possible selection bias, we compared the distribution of parity, age at first birth, and years of education between a subsample of 15 000 of the respondents and the total invited sample from 1991/1992, using national register data. No difference was found other than that the response rate increased with increased education (data not shown). Further, by using the answers from the 1991/1992 questionnaire, the distribution of data for the following variables were compared between the subjects who responded to the second questionnaire in 1998 and all who participated in 1991/1992: smoking, physical activity, geographic, perceived health, parity, BMI, marital status, education, and consumption of fatty fish (data not shown). Again, a selection bias related to education was found in addition to smoking, perceived health, and marital status.

Questionnaire

The subjects answered an eight page self-administered questionnaire, which included questions on height, weight, physical activity, smoking habits, diseases, perceived health, marital status, and diet. A revised version of the food frequency questionnaire described by Hjartaker and Lund (1998) constituted a major part of the questionnaire. This food frequency questionnaire was aimed to cover total diet; however, the main purpose was to assess consumption of marine foods. There were altogether 85 frequency questions on common food items consumed in Norway. The questions on cod-liver oil supplements were: 'do you use cod-liver oil supplements (liquid)?' and 'do you use cod-liver oil capsules?', with answering options 'yes' or 'no' for both. Further the subjects were asked to record how often they used cod-liver oil in either liquid or capsule form in relation to seasonal variation ('during winter' and 'rest of the year'). The frequency categories were as follows: 'seldom/never', 'one to three times per month', 'once per week', 'twice to six times per week', and 'daily'.

The food frequency questionnaire was equal to the one described by Hjartaker and Lund (1998) despite that the food items: juice, desserts, cakes, and salty snack were included. An evaluation of the part in the questionnaire covering marine foods against serum phospholipid fatty acid composition in 234 middle-aged women, showed significant correlations between calculated intake of n-3 fatty acids and serum phospholipid n-3 fatty acids. Cod-liver oil consumption was strongly related to the phospholipid n-3 fatty acid composition ($r = 0.46$, $P = < 0.001$) (Hjartaker *et al*, 1997).

Daily intake of energy and nutrients were computed based on the Norwegian Food Composition Table (Rimestad *et al*, 2001). The Central Bureau of Statistics Norway provided data on age and place of residence. Physical activity was recorded in the questionnaire on a scale ranging from 1 to 10 and collapsed into three categories 'low' (1–3), 'moderate' (4–7), and 'high' (8–10).

Cod-liver oil use

In the analysis, use of cod-liver oil was divided into four groups: nonusers, occasional users, daily users part of the year, and whole-year daily users. Subjects were classified as nonusers if they never took cod-liver oil, or did so less frequently than once a week (during winter and the rest of the year). 'Occasional users' were defined as subjects never taking cod-liver oil supplements daily, but using it between 1 and 6 days per week either during winter months or the rest of the year. 'Daily users part of the year' were defined as subjects taking cod-liver oil supplements daily during either summer or winter, and the 'whole-year daily users' constituted those taking cod-liver oil supplements daily both during winter and the rest of the year. In the analysis, no discrimination was made based on whether the cod-liver oil was consumed as capsules or in liquid form.

Exclusion criteria

Subjects with missing information on cod-liver oil supplement use were excluded from the analysis ($n=334$). In addition, 329 subjects were excluded from the analysis where variables on intake of food items and vitamin D were included. For these latter analyses, subjects were excluded if the estimated daily energy intake was ≥15 000 kJ ($n=43$), ≤2500 kJ ($n=163$), or the number of blank (unanswered) items in the food frequency questionnaire was ≥41 (50% of the total number of questions). When summarising the number of blank items, each of the frequency questions per food items was counted, with the exception of three questions each on different milk types and coffee; in this case they were merged into one. In total, 193 subjects had 41 or more blank items, of whom 70 subjects had daily energy intake estimated to be 2500 kJ or less.

Statistical analysis

SAS version 8.02 was used for nutrient calculations and statistical analysis. The relation between the use of cod-liver oil and selected variables was examined by applying a logistic regression model to calculate OR with corresponding 95% CI. The variables in the statistical model were selected based on dietary and lifestyle variables of interest. When analysing energy intake by cod-liver oil use, a linear regression analysis was performed where cod-liver oil use was recoded into a set of indicator variables, and nonusers were defined as reference group. The Kruskal–Wallis test was applied to compare dietary intake of vitamin D and intake of grams of vegetables, fruit, fatty- and lean fish, and fish products per day between different cod-liver oil use categories. A nonparametric method was required for these analyses, since the data were not normally distributed. The selected dietary variables were chosen because they can be considered to indicate a healthy diet, and intake of some of these food items are important sources of vitamin D. When assessing intake of vitamin D in the diet by cod-liver oil use, the recommended daily intake of 5 μg was chosen as the lower cut-off point and 50 μg was chosen as the upper limit according to the Nordic dietary recommendations (Sandström *et al*, 1996).

Results

Some characteristics of the study participants are presented in Table 1. The average age was 47.7 y (s.d. = 4.3). Average BMI, calculated from self-reported weight and height was 24.4 kg/m^2 (s.d. = 4.1). Three-quarters of the respondents were married and around 40% of them had more than 12 years of education.

Table 1 Characteristics of the study sample (n=36 882)[a]

Characteristics	n	%
Age (y)		
41–45	13 211	35.8
46–50	12 134	32.9
51–55	11 537	31.2
BMI (kg/m^2)		
<20	2854	7.9
20–24.9	20 404	56.4
25–29.9	9903	27.4
≥30	3010	8.3
Education (y)		
≤9	8128	22.3
10–12	13 220	36.3
>12	15 072	41.4
Marital status		
Married	26 685	74.6
Cohabitee	3342	9.3
Other	5750	16.1
Geographic		
Oslo region (capital city)	8035	21.8
East Norway	10 341	28.0
South coast	2009	5.4
West Norway	9136	24.8
Mid Norway	3199	8.7
North Norway	4162	11.3
Smoking		
Current	11 628	32.3
Ex	10 569	29.4
Never	13 743	38.3
Physical activity		
Low	4256	12.3
Moderate	26 024	75.0
High	4437	12.8
Perceived health		
Very good	11 895	33.5
Good	21 278	59.9
Poor	2336	6.6
Supplement use other than cod-liver oil		
Daily	14 235	40.2
Occasionally	16 233	13.9
Nonusers	4927	45.9

[a]Subgroups may not total 36 882 because of missing values.

Cod-liver oil use

Cod-liver oil supplements were taken by 44.7% ($n = 16481$) of the participating women. In total, 6046 (16.4%) used the supplement daily during the whole year, 6871 (18.6%) used it daily part of the year, and 3564 (9.7%) on an occasional basis. Of the cod-liver oil supplement takers (both daily and occasional), 7739 (47.0%) took it only during the winter, 8735 (53.0%) both in summer and winter, and 7 (<0.1%) only during the summer months.

Cod-liver oil use and various characteristics

The percentage distribution of selected health, demographic, and lifestyle variables with respect to cod-liver oil use is shown in Table 2. In Table 3, the results of a multivariate analysis of cod-liver oil use for these selected variables are presented. The OR are calculated relative to nonusers. The use of cod-liver oil increased with increased age. About 39% of the subjects who took cod-liver oil daily during the whole year were in the age group 51–55 compared to 29% of the

Table 2 Percentage distribution of different respondent characteristics for non-, occasional, daily, and whole-year daily users (n=36 882)[a]

Variable	*Nonusers* n=*20401*	*Occasional users* n=*3564*	*Daily users part of the year* n=*6871*	*Whole-year daily users* n=*6046*
Age (y)				
41–45	37.9	41.0	34.2	27.5
46–50	32.8	30.7	33.4	33.8
51–55	29.2	28.2	32.4	38.7
BMI (kg/m²)				
<20	7.5	8.5	7.8	9.0
20–24.9	53.3	60.3	60.3	60.1
25–29.5	29.2	25.2	25.8	24.3
≥30	10.0	6.1	6.1	6.5
Education (y)				
≤9	24.0	15.0	20.7	22.8
10–12	37.4	32.8	34.2	37.2
>12	38.6	52.2	45.2	40.1
Marital status				
Married	74.8	73.5	75.2	73.8
Cohabitee	9.4	9.2	9.1	9.4
Other	15.8	17.3	15.7	16.8
Geographic				
Oslo region (capital city)	19.8	24.2	23.4	25.3
East Norway	28.7	24.5	29.0	26.7
South coast	5.9	5.0	4.9	5.0
West Norway	25.3	25.9	22.2	25.2
Mid Norway	8.9	8.7	8.7	7.9
North Norway	11.4	11.7	11.9	9.9
Smoking				
Never	37.1	41.2	40.8	37.4
Current	34.4	27.7	29.2	31.7
Ex	28.5	31.1	29.9	31.0
Physical activity				
Low	14.0	10.5	9.9	10.0
Moderate	73.9	78.7	77.0	74.0
High	12.0	10.8	13.1	15.9
Perceived health				
Very good	32.7	34.8	35.1	33.6
Good	60.3	60.2	59.3	59.2
Poor	7.0	5.0	5.6	7.3
Supplements use (other than cod liver oil)				
Daily	36.1	25.0	42.9	60.5
Occasionally	12.2	34.4	14.6	7.0
Nonusers	51.7	40.6	42.6	32.5

[a]Subgroups may not total 36 882 because of missing values.

Table 3 Adjusted[a] odds ratios and 95% confidence limits for use of cod-lier oil supplements relatie to nonusers according to different characteristic ariables (n=36 882)[b]

Variable	Occasional users OR (95% CI)	Daily users part of the year OR (95% CI)	Whole-year daily users OR (95% CI)
Age (y)			
41–45	1.00	1.00	1.00
46–50	0.92 (0.83–1.02)	1.14 (1.06–1.23)	1.29 (1.19–1.40)
51–55	1.09 (0.99–1.21)	1.28 (1.19–1.38)	1.74 (1.61–1.88)
P for trend	*0.11*	*<0.001*	*<0.001*
BMI (kg/m²)			
<20	1.00	1.00	1.00
20–24.9	1.01 (0.87–1.17)	1.09 (0.97–1.23)	0.94 (0.84–1.06)
25–29.5	0.78 (0.66–0.91)	0.86 (0.76–0.97)	0.72 (0.63–0.82)
≥30	0.63 (0.51–0.78)	0.61 (0.52–0.72)	0.60 (0.51–0.71)
P for trend	*<0.001*	*<0.001*	*<0.001*
Education (y)			
≤9	1.00	1.00	1.00
10–12	1.34 (1.18–1.52)	1.08 (0.99–1.18)	1.07 (0.98–1.17)
>12	1.90 (1.68–2.14)	1.33 (1.22–1.45)	1.14 (1.04–1.25)
P for trend	*<0.001*	*<0.001*	*<0.001*
Marital status			
Married	1.00	1.00	1.00
Cohabitee	1.05 (0.91–1.21)	1.04 (0.94–1.16)	1.05 (0.94–1.18)
Other	1.14 (1.02–1.27)	0.99 (0.91–1.07)	1.00 (0.92–1.10)
Geographic			
Oslo region (Capital city)	1.00	1.00	1.00
South east	0.80 (0.72–0.90)	0.90 (0.82–0.98)	0.76 (0.69–0.83)
South coast	0.80 (0.66–0.97)	0.77 (0.66–0.89)	0.70 (0.60–0.82)
West	0.92 (0.82–1.03)	0.78 (0.72–0.86)	0.82 (0.74–0.90)
Trondelag	0.84 (0.71–0.99)	0.87 (0.77–0.98)	0.73 (0.63–0.83)
North Norway	1.01 (0.88–1.17)	0.97 (0.87–1.09)	0.70 (0.62–0.80)
Smoking			
Never	1.00	1.00	1.00
Current	0.78 (0.71–0.87)	0.84 (0.78–0.90)	1.00 (0.92–1.09)
Ex	1.05 (0.95–1.15)	1.00 (0.93–1.08)	1.15 (1.07–1.25)
Physical activity			
Low	1.00	1.00	1.00
Moderate	1.30 (1.14–1.48)	1.41 (1.28–1.57)	1.39 (1.24–1.55)
High	1.11 (0.93–1.33)	1.41 (1.23–1.61)	1.72 (1.50–1.97)
P for trend	*0.21*	*<0.001*	*<0.001*
Perceived health			
Very good	1.00	1.00	1.00
Good	1.08 (0.99–1.18)	1.05 (0.98–1.12)	1.10 (1.02–1.18)
Poor	0.98 (0.80–1.18)	0.96 (0.83–1.11)	1.27 (1.10–1.46)
P for trend	*0.32*	*0.61*	*0.001*
Supplements use (other than cod liver oil)			
Nonusers	1.00	1.00	1.00
Occasionally	3.19 (2.90–3.52)	1.35 (1.23–1.48)	0.83 (0.73–0.95)
Daily	0.80 (0.73–0.89)	1.36 (1.27–1.45)	2.45 (2.28–2.62)

[a]All variables were mutually adjusted for each other.
[b]Subgroups may not total 36 882 because of missing values.

nonusers (Table 2). Quantitatively, the subjects in the eldest age group had a 1.7 times higher odds to be daily users the whole year, compared to the youngest age group (Table 3). For all three user categories, consumption decreased significantly with increased BMI (P-value for trend >0.001). As indicated in Table 2, 39.2% of the nonusers had BMI ≥ 25 compared to around 30% of the cod-liver oil users. Cod-liver use was more common among subjects with higher education. This was more pronounced in the occasional user category, where subjects with higher education (> 12 y) had a OR = 1.9 (95% CI: 1.68–2.14) for taking cod-liver oil supplements compared to subjects with the lowest level of education (≤9 y). Cod-liver oil use seemed to be independent of marital status (Table 3). In the multivariate model, subjects living in northern Norway and in the Oslo region (capital of Norway) had similar odds for using cod-liver oil for both occasional and daily use part of the year. Daily use the whole year was more common in Oslo than any other part of Norway. Current smokers were less likely to use cod-liver oil supplements occasionally or daily part of the year compared to never smokers (OR = 0.78, 95% CI: 0.71–0.87 and OR = 0.84, 95% CI: 0.78–0.90, respectively; Table 3). Ex-smokers were more likely to be daily users the whole year, compared to never smokers (OR = 1.15, 95% CI: 1.07–1.25). Cod-liver oil supplement use increased significantly with increased physical activity level. The subjects with high physical activity had a 1.7 times higher odds to take cod-liver oil the whole year, compared to those reporting low physical activity level (Table 3). Subjects reporting their perceived health to be poor were more likely to be daily users the whole year (OR = 1.27, 95% CI: 1.10–1.46), compared to subjects considering their health to be very good. To further address this issue, intake was compared for nonusers *vs* users (sum of all user categories). In this model OR for 'good health' and 'poor health' compared to 'very good health' were 1.07 (1.02–1.13) and 1.09 (0.98–1.21), respectively (data not reported in Table 3). Daily users of other dietary supplements had an OR of 2.5 of also being cod-liver oil users the whole year, compared to nonusers of dietary supplements other than cod-liver oil (Table 3). Occasional users of food supplements other than cod-liver oil had an OR of 3.2 to be occasional users of cod-liver oil compared to nonusers of dietary supplements.

Cod-liver oil use and diet

Table 4 summarises cod-liver oil use in relation to various dietary variables. Total energy intake was higher among cod-liver oil users than nonusers when adjusting for physical activity in a linear regression model ($P<0.001$). Intake of fatty fish, lean fish, vegetables, and fruits increased by increased cod-liver oil consumption. This was also the case summing the consumption of total potatoes, vegetables, fruits, and juice. The same pattern was found when adjusting for total energy (data not shown), except for 'total fish and fish products' where no difference between cod-liver oil use groups was found. Consumption of total fish and fish products was higher among cod-liver oil users compared to nonusers, but among the cod-liver oil users intake was similar in the different user categories. When stratifying the data by age group, increased food intake by cod-liver oil use was found in all age strata and the Kruskal–Wallis test was highly significant for all food items (data not shown).

Daily vitamin D intake in the diet was significantly higher for the cod-liver oil users than nonusers both when adjusting for total energy and not (data for energy adjusted figures are not shown in Table 5). This was also the case when the vitamin D contribution from the cod-liver oil supplement was subtracted (Table 5). When excluding vitamin D contribution from the cod-liver oil supplements, the proportion of subjects with daily intake of vitamin D in the diet below the recommended 5 μg was nearly 40% in the nonuser group compared to around 30% among the cod-liver oil users. Very few had a vitamin D intake above 50 μg. When vitamin contribution from cod-liver oil was included, the proportion of subjects with intake above the upper limit of 50 μg was the highest (0.5%) among subjects using cod-liver oil daily for the whole year.

Discussion

The main findings in this study were that cod-liver oil users had higher intake of some foods (fish, vegetables, fruits) and higher intake of energy and vitamin D than nonusers. Further, users seemed to report a healthier lifestyle than nonusers.

Our study has several important methodological features. Firstly, the analysis were based on a large nationwide random selected study sample. Secondly, the comprehensive questionnaire applied in the survey provided data on many

Table 4 Daily intake of energy and selected food items by cod-liver oil supplement use (n=36 553)[a]

Food items	*Non-users n=20174*	*Occasional users n=3551*	*Daily users part of the year n=6825*	*Whole-year daily users n=6003*	*P-value[b] unadjusted*
Total energy [c] (kJ) (s.d.)	6802 (1793)	7272 (1783)	7295 (1795)	7257 (1854)	<0.001[d]
Fatty fish (g)	13	16	16	17	<0.001
Lean fish (g)	26	28	30	30	<0.001
Fish and fish products (g)	29	32	32	32	<0.001
Vegetables (g)	103	112	116	121	<0.001
Fruits (g)	119	129	144	152	<0.001
Total potatoes, vegetables, fruits, jam, and juice (g)	401	425	454	469	<0.001

[a]Results are given as median values.
[b]Kruskal–Wallis test.
[c]Values are mean.
[d]Regression model adjusted for physical activity.

Table 5 Daily vitamin D intake by cod-liver oil supplement use (*n*=36 553)

Daily vitamin D intake	*Non-users* n=*20174*	*Occasional users* n=*3551*	*Daily users part of the year* n=*6825*	*Whole-year daily users* n=*6003*	P-*value*[a]
Vitamin D (μg/d[b]) (vitamin contribution from cod-liver oil supplements excluded)	5.9	6.5	6.6	6.7	<0.001
Vitamin D (μg/d [b]) (vitamin contribution from cod-liver oil supplements included)	5.9	10.2	14.3	19.8	<0.001
Proportion below 5 μg vitamin D/day % (vitamin contribution from cod-liver oil supplements excluded)	39.3	30.8	31.6	31.4	
Proportion below 5 μg vitamin D/day % (vitamin contribution from cod-liver oil supplements included)	39.1	11.7	7.3	8.0	

[a]Kruskal–Wallis test.
[b]Figures are median.

lifestyle-, demographic-, and health-related issues that could be taken into account in the analysis. Thirdly, the food frequency questionnaire data, aiming at covering total diet, made it possible to use usual daily intake of both food items and nutrients as independent variables in the analysis. Fourthly, the data on cod-liver oil supplement use was detailed and contained information on both frequency and seasonal variation. Further, these questionnaire data on marine foods, including cod-liver oil, have been independently validated and were shown to be satisfactory (Hjartaker *et al*, 1997).

The comparison of the study sample and source population with respect to selected characteristics supports the external validity of the results. However, the sample in this study was characterised by increased response rate by increased education level. Since education level significantly predicted cod-liver oil use, it is likely that the prevalence of use was higher than in the population from which the study sample was drawn. The average cod-liver oil use found in this study was slightly higher than what has been reported previously for the Norwegian population (Johansson & Solvoll, 1999). However, our findings were in agreement with surveys done on Norwegian women corresponding to the same age group (Hjartaker & Lund, 1998). We assume that there is no reason to believe that pattern of use differed between responders and non responders with respect to other variables that could not be included in the comparison test. Thus, to generalise the findings to the female population aged 40 – 55 y in Norway seems reasonable.

Daily consumption seemed to be the main pattern for cod-liver oil use, since more than three-quarter of the users took it on a daily basis. Nearly half of the daily users took it both in summer and winter, which is in line with the recommendations by the Norwegian National Council on Nutrition and Physical Activity (Press release, 17.09.93).

Messerer *et al* (2001a) have shown that during the last two decades there has been a dramatical increase in the prevalence of dietary supplement use among both men and women. One limitation in our study is that we have no data on time trends. However, when considering production of cod-liver oil, the figures correspond to a supply of 0.3 g per person per day throughout the period 1959–1990, and dietary surveys during 1963–1983 have shown that only 10% of the adult population took cod-liver oil supplement regularly (Johansson *et al*, 1996). Thus, this might indicate relatively stable consumption in this period followed by an increase in the last decade since studies from the 1990s have reported that more than 30% of the population use cod-liver oil supplement (Johansson *et al*, 1997; Hjartaker & Lund, 1998; Johansson & Solvoll, 1999).

The results from our study were in agreement with other studies regarding the association of cod-liver oil supplement use and age, BMI, smoking, and diet (Hjartaker & Lund, 1998; Johansson *et al*, 1998; Egeland *et al*, 2001). Further, our findings support previous studies in which predictors for dietary supplement use have been assessed. Several studies have found that subjects who take dietary supplements also are more likely to have a higher micronutrient intake from food (Koplan *et al*, 1986; Dorant *et al*, 1993; Slesinski *et al*, 1996; Kaartinen *et al*, 1997; Lyle *et al*, 1998; Dwyer *et al*, 2001). In a national dietary survey, Johansson *et al* (1998) found that cod-liver oil contributed 33% of the total intake of very long-chain n-3 fatty acids. They also found that men and women in the highest quartile of intake of these fatty acids had 3 to 4-fold higher intake of retinol and vitamin D, as well as 20–50% higher intake of fruits and vegetables, dietary fibre, and vitamin C. This supports our findings that cod-liver oil use is associated with healthy dietary habits. In contrast, Troppmann *et al* (2002) did not find supplement users to have better dietary habits than nonusers. However, their study was based on single 24-h recalls. Further, in their analysis the study sample was divided into subgroups with a rather small number of subjects in each, thus impairing the ability to detect a difference.

The observed relationship between consumption of fish and use of cod-liver oil supplement in the present study has been found by others (Egeland *et al*, 2001), as well as the association between consumption of fruits and vegetables and use of other dietary supplements (Frank *et al*, 2000).

Supplement use has previously been associated with physical activity, in line with what we observed (Lyle *et al*, 1998; Messerer *et al*, 2001b). Further, total energy intake from the diet was highest among the cod-liver oil users. This might be explained by increased energy demand due to higher activity level. By contrast, this difference in energy intake could not explain increased intake of fatty fish, lean fish, fruits, vegetables, and vitamin D with increased intake of cod-liver oil found in our study; intake of total fish and fish products was the exception.

The finding that a large proportion had vitamin D daily intake below that recommended (Table 5) cannot be interpreted to signify that subjects do not have their vitamin D needs met. This is so because the recommended level has been selected as two standard deviations above the mean physical need for a group (Sandström *et al*, 1996). On the other hand, the figures support the findings of lower vitamin D levels in the diet among subjects not using cod-liver oil compared to subjects taking it. The proportion of subjects having an intake above the upper limit of intake was small. However, subjects taking cod-liver oil were also more likely to use other dietary supplements, but nutrients from these products were not included in the nutrient analysis. Thus, the true vitamin intake for the cod-liver oil users and the proportion above tolerable limit were most likely higher than estimated.

The relationship between intake of dietary supplements and education level has been reported in other studies (Slesinski *et al*, 1996; Ervin *et al*, 1999; Balluz *et al*, 2000; Egeland *et al*, 2001). Observations on the relationship between subjective health and use of dietary supplement have been contradictory. In our study, we observed a small, but significant, decrease in cod-liver oil use with poorer perceived health only for whole-year daily users. For the other user categories, perceived health did not predict use. Messerer *et al* (2001b) found that men who reported excellent health ate less supplements than those who reported poor health. However, this association was weaker among women. By contrast, Ervin *et al* (1999) found that self-reported health status was positively related to supplement use. Our finding might imply that the tendency to polarisation to either no use or use every day of the year becomes more obvious among those who reported poor health. When replacing frequency of consumption with dichotomous responses (yes/no), subjects who reported their health to be good were more likely to use cod-liver oil supplements.

The geographic differences showed that subjects living in Oslo (the capital of Norway) were more likely to take cod-liver oil. Similar observations have been reported in Sweden, where dietary supplement users were more likely to live in Stockholm (Messerer *et al*, 2001b), although this difference disappeared after adjusting for age. Since we adjusted for age in the multivariate analysis, this probably does not explain our findings. It could, however, reflect a selection bias due to a higher proportion of diet and health conscious subjects recruited from the Oslo region compared to the smaller cities or rural areas.

The most obvious predictor for cod-liver oil use was use of other dietary supplements. This supports the assumption that those consuming cod-liver oil also get more nutrients from other sources.

The main argument for the recommendation of The Norwegian National Council on Nutrition and Physical Activity for cod-liver oil supplements is the risk of vitamin D deficiency in populations living in northern areas. However, the pattern in cod-liver oil use observed indicates that it tends to be indiscriminate and not matched to needs. Those who most likely have their vitamin D requirements met through food intake, were significantly more likely to take cod-liver oil as well. It has been suggested that this pattern of supplement use demonstrates a gap between possible need and actual use (Bristow *et al*, 1997). Cod-liver oil was, historically an important source of fat-soluble vitamins in particular vitamin D, especially for people living in the coastal areas (Kloster, 1931; Brustad *et al*, 2003). Our findings suggest that the pattern of use today is associated with factors other than dietary needs.

In conclusion, a substantial proportion of Norwegian women take cod-liver oil supplements. Predictors for cod-liver oil use are similar to those found for consumption of other dietary supplements. Use of cod-liver oil is associated with several sociodemographic factors and self-reported health issues, and intake of some foods. When assessing the relationship between cod-liver oil use and occurrence of chronic diseases, these potential confounders need to be considered. Cod-liver oil use seemed not to be matched with vitamin D needs. Assessment of vitamin D status by measuring its level in blood seems worthy of investigation, in particular among people living in northern latitudes.

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Paper III

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Vitamin D status of middle-aged women at 65–71°N in relation to dietary intake and exposure to ultraviolet radiation

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Abstract
Objective: To determine the vitamin D status of middle-aged women living in the Norwegian arctic and its relationship with vitamin D intake and exposure to ultraviolet (UV) radiation.
Design: Cross-sectional study.
Subjects and setting: This study is based on measurements of 25-hydroxyvitamin D (25(OH)D) levels in a sub-sample of the Norwegian component of the EPIC biological bank, which consists of blood samples from a random selection of participants in the Norwegian Women and Cancer Study. From November 2001 until June 2002, 309 blood samples were collected from a total of 443 invited middle-aged women (44–59 years) in northern Norway (65–71°N) (crude response rate, 69.8%). Questionnaire data provided information on dietary sources of vitamin D and UV exposure.
Results: Median plasma 25(OH)D concentration for the whole group was 55.0 nmol l^{-1} (range 8.1–142.8 nmol l^{-1}). Vitamin D intake was a significant predictor of 25(OH)D status ($P = 0.0003$). The time of the year when the blood sample was collected significantly predicted plasma 25(OH)D level ($P = 0.005$). Levels of 25(OH)D were positively associated ($P = 0.0002$) with estimated hours per day of exposure to UV-B radiation. Residing in northern Norway during the summer prior to blood sampling was negatively associated with 25(OH)D concentration ($P = 0.001$). The prevalence of moderate hypovitaminosis D was highest in January–February, when a quarter of the participants had 25(OH)D concentrations ≤ 37.5 nmol l^{-1}.
Conclusions: Increased ingestion of marine food items that provide vitamin D should be promoted and further studies should be carried out to investigate vitamin D status in arctic populations in relation to both UV exposure and traditional food sources.

Keywords
Vitamin D status
UV-B exposure
Arctic diet
Arctic health
'Vitamin D winter'

Vitamin D is essential for natural bone metabolism and for calcium and phosphorus homeostasis[1]. It is obtained either from the skin upon exposure to ultraviolet (UV) radiation or through dietary sources. Fatty fish, fish liver, cod-liver oil, egg yolk and mushrooms contain vitamin D, as do fortified foods like milk, butter and margarine. Since natural sources of vitamin D are limited, UV exposure has long been recognised as the principal source of vitamin D_3 for humans[2]. However, dramatic influences of seasonal and latitudinal changes of solar UV-B radiation on vitamin D_3 synthesis have been demonstrated by Webb *et al.*[3]. Below a certain threshold of UV radiation, corresponding to cloudless conditions in Boston, USA (43°N) in mid-February, no photoconversion of provitamin D to previtamin D was detected[3]. Because of this seasonal variation in UV-B radiation, cutaneous vitamin D production is absent during part of the winter and the length of the 'vitamin D winter' increases with latitude.

In northern Norway (65–71°N) the sun is below the horizon for up to 2 months during the winter. Owing to this high latitude and limited exposure to sunshine, the population living in this area is likely to be dependent on dietary sources of vitamin D to meet their biological needs during a considerable part of the year. Historically, high amounts of fish liver and fresh fish-liver oil were consumed among people who lived in the northern coastal areas of Norway[4]. The fish liver eaten was mainly from cod and saithe, and consumption followed their seasonal harvests. The season for cod liver was connected with the spawning time, starting around mid-December and lasting until April. Saithe liver was consumed from late summer until September/October. Studies from the first part of the 20th century showed that this food, which is rich in fat-soluble vitamins, constituted the most important source of vitamin D and prevented rickets in the coastal population[5]. Even though there still are areas where fish

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liver is consumed frequently[4], fatty fish and fortified margarine are today considered the main dietary sources of vitamin D in the Norwegian population[6].

In recent years some epidemiological studies have found high prevalences of hypovitaminosis in the Nordic countries[7–10]. Only two studies have examined determinants for vitamin D status in northern Norway[11,12] and both were based on small sample sizes (17 and seven subjects, respectively). To our knowledge, no previous population-based assessment of vitamin D status with random sampling, where both UV exposure and intake have been accounted for, has been conducted in arctic regions of Norway or corresponding latitudes.

Circulating 25-hydroxyvitamin D (25(OH)D) is considered the most sensitive clinical marker for determining nutritional vitamin D status[13]. A plasma 25(OH)D concentration of $\leq 37.5\,\mathrm{nmol\,l^{-1}}$ has been used as an indicator for moderate hypovitaminosis D[14] and 25(OH)D concentration $> 50\,\mathrm{nmol\,l^{-1}}$ has been suggested as the recommended level[15,16].

The aim of this study was to investigate the vitamin D status of middle-aged women living in northern Norway (65–71°N) by determining 25(OH)D levels in blood plasma and assessing its relationship with vitamin D intake and UV exposure.

Method

Study sample

Subjects were recruited from the northern contingent of the Norwegian EPIC (European Prospective Investigation into Cancer and Nutrition) cohort, which has been described in detail elsewhere[17]. In short, the Norwegian EPIC cohort is a sub-sample of the nation-wide Norwegian Women and Cancer Study (NOWAC) consisting of 37 231 participants who, in 1991/1992 and 1998, answered and returned questionnaires regarding lifestyle and health. By random selection, 20 696 of these women were contacted by mail and asked to give blood samples to be included in the EPIC biological bank. These requests were sent out in batches from October 2000 until June 2002. During the period from November 2001 to June 2002, all participating women living in northern Norway were also asked to give an additional blood specimen for vitamin D determination. The blood specimens were collected at local health centres into vacutainer tubes 4.5 ml blue top; Becton-Dickinson, Plymouth, UK containing sodium citrate (3.2%) and returned by mail to the University of Tromsø, northern Norway. A total of 443 subjects were contacted, of whom 309 responded (response rate, 69.8%). Nine of these blood samples could not be used for analysis, leaving 300 subjects for this study.

Questionnaire

The participating subjects answered a two-page questionnaire covering various aspects of UV exposure including solarium use and dietary sources of vitamin D, including the consumption of cod and saithe liver, fresh fish-liver oil, vitamin D-fortified milk and butter/margarine, cod-liver oil supplements, dietary supplements and fatty fish. The questions on fatty fish and cod-liver oil supplements were equal to the questions applied in the NOWAC questionnaire, which has been evaluated and showed a significant correlation between data on n–3 fatty acids intake and phospholipid n–3 fatty acids in serum[18]. In the questions that focused on UV exposure, participants were asked to recall the number of hours they had spent in daylight last week (the week prior to collection of the blood sample), whether they had resided in northern Norway during the whole of summer 2001 (June–August, the summer prior to collection of the blood sample), whether they had been on a sun holiday abroad since September 2001, and whether they had used a solarium during the past month. In the questions regarding fish liver, the participants were asked to recall how often they had consumed cod and saithe liver separately during the 'fish-liver season'.

Determination of 25-hydroxyvitamin D

Blood plasma was collected and kept at −80°C until analysis for 25(OH)D according to a modified version of the method described by Aksnes[19]. Briefly, 0.25 ml plasma samples were spiked with ^{3}H-25(OH)D_3 (for calculation of recovery), and 25(OH)D was extracted with methanol and n-hexane. The n-hexane phase was collected, evaporated to dryness and injected into a reverse-phase high-performance liquid chromatography system. Elution of 25(OH)D was performed with methanol/water (85:15, v/v) and the eluate was monitored at 265 nm by a diode-array detector (UV6000; ThermoFinnigan, San Jose, CA, USA) equipped with a 5 cm detector cuvette. The mean recovery of 25(OH)D was 77.2% (standard deviation (SD) 3.9%) and the interassay variation was 6%, with a detection limit of $6.0\,\mathrm{nmol\,l^{-1}}$. The method determined the sum of 25(OH)D_2 and 25(OH)D_3.

Biological effective UV dose rate

Based on the work by Webb *et al.*[3] and MacLaughlin *et al.*[20], we established a biological effective UV dose rate (BED) for photoconversion of 7-dehydrocholesterol (7-DHC) to previtamin D in skin. Webb *et al.*[3] found no detectable photoconversion of 7-DHC to previtamin D for mid-February and a small production of previtamin D at mid-March. For mid-February in Boston USA, they measured surface irradiances of 0.024, 1.0 and $10\,\mathrm{mW\,m^{-2}\,nm^{-1}}$ with an Optronics 742 spectroradiometer at wavelengths of 300, 306 and 316 nm, respectively. The BED was established by adding the measured surface irradiances weighted by the relative efficiencies for converting 7-DHC to previtamin D_3. The weights are 0.92, 0.45 and 0 for 300, 306 and 316 nm, respectively[3,20]. Below the threshold $BED_{threshold} = 0.024 \times 0.92 + 1.0 \times 0.45 = 0.472$

we assumed that no photoconversion to previtamin D took place. For each day in the period November 2001 to June 2002, we simulated the maximum BED and the amount of time the BED exceeded the UV radiation threshold for vitamin D production described above for all municipalities in northern Norway. We applied the fast yet accurate UV simulation tool FastRT to simulate surface irradiances at 300 and 306 nm as would be measured by a spectroradiometer with an Optronics 742 spectral response function (http://zardoz.nilu.no/~olaeng/fastrt/fastrt.html). The ozone layer thickness was fixed at a typical level (300 Dobson Units). Clouds, altitude and snow were not accounted for in the simulations.

Statistical analysis

SAS version 8.02 (SAS Institute, Cary NC, USA) was used for nutrient calculations and statistical analysis. To assess predictors for plasma 25(OH)D level, general linear models were used. In these analyses the dependent variable 25(OH)D was log-transformed since it was not normally distributed. Daily vitamin D intake was calculated based on the Norwegian Food Composition Table[21] and on vitamin D determination of boiled fish liver and fresh fish-liver oil[4]. Dietary supplements, except for cod-liver oil, were not included in the estimation of daily vitamin D intake owing to limited information on nutrient content in the various products used, but instead were treated as a dichotomous variable. Subjects who reported that they had been on a sun holiday abroad or had used a solarium were excluded from some of the analyses in order to focus on predictors for vitamin D security at high latitudes. A variable named 'UV-hours', representing hours per day with exposure to UV radiation above the threshold for vitamin D production in skin, was devised. It combined questionnaire data on reported hours spent in daylight the week prior to the blood sampling with information on total hours when the simulated BED was above 0.472 (estimated threshold value for photoconversion of vitamin D). For each woman, the quantity was identical to the reported hours spent in daylight the week prior to the blood sampling. However, the time was not allowed to exceed the total hours at which vitamin D production could occur at a participant's geographical location (municipality) in the week the blood sample was collected. For missing values on hours spent in daylight, the 'UV-hours' variable was treated as missing except for women whose blood samples were drawn when BED < 0.472. For the latter, the 'UV-hours' variable was coded as zero. The variable for time of the year when the blood specimen was collected was separated into four 2-month categories. In the season-stratified analysis, only three groups were examined, since November–February were collapsed into a single dark season. The model's ability to explain the variation in plasma 25(OH)D level is given by the adjusted coefficient of determination (R^2_{adj}, adjusted for the number of degrees of freedom). When selecting independent variables to be included in each statistical model, the variance inflation factor (VIF) was applied to determine if collinearity was present. In the statistical tests, the 5% significance level (two-sided) was chosen.

Results

Some characteristics of the study sample are summarised in Table 1. The participants' age ranged from 44 to 59 years. The 5th, 10th, 90th and 95th percentiles for daily vitamin D intake were 0.95, 1.6, 16.9 and 22.8 μg, respectively. The median vitamin D intake among subjects with 25(OH)D concentrations ≥37.5 and <37.5 nmol l^{-1} was 6.8 and 3.2 μg day^{-1}, respectively (Table 2). The main dietary sources of vitamin D were salmon/trout (30.2%), cod-liver oil supplements (23.4%), margarine/butter on bread (23.0%), and fish liver and fresh fish-liver oil (9.4%). There was no significant difference in calculated vitamin D intake by calendar month the women were recruited into the study ($P = 0.46$, Kruskal–Wallis test).

For nearly half of the subjects (45.7%), the 'UV-hours' metric was zero. Among the women who participated in November–February, 23.8% had been on a sun holiday or had used a solarium; this was the case for 34.3% of the

Table 1 Descriptive characteristics of the study sample ($n = 300$)*

Characteristic	Mean (SD) or *n*	Median or %
Age (years)	51.6 (4.2)	51.6
Body mass index (kg m^{-2})	25.1 (3.8)	24.4
Dietary vitamin D intake (μg day^{-1})†	8.1 (7.0)	6.2
Hours in daylight last week prior to blood sampling	10.8 (11.8)	7.0
Latitude		
65–67°N	105	35
68–69°N	153	51
70–71°N	42	14
UV-hours (h day^{-1})		
0	127	46
0.1–1.0	48	17
1.1–2.0	44	16
2.1 +	59	21
Cod-liver oil supplement users (once per week or more)	120	40
Fish liver (cod or saithe) consumption (twice per season or more)	176	59
Sun holiday	51	17
Solarium use	45	15
Dietary supplements other than cod-liver oil	171	58
Residing in northern Norway during the previous summer	157	53

SD – standard deviation.
* Subgroups may not total to 300 due to missing values.
† Contribution to vitamin D from dietary supplements except cod-liver oil was not included.

Table 2 Selected characteristics of the study sample by plasma 25-hydroxyvitamin D (25(OH)D) concentration ($n = 300$)

	Plasma 25(OH)D ($nmol\,l^{-1}$)		
Characteristic	<37.5 ($n = 41$)	≥37.5 ($n = 259$)	*P*-value
Age (years), mean	51.0	51.7	0.09
Body mass index ($kg\,m^{-2}$), mean	26.2	24.9	0.13
Dietary vitamin D intake ($\mu g\,day^{-1}$), median	3.2	6.8	<0.0001*
Hours in daylight last week prior to blood sampling, mean	8.2	11.3	0.08
Latitude (°N), mean	67.9	67.8	0.91
UV-hours ($h\,day^{-1}$), median	0.0	0.57	0.02*

* Wilcoxon two-sample test.

subjects enrolled in March–June. Only 2% of the subjects had been both to a solarium and on a sun holiday.

The median 25(OH)D concentration for the whole group was 55.0 (range 8.1–142.8) $nmol\,l^{-1}$ (Table 3). The prevalence of subjects with 25(OH)D concentrations below 37.5 $nmol\,l^{-1}$ was 13.7%. When excluding subjects who had been on a sun holiday abroad or to a solarium (90 subjects in total), 16.4% had 25(OH)D levels below 37.5 $nmol\,l^{-1}$ and the mean plasma concentration of 25(OH)D dropped to 53.1 (SD 17.6) $nmol\,l^{-1}$, which is significantly lower ($P = 0.03$, Student's *t*-test) than the mean for the whole group. The median 25(OH)D concentration for the subjects with no sun holiday/solarium and no 'UV-hours' ($n = 97$) was 45.9 $nmol\,l^{-1}$. Table 3 also presents plasma 25(OH)D levels by different time intervals for the blood sampling. The prevalence of moderate hypovitaminosis D was highest in January–February, at 23.3%. In March–April the prevalence was around a third of the January–February level. When excluding subjects who had been to a solarium or on a sun holiday, in January–February about a quarter of the subjects had 25(OH)D concentrations below 37.5 $nmol\,l^{-1}$ and almost two-thirds had levels below 50 $nmol\,l^{-1}$.

The adjusted mean values of 25(OH)D concentration in relation to daily duration of vitamin D-productive light ('UV-hours') increased up to 1.1–2.0 UV-hours per day and then seemed to level off (Fig. 1).

As denoted in Table 4, in the multiple linear regression model including all subjects significant predictors for variation in 25(OH)D level were age, dietary vitamin D intake, time of year when the blood sample was collected, sun holiday, solarium use and residing in northern Norway the summer prior to the blood sampling. When stratifying the analysis by subjects who had been on a sun holiday or to a solarium and those who had not, only age was significantly associated for the sun holiday/solarium use group ($P = 0.01$). For the no sun holiday/no solarium use group, dietary vitamin D intake, time of year when the blood sample was collected and residing in northern Norway during the previous summer were highly significant. In further analysis where subjects who had been on a sun holiday or used a solarium were excluded, dietary vitamin D intake was significantly associated with plasma 25(OH)D concentrations throughout the whole time period, but most significantly in November–February ($P = 0.006$) (Table 4). The variable 'residing in northern Norway during the previous summer' significantly predicted 25(OH)D levels in blood in the November–February strata ($P = 0.05$).

When the variables 'hours in daylight last week prior to blood sampling', 'latitude' and 'time of year when the blood sample was collected' (Table 4) were substituted by the variable 'UV-hours', the latter was strongly associated with plasma 25(OH)D concentration for both the whole group ($P = 0.0002$) and the no sun holiday/no solarium use stratum ($P = 0.0002$) (Table 5). However, for subjects who had been on a sun holiday or to a solarium, 'UV-hours' was not significantly associated ($P = 0.64$) with plasma 25(OH)D level. For the no sun holiday/no solarium use group, dietary intake of vitamin D as a

Table 3 Distribution of vitamin D measures in the study sample through the 8-month period ($n = 300$)

	All ($n = 300$)	November–December ($n = 36$)	January–February ($n = 86$)	March–April ($n = 111$)	May–June ($n = 67$)
25(OH)D concentration ($nmol\,l^{-1}$)					
Mean (SD)	56.9 (18.8)	52.8 (16.0)	49.5 (15.6)	60.8 (18.4)	61.9 (21.5)
Median (range)	55.0 (8.1–142.8)	51.7 (22.6–100.1)	46.9 (26.2–98.3)	60.6 (8.1–125.4)	60.8 (22.6–142.8)
25(OH)D below 37.5 $nmol\,l^{-1}$ (%)	13.7	13.9	23.3	8.1	10.5
Exclusion of subjects with solarium use or sun holiday	16.4	19.2	25.4	8.6	14.0
25(OH)D below 50.0 $nmol\,l^{-1}$ (%)	38.0	44.4	58.1	24.3	31.3
Exclusion of subjects with solarium use or sun holiday	46.4	57.7	65.7	28.6	39.5

25(OH)D – 25-hydroxyvitamin D; SD – standard deviation.

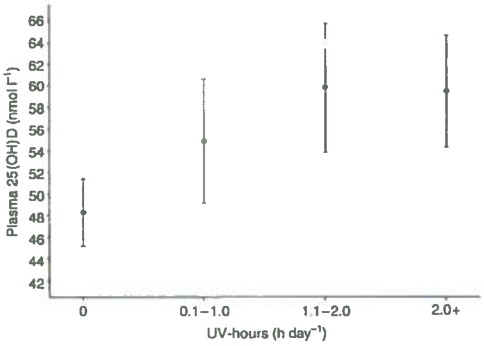

Fig. 1 Adjusted mean values (bars, 95% confidence interval) for plasma 25-hydroxyvitamin D (25(OH)D) by UV-hours (adjusted for age, body mass index, vitamin D intake, use of supplements and residing in northern Norway during the previous summer)

determinant of plasma vitamin D was highly significant when 'UV-hours' was used in the model ($P < 0.0001$). The same was found when looking at the subgroup of women with zero UV-hours and no sun holiday/no solarium use (data not shown).

To assess the association between plasma 25(OH)D and vitamin D contributions from fish-liver oil supplements and fish liver and fresh fish-liver oil separately, the variable 'total vitamin D intake' was split into three categories: 'vitamin D from cod-liver oil supplements', 'vitamin D from fish liver and fresh fish-liver oil' and 'vitamin D from all other sources'. These variables were then included as independent variables in the regression model to assess determinants for plasma 25(OH)D concentration together with age, body mass index, use of dietary supplements, UV-hours and whether or not residing in northern Norway the whole summer prior to blood sampling. This model explained 24% of the variance in plasma 25(OH)D concentration. Dietary vitamin D intake from fish liver and fresh fish-liver oil was positively associated with plasma 25(OH)D concentration, but of borderline significance ($P = 0.06$). The contributions from cod-liver oil supplements and from all other vitamin D sources were positively associated with 25(OH)D ($P = 0.0009$ and 0.02, respectively). (No collinearity between these three variables representing different vitamin D sources was found.)

Discussion

We found that the vitamin D status of subjects who stayed the entire year in northern Norway was dependent on dietary sources of vitamin D throughout the study period (November–June). The prevalence of moderate hypovitaminosis D was highest in January–February, when a quarter of the participants had 25(OH)D concentration ≤ 37.5 nmol l^{-1}. Subjects who had travelled to southern locations during the summer, prior to the blood sampling, had higher vitamin D levels in their blood compared with those who had remained in the north.

This present investigation has several interesting features. First, this study is the only randomised, population-based assessment of vitamin D status measured as plasma 25(OH)D concentrations among middle-aged women in northern Norway. Second, the participants' broad geographical distribution throughout all latitudes in the north made it possible to investigate vitamin D status in a population living at some of the most northerly geographical locations of significant human settlement. Third, the extreme variation in sun exposure found at these high latitudes could be taken into account because the blood samples were collected throughout the dark season when the sun was below the horizon for 24 hours a day, and until summer when the sun never set. Fourth, the focused questionnaire aimed to collect information on both UV radiation-related issues and dietary vitamin D intake, and thus provided detailed data on all sources of vitamin D. Furthermore, the time- and geographically specific simulated UV-radiation measure devised for northern Norway made it possible to develop the 'UV-hours' variable to explain plasma 25(OH)D concentration. This new variable, 'UV-hours' (Table 5), was considered a better metric than the previous 'hours in daylight last week prior to blood sampling', 'time of year when the blood sample was collected' and 'latitude' (Table 4).

It would have been desirable to have a greater number of subjects participating in the study in light of the seasonal variation in plasma vitamin D level, especially for the stratified analysis, which had relatively few subjects assigned to each stratum. The reason for this limited number was that, during the data sampling period (November 2001–June 2002), among the randomly selected women asked to give blood for the Norwegian EPIC biological bank only 443 subjects were living in northern Norway. Further, in this nation-wide sampling, the blood collection was suspended during the summer months to avoid low response rates because of summer holidays. This introduced another limitation in our study because the blood sampling period did not cover the whole year, and it was therefore not possible to assess predictors for vitamin D status in northern Norway for all seasons.

A common problem in cross-sectional studies is that exposure data recalled are biased by the subject's knowledge of their own status with respect to the disease or outcome under investigation. In our study, the participants were unaware of their own plasma vitamin D level when they answered the questionnaire. Thus, food intake recalled in the questionnaire was most likely independent of the women's vitamin D status.

Several studies have concluded that vitamin D insufficiency is a common problem in Europe not only among the

Table 4 Regression models for predictors of log 25(OH)D concentrations in blood plasma*

Variable	All ($n = 260$) β	All ($n = 260$) *P*-value	Sun holiday/solarium use: Yes ($n = 78$) β	Yes *P*-value	Sun holiday/solarium use: No ($n = 182$) β	No *P*-value	Season†: November–February ($n = 86$) β	November–February *P*-value	Season†: March–April ($n = 57$) β	March–April *P*-value	Season†: May–June ($n = 39$) β	May–June *P*-value
Age (years)	0.010	0.02	0.023	0.01	0.004	0.42	−0.008	0.23	0.007	0.42	0.027	0.04
Body mass index (kg m^{-2})	−0.003	0.54	0.002	0.90	−0.004	0.48	−0.002	0.75	0.007	0.38	−0.030	0.07
Dietary vitamin D intake (μg day^{-1})	0.010	0.0003	0.002	0.66	0.013	0.0003	0.014	0.006	0.011	0.04	0.017	0.04
Supplement use‡ (yes/no)	0.022	0.56	−0.004	0.96	0.030	0.49	−0.033	0.58	0.110	0.12	−0.012	0.91
Residing in northern Norway during the previous summer (yes/no)	−0.107	0.004	−0.045	0.54	−0.144	0.0008	−0.118	0.05	−0.120	0.09	−0.159	0.15
Hours in daylight last week prior to blood sampling	0.002	0.36	−0.001	0.75	0.003	0.22	0.003	0.71	−0.004	0.44	0.005	0.09
Time of year when the blood specimen was collected	–	0.005	–	0.62	–	0.002	–	–	–	–	–	–
November–December	ref	ref	ref	ref	ref	ref	–	–	–	–	–	–
January–February	−0.032	0.61	−0.122	0.37	0.013	0.86	–	–	–	–	–	–
March—April	0.125	0.05	−0.046	0.74	0.204	0.005	–	–	–	–	–	–
May–June	0.120	0.12	0.032	0.84	0.139	0.11	–	–	–	–	–	–
Latitude (°N)	0.007	0.60	−0.024	0.31	0.015	0.350	–	–	–	–	–	–
Sun holiday (yes/no)	0.116	0.02	–	–	–	–	–	–	–	–	–	–
Solarium use (yes/no)	0.221	<0.0001	–	–	–	–	–	–	–	–	–	–
Model	$R^2_{adj} = 0.24$, $P < 0.0001$		$R^2_{adj} = 0.05$, $P = 0.21$		$R^2_{adj} = 0.23$, $P < 0.0001$		$R^2_{adj} = 0.10$, $P = 0.03$		$R^2_{adj} = 0.14$, $P = 0.03$		$R^2_{adj} = 0.26$, $P = 0.01$	

25(OH)D – 25-hydroxyvitamin D; ref – reference category.
* Due to missing values the total is less than 300.
† For the seasonal strata, subjects who had been on a sun holiday or used a solarium were excluded.
‡ Cod-liver oil supplement not included.

Table 5 Models for predictors of log25(OH)D concentrations in blood plasma when 'UV-hours' replace 'hours in daylight last week prior to blood sampling', 'latitude' and 'time of year when the blood specimen was collected'

			Analysis stratified by sun holiday/solarium use			
	All ($n = 270$)		Yes ($n = 81$)		No ($n = 190$)	
Variable	β	*P*-value	β	*P*-value	β	*P*-value
Age (years)	0.009	0.03	0.025	0.004	0.002	0.61
Body mass index (kg m^{-2})	−0.003	0.57	0.004	0.75	−0.002	0.65
Dietary vitamin D intake (μg day^{-1})	0.011	<0.0001	0.001	0.79	0.014	<0.0001
Supplement use*	0.025	0.49	−0.001	0.99	0.027	0.52
Residing in northern Norway during the previous summer	−0.117	0.001	−0.066	0.35	−0.149	0.0003
UV-hours (h day^{-1})	–	0.0002	–	0.64	–	0.0002
0	ref	ref	ref	ref	ref	ref
0.1–1.0	0.100	0.04	0.010	0.92	0.128	0.03
1.1–2.0	0.181	0.0005	0.113	0.24	0.203	0.001
2.1 +	0.177	0.0002	0.059	0.53	0.201	0.0003
Sun holiday	0.113	0.02	–	–	–	–
Solarium use	0.224	<0.0001	–	–	–	–
Model	$R^2_{adj} = 0.25$, $P < 0.0001$		$R^2_{adj} = 0.06$, $P = 0.14$		$R^2_{adj} = 0.24$, $P < 0.0001$	

25(OH)D – 25-hydroxyvitamin D; ref – reference category.
* Cod-liver oil supplement not included.

elderly[22], but also for middle-aged[9] and younger populations[7,23]. Van der Wielen *et al.*[22] have shown that, among the elderly, sub-clinical vitamin D deficiency is surprisingly more common in southern Europe than in Scandinavia. This was explained by food fortification and vitamin D supplements that are common in Scandinavia. A recent study from Finland[24] indicated that one-third of a young Finnish population was vitamin D-deficient (<25 nmol l^{-1}) during winter, and suggested that this could be a health concern for the whole of northern Europe. The prevalence of low vitamin D status in the Finnish study was higher than what we observed. This could be due to higher mean daily vitamin D intake, which for the Finnish compared with our northern Norwegian sample was 4.7 ± 2.5 μg versus 8.1 ± 7.0 μg, respectively.

A significant positive correlation between dietary vitamin D intake and 25(OH)D level has previously been reported in subjects with low sun exposure[25,26]. Our findings suggest that the middle-aged female population in northern Norway depends heavily on dietary sources of vitamin D due to insufficient UV exposure. Further, a considerable proportion is at risk of not consuming the amount necessary to cover their needs.

In contrast to Vik *et al.*[11] who did not find any seasonal variation in 25(OH)D level from November until May, our results show an obvious 'dark-season' effect on vitamin D levels. The low level of moderate hypovitaminosis D observed in March–April could be explained by Easter holidays, since there is a tradition in Norway to go skiing at this time in the mountains where reflection of UV radiation from the snow will increase vitamin D production in the skin.

Sun holidays and the use of a solarium were, not surprisingly, strong predictors of 25(OH)D level. In addition, when adjusting for time of year when the blood sample was taken, staying at more southern latitudes during the previous summer was also positively associated with vitamin D in the blood. This indicates a long-term impact of summer sunlight exposure on vitamin D status. The survey by Poskitt *et al.*[27] can be interpreted similarly as they found that, among children from the West Midlands, England, 25(OH)D concentrations were higher in those who had had a seaside holiday the year before blood sampling compared with those who had not.

In our study we found that age was a positive predictor of plasma 25(OH)D among subjects who had been on a sun holiday or spent time in a solarium. This is contradictory to what has been reported in other studies, where age has been associated with an increased risk of low levels of vitamin D in blood. This was thought to reflect the decreased capacity in the elderly of human skin to produce vitamin D_3[28]. However, Need *et al.*[29] found that 25(OH)D levels fell significantly after the age of 69. The age of our participants ranged from 44 to 59 years, and thus was below the age when the capacity of the skin to produce vitamin D is likely reduced. Thus it is probable that the increased 25(OH)D level with age observed in subjects who had been on a sun holiday or used a solarium was due to other factors associated with age that could not be controlled for in the present analysis, such as use of suntan lotion, time spent in direct sun or clothing worn.

When assessing sun exposure in relation to vitamin D status in populations, a 9-point scale has been employed in several studies[14,25,26,30] and has been considered valid for ranking subjects by sunshine exposure. Briefly, the ranking scale is based on recall of the time and degree of exposure to sunshine the week before administration of the questionnaire, sunscreen use, and travel to southern locations during the previous month. Our estimated 'UV-hours' variable correlated well with plasma 25(OH)D level. This suggests that recall of hours spent in daylight the week prior to the blood sampling, weighed for estimated geographic- and time-specific UV radiation relevant for vitamin D photoconversion, can be considered a valid measure for UV-induced vitamin D production. Furthermore, this association indicates that, for middle-aged women living at 65–71°N, seasonal variation in vitamin D status can be explained by variation in UV exposure at these latitudes. The association between 'UV-hours' and vitamin D status does not necessarily mean that blood 25(OH)D concentrations reflect UV exposure the week prior to the blood sampling. Instead it could indicate that recall of the time spent in daylight for one week gives a representative estimate for usual sun exposure per week during the actual season. This interpretation is in line with the discussion above about the long-term impact of summer exposure to sunshine on vitamin D status.

Cod-liver oil supplements, margarine, butter and fatty fish have been established in dietary surveys conducted in Norway as the primary dietary sources of vitamin D[6]. However, the impact of the traditional fish-liver dish *mølje* and fresh fish-liver oil on vitamin D status is a phenomenon characteristic for the population of northern Norway[4,5]. Recently, the Norwegian Food Control Authority has recommended that all women of child-bearing age, pregnant women and children do not to eat fish liver because of the risk of long-term negative health impact due to the presence of dioxins and other persistent organic pollutants (POPs) above tolerable limits[31]. Our study showed that consumption of fish liver was an important contributor to vitamin D intake for the population in the north. Uncertainties regarding the possible negative health effects of POPs versus the nutritional benefit of traditional foods have been discussed previously, in particular in relation to the marine diet among populations living in arctic areas, and has been named the 'Arctic dilemma'[32]. Studies from Barrow, Alaska (71.3°N) have, for example, found a high rate of vitamin D deficiency in adults especially among subjects who were not consuming a traditional diet[33]. From a public health perspective, a change in food habits away from traditional diets, that are rich in essential nutrients such as fat-soluble vitamins and polyunsaturated fatty acids, can cause increased risk of some diseases. For the northern Norwegian population, which is vulnerable to vitamin D deficiency due to living at high geographical latitudes, a reduction in liver consumption during winter can have an influence on vitamin D status and health. Thus, a balance between the nutritional benefits of traditional foods and the possible negative health outcomes caused by toxins such as POPs must always be considered when developing and promoting dietary guidelines.

In conclusion, dietary sources of vitamin D are of essential importance for the inhabitants of northern Norway. At these latitudes, skin synthesis of vitamin D cannot compensate for low intakes during winter. Traditional foods, like fish liver and fish-liver oils, constitute good sources of vitamin D. Travelling to southern locations can also improve vitamin D status and protect against deficiency throughout the winter. However, a considerable proportion of residents do not go abroad on a sun holiday or to the south during the summer, and are therefore at increased risk of low vitamin D levels if they fail to consume sufficient food items rich in vitamin D. Increased ingestion of marine foods that provide vitamin D should be promoted and further studies should be carried out to investigate vitamin D status in arctic areas, in relation to both UV exposure and traditional food sources. Study designs with repeated blood measurements are recommended to assess seasonal variation in vitamin D in combination with UV-exposure measurements.

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Paper IV

Vitamin D status in a rural population of northern Norway with high fish-liver consumption.

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Abstract

Objective: To assess vitamin D status and the impact of three repeated fishmeals consisting of cod-liver and fresh cod-liver oil on the plasma level of vitamin D metabolites in a high cod-liver and cod-liver oil consumption area.

Design: Experimental field study.

Methods: Thirty-two volunteers from the Skjervøy (70^0N) municipality in northern Norway were recruited to consume three traditional "mølje"-meals, consisting of cod, cod-liver, fresh liver oil, and hard roe in one week. The liver and fresh cod-liver oil consumed by the participants were weighed and recorded. Blood samples were collected before the first meal, and subsequently 12 hours and four days after the last meal. The blood samples were analysed for the vitamin D metabolites 25-hydroxy vitamin D [25(OH)D] and 1,25-dihydroxy vitamin D [$1,25(OH)_2D$]. All the participants answered a semi-quantitative food frequency questionnaire, which were used to estimate usual daily nutrient intake. The study was carried out in the last part of March 2001.

Results: The median daily vitamin D intake estimated from the questionnaire was 9.9 μg/day. The proportion of the subjects with baseline 25(OH)D levels below 50 nmol/l was 15.4 % and none were below 37.5 nmol/l. Only "mølje"-consumption and "hours spent in daylight" were significantly associated with baseline log25(OH)D. The mean total intake of vitamin D in the three servings was 272 (SD=94) μg, ranging from 142 – 434 μg. Relative to baseline plasma concentration, the mean level of 25(OH)D decreased slightly in both post consumption samples ($p \leq 0.03$), while $1,25(OH)_2D$ peaked 12 hours after the final meal ($p=0.03$).

Conclusion: Three repeated "mølje"-meals provided on average, an amount of vitamin D equal to 54 times the recommended daily dose. Subjects with food consumption habit that included frequent "mølje"-meals during the winter sustained satisfactory vitamin D levels in their blood, in spite of a long "vitamin D winter" (i.e., absence of UV-induced vitamin D production in skin).

Introduction

Dietary sources of vitamin D are scarce. It is mainly found in fatty fish, cod-liver oil and fortified margarine or butter. Ultraviolet (UV)-radiation induced skin-production constitutes the main contributor to vitamin D in humans. UV-radiation with wavelengths less than 320 nm is needed for this cutaneous photo conversion of provitamin D (7-dehydrocholesterol) to pre-vitamin D which is the precursor to vitamin D [1]. Great seasonal variation in UV-light has been found to cause seasonal fluctuation in vitamin D status in humans [2]. Fish-liver has traditionally been the most important vitamin D source for the coastal population of northern-Norway during the winter months [3], since at these latitudes the sun-induced vitamin D production ceases for a considerably part of the year. The fish liver consumed was mainly from cod (gadus morhua L.) and saithe (pollachius virens) and the primary consumption followed the seasonal harvests. The cod-liver season was linked to the spawning period and lasted about three months during winter (most usually from January until March/April). The saithe-liver was consumed from late summer until September/October.

A recent epidemiological investigation has confirmed the importance of diet to vitamin D status in the northern Norway population [4]. Un-published data from the nationwide Norwegian women and Cancer study (NOWAC) [5] has shown that there are still communities where fish-liver and fresh fish liver oil are consumed frequently. The coastal municipality of Skjervøy which is situated at 70 degrees North, was identified among those with highest frequency of consumption. Fifty percent of the participating subjects reported eating fish liver and fish-liver oil, or "mølje", which is the Norwegian name of the dish, seven times per season or more. In a recent study among volunteers in Tromsø [6], the largest city in northern Norway, it was found that the average vitamin D consumption from one single fish meal containing fish-liver and fresh cod-liver oil was 73.3 μg, which is about 15 times the recommended daily intake (5.0 μg)[7]. According to the un-published NOWAC data, "mølje" seems to be more common in the rural coastal northern areas than among the more urban centres.

The 25-hydroxy vitamin D (25(OH)D) concentration in blood has been the most used metabolite for determining overall vitamin D status of an individual [8]. A 25(OH)D concentration ≤ 37.5 nmol/l in blood has been designated as an indicator of moderate hypovitaminosis D [9,10] and concentrations ≥ 50nmol/l has been suggesteed as the recommended level [11,12]. The 1,25-dihydroxy vitamin D (1,25(OH)$_2$D) metabolite is the biological active form [1].

By recruiting volunteers from the rural costal village of Skjervøy, we wanted to assess the impact of this traditional fish dish containing liver and liver-oil, on plasma levels of vitamin D and its metabolites in a high "mølje"-consumption group and to study the effect of three consecutive meals on these parameters.

Methods and material

Study subject were recruited by announcement in the local newspaper. Inclusions criteria were: either gender, above the age of 20, and living in the municipality of Skjervøy. Thirty-two volunteers, 21 men and 11 women aged 38-61 wanted to take part in the study. This project was approved by the Regional Committee for Research Ethics, and all subjects signed a consent form.

The study schedule is outlined in Figure 1. All participants answered the NOWAC food frequency questionnaire, which were used to estimate usual daily nutrient intake. This questionnaire has been described in details elsewhere [5,13]. A slight alteration of the questionnaire was made to allow discrimination between cod-liver and saith-liver consumption and the recoding of usual consumption patterns. In addition we included questions on hours spent in daylight the previous week, as well as sun-seeking holidays and use of solarium during the last month prior to the study. The questionnaire also contained questions on gender, age, height, and weight of the respondents.

The subjects were served three "mølje"-meals with a two day interval during a seven-day period. All meals were served in the canteen at Skjervøy Upper Secondary School. The "mølje"-meals were prepared in the traditional way by students attending the hotel and food-processing studies at this school. The fish was caught the day before or the same day as it was served. Both the cod and the hard roe were boiled separately in water. The liver was divided and boiled in only small amounts of water and the oil derived from this constituted the fresh cod-liver oil.

Participants served them selves and took as much as he or she wanted at the arranged fish buffet, but the amounts of liver and cod-liver oil at each participant plate were weighed by using digital weights and recorded in grams by trained students at the school. Blood samples were collected before the first meal, and 12 hours and 4 days after the last meal. Body weight and height were measured on day 8 or day 11. The study was carried out in the last part of March 2001. The blood samples were collected employing EDTA-containing vacutainer tubes (Becton-Dickinson, 9 ml lavender top, Plymouth, UK). Participants were asked to maintain their usual diet during the study period.

Usual (i.e. self-reported) daily vitamin D intake was computed using the food questionnaire information and the corresponding nutrient values reported in the Norwegian Food Composition Table [14], as well as our food analysis of liver and fresh cod-liver oil as described below. Due to limited information on the nutrient content of different supplements, vitamin D contributions from dietary supplements other than cod-liver oil were not included in estimating the usual daily vitamin D intake for each participant.

Food sample analyses

Samples from the liver and fresh cod-liver oil servings were analysed for vitamin D according to the method described by Horvli & Lie [15]. In short, vitamin D was extracted using 96 % ethanol/ 60 % KOH, containing pyrogallol, ascorbic acid and an internal standard (vitamin D_2). Heating to 70 °C for 20 minutes saponified the sample. After addition of water, the sample was extracted twice with hexane using a whirl-mixer and centrifuge. The combined hexane phases were extracted with water, and iso-propanol was added before evaporation. The sample was further cleaned up using a HPLC system consisting of a Spectra Physics P1000 isocratic pump, a Shimadzu SPD 6AV UV-detector, a Shimadzu C-3A integrator, fitted with a Brownlee silica column (25 cm x 4.6 mm, 5μm). For the analytical step, a C_{18} column (25 cm x 4.6 mm, 5 μm Supelco Inc., Bellefonte, USA) was used.

For the preparative clean-up step, tetrahydrofurane : n-hexane (12.5:87.5 v/v) was used as the mobile phase. For the analytical step, chloroform : methanol : acetonitrile (6:12:82 v/v) was employed as eluent and the sample was dissolved in methanol. The flow rates were 1 ml/min for both columns. Vitamin D_2 (internal standard) and D_3 were detected on-line by the UV-detector at 265 nm. These analyses were carried out by the Directorate of Fisheries, Institute of Nutrition, Bergen, Norway.

The vitamin D intake from the "mølje"-meal was estimated based on the vitamin D content of the liver and the fresh cod-liver oil served, since the rest of the food items consumed (cod, potatoes and hard roe) contain little or no vitamin D.

Plasma levels of 25(OH)D and 1,25-$(OH)_2D$.

The blood samples were analysed with respect to 25(OH)D and 1,25$(OH)_2D$. Blood plasma was collected and kept at -80°C until analyses for 25(OH)D and 1,25$(OH)_2D$ according to modified versions of the methods described by Aksnes [16,17]. Briefly, 1,5 ml plasma samples were mixed with 2 ml acetonitrile, vortexed and centrifuged at 1.000 x g for 10 min to remove proteins. The supernatants were collected, 3.5 ml 0.1 M K_2HPO_4, (pH 10.5) was added, and the mixture applied to C-18-OH vacuum columns (Varian, USA). The columns were washed with 5 ml distilled H_2O, followed by a second wash with 5 ml methanol:H_20 (70:30, v/v), after which the 25(OH)D and 1,25$(OH)_2D$ fractions were eluted with hexane:isopropanol (95:5, v/v), and evaporated to dryness with a gentle flow of nitrogen. The samples were dissolved in 250 µl hexane:isopropanol:ethanol (95:2.5:2.5, v/v) and the collected fraction was separated on a silica column (Supelcosil, 15 cm x 4.6 mm, 3 µm; Supelco Inc, Bellefonte, USA) by HPLC. The fractions containing 25(OH)D and 1,25$(OH)_2D$ were collected and again evaporated to dryness with nitrogen gas and dissolved in ethanol. 25(OH)D was quantified by a radioreceptor assay (RRA) using human vitamin D binding protein from blood plasma as the binding protein, and 1,25$(OH)_2D$ by a RRA using the 1,25 $(OH)_2D$- receptor from chick duodenal cytosol.

Serum parathyroid hormone (PTH)

Intact serum PTH-levels was measured on an Immulite analyser (Diagnostic Products, Los Angeles, Ca, USA) on the basis of a two-site chemiluminescent immunometric assay. The Immulite analyser has a working range of 0.1-263 pmol/l.

Statistical Analyses

Statistical analyses and nutrient calculations were done by employing the SAS software package, version 8.02. Log transformed values for the variable for 25(OH)D were used in the general linear models and t-tests because this variable was not normally distributed. When general linear models were chosen, test for colinearity (variance of inflation factor) between the independent variables was applied. Independent variables were selected by backward elimination. For the analysis of baseline 25(OH)D levels, the subjects who reported that they had been on sunny holiday or recently used a solarium were excluded (n=4) in addition to subjects for whom this information was missing (n=2). Cod-liver oil supplement use was defined as taking it more than twice per week. Pearson correlation coefficients were calculated for the self-reported daily intakes of vitamin D and the 25(OH)D concentration in blood at baseline. Paired sample t-tests and ANOVA with repeated measurement design were used to compare changes in vitamin D metabolite levels with time.

Results

Some characteristics of the participants are shown in Table 1. The median self-reported usual vitamin D intake estimated from the semi-quantitative food frequency questionnaire, was 9.9 µg/day. According to the questionnaire data, 47 % of the participants ate "mølje" two to three times per months or more and 17 % did so once per week or more during the "mølje"-season (Figure 2).

The served "mølje"-meals

Median intake in grams of cod-liver and fresh cod-liver oil consumed during the three servings are shown in Table 2 as well as total fat percentage and amount of vitamin D per 100 g of food served per meal. The vitamin D content per 100 grams of food varied two-fold between meals, while the fat content was approximately constant. As illustrated in Table 3, the total vitamin D intake from the served meals was higher only for men compared to women ($p=0.004$) and not for any of the other parameter listed. The mean total quantity of vitamin D provided in the three meals was 271.9 (SD=93.9) μg, ranging from 142.4 –434.4 μg; the median intake was 264.1 μg.

Baseline 25(OH)D

The distribution pattern of the observed baseline concentrations of 25(OH)D is depicted in Figure 3, corresponding to a mean concentration of 67.2 nmol/l. The proportion of the subjects with 25(OH)D levels below 50 nmol/l was 15.4 % and none were below 37.5 nmol/l. In the unadjusted analysis (Table 3), cod-liver oil supplement users had significantly higher 25(OH)D levels in blood ($p=0.04$) compared to non-users. Further, subjects who spent less than 7 hours per week in daylight the week prior to the study had significant lower 25(OH)D concentrations in blood compared to those who spent more time in daylight ($p=0.02$). There was a significant trend ($p=0.04$) in baseline 25(OH)D concentration by frequency of recalled "mølje"-consumption. The proportion of subjects with baseline 25(OH)D levels below 50nmol/l did decrease with increased frequency of recalled "mølje"-consumption.

The correlation coefficient for intake of vitamin D and levels in blood was $r=0.30$, but not significant ($p=0.13$). Subjects with a self reported daily intake of vitamin D less than 10 μg had on average a 25(OH)D concentration of 62.4 (SD=13.4) nmol/l at baseline, compared to subjects with a daily intake at 10μg or more; for whom it was 70.6 (SD=18.7) nmol/l (Table

3). However, this difference was not significant. In the multiple regression model only "mølje"-consumption and "hours spent in daylight" was significantly associated with log25(OH)D, adjusted for age and gender, while BMI had no effect as a predictor of vitamin D status at baseline (Table 4).

Changes in the vitamin D metabolites and PTH associated with the "mølje"-meals.

There was a slight decrease in 25(OH)D level at 12 hours ($p=0.03$) and 4 days ($p=0.004$) after the last meal (Figure 4). In the ANOVA for repeated measurement design, there was a significant time effect for log25(OH)D ($p=0.001$) and for 1,25(OH)$_2$D ($p=0.05$). Compared to baseline, there was an increase in 1,25(OH)$_2$D levels at 12 hours ($p=0.03$) after the third serving, but not after 4 days. The change over time in 25(OH)D and 1,25(OH)$_2$D levels were not significantly associated with the total vitamin D consumed in the three served meals, nor with any of the following variables: gender, age, BMI, hours spent in daylight, cod-liver oil supplement use, frequency of "mølje"- consumption, and self-reported daily intake of vitamin D (ANOVA for repeated measurements, data not shown). The mean PTH serum concentrations were 5.0 (SD=2.3) pmol/l, 5.4 (SD=2.9) pmol/l, and 3.8 pmol/l (SD=1.7) at baseline, 12 hours and four days after last meal, respectively. The slight rise in PTH between baseline and 12 hours after last meal was non-significant, while the decrease at four days relative to baseline was highly significant ($p<0.001$) when adjusting for age and sex.

Discussion

We found that the three consecutive "mølje"-meals gave a short-term increase in plasma concentration of the active vitamin D metabolite 1,25(OH)$_2$D and a slight decrease in circulating 25(OH)D levels. However, baseline vitamin D status measured as 25(OH)D concentration was explained by both hours spent in daylight the week before the study and frequency of self-reported "mølje"-consumption. Further, we also found that in the Skjervøy group, the 25(OH)D levels were relatively high and very few subjects had 25(OH)D levels below recommended level.

In the beginning of April 2000, we conducted a similar study in the city of Tromsø, northern Norway (69^{0}N) in which 33 volunteers were served a single "mølje"-meal followed by repeated blood measurements of vitamin D [6]. Around 75% of these subjects had baseline concentrations below the recommended level (50 nmol/l), and one quarter of the subjects were below the limit for moderate hypovitaminosis D (37,5 nmol/l). The relatively high concentrations found in the present study compared to the Tromsø group suggests that the regular consumption of traditional marine food plays an important role in vitamin D status. The recommended dietary intake of vitamin D in the Nordic countries has been set at 5µg per day [7]. The median self-reported vitamin D intake found in the Skjervøy group was more than two-fold of what has been found in nationwide surveys conducted in Norway [5,18]. Further, it is known that significant higher vitamin D intake occurs in northern Norway compared to populations in the more southern parts of the country [19]. By comparing the relative importance of UV-induced- and dietary vitamin D on vitamin D status, a recent study has shown that for northern Norway populations, diet contributes a major source during winter until late spring [4]. The 1930 study by Kloster [3] concluded that the consumption of cod-liver and cod-liver oil was the most important vitamin D source for the costal population, and that rickets was common in places where there was limited access to fresh fish. Our results show that high consumption of "mølje" results in a satisfactory vitamin D status even when measured just after the end of the "vitamin D winter". This suggests that this traditional food compensates for the absence of sufficient sunlight induced vitamin D production.

The finding that 25(OH)D level in blood was not adequately explained by the estimate of total vitamin D intake, but by the frequency of "mølje"-consumption, might be explained by lower occurrence of misclassification on the "mølje"- question compared to the other dietary intake questions. Non-differential misclassification will dilute a true association. It has been shown previously, among subjects in northern Norway, that consumption of "mølje" was associated with vitamin D status [4]. In the mentioned study conducted in Tromsø [6], one meal of "mølje" increased the 25(OH)D level only for subjects with moderate hypovitaminose D (25(OH)D $\leq$ 37.5 nmol/l). Thus, the relatively high baseline levels in the Skjervøy-group could be one explanation for our finding that three "mølje"-meals were not sufficient to raise the 25(OH)D concentration.

The increase in 1,25$(OH)_2$D could be attributed to the short-time increase in PTH, which activates hydroxylation of 25(OH)D in the kidneys[1]. The observed increase in PTH was, however, not significant. This inability to detect a change was most likely explained by low statistical power (small sample size). The observed increase in active vitamin D could also be due to the metabolite being bound to fat in circulation and thereby inactivated, thus causing a need to produce more 1,25$(OH)_2$D.

BMI has been shown to be associated with 25(OH)D levels in blood [6,20,21,22]. This was not found in our study, probably due to the narrow range in the BMI values, as most of the subjects were overweight. The results were, however, in accordance with the "mølje"-study conducted in Tromsø [6] where there also was a short-term reduction in 25(OH)D after a "mølje"-meal among the overweight subjects.

Lack of statistical power due to a small number of participants was a problem in the current study. Thus, substantial differences in 25(OH)D such as reported in Table 3 were found not to be significant. Neither was the study sample randomly selected, as the subjects were recruited based on their own willingness and initiative to participate. However, the participants self-reported frequency of "mølje"-consumption was in line with the unpublished NOWAC-data obtained in the municipality of Skjervøy and the recalled cod-liver oil supplement use in the present study was close to the prevalence found in nation-wide Norwegian [13] and northern Norwegian studies [4,22]. Since the study objective was to investigate the impact of "mølje" on vitamin D status in a high consumption group living in a rural area of northern Norway, external validity of the findings is of less importance.

In conclusion, cod-liver and fresh cod-liver oil can constitute a good vitamin D source. Three consecutive "mølje"-meals on average provided 54 times the recommended daily dose of vitamin D. Subjects with food habits that include frequent "mølje"-meals during the winter can sustain satisfactory vitamin D levels in their blood, despite the lack of UV-induced vitamin D production.

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Table 1. Characteristics of the study sample (n=32)[a].

Characteristic	*Men* n=21 *median or %*	*Women* n=11 *median or %*	*Total* *median or %*	*Range*
Age (y)	52	50	50	38 - 61
BMI (kg/m^2)	29.4	28.3	29.2	19.8 - 35.6
Usual vitamin D intake (µg/day) (supplements other than cod-liver oil excluded)	11.5	5.9	9.9	3.0 - 40.1
Proportion of subjects reporting taking cod-liver oil supplements twice per week or more	52.4	27.3	43.8	
Proportion of subjects who have been on sun holiday or used a solarium the month prior to the study	10.0	20.0	13.3	

[a] Subgroups may not total to 32 due to missing values.

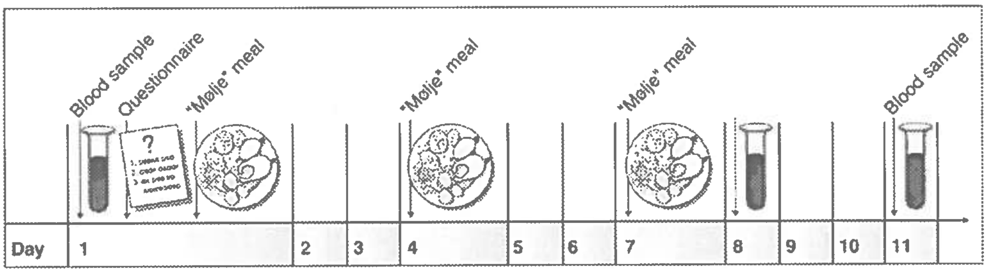


Figure 1. Study design and blood sampling schedule (blood samples were collected before meal 1 and 12 hours and 4 days after meal 3).

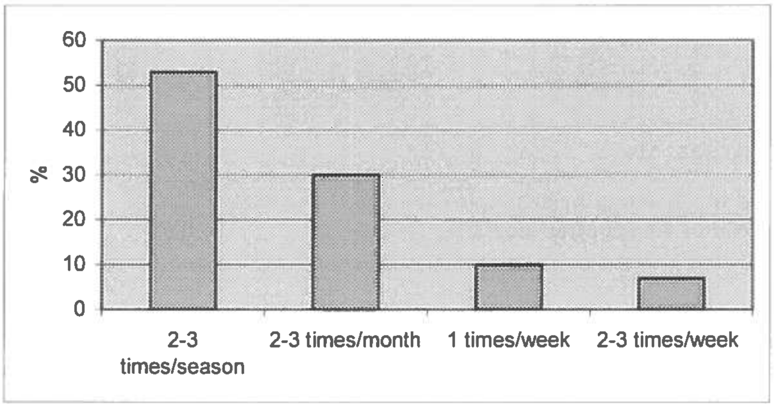


Figure 2. Frequency of consumption during the "Mølje" season among the study participants (a season is estimated to equal three months) (n=30).

Table 2. Median total intake of cod-liver and cod-liver oil from the three served "mølje"-meals and the calculated nutrient content.

Food items and meals	*Median intake (g)*	*Vitamin D (µg/100g)*	*% total fat*
Liver			
meal 1	108	50	48.6
meal 2	115	40	50.9
meal 3	95	80	44.7
Liver-oil			
meal 1	28	90	96.2
meal 2	25	60	96.4
meal 3	25	120	93.8

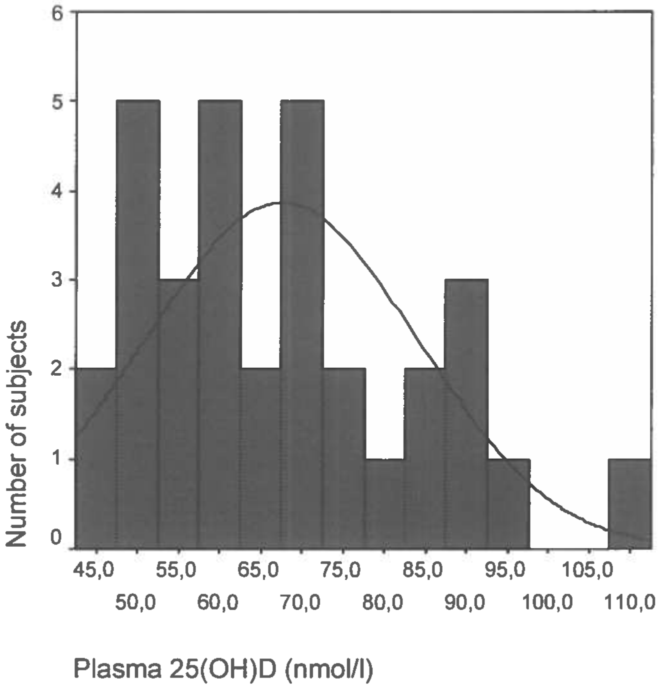


Figure 3. The distribution of baseline plasma 25(OH)D concentrations (n=32)

Table 3. Plasma 25(OH)D levels at baseline and intake of vitamin D through the served "mølje-meals" by different characteristics[a].

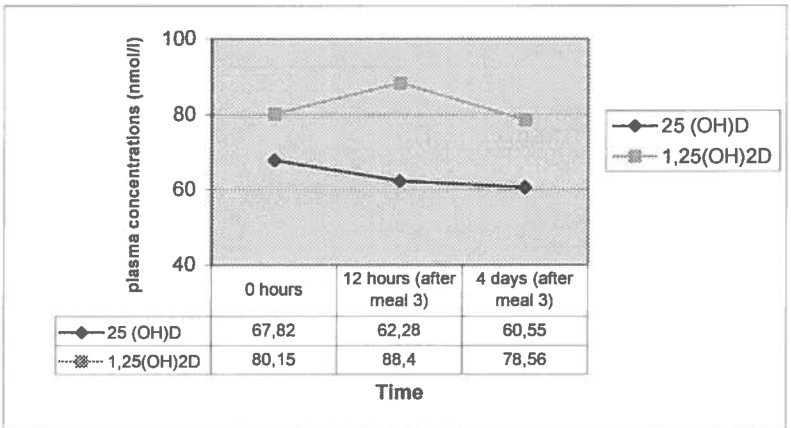
Characteristic	*Baseline 25(OH)D (nmol/l)* [b,c] *Mean (SD)*	*Proportion with baseline 25(OH)D levels below 50 nmol/l*[b] *%*	*Vitamin D consumed (µg) through the "mølje-meals"* [c] *Mean (SD)*
Total	67.2 (16.9)	15.4	272 (94)
Age			
<50 year (n=14)	66.8 (16.5)	21.4	284 (104)
>50 year (n=18)	67.2 (17.8)	11.1	262 (87)
	p=0.92		*p=0.52*
Gender			
Men (n= 21)	68.6 (11.4)	9.5	305 (107)
Women (n=11)	63.9 (13.4)	27.3	209 (75)
	p=0.53		*p=0.004*
BMI (kg/m²)			
<25 (n=9)	67.4 (14.3)	0.0	239 (100)
≥25 (n=23)	67.1 (17.9)	20.0	285 (90)
	p=0.97		*p=0.22*
Cod-liver oil supplement			
Yes (n= 14)	73.8 (18.6)	7.1	260 (76)
No (n= 18)	59.8 (11.3)	22.2	281 (107)
	p=0.04		*p=0.53*
Usual frequency of "mølje" consumption			
3 times per season or less (n=16)	60.7 (14.4)	25.0	262 (96)
2 – 3 times /month or more (n=9)	69.9 (15.1)	11.1	317 (102)
1-3 times per week (n=5)	77.7 (21.7)	0.0	263 (47)
	p=0.04[d]		*p=0.64*[d]
Time spent in daylight			
Less than 7 hours per week (n=7)	53.8 (10.6)	28.6	261 (110)
More than 7 hours per week (n=21)	72.4 (16.1)	4.8	292 (89)
	p=0.02		*p=0.46*
Vitamin D intake/day			
Less than 10µg/day (n=16)	62.4 (13.4)	18.8	245 (97)
10µg/day or more (n=16)	70.6 (18.7)	12.5	299 (85)
	p=0.23		*p=0.11*

[a] All subgroups may not have n=32 due to missing values or exclusions.

[b] Subjects who reported that they had been on a sun holiday or used a solarium during the last month prior to the study (n=4) were excluded.

[c] Statistical test: Student t-test for comparison of means

[d] Test for trend. [e] Paired student t-test calculated on log-transformed values.



	0 hours	12 hours (after meal 3)	4 days (after meal 3)
25 (OH)D	67,82	62,28	60,55
1,25(OH)2D	80,15	88,4	78,56

Figure 4. Plasma concentrations of 25(OH)D and 1,25(OH)$_2$D by time (n=32).

Table 4. Multiple linear regression analysis identifying predictors for baseline log25(OH)D (n=26)[a].

Variables Categories	*t-value*	*p-value*
Cod-liver oil supplement		
Yes (n= 14)	ref.	
No (n= 18)	1.47	0.16
Usual frequency of "mølje" consumption		
3 times per season or less (n=16)	ref.	
2 – 3 times /month or more (n=9)	1.06	0.30
1-3 times per week (n=5)	2.14	0.05
Time spent in daylight		
Less than 7 hours per week (n=7)	ref.	
More than 7 hours per week (n=21)	2.11	0.05
R^2_{adj}		0.51
P-value for model		0.04

Adjusted for age and gender.

[a] Subjects who reported that they had been on sun holiday or used solarium were excluded.

Appendix A

Spørreskjema til møljeforsøket "mølje mot blod"

Vennligst fyll ut dette spørreskjemaet så nøye som mulig. **ID. nummer ....**

Takk for hjelpen.

Alder .... **Høyde ....** **Vekt ......**

Kjønn □ kvinne

□ mann

Fiskelever

I sesongen for fiskelever hvor ofte spiser du <u>torskelever</u> ?

□ aldri
□ 1 gang per sesong
□ 2-3 ganger per sesong
□ 2-3 ganger per mnd
□ 1 gang per uke
□ 2-3 ganger per uke
□ oftere enn 3 ganger per uke

I sesongen for fiskelever hvor ofte spiser du <u>seilever</u> ?

□ aldri
□ 1 gang per sesong
□ 2-3 ganger per sesong
□ 2-3 ganger per mnd
□ 1 gang per uke
□ 2-3 ganger per uke
□ oftere enn 3 ganger per uke

Dersom du spiser fiskelever, hvor mange spiseskjeer pleier du spise hver gang?

□ spiser ikke fiskelever
□ 1 □ 2 □ 3-4 □ 5-6 □ 7-10 □ 10+

Dersom du spiserer fiskelever bruker du da også kraften/skyen som leveren er kokt i?

□ ja □ nei

Hvis ja, hvor mye bruker du hver gang ?

□ 1 spise skje
□ 2 spise skjeer
□ 0,5 dl
□ 1 dl
□ 1,5 dl
□ + 1,5 dl

I sesongen for fiskelever hvor ofte spiser du fiskelever som pålegg på brød?

□ aldri
□ sjeldnere enn 1 gang per uke
□ 1 gang per uke
□ 2-3 ganger per uke
□ 4-6 ganger per uke
□ daglig

Fisk

Hvilke årstider spiser du de ulike fiskeslagene og hvor ofte (sett inn bokstavkoder som tilsvarer ditt forbruk i tabellen) ?

Koder:
a= aldri
b=1-3 ganger per år
c= hver 3 mnd.
d= hver 2. mnd.
e= 1 per mnd
f = 2-3 per mnd.
g= 1 per uke
h= 2 per uke
i= 3+ per uke

Fisk	*like mye hele året*	*vinter*	*vår*	*sommer*	*høst*
Kveite					
Blåkveite					
Brisling					
Makrell					
Rødspette					
Steinbit					
Røye					
Sik					
Sild					
Ørret					
Laks					
Torsk					
Sei					
Uer					

Dersom du spiser fisk, hvor mye spiser du vanligvis per gang? (1 skive/stykke =150 gram)
☐ 1 ☐ 1,5 ☐ 2 ☐ 3 ☐ 4+

Smør/margarin

Hav slags fett bruker du vanligvis <u>på brødet</u>?
☐ bruker ikke fett på brødet
☐ smør
☐ margarin

Hvor mange skiver brød spiser du per dag ….. antall

Dersom du bruker fett på brødet, hvor tykt lag pleier du å smøre på?
(En kuvertpakke med margarin veier 12 gram, sett ett kryss).
☐ skrapet (3g) ☐ tynt lag (5g) ☐ godt dekket (8 g) ☐ tykt lag (12 g)

Hva slags fett blir vanligvis brukt <u>til matlaging</u> i din husholdning? (Sett gjerne flere kryss)
☐ smør
☐ margarin
☐ olje

Hvor mange glass melk drikker du vanligvis av TINE ekstra lett melk (vitamin D beriket)?
☐ aldri/sjelden ☐ 1-4 per uke ☐ 5-6 per uke ☐ 1 per dag ☐ 2-3 per dag ☐ 4+ per dag

Tran

Bruker du tran (flytende)? ☐ Ja ☐ Nei

Hvis ja, hvor ofte tar du tran?

	aldri/ sjelden	1-3 pr mnd	1 per uke	2-6 per uke	daglig
om vinteren					
om sommeren					

Hvor mye tran pleier du å ta hver gang?

☐ 1 ts ☐ 1/2ss ☐ 1+ss

Bruker du tranpiller/kapsler ☐ ja ☐ nei

Hvis ja, hvor ofte tar du tranpiller /kapsler?

	aldri/ sjelden	1-3 pr mnd	1 per uke	2-6 per uke	daglig
om vinteren					
om sommeren					

Bruker du fiskeolje kapsler? ☐ ja ☐ nei

Hvis ja, hvor ofte tar du fiskeoljekapsler?

☐ aldri/ sjelden
☐ 1-3 pr mnd
☐ 1 per uke
☐ 2-6 pr uke
☐ daglig

Hvilke type fiskeoljekapsler bruker du og hvor mange pleier du å ta hver gang?

	ja	antall pr. gang
Triomar	☐	....
Almarin	☐	....
Nykomed Omega-3	☐	....
Annet, navn.		....

Bruker du annet kosttilskudd (eks. vitaminer, minaeraler)? ☐ ja ☐ nei

Hvis ja; hvor ofte tar du slike kosttilskudd?

☐ sjelden/aldri ☐ 1-3 pr. mnd ☐ 1 uke ☐ 2-6 pr uke ☐ daglig

Navn på kosttilskudd:..

....

....

....

Appendix B

Vi ønsker å undersøke D-vitamin-nivåer hos kvinner i Nord-Norge. Vitamin D kan man enten få via kosten eller fra sollys. Håper du tar deg tid til å fylle ut dette spørreskjemaet og returnere det sammen med blodprøven. Det lille blodprøveglasset er for D-vitamin analysene.
Takk for hjelpen!

SOLING

Var du i Nord-Norge hele sommeren 2001 (juni – august) ? ☐ ja ☐ nei

Hvis nei, oppgi sted og varighet?

Sted	Antall uker

Har du vært på solferie i utlandet fra og med september 2001? ☐ ja ☐ nei

Hvis ja, oppgi hvilket land: .... fra dato......... til dato.........

Hvor mye har du vært ute i dagslys i løpet av de siste 7 dagene? .... antall timer total

Har du vært i solarium i løpet av den siste måneden?

☐ nei ☐ 1-2 ganger ☐ 3+ ganger

FISKELEVER

I sesongen for fiskelever hvor ofte spiser du følgende?

	Aldri/ sjelden	1 gang pr. sesong	2-3 ganger pr. sesong	2-3 ganger pr. mnd	1 gang pr. uke	2-3 ganger pr. uke	+3 ganger pr. uke
Torskelever							
Seilever							

Dersom du spiser fiskelever, hvor mange spiseskjeer pleier du spise hver gang?

☐ spiser ikke fiskelever
☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7-10 ☐ 10-13 ☐ 13+

Dersom du spiser fiskelever bruker du da kraften/fettet som leveren er kokt i?

☐ ja ☐ nei

Hvis ja, hvor mye bruker du hver gang ?

☐ 1-2 ss ☐ 0,5 dl ☐ 1 dl ☐ +1 dl

MELK

Hvor mange glass melk drikker du vanligvis av TINE ekstra lett melk (vitamin D beriket, grønn kartong)?

☐ aldri/sjelden ☐ 1-4 per uke ☐ 5-6 per uke ☐ 1 per dag ☐ 2-3 per dag ☐ 4+ per dag

Vennligst snu arket

TRAN OG KOSTTILSKUDD

Bruker du tran (flytende)? ☐ Ja ☐ Nei

Hvis ja, hvor ofte tar du tran?

	aldri/ sjelden	1-3 pr mnd	1 per uke	2-6 per uke	daglig
vinteren					
sommeren					

Hvor mye tran pleier du å ta hver gang?

☐ 1 ts ☐ 1/2ss ☐ 1+ss

Bruker du tranpiller/kapsler? ☐ ja ☐ nei

Hvis ja, hvor ofte tar du tranpiller/kapsler?

	aldri/ sjelden	1-3 pr mnd	1 per uke	2-6 per uke	daglig
vinteren					
sommeren					

Bruker du annet kosttilskudd (eks. vitaminer, mineraler)? ☐ ja ☐ nei

Hvis ja; hvor ofte tar du slike kosttilskudd?

☐ sjelden/aldri ☐ 1-3 pr. mnd ☐ 1 uke ☐ 2-6 pr uke ☐ daglig

Navn på kosttilskudd: ....

FET FISK

Hvor ofte spiser du følgende?

	Aldri/ sjelden	**1 gang pr. mnd**	**2-3 pr mnd**	**1 pr. uke**	**2-3 ganger pr. uke**	**3 + pr. uke**
Laks, ørret						
Makrell						
Sild						

Dersom du spiser fisk, hvor mye spiser du vanligvis per gang? (1 skive/stykke =150 gram)

☐ 1 skive ☐ 1,5 skive ☐ 2 skiver ☐ 3 skiver ☐ 4 + skiver

SMØR OG MARGARIN

Hva slags fett bruker du vanligvis på brødet?

☐ bruker ikke fett på brødet ☐ smør ☐ margarin

Hvor mange skiver brød spiser du per dag ..... antall

Dersom du bruker fett på brødet, hvor tykt lag pleier du å smøre på?

(En kuvertpakke med margarin veier 12 gram, sett ett kryss).

☐ skrapet (3g) ☐ tynt lag (5g) ☐ godt dekket (8 g) ☐ tykt lag (12 g)

Hva slags fett blir vanligvis brukt til matlaging i din husholdning? (Sett gjerne flere kryss)

☐ smør ☐ margarin ☐ olje

Hvor høy er du?............. **Hva er vekten din?.............**

Appendix C

KVINNER OG KREFT

KONFIDENSIELT

Hvis du samtykker i å være med, sett kryss for JA i ruten ved siden av. Dersom du ikke ønsker å delta kan du unngå purring ved å sette kryss for NEI og returnere skjemaet i vedlagte svarkonvolutt.

Hvis du vil være med, så ber vi deg fylle ut spørreskjemaet så nøye som mulig, se orienteringen på brosjyren for nærmere opplysninger.

Med vennlig hilsen

Eiliv Lund
Professor dr. med

Jeg samtykker i å delta i spørreskjema-undersøkelsen JA ☐ NEI ☐

I hvilken kommune har du bodd lengre enn ett år?

Kommune: **Alder**

1. Fødested: .... Fra [0] år til ☐ år
2. .... Fra ☐ år til ☐ år
3. .... Fra ☐ år til ☐ år
4. .... Fra ☐ år til ☐ år
5. .... Fra ☐ år til ☐ år
6. .... Fra ☐ år til ☐ år
7. .... Fra ☐ år til ☐ år

Menstruasjonsforhold

Er menstruasjonen din;

☐ Regelmessig (naturlig)
☐ Uregelmessig
☐ Uteblitt pga. legemiddelbruk, sykdom, trening, annet
☐ Sluttet/stoppet

Hvis du ikke har menstruasjon;

har den stoppet av seg selv? .... ☐
operert vekk begge eggstokkene? .... ☐
operert vekk livmoren? .... ☐
annet, angi .... ☐

Alder da menstruasjonen opphørte? .... år

Graviditeter etter 1991

Fyll ut for hvert barn du har født etter 1991 fødselsår og antall måneder du ammet (fylles også ut for dødfødte eller for barn som er døde senere i livet). Dersom du ikke har født barn, fortsetter du ved neste spørsmål.

Barn Nr.:	Fødselsår	Antall måneder med amming

P-Pillebruk etter 1991

Har du noen gang brukt p-piller, minipiller inkludert, etter 1991? ☐ Ja ☐ Nei

Bruker du p-piller nå? ☐ Ja ☐ Nei

Vi vil be deg om å besvare spørsmålene om p-pillebruk etter 1991 mer nøye. For hver periode med sammenhengende bruk av samme p-pille merke håper vi du kan si oss hvor gammel du var da du startet, hvor lenge du brukte det samme p-pillemerket og navnet på p-pillene.
Dersom du har tatt opphold eller skiftet merke, skal du besvare spørsmålene for en ny periode. Dersom du ikke husker navnet på p-pillen, sett usikker. For å hjelpe deg til å huske navnet på p-pille merkene ber vi deg bruke den vedlagte brosjyren som viser bilder av p-pille- merker som har vært solgt i Norge. Vennligst oppgi også nummeret på p-pillen som står i brosjyren.

Årstall	Alder ved start	Brukt samme p-pille sammenhengende år	måneder	P-pillene (se brosjyren) Nr.	Navn

Hormonspiral

Har du noengang brukt hormonspiral (Levonova)? ☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt hormonspiral i alt? ..... år

Hvor gammel var du første gang du du fikk innsatt hormonspiral? ..... år

Bruker du hormonspiral nå? ☐ Ja ☐ Nei

Holdning til bruk av østrogen

Hvilket av følgende alternativer dekker best ditt syn på østrogenbehandling i forbindelse med overgangsalderen (sett ett kryss)

Positivt - en hjelp som bør tilbys alle kvinner ☐
Et nødvendig onde- bør bare brukes av de med store plager ☐
Negativt- bør ikke «klusse med naturen» ☐

Bruk av hormonpreparater med østrogen i overgangsalderen

Har du noen gang brukt østrogentabletter/plaster?

☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt østrogentabletter/plaster i alt? ..... år

Hvis du har brukt østrogenpreparater i *kun 1 år eller mindre;* hvorfor har du brukt midlene så kort tid?

- Har nettopp startet behandlingen ☐
- Er kvitt plagene ☐
- Redd for skadevirkninger ☐
- Fikk plagsomme bivirkninger ☐
- Annet ☐

Hvor gammel var du første gang du brukte østrogentabletter/plaster? ..... år

Hvorfor begynte du å bruke østrogentabletter/plaster?

- Lindre plager i overgangsalderen (hetetokter, uopplagthet, underlivsplager mm) ☐
- Forebygge benskjørhet (osteoporose) ☐
- Forebygge hjerte/kar sykdom ☐
- Annet ☐

Bruker du tabletter/plaster nå? ☐ Ja ☐ Nei

UTFYLLENDE SPØRSMÅL TIL ALLE SOM HAR BRUKT ELLER BRUKER PREPARATER MED ØSTROGEN I FORM AV TABLETTER ELLER PLASTER.

For hver periode med sammenhengende bruk av samme østrogenpreparat håper vi du kan si oss hvor gammel du var da du startet, hvor lenge du brukte det samme østrogenpreparatet, og navnet på dette. Dersom du har tatt opphold eller skiftet merke, skal du besvare spørsmålene for en ny periode. Dersom du ikke husker navnet på østrogenpreparatet sett «usikker». For å hjelpe deg til å huske navnet på østrogenpreparatene ber vi deg bruke den vedlagte brosjyren som viser bilder av østrogenpreparater som har vært solgt i Norge. Vennligst oppgi også nummer på østrogentabletten/plasteret som står i brosjyren.

Periode	Alder ved start	Brukt samme østrogen-tablett/plaster Sammenhengende år	måned	Østrogentablett/plaster (se brosjyre) Nr.	Navn
Første					
Andre					
Tredje					
Fjerde					
Femte					

Har østrogenpreparatene gitt deg bivirkninger? ☐ Ja ☐ Nei

Hvis Ja; kryss av for hvilke bivirkninger:

- Uregelmessige blødninger ☐
- Brystspenning ☐
- Kvalme/magesmerter ☐
- Hodepine ☐
- Hudreaksjoner ☐
- Vektøkning ☐ ☐ Ant kg
- Annet .... ☐

Førte de overnevnte bivirkninger til at du forandret østrogenbehandlingen din? ☐ Ja ☐ Nei

Hvis ja;

- Skiftet østrogenpreparat ☐
- Sluttet ☐
- Annet, angi ☐

Østrogenpreparat til lokal bruk i skjeden

Har du noen gang brukt østrogenkrem/stikkpille? ☐ Ja ☐ Nei

Bruker du krem/stikkpille nå? ☐ Ja ☐ Nei

Selvopplevd helse

Oppfatter du din egen helse som; (Sett ett kryss)

☐ meget god ☐ god ☐ dårlig ☐ meget dårlig

Sykdom

Har du eller har du hatt noen av følgende sykdommer?

	Ja	Nei	Hvis Ja: Alder ved start
Høyt blodtrykk	☐	☐	
Hjertesvikt/hjertekrampe	☐	☐	
Årebetennelse	☐	☐	
Blodpropp i legg eller lår	☐	☐	
Hjerteinfarkt	☐	☐	
Slag	☐	☐	
Migrene	☐	☐	
Epilepsi	☐	☐	
Sukkersyke (diabetes)	☐	☐	
Endometriose	☐	☐	
Hypothyreose	☐	☐	
Depresjon (oppsøkt lege)	☐	☐	

For følgende tilstander kryss av for hvilket år tilstanden oppsto eller angi årstall for perioden før 1991.

	før 91	91	92	93	94	95	96	97	98
Muskelsmerter (myalgi)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fibromyalgi/Fibrositt	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kronisk tretthetssyndrom	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ryggsmerter ukjent årsak	☐	☐	☐	☐	☐	☐	☐	☐	☐
Nakkeslengskade	☐	☐	☐	☐	☐	☐	☐	☐	☐
Osteoporose/(b.skjørhet)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Brudd									
Underarmen (håndledd)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ryggvirvel (kompresjon)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Andre brudd angi :...........	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sosiale forhold

Er du: (Sett ett kryss) ☐ gift ☐ samboer ☐ annet

Hvor mange personer er det i ditt hushold? ....

Yrke? ....

Hvor høy er bruttoinntekten i husholdet pr. år?

☐ under 150 000 kr ☐ 151 000–300 000 kr
☐ 301 000–450 000 kr ☐ 451 000–600 000 kr
☐ over 600 000 kr

Røykevaner

	Ja	Nei
Har du noen gang røkt?	☐	☐

Hvis Ja, ber vi deg om å fylle ut hvor mange sigaretter du i gjennomsnitt røkte pr. dag i perioden 1991-1998.

	Antall sigaretter hver dag						
Årstall	0	1-4	5-9	10-14	15-19	20-24	25+
1991-94							
1995-98							

	Ja	Nei
Røker du daglig nå?	☐	☐
Bor du sammen med noen som røker?	☐	☐

Hvis Ja, hvor mange sigaretter røker de til sammen pr. dag? ....

Brystkreft i nærmeste familie

Har noen nære slektninger hatt brystkreft;

	Ja	Nei'	Vet ikke	Alder ved start
datter	☐	☐	☐	☐
mor	☐	☐	☐	☐
mormor	☐	☐	☐	☐
farmor	☐	☐	☐	☐
søster	☐	☐	☐	☐

Hvor mange helsøsken har du? ☐ **Søstre** ☐ **Brødre**
(oppgi antall)

Nummer

Hvilket nummer i søskenflokken er du? ☐

Undersøkelser for kreft

Hvor ofte undersøker du brystene dine selv?
(sett ett kryss)

- Aldri .... ☐
- Uregelmessig .... ☐
- Regelmessig (omtrent hver måned) .... ☐

Går du til regelmessig undersøkelse av brystene dine med mammografi? (sett ett kryss)

- Nei .... ☐
- Ja, med to års mellomrom eller mindre .... ☐
- Ja, med to års mellomrom .... ☐

Fysisk aktivitet

Vi ber deg angi din fysiske aktivitet etter en skala fra svært lite til svært mye. Skalaen nedenfor går fra 1-10. Med fysisk aktivitet mener vi både arbeid i hjemmet og i yrkeslivet, samt trening og annen fysisk aktivitet som turgåing o.l. Sett ring rundt det tallet som best angir ditt nivå av fysisk aktivitet.

Alder	Svært lite								Svært mye
30 år	1	2	3	4	5	6	7	8	9	10
I dag	1	2	3	4	5	6	7	8	9	10

Hvor mange timer pr. dag i gjennomsnitt går eller spaserer du utendørs?

	mindre enn ½ time	½-1 time	1-2 timer	mer enn 2 timer
Vinter				
Vår				
Sommer				
Høst				

	Ja	Nei
Arbeider du utendørs i yrkessammenheng?	☐	☐

Hvis ja:
hvor mange timer pr. uke? ....Sommer ....vinter

Høyde og vekt

Hvor høy er du? .... cm

Hvor mye veier du i dag? .... kg

Kosthold

Vi er interessert i å få kjennskap til hvordan kostholdet ditt er **vanligvis.** Kryss av for hvert spørsmål om hvor ofte du **i gjennomsnitt siste året** har brukt den aktuelle matvaren, og hvor mye du pleier å spise/drikke hver gang.

Hvor mange glass melk drikker du vanligvis av hver type? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-4 pr. uke	5-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Helmelk (søt, sur)	☐	☐	☐	☐	☐	☐
Lettmelk (søt, sur)	☐	☐	☐	☐	☐	☐
Skummet (søt, sur)	☐	☐	☐	☐	☐	☐

Hvor mange kopper kaffe drikker du vanligvis av hver sort? (Sett ett kryss for hver linje)

	aldri/ sjelden	1-6 pr. uke	1 pr. dag	2-3 pr. dag	4-5 pr. dag	6-7 pr. dag	8+ pr. dag
Kokekaffe	☐	☐	☐	☐	☐	☐	☐
Traktekaffe	☐	☐	☐	☐	☐	☐	☐
Pulverkaffe	☐	☐	☐	☐	☐	☐	☐

Hvor mange glass juice, saft og brus drikker du vanligvis? (Sett ett kryss for hver linje)

	aldri/ sjelden	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Appelsinjuice	☐	☐	☐	☐	☐	☐
Saft/brus med sukker	☐	☐	☐	☐	☐	☐
Saft/brus sukkerfri	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du yoghurt (1 beger)? (Sett ett kryss)

☐ aldri/sjelden ☐ 1 pr. uke ☐ 2-3 pr. uke ☐ 4+ pr. uke

Hvor ofte har du i gjennomsnitt siste året spist kornblanding, havregryn eller müsli? (Sett ett kryss)

☐ aldri/nesten aldri ☐ 1-3 pr. uke ☐ 4-6 pr. uke ☐ 1 pr. dag

Hvor mange skiver brød/rundstykker og knekkebrød/skonrokker spiser du vanligvis?
(1/2 rundstykke = 1 brødskive) (Sett ett kryss for hver linje)

	aldri/ sjelden	1-4 pr. uke	5-7 pr. uke	2-3 pr. dag	4-5 pr. dag	6+ pr. dag
Grovt brød						
Fint brød						
Knekkebrød o.l.						

Nedenfor er det spørsmål om bruk av ulike påleggstyper. Vi spør om hvor mange brødskiver med det aktuelle pålegget du pleier å spise. Dersom du også bruker matvarene i andre sammenhenger enn til brød (f. eks. til vafler, frokostblandinger, grøt), ber vi om at du tar med dette når du besvarer spørsmålene.

På hvor mange brødskiver bruker du? (Sett ett kryss pr. linje)

	0 pr. uke	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Syltetøy og annet søtt pålegg						
Brun ost, helfet						
Brun ost, halvfet/mager						
Hvit ost, helfet						
Hvit ost, halvfet/mager						
Kjøttpålegg, leverpostei						

Videre kommer spørsmål om fiskepålegg.
På hvor mange brødskiver pr. uke har du i gjennomsnitt siste året spist? (Sett ett kryss pr. linje)

	0 pr. uke	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7-9 pr. uke	10+ pr. uke
Makrell i tomat, røkt makrell						
Kaviar						
Annet fiskepålegg						

Hva slags fett bruker du vanligvis på brødet?
(Sett gjerne flere kryss)

☐ bruker ikke fett på brødet
☐ smør
☐ hard margarin (f. eks. Per, Melange)
☐ myk margarin (f. eks. Soft)
☐ smørblandet margarin (f. eks. Bremykt)
☐ Brelett
☐ lettmargarin (f. eks. Soft light, Letta)

Dersom du bruker fett på brødet, hvor tykt lag pleier du smøre på? (En kuvertpakke med margarin veier 12 gram).
(Sett ett kryss)

☐ skrapet (3 g) ☐ tynt lag (5 g) ☐ godt dekket (8 g)
☐ tykt lag (12 g)

Hvor ofte spiser du frukt? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1 pr. dag	2+ pr. dag
Epler/pærer							
Appelsiner o.l.							
Bananer							
Annen frukt (f.eks. druer, fersken)							

Hvor ofte spiser du ulike typer grønnsaker?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2 pr. uke	3 pr. uke	4-5 pr. uke	6-7 pr. uke
Gulrøtter							
Kål							
Kålrot							
Broccoli/blomkål							
Blandet salat							
Grønnsakblanding (frossen)							
Andre grønnsaker							

For de grønnsakene du spiser, kryss av for hvor mye du spiser hver gang. (Sett ett kryss for hver sort)

- gulrøtter ☐ 1/2 stk. ☐ 1 stk. ☐ 1 1/2 stk. ☐ 2+ stk.
- kål ☐ 1/2 dl ☐ 1 dl ☐ 1 1/2 dl ☐ 2+ dl
- kålrot ☐ 1/2 dl ☐ 1 dl ☐ 1 1/2 dl ☐ 2+ dl
- broccoli/blomkål ☐ 1-2 buketter ☐ 3-4 buketter ☐ 5+ buketter
- blandet salat ☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl
- grønnsakblanding ☐ 1/2 dl ☐ 1 dl ☐ 2 dl ☐ 3+ dl

Hvor mange poteter spiser du vanligvis (kokte, stekte, mos)? (Sett ett kryss)

☐ spiser ikke/spiser sjelden poteter

☐ 1-4 pr. uke ☐ 5-6 pr. uke

☐ 1 pr. dag ☐ 2 pr. dag

☐ 3 pr. dag ☐ 4+ pr dag

Hvor ofte bruker du ris og spaghetti/makaroni ?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2 pr. uke	3+ pr. uke
Ris					
Spaghetti, makaroni					

Hvor ofte spiser du risengrynsgrøt? (Sett ett kryss)

☐ aldri/sjelden ☐ 1 pr. mnd ☐ 2-3 pr. mnd ☐ 1+ pr. uke

Hva slags fett blir vanligvis brukt <u>til matlaging</u> i din husholdning? (Sett gjerne flere kryss)

☐ smør

☐ hard margarin (f. eks. Per, Melange)

☐ myk margarin (f. eks. Soft)

☐ smørblandet margarin (f. eks. Bremykt)

☐ soyaolje ☐ olivenolje ☐ maisolje

Fisk

Vi vil gjerne vite hvor ofte du pleier å spise fisk, og ber deg fylle ut spørsmålene om fiskeforbruk så godt du kan. Tilgangen på fisk kan variere gjennom året. Vær vennlig å markere i hvilke årstider du spiser de ulike fiskeslagene.

	aldri/ sjelden	like mye hele året	vinter	vår	sommer	høst
Torsk, sei, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Sild						

Med tanke på de periodene av året der du spiser fisk, hvor ofte pleier du å spise følgende? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2 pr. uke	3+ pr. uke
Kokt torsk, sei, hyse, lyr						
Stekt torsk, sei, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Sild						

Dersom du spiser fisk, hvor mye spiser du vanligvis pr. gang? (1 skive/stykke = 150 gram)
(Sett ett kryss for hver linje)

- kokt fisk (skive) ☐ 1 ☐ 1,5 ☐ 2 ☐ 3+
- stekt fisk (stykke) ☐ 1 ☐ 1,5 ☐ 2 ☐ 3+

Hvor mange ganger pr. år spiser du fiskeinnmat?
(Sett ett kryss pr. linje)

	0	1-3	4-6	7-9	10+
Rogn	☐	☐	☐	☐	☐
Fiskelever	☐	☐	☐	☐	☐

Dersom du spiser fiskelever, hvor mange spiseskjeer pleier du å spise hver gang? (Sett ett kryss)

☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

Hvor ofte bruker du følgende typer fiskemat?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr. uke
Fiskekaker/pudding/ boller					
Plukkfisk, fiskegrateng					
Fritytfisk, fiskepinner					
Andre fiskeretter					

Hvor stor mengde pleier du vanligvis å spise av de ulike rettene? (Sett ett kryss for hver linje)

- fiskekaker/pudding/boller (stk.) (2 fiskeboller=1 fiskekake) ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- plukkfisk, fiskegrateng (dl) ☐ 1-2 ☐ 3-4 ☐ 5+
- frityrfisk, fiskepinner (stk.) ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7+

Hvor ofte spiser du skalldyr (f. eks. reker, krabbe)**?** (Sett ett kryss)

aldri/ sjelden	1 pr. mnd	2-3 pr mnd	1+ pr. uke
☐	☐	☐	☐

I tillegg til informasjon om fiskeforbruk er det viktig å få kartlagt hvilket tilbehør som blir servert til fisk. Hvor ofte bruker du følgende til fisk? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr. uke
Smeltet eller fast margarin/fett					
Seterrømme (35%)					
Lettrømme (20%)					
Saus med fett (hvit/brun)					
Saus uten fett (hvit/brun)					

For de ulike typene tilbehør du bruker til fisk, vær vennlig å kryss av for hvor mye du vanligvis pleier spise.

- smeltet/fast fett (ss) ☐ 1/2 ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- seterrømme (ss) ☐ 1/2 ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- lettrømme (ss) ☐ 1/2 ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- saus med fett (dl) ☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 2+
- saus uten fett (dl) ☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 2+

Andre matvarer

Hvor ofte spiser du følgende kjøtt- og fjærkreretter? (Sett ett kryss for hver rett)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr. uke
Steik (okse, svin, får)					
Koteletter					
Biff					
Kjøttkaker, karbonader					
Pølser					
Gryterett, lapskaus					
Pizza m/kjøtt					
Kylling					
Andre kjøttretter					

Dersom du spiser følgende retter, oppgi mengden du vanligvis spiser: (Sett ett kryss for hver linje)

- steik (skiver) ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- koteletter (stk.) ☐ 1/2 ☐ 1 ☐ 1,5 ☐ 2+
- kjøttkaker, karbonader (stk.) ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- pølser (stk. à 150g) ☐ 1/2 ☐ 1 ☐ 1,5 ☐ 2+
- gryterett, lapskaus (dl) ☐ 1-2 ☐ 3 ☐ 4 ☐ 5+
- pizza m/kjøtt (stykke à 100 g) ☐ 1 ☐ 2 ☐ 3 ☐ 4+

Hvor mange egg spiser du vanligvis i løpet av en uke (stekte, kokte, eggerøre, omelett)? (Sett ett kryss)

☐ 0 ☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

Vi ber deg fylle ut hovedrettene til middag en gang til som en oppsummering. Kryss av i den ruten som passer hvor ofte du i gjennomsnitt i løpet av siste år har spist slik mat til middag

	5+ pr. uke	4 pr. uke	3 pr. uke	2 pr. uke	1 pr. uke	2-3 pr. mnd	1 pr. mnd	nesten aldri
Rent kjøtt	☐	☐	☐	☐	☐	☐	☐	☐
Oppmalt kjøtt	☐	☐	☐	☐	☐	☐	☐	☐
Fet fisk (makrell, laks o.l.)	☐	☐	☐	☐	☐	☐	☐	☐
Mager fisk (torsk o.l.)	☐	☐	☐	☐	☐	☐	☐	☐
Fiskemat	☐	☐	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du iskrem (til dessert, krone-is osv.)? (Sett ett kryss for hvor ofte du spiser iskrem om sommeren, og ett kryss for resten av året)

	aldri/ sjelden	1-3 pr mnd	1 pr. uke	2-3 pr. uke	4+ pr. uke
– om sommeren	☐	☐	☐	☐	☐
– resten av året	☐	☐	☐	☐	☐

Hvor mye is spiser du vanligvis pr. gang? (Sett ett kryss)

☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

Hvor ofte spiser du bakervarer som boller, kaker, wienerbrød, vafler, småkaker? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Gjærbakst(boller)						
Kaker						
Pannekaker						
Vafler						
Småkaker						

Hvor ofte spiser du dessert? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Pudding Sjokolade/karamell						
Riskrem, fromasj						
Kompott, fruktgrøt hermetisk frukt						

Hvor ofte spiser du sjokolade? (Sett ett kryss)

☐ aldri/sjelden ☐ 1-3 pr. mnd ☐ 1 pr. uke
☐ 2-3 pr. uke ☐ 4-6 pr. uke ☐ 1+ pr. dag

Dersom du spiser sjokolade, hvor mye pleier du vanligvis å spise hver gang? Tenk deg størrelsen på en Kvikk-Lunsj sjokolade, og oppgi hvor mye du spiser i forhold til den.

☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 1,5 ☐ 2+

Hvor ofte spiser du salt snacks? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Potetchips						
Peanøtter						

Tilberedningsmåte

Har du mikrobølgeovn? ☐ Ja ☐ Nei

Hvis Ja; hvor mange ganger pr. uke bruker du mikrobølgeovnen til ganger pr. uke

middagslaging? ....
annet? ....

Hvilken farve foretrekker du på stekeskorpen?

☐ Lys brun ☐ Middels ☐ Mørk brun

Hvor ofte spiser du stekt eller grillet mat?

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Mørkt kjøtt (biff ol.)						
Lyst kjøtt (kylling ol.)						
Oppmalt kjøtt (kjøttkaker ol.)						
Bacon						
Fisk						

Bruker du stekefettet eller sjyen etter steking?

☐ nei, aldri ☐ av og til
☐ som oftest ☐ ja, alltid

Tran og fiskeoljekapsler

Bruker du tran (flytende)? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du tran?
Sett ett kryss for hver linje.

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
- om vinteren	☐	☐	☐	☐	☐
- resten av året	☐	☐	☐	☐	☐

Hvor mye tran pleier du å ta hver gang?

☐ 1 ts ☐ 1/2ss ☐ 1+ss

Bruker du tranpiller/kapsler? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du tranpiller/kapsler?
Sett ett kryss for hver linje.

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
- om vinteren	☐	☐	☐	☐	☐
- resten av året	☐	☐	☐	☐	☐

Hvilken type tranpiller/kapsler bruker du vanligvis, og hvor mange pleier du å ta hver gang?

	ja	antall pr. gang
Møllers trankapsler	☐	....
Møllers omega-3 kapsler	☐	....
Møllers dobbel	☐	....
annet, navn	☐	....

Bruker du fiskeoljekapsler? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du fiskeoljekapsler?

aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
☐	☐	☐	☐	☐

Hvilken type fiskeoljekapsler bruker du vanligvis, og hvor mange pleier du å ta hver gang?

	ja	antall pr. gang
Triomar	☐	....
Almarin	☐	....
Nycomed Omega-3	☐	....
annet, navn	☐	....

Kosttilskudd

Bruker du annet kosttilskudd (eks. vitaminer, mineraler)? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du slike kosttilskudd?

aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
☐	☐	☐	☐	☐

Navn ....

Alkohol

Er du total avholdskvinne? ☐ Ja ☐ Nei

Hvis Nei, hvor ofte og hvor mye drakk du i gjennomsnitt siste året? (Sett ett kryss for hver linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Øl ($^1/_2$ L)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

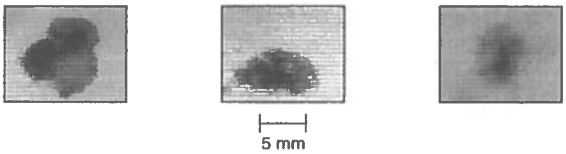
Solvaner

Får du fregner når du soler deg? ☐ Ja ☐ Nei

Hvor mange føflekker har du sammenlagt på begge armer (fra fingertuppene til skuldrene)?

☐ 0 ☐ 1-10 ☐ 11-50 ☐ 51+

Hvor mange uregelmessige føflekker større enn 5 mm har du sammenlagt på begge armene (fra fingrene til armhulene)? Tre eksempler på føflekker større enn 5 mm med uregelmessig form er vist i nedenfor.



☐ 0 ☐ 1 ☐ 2-3 ☐ 4-6 ☐ 7-12 ☐ 13-24 ☐ 25+

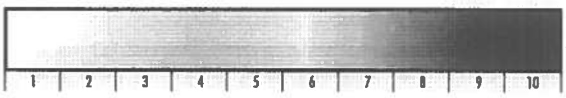
Hvor mange små, regelmessige føflekker har du sammenlagt på begge armene (fra fingrene til armhulene)?

☐ 0 ☐ 1-10 ☐ 11-50 ☐ 51+

Hva er din opprinnelige hårfarge? (sett ett kryss)

☐ mørkbrunt, svart ☐ brun ☐ blond, gul ☐ rød

For å kunne studere effekten av soling på risiko for hudkreft ber vi deg gi opplysninger om hudfarge
Sett ett kryss på den fargen som best passer din hudfarge (uten soling)



Hvor ofte dusjer eller bader du?

	Mer enn 1 g dagl	1 g dagl	4-6 g pr. uke	2-3 g pr. uke	1 g pr. uke	2-3 g pr. mnd.	Sjelden aldri
Med såpe/shampo							
Uten såpe/shampo							

Hvor mange ganger pr. år er du blitt forbrent av solen slik at du har fått svie og blemmer med avflassing etterpå? (ett kryss for hver aldersgruppe)

Årstall	Aldri	Høyst 1 gang pr. år	2-3 g. pr. år	4-5 g. pr. år	6 eller flere ganger
1991-94					
1995-98					

Hvor mange uker soler du deg pr. år i syden?

Årstall	Aldri	1 uke	2-3 uker	4-5 uker	7 uker eller mer
1991-94					
1995-98					

Hvor mange uker pr. år soler du deg i Norge eller utenfor syden?

Årstall	Aldri	1 uke	2-3 uker	4-5 uker	7 uker eller mer
1991-94					
1995-98					

Når bruker du krem med solfaktor (sett evt. flere kryss):

☐ påsken ☐ i Norge eller utenfor syden ☐ solferie i syden

Hvilke solfaktorer bruker du i disse periodene?

	påsken	i Norge eller utenfor syden	solferie i syden
- I dag	....	....	....
- For 10 år siden	....	....	....

Hvilke solkremmerker bruker du? Angi faktor hvis du husker.

	Ja	faktor		Ja	faktor
Piz Buin	☐	....	Cosmica	☐	....
Ambre Solairé	☐	....	Natusan	☐	....
HTH	☐	....	Delial	☐	....
Andre, angi navn...........		....			

Hvor ofte har du solt deg i solarium?

Alder	Aldri	Sjelden	1 gang pr. mnd.	2 ganger pr. mnd.	3-4 ganger pr. mnd	oftere enn1 gang pr. uke
1991-94						
1995-98						

Til slutt vil vi spørre deg om ditt samtykke til å kontakte deg på nytt pr. post.
Vi vil hente adressen fra det sentrale personregister.

☐ Ja ☐ Nei

Takk for at du ville delta i undersøkelsen

Appendix D

Spørreskjema til "Møljeforsøket" - Skjervøy 2001

Vennligst fyll ut dette spørreskjemaet så nøye som mulig og lever det senest ved 3. møljemåltid mandag 19. mars.

Takk for hjelpen!

Alder .... **Høyde ....** **Vekt ......**

Kjønn ☐ kvinne

☐ mann

FISKELEVER

I sesongen for fiskelever hvor ofte spiser du **torskelever ?**

☐ aldri
☐ 1 gang per sesong
☐ 2-3 ganger per sesong
☐ 2-3 ganger per mnd
☐ 1 gang per uke
☐ 2-3 ganger per uke
☐ oftere enn 3 ganger per uke

I sesongen for fiskelever hvor ofte spiser du **seilever ?**

☐ aldri
☐ 1 gang per sesong
☐ 2-3 ganger per sesong
☐ 2-3 ganger per mnd
☐ 1 gang per uke
☐ 2-3 ganger per uke
☐ oftere enn 3 ganger per uke

Dersom du spiser fiskelever, hvor mange spiseskjeer pleier du spise hver gang?

☐ spiser ikke fiskelever
☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7-10 ☐ 10-13 ☐ 13+

Dersom du spiserer fiskelever bruker du da også kraften/skyen som leveren er kokt i?

☐ ja ☐ nei

Hvis ja, hvor mye bruker du hver gang ?

☐ 1 spise skje
☐ 2 spise skjeer
☐ 0,5 dl
☐ 1 dl
☐ 1,5 dl
☐ + 1,5 d

SOLING

Har du vært i Syden eller lignende i løpet av den siste måneden ? ☐ ja ☐ nei

Hvor mye har du vært ***ute i dagslys*** **løpet av de siste 7 dagene?** .... antall timer

Har du vært i solarium i løpet av den siste måneden?

☐ nei ☐ 1-2 gagner ☐ 3+ ganger

Nedenfor er det spørsmål om bruk av ulike påleggstyper. Vi spør om hvor mange brødskiver med det aktuelle pålegget du pleier å spise. Dersom du også bruker matvarene i andre sammenhenger enn til brød (f. eks. til vafler, frokostblandinger, grøt), ber vi om at du tar med dette når du besvarer spørsmålene.

På hvor mange brødskiver bruker du? (Sett ett kryss pr. linje)

	0 pr. uke	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Syltetøy og annet søtt pålegg						
Brun ost, helfet						
Brun ost, halvfet/mager						
Hvit ost, helfet						
Hvit ost, halvfet/mager						
Kjøttpålegg, leverpostei						

Videre kommer spørsmål om fiskepålegg.
På hvor mange brødskiver pr. uke har du i gjennomsnitt siste året spist? (Sett ett kryss pr. linje)

	0 pr. uke	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7-9 pr. uke	10+ pr. uke
Makrell i tomat, røkt makrell						
Kavlar						
Annet fiskepålegg						

Hva slags fett bruker du vanligvis på brødet?
(Sett gjerne flere kryss)

- ☐ bruker ikke fett på brødet
- ☐ smør
- ☐ hard margarin (f. eks. Per, Melange)
- ☐ myk margarin (f. eks. Soft)
- ☐ smørblandet margarin (f. eks. Bremykt)
- ☐ Brelett
- ☐ lettmargarin (f. eks. Soft light, Letta)

Dersom du bruker fett på brødet, hvor tykt lag pleier du smøre på? (En kuvertpakke med margarin veier 12 gram).
(Sett ett kryss)

☐ skrapet (3 g) ☐ tynt lag (5 g) ☐ godt dekket (8 g)
☐ tykt lag (12 g)

Hvor ofte spiser du frukt? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1 pr. dag	2+ pr. dag
Epler/pærer							
Appelsiner o.l.							
Bananer							
Annen frukt (f.eks. druer, fersken)							

Kosthold

Vi er interessert i å få kjennskap til hvordan kostholdet ditt er vanligvis. Kryss av for hvert spørsmål om hvor ofte du i gjennomsnitt siste året har brukt den aktuelle matvaren, og hvor mye du pleier å spise/drikke hver gang.

Hvor mange glass melk drikker du vanligvis av hver type? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-4 pr. uke	5-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Helmelk (søt, sur)	☐	☐	☐	☐	☐	☐
Lettmelk (søt, sur)	☐	☐	☐	☐	☐	☐
Ekstra lettmelk sur)	☐	☐	☐	☐	☐	☐
Skummet (søt, sur)	☐	☐	☐	☐	☐	☐

Hvor mange kopper kaffe drikker du vanligvis av hver sort? (Sett ett kryss for hver linje)

	aldri/ sjelden	1-6 pr. uke	1 pr. dag	2-3 pr. dag	4-5 pr. dag	6-7 pr. dag	8+ pr. dag
Kokekaffe	☐	☐	☐	☐	☐	☐	☐
Traktekaffe	☐	☐	☐	☐	☐	☐	☐
Pulverkaffe	☐	☐	☐	☐	☐	☐	☐

Hvor mange glass juice, saft og brus drikker du vanligvis? (Sett ett kryss for hver linje)

	aldri/ sjelden	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Appelsinjuice	☐	☐	☐	☐	☐	☐
Saft/brus med sukker	☐	☐	☐	☐	☐	☐
Saft/brus sukkerfri	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du yoghurt (1 beger)? (Sett ett kryss)

☐ aldri/sjelden ☐ 1 pr. uke ☐ 2-3 pr. uke ☐ 4+ pr. uke

Hvor ofte har du i gjennomsnitt siste året spist kornblanding, havregryn eller müsli? (Sett ett kryss)

☐ aldri/nesten aldri ☐ 1-3 pr. uke ☐ 4-6 pr. uke ☐ 1 pr. dag

Hvor mange skiver brød/rundstykker og knekkebrød/skonrokker spiser du vanligvis?
(1/2 rundstykke = 1 brødskive) (Sett ett kryss for hver linje)

	aldri/ sjelden	1-4 pr. uke	5-7 pr. uke	2-3 pr. dag	4-5 pr. dag	6+ pr. dag
Grovt brød						
Fint brød						
Knekkebrød o.l.						

Hvor ofte spiser du ulike typer grønnsaker?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2 pr. uke	3 pr. uke	4-5 pr. uke	6-7 pr. uke
Gulrøtter							
Kål							
Kålrot							
Broccoli/blomkål							
Blandet salat							
Grønnsakblanding (frossen)							
Andre grønnsaker							

For de grønnsakene du spiser, kryss av for hvor mye du spiser hver gang. (Sett ett kryss for hver sort)

- gulrotter ☐ 1/2 stk. ☐ 1 stk. ☐ 1 1/2 stk. ☐ 2+ stk.
- kål ☐ 1/2 dl ☐ 1 dl ☐ 1 1/2 dl ☐ 2+ dl
- kålrot ☐ 1/2 dl ☐ 1 dl ☐ 1 1/2 dl ☐ 2+ dl
- broccoli/blomkål ☐ 1-2 buketter ☐ 3-4 buketter ☐ 5+ buketter
- blandet salat ☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl
- grønnsakblanding ☐ 1/2 dl ☐ 1 dl ☐ 2 dl ☐ 3+ dl

Hvor mange poteter spiser du vanligvis (kokte, stekte, mos)? (Sett ett kryss)

☐ spiser ikke/spiser sjelden poteter

☐ 1-4 pr. uke ☐ 5-6 pr. uke

☐ 1 pr. dag ☐ 2 pr. dag

☐ 3 pr. dag ☐ 4+ pr dag

Hvor ofte bruker du ris og spaghetti/makaroni ?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2 pr. uke	3+ pr. uke
Ris					
Spaghetti, makaroni					

Hvor ofte spiser du risengrynsgrøt? (Sett ett kryss)

☐ aldri/sjelden ☐ 1 pr. mnd ☐ 2-3 pr. mnd ☐ 1+ pr. uke

Hva slags fett blir vanligvis brukt til matlaging i din husholdning? (Sett gjerne flere kryss)

☐ smør

☐ hard margarin (f. eks. Per, Melange)

☐ myk margarin (f. eks. Soft)

☐ smørblandet margarin (f. eks. Bremykt)

☐ soyaolje ☐ olivenolje ☐ maisolje

Fisk

Vi vil gjerne vite hvor ofte du pleier å spise fisk, og ber deg fylle ut spørsmålene om fiskeforbruk så godt du kan. Tilgangen på fisk kan variere gjennom året. Vær vennlig å markere i hvilke årstider du spiser de ulike fiskeslagene.

	aldri/ sjelden	like mye hele året	vinter	vår	sommer	høst
Torsk, sei, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Sild						

Med tanke på de periodene av året der du spiser fisk, hvor ofte pleier du å spise følgende? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2 pr. uke	3+ pr. uke
Kokt torsk, sei, hyse, lyr						
Stekt torsk, sei, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Sild						

Dersom du spiser fisk, hvor mye spiser du vanligvis pr. gang? (1 skive/stykke = 150 gram)
(Sett ett kryss for hver linje)

Kokt fisk (skive) ☐ 1 ☐ 1,5 ☐ 2 ☐ 3 ☐ 4+
Stekt fisk (stykke) ☐ 1 ☐ 1,5 ☐ 2 ☐ 3 ☐ 4+

Hvor ofte bruker du følgende typer fiskemat?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr uke
Fiskekaker/pudding/ boller					
Plukkfisk, fiskegrateng					
Frityrfisk, fiskepinner					
Andre fiskeretter					

Hvor stor mengde pleier du vanligvis å spise av de ulike rettene? (Sett ett kryss for hver linje)

- fiskekaker/pudding/boller (stk.) (2 fiskeboller=1 fiskekake) ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- plukkfisk, fiskegrateng (dl) ☐ 1-2 ☐ 3-4 ☐ 5+
- frityrfisk, fiskepinner (stk.) ☐ 1-2 ☐ 3-4 ☐ 5-6 ☐ 7+

Hvor ofte spiser du skalldyr (f. eks. reker, krabbe)? (Sett ett kryss)

aldri/ sjelden	1 pr. mnd	2-3 pr mnd	1+ pr. uke
☐	☐	☐	☐

I tillegg til informasjon om fiskeforbruk er det viktig å få kartlagt hvilket tilbehør som blir servert til fisk. Hvor ofte bruker du følgende til fisk? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr. uke
Smeltet eller fast margarin/fett					
Seterromme (35%)					
Lettromme (20%)					
Saus med fett (hvit/brun)					
Saus uten fett (hvit/brun)					

For de ulike typene tilbehør du bruker til fisk, vær vennlig å kryss av for hvor mye du vanligvis pleier spise.

- smeltet/fast fett (ss) ☐ 1/2 ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- seterromme (ss) ☐ 1/2 ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- lettromme (ss) ☐ 1/2 ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- saus med fett (dl) ☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 2+
- saus uten fett (dl) ☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 2+

Andre matvarer

Hvor ofte spiser du følgende kjøtt- og fjærkreretter? (Sett ett kryss for hver rett)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr. uke
Steik (okse, svin, får)					
Koteletter					
Biff					
Kjøttkaker, karbonader					
Pølser					
Gryterett, lapskaus					
Pizza m/kjøtt					
Kylling					
Andre kjøttretter					

Dersom du spiser følgende retter, oppgi mengden du vanligvis spiser: (Sett ett kryss for hver linje)

- steik (skiver) ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- koteletter (stk.) ☐ 1/2 ☐ 1 ☐ 1,5 ☐ 2+
- kjøttkaker, karbonader (stk.) ☐ 1 ☐ 2 ☐ 3 ☐ 4+
- pølser (stk. à 150g) ☐ 1/2 ☐ 1 ☐ 1,5 ☐ 2+
- gryterett, lapskaus (dl) ☐ 1-2 ☐ 3 ☐ 4 ☐ 5+
- pizza m/kjøtt (stykke à 100 g) ☐ 1 ☐ 2 ☐ 3 ☐ 4+

Hvor mange egg spiser du vanligvis i løpet av en uke (stekte, kokte, eggerøre, omelett)? (Sett ett kryss)

☐ 0 ☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

Vi ber deg fylle ut hovedrettene til middag en gang til som en oppsummering. Kryss av i den ruten som passer hvor ofte du i gjennomsnitt i løpet av siste år har spist slik mat til middag

	5+ pr. uke	4 pr. uke	3 pr. uke	2 pr. uke	1 pr. uke	2-3 pr. mnd	1 pr. mnd	nesten aldri
Rent kjøtt	☐	☐	☐	☐	☐	☐	☐	☐
Oppmalt kjøtt	☐	☐	☐	☐	☐	☐	☐	☐
Fet fisk (makrell, laks o.l.)	☐	☐	☐	☐	☐	☐	☐	☐
Mager fisk (torsk o.l.)	☐	☐	☐	☐	☐	☐	☐	☐
Fiskemat	☐	☐	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du iskrem (til dessert, krone-is osv.)? (Sett ett kryss for hvor ofte du spiser iskrem om sommeren, og ett kryss for resten av året)

	aldri/ sjelden	1-3 pr mnd	1 pr. uke	2-3 pr. uke	4+ pr. uke
– om sommeren	☐	☐	☐	☐	☐
– resten av året	☐	☐	☐	☐	☐

Hvor mye is spiser du vanligvis pr. gang? (Sett ett kryss)

☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

Hvor ofte spiser du bakervarer som boller, kaker, wienerbrød, vafler, småkaker? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Gjærbakst(boller)						
Kaker						
Pannekaker						
Vafler						
Småkaker						

Hvor ofte spiser du dessert? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Pudding - Sjokolade/karamell						
Riskrem, fromasj						
Kompott, fruktgrøt hermetisk frukt						

Hvor ofte spiser du sjokolade? (Sett ett kryss)

☐ aldri/sjelden ☐ 1-3 pr. mnd ☐ 1 pr. uke
☐ 2-3 pr. uke ☐ 4-6 pr. uke ☐ 1+ pr. dag

Dersom du spiser sjokolade, hvor mye pleier du vanligvis å spise hver gang? Tenk deg størrelsen på en Kvikk-Lunsj sjokolade, og oppgi hvor mye du spiser i forhold til den.

☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 1,5 ☐ 2+

Hvor ofte spiser du salt snacks? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Potetchips						
Peanøtter						

Tilberedningsmåte

Har du mikrobølgeovn? ☐ Ja ☐ Nei

Hvis Ja; hvor mange ganger pr. uke bruker du mikrobølgeovnen til — ganger pr. uke
middagslaging? ....
annet? ....

Hvilken farve foretrekker du på stekeskorpen?

☐ Lys brun ☐ Middels ☐ Mørk brun

Hvor ofte spiser du stekt eller grillet mat?

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Mørkt kjøtt (biff ol.)						
Lyst kjøtt (kylling ol.)						
Oppmalt kjøtt (kjøttkaker ol.)						
Bacon						
Fisk						

Bruker du stekefettet eller sjyen etter steking?

☐ nei, aldri ☐ av og til
☐ som oftest ☐ ja, alltid

Tran og fiskeoljekapsler

Bruker du tran (flytende)? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du tran?
Sett ett kryss for hver linje.

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
- om vinteren	☐	☐	☐	☐	☐
- resten av året	☐	☐	☐	☐	☐

Hvor mye tran pleier du å ta hver gang?

☐ 1 ts ☐ 1/2ss ☐ 1+ss

Bruker du tranpiller/kapsler? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du tranpiller/kapsler?
Sett ett kryss for hver linje.

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
- om vinteren	☐	☐	☐	☐	☐
- resten av året	☐	☐	☐	☐	☐

Hvilken type tranpiller/kapsler bruker du vanligvis, og hvor mange pleier du å ta hver gang?

	ja	antall pr. gang
Møllers Basic	☐	....
Møllers dobbel	☐	....
annet, navn	☐	....

Bruker du fiskeoljekapsler? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du fiskeoljekapsler?

aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
☐	☐	☐	☐	☐

Kosttilskudd

Bruker du annet kosttilskudd (eks. vitaminer, mineraler)? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du slike kosttilskudd?

aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-6 pr. uke	daglig
☐	☐	☐	☐	☐

Navn ....

Alkohol

Er du total avholdskvinne? ☐ Ja ☐ Nei

Hvis Nei, hvor ofte og hvor mye drakk du i gjennomsnitt siste året? (Sett ett kryss for hver linje)

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Øl (½ L)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

ISM SKRIFTSERIE - FØR UTGITT:

1. Bidrag til belysning av medisinske og sosiale forhold i Finnmark fylke, med særlig vekt på forholdene blant finskættede i Sør-Varanger kommune.
   Av Anders Forsdahl, 1976. (nytt opplag 1990)

2. Sunnhetstilstanden, hygieniske og sosiale forhold i Sør-Varanger kommune 1869-1975 belyst ved medisinal-beretningene.
   Av Anders Forsdahl, 1977.

3. Hjerte-karundersøkelsen i Finnmark - et eksempel på en populasjonsundersøkelse rettet mot cardiovasculære sykdommer. Beskrivelse og analyse av etterundersøkelsesgruppen.
   Av Jan-Ivar Kvamme og Trond Haider, 1979.

4. The Tromsø Heart Study: Population studies of coronary risk factors with special emphasis on high density lipoprotein and the family occurrence of myocardial infarction.
   Av Olav Helge Førde og Dag Steinar Thelle, 1979.

5. Reformer i distriktshelsetjenesten III: Hypertensjon i distriktshelsetjenesten.
   Av Jan-Ivar Kvamme, 1980.

6. Til professor Knut Westlund på hans 60-års dag, 1983.

7.* Blodtrykksovervåkning og blodtrykksmåling.
   Av Jan-Ivar Kvamme, Bernt Nesje og Anders Forsdahl, 1983.

8.* Merkesteiner i norsk medisin reist av allmennpraktikere - og enkelte utdrag av medisinalberetninger av kulturhistorisk verdi.
   Av Anders Forsdahl, 1984.

9. "Balsfjordsystemet." EDB-basert journal, arkiv og statistikksystem for primærhelsetjenesten.
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