# Dietary habits of fish and dairy products in patients with dyslipidemia referred to Lipid Clinics in Denmark and Norway

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# Abstract

**Background**: Familial hypercholesterolemia (FH) is a common autosomal genetic disease, causing increased levels of low-density lipoprotein cholesterol (LDL-C). Subjects with FH have a higher risk of premature cardiovascular disease (CVD) compared to the general population. A healthy diet is essential for reducing risk of CVD. Having a high consumption of fish as well as choosing low-fat dairy products may be favorable in patients with FH.

**Objectives**: The primary objective of this project was to investigate intake of fish and dairy in a study population of patients with FH in Norway and in a study population suspected of FH in Denmark according to age, sex, body mass index (BMI) and lipid levels, respectively. Furthermore, we aimed to investigate whether intake of fish and dairy products differed in subjects with and without previous or family history of CVD in Danes suspected of FH. We hypothesized that high intakes of fish were associated with higher HDL-C and related to clinical characteristics such as older age, lower BMI, and a history of CVD personally or in the family, and that high intakes of high-fat dairy products were related to higher age, BMI and LDL-C.

**Methods**: This project included 346 subjects from the Danish Find FH study. Subjects were included during visit at the Lipid Clinics in Aalborg and Viborg. Norwegian subjects included 104 patients from the Lipid Clinic in Oslo. Information on fish and dairy intake was collected by mean of the food frequency questionnaires (FFQs) HeartDiet and SmartDiet in Denmark and Norway, respectively.

**Results:** Intake of fish both for lunch and dinner was higher in subjects >50 years of age compared to subjects <50 years of age in both the Norwegian ($p = 0.045$ and $<0.001$, respectively) and the Danish ($p = 0.002$ and 0.028, respectively) populations. Reduced fat cream and other dairy products was related to lower LDL-C in Norwegian subjects ($p = 0.014$). Higher total fish score was statistically significantly associated with higher total cholesterol ($p = 0.032$) and HDL-C ($p <0.001$) in Danish subjects. Danish subjects over 50 years of age consumed more full-fat cheese compared to younger subjects.

**Conclusion**: In both Norwegian patients with FH and Danish subjects suspected for FH, age had the largest impact on intake of fish which indicates that consumption of fish may be an important focus point in dietary counselling of young patients with severe hypercholesterolemia. Higher intakes of fish were also related to higher HDL-C and total cholesterol in Danish subjects.

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# Abbreviations

| | |
|---|---|
| ANOVA | Analyses of variance |
| ASCVD | Atherosclerotic cardiovascular disease |
| CHD | Coronary heart disease |
| CVD | Cardiovascular disease |
| DANSDA | Danish National Survey of Dietary Habits and Physical Activity |
| DHA | Docosahexaenoic acid |
| DLCNS | Dutch Lipid Clinical Network Score |
| EAS | European Atherosclerosis Society |
| EPA | Eicosapentaenoic acid |
| ESC | European Society of Cardiology |
| FA | Fatty acid |
| FFQ | Food frequency questionnaire |
| FH | Familiar hypercholesterolemia |
| HDL | High-density lipoprotein |
| HDL-C | High-density lipoprotein cholesterol |
| HMG-CoA | Hydroxy-3-methyl-glutaryl coenzyme A |
| LDL | Low-density lipoprotein |
| LDL-C | Low-density lipoprotein cholesterol |
| LDLR | Low-density lipoprotein receptor |
| LPL | Lipoprotein lipase |
| MEDPED | Make Early Diagnosis to Prevent Early Death |
| NCEP | National Cholesterol Education Program |
| PCSK9 | Proprotein convertase subtilisin/kexin-type 9 |
| PUFA | Polyunsaturated fatty acid |

| | |
|---|---|
| SFA | Saturated fatty acid |
| TAG | Triacylglycerol |
| TG | Triglyceride |
| VLDL | Very low-density lipoprotein |
| WHO | World Health Organization |

# 1 Introduction

## 1.1 Global and national burden of CVD

Cardiovascular disease (CVD) is the leading cause of death in the world and is responsible for two-thirds of all deaths (1-5). Major CVDs include coronary heart disease (CHD), stroke, peripheral artery disease, and aortic disease (5, 6). The American Heart Association estimates that 2.0 million major CVD events in the United States could be prevented if the adult population achieved better cardiovascular health with recommended physical activity, avoiding or cessation of smoking, and maintaining a healthy weight and diet (7).

The burden of CVD is significant also in Norway and Denmark. In 2020, approximately 200.000 Norwegians were hospitalized or received out-patient care due to CVD (8). In Denmark, more than half a million people were registered with a diagnosis if CVD in 2020, which is an increase of 30% since 2004 (9). However, in Denmark, the incidence of myocardial infarction has declined since 2005 (10). An aging population may in part explain the observed increase in total numbers of CVD. Drugs targeting hypertension and hypercholesterolemia are the most common CVD preventing medications (9). In Norway, medications for preventing or treating CVD were given to 22% of the population in 2020 (8). In Denmark, the total costs of medicine related to CVD were estimated to be 1,81 billion DKK in 2017 (9). CVD has, in other words, major implications on individuals, their families and the society.

## 1.2 Atherosclerosis and CVD

The major diseases of CVDs, CHD and ischemic stroke, are driven by atherosclerosis as the main underlying pathogenesis. Atherosclerosis involves the buildup of cholesterol plaques in arteries which may result in atherosclerotic cardiovascular diseases (ASCVD) both more chronic like angina pectoris and peripheral arterial disease or acute events such as myocardial infarction, ischemic stroke and sudden cardiac death, often elicited by a malignant ventricular arrhythmia like ventricular fibrillation (3, 11).

Several factors are involved in the development and progression of ASCVD. Increased levels of cholesterol in the blood circulation predispose to the retention of low-density lipoproteins (LDL) in the arterial wall (12). LDL is a compound particle consisting of esterified and unesterified cholesterol, phospholipids, triacylglycerol (TAG), and proteins. Endothelial dysfunction is an early event during atherogenesis, and several factors may increase endothelial permeability, such as dyslipidemias, diabetes mellitus, hypertension, obesity, and smoking (13). Increased permeability of the endothelial cells enhances the propensity of LDL to cross the endothelial border leading to increased accumulation in the arterial wall.

Subsequently, LDL particles are phagocytosed by macrophages, which together with endothelial cells play a pivotal role in the atherosclerotic process through production of inflammatory mediators (12, 14). Modifications of the LDL particle such as oxidation, lipolysis, and proteolysis take place inside the arterial wall and enhance the uptake of LDL by macrophages. Lipid-rich macrophages, or foam cells, form “fatty streaks”, which is considered one of the earliest signs of atherosclerosis (11).

Inflammation, together with apoptotic or necrotic death of endothelial and smooth muscle cells and macrophages, may lead to the formation of a necrotic core and destabilization of atherosclerotic plaques (15), which increase the risk of rupture of the fibrous cap covering the lipid-rich core. Disruption of the fibrous cap may initiate a thrombotic response, and the resulting blood clot may result in acute manifestations of CVD such as ischemic stroke and myocardial infarction or malignant arrhythmias (12). Both lipid and connective tissue may be subject to calcification in the atherosclerotic plaque (15). Calcification increases with age and atherosclerotic burden can be determined using cardiac tomography (16).

## **1.3** Cholesterol

### **1.3.1** Absorption and distribution

Dietary cholesterol is absorbed in the small intestine. In the enterocytes, cholesterol is packed together with TAG and apolipoprotein B48 in chylomicrons. The chylomicrons are transported in the lymphatic system and released into the circulation, where they deliver dietary lipids to peripheral tissues. Transfer of TAG and cholesterol to peripheral tissue, mainly adipose and muscle, occurs by interaction with the enzyme lipoprotein lipase (LPL).

The particles shrink due to loss of fatty acids (FAs) and cholesterol and are transformed into chylomicron remnants, which eventually are taken up by the liver. In the liver, both exogenous and endogenous cholesterol is packed in lipoproteins. A large proportion of lipoproteins released from the liver consists of cholesteryl esters and TAG and are called very-low-density lipoprotein (VLDL). The VLDL particle contains apolipoprotein B100 (17). Through the action of the enzymes LPL and hepatic lipase, TAG is transferred to cells in peripheral tissues. The remaining lipoprotein contains a core rich in cholesteryl esters and a surface of phospholipids and free cholesterol. This lipoprotein has a higher density compared to VLDL and is thus called low-density lipoprotein (LDL). LDL delivers cholesterol to tissues by LDL receptor (LDLR) mediated uptake (18, 19) and is reused or removed from the circulation primarily by uptake via hepatic LDLR.

### **1.3.2** Functions

Cholesterol is a part of the lipid bilayer of cell membranes. Cholesterol contributes to maintaining a favorable fluidity and an ordered structure of the membrane as well as regulation of membrane proteins. Several intracellular signaling pathways are dependent on cholesterol (20). Cholesterol is the precursor of steroid hormones such as corticosteroids and sex hormones as well as vitamin D and bile acids. Bile acids aid in the absorption of fat in the intestine (21, 22). Cholesterol is a component of the myelin sheaths covering nerve cells, supporting efficient signal transduction and interestingly, 20% of total body cholesterol is found in the brain (23). Extrahepatic cells can regulate their cholesterol metabolism by a negative feedback control by mean of the rate-limiting enzyme in cholesterol synthesis 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase (19, 24).

### **1.3.3** Role of lipoproteins in atherosclerosis

LDL cholesterol (LDL-C) is considered a causal factor in development of atherosclerosis and the risk of ASCVD increases with high levels of LDL-C in a dose-dependent manner (25). High-density lipoprotein (HDL) is a lipoprotein containing less cholesterol and TAG compared to LDL and is associated with apolipoprotein AI and AII (18). The traditional view has been that HDL was a protective lipoprotein and triglycerides (TG) of minor importance for CVD. This has been challenged as recent data may suggest that HDL cholesterol (HDL-C) is merely a marker of risk, while TG may be causally related to CVD possibly due to their content of (remnant) cholesterol (26).

A large meta-analysis conducted by Baigent et al. found a 22% reduction in cardiovascular mortality with every 1 mmol/l reduction in LDL-C over five years in healthy subjects and in patients with CVD (27). Elevated non-HDL-C and TG have also been found to increase the risk of developing CHD (28). Also, other apolipoprotein B-containing particles have been shown to be atherogenic and several studies have reported a positive association with ASCVD (29-31).

## **1.4** Familial hypercholesterolemia

Familial hypercholesterolemia (FH) is an autosomal dominant disorder causing life-long elevated levels of LDL-C. FH is associated with a significantly increased risk of premature ASCVD and death (14, 32, 33). The frequency of heterozygous FH is about 1:250-300 (34), while homozygous FH is seen in about 1:160.000-300.000 individuals. Homozygous FH leads to severe ASCVD often before 20 years of age (16, 26).

### **1.4.1** Etiology

The ineffective clearance of LDL-C seen in FH is due to mutations mainly in genes encoding either the LDLR present on the surface of hepatocytes, apolipoprotein B, or proprotein convertase subtilisin/kexin-type 9 (PCSK9) (35). Absent or malfunctioning LDLR inhibits hepatic uptake and subsequent catabolism of LDL-C. Apolipoprotein B is a part of the LDL particle and serves as a ligand for the LDLR. PCSK9 binds to the LDLR and inhibits cellular recycling of the receptor, thereby reducing cellular uptake of LDL-C (36). Both gain-of-function and loss-of-function mutations are seen in the gene encoding PCSK9, of which gain-of-function mutations are the ones causing FH. All three types of mutations thus may lead to increased concentrations of LDL-C in the blood circulation. FH is considered an autosomal genetic disease, however, phenotypic FH is seen even though no mutations are found in the PCSK9, APOB, or LDLR genes (37, 38).

### **1.4.2** Diagnosis and symptoms

Genetic testing represents a valuable tool to diagnose FH, but the molecular genetics in FH is complex and the diagnosis is often based on clinical manifestations alone. Several clinical diagnostic criteria for FH exist such as the Dutch Lipid Clinical Network Score (DLCNS)

(39), the Simon Broome diagnostic criteria (40), and the Make Early Diagnosis to Prevent Early Death (MEDPED) criteria (41). The DLCNS and the Simon Broome criteria both include information on clinical data as well as genetics, while the MEDPED criteria only take into account measured cholesterol levels. FH may present with clinical manifestations such as tendon xanthomas, xanthelasmata and corneal arcus due to cholesterol depositions. A diagnosis of FH should be suspected among individuals with severely elevated LDL-C and especially in families with hypercholesterolemia and/or personal or familiar premature onset of CVD (26). However, FH is often asymptomatic and unfortunately unknown until an acute cardiovascular event may occur. Treatment aims to reduce the atherogenic burden and increase years of good health, but primary prevention may be challenged by motivational issues to comply with recommended medication and lifestyle factors such as healthy dietary habits over many years when the disease does not impact current daily life. However, prolonged hyperlipidemia severely increases the risk of CVD later in life, and early diagnosis and treatment are therefore of utmost importance to reduce the risk of ASCVD in these high-risk patients (42-44).

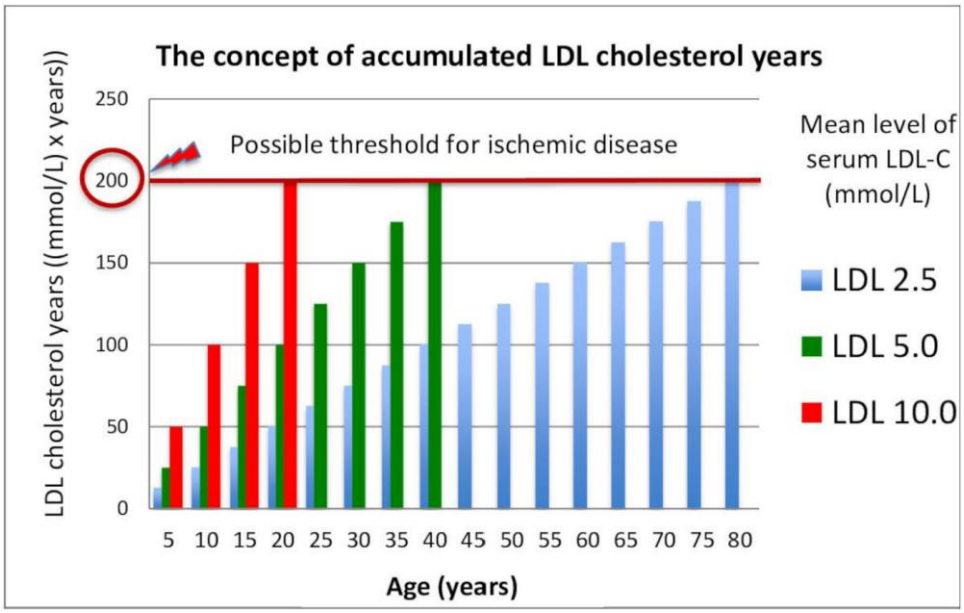
### **1.4.3** Treatment

A healthy lifestyle, including a healthy diet, physical activity and smoking absence, and most often concomitant use of lipid-lowering therapy are the cornerstones in treatment of elevated LDL-C in FH (16, 45). Statins are the most used medications which inhibit *de novo* cholesterol synthesis by blocking the activity of HMG-CoA-reductase (26). When intracellular cholesterol decreases, production of LDLR is enhanced and uptake of circulating cholesterols increases. There are several types of statins, including water and fat soluble (46, 47). Different types are metabolized by different enzymes in the liver (47). Moderate to high-intensity statins typically lower LDL-C by 30-50%. Ezetimibe is another drug typically used in addition to or as an alternative to statins, which may lower LDL-C by 15-20% through inhibition of intestinal uptake of cholesterol (48-50). PCSK9 inhibitors represent a more recent treatment option that may lower LDL-C by approximately 50-60%, but this treatment is expensive and limited to patients whose treatment with statins and/or ezetimibe has not been sufficient (51).

The treatment goals of FH patients according to the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) *Guidelines for the management of*

*dyslipidemias* is LDL-C <1.8 mmol/L in those without major ASCVD risk factors and LDL-C <1.4 mmol/L in FH patients with or at very-high risk of ASCVD. The concept of life-long cholesterol burden shows the significance of early detection and treatment in order to reduce the accumulating burden of increased LDL-C, as illustrated in **Figure 1**, printed with permission (49, 52). If diagnosed and treated early, the risk of early CVD in patients with FH may be no higher than in the general population, and life expectancy is approximately similar (53). Male sex, smoking, hypertension, diabetes, and high TG/low HDL-C are additional risk factors in FH (26). Thus, treatment should also focus on controlling blood glucose and blood pressure as well as on smoking cessation.

**Figure 1**. Accumulating burden of LDL-C




Accumulating burden of low-density lipoprotein cholesterol (LDL-C). With permission to use from © Schmidt, Hedegaard, and Retterstøl 2020. Published by BMJ Publishing Group Ltd. on behalf of British Cardiovascular Society (52).

## **1.5** Relationship between dietary fats and lipids

Dietary SFAs and trans-FAs may raise serum cholesterol levels (54, 55). Especially the long-chain FAs myristic, lauric and palmitic acid may possess LDL-C-raising properties (56). Replacing SFAs with polyunsaturated FAs (PUFAs) has been found to be the most efficient dietary measure for reducing LDL-C (56, 57). The marine omega-3 FAs eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) lower TG, which in part may be due to reduced hepatic synthesis of VLDL (58, 59) but have minor effects on LDL cholesterol levels.

### **1.5.1** Dietary FAs and risk of CVD

In addition to the LDL-C-lowering effect, the replacement of SFAs with PUFAs has been associated with a reduced risk of CVD. Thus, in a systematic review and meta-analysis of randomized controlled trials, Mozaffarian et al. found a 10% reduced risk of CHD with every 5% energy of increased from PUFAs instead of SFAs (60). These findings were in line with Jakobsen et al.'s who found a significant inverse association between intake of PUFAs when replacing SFAs and risk of coronary events and -death (61). Sacks. et al show in the presidential advisory from AHA on dietary fats and CVD published in 2017 that replacement of SFAs with PUFAs lowers both LDL-C and the risk of CVD. This effect is not seen when SFAs are replaced with carbohydrates (62). Avoiding trans-FAs has been an important dietary measure to reduce the risk of CVD, due to the LDL-C-increasing effect (49), but in most countries, intake of trans-FAs has been reduced considerably due to regulatory efforts during recent years and now trans-FAs have a limited impact on CVD risk compared to SFAs.

Intake of long-chain omega-3 FAs has been suggested to have a beneficial effect on atherosclerosis and CVD (58, 63). Marine omega-3 FAs have beneficial effects with respect to CVD like platelet inhibitory effects, anti-inflammatory effects, a small lowering of blood pressure and suggestions for plaque stabilizing effects as well as lowering of plasma triglycerides (63, 64). Early clinical trials suggested a beneficial effect on clinical events but more recent studies have not been able to confirm this and have reported neutral results (64).

## **1.6** Dietary guidelines and habits

### **1.6.1** Official dietary guidelines

In both Denmark and Norway, there are official dietary guidelines for achieving and maintaining good cardiovascular health. The purpose of the guidelines is to reduce the risk of diet- and lifestyle-related diseases and ensure adequate nutrient intake. In Denmark, the dietary guidelines were updated in 2021 to include the aspect of sustainability and the dietary effects on the climate as well as on human health. The current Norwegian guidelines were published in 2014 and were based on the "Nordic Nutrition Recommendations 2012 – integrating nutrition and physical activity" (NNR 2012) and the report from *Nasjonalt råd for ernæring "Kostråd for å fremme folkehelsen og forebygge kroniske sykdommer"* (65, 66).

Recommendations for fish and dairy are included in the official dietary guidelines in both Norway and Denmark. The Norwegian Health Directorate recommends eating fish for dinner two to three times per week. This corresponds to 300-450 g per week, out of which oily fish should account for at least 200 g. Six portions of fish spread correspond to one portion of fish for dinner. The Norwegian Health Directorate recommends reducing the intake of full-fat dairy products and including dairy products low on fat, added sugars, and salt in the everyday diet (67). Three daily portions of low fat dairy products such as milk, yogurt, and cheese are recommended.

In the updated dietary guidelines from 2021, the Danish Veterinary and Food Administration recommends choosing legumes and fish over meat as well as vegetable oils and low fat dairy products over butter and full fat dairy products. The recommended intake of fish is 350 g weekly, of which 200 g should be oily fatty fish. The suggested amount of low fat milk and milk products (<1.5% fat) is 250 ml per day in addition to 20 g of low fat cheese (<17% fat), alternatively 350 ml of milk and milk products and no cheese (68).

### **1.6.2** Dietary habits

Norkost is a national dietary survey conducted by the Department of Nutrition, University of Oslo, which was conducted in 1993-94 (Norkost 1), 1997 (Norkost 2), and 2010-2011 (Norkost 3). The surveys aimed to assess dietary habits in Norwegian adults. A self-administered food frequency questionnaire (FFQ) was used to collect dietary information (69).

In Norkost 3, the daily intake of fish in male subjects was 79 g, of which 15 g was oily fish. In female subjects, the daily intake of fish was 56 g/d, of which 14 g was oily fish. Most adults in Norway thus adhered to the Norwegian recommendations of about 45-65 g of fish per day. However, the recommended ~30 g of oily fish per day was not fulfilled. Intake of milk and yogurt in women was 249 g per day, of which 24 g were full-fat products. Female subjects consumed on average 21 g of cream and cream products and 42 g of cheese, of which 30 g was full-fat cheese. Intake of milk and yogurt in men was on average 384 g/d, of which 29 g was full-fat products. Intake of cream and cream products was on average 22 g/d, and intake of cheese was 46 g/d, of which 31 g full fat. Saturated FAs (SFAs) accounted for 13% of total energy intake in both men and women, which exceeds the recommended 10% as outlined in

the Norwegian dietary guidelines. One portion of low-fat dairy product is in the Norwegian dietary guidelines considered as one glass of milk (200 ml), one carton of yoghurt (125 g), or cheese for one slice of bread (20 g). Only Norwegian men adhered to the recommendation of three daily portions of low-fat dairy products.

A similar survey was conducted by the National Food Institute at the Technical University of Denmark among Danes in 2011-2013, named the Danish National Survey of Dietary Habits and Physical Activity (DANSDA). Female subjects consumed on average 295 g/d of milk and milk products, 37 g/d of cheese and cheese products, and 29 g/d of fish. Male subjects consumed on average 368 g/d of milk and milk products, 42 g/d of cheese and cheese products, and 35 g/d of fish. Hence, most Danes did not fulfill the recommended intake of fish compared to the Danish recommendations of about 50 g of fish per day. However, the DANSDA study did not discern between lean and oily fish, nor between milk and milk products with different fat content. SFAs constituted 16 E% in adults (70).

## **1.7** Dietary recommendations for the prevention of ASCVD

Diet is considered a risk factor with a significant impact on the development of ASCVD (71, 72). In addition to an increased intake of fruits and vegetables, nuts, and whole grains, it is, as mentioned above, recommended to increase the intake of fish and to reduce the intake of salt and SFAs (73). In the report *"National klinisk retningslinje for hjerterehabilitering"* from the Danish Health Authority, it is stated that these recommendations are in large applicable as secondary prevention in patients having developed ASCVD as well (74). *Fagligt selskap af kliniske diætister* recommends, however, in the report *"Diætbehandling af dyslipidæmi og iskæmisk hjertesygdom*" that oily fish should constitute 300 g weekly in these patients.

Correspondingly, the literature reviewed by the Norwegian Directorate of Health in «Kostråd for å fremme folkehelsen of forebygge kroniske sykdommer» showed a «convincing relationship» between replacing SFAs with PUFAs and reduced risk of death from CHD (66). This was also true for intake of <7 E% SFA. A diet rich in fruits, vegetables and low-fat dairy products may lower the risk of hypertension, which is an important risk factor for atherosclerosis development and CVD risk (75).

For reduction of LDL-C, the EAS recommends reducing intake of SFA to <10 E% (<7 E% in

hypercholesterolemia) and dietary cholesterol to <300 mg/d, increasing intake of dietary fiber to 25-40 g/d of which 7-13 g soluble fiber and using products containing plant sterols (49). The National Cholesterol Education Program (NCEP) from the US recommends, correspondingly, an intake of <7 E% SFA, <200 mg/d dietary cholesterol, and 20-30 g/d of dietary fiber. NCEP also recommends the use of 2 g of plant sterols daily (76, 77).

### **1.7.1** Fish consumption and CVD

The Norwegian and Danish health authorities recommend an increased intake of fish due to its content of several beneficial nutrients such as iodine, selenium, vitamin B12, and vitamin D. Additionally, fish is the main source of the marine long-chain omega-3 FAs EPA and DHA, which have been linked to several beneficial effects important for human health (68, 73, 75). The Norwegian recommendations are based on reports from the American Dietetic Association and Food and Agriculture Organization/WHO from 2008 and 2009, respectively. The reports concluded that EPA and DHA may lower the risk of cardiovascular death (78, 79). High consumption of fish has been associated with a more favorable HDL-C profile compared to low consumption and concomitantly reduced levels of inflammatory markers, which may be protective against CVD (80, 81).

The updated Danish guidelines on fish consumption were based on recent reviews of prospective cohort studies, a science advisory from American Heart Association published in 2018 as well as the EAT-Lancet commission's report from 2019 (68). The reviews by Jayedi et al. and Bechthold et al. conclude that a high consumption of fish was associated with a lower risk of CVD death (82-84). The EAT-Lancet commission's recommendation of 28 g of fish per day was based on studies showing an inverse association between fish intake and CVD risk. The report also considers the environment and the aspect of sustainability (85). However, intakes of up to 100 g per day have been associated with health benefits (85). The American Heart Association have previously suggested that a beneficial effect on health may be mediated by fish replacing less favorable foods in addition to being a source of EPA and DHA (86). In the Global Burden of Disease Study, Afshin et al. found that the optimal intake of EPA and DHA from fish to lower the risk of morbidity and mortality from non-communicable diseases was 200-300 mg per day (87). This corresponds to approximately 21 g of raw farmed salmon, 26 g of raw mackerel or 14 g of farmed trout (88).

### **1.7.2** Dairy products in relation to CVD

Full fat milk contains 3,5-4% of fat. About two-thirds of dairy fat is SFAs, mainly myristic, stearic, and palmitic acid (75). The Norwegian and Danish health authorities state that low fat dairy products are to be preferred as evidence suggest that reduction of dietary SFAs is beneficial for cardiac health (68, 75). A survey of dairy intake in participants of the US studies Health Professionals Follow-up Study and Nurses' Health Study, found that replacement of 5% of dairy fat with PUFAs or vegetable fat was associated with 24% and 10% lower risk of CVD, respectively (89). Bernstein et al. found in the Nurses' Health Study that high fat dairy was significantly associated with an increased risk of CHD (90). Nevertheless, dairy products are an important source of calcium, vitamin A, vitamin B12, riboflavin, and iodine as well as proteins with high biologic value (75). Because dairy products are such an important source of several nutrients, most dietary guidelines recommend daily consumption of low fat or non-fat dairy products (91).

## **1.8** Diet and FH

In a consensus statement of the EAS Consensus Panel the importance of early diagnosis and implementation of lifestyle interventions in patients with FH, herein dietary interventions were evaluated (16). The conclusion was that total fats should contribute with <30% of total energy, and SFAs <7%. Dietary cholesterol should be restricted to <200 mg per day. Intake of fruits and vegetables, whole grains, lean meats, beans, and fish as well as low-fat dairy products should be promoted (16). This is in line with the American National Lipid Association, which in the 2011 clinical guidance from an expert panel on FH recommends that total fat should constitute 25-35% of energy intake, SFAs <7% and an intake of dietary cholesterol <200 mg per day. Additionally, the US expert panel recommends the use of 2 g/d of stanol or sterol esters and 10-20 g/d of soluble fiber (92).

National center of competence for FH in Norway has together with the Lipid Clinic at Oslo University Hospital developed dietary advice especially for persons with elevated cholesterol or TG levels (93). The recommendations are in line with the EAS Consensus Panel and the American National Lipid Association. Additionally, specific recommendations for different food groups are emphasized. Regarding dairy products, it is recommended to choose milk and yogurt products with <0.7% fat, and cream and other cream products with <10% fat. Cheese

should contain <20% fat and should not be used on more than one slice of bread per day. In terms of fish, 350-400 g per week is recommended, of which oily fish should constitute 200 g (93).

## **1.9** Knowledge gaps

The importance of a heart-healthy diet in patients with FH is established. Dairy products constitute a substantial part of the Norwegian and Danish diets, and it is unknown whether adults referred to lipid clinics due to elevated cholesterol levels do make heart-healthy dairy choices. To the best of our knowledge, no research has been conducted on differences in dietary habits between Norwegian and Danish patients with severe hypercholesterolemia.

# 2 Objectives of current study

The aims of the present master's thesis were as follows:

- Describe the dietary habits of fish and dairy consumption in Danish and Norwegian patients with hypercholesterolemia according to clinical characteristics such as age, sex, lipid levels, and BMI. Furthermore, investigate the significance of familial and personal history of CVD for diet in the Danish population
- Investigate the associations between measures of fish and dairy consumption and plasma lipid and lipoprotein levels including total cholesterol, LDL-C, HDL, and TG

**Hypotheses**

Including a larger amount of fish in the diet and choosing low-fat dairy products may be related to clinical characteristics and influence lipid levels in subjects with increased cholesterol levels. We hypothesized that:

1. Individuals with severe hypercholesterolemia and a high intake of fish have a lower BMI and TG levels, are of older age, have premature CVD or CVD in the family, and higher levels of HDL-C
2. Individuals with severe hypercholesterolemia and a high intake of high-fat dairy products corresponds to higher age, BMI and LDL-C

# 3 **Materials and Methods**

### **3.1.1** Danish population - The Find Familial Hypercholesterolemia study

The Find Familial Hypercholesterolemia (FFH) study was a collaboration between all 15 lipid clinics in Denmark. More than 1500 patients with suspected FH were recruited between 1st September 2020 and 30th November 2021. FH was suspected based on the following criteria used in Denmark for referral to Danish lipid clinics:

- LDL-C ≥5.0 mmol/L in persons >40 years
- LDL-C ≥4.0 mmol/L in persons aged 18 to 40 years
- LDL-C ≥4.0 mmol/L and premature CVD (men <55 years, women <60 years)

Subjects were interviewed at the lipid clinics about personal and familial CVD, diet, lifestyle, and relevant medical treatment. A clinical examination of potential cholesterol deposits was carried out by a doctor or specialized lipid nurse. All patients were asked to fill out the HeartDiet questionnaire. Subjects were classified according to the DLCNS for FH. The purpose of the study was to examine the prevalence of FH amongst patients referred based on referral criteria described above. Written consent was given by all participants. In the current master's thesis, we have included subjects from two major lipid clinics in Denmark: Aalborg and Viborg.

### **3.1.2** HeartDiet questionnaire

The HeartDiet questionnaire **(Appendix 5)** was developed by the lipid clinic in Aalborg together with the Danish Heart Association. The HeartDiet questionnaire was inspired by the Norwegian SmartDiet questionnaire (94). A previous study validated the HeartDiet questionnaire against a longer and already validated 198-item FFQ as well as with serum β-carotene and omega-3 PUFAs as biomarkers for intake of fruit and vegetables and fish, respectively (95). A highly significant statistical correlation was found between the intake of fruit, vegetables, fish, and SFAs in HeartDiet and the 198-item FFQ (95). Spearman's rank correlation coefficient for intake of fish in HeartDiet and the 198-item FFQ was 0.75 (95).

The HeartDiet questionnaire consists of 19 questions, of which three evaluate the intake of milk and fermented milk products, cream and other milk products such as crème fraiche and curd, and cheese as well as the fat content of the dairy products usually consumed. Two

questions concern the use of fats in cooking and on bread and two regard consumption of meat both as a spread and for dinner, while two questions concern the intake of cake, chocolate, ice cream, fast-food, and crisps. These first nine questions underpin the fat score. The following 10 questions concern fish for lunch and dinner, vegetables and legumes, fruits and berries, bread, cereals, potatoes, rice and pasta, and nuts as well as sweet foods such as jam, sugar-sweetened beverages, and candy. Together, these 10 questions constitute a fish-fruit-vegetable score.

The answer options were assigned points ranging from 0 to 12 based on the degree to which the option is regarded as heart-healthy. A score of more than 75 point in the fish-fruit-vegetable- and fat score is considered a heart-healthy diet. In addition, six questions note the participant's age, sex, smoking status, and habits of exercise and alcohol as well as the use of fish oil supplements.

### **3.1.3** FFH form

All eligible subjects had a FFH registration form filled in by a physician or lipid nurse during clinical evaluation **(Appendix 4)**. The form included information about referral criteria, secondary dyslipidemia, and anthropometric measures as well as the fish-fruit-vegetable and fat scores from the HeartDiet questionnaire. Furthermore, the highest measured level of cholesterol, medical treatment, and plasma lipids and lipoproteins at referral as well as plasma Lipoprotein(a) was registered. Based on the information collected from the interview, clinical examination and blood samples, the Dutch Lipid Clinical Network Score (DLCNS) score was determined for each participant (see below).

### **3.1.4** DLCNS

The DLCNS is a set of criteria for clinical diagnosis of FH. A DLCN score is calculated based on points given within four categories including family history of premature CVD or elevated LDL-C, personal history of CVD, physical examination, and LDL-C levels. A score of less than three points indicate "unlikely FH". A diagnosis of FH is "probable" if a patient attains six to eight points, and "possible" if the score is three to five (26). A definite FH diagnosis can be made if the score is more than eight points. A positive genetic test for FH yields eight points.

### **3.1.5** Norwegian population

Patients with FH above 18 years of age have previously been recruited from the outpatient lipid clinic at Oslo University Hospital. All participants had genetically verified FH or a DLCNS >8. Patients with diabetes mellitus type 1, uncontrolled hypertension, as well as pregnant or lactating women, were not included. Anthropometric measures, a non-fasting blood sample as well as information on previous history of CHD and lipid-lowering treatment were obtained at the study visits. Participants were recruited between September 2016 and September 2017. Informed consent was provided by all participants.

### **3.1.6** SmartDiet questionnaire

The SmartDiet questionnaire **(Appendix 6)** was used to collect dietary information in the Norwegian population. SmartDiet is an FFQ developed at the Lipid Clinic in Oslo. SmartDiet was validated by Svilaas et al. against a 7-day weighed food record. They found a high correlation between SmartDiet and the weighed food record in items regarding milk, bread and cereals, butter and margarine, cheese, meat, and fruit. Lower agreement coefficients were found in fish, vegetables, and snacks (96).

The SmartDiet questionnaire consists of two parts: 15 questions about diet that compose the basis for the calculation of the SmartDiet score and 11 questions that provide supplementary information about diet, anthropometry and lifestyle. Among the first 15 questions, the SmartDiet questionnaire include three questions regarding dairy products and two regarding meat as well as the fat percentage of the dairy and meat products usually consumed. Two questions relate to the frequency of fish consumption for lunch and dinner, while three questions relate to high-fat products, such as dressing, mayonnaise, and oils as well as butter on bread and in cooking. Also, information on products containing plant sterols is included in the SmartDiet questionnaire as well as one question about bread, crispbread, and cereals, one question about vegetables, fruits, and berries, and two questions concerning soft drinks, sweet spreads, cakes, sweets, and crisps.

The answer options for each question are allocated either one, two, or three points, depending on which alternatives are regarded as the least, medium, and most favorable, respectively. Thus, the maximum total score is 45. Twenty-seven points or less is considered not a heart-

healthy diet whereas 35 points or more is considered as a heart-healthy diet. Twenty-eight to 35 points is regarded as improvable.

In some of the questions, quantity is included in addition to frequency and/or quality. E.g., the respondent is asked to estimate how many glasses and cartons of milk and yogurt are consumed daily and weekly, respectively. In the item regarding cheese, the respondent is asked about number of daily portions of cheese used as spread and number of weekly portions of cheese-containing dinners. The same applies to the consumption of oily fish, bread, cereals, vegetables, and fruits. However, quantities do not affect the total SmartDiet score and were not included in the current master's thesis. The remaining six questions about diet, which are not included in the total score, regard consumption of rice, pasta and potatoes, legumes, nuts and avocado, coffee, alcohol, and eggs. Furthermore, the five last questions of the questionnaire explore habitual meal frequency, anthropometry, alcohol consumption, smoke and snuff, and exercise as well as use of dietary supplements.

### **3.1.7** Harmonizing the SmartDiet and HeartDiet questionnaires

The number of answer options for several items in the HeartDiet and SmartDiet is not exactly similar, e.g., five options are available with regard to the question of how many times one eats fish for dinner, ranging from less than 1 portion per month to 3 times or more per week in the HeartDiet questionnaire. In comparison, the corresponding item in SmartDiet has only three options: "1 time or less per week", "2 times per week" or "3 times or more per week". We adjusted the five options in HeartDiet by merging "0-1 portions per month", "2 portions per month" and "3-4 portions per month". Together, these options corresponded to the option with the lowest frequency of fish for dinner in SmartDiet; "1 portion or less per week". The further two options in HeartDiet, "2 times per week" and "3 times or more per week" are in accordance with SmartDiet. Similarly, the options "1-2 portions per week" and "3-6 portions per week" of fish for lunch in HeartDiet were merged to fit "2-4 portions per week" in SmartDiet, and "1 portion per day" and "2 or more portions per day" were merged to match "5 or more portions per week" **(Table 1)**. The options in the questions about dairy products were matched in a similar fashion, which is illustrated in **Table 2.**

**Table 1.** Harmonizing questions regarding fish

| Fish for lunch | | | | | Fish for dinner | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | HeartDiet | | SmartDiet | | | HeartDiet | | SmartDiet | |
| **New category** | Frequency | Points | Frequency | Points | **New category** | Frequency | Points | Frequency | Points |
| **1** | <1 portion/wk | 0 | ≤1 portion/wk | 1 | **1** | ≥1 time/mo<br>2 times/mo<br>3-4 times/mo | 0<br>4<br>9 | ≤1 time/wk | 1 |
| **2** | 1-2 portions/wk<br>3-6 portions/wk | 4<br>9 | 2-4 portions/wk | 2 | **2** | 2 times/wk | 10 | 2 times/wk | 2 |
| **3** | 1 portion/d<br>≥2 portions/d | 10<br>12 | ≥5 portions/wk | 3 | **3** | ≥3 times/wk | 12 | ≥3 times/wk | 3 |

Harmonizing questions regarding fish for lunch and for dinner in the HeartDiet and SmartDiet questionnaires
wk, week; mo, month; d, day

**Table 2.** Harmonizing questions regarding dairy products

| Milk and yogurt | | | | | Cream and other dairy products | | | | | Cheese | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HeartDiet | | SmartDiet | | | HeartDiet | | SmartDiet | | | HeartDiet | | SmartDíet | |
| **New category** | Fat% | Points | Fat% | Points | **New category** | Fat% | Points | Fat% | Points | **New category** | Fat% | Points | Fat% | Points |
| **1** | >2 | 0 | >3 | 1 | **1** | >16 | 0 | >20 | 1 | **1** | >27 | 0 | >20 | 1 |
| **2** | 1-2<br><1 time/wk* | 6<br>6 | 0.5-1<br>≤1 time/wk* | 2<br>2 | **2** | 9-15 | 3 | 10-20 | 2 | **2** | 13-18 | 9 | 10-20 | 2 |
| **3** | ≤1 | 9 | <0.5 | 3 | **3** | ≤7<br>≤1 time/wk* | 6<br>10 | 5-10<br>≤1 time/wk* | 3<br>3 | **3** | <13<br>≤1 time/wk* | 12<br>12 | <10<br>≤1 time/wk* | 3<br>3 |

Harmonizing questions regarding dairy products in the HeartDiet and SmartDiet questionnaires
wk, week
*frequency of consumption

### **3.1.8** Total scores for fish and dairy based on the HeartDiet questionnaire

Total scores for fish and dairy were created by merging all questions regarding the respective food groups in the HeartDiet questionnaire. **Table 3** shows how many points each answer option yielded. The fish score was made by combining the maximum possible points from the questions "How often do you eat fish for lunch" and "How often do you eat fish for dinner". The most favorable option in both questions - two portions or more per day and three times or more per week, respectively - yields 12 points each. Thus, the largest possible sum of points in the total fish score was 24. Accordingly, the maximum points in the three questions regarding dairy products are nine, 10, and 12, resulting in a dairy score of 31 points in total. Since 0 points is an option in every question, a given subject will attain between 0 and 24 or 31 points in total fish or dairy score, respectively. Higher total scores indicate more advantageous dietary habits regarding fish and dairy.

**Table 3**. HeartDiet scores

| **Fish score** | | | | **Dairy score** | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Points** | **Fish for lunch** | **Points** | **Fish for dinner** | **Points** | **Milk and milk products** | **Points** | **Cream and other milk products** | **Points** | **Cheese** |
| 0 | <1 portion/ wk | 0 | 0-1 times/mo | 0 | Full-fat (>2%) | 0 | Full-fat (>16 %) | 0 | Full-fat (≥27%) |
| 4 | 1-2 portions/ wk | 4 | 2 times/mo | 6 | Low fat (1.5-2%) | 3 | Reduced fat (9-15%) | 9 | Reduced fat (≤18%) |
| 9 | 3-6 portions/ wk | 9 | 3-4 times/mo | 6 | ≤1 time/wk | 6 | Low fat (<7%) | 12 | Low fat (≤13%) |
| 10 | 1 portion/d | 10 | 2 times/wk | 9 | Skimmed (<1%) | 10 | ≤1 time/wk | 12 | ≤1 time/wk |
| 12 | ≥2 portions/ d | 12 | ≥3 times/wk | | | | | | |

Points allocated to each answer option in questions regarding fish and dairy intake in the HeartDiet questionnaire
wk, week; mo, month; d, day

### **3.1.9** Statistical analyses

All statistical analyses were performed in StataSE 17. Categorical data was presented as frequencies (*n*) and percentages across exposures of interest. Continuous data was presented as mean with standard deviations. Fisher's exact test was used to compare categorical data. One-way analyses of variance (ANOVA) were used to compare means between multiple groups. Linear regressions were conducted across levels of exposures of interest and lipid levels. BMI was categorized according to the definition of WHO (97). BMI <25 was regarded as normal weight, 25-29.9 as overweight and ≥30 obese. P-values <0.05 were considered statistically significant.

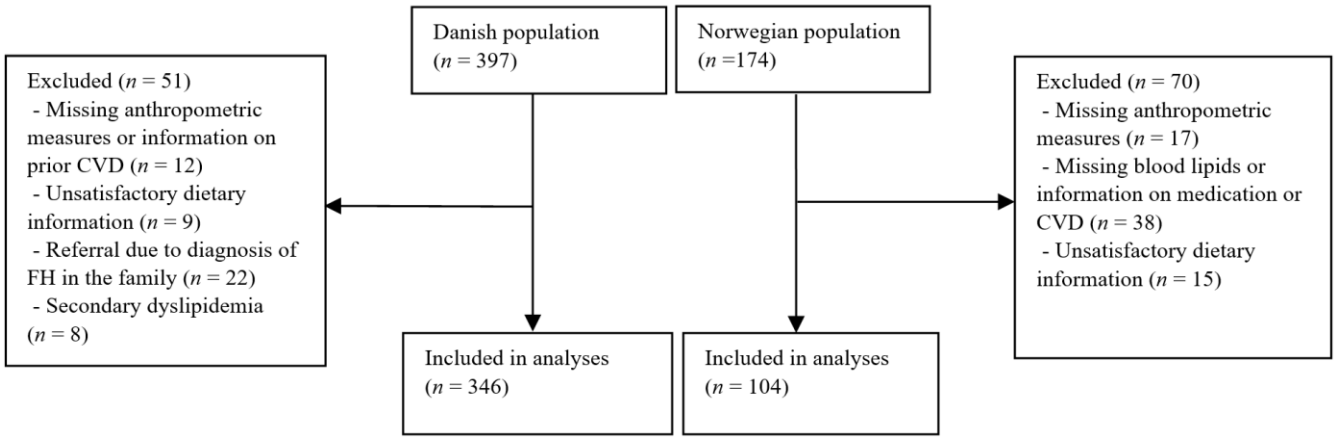
# 4 Results

## 4.1 Study populations

In total, 346 patients from Aalborg and Viborg lipid clinics and 104 patients from the lipid clinic in Oslo were included in the analyses, as illustrated in **Figure 2**. In the Danish population, 48% were men. Subjects 50 years of age or older constituted 58%. Twenty-five percent were categorized as having "probable" or "definite" FH according to DLCNS, and 67% as "possible" FH. Eleven percent of the population had a genetically verified FH and are included in the group of "definite" FH. Sixteen percent had a personal history of ASCVD, and 70% had a family history of CVD. Twenty-eight percent of the subjects received statin treatment. Twenty-nine percent were categorized as normal weight, 45% as overweight, and 27% as obese.

In the Norwegian population, 45% were men and 40% were 50 years of age or older. One subject had a clinical diagnosis of FH and 103 subjects had genetically verified FH. Ninety-two percent received medical treatment, and 11% had a previous history of ASCVD. Forty-five percent were normal weight, 34% overweight, and 21% obese. Characteristics of the Norwegian and the Danish population as well as the group of Danish subjects with a diagnosis of FH are shown in **Table 4.**

**Figure 2.** Danish and Norwegian study populations




Inclusions and exclusions in the Norwegian and Danish populations.

**Table 4**. Baseline characteristics

| | Total, *n* (%) | | |
|---|---|---|---|
| | Denmark *n* = 346 | FH Denmark *n* = 88 | FH Norway *n* = 104 |
| All subjects | | | |
| Men | 165 (48) | 41 (47) | 47 (45) |
| Women | 181 (52) | 47 (53) | 57 (55) |
| Age groups | | | |
| <50 | 147 (42) | 33 (38) | 62 (60) |
| ≥50 | 199 (58) | 55 (62) | 42 (40) |
| BMI | | | |
| <25 | 100 (29) | 26 (30) | 47 (45) |
| 25-29,9 | 154 (45) | 41 (47) | 35 (34) |
| ≥30 | 92 (27) | 21 (23) | 22 (21) |
| DLCNS | | | |
| Unlikely | 26 (8) | - | - |
| Possible | 232 (67) | - | - |
| Probable + definite | 88 (25) | 88 (100) | 104 (100) |
| FH mutation | | | |
| No | 168 (49) | 33 (38) | 0 (0) |
| Yes | 38 (11) | 38 (43) | 104 (100) |
| Unknown | 140 (40) | 17 (19) | - |
| Previous history of ASCVD | | | |
| No | 291 (84) | 65 (74) | 93 (89)* |
| Yes | 55 (16) | 23 (26) | 11 (11)* |
| Family history of ASCVD | | | |
| No | 105 (30) | 36 (41) | - |
| Yes | 141 (70) | 52 (59) | - |
| Current smokers | | | |
| Never | 154 (45) | 34 (39) | 82 (79) |
| Former | 134 (39) | 38 (43) | 8 (8) |
| Current | 58 (17) | 16 (18) | 14 (13) |
| Alcohol (drinks/wk) | | | |
| 0-7 | 281 (81) | 66 (75) | 83 (91) |
| 8-14 | 51 (15) | 15 (17) | 8 (8) |
| ≥15 | 14 (4) | 7 (8) | 1 (1) |
| Statin treatment | | | |
| No | 248 (72) | 52 (59) | 8 (8) |
| Yes | 98 (28) | 36 (41) | 96 (92) |

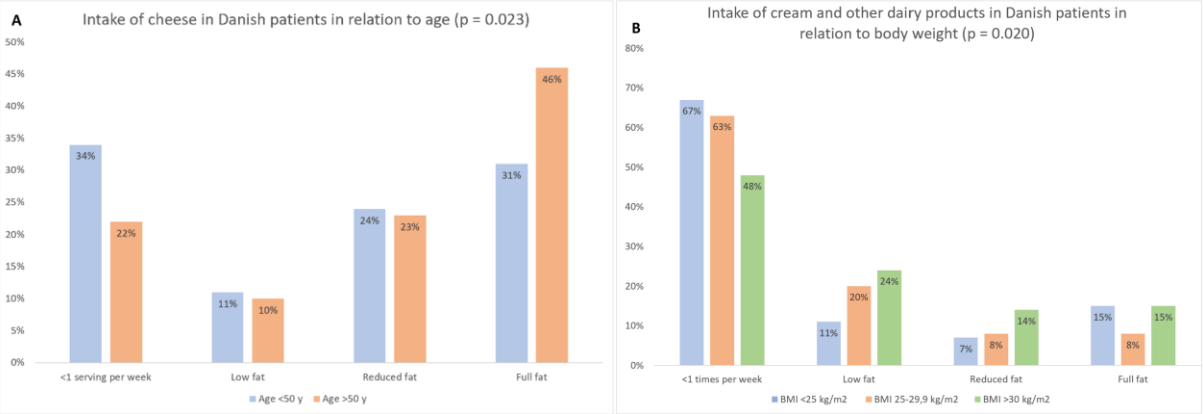
Baseline characteristics among all Danish subjects, Danish subjects diagnosed with familial hypercholesterolemia, and Norwegian FH subjects.
BMI, body mass index; DLCNS, Dutch Lipid Clinic Network Score; ASCVD, atherosclerotic cardiovascular disease
*CHD

# **4.2** Intake of dairy products in the Danish population

Intake of dairy products did not differ between men and women and persons with and without a previous family history of CVD or personal history of CVD, as shown in **Table 5**. Subjects above 50 years of age consumed more full fat cheese compared to subjects under 50 years of age (p = 0.023) as illustrated in **Figure 3**. Also, we observed a statistically significant

difference with regard to cheese intake across DLCN criteria (p = 0.040). Thus, the largest proportion of subjects consuming full fat cheese were categorized with possible FH according to DLCNS. A larger proportion of subjects under 50 years reported eating cheese one time or less per week. A higher percentage of subjects with BMI <25 and 25-29.9 reported consuming cream and other dairy products one time or less per week compared to subjects with BMI >30 (p = 0.020) **(Figure 3)**.

**Figure 3.** Intake of dairy products in the Danish population




Intake of cheese according to age (A) and cream and other dairy products according to body mass index (BMI) in the Danish population (B)
y, years

**Table 5**. Intake of dairy products in Danish subjects (*n* = 346)

| | **Milk and yoghurt, *n* (%)** | | | | | **Cream and other dairy products, *n* (%)** | | | | | **Cheese, *n* (%)** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ≤1 times/ wk | Skimmed (<1%) | Low fat (1,5-2%) | Full fat (2-10%) | p | ≤1 times/ wk | Low fat (≤7%) | Reduced fat (9-15%) | Full fat (>16%) | p | ≤1 times/ wk | Low fat (≤13%) | Reduced fat (≤18%) | Full fat (≥27%) | p |
| All subjects | | | | | | | | | | | | | | | |
| Men | 25 (15) | 96 (58) | 37 (22) | 7 (4) | 0.090 | 103 (62) | 27 (16) | 19 (12) | 16 (10) | 0.269 | 40 (24) | 13 (8) | 43 (26) | 69 (42) | 0.300 |
| Women | 38 (21) | 101 (56) | 27 (15) | 15 (8) | | 104 (57) | 37 (20) | 14 (8) | 26 (14) | | 53 (29) | 22 (12) | 38 (21) | 68 (38) | |
| Age groups | | | | | | | | | | | | | | | |
| <50 | 22 (15) | 87 (59) | 30 (20) | 8 (5) | 0.476 | 84 (57) | 28 (19) | 13 (9) | 22 (15) | 0.547 | 50 (34) | 16 (11) | 35 (24) | 46 (31) | **0.023** |
| ≥50 | 41 (21) | 110 (55) | 34 (17) | 14 (7) | | 123 (62) | 36 (18) | 20 (10) | 20 (10) | | 43 (22) | 19 (10) | 46 (23) | 91 (46) | |
| BMI | | | | | | | | | | | | | | | |
| <25 | 24 (24) | 53 (53) | 14 (14) | 9 (9) | | 67 (67) | 11 (11) | 7 (7) | 15 (15) | | 32 (32) | 12 (12) | 19 (19) | 37 (37) | |
| 25-29,9 | 22 (14) | 90 (58) | 32 (21) | 10 (6) | 0.269 | 97 (63) | 31 (20) | 13 (8) | 13 (8) | **0.020** | 37 (24) | 10 (6) | 38 (25) | 69 (45) | 0.191 |
| ≥30 | 17 (18) | 54 (59) | 18 (20) | 3 (3) | | 43 (48) | 22 (24) | 13 (14) | 14 (15) | | 24 (26) | 13 (14) | 24 (26) | 31 (34) | |
| DLCNS | | | | | | | | | | | | | | | |
| Unlikely | 5 (19) | 13 (50) | 6 (23) | 2 (8) | | 12 (46) | 5 (19) | 5 (19) | 4 (15) | | 11 (42) | 3 (12) | 6 (23) | 6 (23) | |
| Possible | 41 (18) | 136 (59) | 40 (17) | 15 (6) | 0.941 | 146 (63) | 40 (17) | 20 (9) | 26 (11) | 0.447 | 50 (22) | 22 (9) | 59 (25) | 101 (44) | **0.040** |
| Probable + definite | 17 (19) | 48 (55) | 18 (20) | 5 (6) | | 49 (56) | 19 (22) | 8 (9) | 12 (14) | | 32 (36) | 10 (11) | 16 (18) | 30 (34) | |
| Previous history of ASCVD | | | | | | | | | | | | | | | |
| No | 52 (18) | 170 (58) | 52 (18) | 17 (6) | 0.522 | 170 (58) | 51 (18) | 31 (11) | 39 (13) | 0.095 | 77 (26) | 30 (10) | 67 (23) | 117 (40) | 0.928 |
| Yes | 11 (20) | 27 (49) | 12 (22) | 5 (9) | | 37 (67) | 13 (24) | 2 (4) | 3 (5) | | 16 (29) | 5 (9) | 14 (25) | 20 (36) | |
| Family history of ASCVD | | | | | | | | | | | | | | | |
| No | 36 (18) | 123 (60) | 34 (17) | 12 (6) | 0.529 | 125 (61) | 37 (18) | 17 (8) | 26 (13) | 0.771 | 55 (27) | 21 (10) | 49 (24) | 80 (39) | 0.992 |
| Yes | 27 (19) | 74 (52) | 30 (21) | 10 (7) | | 82 (58) | 27 (19) | 16 (11) | 16 (11) | | 38 (27) | 14 (10) | 32 (23) | 57 (40) | |

Intake of dairy products related to sex, age, body mass index (BMI), Dutch Lipid Clinic Network Score (DLCNS), and previous and family history of atherosclerotic cardiovascular disease (ASCVD) in Danish subjects

## **4.3** Intake of fish in the Danish population

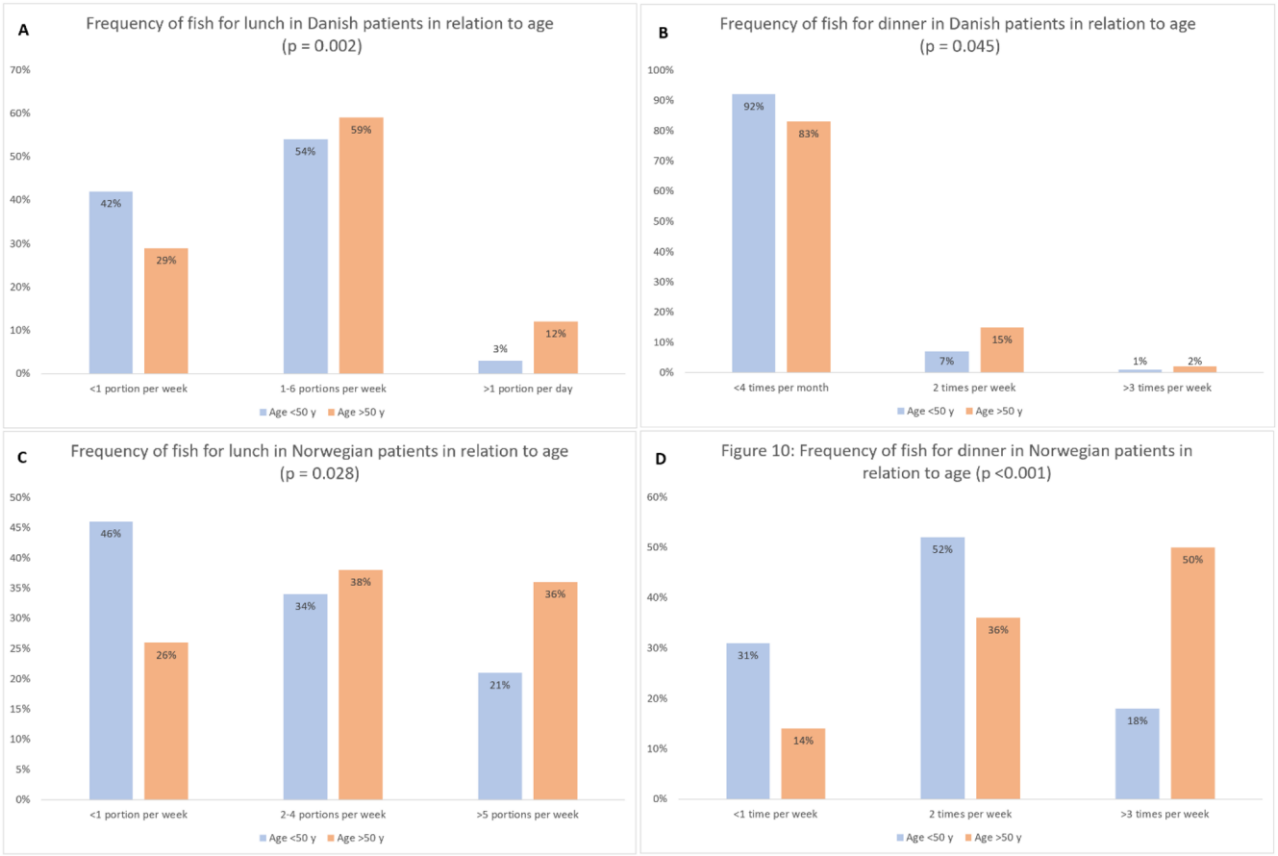
Subjects above 50 years of age consumed statistically significantly more fish both for lunch and for dinner compared to younger subjects (p = 0.002 and p = 0.045, respectively) as shown in **Table 6** and **Figure 4.** Subjects with "possible", "probable" or "definite" FH had fish for lunch more often than subjects with "unlikely" FH (p = 0.031). Beyond age and DLCNS score, no statistically significant differences were observed for fish intake with regard to sex, BMI or personal or family history of CVD.

**Table 6**. Intake of fish in Danish subjects (*n* = 346)

| | **Fish for lunch, *n* (%)** | | | | **Fish for dinner, *n* (%)** | | | |
|---|---|---|---|---|---|---|---|---|
| | <1 portions/ week | 1-6 portions/ week | ≥1 portions/ day | p | ≤4 times/ month | 2 times/ week | ≥3 times/ week | p |
| All subjects | | | | | | | | |
| Men | 57 (35) | 98 (59) | 10 (6) | 0.319 | 146 (88) | 19 (12) | - | 0.109 |
| Women | 62 (34) | 100 (55) | 19 (11) | | 154 (85) | 22 (12) | 5 (3) | |
| Age groups | | | | | | | | |
| <50 | 62 (42) | 80 (54) | 5 (3) | **0.002** | 135 (92) | 11 (7) | 1 (1) | **0.045** |
| ≥50 | 57 (29) | 118 (59) | 24 (12) | | 165 (83) | 30 (15) | 4 (2) | |
| BMI | | | | | | | | |
| <25 | 37 (37) | 51 (51) | 12 (12) | | 86 (86) | 12 (12) | 2 (2) | |
| 25-29,9 | 45 (29) | 96 (62) | 13 (8) | 0.129 | 129 (84) | 22 (14) | 3 (2) | 0.330 |
| ≥30 | 37 (40) | 51 (55) | 4 (4) | | 85 (92) | 7 (8) | - | |
| DLCNS | | | | | | | | |
| Unlikely | 15 (58) | 11 (42) | - | | 23 (88) | 3 (12) | - | |
| Possible | 78 (34) | 137 (59) | 17 (7) | **0.031** | 206 (89) | 22 (9) | 4 (2) | 0.272 |
| Probable + definite | 26 (30) | 50 (57) | 12 (14) | | 71 (81) | 16 (18) | 1 (1) | |
| Previous history of ASCVD | | | | | | | | |
| No | 102 (35) | 166 (57) | 23 (8) | 0.638 | 253 (87) | 34 (12) | 4 (1) | 0.782 |
| Yes | 17 (31) | 32 (58) | 6 (11) | | 47 (85) | 7 (13) | 1 (2) | |
| Family history of ASCVD | | | | | | | | |
| No | 72 (35) | 114 (56) | 19 (9) | 0.693 | 178 (87) | 23 (11) | 4 (2) | 0.631 |
| Yes | 47 (33) | 84 (60) | 10 (7) | | 122 (87) | 18 (13) | 1 (1) | |

Intake of fish in Danish subjects related to body mass index (BMI), Dutch Lipid Clinic Network Score (DLCNS), and previous and family history of atherosclerotic cardiovascular disease (ASCVD)

**Figure 4.** Intake of fish in relation to age in the Danish and Norwegian populations




Intake of fish for lunch (A) and dinner (B) in relation to age in the Danish population and intake of fish for lunch (C) and dinner (D) in relation to age in the Norwegian population
y, years

## **4.4** Intake of dairy products in the Norwegian population

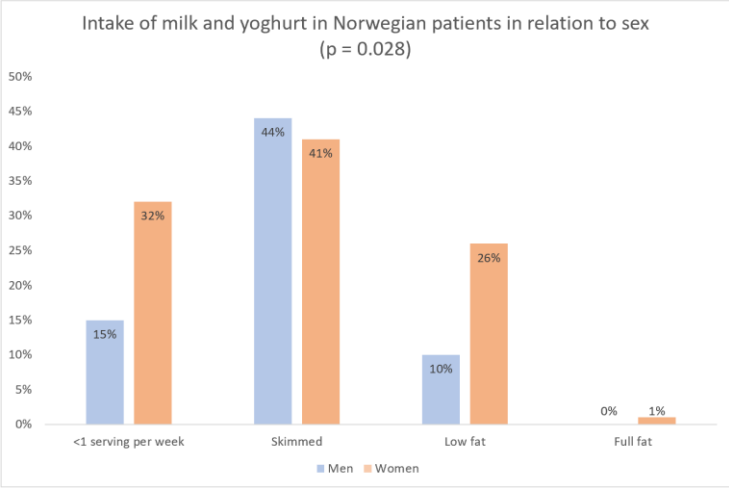
Intake of dairy products in the Norwegian population is shown in **Table 7**. More women than men consumed milk and yogurt one time or less per week. Furthermore, a larger proportion of men consumed skimmed milk compared to women (p = 0.028), as illustrated in **Figure 5**. However, no statistically significant differences were observed with regard to milk and yogurt, cream and other milk products, or cheese for age and BMI.

**Table 7.** Intake of dairy products in Norwegian FH subjects (*n* = 104)

| | **Milk and yoghurt, *n* (%)** | | | | | **Cream and other dairy products, *n* (%)** | | | | | **Cheese, *n* (%)** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0-1 times/ week | Skimmed (<1%) | Low fat (1,5-2%) | Full fat (2-10%) | p | 0-1 times/ week | Low fat (≤7%) | Reduced fat (9-15%) | Full fat (>16%) | p | 0-1 times/ week | Low fat (≤13%) | Reduced fat (≤18%) | Full fat (≥27%) | p |
| All subjects | | | | | | | | | | | | | | | |
| Men | 15 (22) | 44 (64) | 10 (15) | 0 (0) | **0.028** | 28 (41) | 22 (32) | 16 (23) | 3 (4) | 0.543 | 9 (13) | 15 (22) | 21 (30) | 24 (35) | 0.842 |
| Women | 23 (32) | 30 (41) | 19 (26) | 1 (1) | | 22 (30) | 31 (42) | 17 (23) | 3 (4) | | 7 (10) | 15 (21) | 27 (37) | 24 (33) | |
| Age groups | | | | | | | | | | | | | | | |
| <50 | 16 (24) | 33 (49) | 18 (26) | 1 (1) | 0.199 | 21 (31) | 28 (41) | 17 (25) | 2 (3) | 0.610 | 9 (13) | 12 (18) | 25 (37) | 22 (32) | 0.666 |
| ≥50 | 22 (30) | 41 (55) | 11 (15) | 0 (0) | | 29 (39) | 25 (34) | 16 (22) | 4 (5) | | 7 (9) | 18 (24) | 23 (31) | 26 (35) | |
| BMI | | | | | | | | | | | | | | | |
| <25 | 20 (32) | 30 (48) | 13 (21) | 0 (0) | | 26 (41) | 20 (32) | 14 (22) | 3 (5) | | 9 (14) | 10 (16) | 24 (38) | 20 (32) | |
| 25-29,9 | 16 (29) | 28 (51) | 10 (18) | 1 (2) | 0.230 | 20 (36) | 22 (40) | 10 (18) | 3 (5) | 0.230 | 4 (7) | 14 (25) | 15 (27) | 22 (40) | 0.502 |
| ≥30 | 2 (8) | 16 (67) | 6 (25) | 0 (0) | | 4 (17) | 11 (46) | 9 (38) | 0 (0) | | 3 (13) | 6 (25) | 9 (38) | 6 (25) | |

Intake of dairy products in Norwegian subjects with familial hypercholesterolemia (FH) related to sex, age, and body mass index (BMI).

**Figure 5.** Intake of milk and yogurt in relation to sex in the Norwegian population




Intake of milk and yoghurt in male and female subjects in the Norwegian population

## **4.5** Intake of fish in the Norwegian population

Corresponding to the Danish population, subjects over 50 years of age in the Norwegian population consumed fish significantly more frequently both for lunch (p = 0.028) and dinner (p <0.001) compared to younger subjects as shown in **Table 8** and illustrated in **Figure 4**. Consumption of fish did not statistically significantly differ between men and women or between lean, overweight, and obese subjects.

**Table 8.** Intake of fish in Norwegian FH subjects (*n* = 104)

| | **Fish for lunch, *n* (%)** | | | | **Fish for dinner, *n* (%)** | | | |
|---|---|---|---|---|---|---|---|---|
| | ≤1 portion/ week | 2-4 portions/ week | ≥5 portions/ week | p | ≤1 times/ week | 2 times/ week | ≥3 times/ week | p |
| All subjects | | | | | | | | |
| Men | 24 (35) | 20 (29) | 25 (36) | 0.119 | 13 (19) | 28 (41) | 28 (41) | 0.324 |
| Women | 26 (36) | 31 (42) | 16 (22) | | 18 (25) | 34 (47) | 21 (29) | |
| Age groups | | | | | | | | |
| <50 | 31 (46) | 23 (34) | 14 (21) | **0.028** | 21 (31) | 35 (52) | 12 (18) | **<0.001** |
| ≥50 | 19 (26) | 28 (38) | 27 (36) | | 10 (14) | 27 (36) | 37 (50) | |
| BMI | | | | | | | | |
| <25 | 26 (41) | 25 (40) | 12 (19) | | 16 (25) | 26 (41) | 21 (33) | |
| 25-29,9 | 18 (33) | 16 (29) | 21 (18) | 0.153 | 10 (18) | 24 (44) | 21 (38) | 0.852 |
| ≥30 | 6 (25) | 10 (44) | 8 (33) | | 5 (21) | 12 (50) | 7 (29) | |

Intake of fish in Norwegian subjects with familial hypercholesterolemia (FH) related to sex, age, and body mass index (BMI)

## **4.6** Lipid levels in the Danish population

### **4.6.1** Mean lipid levels in subjects receiving lipid-lowering treatment

In subjects receiving lipid-lowering treatment, the mean HDL-C was 1.50 mmol/L in patients eating milk and yogurt once per week or less and 1.27 mmol/L in patients using full fat milk and yogurt **(Appendix 1)**. Beyond this, there were no appreciable nor statistically significant differences between the fat content of dairy products and lipid levels in subjects receiving lipid-lowering treatment. Subjects eating one or more portions of fish spread per day had a mean HDL-C of 1.53 mmol/L and a mean level of TG of 1.63 mmol/L, which was 0.22 mmol/L higher and 0.47 mmol/L lower than subjects eating one or fewer portions per week, respectively.

### **4.6.2** Mean lipid levels in subjects not receiving lipid-lowering treatment

Mean HDL-C was 0.33 mmol/L higher in patients eating one portion or more of fish spread per day compared to patients eating fish for lunch one time or less per week **(Appendix1)**. Mean levels of TG were 2.36 mmol/L and 2.03 mmol/L in the highest-frequency and lowest-frequency groups, respectively. Accordingly, mean levels of TG were 2.22 mmol/L and 1.45 mmol/L in the groups of most-frequent and least-frequent intakes of fish for dinner, respectively. Mean HDL-C was 1.36 mmol/L and 1.63 mmol/L in the corresponding groups.

### **4.6.3** Mean lipid levels in subjects with FH

The mean HDL-C was 0.44 mmol/L higher in Danish subjects with FH eating milk and yogurt once per week or less compared to Danish subjects with FH eating full-fat dairy products **(Appendix 3)**. Mean HDL-C was 0.22 mmol/L higher in subjects eating five portions of fish for lunch or more compared to subjects eating fish for lunch once per week or less.

### **4.6.4** Lipid and lipoprotein levels and fish and dairy consumption

In linear regression analyses of dairy products, consumption of once per week or less was used as reference. The analyses were adjusted for use of lipid-lowering medication. No statistically significant associations between milk and yogurt and cream and other milk products and total cholesterol, HDL-C, LDL-C, or TG were found **(Table 9)**. However, subjects consuming low fat cheese and full fat cheese had 0.22 mmol/L and 0.13 mmol/L higher mean HDL-C levels compared to the reference group ($p = 0.003$ and 0.010, respectively). In the regression analyses of fish consumption, subjects eating one portion or less of fish spread per week were used as references. Subjects eating five or more portions of fish spread per week had 0.46 mmol/L higher mean total cholesterol compared to the reference group ($p = 0.044$), while the mean HDL-C was 0.30 mmol/L higher compared to the reference group ($p < 0.001$). Furthermore, mean HDL-C was 0.22 mmol/L higher in subjects eating fish for dinner two times per week ($p < 0.001$). No appreciable nor significant differences were observed for LDL-C and TG according to dairy products with different fat content nor groups with different frequencies of fish consumption.

In linear regression analyses of consumption of fish and dairy in Danish subjects with FH, subjects consuming low fat milk and yogurt had 0.28 mmol/L lower HDL-C ($p = 0.023$)

compared to the reference group, and subjects consuming full fat milk and yogurt had 0.48 mmol/L lower HDL-C compared to the reference group (p = 0.013) **(Table 10)**. Danish subjects with FH consuming low fat and full fat cream and other dairy products had 0.75 mmol/L (p = 0.014) and 0.73 mmol/L (p = 0.045) lower total cholesterol compared to the reference group. Consumption of reduced fat cream and other dairy products was statistically significantly associated with 0.30 mmol/L lower HDL-C (p = 0.034) and eating fish for dinner two times per week was statistically significantly associated with 0.25 mmol/l higher HDL-C (p = 0.012) compared to the reference groups. The analyses were adjusted for lipid-lowering medication.

**Table 9.** Lipid and lipoprotein levels in Danish subjects (*n* = 346)

| | Total cholesterol | | HDL-C | | LDL-C | | TG | |
|---|---|---|---|---|---|---|---|---|
| | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** |
| **Milk and yoghurt** | | | | | | | | |
| ≤1 times/week | reference | | reference | | reference | | reference | |
| Skimmed (<1%) | 0.02 (-0.30, 0.34) | 0.900 | -0.06 (-0.17, 0.044) | 0.251 | 0.01 (-0.26, 0.27) | 0.940 | -0.12 (-0.52, 0.28) | 0.553 |
| Low fat (1,5-2%) | -0.01 (-0.39, 0.38) | 0.979 | -0.12 (-0.25-0.01) | 0.065 | 0.00 (-0.32, 0.33) | 0.983 | -0.04 (-0.53, 0.44) | 0.857 |
| Full fat (2-10%) | 0.15 (-0.39, 0.70) | 0.581 | -0.12 (-0.30, 0.07) | 0.213 | 0.20 (-0.25, 0.65) | 0.379 | -0.14 (-0.83, 0.54) | 0.678 |
| **Cream and other dairy products** | | | | | | | | |
| ≤1 times/ week | reference | | reference | | reference | | reference | |
| Low fat (≤7%) | -0.00 (-0.32, 0.31) | 0.986 | -0.31 (-0.14, 0.07) | 0.561 | 0.09 (-0.17, 0.35) | 0.517 | -0.20 (-0.60, 0.19) | 0.308 |
| Reduced fat (9-15%) | 0.14 (-0.27, 0.55) | 0.498 | -0.06 (-0.19, 0.8) | 0.432 | 0.15 (-0.19, 0.49) | 0.387 | 0.14 (-0.38, 0.65) | 0.597 |
| Full fat (≥16%) | 0.21 (-0.16, 0.58) | 0.264 | 0.04 (-0.09, 0.16) | 0.566 | 0.06 (-0.25, 0.37) | 0.711 | 0.24 (-0.23, 0.70) | 0.317 |
| **Cheese** | | | | | | | | |
| ≤1 time/week | reference | | reference | | reference | | reference | |
| Low fat (≤13%) | 0.36 (-0.73, 0.79) | 0.103 | 0.22 (0.08, 0.36) | **0.003** | 0.24 (-0.13, 0.60) | 0.200 | -0.34 (-0.89, 0.20) | 0.215 |
| Reduced fat (≤18%) | 0.10 (-0.23, 0.43) | 0.558 | 0.04 (-0.07, 0.15) | 0.479 | 0.43 (-0.23, 0.32) | 0.760 | -0.07 (-0.48, 0.35) | 0.755 |
| Full fat (≥27%) | 0.22 (-0.73, 0.52) | 0.140 | 0.13 (0.03, 0.23) | **0.010** | 0.12 (-0.13, 0.36) | 0.356 | 0.06 (-0.31, 0.43) | 0.737 |
| **Fish for lunch** | | | | | | | | |
| ≤1 portion/week | reference | | reference | | reference | | reference | |
| 2-4 portions/week | 0.20 (-0.58, 0.45) | 0.130 | 0.063 (-0.02, 0.14) | 0.139 | 0.09 (-0.12, 0.30) | 0.381 | -0.22 (-0.54, 0.09) | 0.165 |
| ≥ 5 portions/week | 0.46 (0.01, 0.91) | **0.044** | 0.30 (0.15, 0.45) | **<0.001** | 0.21 (-0.17, 0.59) | 0.286 | -0.36 (-0.93, 0.20) | 0.207 |
| **Fish for dinner** | | | | | | | | |
| ≤ 1 time/week | reference | | reference | | reference | | reference | |
| 2 times/week | 0.24 (-0.13, 0.60) | 0.204 | 0.22 (0.10, 0.34) | **<0.001** | 0.07 (-0.23, 0.37) | 0.635 | -0.00 (-0.46, 0.46) | 0.995 |
| ≥ 3 times/week | 0.40 (-0.59, 1.38) | 0.428 | 0.26 (-0.07, 0.58) | 0.118 | 0.36 (-0.46, 1.18) | 0.395 | -0.78 (-2.02, 0.46) | 0.216 |

Regression analysis of lipid levels and consumption of fish and dairy products in Danish subjects. Adjusted for lipid-lowering treatment.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides

**Table 10.** Lipid and lipoprotein levels in Danish subjects with FH (*n* = 88)

| | Total cholesterol | | HDL-C | | LDL-C | | TG | |
|---|---|---|---|---|---|---|---|---|
| | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** |
| **Milk and yoghurt** | | | | | | | | |
| ≤1 times/week | reference | | reference | | reference | | reference | |
| Skimmed (<1%) | -0.15 (-0.80, 0.50) | 0.648 | -0.15 (-0.35, 0.05) | 0.148 | 0.62 (-0.51, 0.64) | 0.831 | -0.46 (-1.08, 0.17) | 0.153 |
| Low fat (1,5-2%) | -0.21 (-0.99, 0.57) | 0.591 | -0.28 (-0.52, -0.04) | **0.023** | -0.04 (-0.72, 0.65) | 0.916 | -0.05 (-0.80, 0.70) | 0.893 |
| Full fat (2-10%) | -0.14 (-1.36, 1.08) | 0.824 | -0.48 (-0.85, -0.10) | **0.013** | 0.33 (-0.75, 1.41) | 0.544 | -0.34 (-1.52, 0.84) | 0.564 |
| **Cream and other dairy products** | | | | | | | | |
| ≤1 times/ week | reference | | reference | | reference | | reference | |
| Low fat (≤7%) | -0.75 (-1.34, -0.15) | **0.014** | -0.13 (-0.32, 0.07) | 0.192 | -0.46 (-1.00, 0.07) | 0.090 | -0.29 (-0.89, 0.31) | 0.346 |
| Reduced fat (9-15%) | -0.17 (-1.00, 0.67) | 0.691 | -0.30 (-0.57, -0.02) | **0.034** | 0.03 (-0.73, 0.78) | 0.947 | 0.16 (-0.69, 1.00) | 0.711 |
| Full fat (≥16%) | -0.73 (-1.44, -0.02) | **0.045** | -0.10 (-0.34, 0.13) | 0.374 | -0.59 (-1.23, 0.05) | 0.071 | 0.49 (-0.23, 1.20) | 0.182 |
| **Cheese** | | | | | | | | |
| ≤1 time/week | reference | | reference | | reference | | reference | |
| Low fat (≤13%) | -0.13 (-0.96, 0.71) | 0.760 | 0.25 (-0.02, 0.51) | 0.066 | -0.08 (-0.81, 0.66) | 0.835 | -0.53 (-1.33, 0.28) | 0.198 |
| Reduced fat (≤18%) | 0.22 (-0.48, 0,93) | 0.528 | 0.09 (-0.13, 0.31) | 0.423 | 0.21 (-0.41, 0.82) | 0.508 | -0.27 (-0.95, 0.41) | 0.436 |
| Full fat (≥27%) | -0.19 (-0,78, 0.40) | 0.510 | 0.12 (-0.07, 0.30) | 0.205 | -0.24 (-0.75, 0.27) | 0.356 | 0.16 (-0.41, 0.72) | 0.580 |
| **Fish for lunch** | | | | | | | | |
| ≤1 portion/week | reference | | reference | | reference | | reference | |
| 2-4 portions/week | 0.21 (-0.34, 0.77) | 0.445 | 0.08 (-0.10, 0.25) | 0.385 | -0.02 (-0.51, 0.47) | 0.945 | 0.35 (-0.18, 0.89) | 0.196 |
| ≥ 5 portions/week | 0.08 (-0.72, 0.88) | 0.838 | 0.22 (-0.03, 0.47) | 0.087 | -0.11 (-0.81, 0.60) | 0.766 | -0.14 (-0.91, 0.64) | 0.728 |
| **Fish for dinner** | | | | | | | | |
| ≤ 1 time/week | reference | | reference | | reference | | reference | |
| 2 times/week | 0.05 (-0.58, 0.68) | 0.876 | 0.25 (0.06, 0.45) | **0.012** | -0.15 (-0.70, 0.41) | 0.606 | 0.28 (-0.34, 0.90) | 0.373 |
| ≥ 3 times/week | -1.49 (-3.78, 0.81) | 0.202 | -0.27 (-0.99, 0.44) | 0.450 | -0.82 (-2.86, 1.22) | 0.425 | -0.86 (-3.12, 1.39) | 0.449 |

Regression analysis of lipid levels and consumption of fish and dairy in Danish subjects with familial hypercholesterolemia (FH). Adjusted for lipid-lowering treatment.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides

### **4.6.5** Regression analyses of total fish and dairy scores in the Danish population

The regression analysis of total fish score in the Danish population showed a 0.19 mmol/L increase in total cholesterol (p = 0.032) and 0.12 mmol/L increase in HDL-C (p <0.001) per every 10-point increase **(Table 11)**. No appreciable nor statistically significant differences were observed for total cholesterol, HDL-C, LDL-C or TG with increasing dairy score. The analysis was adjusted for use of lipid-lowering medication.

**Table 11**. Regression of total scores in Danish subjects (*n* = 346)

| | **Fish** | | **Dairy** | |
|---|---|---|---|---|
| | **Difference, mmol/L* (95% CI)** | **p** | **Difference, mmol/L* (95% CI)** | **p** |
| Total cholesterol | 0.19 (0.02, 0.36) | **0.032** | -0.11 (-0.27, 0.05) | 0.164 |
| HDL-C | 0.12 (0.07, 0.18) | **<0.001** | -0.03 (-0.08, 0.02) | 0.268 |
| LDL-C | 0.08 (-0.07, 0.22) | 0.293 | -0.07 (-0.20, 0.07) | 0.320 |
| TG | -0.17 (-0.38, 0.05) | 0.122 | -0.11 (-0.27, 0.05) | 0.164 |

Regression analysis of lipid levels and total scores for fish and dairy in Danish subjects. Adjusted for lipid-lowering treatment.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides
*Per 10-point increase

## **4.7** Lipid levels in the Norwegian population

### **4.7.1** Mean lipid levels

Norwegian subjects eating cheese once a week or less had a mean LDL-C of 3.45 mmol/L, compared to 2.91 mmol/L for subjects using full fat cheese **(Appendix 2)**. Mean LDL-C for subjects eating one or fewer portions of fish spread per week was 0.22 mmol/L higher than subjects eating five or more portions.

### **4.7.2** Lipid and lipoprotein levels and consumption of fish and dairy in the Norwegian population

Subjects choosing reduced fat cream and other milk products had lower mean LDL-C compared to the reference group (p = 0.014), as described in **Table 12**. Beyond this, no statistically significant differences in lipid and lipoprotein levels were seen between the different groups of dairy and fish in Norwegian patients.

**Table 12**. Lipid and lipoprotein levels in Norwegian FH subjects (*n* = 104)

| | Total cholesterol | | HDL-C | | LDL-C | | TG | |
|---|---|---|---|---|---|---|---|---|
| | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** | **Difference (mmol/L)** | **p** |
| **Milk and yoghurt** | | | | | | | | |
| ≤1 times/week | reference | | reference | | reference | | reference | |
| Skimmed (<1%) | 0.19 (-0.35, 0.73) | 0.487 | -0.02 (-0.21, 0.17) | 0.806 | 0.08 (-0.40, 0.57) | 0.736 | 0.14 (-0.18, 0.47) | 0.379 |
| Low fat (1,5-2%) | 0.43 (-0.25, 1.10) | 0.214 | 0.07 (-0.17, 0.31) | 0.547 | 0.22 (-0.39, 0.83) | 0.477 | 0.03 (-0.38, 0.43) | 0.901 |
| Full fat (2-10%) | 2.01 (-0.44, 4.45) | 0.107 | -0.24 (-1.10, 0.62) | 0.528 | 1.66 (-0.53, 3.85) | 0.136 | 1.31 (-0.16, 2.78) | 0.079 |
| **Cream and other dairy products** | | | | | | | | |
| ≤1 times/ week | reference | | reference | | reference | | reference | |
| Low fat (≤7%) | -0.35 (-0.87, 0.18) | 0.196 | 0.07 (-0.11, 0.26) | 0.453 | -0.38 (-0.84, 0.09) | 0.111 | 0.07 (-0.25, 0.39) | 0.674 |
| Reduced fat (9-15%) | -0.62 (-1.24, 0.002) | 0.051 | 0.00 (-0.22, 0.21) | 0.965 | -0.69 (-1.24, -0.14) | **0.014** | 0.23 (-0.15, 0.60) | 0.237 |
| Full fat (≥16%) | -0.43 (-1.52, 0.66) | 0.437 | -0.18 (-0.56, 0.20) | 0.350 | -0.41 (-1.38, 0.55) | 0.394 | 0.41 (-0.25, 1.07) | 0.220 |
| **Cheese** | | | | | | | | |
| ≤1 time/week | reference | | reference | | reference | | reference | |
| Low fat (≤13%) | 0.32 (-0.52, 1.16) | 0.244 | 0.13 (-0.16, 0.42) | 0.167 | 0.17 (-0.58, 0.92) | 0.652 | -0.16 (-0.66, 0.34) | 0.522 |
| Reduced fat (≤18%) | 0.28 (-0.47, 1.02) | 0.467 | 0.17 (-0.09, 0.43) | 0.196 | 0.12 (-0.55, 0.79) | 0.721 | 0.06 (-0.38, 0.51) | 0.787 |
| Full fat (≥27%) | 0.46 (-0.32, 1.24) | 0.450 | 0.19 (-0.08, 0.46) | 0.380 | 0.26 (-0.44, 0.95) | 0.470 | 0.20 (-0.27, 0.66) | 0.397 |
| **Fish for lunch** | | | | | | | | |
| ≤1 portion/week | reference | | reference | | reference | | reference | |
| 2-4 portions/week | -0.17 (-0.70, 0.35) | 0.513 | 0.14 (-0.04, 0.32) | 0.122 | -0.31 (-0.77, 0.15) | 0.189 | -0.03 (-0.34, 0.28) | 0.858 |
| ≥ 5 portions/week | -0.05 (-0.63, 0.53) | 0.862 | 0.13 (-0.07, 0.33) | 0.199 | -0.34 (-0.85, 0.17) | 0.187 | 0.26 (-0.09, 0.60) | 0.145 |
| **Fish for dinner** | | | | | | | | |
| ≤ 1 time/week | reference | | reference | | reference | | reference | |
| 2 times/week | 0.36 (-0.21, 0.92) | 0.213 | 0.04 (-0.15, 0.24) | 0.655 | 0.21 (-0.29, 0.71) | 0.404 | 0.22 (-0.13, 0.56) | 0.213 |
| ≥ 3 times/week | -0.04 (-0.67, 0.59) | 0.120 | 0.05 (-0.17, 0.27) | 0.670 | -0.23 (-0.79, 0.33) | 0.415 | 0.19 (-0.19, 0.57) | 0.320 |

Regression analysis of lipid levels and consumption of fish and dairy in Norwegian subjects with familial hypercholesterolemia (FH). Adjusted for lipid-lowering treatment.
HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides

# 5 Discussion

In this master's thesis, the consumption of fish and dairy in patients with FH in Norway and in patients suspected for FH in Denmark was investigated. Consumption of fish and dairy was assessed in relation to age, sex, and BMI in the Norwegian population, and in relation to age, sex, BMI, DLCNS, and previous history of ASCVD as well as family history of ASCVD in the Danish population. Furthermore, we investigated associations between plasma lipid and lipoprotein levels and consumption of dairy products with different fat content as well as different frequencies of fish consumption.

In summary, it was found that Danish and Norwegian patients had similar habits of fish and dairy consumption with regard to age, BMI, and sex. Age had the largest impact on the consumption of fish both in the Danish and the Norwegian study population, with subjects over 50 years eating fish both for dinner and lunch statistically significantly more frequent than subjects under 50 years of age. In the Danish population, subjects over 50 years of age also consumed more full fat cheese compared to younger subjects, which was not seen in the Norwegian population. When comparing plasma lipid levels in patients consuming dairy products of different fat content, both low fat cheese and full fat cheese were associated with higher HDL-C in Danish patients. Furthermore, a higher frequency of fish consumption was associated with higher total cholesterol and HDL-C levels in Danish subjects. These associations were not found in the Norwegian population.

## 5.1 Discussion of results

### 5.1.1 Study populations

A larger proportion of the Danish population was above 50 years of age compared to the Norwegian population, namely 58% of Danish subjects and 40% of Norwegian subjects. This may be due to the fact that Danish subjects are only suspected for FH based on high plasma lipid levels. It is more common for persons of older age to have their plasma lipid levels measured at the General Practitioner, as high lipid levels generally are not a problem in younger subjects unless a predisposition exists, such as for instance in FH.

BMI was approximately evenly distributed in the Danish and the Norwegian population. However, 45% of the Norwegian population had a BMI <25 and was categorized as normal weight compared to 29% of the Danish population. Since high BMI is a risk factor for CVD, Norwegian subjects have most likely previously received dietary and lifestyle guidance to avoid obesity, considering they all have a diagnosis of FH. As expected, a significantly larger proportion of the Norwegian population received statin treatment compared to the Danish population, namely 92% and 28%.

### **5.1.2** Intake of fish

Intake of fish was higher in persons above 50 years of age. A major explanation for this may be that older persons were more accustomed to eating more fish compared to younger generations. It is also likely that fish is one of the dietary components with advantageous health effects best known to the general population, and that buying and eating fish is prioritized to a larger extent in persons of older age at higher risk of CVD. Finally, personal economy may be a factor of significance since fish is relatively expensive. Surprisingly, premature CVD or family history of CVD was not associated with higher fish intake. These findings may suggest that fish intake should be a focus point during dietary counselling of young individuals in particular.

Considerably more subjects in the Norwegian population consumed fish for dinner three or more times per week compared to the Danish population, namely 50% of subjects over 50 years of age and 18% of subjects under 18 years of age, compared to 2% and 1% of Danish subjects over and under the age of 50, respectively. This implies that there were national differences regarding fish consumption which might in part be due to local dietary habits and access to fish. Also, the findings may in part be ascribed to the fact that all Norwegian subjects had FH whereas Danish subjects were only suspected to have FH, which would be in line with Arroyo-Olivares et al. who found that consumption of fish was higher in patients with FH compared to their non-affected relatives (98). Correspondingly, Molven et al. found that more children with FH had a high frequency of fish consumption for dinner compared to non-FH children (99).

### **5.1.3** Intake of dairy products

In the Danish population, subjects over 50 years of age consumed more full fat cheese compared to younger subjects. Furthermore, more subjects under the age of 50 reported consuming cheese once per week or less. The age differences in consumption of cheese may be due to different habits in younger and older persons as may also be the cause regarding fish intake, in that older persons may be more accustomed to using full fat products whereas younger persons may be used to having greater access to reduced fat and low fat alternatives as a result of developments in the food market. Considering the dietary guidelines, older persons with high risk of developing CVD would presumably benefit from exchanging full fat dairy products with low fat products. However, some studies have found a neutral association between dairy intake and risk of CVD (100, 101). Especially the association between fermented products such as yogurt and cheese in relation to CVD risk has been ambiguous (101). Kvist et al. found that consumption of full fat yogurt products or cheese instead of milk, regardless of fat content, was associated with a lower risk of development of myocardial infarction among middle-aged Danish men and women (102).

### **5.1.4** Lipid and lipoprotein levels

In this project, full fat dairy products were not associated with increased levels of neither LDL-C nor TG. Both low fat and full fat cheese were associated with higher HDL-C levels. The neutral effect of higher intake of dairy fat on LDL-C in this project is in line with the findings of Antoniazzi et al., who found no association between SFA and LDL-C in a study of FH patients from Spain and Brazil (103). However, dairy products as investigated in this project are only one source of SFA and do not constitute the total amount of dietary SFA.

Studies have been ambiguous in regard to the effect of diet in patients with FH. Malhotra et al. and Barkas et al. found in their systematic reviews that no conclusion could be made about the effectiveness of a cholesterol-lowering diet for reducing risk of CVD in patients with FH (104, 105). However, Roy et al. concluded that the apparent lack of effectiveness of diet in modulating plasma LDL-C levels most likely is due to biases in study designs (106). In the current study, diet seemed to have a larger impact on lipid and lipoprotein levels in the Danish subjects with FH compared to Norwegian FH subjects since both low fat and full fat milk and yogurt as well as reduced fat cream and other dairy products were related to lower HDL-C, and low fat and full fat cream and other dairy products were related to lower total cholesterol in Danish FH subjects. In comparison, only reduced fat cream and other dairy products was

related to lower LDL-C in the Norwegian population. Drouin-Chartier et al. found that diet quality was inversely associated with coronary artery calcification which is an important risk factor for incident CVD in subjects with FH receiving concomitant lipid-lowering treatment (107). Furthermore, Torvik et al. found that dietary counselling of children with FH had a positive effect on intake of SFA as well as on plasma lipid profile (108).

## **5.2** Limitations of the study

### **5.2.1** Collection of dietary information

A major limitation in this project was information bias as information on diet relied on self-reported intake of fish and dairy products, which is prone to measurement error as well as potential recall and memory biases and variations in food intake over time. Thus, participants may want to present a more advantageous portrayal of their diet when interviewed by a nurse or nutritionist and dietary information is therefore prone to over- and under reporting, depending on what is perceived as beneficial (109). With regard to recall bias, a diagnosis of CVD or FH might affect a subject's response in dietary questionnaires influenced by an idea of what is regarded as desirable (109). Also, patients with such diagnoses may have received dietary guidance previously which is a major limitation. Additionally, collecting dietary information by means of a dietary questionnaire is a retrospective method, which requires that the respondent to a certain degree is aware of their habitual diet and able to report portion sizes, frequencies and type of foods accurately.

Furthermore, the accuracy of the questionnaires for the purpose of this project was limited to categorization of fish and dairy intake and no information was available for intake of oily fish in the Danish population. Discerning between lean and oily fish would have been of interest due to the higher levels of EPA and DHA in oily fish. Additionally, developments in the food market might have reduced the questionnaire's relevance and ability to detect the participant's true intake of fish and dairy products. Many new dairy products, in particular, have been developed during recent years and these may not have been captured by the dietary questionnaires. The SmartDiet and HeartDiet questionnaires report only frequencies of consumption and/or type of the foods of interest. Regarding milk products, subjects are categorized based on fat content of the dairy products they use *most often*. Only subjects consuming milk and milk products once per week or less are categorized based on frequency.

Therefore, the amount of dairy consumed during a week is likely to vary widely. Plasma LDL-C may increase with increasing intake of SFAs, and total amount of dairy would thus be of relevance for this project. The same is true for consumption of fish.

Even though both the HeartDiet and the SmartDiet questionnaires have previously been validated, a correlation coefficient for intake of dairy was not reported in either validation studies. However, the conclusions of both validation studies were that the HeartDiet and the SmartDiet questionnaires are useful tools for evaluation of diet in clinical practice.

### **5.2.2** Methodological considerations

Methodological limitations in this project include small sample sizes and some cross tabulations only had limited number of subjects. The generalizability of the study findings may be limited since participants were included from only two cities in Denmark and one city in Norway. Another limitation is that butter was not included in the dairy score. In both SmartDiet and HeartDiet questionnaire, butter is included in the questions regarding fat on bread and in cooking. However, butter may constitute a significant part of dairy intake and would thus have been of interest to explore in this project.

Comparing the Norwegian and the Danish populations imposed several challenges. Firstly, the dietary questionnaires used to assess intake of fish and dairy were not identical. Even though HeartDiet is based on SmartDiet, they are different in several ways. The number of answer options as well as points allocated to each category in HeartDiet vary, whereas SmartDiet consequently has three categories associated with one, two or three points. The design of HeartDiet allows for collection of more detailed information, which is in risk of being lost when being harmonized to fewer categories as in SmartDiet. Furthermore, foods included in HeartDiet and SmartDiet are designed to fit the population and food market of the respective countries.

Secondly, the Norwegian and Danish populations included in the current thesis differed as the Danish populations included subjects referred to two large lipid clinics suspected for FH, while the Norwegian population included individuals diagnosed with FH who have been enrolled at the lipid clinic in Oslo. Danish subjects were referred to the lipid clinics based on aforementioned referral criteria, and may have made changes in dietary habits during the

period of time between measuring high plasma lipid levels at their General Practitioner and visit at the lipid clinic.

## **5.3** Strengths

Strengths of the current thesis include the recruitment of patients in lipid clinics from both Denmark and Norway. There was a high degree of agreement to participate in the study populations. Patients were diagnosed with FH by genetic testing and by highly specialized units. The FFQ was filled out together with or reviewed by a dietitian or a nurse. This allowed for the participant to ask questions and to be assisted if needed. Self-administered questionnaires require a certain level of nutrition literacy, and a health professional can be helpful for ensuring that the form is understood correctly. Additionally, the paper-format of the questionnaires provided that no technological skills were demanded. Both HeartDiet and SmartDiet have previously been validated and found to be appropriate tools for measuring an individual's habitual diet.

## **5.4** Perspectives for future research: from fish and dairy products to dietary patterns

In this master's thesis, the exposures of interest were limited to intake of fish and dairy products and investigation of complex dietary patterns were considered beyond the scope if this project. However, recent evidence emphasizes the importance of regarding the diet as a whole, contrary to focusing on adding or removing one or a few dietary components, which has been the traditional approach over the past decades. Thus, increasing weekly portions of fish, e.g., will necessarily lead to a decrease in the intake of the foods which are replaced by fish and such substitutional aspects may be of importance. Also, having a high consumption of fish and/or low-fat dairy products may be accompanied by other foods choices, and it is likely that fish and low-fat dairy products not alone constitute, but are components of, a healthy diet with beneficial impact on risk of CVD. Interestingly, a study by Fahed et al. showed that FH patients adhering to a favorable lifestyle had 86% lower risk of coronary heart disease compared with subjects leading an unhealthy lifestyle (110). Furthermore, the results showed that FH patients with a favorable lifestyle could have lower risk of CHD compared to subjects without FH leading an unhealthy lifestyle (110). A healthy lifestyle was

defined as having three out of four of the following characteristics: doing regular exercise, not currently smoking, having a BMI of less than 30 and adhering to a healthy dietary pattern.

The Mediterranean diet is considered the most advantageous dietary pattern for the prevention of CVD (111) and the ESC recommended in the most recent guidelines (2021) on the prevention of CVD to eat according to the Mediterranean or similar diet to lower the risk of CVD (112). Thus, observational cohorts have shown a consistent association between adherence to a Mediterranean diet and lower cardiovascular risk (111, 113). Also, in the landmark PREDIMED study, Estruch et al. found a significantly lower incidence of major cardiovascular events in persons with high cardiovascular risk eating a Mediterranean diet compared to a control group (114). The intervention groups eating a Mediterranean diet were supplemented with either olive oil or unsalted nuts. The study demonstrated that a diet based on vegetables with high contents of unsaturated fat was effective in the prevention of CVD (114). Other well-described dietary patterns include The DASH diet and the healthy Nordic diet which are characterized by large amounts of whole grains, fruits, vegetables, and moderate amounts of fish and low-fat dairy products as well as reduced amounts of red and processed meats (115, 116).

Due to differences in availability of foods and food culture, the optimal diet may differ between regions. Adherence to, and sustainability of, a certain diet may be increased if regional differences are considered (117). The healthy Nordic diet has been proposed to be the Nordic equivalent to the Mediterranean diet (118). The healthy Nordic diet is based on the 2004 Nordic Nutrition Recommendations and contains foods originating from Nordic countries, including fruits and berries, vegetables, legumes, low-fat dairy products, oily fish such as salmon, herring, and mackerel, and cereals such as oats and barley as well as rapeseed oil. The diet is low on sugar-sweetened beverages, saturated fats, and salt (119). Dietary intervention studies such as the NoMa study conducted in Norway, the NORDIET study conducted in Sweden, SYSDIET conducted in Finland, Sweden and Denmark, and the New Nordic Diet study conducted in Denmark have shown beneficial effects of the healthy Nordic diet on lipid profile, blood pressure, and insulin sensitivity as well as on low-grade inflammation (116, 117, 119, 120).

A major advantage of dietary pattern analysis is that the combined effects of all foods

consumed can be investigated. Investigation of dietary patterns in relation to lipid profile and CVD risk in patients with FH requires detailed FFQs, but indeed represent an interesting area of research that warrant further investigation.

# 6 Conclusion

In conclusion:

1. We found our hypothesis regarding fish being associated with older age to be correct. Additionally, Danish subjects with severe hypercholesterolemia and a high intake of fish did have higher levels of HDL-C. However, BMI and premature CVD or CVD in the family as well as TG levels were not statistically significantly associated with consumption of fish.

2. Our hypothesis that individuals with severe hypercholesterolemia and a high intake of high-fat dairy products were of older age and had a higher BMI was found to be correct in the Danish population. However, age and BMI were not statistically significantly associated to dairy intake in the Norwegian population. Contrary to our expectations, subjects with high intake of high-fat dairy products did not have significantly higher LDL-C levels compared to subjects with lower intake of high-fat dairy products.

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# 8 Appendices 1-6

**Appendix 1. Mean lipid levels in Danish subjects (*n* = 346)**

| | Untreated (*n*=248) | | | | | Treated (*n*=98) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | Total cholesterol, mmol/l (SD) | HDL, mmol/l (SD) | LDL, mmol/l (SD) | TG, mmol/l (SD) | *n* | Total cholesterol, mmol/l (SD) | HDL mmol/l, (SD) | LDL mmol/l, (SD) | TG mmol/l, (SD) |
| **Milk and yoghurt** | | | | | | | | | | |
| 0-1 times/wk | 45 | 7.70 (0.93) | 1.44 (0.43) | 5.44 (0.70) | 2.47 (2.26) | 17 | 5.23 (1.27) | 1.50 (0.37) | 3.02 (1.08) | 1.53 (0.67) |
| Skimmed (<1%) | 142 | 7.57 (1.00) | 1.41 (0.41) | 5.29 (0.86) | 2.14 (1.20) | 55 | 5.64 (1.42) | 1.35 (0.32) | 3.46 (1.11) | 1.97 (1.35) |
| Low fat (1,5-2%) | 48 | 7.66 (0.89) | 1.34 (0.32) | 5.40 (0.74) | 2.18 (1.18) | 16 | 5.29 (1.35) | 1.30 (0.24) | 3.10 (1.20) | 2.16 (1.24) |
| Full fat (2-10%) | 12 | 7.35 (1.13) | 1.39 (0.27) | 5.08 (0.76) | 2.03 (1.08) | 10 | 6.14 (1.58) | 1.27 (0.31) | 4.09 (1.35) | 2.01 (1.53) |
| **Cream and other dairy products** | | | | | | | | | | |
| 0-1 times/wk | 148 | 7.55 (0.99) | 1.40 (0.41) | 5.26 (0.83) | 2.23 (1.57) | 59 | 5.57 (1.41) | 1.37 (0.32) | 3.42 (1.16) | 1.85 (1.07) |
| Low fat (≤7%) | 43 | 7.64 (0.87) | 1.37 (0.30) | 5.47 (0.81) | 1.99 (1.07) | 21 | 5.35 (1.35) | 1.34 (0.29) | 3.24 (1.27) | 1.72 (0.71) |
| Reduced fat (9-15%) | 25 | 7.73 (0.82) | 1.30 (0.31) | 5.45 (0.67) | 2.42 (1.34) | 8 | 5.60 (1.15) | 1.48 (0.44) | 3.46 (0.91) | 1.80 (1.37) |
| Full fat (≥16%) | 32 | 7.71 (1.12) | 1.48 (0.45) | 5.34 (0.78) | 2.21 (1.35) | 10 | 5.94 (1.74) | 1.28 (0.30) | 3.44 (1.33) | 2.88 (2.43) |
| **Cheese** | | | | | | | | | | |
| 0-1 times/wk | 61 | 7.41 (0.92) | 1.32 (0.37) | 5.18 (0.66) | 2.35 (1.51) | 32 | 5.51 (1.26) | 1.26 (0.27) | 3.43 (1.07) | 1.72 (0.66) |
| Low fat (≤13%) | 25 | 7.68 (0.97) | 1.52 (0.43) | 5.44 (0.82) | 1.62 (0.87) | 10 | 6.11 (1.55) | 1.52 (0.40) | 3.66 (1.22) | 2.26 (2.7) |
| Reduced fat (≤18%) | 61 | 7.59 (1.08) | 1.34 (0.37) | 5.32 (1.05) | 2.20 (1.28) | 20 | 5.41 (1.46) | 1.36 (0.31) | 3.25 (1.27) | 1.78 (0.91) |
| Full fat (≥27%) | 101 | 7.71 (0.93) | 1.44 (0.40) | 5.39 (0.71) | 2.27 (1.59) | 36 | 5.55 (1.48) | 1.40 (0.32) | 3.35 (1.21) | 2.08 (1.25) |
| **Fish for lunch** | | | | | | | | | | |
| <1 portion/wk | 84 | 7.38 (0.91) | 1.33 (0.40) | 5.20 (0.86) | 2.36 (1.86) | 35 | 5.60 (1.47) | 1.31 (0.33) | 3.44 (1.28) | 2.10 (1.21) |
| 1-6 portions/wk | 142 | 7.69 (0.98) | 1.40 (0.35) | 5.38 (0.77) | 2.14 (1.15) | 56 | 5.51 (1.39) | 1.37 (0.30) | 3.33 (1.13) | 1.85 (1.32) |
| ≥1 portion/d | 22 | 7.93 (1.02) | 1.66 (0.50) | 5.45 (0.82) | 2.03 (1.34) | 7 | 5.83 (1.31) | 1.53 (0.38) | 3.57 (0.94) | 1.63 (1.05) |
| **Fish for dinner** | | | | | | | | | | |
| 0-4 times/mo | 214 | 7.54 (0.96) | 1.36 (0.35) | 5.29 (0.82) | 2.22 (1.48) | 86 | 5.61 (1.42) | 1.36 (0.32) | 3.44 (1.15) | 1.92 (1.29) |
| 2 times/wk | 30 | 8.06 (0.96) | 1.67 (0.52) | 5.61 (0.72) | 2.18 (1.26) | 11 | 5.08 (1.27) | 1.32 (0.33) | 2.85 (1.24) | 1.04 (1.04) |
| ≥ 3 times/wk | 4 | 7.75 (0.99) | 1.63 (0.54) | 5.42 (0.65) | 1.45 (0.30) | 1 | 6.80 (-) | 1.60 (-) | 4.70 (-) | 1.10 (-) |

Mean lipid levels in Danish subjects with and without lipid-lowering treatment across levels of exposures.
wk, week; d, d; mo, month

**Appendix 2. Mean lipid levels in Norwegian FH subjects (*n* = 104)**

| | *n* | Total cholesterol, mmol/l (SD) | HDL, mmol/l (SD) | LDL, mmol/l (SD) | TG, mmol/l (SD) |
|---|---|---|---|---|---|
| **Milk and yoghurt** | | | | | |
| ≤1 times/wk | 28 | 4.88 (1.86) | 1.43 (0.49) | 3.11 (1.58) | 1.10 (0.57) |
| Skimmed (<1%) | 56 | 4.60 (1.39) | 1.39 (0.38) | 2.76 (1.31) | 1.25 (0.76) |
| Low fat (1,5-2%) | 19 | 5.17 (1.03) | 1.50 (0.34) | 3.20 (1.06) | 1.13 (0.60) |
| Full fat (2-10%) | 1 | 10.10 (-) | 1.30 (-) | 7.80 (-) | 2.40 (-) |
| **Cream and other dairy products** | | | | | |
| ≤1 times/wk | 34 | 5.29 (2.00) | 1.41 (0.37) | 3.45 (1.82) | 1.10 (0.60) |
| Low fat (≤7%) | 22 | 4.56 (1.29) | 1.40 (0.31) | 2.66 (1.19) | 1.33 (0.94) |
| Reduced fat (9-15%) | 43 | 4.57 (1.00) | 1.47 (0.46) | 2.73 (0.86) | 1.17 (0.58) |
| Full fat (≥16%) | 5 | 5.18 (2.80) | 1.24 (0.38) | 3.34 (2.54) | 1.52 (0.88) |
| **Cheese** | | | | | |
| ≤1 time/wk | 13 | 5.15 (2.14) | 1.30 (0.56) | 3.41 (1.90) | 1.16 (0.72) |
| Low fat (≤13%) | 40 | 4.80 (1.73) | 1.45 (0.43) | 2.94 (1.60) | 1.21 (0.51) |
| Reduced fat (≤18%) | 20 | 4.74 (1.15) | 1.40 (0.29) | 2.90 (1.08) | 0.98 (0.37) |
| Full fat (≥27%) | 31 | 4.81 (1.32) | 1.46 (0.35) | 2.91 (1.19) | 1.13 (0.98) |
| **Fish for lunch** | | | | | |
| ≤1 portion/wk | 43 | 4.79 (1.16) | 1.34 (0.36) | 3.06 (1.08) | 1.14 (0.59) |
| 2-4 portions/wk | 36 | 4.87 (1.65) | 1.49 (0.46) | 2.99 (1.42) | 1.12 (0.55) |
| ≥ 5 portions/wk | 25 | 4.87 (2.02) | 1.47 (0.36) | 2.84 (1.93) | 1.40 (0.96) |
| **Fish for dinner** | | | | | |
| ≤ 1 time/wk | 24 | 4.70 (1.03) | 1.39 (0.35) | 2.97 (1.00) | 1.04 (0.48) |
| 2 times/wk | 51 | 4.87 (1.40) | 1.43 (0.45) | 3.01 (1.23) | 1.25 (0.82) |
| ≥ 3 times/wk | 29 | 4.88 (2.13) | 1.44 (0.36) | 2.94 (1.99) | 1.23 (0.58) |

Mean lipid levels in Norwegian subjects with familial hypercholesterolemia (FH) across levels of exposures
wk, week

**Appendix 3. Mean lipid levels in Danish subjects with FH (*n* = 88)**

| | *n* | Total cholesterol, mmol/l (SD) | HDL, mmol/l (SD) | LDL, mmol/l (SD) | TG, mmol/l (SD) |
|---|---|---|---|---|---|
| **Milk and yoghurt** | | | | | |
| ≤1 times/wk | 17 | 7.31 (1.88) | 1.58 (0.37) | 4.90 (1.83) | 2.14 (1.60) |
| Skimmed (<1%) | 48 | 7.04 (1.71) | 1.44 (0.38) | 4.85 (1.55) | 1.67 (0.83) |
| Low fat (1,5-2%) | 18 | 7.31 (1.80) | 1.30 (0.30) | 5.07 (1.71) | 2.11 (1.35) |
| Full fat (2-10%) | 5 | 5.36 (1.70) | 1.14 (0.21) | 3.48 (1.43) | 1.56 (0.75) |
| **Cream and other dairy products** | | | | | |
| ≤1 times/wk | 49 | 7.30 (1.73) | 1.49 (0.41) | 4.97 (1.54) | 1.82 (1.13) |
| Low fat (≤7%) | 19 | 6.37 (1.95) | 1.36 (0.26) | 4.34 (1.95) | 1.51 (0.80) |
| Reduced fat (9-15%) | 8 | 7.23 (1.82) | 1.19 (0.23) | 5.09 (1.54) | 1.99 (1.32) |
| Full fat (≥16%) | 12 | 7.02 (1.65) | 1.38 (0.33) | 4.81 (1.69) | 2.36 (1.36) |
| **Cheese** | | | | | |
| ≤1 time/wk | 32 | 6.89 (1.71) | 1.34 (0.41) | 4.69 (1.49) | 1.87 (1.13) |
| Low fat (≤13%) | 10 | 7.24 (1.41) | 1.58 (0.33) | 5.06 (1.43) | 1.41 (0.78) |
| Reduced fat (≤18%) | 16 | 7.38 (2.22) | 1.42 (0.39) | 5.14 (2.07) | 1.64 (1.09) |
| Full fat (≥27%) | 30 | 6.99 (1.78) | 1.45 (0.30) | 4.72 (1.68) | 2.07 (1.23) |
| **Fish for lunch** | | | | | |
| ≤1 portion/wk | 26 | 6.85 (1.76) | 1.35 (0.35) | 4.78 (1.74) | 1.59 (0.99) |
| 2-4 portions/wk | 50 | 7.18 (1.87) | 1.42 (0.37) | 4.88 (1.69) | 2.02 (1.25) |
| ≥ 5 portions/wk | 12 | 6.95 (1.56) | 1.57 (0.36) | 4.69 (1.36) | 1.52 (0.77) |
| **Fish for dinner** | | | | | |
| ≤ 1 time/wk | 71 | 7.03 (1.78) | 1.38 (0.31) | 4.83 (1.63) | 1.80 (1.08) |
| 2 times/wk | 16 | 7.18 (1.92) | 1.63 (0.52) | 4.78 (1.83) | 2.09 (1.35) |
| ≥ 3 times/wk | 1 | 6.70 (-) | 1.1 (-) | 5.01 (-) | 1.1 (-) |

Mean lipid levels in Danish subjects diagnosed with familial hypercholesterolemia (FH) across levels of exposures
wk, week

**Appendix 4.** Find Familial Hypercholesterolemia (FFH) form

# Projekt FFH

Udfyldt af:_____ Dato: _____/_____/_____(dd/mm/åå)

**Navn** ..... **CPR** ..... **REDCap ID** .....

Udgave 3/December 2020

**Henvisningsårsag** (sæt kryds(er)):

☐ Alder > 40 år og LDL-kolesterol (LDL-k) ≥ 5 mmol/l Alder 18 - 40 år og
☐ LDL-k ≥ 4 mmol/l
☐ LDL-k ≥ 4 mmol/l og tidlig personlig hjertekarsygdom (mænd < 55 år, kvinder < 60 år) Antal LDL-k værdier der

opfylder det givne henvisningskriterie: 0 ☐ 1 ☐ 2 ☐ >2 ☐

☐ Henvist efter påvist FH hos slægtning

| | Ja | Nej |
|---|---|---|
| **Sekundær dyslipidæmi udelukket som årsag til hyperkolesterolæmi** | ☐ | ☐ |
| Hvis nej, angiv type | | |

**Højde** (cm) ..... **Vægt** (kg) ..... **Livvidde** (cm) .....

**Fedt-score** ..... **FiskFrugtGrønt-score** .....

**Rygning** Aldrig ☐ Tidligere ☐ Aktuel ☐ **Pakkeår** .....

**Alkohol** (genstande pr. uge) 0-7 ☐ 8-14 ☐ ≥15 ☐

| | Ja | Nej |
|---|---|---|
| **Hjertekarsygdom** | ☐ | ☐ |

Hvis ja, hvilke(n)

☐ Angina pectoris
☐ AMI
☐ PCI
☐ CABG
☐ Påvist aortastenose
☐ Iskæmisk apopleksi/behandlet TCI
☐ PAD (Symptomgivende + ABI< 0,9 og/eller revaskularisering)

Aterosklerose/iskæmi påvist ved
☐ KAG (diffus, insignifikante og signifikante stenoser)
☐ CT-angio
☐ Hjerte-CT, CAC score.....
☐ Ultralyd af karotider
☐ Anden billeddiagnostik (fx stress MR, RbPET, myokardieskintigrafi m.f.)

| | Ja | Nej |
|---|---|---|
| **Diabetes Mellitus** | ☐ | ☐ |
| Hvis ja, angiv type Type 1 ☐ Type 2 ☐ Anden type ☐ | | |
| | **Ja** | **Nej** |
| **I behandling for hypertension** | ☐ | ☐ |

**Kolesterolværdier ved henvisningstidspunktet (mmol/L)**
Behandlet* ☐ Ubehandlet ☐

Total-k ..... HDL-k ..... LDL-k ..... Triglycerid .....

* Hvis behandlet, angiv type, dosis og frekvens:

Præparat 1:..... dosis: ..... frekvens: .....

Præparat 2:..... dosis: ..... frekvens: .....

**Lp(a) målt i lipidklinikken:** ..... mg/L; ved anden måleenhed angiv denne: .....

| Dutch Lipid Clinic Network Score for FH | Point | Kriterie opfyldt |
|---|---|---|
| **1. Familiehistorie** | | |
| Førstegradsslægtning med præmatur (mænd < 55 år, kvinder < 60 år) kardiovaskulær sygdom *eller* førstegradsslægtning med LDL-k over 95. percentilen for alder og køn[se tabel 1] | 1 | ☐ |
| Førstegradsslægtning med senexanthomer og/eller arcus cornealis *eller* børn < 18 år med LDL-k over 95. percentilen for alder og køn[se tabel 1] | 2 | ☐ |
| **2. Klinisk anamnese** | | |
| Præmatur koronararteriesygdom (mænd < 55 år, kvinder < 60 år) | 2 | ☐ |
| Præmatur cerebral eller perifer arteriesygdom (mænd < 55 år, kvinder < 60 år) | 1 | ☐ |
| **3. Objektiv undersøgelse** | | |
| Senexanthomer | 6 | |
| Arcus cornealis før 45 års alderen | 4 | ☐ |
| Xanthelasmata | 0 | ☐ |
| **4. LDL-k niveau** | | |
| Højeste ubehandlede LDL-k* _____ mmol/L | | |
| LDL-k ≥ 8.5 mmol/L | 8 | ☐ |
| LDL-k 6.5–8.4 mmol/L | 5 | ☐ |
| LDL-k 5.0–6.4 mmol/L | 3 | |
| LDL-k 4.0–4.9 mmol/L | 1 | ☐ |
| **5. DNA analyse** | | |
| Er gentest foretaget? Ja ☐ Nej ☐ | | |
| Hvis ja, afventer svar ☐ | | |
| Sygdomsassocieret mutation påvist (LDL-receptor-, ApoB- eller PCSK9 gen) | 8 | ☐ |

*Kun højeste score tæller indenfor hver af de 5 områder*

**Angiv total DLCN Score** .....

Definitiv FH (>8 points), Sandsynlig FH (6–8 points), Mulig FH (3–5 points)

*foreligger der ikke en ubehandlet LDL-k værdi, angives den højeste LDL-k på den mest LDL-reducerende behandling mhp. senere beregning af korrigeret LDL-k værdi:

Behandlet LDL-k (mmol/L): ..... Præparat: ..... dosis: ..... frekvens: .....

**Tabel 1**. 95% percentilen af LDL-kolesterol i Herlev-Østerbroundersøgelsen

| Alder | Mænd | Kvinder |
|---|---|---|
| < 30 | 4.2 | 3.9 |
| 30-34 | 4.7 | 4.0 |
| 35-39 | 4.9 | 4.1 |
| 40-44 | 5.0 | 4.3 |
| 45-49 | 5.0 | 4.6 |
| 50-54 | 5.1 | 4.9 |
| 55-59 | 5.1 | 5.1 |
| 60-64 | 5.0 | 5.2 |
| 65-69 | 4.9 | 5.2 |
| 70-74 | 4.8 | 5.2 |
| 75-79 | 4.7 | 5.1 |
| 80-84 | 4.6 | 5.1 |

Evt. yderligere kommentarer:

**Appendix 5.** HeartDiet questionnaire

Navn .....
Cpr. nr. .....
Dato .....

# HjerteKost

Læs spørgsmålene grundigt, og sæt for hvert spørgsmål et kryds i den rubrik, der passer bedst til dine generelle kostvaner.

**Du må kun sætte ét kryds ud for hvert spørgsmål.**

**Vurdering af dine kostvaner**

Når du har udfyldt skemaet, føres resultaterne af Fedtscoren og FiskFrugtGrøntscoren ind i skemaet nedenfor. Den samlede pointscore fås ved at lægge pointene fra de enkelte spørgsmål sammen.

Din kost vurderes på baggrund af, hvor højt du scorer.

For at kunne opnå betegnelsen "HjerteSund" skal scoren være mindst 75% i både Fedtscoren og FiskFrugtGrøntscoren.

| Dato og år | Fedtscore % | FiskFrugtGrønt-score % | Kommentar |
|---|---|---|---|
| | | | |

HJERTEFORENINGEN
PÅ RETTE STED

Lipidklinikken
Kardiologisk Afdeling
AALBORG UNIVERSITETSHOSPITAL

Dette skema er udarbejdet af Lipidklinikken, Aalborg Universitetshospital, i samarbejde med Hjerteforeningen.
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## Mælk og surmælksprodukter

Hvilken typer mælk/surmælksprodukt bruger du oftest?.....sæt 1 X

Drikker/spiser mælk/surmælksprodukter 0 - 1 gang om ugen..... 6 ☐

Sødmælk, tykmælk, ymer, A38 (3,5% fedt), sødmælksyoghurt, koldskål (mere end 2% fedt), græsk yoghurt 10%..... 0 ☐

Letmælk, ylette, letmælksyoghurt, A38 (1,5% fedt), Cultura, græsk yoghurt (højst 2% fedt), koldskål (højst 2% fedt)..... 6 ☐

Skummetmælk, minimælk, kærnemælk, koldskål (højst 1% fedt), skummetmælksyoghurt, Cheasy yoghurt, A38 0,5%, drikkeyoghurt, skyr..... 9 ☐

## Øvrige mælkeprodukter

Hvilke typer øvrige mælkeprodukter bruger du oftest?
*I madlavning, til kager, i kaffe/te, som dressing o.l.* .....sæt 1 X

Bruger nedenstående typer mælkeprodukter, 0 - 1 gang om ugen..... 10 ☐

Piskefløde, Cremefine til piskning, cremefraiche 18%, cremefraiche 38%, madlavningsfløde (over 16%)..... 0 ☐

Kaffefløde 12%, fløde 9%, cremefraiche 9%, græsk yoghurt 10%, Cremefine til madlavning 15%..... 3 ☐

Madlavningsfløde (højst 7%), græsk yoghurt (højst 5% fedt), fromage frais, kvark, cremefraiche 6%..... 6 ☐

## Ost

Hvilken type ost spiser du oftest?.....sæt 1 X

Spiser ost 0 - 1 gang om ugen.....12 ☐

Skæreost 45+, flødeoste, blå- og hvidskimmel oste, mozzarella, gratineringsost, parmesan, grana, feta/salattern (27% fedt)..... 0 ☐

Skæreost 30+ (18%), friskost (højst 18% fedt), smelteost (højst 18% fedt), gratineringsost (højst 18% fedt)..... 9 ☐

Skæreost 20+ (13%) og 10+ (6%), friskost (højst 13% fedt), hytteost, feta/salattern (højst 10% fedt), brie light, Castello light, mozzarella light, gratineringsost light.....12 ☐

## Fedtstof på brød

Hvilken type fedtstof bruger du oftest?.....sæt 1 X

Bruger normalt ikke fedtstof på brød.....15 ☐

Smør, smørbare blandingsprodukter, fx Bakkedal, Kærgården original 75%, svinefedt..... 0 ☐

Kærgården 43%/60%, bløde plantemargariner..... 6 ☐

Minariner med højst 40% fedt, mayonnaise.....15 ☐

## Fedtstof til madlavning

Hvilken type fedtstof bruger du oftest til madlavning?
*Stegning, bagning, i sovs, som dressing o.l.* ..... sæt 1 X

Bruger normalt ikke fedtstof til madlavning.....15 ☐

Smør, smørbare blandingsprodukter, stege-/bagemargarine, palmin..... 0 ☐

Bløde plantemargariner..... 3 ☐

Flydende margariner, planteolier.....15 ☐

## Kødpålæg- og pålægssalater

Hvilken type pålæg spiser du oftest?.....sæt 1 X

Spiser kødpålæg, æg og pålægssalater 0 - 1 gang om ugen..... 9 ☐

Leverpostej, paté, spegepølse, kødpølse, rullepølse, sylte..... 0 ☐

Leverpostej (højst 14% fedt), mager kød-/spegepølse, mayonnaisesalater som fx skinke-, hønse- og rejesalat, æg..... 6 ☐

Skinke, hamburgerryg, saltkød, roastbeef, kyllinge-/kalkunpålæg, steg/kødpålæg u/synligt fedt, kødpålæg (højst 5% fedt), leverpostej (højst 6%)..... 9 ☐

## Kød som varm ret

Hvilken type kød spiser du oftest
*Inklusive kød i sammensatte retter som gryderetter, pizza, lasagne, pastaretter, tortilla o.l.?*.....sæt 1 X

Spiser kød 0 - 1 gang om ugen.....12 ☐

Hakkekød (over 12% fedt), nakkekoteletter m/fedtkant, steg m/fedtkant, lammekoteletter, wienerschnitzel, pølse, medisterpølse, bacon, grillben/spareribs, and, gås, færdigkøbte frikadeller, karbonader, hamburgerbøf..... 0 ☐

Hakkekød (højst 12% fedt), kylling og kalkun m/skind, steg u/fedtkant, skinke medisterpølse, kyllingepølse..... 9 ☐

Hakkekød (højst 6% fedt), kylling og kalkun u/skind, kød uden synligt fedt, skinke, svinekotelet uden fedtkant, kalvekød, vildtkød.....12 ☐

## Kage, chokolade og flødeis

Hvor ofte spiser du kage, chokolade og flødeis?
*1 portion = 1 stk. kage, 50 g chokolade eller 1 portion flødeis*.....sæt 1 X

4 eller flere portioner om ugen..... 0 ☐

2-3 portioner om ugen..... 3 ☐

1 portion om ugen..... 6 ☐

Ikke hver uge..... 9 ☐

## Fastfood og chips

Hvor ofte spiser du fastfood og chips?
*Eks. burger, pommes frites, kinarulle, pizza, hotdog, pølser, kartoffelchips, tortilla chips*.....sæt 1 X

2 eller flere gange om ugen..... 0 ☐

1 gang om ugen..... 3 ☐

2-3 gange om måneden..... 6 ☐

1 gang om måneden eller sjældnere..... 9 ☐

**Samlet Fedtscore:**_____

## Fisk til frokost

Hvor ofte spiser du fiskepålæg til frokost eller andre måltider?
*Eks. laks, makrel, sild, sardiner, ørred, forel, tun, fiskefilet, fiskefrikadelle, torskerogn, rejer og andre skaldyr*
*OBS: 1 portion = pålæg på ½ skive brød / 35 g, 2 portioner = pålæg på 1 skive rugbrød.* ..... sæt 1 X

| | | |
|---|---|---|
| Mindre end 1 portion om ugen | 0 | ☐ |
| 1-2 portioner om ugen | 4 | ☐ |
| 3-6 portioner om ugen | 9 | ☐ |
| 1 portion om dagen | 10 | ☐ |
| 2 eller flere portioner om dagen | 12 | ☐ |

## Fisk til varm mad

Hvor ofte spiser du fiskeretter eller fisk til varm mad? ..... sæt 1 X

| | | |
|---|---|---|
| 0-1 gang om måneden | 0 | ☐ |
| 2 gange om måneden | 4 | ☐ |
| 3-4 gange om måneden | 9 | ☐ |
| 2 gange om ugen | 10 | ☐ |
| 3 eller flere gange om ugen | 12 | ☐ |

## Grøntsager og bælgfrugter

Hvor mange portioner grøntsager (rå, kogte, stegte, bagte, syltede) og/eller bælgfrugter (tørrede bønner, linser, ærter) spiser du om dagen? (Husk også grøntsager i sammenkogte retter, wok m.m)
*OBS: 1 portion = 1 dl / 100 g grøntsager eller kogte bælgfrugter.*
*½ tallerken fyldt med grøntsager svarer til 300 g (og dermed til 3 portioner)* ..... sæt 1 X

| | | |
|---|---|---|
| Ikke hver dag | 0 | ☐ |
| 1 portion om dagen | 6 | ☐ |
| 2 portioner om dagen | 12 | ☐ |
| 3 portioner om dagen | 18 | ☐ |

## Frugt og bær

Hvor mange portioner frugt og bær spiser du om dagen?
*Eks. æble, pære, banan, appelsin, vindruer, bær, melon, frugtgrød*
*OBS: 1 portion = 1 dl / 1 stk. / 100 g* ..... sæt 1 X

| | | |
|---|---|---|
| Ikke hver dag | 0 | ☐ |
| 1 portion om dagen | 6 | ☐ |
| 2 portioner om dagen | 12 | ☐ |
| 3 portioner om dagen | 18 | ☐ |

## Brød

Hvor mange skiver fuldkornsbrød spiser du om dagen?
*Eks. rugbrød, Levebrød, fiberbrød/-boller, groft knækbrød, brød m/fuldkornsmærke* ..... sæt 1 X

| | | |
|---|---|---|
| Spiser ikke fuldkornsbrød hver dag | 0 | ☐ |
| 1 skive om dagen | 2 | ☐ |
| 2 skiver om dagen | 6 | ☐ |
| 3 eller flere skiver om dagen | 8 | ☐ |

## Morgenmadsprodukter

Hvor ofte spiser du morgenmadsprodukter, der er rige på fuldkorn og/eller fiber?
*Eks. havregryn, Havrefras, Rugfras, mysli, FiberSund, Weetabix, All Bran, rugbrød* ..... sæt 1 X

| | | |
|---|---|---|
| Spiser normalt ikke morgenmadsprodukter rige på fuldkorn | 0 | ☐ |
| 1-2 gange om ugen | 2 | ☐ |
| 3-4 gange om ugen | 4 | ☐ |
| 5-7 gange om ugen | 6 | ☐ |

## Kartofler, ris og pasta

Hvor ofte spiser du kartofler, ris eller pasta som tilbehør til det varme måltid? ..... sæt 1 X

| | | |
|---|---|---|
| 0-1 gang om ugen | 0 | ☐ |
| 2-3 gange om ugen | 4 | ☐ |
| 4-7 gange om ugen | 6 | ☐ |

## Nødder

Hvor ofte spiser du nødder?
*Eks. mandler, val-, pistacie-, cashew-, para- og hasselnødder, peanuts*
*OBS: 1 portion = 1 lille håndfuld / 30 g ( 3 håndfulde på en gang, 1 x om ugen = 3 portioner)* ..... sæt 1 X

| | | |
|---|---|---|
| Mindre end 1 portion om måneden | 0 | ☐ |
| 1-3 portioner om måneden | 2 | ☐ |
| 1-2 portioner om ugen | 4 | ☐ |
| 3 eller flere portioner om ugen | 8 | ☐ |

## Sukker, marmelade og søde drikke

Hvor ofte spiser du eksempelvis sukker eller marmelade og drikker søde drikke?
*1 skive brød med honning, marmelade, Nutella eller*
*1 glas sød saft, sodavand, frugtjuice eller*
*4 sukkerknalder, ½ spsk. sukker* ..... sæt 1 X

| | | |
|---|---|---|
| 4 eller flere gange om dagen | 0 | ☐ |
| 2-3 gange om dagen | 2 | ☐ |
| 0-1 gang om dagen | 6 | ☐ |

## Slik

Hvor ofte spiser du slik (vingummi, lakrids, bolcher)?
*1 portion = 1 dl / 75 g* ..... sæt 1 X

| | | |
|---|---|---|
| 3 eller flere portioner om ugen | 0 | ☐ |
| 2 portioner om ugen | 4 | ☐ |
| 0-1 portion om ugen | 6 | ☐ |

**Samlet FiskFrugtGrøntscore:** _____

Du er nu færdig med kostspørgeskemaet.
Det er en god idé at se skemaet igennem, så du er sikker på, at du har besvaret alle spørgsmålene.

# Livsstil

## Alder

_____år

## Køn

Kvinde ☐
Mand ☐

## Rygning

Tidligere ryger ☐
Ryger ☐
Ikke ryger ☐

## Motion

Hvor ofte motionerer du mindst 30 minutter om dagen?
Eks. rask gang, løb, cykling, svømning
Antal gange pr. uge:

0 ☐
1 ☐
2 ☐
3 ☐
4 ☐
5 ☐
6 ☐
7 ☐
>7 ☐

## Alkohol

Hvor mange genstande drikker du i gennemsnit om ugen?

0-7 ☐
8-14 ☐
≥15 ☐

1 genstand = 1 glas vin (12,5 cl), eller 1 øl (33 cl), eller 4 cl spiritus

## Kosttilskud

Tager du tilskud af fiskeolie?

Nej ☐
Fiskeoliekapsler ☐
Torskelevertran ☐

**Appendix 6.** SmartDiet questionnaire

## De gode rådene finner du her

Mettet fett er kolesteroløkende. Reduser derfor inntaket av matvarer med mye mettet fett. Velg i stedet matvarer med umettet fett som kan senke kolesterolet.

Drikk mager melk, ½ liter skummet, søt eller sur, daglig. Dersom du ikke drikker melk daglig, kan det føre til et for lavt inntak av kalsium.

Alle fløte- og rømmetyper inneholder mye mettet fett og anbefales ikke i hverdagskostholdet. Cultura, skummet kultur, lettmelk, ekstra lett melk, skummet melk, yoghurt, lett Créme Fraiche (10 % fett) og Kesam (1 % fett) kan brukes i matlaging, til sauser og dressing.

Ost er en kilde til store mengder mettet fett. Velg lettere eller mager ost (ost med mindre enn 10 % fett) til hverdags. Ikke bruk lettere ost som pålegg på mer enn en tredel av dagens brødskiver. Vær også oppmerksom på mengde og type ost du bruker i matlagingen. Velg gjerne planteoljebaserte oster som pålegg og i matlagingen.

Fett kjøtt er også en kilde til store mengder mettet fett. Velg kjøtt med mindre enn 10 % fett både som middagsmat og som pålegg. Skjær bort alt synlig fett, og spis minst mulig oppblandede kjøttprodukter. Velg for eksempel karbonadedeig eller kylling-/ svinekjøtt-deig fremfor kjøttdeig. Fjern skinnet på kylling, kalkun og annet fjærkre. Velg skinkeprodukter som pålegg fremfor salami, fårepølse og lignende.

Spis alle typer fisk til middag flere ganger i uken. Fet fisk som makrell, sild, laks og ørret inneholder umettet fett (omega-3) og er derfor spesielt gunstig. Spis fisk som pålegg daglig. Ta i tillegg 1 skje tran, eventuelt 2 fiskeoljekapsler, daglig året rundt.

Bruk gjerne majonespålegg daglig, men i moderate mengder. De fleste majonesprodukter inneholder mye olje og derfor mye fett (og kalorier), men fettet er umettet og derfor gunstig.

Myk plantemargarin er en god kilde til umettet fett. Velg typer med mer enn 75 % umettet fett. Velg gjerne margarin med plantesteroler. Plantesteroler er gunstig for kolesterolet. Ved bruk av medikamentet Ezetrol® (ezetimib) forventes imidlertid ikke plantesteroler å gi noen ytterligere kolesterolreduksjon.

Bruk gjerne olje, flytende eller myk plantemargarin i matlagingen (velg typer med mer enn 75 % umettet fett). Spis mindre stekt mat. Velg heller kokt eller ovnsstekt mat, da vil behovet for fett i matlagingen reduseres.

Grove kornprodukter er viktig i hverdagskostholdet. Spis mye av alle sorter fiberrike kornprodukter. Havre er spesielt gunstig og bør brukes regelmessig. Brødet bør inneholde mer enn 6 gram fiber pr 100 gram brød og ha over 75 % grovhet. Se etter Brødskala'n på emballasjen.

Husk "5-om-dagen". Spis minst tre porsjoner grønnsaker og to porsjoner frukt hver dag. Fyll halve middagstallerkenen med grønnsaker, både rå og lettkokte. Spis frukt og grønnsaker som mellom-måltid, som pålegg og som pynt på pålegget. Vær raus med porsjonene. Erter, bønner og linser kan med fordel spises ofte.

En porsjon poteter, ris eller pasta daglig er et fint tilbehør til middagen.

Bruk minst mulig sukker, sukkerholdig mat og drikke, som kjeks, kaker, is, søtt pålegg, sukker-godt, sjokolade, juice, nektar, saft og brus. Med unntak av fruktjuice gir disse produktene ingen eller få næringsstoffer, men kan bidra til økt vekt. Sukker (inkludert fruktsukker) kan også øke triglyseridverdiene.

Nøtter og mandler inneholder gunstig umettet fett, men er veldig kaloririke. Bruk det derfor gjerne, men i begrenset mengde. Kokosnøtten og chillinøttene inneholder mye mettet fett og bør derfor unngås.

Kaffebønnen inneholder fettstoffer som øker kole-sterolet. Velg derfor pulverkaffe (inneholder ikke fett) eller kaffe som blir filtrert, da filteret fjerner det meste av fettstoffene. Husk at kaffe tilsatt melk (for eksempel café latte, cappuccino) kan være en kilde til mettet fett avhengig av melketypen som brukes og mengde kaffe som drikkes.

Alkohol inneholder mye kalorier og kan derfor føre til vektøkning. Alkohol kan også øke triglyseridverdiene.

Eggeplommen inneholder mye kolesterol. Begrens inntaket til to eggeplommer per uke. Den største årsaken til økning av kolesterolet i blodet er likevel matvarer rike på mettet fett.

Spørreskjemaet vil ikke nødvendigvis gi et komplett bilde av ditt kosthold. Du kan få mer informasjon om kostholdet i heftet "Kostbehandling ved høye blodlipider hos voksne" (Lipidklinikken 2006).

Spørsmål 1-15 med unntak av spørsmål 10 er evaluert i forhold til veid kostholdsregistrering.

Kilde: Svilaas A, Strøm EC, Svilaas T, Borgejordet Å, Thoresen M, Ose L. SmartDietTM, a health educational tool. Reproducibility and validity of a short food questionnaire for assessment of dietary habits. Nutr Metab Cardiovasc Dis 2002; 12: 60-70. Fjerde revidering av skjemaet november 2019.

74841 Wera AS, Porsgrunn

# SmartDiet™

## 26 spørsmål om ditt kosthold og din livsstil



Les spørsmålene og de angitte svarmulighetene nøye!

Sett kryss ved det svaret som passer best med det du vanligvis spiser.

Kommentarer:

Antall poeng: _____

| Kostholdsvurdering | |
|---|---|
| 27 poeng eller mindre: | Du bør forbedre kostholdet ditt på mange punkter, for å gjøre det mer helse- og hjertevennlig. |
| 28-35 poeng: | Du kan forbedre kostholdet ditt på en del punkter, slik at det blir mer helse- og hjertevennlig. |
| 36 poeng eller mer: | Du har sunne kostholdsvaner. |

Navn: .....

Fødselsdato: ..... Dato for besvarelsen: .....

Navn på fastlege: .....

Adresse til fastlege: .....

Sett ett kryss til hvert spørsmål ved å krysse av i sirkelen ved det alternativet som passer best med det du vanligvis spiser.
Vær oppmerksom på at spørsmålene veksler mellom å spørre etter daglig og ukentlig forbruk.
*Kun utvalgte matvarer er listet opp.*

1. Melk (sur/søt) og yoghurt

Hvor mange glass (2dl) melk drikker/bruker du daglig som drikke, i matlagingen, på gryn, i grøt, i dessert, i kaffe, te o.l.? Antall:.....

Hvor mange små beger med yoghurt (ca 125g) spiser du i løpet av en uke? Antall:.....

Hvilken type melk bruker du oftest?

Melk med > 3 % fett • Helmelk • Kulturmelk • Kefir • Kokosdrikk .....
Melk med 0,5-1 % fett • Lettmelk (vanlig/laktosefri) • Cultura • Biola naturell • Melk med smak.....
Melk med < 0,5 % fett • Skummet melk • Skummet kulturmelk • Biola bærdrikk 0,1 % fett • Styrk 0,1 % •
Melkeerstatninger som soya-, havre- og mandeldrikk (ikke kokosdrikk) .....
Drikker ikke/bruker mindre enn 1 liter i uken eller bruker aldri .....

2. Fløte, rømme o.l.

Hvilken type bruker du oftest i matlagingen, i dressing, i dip, i kaker, i kaffe, i te o.l.

Inneholder > 20 % fett • Kremfløte • Lett piskbar fløte • Créme Fraiche • Seterrømme • Kokosmelk.....
Inneholder 10-20 % fett • Matfløte • Lettrømme 18 % (vanlig/laktosefri) • Lett Créme Fraiche 18 % ....
Inneholder 5-10 % fett • Lett matfløte • Kaffefløte • Lett rømme 10 % • Vikingmelk • Kesam • Matyoghurt •
Lett Créme Fraiche 10 % fett • Lett Kokosmelk .....
Inneholder < 5 % fett • Drømmelett • Kesam Mager .....
Bruker ikke dette ukentlig eller bruker aldri .....

3. Ost på brødmaten, i matlaging, på pizza o.l.

Hvor mye ost som pålegg, regnet i osteskiver eller i spiseskjeer (for smørbar ost), spiser du daglig? Antall:.....

Til hvor mange middager per uke bruker du ost?
Eksempel: På pizza, på lasagne, i saus, i salat o.l. Antall:.....

Hvilken type ost bruker du oftest?

Ost med > 20 % fett • Hvitost • Nøkkelost • Gauda • Cheddar • Edamer • Gräddost • Taffelost •
Gudbrandsdalsost (G35) • Ekte geitost • Fløtemysost • "Dessert-oster" • Fete krem- og tubeoster •
Snøfrisk • Fetaost • Mozzarella • Parmesan • Revet ost • GO'Vegan Cheddar/Skivet/Bit (erstatning til ost) .
Ost med 10-20 % fett • Lettere hvitost • Lettere nøkkelost • Lettere Fløtemysost/Gudbrandsdalsost •
Lettere krem- og tubeoster • Snøfrisk Lett • Mozzarella Lett • Lett revet ost • Go'Vegan Revet .....
Ost med <10 % fett • Cottage cheese • Mager Cottage cheese • Mager Cottage cheese og yohurt •
Mager fetaost • Gammalost • Pultost • Skjørost • Mager mysost • Prim • Prim Lett.....
Bruker ost kun en gang i uken eller bruker aldri .....

4. Kjøttpålegg

Hvilken type kjøttpålegg bruker du oftest?

Pålegg med > 10 % fett • Salami • Servelat • Fårepølse • Morrpølse • Reinsdyr- og elgpølse • Falukorv •
Kalkunkorv • Sylte • Lammerull • Kalverullade • Fenalår • Chorizo • Pepperoni • Patè • Leverpostei .....
Pålegg med < 10 % fett • Mager skinke • Hamburgerrygg • Roastbiff • Kylling-/kalkunfilet •
Lett servelat • Speket skinke uten fettrand • Skinkestek uten fettrand • Lett salami • Speket biff •
Okserull • Oljebaserte posteier • Mager leverpostei .....
Bruker kjøttpålegg kun en gang i uken eller bruker aldri .....

5. Kjøtt til middag

Hvilken type kjøtt bruker du oftest?

Kjøtt med > 15 % fett • Familiedeig • Mediterdeig • Grillpølse • Wienerpølse • Kjøttpølse • Mediterpølse •
Nakkekoteletter • Lammekjøtt • Medisterkake • Wienerschnitzel • Bacon av svin • Grillbøn (spareribs) •
Steik med fettrand • Entrecôte • Kjøttpudding • And .....
Kjøtt med 10-15 % fett • Kjøttdeig (okse, lam) • Kyllingpølse • Lettpølse • Karbonade • Hamburger •
Kebabkjøtt • Kjøttkaker • Koteletter med fettrand • Bayonneskinke med fettrand • Kjøttboller • Kylling,
kalkun og høne med skinn • Kyllingvinger • Kyllingklubber .....
Kjøtt med < 10 % fett • Karbonadedeig • Kjøttdeig (svin, kylling) • Biff • Filet (kylling, svin, okse,
lam) • Viltkjøtt • Stek uten fettrand • Bogskinke • Koteletter uten fettrand • "Go og mager"- pølser •
Kjøtt uten synlig fett • Strimler av mager biff, svin og kylling • Kylling, kalkun og høne uten skinn •
Kyllingkjøttboller (< 10 % fett) • Kalkunbacon .....
Spiser kjøtt kun en gang i uken eller spiser aldri .....

6. Fiskepålegg

Hvor ofte har du fisk som pålegg eller i salater til lunsj?

Laks • Makrell • Sild • Sardiner • Brisling • Tunfisk • Reker • Krabbe • Crab-sticks • Fiskepudding/-kake o.l.
På inntil 1 brødskive i uken eller aldri .....
På 2-4 brødskiver i uken .....
På 5 eller flere brødskiver per uke .....

7. Fisk til middag

Hvor ofte spiser du fisk, fiskemat og/eller fiskeretter?

Inntil en gang i uken eller aldri .....
2 ganger i uken .....
3 eller flere ganger i uken .....

Til hvor mange av disse middagene spiser du fet fisk ukentlig? Antall:.....
Eksempel: Ørret • Laks • Makrell • Kveite • Sild

8. Majonesprodukter, dressing, remulade, kaviar o.l.

Hvor ofte bruker du majonesprodukter, dressing, remulade og/eller kaviar på brødmaten?
Eksempel: Majones • Rekesalat • Italiensk salat • Crab-stick salat • Skagensalat • Frokostsalat • Remulade •
Potetsalat • Kaviar/kaviarmix • Dressing • Pesto • Aioli
På inntil 1 brødskive i uken eller aldri .....
På 2-7 brødskiver i uken .....
På 8 eller flere brødskiver per uke .....

9. Smør eller margarin på brødmaten

Hvilken type bruker du oftest?

Meierismør og andre typer smør • Melange margarin • Bremykt Original • Bremykt Mykere • Olivero ....
Brelett • Plantego` .....
Soft FLora (Original, Lett, Spesial) • Smøremyk • Smørelett • Vita • Vita Lett • Vita Pro-Aktiv •
Becel Pro-active .....
Bruker vanligvis ikke smør eller margarin på brødmaten .....

10. Plantesteroler

Bruker du et produkt som inneholder plantesteroler?
Eksempel: Vita Pro-aktiv • Becel Pro-aktiv ◯ Ja ◯ Nei

11. Fett i matlagingen

Hvilken type fett bruker du oftest til steking, baking, i saus, som dressing o.l.

Meierismør og andre typer smør • Melange margarin og andre typer hard margarin • Olivero Steke og
Bake • Soft Flora Steke og Bake • Soft margarin uten salt og melk • Kokosolje • Kokosfett .....
Olje • Flytende margarin .....
Bruker vanligvis ikke fett i matlagingen .....

12. Brød, knekkebrød og andre kornprodukter

Hvor mange skiver brød, rundstykker eller knekkebrød spiser du daglig? Antall:.....

Hvor mange porsjoner havregrøt, kornblanding eller andre typer frokost-blandinger spiser du ukentlig? Antall:.....

Hvilken type brød og kornprodukter spiser du oftest?

Brød med < 75 % grovhet • Kneippbrød • Firkornbrød • Landbrød • Jegerbrød • Loff • Fine rundstykker
eller baguetter • Polarbrød (hvete, havre, fullkorn) • Ciabatta • Lyst knekkebrød • Pitabrød • Riskaker •
Puffet ris • Cornflakes • Havrenøtter • Granola • Frokostblanding med sjokolade, honning, sukker o.l. ....
Brød med > 75 % grovhet • Grovbrød • Naturlig sunt (havre, rug og spelt) • Coop Fiber og Frø •
Rugbrød • Pumpernikkel • Vita brød • Polarbrød (flerkorn) • Grove knekkebrød • Havreknekkebrød •
Rugsprø • Fiberrik • Havregryn • Weetabix • Frokostblanding merket med nøkkelhullet.....
Spiser ikke brød, knekkebrød eller andre kornprodukter.....

13. Grønnsaker, frukt og bær

Hvor mange porsjoner grønnsaker, frukt og bær spiser du daglig?
1 porsjon = 150 g som tilsvarer ca 2 gulrøtter eller ca et stort eple
Mindre enn 2 porsjoner (< 300 g) daglig .....
2-4 porsjoner (300-600 g) daglig .....
Mer enn 4 porsjoner (> 600 g) daglig .....

Hvor mange av dagens porsjoner er grønnsaker eller salat? Antall:.....

Hvor mange av dagens porsjoner er frukt eller bær? Antall:.....

14. Søtt pålegg og søt drikke

Hvor ofte bruker du søtt pålegg eller søt drikke med sukker eller fruktsukker?
Eksempel: Syltetøy • Marmelade • Prim • Geitost • Sjokoladepålegg • Honning • Brus • Saft • Smoothie •
Iskaffe • Fruktjuice • Nektar o.l.
0-1 ganger daglig .....
2 ganger daglig .....
3 eller flere ganger daglig .....

15. Sjokolade, snacks, kaker, kjeks o.l.

Hvor ofte spiser du sjokolade, snacks o.l.?
Eksempel: Sjokolade (lys/mørk) • Fløteis • Potetgull • Ostepop • Baconcrisp • Tortilla chips • Kaker • Kjeks •
Wienerbrød • Boller • Skolebrød • Smågodt o.l.
0-1 ganger ukentlig .....
2 ganger ukentlig .....
3 eller flere ganger ukentlig .....

Totalt antall poeng: =

16. Potet, ris, pasta o.l.

Hvor mange porsjoner spiser du ukentlig? En porsjon tilsvarer 2 kokte poteter eller 2 dl kokt ris, pasta o.l.
Eksempel: Potet • Ris • Pasta • Byggryn • Cousous • Bulgur • Quinoa o.l.
◯ Spiser ikke ◯ 0-1 porsjon ◯ 2 porsjoner ◯ 3 porsjoner eller fler

Hva spiser du oftest? ◯ Fullkorn ◯ Ikke fullkorn ◯ Fritert

17. Belgvekster

Spiser du belgvekster ukentlig? ◯ Ja ◯ Nei
Eksempel: Bønner • Kikerter • Linser • Erter • Grønnsaks- og bønneblanding o.l.

18. Nøtter, musli- og nøttebarer, avokado o.l.

Spiser du nøtter, mandler, musli- og nøttebarer ukentlig? ◯ Ja ◯ Nei
Spiser du avokado eller oliven ukentlig? ◯ Ja ◯ Nei

19. Kaffe

Drikker du kaffe? ◯ Ja ◯ Nei
Hvis ja, hvilken type? .....
Eksempel: Traktekaffe • Pulverkaffe • Presskannekaffe • Kapselkaffe • Kokekaffe • Café latte • Cappuccino, iskaffe o.l.

20. Alkohol

Drikker du alkohol? ◯ Ja ◯ Nei
Hvis ja, hvor mange enheter drikker du til sammen per uke?
◯ Mindre enn 1 ◯ 1-3 ◯ 4-7
◯ 8-14 ◯ 15 enheter eller flere

1 enhet =
1 glass vin (125 ml)
1 glass øl (0.33 l)
4 cl brennevin

21. Egg

Hvor mange egg, inkludert i matlaging, spiser du per uke? Antall.....

1. Måltidsmønster

Hvor mange måltider, inkludert mellommåltider, spiser du daglig?
◯ 1-2 måltid ◯ 3 måltider
◯ 4 måltider ◯ 5 eller flere måltider

2. Høyde, vekt og midjemål

Høyde: ..... cm Vekt: ..... kg
Ønsker du å gå ned i vekt? ◯ Nei ◯ Ja
Hvis ja, hvor mange kilo ønsker du å gå ned i vekt? ..... kg
Midjemål: ..... cm

3. Røyk/snus

Røyker du?
◯ Nei, aldri ◯ Nei, tidligere røyker ◯ Ja ◯ Ja, av og til ◯ Passiv røyker

Hvis ja, hvor mange sigaretter/piper røyker du i gjennomsnitt per dag? Antall .....

Snuser du?
◯ Nei, aldri ◯ Nei, tidligere snuser ◯ Ja ◯ Ja, av og til

Hvis ja, hvor mange porsjoner snuser du i gjennomsnitt per dag? Antall .....

4. Mosjon

Hvor ofte mosjonerer du i minst 30 minutter slik at du blir andpusten eller svett?
Eksempel: Rask gange • Løping • Skigåing • Svømming • Sykling • Saltrening • Styrke • Fysikalsk trening o.l.
◯ Sjeldnere enn 1 gang per uke eller aldri
◯ 1 til 2 ganger per uke
◯ 3 eller flere ganger per uke

Hvilken type mosjon bedriver du? .....

5. Kosttilskudd

Bruker du regelmessig kosttilskudd?
◯ Nei ◯ Tran ◯ Fiskeoljekapsler/omega3-kapsler
◯ Vitamin D ◯ Multivitaminpreparat ◯ Annet .....