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Evaluation of Selected Food Categories in a Short FFQ Covering Questions regarding Dairy and Meat Products Among Participants with Moderate to High Risk of Cardiovascular Disease

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Preface

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Abstract

Introduction: This study is a part of the nationwide VISA-project. Validation of FFQ is crucial to obtain valid information within nutritional epidemiology. The diet in Norway shows a high intake of dairy and meat products rich in fat. These fatty acids affect the cholesterol, which is one of the risk factors for developing cardiovascular disease (CVD). As CVD is still the leading cause of mortality, both dietary assessment and investigation of dietary risk factors are crucial.

Aim: The primary aim of this master thesis is to evaluate the relative validity and reproducibility of selected food categories in a short FFQ, and explore possible associations between food categories and fatty acids in blood among Norwegian adults with moderate to high risk of CVD.

Method: A sub-group of 500 participants from the VISA-project was included in this study and divided in two groups. 318 qualified for the validation-biomarker study (VB) where they completed a short FFQ and gave blood samples by Dried Blood Spots at 48 Boots pharmacies. Four weeks later 122 participants completed the same FFQ in their homes in the validation test-retest study (VTR). The reproducibility of the FFQ was tested with a test-retest, and the validity was tested using fatty acids measured in blood as reference measurement.

Results and conclusion: VB: 82 men and 234 women with a mean age of 58.32 (±13.43) years and mean total-cholesterol on 6.50 (±1.17) mmol/L participated. VTR: 26 men and 96 women with a median age of 60.50 (50, 70) years and a mean BMI of 27.0 (±3.70) kg/m^2 participated. Satisfactory correlations (> 0.50) were seen for 12/18 questions and C15:0 had correlations with high-fat dairy products. The short FFQ can measure the intake of dairy products, eggs and the use of cholesterol lowering margarine among adults with slightly elevated risk for CVD.

Sammendrag

Introduksjon: Denne studien er en del av det landsomfattende VISA-prosjektet. Validering av matvarefrekvens spørreskjema (FFQ) brukt i ernæringsforskning er essensielt for å kunne arbeide med troverdig informasjon innen ernæringsepidemiologien. Kostholdet i Norge viser et høyt inntak av fete meieri- og kjøttprodukter. Kolesterolet blir påvirket av disse mettede fettsyrene og er en av risikofaktorene for å utvikle hjerte- og karsykdommer (HKS). Videre er HKS fortsatt hovedårsaken til dødelighet, og en kartlegging av kostholdet er viktig for å finne eventuelle risikofaktorer som kan lede til sykdom.

Problemstilling: Hovedmålet med denne masteroppgaven er å evaluere den relative validiteten og reproduserbarheten til ulike mat-kategorier i et kort FFQ, og undersøke mulige sammenhenger mellom matvaregrupper og fettsyrer målt i blod hos norske voksne med moderat til høy risiko for HKS.

Metode: Et underutvalg av 500 deltakere fra VISA-prosjektet ble inkludert i denne studien og videre delt i to grupper. 318 deltakere kvalifiserte til validerings-biomarkør studien (VB), hvor deltakerene fylte ut et kort FFQ og tok blodprøver med Dried Blood Spots i 48 Boots apotek. Fire uker senere fullførte 122 deltakere det samme spørreskjemaet for andre gang i deres hjem i validerings test-retest studien (VTR). Reproduserbarheten av spørreskjemaet ble testet med test-retest, videre ble validiteten testet ved hjelp av fettsyrer målt i blod som referansemetode.

Resultater og konklusjon: VB: 82 menn og 234 kvinner med en gjennomsnittsalder på 58,32 (±13,43) år og et gjennomsnittlig totalkolesterol på 6,50 (±1,17) mmol/L deltok. VTR: 26 menn og 96 kvinner med en median alder på 60,50 (50, 70) år og en gjennomsnittlig BMI på 27,0 (±3,70) kg/m^2 deltok. Tilfredsstillende korrelasjoner (> 0,50) ble observert for 12/18 spørsmål, og C15:0 hadde korrelasjoner med fete meieriprodukter. Den korte FFQ'en kan måle inntaket av meieriprodukter, egg og bruk av kolesterolsenkende margarin hos voksne med moderat til høy risiko for hjerte-og karsykdom.

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List of abbreviation

AA	Arachidonic acid
AHA	American Heart Association
ALA	Alfa-linolenic acid
BMI	Body mass index
BP	Blood pressure
CC	Correlation coefficients
CHD	Coronary heart disease
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DBS	Dried blood spots
DHA	Docosahexaenoic acid
EPA	Eicosapentaenoic acid
FA	Fatty acids
FAME	Fatty acids methyl esters
FAO	Food and Agriculture Organization of the United Nations
FFQ	Food frequency questionnaire
FNL	Functional nutrition litteracy
HbA1c	Long-term blood glucose
HDL	High-density lipoprotein
HDL-C	High-density lipoprotein-cholesterol
HF	High-fat
HUFA	Highly unsaturated fatty acids
HUNT	Helseundersøkelsen i Nord-Trøndelag
LA	Linoleic acid
LDL	Low-density lipoprotein
LDL-C	Low-density lipoprotein-cholesterol
LF	Low-fat
MedD	Mediterranean diet
MF	Medium-fat
MUFA	Mono unsaturated fatty acids
NCD	Non-communicable diseases
NSD	Norwegian Center for Research

PA	Physical activity
PUFA	Poly unsaturated fatty acids
RBC	Red blood cells
RCT	Randomized controlled trail
REK	National Committee for Research Ethics in Norway
RI	Recommended intake
SBP	Systolic blood pressure
SFA	Saturated fatty acids
TC	Total cholesterol
TFA	Trans fatty acids
TG	Triglyceride
UFA	Unsaturated fatty acids
UiO	University in Oslo
VB	Validation-biomarker study
VISA	Vascular lifestyle-Intervention and Screening in Pharmacy
TMAO	Trimethylamine-N-oxide
VLDL	very low-density lipoprotein
VTR	Validation test-retest study
V3-FFQ	First time completing the FFQ
V4-FFQ	Second time completing the FFQ
V3	Visit 3 – start of the current study
V4	Visit 4 – second visit in the current study
WCRF	World Cancer Research Fund International
WCRF/AICR	World Cancer Research Fund International/American Institute of Cancer Research
WHO	World Health Organization
WR	Weighed registration

1 Introduction

This master thesis is a part of the nationwide screening project "Vascular lifestyle-Intervention and Screening in Pharmacy (VISA)-Project" carried out by researchers at the Department of Nutrition, University of Oslo. The screening took place at 149 Boots pharmacies across Norway. Participants were stratified in accordance to risk factors and those identified as having moderate to high risk of cardiovascular disease (CVD) was included in an 8-week randomized controlled trial (RCT). The aim of VISA-Project is to assess the effect of identifying high risk of CVD in a low-threshold screening of risk factors for CVD preformed in pharmacies. In September 2015 participants stratified to high-risk of CVD in the screening showed up at Boots pharmacies across Norway for 1-year follow up, and an additional last intervention in the RCT. This master thesis is based on the data collected in September 2015. My role in the project was to be involved in the 1-year follow up of participants stratified to high risk.

1.1 Diet survey

Diet surveys are crucial for mapping of the intake of foods in relation to health status in both developed and developing countries (Albani et al., 2016). The intake of different foods will vary in relation to season, different culture and geography (Willet, 2013). Surveys can be divided into *retrospective* and *prospective* methods and further divided into closed and open questions (Hjartåker & Veierod, 2007). Food frequency questionnaires (FFQ), dietary history interview and 24-hour recall are all examples of retrospective methods including both open and closed questions. Hence these methods rely on the participant's memory. Methods used in prospective measurements are food diaries and weighed registration (WR). In contrast to retrospective methods, here the diet is registered at the time of event (Hjartåker & Veierod, 2007; Willet, 2013). WR is often used as a reference measurement in validation studies of FFQs (Hjartåker & Veierod, 2007). There is no method that measures the intake accurately, as report errors are connected to all measurements. For this reason the relative intake is registered (Hjartåker & Veierod, 2007).

FFQ is a method with closed questions, and it can ask for the diet over the last two years or two months. It can assess the intake of macro- and micronutrients along with energy intake, but the design of the questionnaires varies. For diet mapping covering shorter periods the questionnaires are often shorter and are sometimes referred to as short FFQs (Hjartåker &

Veierod, 2007; Lillegaard, Øverby, & Andersen, 2012). FFQs often contain up to 100 questions and aim to map the diet over 1-2 years. As to many detailed questions, participants may spend a long time filling them out, and it can be rather challenging for them to accomplish. This could result in FFQ's only completed by highly motivated individuals, and for this reason will not serve as an accurate representation of the population (Hjartåker & Veierod, 2007; Willet, 2013). However, several short FFQs have been developed the last years and are specifically useful when only certain foods are of interest. Food groups such as dairy products, meat products or fruits and vegetables (Hjartåker & Veierod, 2007; Lillegaard et al., 2012). Short FFQs may not always be designed to cover energy intake, and often it seek information of the number of food groups consumed per day. They are shorter (approximately 10 minutes to complete) and hence less challenging to accomplish (Lillegaard et al., 2012). It is also crucial for the participants to be able to read and understand the language of the questionnaire, as well as have a cultural affinity to the diet and food in question. Recruitment of participants over a larger geographic area is also possible when mailing out a questionnaire (Hjartåker & Veierod, 2007). Short FFQs are practical tools and are often used in both larger studies and smaller studies (Subar et al., 2001).

1.2 Validation of food frequency questionnaires

From a public health perspective validation of tools used in assessment of risk factors for disease is important in primordial prevention. In order to do improvements in prevention work it is essential to have valid tools in the mapping of risk factors (Masson et al., 2003). Instruments used in dietary research need to be able to give good estimations on what we are measuring, and it is important that they give the same result when measuring several times for a given population (Willet, 2013). Statistical measurements such as correlations coefficients (CC) and Bland Altman plots are often used in the evaluation of questionnaires validity (Bland & Altman, 2010; Schmidt & Steindorf, 2006). Even though this does not give the full truth it is a part of the evaluation of FFQs. Moreover, there are several other determinants to take into considerations such as study design, participant rate and selection when evaluating the validity of a questionnaire.

Reproducibility and validity are key words in validation studies (Willet, 2013), and will be further explained. The degree of reproducibility is a crucial determinant in the validation of FFQs (Hjartåker & Veierod, 2007), and refers to the degree a questionnaire will give the same results for the same persons when testing the same questionnaire at two different times by a test-retest (Eng & Moy, 2011; Hjartåker & Veierod, 2007). When asking

about the diet for previous two months a period of four weeks will be sufficient time for a test-retest. Thus one month will overlap in both test and the re-test (Cantin et al., 2016; Hjartåker & Veierod, 2007; Willet, 2013). According to Willet the time in between tests should be long enough for the participants to forget their first answers, yet short enough that they do not make any dietary changes (Willet, 2013). The validity of a FFQ is to what extent it is measuring what it is supposed to measure. Since there is no such thing as a gold standard within dietary research a reference method that is considered more valid then the test method is often used. Further, there are also some criteria that shall be considered in the evaluation of validity and choice of reference method (Willet, 2013). Walter Willet has compiled some guidance criteria to follow in validation studies and comprises the following: a) the errors addressing the measurement shall be independent of each other. The errors in the reference measure shall not include same errors as in the test measure; b) the reference measurement must be considered more accurate than the test method. WR is considered a good choice because its estimates are more precise then the FFQ and the errors connected to it is of another degree then the errors in the FFQ. Though, if there is a possibility to use biomarkers it is highly recommended; c) the test measurement and the reference measurement shall be done on the same level. The measurements must be similar in time frame, and in regard to individual or group-level; d) the order of data collection from test and reference measurement is important; e) if possible, it is a strength to have two different reference measures, and f) the participants in the study should be a sub group of the study population (Willet, 2013). Since there is no ideal reference measurement all different factors have to be evaluated together. However, the use of biochemical indicators in nutritional epidemiology is often seen as a highly trusted reference measurement (Willet, 2013).

1.2.1 Use of biomarkers in validation studies

Biochemical indicators can be used as reference measurement to further strengthen a validation study. They are however often expensive and not viable for smaller studies (Willet, 2013). Biochemical indicators are valuable as reference measurements when validating FFQs because the errors are approximately completely independent of the test method. It is also an objective measurement because the participants are not able to make an impact on the outcome of it in contrast to questionnaires (Hjartåker & Veierod, 2007; Willet, 2013). This makes biochemical indicators as close to a gold standard if there is one. There are however biological variations associated with the indicators such as individual differences in

absorption and metabolism, in addition to age, gender, diseases and use of medications. Indicators may be compounds taken as samples from tissue, urine or as biomarkers from blood (Willet, 2013). Biomarkers cannot reflect a full diet, but some can reveal energy intake and also intake of specific food groups (Brevik, Veierød, Drevon, & Andersen, 2005; Hjartåker & Veierod, 2007). There are only a few reliable methods in use of biomarkers. Double-labeled water, which reflects energy-intake over a 2-3 week period, and 24-hour urine collection of nitrogen, which mirrors the intake of protein, potassium and sodium (Hjartåker & Veierod, 2007). Carotenoids are often used in the assessment of fruit and vegetable intake, whereas fatty acids can be used to reflect intake of fat containing foods. Polyunsaturated fatty acids (PUFA) can reflect the intake of fat fish, and some saturated fatty acids (SFA), such as C15:0 and C17:0, may also give an indication of intake of milk and dairy products (Albani et al., 2016; Brevik et al., 2005; Hjartåker & Veierod, 2007; Samuelson, Bratteby, Mohsen, & Vessby, 2001). Other SFAs may also reflect the intake of high-fat food groups, such as high-fat dairy and potentially high-fat meat products (Albani et al., 2016; Samuelson et al., 2001). Exploring reliable biomarkers in future research will make dietary surveys more reliable than they are today, and maybe some day they will play a crucial role in the assessment of diet and risk factors for different lifestyle diseases (Willet, 2013).

It is not possible to measure absolute fat intake, but fatty acids as biomarkers are more frequently used within nutritional epidemiology (Hodge et al., 2007). A measurement of fatty acids from adipose tissue is the most consistent measurement of long-term fat intake, but this can be rather challenging for the participants to go through with. For this reason, fatty acids (FA) from plasma and whole blood are used to measure the intake of fat containing food. This can give an indication of the dietary fat consumed over the past few days (Hodge et al., 2007; Holen et al., 2016). The body is also able to synthesize fatty acids itself, and there are only two dietary essential FA: Linoleic acid (LA) (C18:2n6), which is the precursor to the partly essential arachidonic acid (AA) (C20:4n6), and α-linolenic acid (ALA) (C18:3n3) (Harvey & Ferrier, 2011). AA is the substrate for prostaglandins, which is one of the important eicosanoids that affect inflammatory processes among other responses. ALA plays a role for growth and development together with other n-3 FAs. LA and ALA are both compounds in plants (Harvey & Ferrier, 2011). When these FA are found in plasma they are indicators of dietary fat intake (Hodge et al., 2007). AA is also found in lard and beef meat, and it might be able to reflect a diet pattern high in meat (Fødevareinstitutt., 2016; Mahan & Escott-Stump, 2008; Marangoni, Colombo, & Galli, 2004).

1.3 Cardiovascular disease – epidemiology

Non-communicable diseases (NCD), also known as lifestyle diseases, as cancer, cardiovascular diseases (CVD) and diabetes mellitus, are the main causes of mortality worldwide. According to World Health Organization (WHO), they are responsible for 82 % of the mortality from NCD (World Health organization[WHO]2014).

In Norway, other countries in Northern Europe and USA there was an increased mortality rate from CVD in the late 40's, which reached a peak during the 1970's (Helsedirektoratet, 2009). It is particularly coronary heart disease (CHD) and stroke that are the dominant diseases in Europe, and the numbers affected varies widely between the countries (Townsend, Nichols, Scarborough, & Rayner, 2015). The mortality rate from CVD has went down over the past 40 years in Norway, but still represents the main cause of death amongst all age-groups (Folkehelseinstituttet, 2015a). Although men are the ones most frequently affected by CVD, mortality from CVD occurs in higher age especially among women (Folkehelseinstituttet, 2015a). However, there is an alarming increase among young adults, in the age 25-44 years old, with a first-time myocardial infraction, which has shown no decrease since 2001 (Folkehelseinstituttet, 2015b; Sulo et al., 2014).

CVDs are all caused by biological changes due to lifestyle, and the major risk factors are elevated cholesterol, elevated plasma glucose, overweight and obesity, hypertension, tobacco use and inactivity (Sotos-Prieto et al., 2016; World Health Organization/Food and Agriculture Organization of the United Nations[WHO/FAO] 2003). The main cause of mortality from CVD in Norway is infraction, which is a result of unhealthy lifestyle, overweight, and the relationship between cholesterol, smoking and hypertension, which gives a specific high risk of CHD (Selmer & Tverdal, 2003). There has been an increase in sedentary lifestyle among Norwegians over the past few years, which also contributes to overweight and obesity and a higher disease rate (Graff-Iversen, Selmer, & Søgaard, 2007). According to the national wide survey HUNT, which maps the health status among Norwegians from 1984-2008, they see a prevalence of 20 % of the men and 17 % of the women that suffer from obesity (> 30) in the age of 40-45 years old (Krokstad & Knudtsen, 2011).

These risk factors all contribute to different physiological changes in the blood vessels. CVD refers to disorders in the heart and blood vessels and can be divided in several diseases where all are caused by the same natural process of atherosclerosis (Folkehelseinstituttet, 2015b; Lusis, 2000; World Health Organization[WHO]2016a). The development of CVD is grounded in genes, culture, environment, political system and

lifestyle. Despite the complex causes, research shows that small changes in lifestyle, especially regarding diet, physical activity (PA) and tobacco use, can make a difference (WHO/FAO, 2003). WHO states that 80% of all CVD events and 90% of all new events of diabetes mellitus type 2 could have been prevented with diet, PA and tobacco use (WHO, 2014). High cholesterol is a major risk factor for developing CVD because of its damaging impact on the inflammatory process of atherosclerosis (Lusis, 2000). In short elevated cholesterol, in particular low-density lipoprotein (LDL), can accumulate together with other substances in intima and form a plaque in medium-sized and large arteries, which will lead to a constricted lumen. These physiological changes can lead to a CVD event (Lusis, 2000). These diseases may be reduced in many cases by small modifications in lifestyle, which impacts the risk factors.

1.3.1 Cholesterol and risk factors

Plasma cholesterol and triglycerides are the two most important lipid measurements in the examination of CVD and constitute the lipid profile (Nordestgaard & Varbo, 2014). Lipids are fat-soluble and together with cholesterol, they are carried in plasma by compounds known as lipoproteins (Frayn, 2010). Lipoproteins are dynamic structures that continuously exchange lipids and cholesterol. LDL-cholesterol (LDL-C) is the most cholesterol rich lipoprotein. Its function is to supply cholesterol to cells in the body, and it is also known as the bad cholesterol. On the other hand high-density lipoprotein cholesterol (HDL-C), is both the smallest and heaviest lipoprotein due to its low content of lipids and high content of proteins. HDL's compound is a result of its ability to remove cholesterol from tissues and transport it to the liver for excretion. It is referred to as the good cholesterol. The body obtains cholesterol from its own synthesizing and from diet (Frayn, 2010; WHO/FAO, 2003). TC, LDL-C and HDL-C, are the best predictors for CVD of the lipoproteins. Low levels of LDL-C are considered protective, and new research implies that a not too low level of HDL-C, will protect against CVD (Nordestgaard & Varbo, 2014; Rader & Hovingh, 2014). Rader & Hovingh raise questions about the HDL-hypotheses, as recent research suggest that it is rather HDL's function, which plays a protective role against CVD as opposed to the current hypothesis of high levels of HDL-C. This is still uncertain and further research and validation is necessary (Rader & Hovingh, 2014). The HDL level should not be to low, and recent studies show no effect with increasing HDL levels (Juel Christiansen, 2014). To achieve satisfying levels of HDL-C a healthy diet and regular PA is recommended (WHO/FAO, 2003).

Blood pressure, cholesterol, blood glucose, stress, smoking and BMI are all modifiable factors, which can be reversed by healthy eating, regular exercise, smoke cessation and weight loss (Oggioni et al., 2015; Selmer & Tverdal, 2003). These are all factors that comprise WHO Global Targets 2025 in order to reduce NCDs worldwide (WHO, 2014). Non-modifiable factors such as gender, age, and first relatives like parents or children with CVD, also give a higher risk of disease. Blood pressure and cholesterol naturally increases with higher age, which highlights the importance of regular exercise and healthy eating regardless of ones age (WHO/FAO, 2003). In **Table 1** the preferred values of risk factors are presented.

Table 1: Preferred values of risk factors for CVD.

Risk factors [1]	Men	Women
Systolic blood pressure (mmHg)	< 140	< 140
Diastolic blood pressure (mmHg)	< 90	< 90
Total-cholesterol (mmol/L)	< 5.0	< 5.0
LDL-cholesterol (mmol/L)	< 3.0	< 3.0
HDL-cholesterol (mmol/L)	≥ 1.0	≥ 1.3
Triglycerides (mmol/L)	≤ 1.7	≤ 1.7
Blood glucose (mmol/L)	< 7.0	< 7.0
Body mass index (kg/m^2)	< 24	< 24

[1] (Helsedirektoratet, 2009)

1.4 Diet related risk factors for cardiovascular disease

The Norwegian recommendations for fat is between 25 and 40 energy % (E%), which comprise < 10 E% from SFAs, 10-20 E% from monounsaturated fatty acids (MUFA), 5-10 E% from polyunsaturated fatty acids (PUFAs) of which 1 E% make up n-3 fatty acids (Helsedirektoratet, 2014). Foods such as fruits and vegetables, whole grains, legumes, nuts, seeds, olive oil, rapeseed oil, fatty fish, low-fat dairy products, little or no salt, small amounts of red meat and poultry are seen as heart friendly food because of its positive effects on blood pressure, cholesterol and weight control (Helsedirektoratet, 2014; Sacks et al., 2001). Aside from diet, PA and smoking also determine the cholesterol (Freund, Belanger, D'Agostino, & Kannel, 1993). PA such as frequent endurance training is recommended and the national guidelines for hyperlipidemias are 30-45 minutes exercise every day (Björk & Thelle, 2008; Couillard, Despres, Lamarche, & Bergeron, 2001). Further, are the daily recommendations for PA for adults in prevention of lifestyle diseases is as following:

- 150 minutes moderate exercise per week or 75 minutes high intensity exercise per week.
- Training of the main muscle groups twice a week.
  (Helsedirektoratet, 2014)

However, to reduce the TGs and raise the HDL-C one should exercise an amount, which is equivalent to an expenditure of 1200-2200 kcal per week. This will reduce the TGs and increase the HDL-C by 10 and 5-8 % respectively (Björk & Thelle, 2008). Smoking is considered the most pronounced risk factors for developing CVD (American Heart Association[AHA]2015a; Freund et al., 1993) Research over many years documents the damaging effects of smoking on lipoprotein metabolism, especially its ability to oxidize LDL-C and accelerate the atherosclerosis process (Freund et al., 1993). It is still necessary for the health sector to continue the counseling for cessation of smoking in order to lower the overall CVD diseases and mortality (Holme, Retterstol, Norum, & Hjermann, 2016; Oggioni et al., 2015).

1.4.1 Diet and fat composition

Our diet is also a key point in further lifestyle counseling in the fight against diseases. The composition of our total daily diet with all the different components is of importance. The FAs in our food have an impact on our cholesterol and research shows a protective effect for CVD by replacing the SFAs with MUFAs and PUFAs from plant food in the diet (Helsedirektoratet, 2014; Jakobsen et al., 2009). However, recent years controversy opinions among scientists about the SFAs role in the diet and its actual impact on disease has arisen (de Souza et al., 2015; Pedersen et al., 2011). In a review by de Souza and coworkers they are critical to the dietary guidelines regarding fat and other macronutrients because of limitations in several larger studies that document health effects from SFAs (de Souza et al., 2015). Regardless, the current recommendations say it is convincing documentation of replacing SFs with UFAs to reduce the risk of CHD (Nasjonalt Råd for Ernæring[NRE]2011). Furthermore, there is convincing documentation that trans fatty acids (TFA) increase the risk for CHD (de Souza et al., 2015; World Health Organization/Food and Agriculture Organization of the United Nations[WHO/FAO]2008).

However, certain SFAs have more profound effect with regards to increasing LDL-C such as FAs from dairy products and meat. Lauric acid (C12:0), myristic acid (C14:0) and palmitic acid (C16:0) are the most potent ones (Helsedirektoratet, 2014; WHO/FAO, 2003).

These FAs are commonly found in butter, animal fat, coconut oil and palm oil (Mahan & Escott-Stump, 2008). Other FAs as PUFAs like n-6 have been shown to decrease the total cholesterol (TC) and LDL-C. The long chained marine n-3 acids eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), have a number of health promoting effects in the human body, but all of them are not fully known. They appear to reduce the triglycerides (TGs) in serum, which has a positive effect on the HDL-C. Conversely some of the long-chained n-3 FAs may increase the LDL-C, therefore their role in prevention of CVD is not fully assessed (Harris, 1997; Ohnishi & Saiti, 2013; WHO/FAO, 2003). EPA and DHA are both essential FAs, and when found in the plasma or whole blood it is an indication of dietary intake, typically from fat fish (Mahan & Escott-Stump, 2008). Studies show that a diet rich in PUFAs and monounsaturated fatty acids (MUFAs) is recommended to prevent risk factors that lead to CVD (Mente, de Koning, Shannon, & Anand, 2009; Yubero-Serrano et al., 2015). Similarly, SFAs from animal products such as milk and dairy products, meat and meat products and eggs are recommended in very small amounts because of their high SFA content (WHO/FAO, 2003). Additional FAs found in dairy products and milk, which originate from animals, are C15:0, C17:0, C16:1n9 and the trans-FA C18:1t11 (Mahan & Escott-Stump, 2008).

Replacing SFAs with UFAs shows a decrease in the cholesterol in many western societies largely because of changes in diet and lifestyle (Holme et al., 2016; Thorsson et al., 2013; Valsta et al., 2010). Thorsson and colleagues observed a major drop in the total–cholesterol of the Icelandic population between 1980 and 2006, which occurred simultaneously with a shift in the diet. In the early 1970s their diet was characterized by a high consumption of whole milk, dairy products and butter, later shifting towards oils and low-fat dairy products (Thorsson et al., 2013). Further, the 40-year follow-up of the Oslo-study highlights the importance of continuously giving counseling regarding healthy lifestyle where foods high in SFA will be replaced by foods high in UFAs like fat fish products, oils and nuts (Holme et al., 2016). It is however important to remember that diet is not solely comprised by FAs, and that a holistic diet is therefore important to consider from a health perspective.

Certain food diets, such as the Mediterranean diet (MedDiet), are richer in specific FAs. The MedDiet is especially high in MUFAs (18:1n9 in olive oil), as well as PUFAs (n-3), found in fat fish and plants, and it is also rich in fiber, vitamins, minerals and phytochemicals (NRE, 2011). This diet is typical for people living in Crete, Greece and Southern Italy. It has been of particular interests to scientists as inhabitants from these regions have had low rates

of CVD, and certain cancer types, as well as long life expectancy during the 1960's (Willet et al., 1995). The diet is rich in fruits, vegetables, whole grains, potatoes, beans, nuts and seeds. Its main source of dairy comes from cheese and yoghurt, and includes moderate to low intake of fish, poultry and eggs, low amounts of red meat and moderately amounts of wine consumed with meals. The main source of fat is olive oil (Willet et al., 1995). Several studies observe beneficial effects related to risk factors such as metabolic syndrome, diabetes mellitus 2 and overweight with adherence to this diet (Esposito, Kastorini, Panagiotakos, & Giugliano, 2013; Hu et al., 1998; Salas-Salvado et al., 2011). Estruch et al. observe a reduction in major cardiovascular events in 4997 subjects at risk with adherence to MedDiet enriched with olive oil and nuts in a large cohort (Estruch et al., 2013). Despite the beneficial improvements related to risk factors with adherence to MedDiet it is important to remember it is dependent upon lifestyle and culture (Esposito et al., 2013). Researchers have suggested several mechanisms that mediate these benefits, but the true physiological pathway through which the diet affects disease remains unknown (Martinez-Gonzalez et al., 2016). Daily activity is a part of this lifestyle and genes also have an influence (Esposito et al., 2013). However, Menotti and colleagues discovered an interesting result showing an increased risk of CVD mortality in subjects with high cholesterol, despite differences in culture between countries in the subjects (Menotti et al., 2008).

Despite cultural differences in diet pattern it is important to choose the correct type of dairy products and meat products to maintain a good health, but there is still work that has to be done to get the population to eat the recommended FA.

1.4.2 Dairy and meat intake in Norway

According to the latest report from the Norwegian Directorate of Health, where they focus on the progress in Norwegian diet, they have found an increasing tendency in the consumption of dairy products and meat products high in SFAs over several periods during the last 60 years on a wholesale level (Helsedirektoratet, 2015). Consumption of milk and dairy products has increased, and is the biggest source of SFAs in the Norwegian diet. In 2014 the intake of high-fat cheese was still increasing. Furthermore, the intake of cooking oils has increased while the consumption of butter and butter products such as mixed margarine have been stable over the pas few years.

The consumption of meat has also increased over the 60 years. From 1989 to 2008 the average consumption of meat per person increased from 53 kg to 76 kg respectively. Over the last seven years the intake of meat has decreased, but has now stabilized between 74 and 76

kg from 2009 to 2014. This mainly includes meat from pork, poultry and cattle. These numbers do not include the amount of meat eaten from kiosks, cafes and other fast-food stores (Helsedirektoratet, 2015).

The majority of dietary fat in the Norwegian diet comes from milk and dairy products, meat and meat products and cooking oils. The daily recommendations consists of less than 10 E% from SFA, but today (2016) the level is 15 E% and it has increased over the past few years. The intake of trans fatty acids (TFA) has maintained a low level close to 1 E%. It is possible to keep the intake low, mainly because fewer foods today contain TFA compared to earlier. The main sources of TFA are dairy products and meat products (Helsedirektoratet, 2015). This shows that the Norwegian diet is still very high in SFAs and a mapping of intake of fat containing food from diet, and how they affect the cholesterol, is of importance to better understand the development of diseases. The diet as a whole should be considered together with the physical and mental health. The compounds of different fatty acids in the diet should also be investigated, like the MedDiet and its effect on human health.

1.5 Biomarkers with dried blood spots

The foods we ingest contain compounds of macro- and micronutrients comprising of several substances of both edible and not-edible nature. Substances in the food can, as previously mentioned, work as biomarkers. The FAs can reflect different dietary patterns with regard to high or low fat-intake, vegetarians vs. carnivores, as well as milk and dairy intake (Albani et al., 2016; Brevik et al., 2005). Biomarkers are an objectively characterization of nutrient intake (Holen et al., 2016). There are several methods to use to collect samples, and one of them is presented here: Dried Blood Spots (DBS).

Samples from Dried blood spots (DBS) can be used to analyze thousands of metabolites, also nutrients, peptides, proteins and hormones in very small biological samples (Holen et al., 2016). DBS were originally used for screening of infants for inherited metabolic disorders (Vitas Oslo). It was first used in the 1960s and is now also used to collects samples in quantitative research. In large-scale research, the costs for collecting biomarkers are high, hence making DBS an attractive low cost alternative. It is also simple in use and does not require authorized heath personnel to perform the tests. The participant in a study can obtain blood samples themselves by using an automatic finger prick lancet and provide blood on the filter card. Another advantage of DBS are that the tests can be performed at the participants home, in a classroom, when seeing a nutritionist, at a pharmacy, before, during and after sports competition, as well within field work (Vitas Oslo).

Temperature and the light may have an impact on the fatty acids. The recommended method of preservation is to dry the samples at room temperature for 5 hours before preserving them in a fridge at 4-6 degrees Celsius and later in a freezer at -20 degrees Celsius (Bastani, Gundersen, & Blomhoff, 2012; Holen et al., 2016). Screening in clinical studies in the field can involve several challenges with regards to storage of FAs, particularly highly unsaturated fatty acids, (HUFAs) (≥20 carbons and ≥3 carbon-carbon double bounds), as they are prone to oxidation (Metherel & Stark, 2015). The filter cards used for blotting are impregnated with antioxidants in order to prevent loss of HUFAs, such as the long-chained n-3 FAs. Research also shows that other factors such as the oxidation of iron in red blood cells (RBC) is likely to have an impact on the oxidation process (Metherel & Stark, 2015). Chelation on the cards will prevent this process (Marangoni et al., 2004). The current study focuses primarily on SFAs, and for this reason it does not need to take the above mentioned problems associated with oxidation into consideration.

1.6 Theory

Studies have shown that the saturated fatty acids (SFAs) C15:0 and C17:0 may work as biomarkers for milk and dairy products (Albani et al., 2016; Brevik et al., 2005; Samuelson et al., 2001). There are several studies that have suggested that C15:0 is a good biomarker for high-fat containing food groups, whereas the results from C17:0 are more varied (Albani et al., 2016; Brevik et al., 2005). There are also a number of other SFAs found in animal products that may work as biomarkers for the intake of meat and meat products. Stearic (C18:0) and the unsaturated fatty acid (UFA) palmitoleic (C16:1) have been measured in cholesterol esters and may work as biomarkers for intake of meat from diet (Samuelson et al., 2001). Arachidonic acid (AA) (C20:4n6) is also abundant in meat and may reflect a diet pattern with high meat intake (Marangoni et al., 2004). Other substances such as carnitine and trimethylamine-N-oxide (TMAO) are also used as measurements for intake of meat, however several factors make them unpredictable as biomarkers for meat intake (O'Gorman, Gibbons, & Brennan, 2013). For instance, the levels of carnitine and TMAO are high in individuals who eat both meat and fish. Their role as biomarkers for certain food items is imprecise as they reflect more a certain diet pattern for vegetarians, omnivores or carnivores (Koeth et al., 2013; O'Gorman et al., 2013).

Because of the increasing intake of dairy and meat products, as well as the increasing mortality from CVD among young adults in Norway, further assessment and mapping of the

diet is essential. In order to perform a valid assessment, validation of tools used in dietary research is essential.

2 Purpose of study

The primary aim of this master thesis is to evaluate the relative validity and reproducibility of selected food categories in a short FFQ, and explore possible associations between food categories and fatty acids in blood among Norwegian adults with moderate to high risk of CVD.

The objectives of this master thesis are:

Primary objective:

- Investigate if the questionnaire is valid to measure intake of milk and dairy products, meat and meat products and eggs.
- To test the reproducibility of the questionnaire by measuring intake of milk and dairy products, meat and meat products, eggs, use of cholesterol lowering margarine and number of cigarettes.

Secondary objective:

- Explore possible associations between intake of milk and dairy products, meat and meat products and fatty acids in whole blood.

3 Method and sample

3.1 Study design

The ongoing RCT VISA-project conducted its last intervention in September 2015. Data used in the current master thesis is taken from the third and fourth visit (V3 and V4) in the same project.

V3 took place at 48 Boots pharmacies across Norway and V4 took place in the participant's homes. In the VISA-project, 500 individuals were invited to V3 at 48 Boots pharmacies. The pharmacies were randomly split into either intervention- (n = 23) or control- (n = 25) pharmacies. The pharmacies were again divided in two study branches in this master

thesis: validation-biomarker study (VB) and validation test-retest study (VTR). See the flow chart below (**Figure 1**) for the design of the study. Only the control pharmacies were qualified for test-retest.

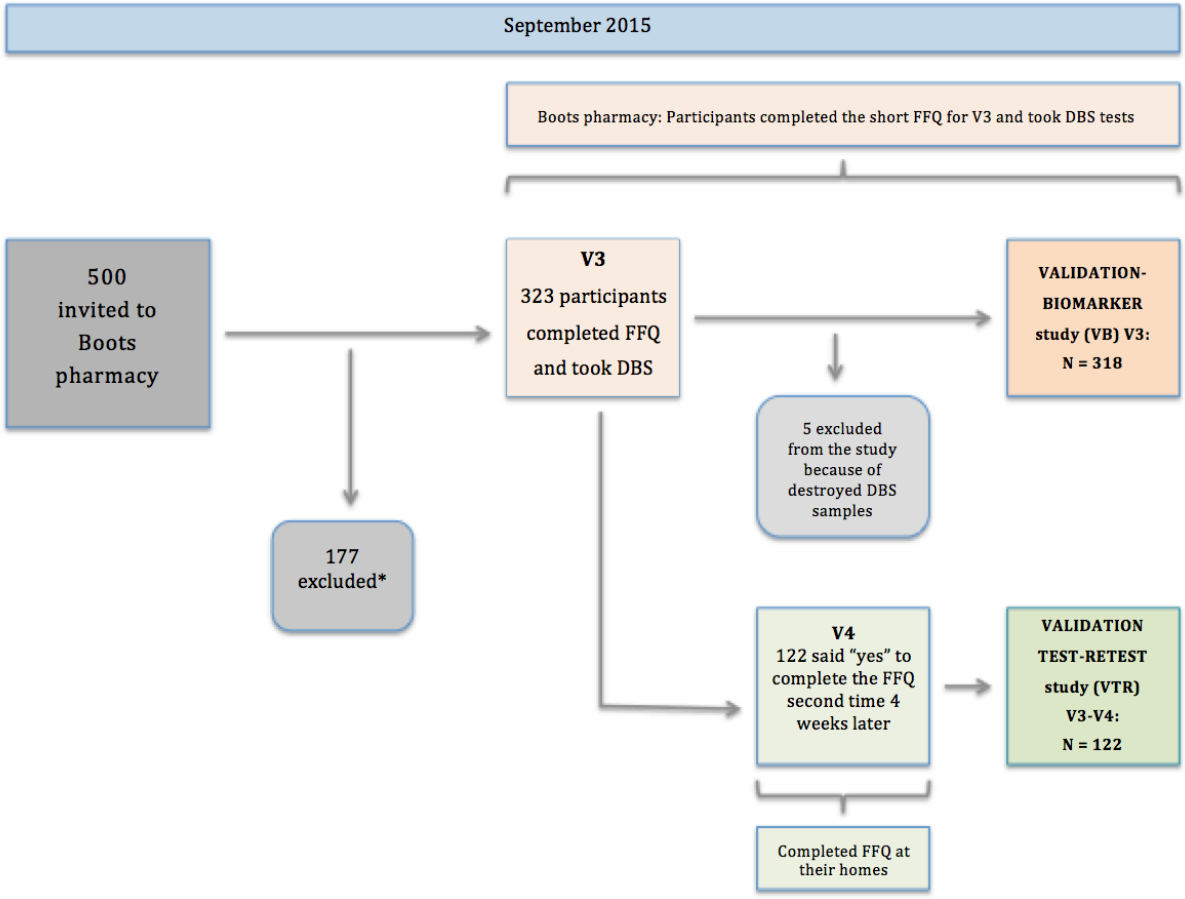

Figure 1: Study design, time and location for the two different study branches validation-biomarker study (VB) and the validation test-retest study (VTR). *177 were excluded because they were exposed for an intervention in the VISA-project thus they are not qualified for this master thesis.

Data from both V3 and V4 is used in the validation of food categories of milk and dairy products, meat and meat products and eggs in the short FFQ. The validation and the reproducibility were tested. FAs measured in whole blood at V3 were used to explore correlations between them and the previous mentioned food. All participants have given their written consent and the project is approved by the National Committee for Research Ethics in Norway (REK), and is registered with the reference-number 2013/-1660-/REK sør-øst D (attachment 1, 2). The study was also reported to Norwegian Center for Research (NSD) (attachment 3, 4).

3.2 Sample

The participants in this study were characterized as healthy individuals with moderate to high-risk of CVD. Inclusion criterions were no previous CVD, no blood pressure- cholesterol and/or blood glucose lowering medications, age above 18 years of age, not pregnant or lactating. All participants were required to be able to read and understand Norwegian. All participants completed a questionnaire regarding background information (attachment 5) and signed a consent form (attachment 6).

3.2.1 Sample validation-biomarker study (VB)

A number of 318 qualified and consented to complete both the short FFQ (attachment 7) and take blood samples by DBS at the same time at the pharmacy (V3). Participants were between 23-88 years old.

3.2.2 Sample validation test-retest study (VTR)

Of the 318 who consented, 122 were in the control pharmacies with no intervention, and therefore qualified for the test-retest study. Participants filled out the short FFQ at V3 and completed the same questionnaire four weeks later in their homes (V4). The participants were between 21 and 84 years old.

3.3 Method

3.3.1 Measurements

Trained authorized health care providers at Boots pharmacy performed all biochemical and anthropometric measurements at V3. Anthropometrical measurements (height, weight) were taken for 316 participants. A standard height meter was mounted on the wall and weight was measured with a standard digital scale at V3. The participants were weighted in light clothes and without shoes. Both measurements were rounded to the closest 0.1 cm. 316 individuals were also measured for blood pressure (BP), HbA1c, TC, HDL and TG. Information on LDL-levels exists for 307 participants. The BP was measured twice using an A&D Medical Blood Pressure Monitor Model UA-767Plus30 and the mean BP was used as the current value. Afinion AS100 was used to measure HbA1c, TC, HDL and TG by a disposable finger-prick lancet pricked on the side of the ring finger. The device calculated LDL levels. The health personnel recorded all measurements in a table, which was marked with the participants ID-number. Participants who had eaten before they gave blood samples were registered by number of hours in advance they had eaten before the blood tests.

3.3.1.1 FA-profile by DBS

318 participants in pharmacies during V3 consented to take blood sample using DBS collection kit (Vitas, Oslo). The kit contains a filter card with five spots, disposable Cutisoft disinfection, Accu-check safe-t-pro disposable lancet and an aluminum preservation bag. The drop of blood was obtained by puncturing a cleansed fingertip with the automatic lancet. Blood was provided to the spot, which was 13mm in diameter. Minimum three full spots of blood were provided to the filter card. A full spot was satisfactory filled when completely filled or almost completely filled with blood. When all spots were filled satisfactory, the card was dried for five hours at room temperature before it was put in an aluminum bag, closed, and preserved in the fridge. The samples were sent by mail to Vitas Laboratory in Oslo where they performed analysis of whole blood FAs. The FAs analyzed by this method are presented in **Table 2**. The results are given in % of FAME. Participants were asked to refrain from eating fatty fish, taking "tran" (fish oil supplement) and omega-3 neither the same day nor the day before the measurement. These supplements and foods may affect the DHA and EPA analysis. Any exceptions were noted.

Table 2: Fatty acids measured in blood by the method Dried Blood Spots.

SFA[1]	MUFA[2]	PUFA[3]
Lauric acid C12:0	Palmitoleic acid C16:1n9	Linoleic acid C18:2n6
Myristic acid C14:0	Oleic acid C18:1c9	Gamma-linolenic acid C18:3n6
Pentadecyclic acid C15:0	cisVaccenic acid C18:1c11	Alpha-linolenic acid C18:3n3
Palmitic acid C16:0	Eicosenoic acid C20:1n9	Dihomogammalinolenic acid C20:3n6
Margaric acid C17:0		Arachidonic acid C20:4n6
Stearic acid C18:0		Eicosapentaenoic acid C20:5n3
Arachidic C20:0		Docosapentaenoic acid C22:5n3
		Docosahexaenoic acid C22:6n3

[1] saturated fatty acids, [2]monounsatturated fatty acids, [3] polyunsatturated fatty acids.

The analysis at Vitas started with extracting fatty acids methyl esters (FAME). FAME, were further Analyzed using the analytical technique Gas Chromatography – Flame Ionization Detector (GC-FID) after direct transmethylation.

3.3.2 Short FFQ

Participants filled out the short FFQ and an additional questionnaire regarding background characteristics. The short FFQ was originally used to investigate the compliance to the Norwegian dietary recommendations (Hege Berg Henriksen, UiO). The short FFQ used in this thesis is modified in accordance with the aim of the VISA-project and contains more detailed questions regarding intake of products high in fat.

The questionnaire is designed to give information regarding whole food groups and cannot compute energy intake. It provides information regarding the daily diet, smoking habits and physical activity based on the regular intake and activity over the last 1-2 months. The main food groups included in the questionnaire are fruit, nuts, vegetables (not potato), grains, drinks, dairy products, bread, spreads, eggs, butter/margarine/oils, cholesterol lowering margarine, fish, meat, rice and pasta and cakes/desert/candy divided into 62 questions including questions regarding smoking and exercise. Within each food category it asks for how many times per week a food was eaten (frequency), and the amount eaten each time (amount). The spread category asks what the participant usually eats on bread during a week. The egg category only asks for number. Butter/margarine/oils category is divided in use (yes, no) and use for baking or daily on bread. Cholesterol lowering margarine category is divided into "use" (yes, no), "if used", and how often. Smoking category is divided into if you smoke, how often and how many cigarettes per day. The questions validated in this thesis are questions regarding milk and dairy products, cholesterol lowering margarine, meat and meat products, eggs and number of cigarettes per day, which gives a total on 18 questions.

Questionnaires were scanned using the program Teleform^{TM} belonging to the Department of Nutrition, UiO. After scanning, the questionnaires had to be verified to avoid mistakes made by respondents or the program itself. When verifying the completed questionnaire all numbers got checked, all automatic suggested corrections from Teleform were checked twice, for every third questionnaire random checks were performed on each page. When values were missing the following rules were used; when frequency was registered but no amount, the smallest amount was registered; when registered amount but no frequency, the smallest frequency above 0 was registered; when both frequency and amount were missing they remained as missing values; if registered an amount and 0 on frequency the cross for amount got removed ant the values were registered as missing values.

Hege Berg Henriksen at UiO created an SPSS-syntax for the short FFQ. All values in the questionnaire were recomputed into grams per day in the syntax. The values and grams for the specific foods behind every question are based on data from NORKOST 3 survey

(Andersen, Totland, & Kigen, 2010). The alternative for the amount 6-7 was computed as 6 + 7 / 2. The alternative for 8+ was computed as 8 + 20 %. The food categories in the questionnaire that are used to explain the results are listed in **Table 3**.

Table 3: Food items behind the questions used in the short-FFQ.

Food categories	Food content
Milk high fat (HF)	Whole or full fat milk, sour milk, kefir
Milk medium fat (MF)	Semi skimmed milk, double semi skimmed milk, "Cultura" (MF sour milk), "Biola naturell" (natural MF sour milk)
Milk low fat (LF)	Skimmed milk, sour milk, "Biola bærdrikk 0.1 % (LF berry sour milk)
Dairy high fat (HF)	Double cream, cream fraiche, full fat sour cream
Dairy medium fat (MF)	Single cream, diet (MF) sour cream, yoghurt with sugar, diet cream fraiche
Dairy low fat (LF)	Coffee cream, extra diet (LF) sour cream, quark, yoghurt natural/0 % fat
Cheese high fat (HF)	Yellow cheese, brown cheese, brie
Cheese medium fat (MF)	MF yellow and brown cheese, MF cream cheese, "Prim" (cream cheese made of brown cheese)
Cheese low fat (LF)	"Vita" yellow cheese (cholesterol lowering cheese), cottage cheese, diet "Prim", yellow cheese 10 % fat
Meat spread high fat (HF)	Saveloy sausage, liver pate, salami
Meat spread low fat (LF)	Ham, chicken, turkey, oil-based pate, diet savely sausage
Meat dinner/hot lunch high fat (HF)	HF minced meat, sausage, full roast, bacon
Meat dinner/hot lunch medium fat (MF)	MF minced meat (lamb, beef), chicken sausage, diet sausage, hamburger, chicken with skin
Meat dinner/hot lunch low fat (LF)	LF minced meat, minced meat (pork, chicken), steak, fillet of chicken, pork, beef or lamb, game meat and "Go og mager" sausage
Dairy products high fat (HF)	Milk HF, dairy HF, cheese HF
Dairy products medium fat (MF)	Milk MF, dairy MF, cheese MF
Dairy products low fat (LF)	Milk LF, dairy LF, cheese LF
Total dairy products	Milk, dairy and cheese (HF, MF, LF)
Total meat products	Meat lunch/dinner and meat spread (HF, MF, LF)

3.3.3 Statistical analysis

All analysis was performed in IBM SPSS version 23 for Mac. Categorical and continuous variables were checked for "outliers" and errors and corrected if needed. A significance level on 5 and 1 % was used and all p-values are 2-tailed. Normal distribution was checked using histograms, Q-Q plots and Kolmogorov-Smirnov ($p = < 0,05$).

The continuous variables, which describe the sample in the VB were normally distributed and are presented as mean with standard deviation. In the VTR some data were non-normally distributed thus they are presented as median with 25 and 75 percentiles. The

categorical variables in both study branches are presented with percentages. When comparing two groups independent-samples t-test was used for normally distributed continuous variables in both study branches. For non-normally distributed variables in the VTR study Mann-Whitney U test was used. All categorical variables were compared by chi-square test for independence.

3.3.3.1 Power calculations

A power calculation was performed to determine how many participants required when splitting the results into two groups to expect a correlation on 0.4 or higher with a significance level on 0.05 % and 80 % power.

3.3.3.2 Statistical methods

The reproducibility of the questionnaire was tested by a test-retest, which was performed by approximately half of the participants. There were 4 weeks in between the test and the retest, and the first time participants completed the short-FFQ at Boots pharmacy (V3) and later in their homes (V4). Further Spearman's rho correlation coefficient (CC) was calculated to test if there was a correlation between the intake at V3 and V4. CCs of > 0.50 were defined as "satisfactory or good", 0.30-0.49 were defined as "fair" and CCs < 0.30 were defined as poor as proposed by Hankin and colleagues (Hankin, Wilkens, Kolonel, & Yoshizawa, 1991).

To describe the sample in both VTR and the VB, median with 25 and 75 percentile were used because the data was not normally distributed. Wilcoxon's signed-rank test was used to test the difference in median intake between the two visits. A significance level on 5 and 1 % is used. The agreement between the measurements (V3-V4) is described using Bland Altman plots. The difference in intakes between the two visits was plotted up against the mean intake from both visits. The plot shows the mean difference in intake by the solid line and limits of agreement defined as mean difference ± 1.96 SD by the dotted line. The limits of agreement show the range of differences in intake, which comprise most of the cases within this range with a probability of 95 % as long as the data is normal distributed. The results from the Bland Altman plots, difference in median intake between V3 and V4 and the CCs shall be evaluated together.

To test the relative validity of the short FFQ C15:0 and C17:0 measured by DBS were analyzed and used as the reference measurement for intake of milk and dairy products. Spearman's rho CC was calculated to test if there was a correlation between the FA in blood and the intake of milk and dairy products.

Further was 19 fatty acids measured in whole blood by DBS and analyzed by Spearman's rho correlations to explore associations between FAs and intake of milk, dairy and meat products. By associations between FAs and intake of milk, dairy and meat products it is in the sense of correlations between them. Not absolute associations.

4 Results

4.1 Background characteristic

4.1.1 Characteristics of the sample in validation-biomarker study (VB)

The background characteristics of the participants at baseline (V3) for the validation-biomarker study (VB) of this thesis are presented in both **Table 4** and **6.** A mean age of 58.32 (±13.43) was seen among 234 women and 82 men in the VB (**Table 4**). Age, martial status, level of high education, blood pressure, total-cholesterol, LDL-cholesterol and HDL-cholesterol were statistical different between genders (**Table 4**). Further, a mean BMI (27 kg/m^2) characterized as overweight (25-29.9 g/m^2) was seen among all subjects (WHO, 2016a). Over halve of the participants in VB had secondary school as their highest achieved education, and the share of participants living alone was highest for women on 41 % (VB). All participants in VB gave blood samples by DBS and answered the short-FFQ at V3. The lipid profile is presented in **Table 4**. The mean TC was 6.50 mmol/L, whereas the mean LDL was 3.91 mmol/L for both genders at baseline. When dividing the results from VB into age groups there were no differences in the levels of lipoproteins from the mean values in **Table 4**.

Table 4: Background characteristics of the participants in the validation-biomarker study (VB) presented as mean and percent (%) for total, men and women

	Total (N = 316)	Male (n = 82)	Female (n = 234)	p[a]
Age[1] (mean, SD)	58.32 (13.43)	55.60 (13.76)	59.27[d] (13.20)	0.033[b, 6]
Living alone[2] (%)	36.8	25.6	41	0.019[c]
Physical inactive[3] (%)	21.1	20.7	21.4	1.00[c]
Everyday smokers (%)	9.4	7.3	10.3	0.574[c]
Ethnicity outside Northern countries[4] (%)	12.3	17.1	10.7	1.174[c]
Low education[5] (%)	52.8	62.2	50.0	0.076[c]
High education[6] (%)	36.8	25.6	41.0	0.019[c]
BMI[1] (kg/m^2)	27.00 (4.50)	26.89 (3.60)	27.03 (4.78)	0.782[b]
HbA1C[1] (mmol/L)	5.53 (0.32)	5.55 (0.40)	5.53 (0.29)	0.738[b]
Systolic blood pressure[1] (mmHg)	127.40 (16.29)	134.57 (16.76)	124.89 (15.39)	0.000[b]
Diastolic blood pressure[1] (mmHg)	80.11 (9.95)	83.02 (10.21)	79.10 (9.67)	0.002[b]
Total cholesterol (mean, SD)	6.50 (1.17)	6.11 (1.24)	6.64 (1.12)	0.000[b]
HDL-cholesterol (mean, SD)	1.77 (0.48)	1.58 (0.54)	1.84 (0.44)	0.000[b]
LDL-cholesterol (mean, SD)	3.91[7] (0.98)	3.70[8] (0.90)	4.0[9] (0.99)	0.018[b]
Triglycerides (mean, SD)	1.90 (1.06)	2.06 (1.24)	1.89 (0.98)	0.172[b]

[a] p-value which shows the difference between men and women is estimated by independent-samples t-test[b], chi-square for independence[c] on a 0.05 significance level.
[1] value is given in mean, standard deviation is given in parenthesis.
[2] includes not married/cohabitating, widow/widower or divorced participants.
[3] includes participants who are inactive or exercise less than once a week.
[4] includes participants born outside, or with both parents born outside of Northern countries.
[5] includes participants with junior high school (10 years) as highest achieved education.
[6] includes participants with 1-5 years of university/university college as highest achieved education.
[7] 9 missing, [8] 4 missing, [9] 5 missing.

4.1.2 Characteristics of sample in validation test-retest study (VTR)

The participants in the VTR (**Table 5**) are more homogeneous with only statistical differences in blood pressure between the genders compared to participants in VB. A median age of 60.5 (50, 70) with a share of 96 women and 26 men participated in the VTR (**Table 5**). BMI was characterized as overweight (25-29.9 kg/m^2) (WHO, 2016a), with a mean on 25.90 kg/m^2. The participants had 1-6 years of university degree as their highest achieved education, and the share of participants living alone is highest for women on 43.8 (VTR).

Table 5: Background characteristics of the participants in the validation test-retest study (VTR) presented as median, mean and percent (%) for total, men and women.

	Total (N = 122)	Male (n = 26)	Female (n = 96)	p[a]
Age[1]	60.50 (50, 70)	64.00 (45, 69)	60.00 (52, 70)	0.79[b]
Living alone[2] (%)	40.2	26.9	43.8	0.18[c]
Physical inactive[3] (%)	2.5	0	3.1	0.37[c]
Everyday smokers (%)	10.7	7.7	11.5	0.85[c]
Ethnicity outside Northern countries[4] (%)	13.9	23.1	11.5	0.21[c]
Low education[5] (%)	12.3	7.7	13.5	0.64[c]
High education[6] (%)	50.8	61.5	47.9	0.31[c]
BMI[7] (kg/m^2)	25.90 (3.70)	25.07 (1.89)	26.13 (4.03)	0.06[d]
HbA1C[7] (mmol/L)	5.51 (0.34)	5.59 (0.51)	5.49 (0.28)	0.345[b]
Systolic blood pressure[7] (mmHg)	126.76 (17.61)	136.61 (17.79)	124.09 (16.67)	0.003[b]
Diastolic blood pressure[7] (mmHg)	78.23 (10.27)	82.96 (11.09)	76.94 (9.71)	0.016[b]

[1] value is shown in median with 25 and 75 percentiles in parenthesis.
[2] includes not married/cohabitating, widow/widower or divorced participants.
[3] includes participants who are inactive or exercise less than once a week.
[4] includes participants born outside, or with both parents born outside of Northern countries.
[5] includes participants with junior high school (10 years) as highest achieved education.
[6] includes participants with 1-5 years of university/university college as highest achieved education.
[7] value is given in mean, standard deviation is given in parenthesis.
[a] p-value which shows the difference between men and women is estimated by Mann-Whitney U test [b], chi-square for independence[c], independent-samples t-test[d] on a 0.05 significance level.

4.1.3 Geographically extensiveness of the study population in VB and VTR

As shown in **Table 6**, the majority of the participants in both VB and VTR were from Akershus (approximately 11 %) and Oslo (13.1 % VTR, 10.7 % VB). There were no participants from the counties Finmark, Hedemark, Troms and Vest-Agder in VTR.

Table 6: County of residence for participants in both validation test-retest (VTR) and validation-biomarker (VB) study.

County	VTR (%) (n = 122)	VB (%) (n = 318[1])
Akershus	11.5	11.3
Aust-Agder	2.5	1.6
Buskerud	9	5.7
Finnmark		2.8
Hedemark		7.5
Hordaland	4.9	10.4
Møre og Romsdal	9	3.8
Nord-Trøndelag	1.6	0.9
Nordland		6.3
Oslo	13.1	10.7
Rogaland	0.8	2.2
Sør-Trøndelag	17.2	11.6
Telemark	0.8	0.3
Troms		2.5
Vest-Agder		1.9
Vestfold	17.2	9.1
Østfold	10.7	10.4

[1] 2 missing

4.2 Validation test-retest study

4.2.1 Test-retest of the short-FFQ

The CCs of milk products, dairy products, meat products, and number of eggs and cigarettes at V3 and V4 are presented in **Table 7** and **8** as gram/day (number eggs and cigarettes) for total, men and women. Further is the median intake between V3 and V4, along with p-values that indicates a statistical difference in intake, presented in **Table 9** where no statistical differences in median intake were observed between V3 and V4 in 14 out of 16 questions.

Satisfactory correlations (> 0.50) were found for milk HF and LF, dairy HF and LF, cheese HF, meat spread HF and LF, number eggs, meat dinner HF, number cigarettes, and for the categorical variables cholesterol lowering margarine and smokers (**Table 7** and **8**). Further, there were no statistical differences in median intake between V3 and V4 for the mentioned food groups with the exception of cheese HF ($p = 0.033$) (**Table 9**). Fair correlations coefficients (0.30-0.49) were found for the remaining foods: milk HF, dairy MF, cheese MF and LF and meat dinner MF and LF (**Table 7** and **8**). No statistical differences in median intake between V3 and V4 for these food groups with the exception of milk HF ($p = 0.033$) (**Table 9**).

When dividing the sample into gender (**Table 7**), there were significant correlations that differed between men and women. In general, women tended to have higher correlations compared to men for all food groups except for MF dairy and cheese, LF dairy and meat products, eggs and HF meat products.

Table 7: Correlation coefficients after repeated measurements of short FFQ (test-retest) between visit 3 (V3) and visit 4 (V4) for total, men and women.

	V3-V4	V3	V4
	Total N = 122	Males n = 26	Females n = 96
	rho[a]	rho[a]	rho[a]
Drinks[1] (g/day)			
Milk HF[2]	0.449**	0.422*	0.458**
Milk MF[3]	0.812**	0.757**	0.843**
Milk LF[4]	0.680**	0.618**	0.692**
Dairy[1] (g/day)			
Dairy HF	0.503**	0.423*	0.513**
Dairy MF	0.477**	0.651**	0.421**
Dairy LF	0.525**	0.561**	0.529**
Spread[1] (g/day)			
Cheese HF	0.514**	0.482*	0.526**
Cheese MF	0.410**	0.595**	0.337**
Cheese LF	0.470**	0.090	0.559**
Meat HF	0.546**	0.264	0.583**
Meat LF	0.640**	0.542**	0.604**
Eggs			
Number eggs[5]	0.758**	0.848**	0.708**
Meat dinner/hot lunch[1] (g/day)			
Meat dinner HF	0.518**	0.565**	0.508**
Meat dinner MF	0.438**	0.350	0.448**
Meat dinner LF	0.462**	0.537**	0.452**
Smoking			
Number cigarettes[6]	0.919**		0.919**

[a] Spearman's rho correlation coefficient.

**Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed).

[1] see table 6 for list of food items.

[2] high-fat, [3] medium-fat, [4] low-fat, [5] 6 missing, [6] 111 missing.

Table 8: Correlation coefficients after repeated measurements of short FFQ (test-retest) between visit 3 (V3) and visit 4 (V4) for the categorical variables cholesterol lowering margarine and smoking.

	V3-V4 Total (N = 122)	Males (n = 26)	Females (n = 96)
	rho[a]	rho[a]	rho[a]
Cholesterol lowering margarine	0.576**[1]	0.733**	0.516**[1]
Smoking	0.905**[2]	-	0.906**[2]

[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01-level (2-tailed).
[1] = 4 missing, [2] = 1 missing.

Table 9: Median intakes at visit 3 (V3) and visit 4 (V4) for total, and p-value for difference in intake between V3 and V4 for total, men and women.

	V3	V4	V3-V4		
	Total N = 122	Total N = 122	Total N = 122	Males n = 26	Females n = 96
	Median (P_{25}, P_{75})[a]	Median (P_{25}, P_{75})[a]	p[c]	p[c]	p[c]
Drinks[1] (g/day)					
Milk HF[2]	0 (0, 0) 23.89[b] (72.89)	0 (0, 0) 14.89[b] (52.10)	0.033	0.123	0.109
Milk MF[3]	58 (0, 142)	50 (0, 186)	0.954	0.327	0.524
Milk LF[4]	0 (0, 14)	0 (0, 28)	0.937	0.953	0.852
Dairy[1] (g/day)					
Dairy HF	0 (0, 7)	0 (0, 3.50)	0.673	0.501	0.839
Dairy MF	7 (0, 17.75)	7 (0, 14.50)	0.371	0.840	0.274
Dairy LF	3.5 (0, 14.50)	7 (0, 23.25)	0.631	0.064	0.792
Spread[1] (g/day)					
Cheese HF	3.57 (1.43, 9.29)	6.43 (1.43, 9.29)	0.033	0.162	0.075
Cheese MF	0 (0, 3.57)	0 (0, 3.57)	0.502	0.722	0.311
Cheese LF	0 (0, 1.43)	0 (0, 1.43)	0.671	0.686	0.625
Meat HF	1.43 (0, 6.43)	0 (0, 3.57)	0.759	0.727	0.483
Meat LF	3.57 (0, 6.43)	3.57 (0, 6.43)	0.760	0.662	0.919
Eggs					
Number eggs[5]	4 (2, 6)	3 (2, 5)	0.293	0.437	0.495
Meat dinner/hot lunch[1] (g/day)					
Meat dinner HF	10.50 (0, 42)	10.50 (0, 21)	0.148	0.608	0.178
Meat dinner MF	15.75 (0, 43.50)	21 (0, 43.50)	0.101	0.588	0.113
Meat dinner LF	43.50 (21, 64.50)	43.50 (21, 64.50)	0.454	0.752	0.276
Smoking					
Number cigarettes[6]	10 (8, 15)	8 (2, 5)	0.102		0.102

[a] P_{25} = 25 percentile, P_{75} = 75 percentile (Tukey's Hinges).
[b] mean (SD).
[c] P-value which shows the difference in median intake between V3 and V4 is estimated by Wilcoxon Signed Ranks tests. [1] see table 6 for list of food items, [2] high-fat, [3] medium-fat, [4] low-fat, [5] 6 missing, [6] 111 missing.

When divided the data into age groups; 20-45 (n = 21); 46-65 (n = 53); and 66-85 (n = 48) the highest age group represented the correlation closest to the total in **Table 7**, while the lowest age group showed the opposite and varied more in the results (data not shown). There was no correlation specifically higher or lower then the values in **Table 7** when dividing the results into BMI groups of underweight; normal weight; or overweight. There were however more varied correlations between V3 and V4 observed for participants characterized with BMI >30. There were no statistical differences for the participants with BMI >30 between median intakes for most food groups between the visits (data not shown).

When splitting the results into high education and low education the correlations for participants with high education had higher correlations for food groups characterized as healthy (MF, LF) compared to participants with low education (data not shown).

4.2.2 Bland-Altman plot

Bland Altman plots for all foods and amount of cigarettes are analyzed. **Figure 2** presents the Bland Altman plots showing the difference in intake between the test measurement at V3 and retest measurement at V4 against the mean intake from both visits, presented only for the eight highest correlations (continuous variables) from the test-retest: medium-fat milk, low-fat milk, low-fat dairy, high-fat cheese, high-fat meat spread, low-fat meat spread, number eggs and high-fat meat dinner.

A. Medium-fat milk

The plot shows a small overestimation in intake for V3 with a mean difference in intake between the visits on 15.9 g/day. The observations are clustered together within the upper and lower limit of agreement of respectively -436.2 and 468.0 g/day.

B. Low-fat milk

V3 slightly underestimates the intake with a mean difference between the visits of -5.7 g/day (**Figure 2**). The individual observations are spread out within the limits of agreement of -146.2 and 134.7 g/day. There is an increasing tendency in the variation in intake by increasing intake.

C. Low-fat dairy

The plot presents a mean difference in intake between the visits of -1.8 g/day, which is a slightly underestimation in intake from V4 (**Figure 2**). Most of the observations are clustered together within the limits of agreement of -62.9 and 59.4 g/day.

D. High-fat cheese

The mean difference in intake between the visits is -2.00 g/day, and the observations are evenly spread out within the limit of agreement of 15.7 and -19.7 g/day (**Figure 2**).

E. High-fat meat spread

Difference in intake is close to zero with a value of 0.07 g/day, and the observations are spread evenly out within the limits of agreement from -7.4 and 7.2 g/day (**Figure 2**).

F. Low-fat meat spread

The mean difference in intake between the visits is also close to zero, with a value of -0.08 g/day. Most of the observations are within the limits of agreement from -11.9 and 11.8 g/day (**Figure 2**) and with increasing difference in intake with increasing intake.

G. Number eggs

The observations are spread out within the limits of agreement of -4.4 and 4.9 eggs with an increasing difference with increasing intake. The mean difference in intake between the visits is 0.3 eggs (**Figure 2**).

H. High-fat meat dinner

The plot shows that the observations are spread out, and most are within the limits of agreement on -62.5 and 69.3 g/day (**Figure 2**). There is an increasing variation in intake with increasing intake. There is also an overestimation in intake at V3 with a mean difference of 3.4 g/day.

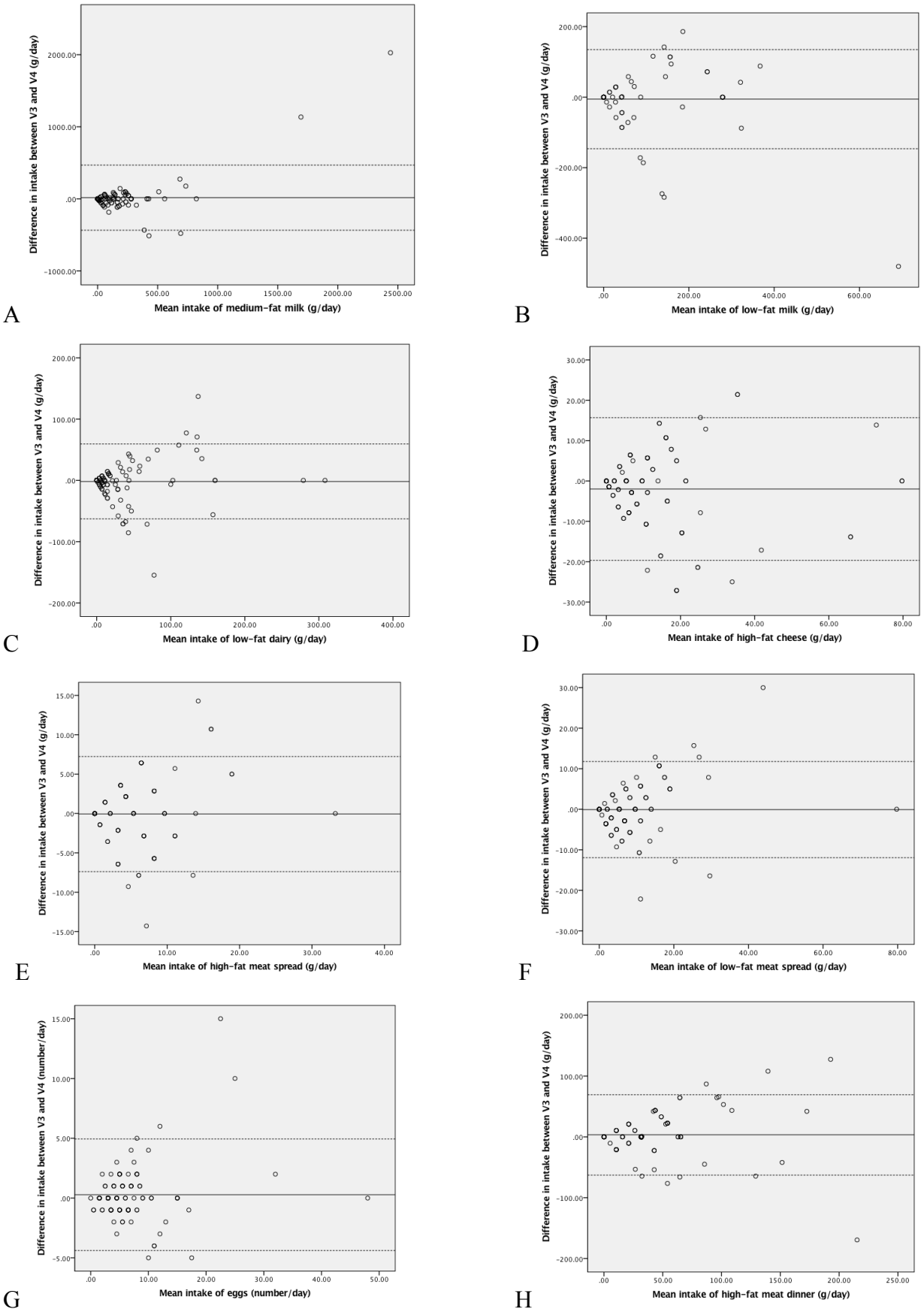

Figure 2: Bland-Altman plot of the difference in intake between V3 and V4 against the mean intake from both visits of A) Medium-fat milk, B) low-fat milk, C) low-fat dairy, D) high-fat cheese, E) high-fat meat spread, F) low-fat meat spread, G) number eggs and H) high-fat meat dinner. The solid line represent the mean intake for both visits and the dotted lines present the limit of agreement (± 1.96 SD). The circles represent a participant. The plot shows the degree of agreement on a group-level.

The remaining eight plots not presented in figures have a similar tendency in variation. When divided the results by gender there were not enough participants that had answered questions within a food group to create a plot. Questions with insufficient answers in FFQ to create a plot comprise skimmed milk, dairy MF, dairy LF, amount eggs, cholesterol lowering margarine and question regarding smoking habits for men and women.

4.3 Validation-biomarkers study

The short-FFQ was validated using biomarkers as reference measurements. C15:0 and C17:0 were used as biomarkers for intake of milk and dairy products. FAs drawn from blood by DBS are presented as mean levels in all participants in **table 10**. The values are given in % of FAME. 318 participants gave blood samples and answered the short-FFQ at V3.

Tabel 10: Mean and standard deviation (SD) for all fatty acids measured in whole blood taken by Dried Blood Spots for total, males and females shown in % of fatty acid methyl esters (FAME).

SFA[a]				MUFA[c]				PUFA[d]			
	Mean[h] (SD[b])				Mean (SD)				Mean (SD)		
	Total[e]	Male[f]	Female[g]		Total[e]	Male[f]	Female[g]		Total[e]	Male[f]	Female[g]
Lauric acid C12:0	0.13 (0.10)	0.14 (0.12)	1.12 (0.09)	*Palmitoleic acid C16:1n9*	1.53 (0.57)	1.35 (0.51)	1.60 (0.57)	*Linoleic acid C18:2n6*	19.92 (2.63)	19.34 (2.79)	20.10 (2.53)
Myristic acid C14:0	0.99 (0.36	1.03 (0.45)	0.97 (0.33)	*Oleic acid C18:1n9*	20.51 (2.35)	20.94 (2.73)	20.37 (2.20)	*Gamma-linolenic acid C18:3n6*	0.21 (0.10)	0.20 (0.10)	0.21 (0.09)
Pentadecyclic acid C15:0	0.25 (0.05)	0.24 (0.05)	0.25 (0.05)	*cisVaccenic acid C18:1c11**	1.52 (0.27)	1.49 (0.28)	1.52 (0.26)	*Alpha-linolenic acid C18:3n3*	0.54 (0.18)	0.55 (0.18)	0.54 (0.18)
Palmitic acid C16:0	21.68 (1.44)	21.88 (1.48)	21.62 (1.41)	*Eicosenoic acid C20:1n9*	0.24 (0.06)	0.26 (0.07)	0.24 (0.06)	*Dihomogammalinolenic acid C20:3n6*	1.39 (0.27)	1.37 (0.27)	1.40 (0.27)
Margaric acid C17:0	0.35 (0.06)	0.35 (0.06)	0.34 (0.06)					*Arachidonic acid C20:4n6*	7.59 (1.41)	7.59 (1.56)	7.58 (1.37)
Stearic acid C18:0	11.39 (0.96)	11.59 (1.05)	11.32 (0.92)					*Eicosapentaenoic acid C20:5n3*	1.44 (0.98)	1.45 (1.43)	1.44 (0.77)
Arachidic acid C20:0	0.09 (0.02)	0.09 (0.03)	0.08 (0.10)					*Docosapentaenoic acid C22:5n3*	1.32 (0.29)	1.39 (0.35)	1.30 (0.26)
								Docosahexaenoic acid C22:6n3	3.33 (0.91)	3.27 (1.01)	3.35 (0.88)

[a] saturated fatty acids, [b] standard deviation, [c] monounsaturated acids, [d] polyunsaturated acids, [e] n = 318, [f] n = 82, [g] n = 234, [h] all mean values are shown in % of FAME
*Naturally occurring trans fatty acid.

Further Spearman's correlation coefficients were calculated for questions regarding milk, dairy, spread and meat dinner for all FA and are presented in **Table 11**, **12**, **13** and **14**. For all correlations presented further the significance level for the correlation will be on the 0.01-level unless other is mentioned.

Positive correlations < 0.3 were observed within the food groups milk (HF, MF) and dairy (HF, MF, LF) for some or all of the FAs C12:0, C14:0, C15:0, C22:5n3 and C18:2n6. An inverse correlation < 0.3 was seen for C20:4n6 and milk HF.

Only one correlation was significant on the 0.01-level for cheese HF and C15:0 (<0.3). Meat spread HF had negative correlations for C16:1n9, C18:1c11 and C20:0 (< -0.3) and a positive association for C20:0.

Further had meat dinner MF and C14:0, C15:0 and C20:4n6 inverse associations (< 0.3). Positive correlations were seen for meat dinner (HF, MF) for C20:4n6 (< 0.3). There were no significant correlations between C17:0 and any of the foods analyzed.

Table 11: Correlation coefficients between high-fat, medium-fat and low-fat milk and levels of fatty acids (FA) in blood measured in total.

MILK N = 318	High-fat[1]	Medium-fat[2]	Low-fat[3]
	rho[a]	rho[a]	rho[a]
C12:0	0.182**	-0.051	0.041
C14:0	0.160**	-0.055	0.059
C15:0	0.145**	0.099	0.040
C16:0	0.115*	-0.086	-0.038
C16:1n9	0.079	-0.086	0.010
C17:0	0.075	0.019	0.021
C18:0	-0.038	0.113*	0.055
C18:1c9	0.097	-0.053	-0.085
C18:1c11	0.014	0.065	-0.018
C18:2n6	-0.094	0.006	0.011
C18:3n6	-0.030	-0.041	-0.019
C18:3n3	0.100	-0.015	-0.065
C20:0	-0.008	0.052	0.049
C20:1n9	-0.002	0.099	-0.035
C20:3n6	-0.103	-0.080	-0.009
C20:4n6	-0.115**	0.051	-0.017
C20:5n3	0.004	0.106	0.109
C22:5n3	-0.086	0.179**	0.073
C22:6n3	-0.056	0.083	0.099

[1] Includes whole or full fat milk, sour milk, kefir.
[2] includes semi skimmed milk, double semi skimmed milk, "Cultura" (MF sour milk), "Biola naturell" (natural MF sour milk).
[3] includes skimmed milk, sour milk, "Biola bærdrikk 0.1 % (LF berry sour milk).
[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table 12: Correlation coefficients between high-fat, medium-fat and low-fat dairy foods and levels of fatty acids (FA) in blood measured in total.

DAIRY N = 318	High-fat[1]	Medium-fat[2]	Low-fat[3]
	rho[a]	rho[a]	rho[a]
C12:0	0.003	-0.028	-0.047
C14:0	0.021	-0.068	-0.031
C15:0	0.195**	0.022	-0.003
C16:0	0.030	-0.142*	-0.113*
C16:1n9	0.042	-0.085	-0.023
C17:0	0.057	0.072	0.012
C18:0	-0.084	0.007	-0.027
C18:1c9	0.016	-0.132*	-0.110
C18:1c11	-0.005	-0.069	-0.019
C18:2n6	-0.018	0.150**	0.154**
C18:3n6	-0.085	-0.096	-0.001
C18:3n3	0.079	-0.009	0.016
C20:0	-0.041	-0.020	-0.112*
C20:1n9	0.003	-0.008	-0.039
C20:3n6	-0.049	0.002	0.078
C20:4n6	-0.090	0.025	0.015
C20:5n3	0.107	0.116*	0.059
C22:5n3	-0.009	0.034	0.042
C22:6n3	0.070	0.082	0.036

[1] Includes double cream, cream fraiche, full fat sour cream.
[2] includes single cream, diet (MF) sour cream, yoghurt with sugar, diet cream fraiche.
[3] includes coffee cream, extra diet (LF) sour cream, quark, yoghurt natural/0 % fat.
[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table 13: Correlation coefficients between high-fat, medium-fat and low-fat cheese, and high-fat and low-fat meat and levels of fatty acids (FA) in blood measured in total.

SPREAD N = 318	Cheese			Meat	
	High-fat[1]	Medium-fat[2]	Low-fat[3]	High-fat[4]	Low-fat[5]
	rho[a]	rho[a]	rho[a]	rho[a]	rho[a]
C12:0	0.054	0.045	-0.003	0.052	0.006
C14:0	0.089	0.017	0.022	0.007	-0.014
C15:0	0.220**	0.020	0.051	-0.059	-0.027
C16:0	-0.004	-0.041	-0.038	-0.081	-0.016
C16:1n9	-0.051	0.049	-0.025	-0.152**	0.007
C17:0	0.108	0.076	0.073	-0.029	-0.065
C18:0	0.067	-0.017	-0.114*	0.080	0.001
C18:1c9	-0.056	-0.045	-0.016	0.106	0.063
C18:1c11	-0.139*	0.024	0.012	-0.118*	0.010
C18:2n6	0.062	-0.008	0.053	0.027	0.000
C18:3n6	-0.052	0.047	-0.063	-0.003	0.073
C18:3n3	0.000	0.021	0.035	-0.002	-0.015
C20:0	0.030	0.034	-0.025	0.154**	-0.020
C20:1n9	-0.041	0.096	0.027	0.031	-0.022
C20:3n6	0.046	0.039	-0.081	-0.020	0.065
C20:4n6	0.014	0.001	-0.091	0.037	0.054
C20:5n3	-0.003	0.075	0.142*	-0.087	-0.041
C22:5n3	0.018	0.084	0.028	-0.026	-0.041
C22:6n3	-0.059	0.054	0.124*	-0.091	-0.077

[1] Includes yellow cheese, brown cheese, brie.
[2] includes MF yellow and brown cheese, MF cream cheese, "Prim".
[3] includes "Vita" yellow cheese .
(cholesterol lowering cheese), cottage cheese, diet "Prim", yellow cheese 10 % fat.
[4] includes saveloy sausage, liver pate, salami.
[5] includes ham, chicken, turkey, oil-based pate, diet savely sausage.
[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Table 14: Correlation coefficients between high-fat, medium-fat and low-fat meat dinner and levels of fatty acids (FA) in blood measured in total.

MEAT DINNER N = 318	High-fat[1]	Medium-fat[2]	Low-fat[3]
	rho[a]	rho[a]	rho[a]
C12:0	0.019	-0.073	0.014
C14:0	-0.048	-0.118*	0.006
C15:0	-0.047	-0.182**	0.012
C16:0	-0.072	-0.083	-0.081
C16:1n9	-0.072	-0.112*	-0.002
C17:0	-0.008	-0.038	0.014
C18:0	0.007	0.055	-0.006
C18:1c9	0.063	-0.045	0.026
C18:1c11	-0.088	-0.083	0.012
C18:2n6	-0.004	0.004	-0.014
C18:3n6	-0.015	0.087	0.070
C18:3n3	-0.029	-0.037	0.024
C20:0	0.056	0.057	0.005
C20:1n9	0.030	0.004	-0.017
C20:3n6	0.042	0.095	0.088
C20:4n6	0.110*	0.174**	0.093
C20:5n3	-0.061	-0.020	-0.020
C22:5n3	-0.058	0.021	0.023
C22:6n3	-0.062	-0.018	-0.049

[1] Includes HF minced meat, sausage, full roast, bacon.
[2] includes MF minced meat (lamb, beef), chicken sausage, diet sausage, hamburger, chicken with skin.
[3] includes LF minced meat, minced meat (pork, chicken), steak, fillet of chicken, pork, beef or lamb, game. meat and "Go og mager" sausage.
[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

When splitting the results into gender for milk, dairy and cheese products, the significant correlations disappeared for milk HF. Further, there were positive associations for C15:0 for

dairy HF (women) and cheese HF (men, women) (rho < 0.3) (**Table 15**). Cheese HF was positive associated (rho < 0.3) with C17:0 on a 0.05-level for women (**Table 15**).

Table 15: Correlation coefficients between milk dairy and cheese products and levels of C15:0 and C17:0 measured in blood in men and women.

	Milk[1]			Dairy[1]			Cheese[1]		
	HF[2]	MF[3]	LF[4]	HF[2]	MF[3]	LF[4]	HF[2]	MF[3]	LF[4]
Pentadecyclic acid C15:0									
Male[b]									
rho[a]	0.170	0.056	0.039	0.225*	0.087	0.002	0.290**	0.124	0.003
Female[c]									
rho[a]	0.142*	0.113	0.042	0.174**	-0.019	-0.033	0.214**	0.008	0.054
Margaric acid C17:0									
Male[b]									
rho[a]	0.163	-0.082	0.056	0.149	0.072	-0.020	0.026	0.080	0.036
Female[c]									
rho[a]	0.037	0.042	0.011	0.023	0.081	0.031	0.147*	0.083	0.089

[1] see table 6 for list of food items, [2] high fat, [3] medium fat, [4] low fat.
[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
[b] n = 82, [c] n = 234.

All HF dairy products (milk, dairy, cheese) gave a significant positive correlation for C15:0, for women and all subjects (< 0.3) (**Table 16**).

Total dairy products (HF, MF, LF) gave positive correlation (< 0.3) for C15:0 for all subjects, with a higher correlation for women (0.156) then men (0.088) on the 0.05-significance level (**Table 16**).

Table 16: Correlation coefficients between total dairy products (high-fat, medium-fat, low-fat), high-fat (HF) dairy products, medium-fat (MF) dairy products, and low-fat (LF) dairy products and levels of C15:0 and C17:0 measured in blood in men and women.

	Total dairy products[1]	Dairy products HF[1]	Dairy products MF[1]	Dairy products LF[1]
	rho[a]	rho[a]	rho[a]	rho[a]
Pentadecyclic acid C15:0				
Total[b]	0.141*	0.267**	0.102	0.006
Male[c]	0.088	0.267*	0.079	0.071
Female[d]	0.156*	0.282**	0.109	-0.030
Margaric acid C17:0				
Total[b]	0.078	0.116*	0.037	0.025
Male[c]	-0.023	0.110	-0.061	0.003
Female[d]	0.106	0.113	0.066	0.035

[1] See table 6 for list of food items.
[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
[b] n = 318, [c] n = 82, [d] n = 234.

When dividing the results into age groups, participants between 20 and 45 (7 men, 14 women, 42.9 % normal weight, 38.1 % over weight) had a significant correlation between 0.3 and 0.49 for C15:0 for dairy products (HF, MF) and total dairy products (**Table 16**). The remaining age groups did not have any strong correlation between C15:0, C17:0 and dairy products with an acceptance for 66-85 years old where a significant correlation on 0.319 was found between C15:0 and dairy products HF. A significant correlation on 0.05-level on 0.167 was covered between C15:0 and dairy products HF for the age group 46-65 (**Table 17**).

Table 17: Correlation coefficients for C15:0 and total dairy products, high-fat- medium-fat- and low-fat dairy products divided on age groups.

	Pentadecyclic acid C15:0			
	Total dairy products[1]	Dairy products HF[1]	Dairy products MF[1]	Dairy products LF[1]
Age groups	rho[a]	rho[a]	rho[a]	rho[a]
20-45 (n = 58)	0.405**	0.409**	0.422**	-0.046
46-65 (n = 148)	0.041	0.167*	0.059	0.046
66-85 (n = 108)	0.006	0.319**	-0.016	-0.042

[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
[1] see table 6 for list of food items.

Most of the participants in this thesis have a BMI between 25 and 29.9, and they have a higher correlation for C15:0 and dairy products HF compared to the other BMI groups. For dairy products HF and MF there are significant correlations with C15:0 on 0.335 and 0.237 (**Table 18**).

Table 18: Correlation coefficients for C15:0 and total dairy products, high-fat- medium-fat- and low-fat dairy products divided on BMI:

	Pentadecyclic acid C15:0			
	Total dairy products[1]	Dairy products HF[1]	Dairy products MF[1]	Dairy products LF[1]
BMI (g/m^2)	rho[a]	rho[a]	rho[a]	rho[a]
<18.9[2] (0 %)				
19-24.9 (42.9 %)	0.137	0.244**	0.035	0.035
25-29.9 (38.1 %)	0.146	0.335**	0.237**	0.021
>30 (22.6 %)	0.098	0.239*	-0.043	-0.046

[a] Spearman's rho correlation coefficient.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
[1] see table 6 for list of food items, [2]no data.

When dividing the sample in gender there were significant inverse correlations between -0.227 ($p > 0.05$) and -0.301($p > 0.01$) for meat products HF (spread, lunch, dinner) for men with C15:0, C17:0 (**Table 19**). A significant positive association (0.309) ($p > 0.01$) was seen between meat HF and C20:4n6 for men. Women had only significant correlation between meat MF and C15:0 (0.182) ($p > 0.001$). For all meat products together there were significant

positive correlations for C20:4n6 for total (0.186), men (0.290) and women (0.140). For men there were negative correlations for C15:0
(-0.250) and C17:0 (-0.241) (**Table 19**).

Table 19: Correlation coefficients for C15:0, C17:0 and C20:4n6 and total meat products, high-fat- medium-fat- and low-fat meat products (spread, lunch, dinner) for total, men and women.

	Total meat products[1]	Meat products HF[1]	Meat products MF[1]	Meat products LF[1]
	rho[a]	rho[a]	rho[a]	rho[a]
Pentadecyclic acid C15:0				
Total[b]	-0.155**	-0.074	-0.182**	0.001
Male[c]	-0.250*	-0.301**	-0.132	-0.021
Female[d]	-0.089	0.027	-0.182**	0.023
Margaric acid C17:0				
Total[b]	-0.030	-0.022	-0.038	-0.004
Male[c]	-0.241*	-0.227*	-0.090	-0.156
Female[d]	0.037	0.030	-0.033	0.053
Arachidonic acid C20:4n6				
Total[b]	0.186**	0.107	0.174*	0.090
Male[c]	0.290**	0.309**	0.288**	0.041
Female[d]	0.140*	0.029	0.125	0.109

[a] Spearman's rho correlation coefficient.
[b] n = 318, [c] n = 82, [d] n = 234.
**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
[1] see table 6 for list of food items, [2]no data.

5 Discussion

This study population contains of a sub group that were a part of an RCT in the national wide VISA-project. Participants were stratified in accordance to risk factors and those identified as having moderate to high risk of CVD were included in the cholesterol screening in pharmacies in 2014. Among the study population in the current study there was performed a validation of selected questions in a short FFQ, covering questions regarding fat containing foods. A test-retest (VTR) of the short FFQ was performed and FAs were used as biomarkers as the reference measurement (VB). Relative validity and the reproducibility of the short FFQ were assessed through correlations and agreement between the methods, through distribution in percentiles (25p, 75p) and comparison with biomarkers.

5.1 Method and sample

5.1.1 Participation

As mentioned previously, participation in a validation study requires a high level of motivation. It is challenging to have a representative selection in validation studies because of this high degree of motivation (Andersen Frost, 2000). The sample in this study is a sub group of the participants in the VISA-project, which started in 2014 and had its last visit in the pharmacy in 2015. It is therefore likely to believe that the participants in the current study are highly motivated and also have a greater interest and awareness of their health. This can be an explanation for the high participant rate of 318 for the validation-biomarker study (VB) (64 %). According to Willet a number of 100-200 would be sufficient in order to explain aspects regarding the validity, and also sufficient to account for a possible loss of participants during the study (Willet, 2013). The validation test-retest study (VTR) consisted of 122 participants, which is comparable to sample sizes used previously when testing reproducibility and validity. Two other studies used sample groups of 121 and 102 (Hebden, Kostan, O'Leary, Hodge, & Allman-Farinelli, 2013; Ocké et al., 1997). In similarity to the VISA-project, the VB study covered a large part of Norway's counties. The majority of those participants were however from Oslo and Akershus. The VTR study was less extensive and could have been strengthen with a wider geographic sample size. The high participant rate is yet a factor that strengthens this study.

5.1.2 Characteristics of participants

5.1.2.1 Participants and their risk for CVD

Validation test-retest study

There were no significant differences in background characteristics between the participants in the control and intervention pharmacies in the VISA-project, thus selection bias in this regard did not occur in the test-retest population (VTR, in current study) (data not shown).

Further, there were no statistical differences between men and women at baseline in the VTR study regarding age, living situation, physical inactivity level, smoking habits, born outside or with parents born outside Northern countries, low or high education, BMI and long term blood glucose with the exception of blood pressure. Both systolic and diastolic blood pressure was significantly higher among men than women. Despite non-significant differences between genders the median age was higher, along with a higher share of inactive participants among men compared to women. High age and especially inactivity are two

factors, which increases the blood pressure (Couillard et al., 2001; WHO/FAO, 2003). The mean BP for men in VTR study is characterized as normal high blood pressure (Helsedirektoratet, 2009). Nevertheless, slightly elevated blood pressure gives a higher risk for developing stroke and heart infraction (Helsedirektoratet, 2009).

Validation-biomarker study

In the VB study there were significant differences between men and women for CVD risk factors such as SBP, DBP, TC, LDL-C and HDL-C. Here both BP and lipid-profile are considered risk factors for developing CVD. After calculating the 10-year risk of mortality from CVD in the risk-table by the Directorate of Health men have a higher 10-year CVD mortality risk between 3-4 % and 5-9 % compared to women, who have a risk between 2 % and 3-4 % in the VB sample (Helsedirektoratet, 2009). The calculation of risk is based on the factors gender, smoking habits, age, SBP and TC. However, other risk factors such as genes, diabetes mellitus 2, overweight, diet and physical activity, dyslipidemia or psychological factors such as stress and home situation will give an additional risk to this estimation (Helsedirektoratet, 2009).

5.1.2.2 Factors that may influence reporting

The participants in the VB study were less homogeneous than the participants in the VTR study. Age, living situation and high education were significantly different between men and women (VB). The share of men is approximately similar in both groups with 25.8 % (VTR) and 21.3 % (VB).

There are many studies that suggest that factors like education level, smoking habits, activity level, body image, gender and BMI have an impact on reporting during a diet record period (Bedard, Shatenstein, & Nadon, 2004; Johansson, Wikman, Åhrén, Hallmans, & Johansson, 2007). In both study branches there were more than three times as many women when compared with men who answered the questionnaire and gave blood samples. Studies show that women more frequently participate in studies than men, and also underreport more frequently (Antonsen, 2005; Johansson et al., 2007). In the present study this may also have occurred, however our data cannot support this.

In a study from Samaras and colleagues they saw a trend among women underreporting high-fat containing food, and that the underreporting was greater among those with higher BMI, but not necessarily higher % of body fat (Samaras, Kelly, & Campbell, 1999). Several studies show that underreporting increases with increasing BMI (Johansson et al., 2007; Poslusna, Ruprich, de Vries, Jakubikova, & van't Veer, 2009). Most participants in

this study were characterized as overweight (BMI 25-29.9 kg/m^2), where a mean BMI of 26 kg/m^2 (VTR) and 27 kg/m^2 (VB) was observed. A share of 40.2 % (VTR) and 38.4 % (VB) are overweight. Further, 11.5 % (VTR) and 22.6 % (VB) are considered obese.

Nevertheless, it did not change the CC from the total when dividing the results into BMI groups; underweight, normal weight; and overweight, except for the participants with BMI >30 characterized as obese. Here the results for all food groups were more varied with lower CCs, but it did not show any statistical differences in median intake between the test (V3) and the retest (V4) for participants with BMI >30. The factors such as body image and also that what is considered socially accepted may have played a role in the answers as a consequence of the higher BMI. As every question was not answered by all participants, there were not enough participants to create any Bland Altman plots for those with BMI >30, that could have revealed possible underestimations in this group.

A study among 436 British women it did not show an impact of the reporting with higher body fat, but did show more underreporting with increasing BMI (Samaras et al., 1999). Further, BMI measurement is associated with some degree of imprecise measure because people with high muscle mass and low height will tend to have a BMI that is too high (Frayn, 2010), yet WHO recommend the use of BMI in the mapping of health status (WHO, 2016b).

Many of the participants in the study population in both VTR and VB are characterized as overweight and the sample in VB has a slightly elevated mean TC, LDL-C and mean BP. This gives the participants a moderate to high risk for CVD and is hence a reflection of the selection in the VISA-project. However, after evaluating this sample with the various background characteristics one can argue that this study is mostly countable for overweight, middle aged women with moderate risk for CVD.

The number of smokers (n = 13) and physical inactive (n = 3) in the current study was low, and hence there is no data that can explain any differences in this concern. The level of education will be further discussed later.

5.1.3 Implementation of study

This study started out at the pharmacy where the participants measured their cholesterol, blood glucose and blood samples by DBS. When all biochemical indicators were collected the participants completed the short FFQ as the first step in the validation (V3) and test-retest study (V4). Therefore, all blood samples were taken before the participants answered the questionnaire. When participants answered the short FFQ four weeks later (V4) they did not

do it at the same location but in their homes. This may affect the results from the test-retest because it was not performed under the same circumstances (Andersen Frost, 2000). Participants might have felt more stressed after taking different measurements and blood samples at the pharmacy, compared to being home in calm and safe surroundings (Ko & Lin, 2012). Some participants may also have received help in completing the questionnaire the second time. This can cause a discrepancy in the answers in the questionnaire that can create artificial low CCs on the test-retest.

5.1.3.1 Criteria for validation studies

To address the validity of dietary surveys in general terms is not possible because it is dependent upon different factors such as study design, implementation and study population included in the study (Andersen Frost, 2000). Furthermore, there are the previous mentioned criteria, which the study must conform to in order to be of good quality, which will be further discussed.

In this study the reference measurements were biomarkers, which are considered a more accurate measurement then the short FFQ, which is one of the strengths (Albani et al., 2016; Willett et al., 2001). Further another strength is that both measurements are performed on an individual level and the errors connected to both measurements were approximately independent of each other because of the use of biomarkers (Willett et al., 2001). However, this study had only one reference measurement and could have been strengthened by using an additional measurement such as weighted registration (WR) or 24-hour recall, a so-called *triangulation* (Hjartåker & Veierod, 2007) Due to the time limit on this thesis it was not possible to accomplish. The DBS tests were performed right before the participants answered the short-FFQ and could affect the estimates in the test-retest. Despite that, biomarkers can be collected simultaneously with the completion of a questionnaire without risking getting artificial CC (Willet, 2013). As mentioned previously the participation rate was high and the participants present a sub group of the study population in the VISA-project. Several criteria are carried out in the performance of this study and are among this study's strengths.

5.1.3.2 Measurements performed by health care providers in pharmacy

The utilization of pharmacies as a place to recognize patients at risk for diseases is underestimated (Lai, Poblet, & Bello, 2000). Pharmacies are a place often visited and easily accessible for most people, and studies show that pharmacies are an arena that can contribute to the assessment of risk factors within primary health care (Houle, Charrois, Faruquee, Tsuyuki, & Rosenthal, 2016; Tsuyuki et al., 2002). Lowering the modifiable risk factors for

CVD such as controlling blood glucose and measuring cholesterol and BP shows a decrease in mortality from CVD (Forrester, 1996). Collaboration between pharmacies and the primary health care can contribute to discovering more people at risk and thus may prevent further development of disease (Tsuyuki et al., 2002).

Despite the practical utilization of pharmacies in public health work there are several challenges related to it (Houle et al., 2016). Pharmacists experience the extra work as time-consuming and also the deviation from traditional practice models has been an issue. Pharmacists also imply the requisite for reimbursement and recognition for the service (Houle et al., 2016).

Despite there being trained authorized health care providers in the pharmacies in the current study that performed the measurements, it is important to remember that the pharmacy is neither a hospital nor a research institution. The training of how to perform the measurements with DBS could have been more detailed and improved. In the present study, only health personnel that were present on a one-day seminar with various activities, including a demonstration of DBS, had the opportunity to get a training of performance of DBS measurements. Apart from the demonstration, health personnel had to learn the method themselves by watching a video and practice (only one time) on each other. The pharmacists had to adapt new routines that were challenging for many of them. This indicates that including all of these services at all times may not be feasible (Houle et al., 2016).

5.1.4 Statistical tests

In validation studies there are different statistical approaches used to describe the relative validity and reproducibility such as CC, Bland Altman plots, t-tests and Wilcoxon signed rank test (Hebden et al., 2013; Schmidt & Steindorf, 2006). CCs are commonly used to assess how much of the same variance two variables have in common such as the intake measured twice by a test-retest of a FFQ. CCs for intake of foods and nutrients between 0.5 and 0.7 is frequently seen in validation studies of FFQ and are considered good (Subar et al., 2001; Willet, 2013). CC of 0.4 is also considered fair (Hankin et al., 1991; Subar et al., 2001). It is important to be aware that CCs increases by higher variance in intake and is often significant with a large sample size (> 100). The significant level connected to CC says how much confidence one can have in the CC, and it does not say to which degree the two variables are associated. On the contrary the CCs can be lower for foods eaten rarely or with less variance in intake (Andersen Frost, 2000; Pallant, 2013). In a review by Schmidt and coworkers they found that 89.1 % (out of 46 articles) of validation studies use CCs in the evaluation of the

validity, but it is inadequate to only relay on this one method (Schmidt & Steindorf, 2006). Since CCs only measure an association between two variables, it is necessary with an additional analysis that gives information about errors and the agreement between the test method and reference method. One method used to describe this is the use of Bland Altman plots, which describe the difference in intake between the test and retest along with mean intake from both tests with an upper and lower limit of two standard deviations (± 1.96 SD) (Schmidt & Steindorf, 2006). Within the limits of agreement there is a variation that is expected to count for a subject in the population with 95 % probability. The Bland Altman plot will also reveal under- and overestimation (Schmidt & Steindorf, 2006). On the other hand, in nutrition research it is important to evaluate what these differences mean in practical terms and it requires knowledge of the research topic. A seemingly small variation in intake of food in g/day may be of considerable importance. The results from the Bland Altman plots will be further discussed later in this chapter.

For the validation of the short FFQ with biomarkers there are only CCs available in the evaluation. In order to describe which foods cause changes in the FA measured in blood, multiple regression analysis would be an additional appropriate method to use. Because of the time limit on this thesis, there was not enough time for the master student to learn the method properly in order to use it adequately. Therefore the methods used here are considered sufficient. Classifications of intake in quartiles on an individual level, used to study if participants with high intake at V3 will end up in the same quartile at V4, could also contribute to the validation. However, there is no consensus in the literature on the best statistical approaches for assessing the validity of dietary assessment tools (Masson et al., 2003). Therefore, the choice of methods used in this master thesis was based on the methods considered most appropriate to evaluate relative validity on a group level with limited time.

5.1.5 Short food frequency questionnaire

This thesis uses a short FFQ and not a full version. There are many studies that have carried out the use of various short FFQ to investigate the intake of certain food groups such as dairy products, fruit and vegetables (Bogers, van Assema, Kester, Westerterp, & Dagnelie, 2003; Dahl, Maeland, & Bjorkkjaer, 2011; Macdonald et al., 2014). Lillegaard and coworkers reported a high association for foods eaten frequently as low-fat milk on 0.67, when compared with foods eaten rarely as pizza on 0.11 measured with a short FFQ among adolescents in Norway. The study concluded that the short FFQ had valid estimates for foods eaten frequently compared to foods eaten rarely (Lillegaard et al., 2012). Other studies conclude

that the use of a short FFQ is a valid method to measure specific food groups commonly eaten, such as fruits and vegetables, meat products, dairy and milk products (Bogers et al., 2003; Giovannelli et al., 2014). Albani and colleagues measured the intake of different dairy products high and low in fat using C15:0 and C17:0 as biomarker measured with DBS (Albani et al., 2016).

Nevertheless, there are also several limitations connected to the short-FFQ, such as no alternatives for people with food intolerances as gluten intolerance, lactose intolerance, allergies, or for people who eat special products and follows a diet. It does not capture a day-to-day variability, and rare food groups and food eaten rarely will not be caught. It is based on a typical Norwegian diet and does not take other diet patterns from other cultures into consideration and may therefore omit essential foods. There was an average of 12.3 % (VB) and 13.9 % (VTR) for participants with ethnicity outside of northern countries. Whether this group has obtained Norwegian diet pattern is unknown, and may create dispersion in the CCs.

An inclusion criteria in this study was that the participants had to know how to read and understand Norwegian. Despite that, some persons might find it challenging to understand and interpret the questionnaire. The degree of their ability to understand and comprehend the questionnaire may differ between the subjects. Nutbeam describes one's own capacity to conceive and obtain knowledge and understand messages regarding own health as *health literacy* (Nutbeam, 2006). From this composite term, *nutrition literacy* has raised and comprises the understanding regarding nutrition and health (Guttersrud, Dalane, & Pettersen, 2014). Nutrition literacy can be divided into three levels of how to obtain nutritional health messages; one of them is called *functional nutrition literacy (FNL).* This term refers to "proficiency in applying basic literacy skills such as reading and understanding food labeling and grasping the essence of nutrition information guidelines" (Guttersrud et al., 2014, p. 877). It is likely to believe that not all participants hold the same capacity of FNL and may further give a discrepancy in the results. In some cases the usage of images, or figures of food measurements, depicting in a questionnaire could be helpful (Masson et al., 2003).

In the VTR sample, half of the participants gave information that their highest achieved education was 1-5 years of university or university-college degree (high education). 12.3 % gave information that their highest achieved education is completion of junior high school (low education). There is no information about education level for the remaining sample. Further, there were no statistical differences between genders for high education, although men made up a higher proportion. However, there were higher correlations for the FFQ observed for participants with high education compared to those with lower education

(no data shown). In a study among 1015 women, which tested the reproducibility and validity of an FFQ, they found weak correlations for participants with low education (> 12 years). On the other hand, in the follow-up, first 6 months, and then one year later, showed that validity increased in all education groups and there were mostly non-significant differences in reporting for those with low education (Kristal, Feng, Coates, Oberman, & George, 1997). Further, Johansson and coworkers found no significant difference in reporting divided on educational level among 193 Swedes (Johansson et al., 2007).

However, the current short FFQ was explained well, with examples of food items related to each questions written in parenthesis. The amount was articulated as portions as cheese slices, salami slice, cups/glass, which is easy for most people to relate to. The short FFQ is a less expensive method, fast for the participants to complete but on the other hand it may not be precise enough, and miss out on important foods in the diet.

5.1.6 Biomarkers by dried blood spots

There is no gold standard of biomarkers that can reflect the intake of certain fat containing food, but research shows that there are good indicators of certain FAs as biomarkers for the intake of milk and dairy products (Albani et al., 2016; Brevik et al., 2005; Samuelson et al., 2001). There are also several short FFQs that utilize biomarkers as reference measurements (Dahl et al., 2011; Giovannelli et al., 2014; McNaughton, Hughes, & Marks, 2007). The present study used biomarkers as a reference method when validating the short-FFQ, and is one of the strengths with this study (Andersen Frost, 2000).

However, there are some challenges associated with the procedure of the DBS. The samples are taken from whole blood and there is little information about metabolites and nutrients in whole blood compared to plasma/serum samples (Holen et al., 2016). Whole blood has also several other physiological qualities that make it more challenging to measure biomarkers in it than plasma. Since the DBS samples can be performed by anyone anywhere the quality of the samples may differ with regard to correct performance (time drying in air temperature, fridge) (Holen et al., 2016). Further, the spot on the card is 13 mm in diameter and blood shall cover the whole spot. A DBS kit only contains two finger-prick lancets and in some cases it can be insufficient because two finger pricks can provide small amounts of blood. Health care providers at the pharmacy performed the DBS tests in this study and several finger-prick lancets (> 2) were used to provide enough blood for three full spots. It is crucial to be warm in your hands and perform the fingertip prick standing with your hands lower than your heart, in order to ensure the blood flow.

The DBS tests in this study were preserved at room temperature for not more than 5 hours before being placed in the fridge at the pharmacy and then sent by mail to Vitas, Oslo. Later they were preserved in the freezer at -20 degrees Celsius. As mentioned previously, how the samples are stored may affect the FAs, and it is the HUFAs, which are especially sensitive for changes in temperature and light, which can start an oxidation. However, this study focused on SFAs, which are stable and not sensitive for oxidation due to temperature and are therefore suitable as biomarkers in DBS. Further, some of the samples were excluded because; a) Id-numbers were missing; b) cards were dried at room temperature too long before being put in the fridge; and c) the cards were not put in the aluminum preservation bag. Even though these tests were excluded there still might be some differences in the samples. Information about the procedure was given to all pharmacies that performed DBS tests, but some of the health care providers may have forgotten some tests and therefore refrained to give information if samples were in room temperature for more than five hours.

When following the correct procedure, and using cards with impregnation of antioxidants and chelation, the method of DBS is a cheap and simple way of collecting biomarkers especially over a large geographic area. In the future, DBS may play a crucial role in dietary research when collecting biomarkers is essential for a low cost. Further, it is important that biomarkers will be validated for such use.

The current study mainly focuses on pentadecyclic acid (C15:0) and margaric acid (C17:0), which may reflect the dairy and milk intake. Carnitine and TMAO are not considered as potential biomarkers for meat in this study because they are less accurate due to physiological variations between vegetarians and omnivores. Further, carnitine works as a carrier for lipids into mitochondria in muscles and is therefore abundant in muscle mass (Dragsted, 2010). This indicates that men, who have higher muscle mass, and persons with high exercise level, will have higher levels of carnitine (Dragsted, 2010). There are however also other biomarkers in use in research, and also some that might have been suitable for this study but are unknown to the author of this thesis.

5.3 Validation of short food frequency questionnaire

Validation studies are primarily carried out to evaluate the validity of a FFQ for the specific study population tested, and therefore the internal validity is evaluated (Lillegaard et al., 2012). To evaluate the external validity, which refers to the degree in which the FFQ is generalizable outside the study population is often very hard to evaluate. (Svensson, Hjartåker, & Laake, 2007).

Moreover, there are several errors connected to dietary research, but a good study design will reduce the systematic and random errors and strengthen the validity and the reproducibility (Laake, Hjartåker, Thelle, & Veierod, 2007). Systematic errors refer to bias in the measurements or estimates, and will reduce the validity of the study. Systematic bias can rise from selection bias of the study population and affect the internal validity. Bias can also rise from errors in information the participants report in a study. The errors can be repetitive when performing both the test and the retest due to conscious or unconscious reporting from the participants. Statistical methods used to validate are also crucial for obtaining valid results. On the contrary, random errors will give a less precise estimation resulting in larger variation in the estimates (Laake et al., 2007). Systematic bias, and errors in the tools used for measurement, can also be repeated and is hard to manage statistically. Random errors can, in contrast to systematic errors threaten the reproducibility of the measurements in a study (Laake et al., 2007). Both errors have to be avoided in order to have a valid result, and it is often very challenging to evaluate the validity of a questionnaire, as to many factors impact one another (Laake et al., 2007; Willet, 2013). The reproducibility and the validity are specific for the study population tested (Svensson et al., 2007).

Underreporting is a widespread phenomenon in all populations regardless of gender, BMI, degree of activity, smoking habits, educational status and living situation (Johansson et al., 2007; Krebs-Smith et al., 2000; Schmidt & Steindorf, 2006). Research suggests that underreporting can be a result of social preoccupation regarding weight control and body image, consciously omitting foods that are seen as unhealthy and also changes in dietary habits when undertaking the dietary survey (Samaras et al., 1999). The use of Bland Altman plots will reveal this phenomenon. Since this study population consented to participate in a study regarding cholesterol and heart health it is not unlikely to believe that the reporting is due to what the participants recognize as “good” and “bad” food in regard to CVD. The answers will regardless differ between subjects based on their knowledge about food, portion size and heart health.

The results from the validation have been compared with short and long FFQs that utilize biomarkers as reference method. Biomarkers measured in whole blood, plasma and serum. Reproducibility has been compared with results from test-retest in other studies, where the test-retest had a period of four weeks and up to one year in between the tests.

5.3.1 Test-retest of short food frequency questionnaire

The test method is referred to as V3-FFQ and the retest method V4-FFQ.

The questions in the short FFQ are divided into categories when the results are discussed: dairy products (milk, dairy, cheese), meat (spread, dinner), number of eggs and cigarettes, and the categorical variables (cholesterol lowering margarine and smoking). The results from Spearman's rho correlation, Wilcoxon Signed rank test, distribution in percentiles (25p, 75p) and the Bland Altman plots are further discussed in the light of the questionnaires reproducibility. It is important to bear in mind that these individuals measured their cholesterol at V3 and received information that their TC was slightly elevated. This might affect further food choice and may facilitate dietary changes among the participants when they completed the questionnaire four weeks later. On the other hand, participants may also just imply they have done changes without actually doing so. Further, there are few studies that test the reproducibility of questionnaires containing food groups calculated in g/day because several studies measure the energy intake.

5.3.1.1 Dairy products

Milk

The questions regarding milk are divided into three categories: high-fat, medium-fat and low-fat. For these categories there are only correlations seen as good (>0.5) (Hankin et al., 1991) for milk medium-fat (0.81) and low-fat (0.68) and they are among the highest correlations overall. Ocké and colleagues found similar correlations for milk in the Dutch EPIC study on 0.85 that measured intake of different food groups (Ocké et al., 1997). Further, in the current study there is a significant mean difference in intake of high-fat milk between the visits, and an overestimation for high-fat milk for V3-FFQ is observed. The median and percentiles are similar despite significant differences in intake between the measurements. When looking at the mean (SD), there is a mean difference on 9 g (±20.79) between the intakes of high-fat milk. The cause could be one outlier that consumes three times as much milk compared to the trend in variation. On the other hand, there is a change towards lower consumption of high-fat milk at V4.

The Bland Altman plot for medium-fat milk appears rather clustered together but the difference varies with approximately 400 g/day, which equals two glasses of medium-fat milk a day. With a closer look at the plot there are two outliers that probably cause the large variation in intake on a group level, if they were removed the plot would look different with a narrower variation in intake. On an individual level the variations in observations are close to one glass a day, one can assume that if the outliers were removed the variation would be closer to this estimation.

The plot for low-fat milk has a fan-shape, which is typical for plots with FFQ-data. This plot shows a variation in less than a glass of milk a day, along with an increasing overestimation in intake with higher consumption. This is a typical trend for healthy foods, which is often overestimated (Fallaize et al., 2014). The correlation is good, and the difference in intake is very small together with an approximately equal distribution in percentiles for both visits. This indicates a satisfactory estimation for low-fat milk in the V3-FFQ.

In a study by Bogers and coworkers where they performed a test-retest with four weeks in between the tests, they found correlations between 0.49 and 0.82. Those CCs were stronger than those in the current study (except from milk MF and LF), but on the other hand they estimated fruit and vegetable intake (Bogers et al., 2003). It is easier for respondents to know how many apples they eat a day compared to intake of dairy products, which include different items. The lowest correlation in Bogers and coworkers' study was 0.49 for the category "other fruits". This can be compared to some degree with the results in the present study with the basics of several different food items included in one question. However, the reproducibility of the V3-FFQ shows adequately good estimations for both medium- and low-fat milk. Further, it did not give a good estimation for high-fat milk, and the reasons for the significant difference is probably the outlier of one individual that consumed over halve a liter milk a day that violate the data.

Dairy

High-fat dairy is among the highest correlation (>0.5) with close to zero difference in intake between the methods. The distribution in percentiles is approximately the same for both visits, which indicates nearly the same distribution in median intake. Food items in this category comprise double cream, cream fraiche and full fat sour cream. These are foods often used in cooking, as dinner and desert and the amount can be hard to calculate. The variation in intake is 15 g/day, which can be compared with one tablespoon of sour cream or almost two tablespoons of double cream (Helsedirektoratet/Mattilsynet). This is considered a small difference in intake between the methods, and the V3-FFQ estimates the intake of high-fat dairy as good on a group level.

Medium-fat dairy covers food such as single cream, MF-sour cream, yoghurt with sugar and MF-cream fraiche and also has a difference in intake between the methods close to zero on a group level. The amount that varies is equal to a third of a cup of yoghurt of 125 g, which is a normal amount of yoghurt found in Norwegian stores (Go'morgen yoghurt 195 g)

(Helsedirektoratet/Mattilsynet). The Bland Altman plot shows a tendency to overestimate the intake on an individual level when the amount of intake also increases, and most participants are in the same percentiles for both visits (2.25 g higher for V4). The V3-FFQ estimates the intake of medium-fat dairy as good on a group level.

When looking at the plot for low-fat dairy, which contains dairy products like LF-sour cream, quark, "yoghurt 0 % fat" and coffee cream there is a trend in the variation in halve a cup of yoghurt (125 g) or 2-3 tablespoons of sour cream (Helsedirektoratet/Mattilsynet). The distribution in percentiles differs between the visits with the 75 percentile being 8 g higher at V4-FFQ. This indicates that more participants choose a higher amount eaten at V4 compared to V3. When the intake is increasing there is also an increasing overestimation in the intake on an individual level. On a group level the V3-FFQ slightly underestimates the difference in intake on -1.8 g, which is insignificant for this instance.

There is uncertainty if the study population compared their intake with the same foods that are used as examples in this discussion. The comparison is done based on foods most commonly eaten and also the foods most easily to compare the amount with. Dairy products comprise foods from sour cream used in cooking to yoghurt, and it can be hard for the participants to calculate sour cream used for dinners over the last two months compared to one cup of yoghurt. The two lowest correlations for dairy (0.48 and 0.50) shows the smallest variation in intake out of the Bland Altman plots compared to the highest correlation (0.53) for low-fat dairy which has the highest variation in intake of the three categories. Hu and coworkers tested the reproducibility of a questionnaire with food groups such as dairy HF and LF, and found correlations on 0.58 (HF) and 0.69 (LF). Although the LF dairy comprised LF milk and diet ice cream. While the HF dairy contained HF milk, sour cream, cream cheese and cream, which is more similar to the food items in this category tested (Hu et al., 1998). The discrepancy in the distribution in percentiles for all dairy categories is considered low, except for the 75 percentile at V4 for LF dairy. The difference in intake is close to zero on all dairy categories and the V3-FFQ estimates intake of the different fat containing food questions good on a group level.

Cheese

There is a typical fan-shape in the plot for high-fat cheese, which shows a slightly underestimation in intake on a group level (-2), and both under- and overestimation on individual level. Most observations are spread out over a variation in intake of approximately 1 portion of pre-sliced cheese a day, which is a portion for a slice of bread

(Helsedirektoratet/Mattilsynet). There is a significant difference in intake between V3-FFQ and V4-FFQ, but on the other hand both 25 and 75 percentiles are in the same groups for both visits.

For both medium- and low-fat cheese there are fair correlations (0.3-0.49) (Hankin et al., 1991) with a difference in intake close to zero. The variation in intake between the measurements is less than one slice of cheese (10 g) for both and all participants are in the same percentiles for both visits. The V3-FFQ gives good estimations for medium- and low-fat cheese. The reasons for the low correlations for these food groups can be due to less variation in intake and lower number of participants that consume dairy foods (Andersen Frost, 2000). In a German and Dutch study (Bohlscheid-Thomas, Hoting, Boeing, & Wahrendorf, 1997; Ocké et al., 1997) they found higher correlations for cheese that showed 0.61 to 0.77. The higher correlations can also be due to cultural differences in diet between countries.

All dairy products in a public health perspective

These variations may seem small, but when considering these variations in the light of the Norwegian dietary guidelines it has a different meaning. To cover the need of calcium the recommended intake (RI) is 800 mg/d (Nordic Council of Ministers[NCM]2012). To achieve this amount of calcium from solely dairy products a person has to eat for example 1.5 glass (300 g) of medium-fat milk, two slices of low-fat cheese (20 g) and a cup of fruit yoghurt (125 g) a day, which gives a total on 765 mg of calcium (Helsedirektoratet/Mattilsynet). When the variation in plot is up to two glasses of milk a day it is a skew distribution in intake. Considering that there are more women in this study with Caucasian origin and a mean age of 60, the RI of calcium, and also vitamin-D (10 μg > 60 years), is important to meet to achieve good bone health and prevent osteoporosis (NRE, 2011; NCM, 2012). There is not a recommended amount in gram for dairy products in Norway except from the advice of including low-fat dairy products in our daily diet. This is due to both positive and negative physiological effects of calcium (NRE, 2011). Several other countries have specific recommendations of dairy like Denmark and Australia (Fødevarestyrelsen; National Health and Medical Research Council, 2013). Our neighboring country, Denmark, recommends ¼-½ l milk together with 25 g of cheese a day (Fødevarestyrelsen). Seen from the perspective of the Danish recommendations, but also the Norwegian, the variation in intake of milk and cheese, and the study population, it may be of importance in the prevention of osteoporosis. Further it is important to cover the RI of calcium (Fødevarestyrelsen; NCM, 2012).

When looking at the percentiles for dairy products they are mostly equal. Though there is a tendency with change in dietary fat towards an increasing intake of low-fat dairy products at V4 for milk and dairy. On the other hand the intake of dairy HF has slightly decreased at V4. There are several studies that show higher correlations for milk, dairy and cheese (0.6-0.8) and it is important to bear in mind cultural differences between countries. Studies with approximately same study design as the current study had study populations from the Netherlands, Spain, USA and Germany (Bohlscheid-Thomas et al., 1997; Fernandez-Ballart et al., 2010; Ocké et al., 1997). These countries have a different diet from the Norwegian, and some especially higher dairy consumption such as the Netherlands (Ocké et al., 1997).

5.3.1.2 Meat

Spreads

The correlations for high-fat- and low-fat meat spread are satisfactory (> 0.5) with no differences in intake between the methods, which are close to zero (0.07 and -0.08) on a group level. For low-fat all participants are in the same percentiles as for high-fat there is a change to lower intake at V4. Both plots have a fan-shape with approximately evenly distributed individual observations over and under the mean intake from both V3 and V4, which indicates that V3-FFQ over- and underestimate the intake at the same time as the intake is increasing on individual level.

Dinner

For the intake of high-fat meat for dinner or lunch there is a variation in intake of approximately 60-70 g/day. This amount equals one sausage, or less than half a portion of a full-fat roast. The mean difference in intake between the visits is 3.4 g meat a day, which is considered very small and there is no significant difference in median intake between the visits. All participants are approximately in the same percentiles with the exception of high-fat meat dinner where the intake has decreased at V4. Estimations of high-fat meat on group level are well assessed by the V3-FFQ.

Both medium- and low-fat meat for dinner show a slightly underestimation in mean difference in intake between the visits of 4.5 g meat, this is considered a small amount and there are no significant differences in median intake. The variation is 60-70 g for medium-fat meat that comprise hamburgers, chicken sausage or medium-fat minced meat, the variation can then vary from one piece of sausage to a forth of a hamburger.

Low-fat meat dinner has the largest variation on almost half a meat portion a day (90 g). There is a small tendency for overestimation of the intake when the intake is increasing on an individual level.

Other studies tend to find higher correlations for meat than this current study ranging from 0.70 to 0.88 (Fallaize et al., 2014; Hu et al., 1998; Ocké et al., 1997). The reasons for this could be larger FFQs with more detailed questions. Further, Ocké and coworkers developed the questionnaire to assess, among other parameters, meat intake in relation to cancer (Ocké et al., 1997). Hu and colleagues enrolled participants from the Health Professional Follow-up Study, a prospective study of risk factors for cancer and CVD (Hu et al., 1998), which may result in highly motivated and experienced study population. In the Food4Me FFQ there were images of food portion sizes, which can make it easier for participants to estimate portions (Fallaize et al., 2014). On the basis of the mentioned arguments for higher correlations in other studies, but also fair correlation (0.3-0.49) (Hankin et al., 1991) observed in the current study, with small to moderate variation in intake of meat with close to zero difference in intake between the measurements, the V3-FFQ captures moderately estimations for high-fat- and low-fat meat spread and intake of meat dinner on a group level (Subar et al., 2001).

Meat in a public health perspective

In a health perspective it is recommended to reduce the intake of red meat and rather eat low-fat meat (also white meat) as poultry and lean pork, lamb and steak (NRE, 2011). The recommendations are not more than 500 g red and processed meat per week including meat from spread. This equals 2-3 dinners of meat weekly (NRE, 2011). Other diets, such as the Mediterranean diet, consist of meat in even smaller quantities than the Norwegian recommendations and are considered a heart friendly diet. Red meat here is only recommended twice a month (Huedo-Medina, Garcia, Bihuniak, Kenny, & Kerstetter, 2016). The median intake per week of meat from spread, lunch and dinner among the participants (n = 122) at V3 is 599 g/week (349, 953). It is important to be aware that this includes total meat intake from high to low fat content: HF-LF red meat and HF-LF white meat. The FFQ cannot separate between intake of white and red meat. There are only 15 % (18/122) of the participants who eat between 400-500 g meat per week, and 57 % (70/122) eat over 500 g/week. This intake is high, and it seems to follow the trend in the development in meat consumption the last 25 years from the report of development in the Norwegian diet (Helsedirektoratet, 2015). This high meat consumption is a threat for the public health. In the

developing of cancer, red and processed meat constitute for several types of cancer in digestive organs (World Cancer Research Fund International [WCRF]2007). In the latest, and largest study, about stomach cancer, PA and nutrition from World Cancer Research Found International (World Cancer Research Fund International/American Institute of Cancer Research [WCRF/AICR]2016) they updated their recommendations because of the latest findings. Processed meat (smoking, curing, salting) have strong evidence of causing stomach cancer, and comprise food as ham, bacon, pastrami, salami, hot dogs and some sausages, which all are common meat spreads in the FFQ used in the current study (WCRF/AICR, 2016). High-fat meat and processed meat (salted: salami, pastrami, minced meat) also have convincing evidence to cause CHD, hypertension and CVD (NRE, 2011). Further, American Heart Association (AHA) recommend not to eat SFAs and TFA found in the previous mentioned spreads, and rather replace them with MUFAs and PUFAs, which is similar to the fat composition in the Mediterranean diet (AHA, 2015a; Estruch et al., 2013).

Another perspective in meat consumption is environmental factors. The conventional agriculture, with food production, processing and trade, stands for nearly the majority of greenhouse gas emissions in the world (Oosterveer & Sonnenfeld, 2012). By reducing the intake of meat, it has not only a positive effect on health, but also contributes to reducing emissions of greenhouse gas. As AHA and Bere and colleagues recommends, seasonal eating is both suggested heart- and environmental friendly (American Heart Association[AHA]2015b; Bere & Brug, 2009).

The small changes seen in the intake among the study population between V3 and V4 is directed towards less intake of meat HF and MF. Identical intake (median and percentiles) is observed for low-fat meat at V4.

5.3.1.3 Number of eggs and cigarettes

The difference in intake of eggs between the measurements is close to zero (0.3) and all participants are almost in the same percentiles. The correlation is high (0.76) and the variation in intake differs from 0 to 4 eggs, which is considered small. Two studies, which tested the reproducibility of a questionnaire up against food groups, found similar correlations on 0.71 and 0.73, both with 6 months intervals (Bohlscheid-Thomas et al., 1997; Ocké et al., 1997). Further in two other studies they found a lower correlation of 0.69 (Fallaize et al., 2014; Hu et al., 1998). Several other studies show correlation for eggs on 0.7.

The correlation for number of cigarettes is the highest on 0.92 and the percentiles shows a trend towards fewer cigarettes at V4, 11 vs. 14. There are only eight smokers in this sample, thus it was not possible to create a Bland Altman plot.

To include number of eggs and cigarettes in the validation is a factor that can participate in the evaluation of the validity. Number of eggs and cigarettes are of a definite size hence it is easier for participants to relate to. V3-FFQ gives good estimations for intake of eggs in the reproducibility test.

5.3.1.4 Categorical variables

For the categorical variables "smoking habits" and "cholesterol lowering margarine" the correlations are on 0.91 and 0.58. The number in the different categories is equal for both samples (data not shown). For cholesterol lowering margarine there is a trend with slightly more users of margarine at V4 with 2 more at "use every day" (16 vs. 18) and 3 more at " use every now and then" (23 vs. 26). This indicates small changes when completing the short FFQ at V4.

Cholesterol lowering margarine (Müller et al., 1997) contains several MUFAs and PUFAs that have cholesterol lowering effect, as well as beta-glucans and plant sterols (Mills DA; Müller et al., 1997). After the participants measured their TC at V3 it is not unlikely that it is the cause of the slightly increased consumption of cholesterol lowering margarine at V4.

5.3.1.5 Summary of test-retest of the short FFQ

The responses in the FFQ are dependent upon the participant's memory, the design and properties of the questionnaire and actual changes in dietary pattern among the study population (Bogers et al., 2003). Evaluating after the changes in median intake and the distribution in percentiles, the changes in diet seen at V4-FFQ are towards a lower consumption of high-fat food and higher consumption of low-fat food. The fact that the study population's cholesterol measured slightly elevated at V3 may have affected the responds at V4.

Bogers and coworkers conducted a study concerning validation of FFQ utilizing a test-retest and biomarkers as reference method. They evaluated fruit and vegetable intake among 157 Dutch women using carotenoids as biomarkers. After four weeks the test-retest of the FFQ showed Spearman's rho correlations ranging from 0.4 to 0.8. Further, the significant correlations between biomarkers and food categories ranging mostly between 0.2 and 0.3 (highest rho = 0.57) (Bogers et al., 2003). The correlations in the current study range from 0.4 to 0.9 with the majority being between 0.5 and 0.9 when testing the reproducibility. After a

reproducibility-test most correlations turn out between 0.5-0.7 (Willet, 2013) hence the correlations in the current study are within a normal range. Further, Albani and coworkers observed differences in intake of dairy products between countries when performing the Food4Me study. The countries included in their study were Germany, Greece, Ireland, the Netherlands, Poland, Spain and UK (Albani et al., 2016).

After dividing the sample by gender there were higher correlations among women than men, though not any statistical differences in intake between the measurements for both genders separately. An explanation for this might be that women are more aware of their habitual diet than men, and also better at estimating portion (Masson et al., 2003). Another factor that can influence differences in estimation is due to whom is doing the grocery shopping in the household (Cade, Thompson, Burley, & Warm, 2002). Most of the Bland Altman plots divided by gender were incomplete as a result of that it was only a few individuals in each category.

5.3.2 Reference measurement – biomarkers by Dried Blood Spots

The significant correlations between the FAs and the FFQ are low, ranging from 0.12-0.22 for all participants, and up to 0.31 when divided by gender. In a large sample low correlations can be significant (Pallant, 2013).

DBS collect FAs from whole blood cells that reflect the fat intake over the last few days, while the FFQ captures the intake over the past two months. In addition to a day-to-day variation in intake, this can result in low correlations between FAs and FFQ. This might imply that DBS samples will be more suitable when carrying out a dietary record, or a WR, over a few days. In order to capture the long-term intake, samples of FAs from adipose tissue should be measured (Holen et al., 2016). Nevertheless, when using two different measuring instruments, as an FFQ and blood samples, the CC will always be lower (Bland & Altman, 2010). Another reason may be because some foods are eaten less often than others. Meat is an example that is eaten less often than other foods. Even so, there are several other studies that have discovered the same correlations as in the current study using DBS and other methods (Albani et al., 2016; Brevik et al., 2005; Smedman, Gustafson, Bergrus, & Vessby, 1999; Sun, Campos, & Hu, 2007).

However, the percentage of FAs in blood may also reflect consumption of other foods rich in fat such as fish, cakes, cookies, chocolate, potato chips and other highly processed foods. In this regard, TFA are more abundant and can be a more precise indicator to reflect

the intake, which is also suggested by researchers (Holen et al., 2016; Mahan & Escott-Stump, 2008).

Studies often use C15:0 and C17:0 as biomarkers for milk and dairy fat intake (Brevik et al., 2005; Smedman et al., 1999). Since both contain odd-number-carbon chains the human body is unable to synthesize them, but on the contrary the bacterial flora in rumen in ruminants are able to. Hence these are suggested as biomarkers for intake of dairy products (Albani et al., 2016; Sun et al., 2007; Wolk, Furuheim, & Vessby, 2001). The body synthesizes FAs itself and palmitic acid (C16:0) is the end product of de novo synthesis primarily in the liver. Further elongation of FA requires other enzymes and takes place in the smooth endoplasmatic reticulum. The brain holds the required enzymes and is therefore capable to elongate FA up to 22 carbon atoms (Harvey & Ferrier, 2011).

5.3.2.1 Dairy products and fatty acids

In the following paragraphs all dairy products are discussed together: milk, dairy and cheese.

In this study only observed associations are discussed. In future work a multiple regression analysis will further describe how much of the variation in FAs can be explained by intake of milk, dairy products, meat and meat products. Possible interaction and confounding factors are not taken into consideration in this thesis. I will however point out that the following are only observations and are not absolute associations or explanations.

High-fat dairy

The strongest correlations between the FA and FFQ were found for the category high-fat dairy products, which is obvious because of exactly the high fat content. Further, the significant correlations were mostly dominated by the SFAs: C12:0 (milk: 0.182), C14:0 (milk: 0.160) and C15:0 (milk: 0.145); (dairy: 0.195); (cheese: 0.220). Sun and colleagues found similar correlations for intake of dairy products and SFA on 0.18 (C14:0) and 0.28 (C15:0). The sample was similar for 313 participants, but the measurements were taken from plasma (Sun et al., 2007). The dairy product category in Sun and colleague's study comprised milk, yoghurt, ice cream, sour cream and cheese (Sun et al., 2007). Among 205 individuals non-significant correlations were observed for milk high-fat and C14:0 (0.08), and further cheese (0.11) in a study by Biong and coworkers. C15:0 was significant for dairy (0.14). All of the samples were measured in FA in serum (Biong, Berstad, & Pedersen).

High-fat milk had an inverse significant correlation with arachidonic acid (C20:4n6), which is the derivate from the essential FA linoleic acid (LA) (18:2n6) (Harvey & Ferrier, 2011). Meat is rich in AA, and accordingly can cowmilk contribute with this FA (Abedi &

Sahari, 2014). AA is not essential by itself, but can be if its precursor LA is lacking (Lippincott). Inflammation is a part of CHD and there are several studies on the effect of n-3 on this disease (Ohnishi & Saiti, 2013; Russo, 2009). And further research is necessary to investigate possible mechanism between FA and CVD.

Medium-fat dairy

There was no specific FA composition that dominated for medium-fat dairy products, though the two strongest significant correlations were one n-3 and one n-6 FA. Docosapentaenoic acid (DPA) (C22:5n3) had a correlation on 0.179 for milk and LA had a correlation on 0.150 for dairy. LA is the most common n-6 FA found in milk, but both FA are found in plants, and LA is mainly found in vegetable oils and soybeans (Mahan & Escott-Stump, 2008; Srednicka-Tober et al., 2016). The dairy MF category contain single cream, yoghurt with sugar and cream fraiche, which are all made of milk. In a review of Srednicka-Tober and coworkers they found a significantly higher content of DPA (also EPA and ALA) in organic milk compared to conventional produced milk where 19 previous studies were analyzed (Srednicka-Tober et al., 2016). Conversely, and according to the Danish food table there is no DPA or EPA in conventional or organic produced MF milk, and the content of ALA is the same in both types (Fødevareinstitutt., 2016). The FFQ used in the study did not separate organic and conventional produced milk. Because of different findings in organic vs. conventional produced milk it would be interesting to create a questionnaire that separate the two categories. Further, comparison can be made by measuring FA content or other nutrients in blood/plasma and investigate any possibly differences and explanations by multiple regressions.

Low-fat dairy

The participants in the current study have a higher percentage (% of FAME) of LA, EPA, DHA than the levels found in 100 healthy subjects in a study by Marangoni and colleagues (Marangoni et al., 2004). They found a mean level of LA on 16.74 ±5.86, EPA on 0.59 ±0.47 and DHA on 1.75 ±0.59 and the findings in the current study are 19.92 ±2.63 (LA), 1.44 ±0.98 (EPA) and 3.33 ±0.91 (DHA) for all subjects. The highest correlations between the FAs and dairy products are between dairy and LA (0.154), cheese and EPA (-0.142), and cheese and DHA (0.124). Organically produced milk (organic milk) has a similar content of SFAs and MUFAs as conventional produced milk, but researchers found higher content of PUFAs in organic milk (Srednicka-Tober et al., 2016). In this study it is unclear whether the study population eat organic dairy or not.

There may be other more reasonable explanations for the higher percentage of LA, EPA and DHA in the subjects. When looking at the results in a study by Saga and coworkers they found a difference in levels of LA, EPA and DHA between Norwegian individuals using n-3 supplements and those who were not (Saga, Liland, Leistad, Reimers, & Rukke, 2012). The percentage of FA in those using n-3 supplement are slightly higher than the levels in the individuals in the current study. However, the participants were asked not to take n-3 supplements before taking DBS samples at V3. EPA and DHA are the long-chained n-3 FA found in fat fish and seashell and the content varies between fish in regard to their fodder or if its wild fish and also origin (Mahan & Escott-Stump, 2008; Sissener, Torstensen, Stubhaug, & Rosenlund, 2016). LA, together with ALA, are also found in cholesterol lowering margarine, rapeseed oil, soybean oil, walnuts, and linseeds (Mills DA; Müller et al., 1997). It is therefore many different sources of n-3.

C15:0 and C17:0 and high-fat dairy products

Men and women have different body composition where women have higher fat tissue than men (Frayn, 2010). When dividing the results between gender women tended to have more and higher significant correlations than men between C15:0 and high-fat dairy and cheese and all dairy products together (milk, cheese, dairy). The correlations for women ranged from 0.174-0.282. On the other side, men had only high correlations for C15:0 and high-fat cheese. For all dairy products together the highest correlations for total, men and women were observed for the high-fat category (0.267-0.282). Further, when dividing the sample into BMI categories the strongest significant correlation was found for high-fat dairy products for those characterized as overweight, which is the mean BMI among this study population (38.1 %). When dividing into age groups, the highest significant correlations observed overall were for the age group 20-45 years old with CC between 0.405-0.422 for C15:0 and total dairy products and medium- and high-fat dairy products.

The results show that C15:0 is predominant for all the high-fat dairy categories. In the large international study Food4Me, by Albani and coworkers they found CCs for C15:0 to be high for all dairy products, especially high-fat (Albani et al., 2016). Further, they found stronger CC for C15:0 than for C17:0. The intake of dairy products varied between the countries included in the study: Poland, the Netherlands, Ireland, Germany, Spain, Greece and UK. Greece and Spain reported no consumption of butter and cream in contrast to Germany and Poland where the intake was higher. They found the lowest levels of C15:0 in Spain and Greece, and the highest levels in Germany. C17:0 was similar in all countries except from in

Germany and Poland where it was higher. They also found differences between gender for all countries in regard to C17:0 (Albani et al., 2016).

As mentioned earlier the mean BMI is slightly higher for women than for men in this study population, indicating that some of the participants are overweight. The intake of dairy products among this study population is not considered specifically high. 57 % of the men had an intake of total dairy products (HF, MF, LF) of 100-400 g/day, and only 18 % with higher intake (>400g/d). Among the women 61 % had the same intake and 13 % an intake over 400g/d. An intake of 100-400 g of dairy can vary from ½ glass of milk to one glass and one yoghurt (Helsedirektoratet/Mattilsynet). This is not considered a high intake of dairy and it is important that the RI for calcium is fulfilled (NCM, 2012).

Conversely C17:0 did not show any significant correlations except for cheese HF for women, and between total and dairy products HF. According to other research it appears as though C17:0 is less precise for single dairy items, but rather reflect the intake of total dairy products (Albani et al., 2016; Johansson et al., 2007). C17:0 is also a good biomarker for long-term intake of dairy fat intake measured in adipose tissue (Sun et al., 2007).

Both C15:0 and C17:0 is higher among women in the current study, which is also observed in the case-control study by Warensjö and colleagues (Warensjö et al., 2009). They found an inverse relation to the risk of a first event stroke with C17:0 in phospholipids in plasma. The associations between intake of dairy fat and CVD is contradictory, and several other studies have found inverse associations with FA-biomarkers (C15:0 and C17:0) and risk factors for CHD, metabolic syndrome and diabetes mellitus 2 (Drehmer et al., 2016; Krachler et al., 2008; Warensjo et al., 2004).

5.3.2.2 Meat products and fatty acids

In the following paragraphs all meat intake will be discussed together (spread, lunch, dinner). A small note to bear in mind is that the FA samples were taken in September, which is the hunting season for game in Norway. Game meat (reindeer, moose, grouse) is considered leaner with less total fat little SFAs than conventional produced meat (Hassan, Sandanger, & Brustad, 2012). This may result in different meat intake in this certain period compared to rest of the year.

Further, there are only statistical correlations for high- and medium- fat meat, not for low-fat. Therefore the two first categories will be discussed.

High-fat and medium-fat meat

Among the FAs with significant correlations for high-fat meat there were two, with the exception of an inverse association for C16:1n9 (-0.152). This FA is synthesized from the body from C16:0 (Harvey & Ferrier, 2011). The negative associations may imply that low intake of meat may reduce this FA in blood, but this cannot be explained without performing regression analysis. Further, correlations for C20:0 were 0.154, and for AA 0.110.

Medium-fat meat had a negative correlation (-0.182) for C15:0, whereas AA had 0.174. Baylin and coworkers compared biomarkers from plasma, whole blood and adipose tissue to investigate which method that most accurately reflected the diet (Baylin et al., 2005). They found that adipose tissue had the highest correlations for the diet and especially ALA, LA and 18:2 trans-fatty acids. In contrast they did not find any good biomarkers for AA in the different tissues (Baylin et al., 2005).

Fatty acids and meat products

There were not many studies known by the author of this thesis at the present moment (May, 2016) that considered SFAs or other FAs as biomarkers for intake of meat in humans in dietary surveys. There are several studies that look at dairy and milk intake in comparison with FA in blood/plasma in validation studies (Biong et al., 2006; Smedman et al., 1999; Sun et al., 2007), but not regarding meat. There were some studies that had investigated meat intake with percentage in plasma/blood, but had not utilized correlations between diet intake and FA (Marangoni et al., 2004; Welch, Shakya-Shrestha, Lentjes, Wareham, & Khaw, 2010). Welch and coworkers investigated different diet pattern (vegan, vegetarian, and carnivore) and percentage of PUFAs in plasma. They found ALA to be lowest among meat-eaters, along with low levels of EPA compared to the other groups. Among meat-eaters 93 % of the DHA was supplied through poultry (Welch et al., 2010). Further, Baylin and colleagues found that diet-whole blood correlations in general are lower than diet-plasma correlations (Baylin et al., 2005).

However, in a study by Marangoni and coworkers they studied FAs in blood and different diet patterns among 100 subjects (46 males, 54 women). They found AA (C20:4n6) to be significantly high in subjects with high meat consumption (2-3 servings/week). The mean percentage (FAME) of intake for those with high meat consumption was 8.10 ±2.48 (n = 61). In the current study the mean value is 7.59 ±1.41 (n = 318). Further, the median weekly intake of all meat (dinner, lunch, spread) among the current study population is

approximately equal to 2-3 servings a week. For all subjects in Marangoni and coworkers' study the mean percentage for AA was 6.65 ±2.47 (n = 100) (Marangoni et al., 2004).

The data analyzed in this study is not adjusted for any confounding factors and there are other reasonable reasons for high levels of AA and other FAs. It does get elongated from LA, which is abundant in plant oils and also cholesterol lowering margarine that contains these oils (Mahan & Escott-Stump, 2008; Ohnishi & Saiti, 2013). Even so, the fatty acid composition in meat from beef, pork, lamb and poultry varies in terms of which part of the animal it is concerned, and to region of origin (Wood & Enser, 1997).

5.4 Future work

There is a need to take a closer look at dietary fat from milk, dairy and meat products in association with the variation of FA found in blood.

To further strengthen the validation of this short FFQ, and potentially find to what extent the variation in different FAs in blood can be described by the intake of milk, dairy and meat products further analysis is needed.

The FA found in blood discussed here can reflect intake of a selection of different fat rich foods. An additional future aim would be to investigate any possible associations between the study population's lipid profile, FAs measured in blood and intake of milk, dairy and meat products.

Discovering reliable biomarkers for meat intake that can be measured in blood, plasma and serum would bring nutrition research one-step forward. For any future modifications of the short FFQ it might be useful to separate the questions regarding meat into intake of white and red meat, hence I suggest that low-fat category will include only white meat.

6 Conclusion

The primary aim of this master thesis was to evaluate the relative validity and reproducibility of selected food categories in a short FFQ, and explore possible associations between food categories and fatty acids in blood among Norwegian adults with moderate to high risk of CVD.

The current study did not adjust for any confounding factors and there is uncertainty connected to the results. However, there were no significant differences in intake between V3 and V4 for nearly all food groups. For those with statistical difference there was a tendency to

overestimate the intake by the short FFQ. Furthermore, the study population was approximately in the same percentiles for both visits.

Considering the results from both test-retest and the validation, in addition to other results, the total evaluation gives indications that the short FFQ can measure the intake of dairy products, eggs and the use of cholesterol lowering margarine among adults with slightly elevated risk for CVD. There were possible associations discovered between food items and FA that might be interesting to look further into in the future. The results from this evaluation can contribute to further validation of the short FFQ.

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Attachment 1

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Gjøril Bergva	22845529	16.12.2013	2013/1660/REK sør-øst D
			Deres dato:	**Deres referanse:**
			29.10.2013	

Vår referanse må oppgis ved alle henvendelser

Til: Kjetil Retterstøl

2013/1660 D Effekt av screening av risikofaktorer for hjerte- og karsykdom i apotek

Vi viser til klage, mottatt 29.10.2013, på komiteens behandling av ovennevnte søknad. Klagen ble behandlet på komiteens møte 27.11.2013.

Forskningsansvarlig: Universitetet i Oslo
Prosjektleder: Kjetil Retterstøl

Prosjektomtale
Utgangspunkt for prosjektet er at blodtrykk, kolesterolnivå og blodsukker er viktige risikofaktorer for hjerte og karsykdommer (HKS). I prosjektet skal man gjennomføre en gratis screening med målinger av disse risikofaktorene samt midjemål og vekt i ca. 150 apoteker i landet. Deltakerne skal i tillegg besvare et spørreskjema. Basert på resultatene fra målingene og spørreskjemaet, vil helsepersonell ved apotek regne ut deltakernes individuelle risikoscore. De med høy risiko for HKS, vil bli bedt om å screene seg på nytt etter 8 uker. 10 % av dem som oppsøker apotek vil ikke bli screenet første gang, men bli forespurt om å komme tilbake om 8 uker. Formålet med prosjektet er å vurdere om kunnskap om egen risiko for HKS har effekt på livsstil etter 8 uker og 1 år. Det skal inkluderes 25 000 forskningsdeltakere. Data fra intervensjonsgruppen skal kobles til Norsk pasientregister, Reseptregisteret og Dødsårsaksregisteret etter 2 og 5 år.

Det er tidligere gjennomført en kolesterolkampanje i apotek som la grunnlag for stipendiatens masteroppgave. Prosjektet ble framlagt for REK og ble vurdert til å falle utenfor REKs mandat (2012/517).

Saksgang
Søknaden ble første gang behandlet i møtet 23.09.2013. Komiteen avslo prosjektet med følgende begrunnelse: «Etter komiteens syn er det ikke et rimelig forhold mellom forutsigbar nytte og ulempe for deltagerne. Gevinsten av screeningen er såpass marginal at den ikke berettiger den uro og bekymring deltagelse i prosjektet kan medføre. Komiteen finner ikke at hensynet til deltagernes velferd og integritet er ivaretatt på en tilfredsstillende måte, jfr helseforskningsloven § 5».

Prosjektleders klage ble mottatt 29.10.2013

Klagers anførsler
I klagen viser prosjektleder til at ny styrkeberegning er utført og at antall deltagere er redusert for å bedre ivareta forholdet mellom nytte og ulempe. Nytten for den enkelte vil, ifølge søker, primært bestå i at uoppdaget diabetes, hypertensjon eller hyperkolesterolemi kan avdekkes, og at de vil få livsstilsråd i henhold til retningslinjene. Prosjektleder viser til erfaringer og tidligere studier som viser at deltakere i slike undersøkelser i hovedsak er fornøyde med å bli undersøkt. Det vises også til samfunnsnytten i at prosjektet har en forebyggende karakter. Det er redegjort nærmere for rekrutteringen til studien, behovet for

Besøksadresse:
Gullhaugveien 1-3, 0484 Oslo

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

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

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

registerkobling er begrunnet og metode for gjennomføring av registerkobling er beskrevet. Søker erkjenner at det er vanskelig å finne egnet kontrollgruppe, men en ny runde i Tromsøundersøkelsen i 2014 vil kunne gi mulighet til å finne matchede kontroller på en rekke parametre.

Komiteens vurdering
Komiteen konstaterer at prosjektleder har gitt et grundig tilsvar, og det er lagt inn en rekke endringer i prosjektets design for å imøtekomme komiteens innvendinger. Etter en helhetlig vurdering har komiteen kommet til at studien, slik den nå er fremlagt, er forsvarlig å gjennomføre.

Komiteen legger merke til at det er diskrepans mellom protokoll og informasjonsskriv når det gjelder registerkobling. Komiteen setter derfor som vilkår for godkjenning at informasjonsskrivene oppdateres i tråd med den reviderte protokollen. Skrivene skal sendes komiteen til orientering.

Vedtak
Komiteen omgjør sitt opprinnelige vedtak, jfr. forvaltningsloven § 33, annet ledd.

Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres under forutsetning av at ovennevnte vilkår oppfylles.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, klage og revidert protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2020. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 31.12.2025. Forskningsfilen skal oppbevares avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

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

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen,

Finn Wisløff
Professor em. dr. med.
Leder

Gjøril Bergva
Rådgiver

Kopi til: e.h.mjelde@medisin.uio.no, Universitetet i Oslo

Attachment 2

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Ingrid Dønåsen	22845523	16.02.2016	2013/1660 REK sør-øst D
			Deres dato:	**Deres referanse:**
			23.10.2015	

Vår referanse må oppgis ved alle henvendelser

Kjetil Retterstøl
Universitetet i Oslo

2013/1660 Effekt av screening av risikofaktorer for hjerte- og karsykdom i apotek

Forskningsansvarlig: Universitetet i Oslo
Prosjektleder: Kjetil Retterstøl

Vi viser til søknad om prosjektendring datert 23.10.2015 for ovennevnte forskningsprosjekt, samt supplerende informasjon innsendt via e-post 13.02.2016. Søknaden er behandlet av leder for REK sør-øst D på fullmakt, med hjemmel i helseforskningsloven § 11.

Endringene innebærer:
- To nye prosjektmedarbeidere: Ida Tonning Røyseth og Beate Østengen.

De nye prosjektmedarbeiderne skal skrive hver sin masteroppgave basert på data innhentet i prosjektet. Prosjektbeskrivelse for de to masteroppgavene er ettersendt i e-post datert 13.02.2016.

Vurdering
REK har vurdert endringssøknaden og har ingen forskningsetiske innvendinger til endringene slik de er beskrevet i skjema for prosjektendring.

Vedtak
REK godkjenner prosjektet slik det nå foreligger, jfr. helseforskningsloven § 11, annet ledd.

Godkjenningen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, endringssøknad, oppdatert protokoll og de bestemmelser som følger av helseforskningsloven med forskrifter.

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

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Besøksadresse:
Gullhaugveien 1-3, 0484 Oslo

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

Med vennlig hilsen

Finn Wisløff
Professor em. dr. med.
Leder

Ingrid Dønåsen
førstekonsulent

Kopi til:
Eva Helene Mjelde: e.h.mjelde@medisin.uio.no
Universitetet i Oslo ved øverste administrative ledelse: universitetsdirektor@uio.no
Universitetet i Oslo, medisinsk fakultet ved øverste administrative ledelse: postmottak@medisin.uio.no

Attachment 3

Norsk samfunnsvitenskapelig datatjeneste AS
NORWEGIAN SOCIAL SCIENCE DATA SERVICES

MELDESKJEMA

Meldeskjema (versjon 1.4) for forsknings- og studentprosjekt som medfører meldeplikt eller konsesjonsplikt (jf. personopplysningsloven og helseregisterloven med forskrifter).

1. Prosjekttittel		
Tittel	Vaskulære helseundersøkelser i apotek. En randomisert, kontrollert studie av effekten av risikoidentifisering i apotek, og en studie for å monitorere endringer i risikofaktorer i populasjonen fra 2012-2014.	
2. Behandlingsansvarlig institusjon		
Institusjon	Universitetet i Oslo	Velg den institusjonen du er tilknyttet. Alle nivå må oppgis. Ved studentprosjekt er det studentens tilknytning som er avgjørende. Dersom institusjonen ikke finnes på listen, vennligst ta kontakt med personvernombudet.
Avdeling/Fakultet	Det medisinske fakultet	
Institutt	Institutt for medisinske basalfag	
3. Daglig ansvarlig (forsker, veileder, stipendiat)		
Fornavn	Karianne	Før opp navnet på den som har det daglige ansvaret for prosjektet.Veileder er vanligvis daglig ansvarlig ved studentprosjekt. Veileder og student må være tilknyttet samme institusjon. Dersom studenten har ekstern veileder, kan biveileder eller fagansvarlig ved studiestedet stå som daglig ansvarlig.Arbeidssted må være tilknyttet behandlingsansvarlig institusjon, f.eks. underavdeling, institutt etc. NB! Det er viktig at du oppgir en e-postadresse som brukes aktivt. Vennligst gi oss beskjed dersom den endres.
Etternavn	Svendsen	
Akademisk grad	Høyere grad	
Stilling	Stipendiat	
Arbeidssted	Universitetet i Oslo	
Adresse (arb.sted)	Postboks 1046 Blindern	
Postnr/sted (arb.sted)	0317 Oslo	
Telefon/mobil (arb.sted)	22851210 / 95026445	
E-post	kariannes.svendsen@medisin.uio.no	
4. Student (master, bachelor)		
Studentprosjekt	Ja ○ Nei ●	
5. Formålet med prosjektet		
Formål	Det overordnede målet med prosjektet er å bidra med ny kunnskap om helseundersøkelser (screening) i apotek. Vi ønsker å vurdere om det å få kunnskap om ukjent høy risiko for hjerte-kar sykdommer vil føre til positive endringer i verdier av risikofaktorene, kosthold, livsstil, og fysisk aktivitet etter 8 og 52 uker. Videre vil langtidseffekten av kunnskap om egen risiko vurderes i ett langtidsperspektiv ved å utføre koblinger til sentrale helseregistre etter 2 og 5 år.	Redegjør kort for prosjektets formål, problemstilling, forskningsspørsmål e.l. Maks 750 tegn.
6. Prosjektomfang		
Velg omfang	○ Enkel institusjon ○ Nasjonalt samarbeidsprosjekt ● Internasjonalt samarbeidsprosjekt	Med samarbeidsprosjekt menes prosjekt som gjennomføres av flere institusjoner samtidig, som har samme formål og hvor personopplysninger utveksles.
Oppgi øvrige institusjoner	Boot apotek, Mills DA, Universitetet i Tromsø, Universitetet i Minnesota	
Oppgi hvordan samarbeidet foregår	Mills, Boots og Universitetet i Oslo samarbeider tett, og har møter på en jevnlig basis. Dette samarbeidet går mest på den praktiske gjennomføringen av studien i apotek. Samarbeidspartnere på Universitetet i Tromsø og Universitetet i Minnesota vil foregå pr mail og telefon, og er mindre frekvent. Med våre kontaktpersoner her diskuteres studiedesign i hovedsak.	
7. Utvalgsbeskrivelse		

Utvalget	Vi skal gjennomføre gratis kolesterolmålinger i apotek i 150 Boots apotek. I 50 av Boots apotekene kan man samtykke til å måle blodtrykk, HbA1c (langtidsblodsukker) , LDL- og HDL-kolesterol, triglyserider, vekt og høyde i tillegg til målingen av totalkolesterol. Alle i Norge som har mulighet og ønsker det kan måle kolesterolet sitt gratis i apotek i studieuken. Basert på tidligere erfaringer, og det at 50 av apotekene skal tilby flere målinger enn bare totalkolesterol, estimerer vi 10-15000 deltagere, omtrent 4000 av dem skal rekrutteres til studien.	Med utvalg menes dem som deltar i undersøkelsen eller dem det innhentes opplysninger om. F.eks. et representativt utvalg av befolkningen, skoleelever med lese- og skrivevansker, pasienter, innsatte.
Rekruttering og trekking	Alle som ønsker det kan måle kolesterolet sitt gratis i en uke 150 apotek over hele landet. I de 50 utvalget studieapotekene blir alle som ønsker å måle kolesterolverdiene spurt om de vil delta i studien hvor de får mulighet til å måle flere hjerte-kar risikofaktorer. De som samtykker til å delta, og tilfredstiller inklusjonskriteriene vil få deres risikoscore kalkuleres på bakgrunn av deres målte verdier, og deltagerne vil strategisk fordeles i to grupper; lav og høy risiko. I høy risikogruppen skal deltagerne blokk-randomiseres til 3 grupper; 1 intervensjon og 2 kontrollgrupper ved hjelp av ett web basert program utviklet at LINK medical.	Beskriv hvordan utvalget trekkes eller rekrutteres og oppgi hvem som foretar den. Et utvalg kan trekkes fra registre som f.eks. Folkeregisteret, SSB-registre, pasientregistre, eller det kan rekrutteres gjennom f.eks. en bedrift, skole, idrettsmiljø, eget nettverk.
Førstegangskontakt	Deltagerne som møter opp kan enten ha sett reklame om kolesterolmålingene eller møtt opp i apotek grunnet andre ærender og så sett tilbudet om kolesterolmålinger. I de 50 studie-apotekene vil alle som kommer inn i apotek, som ønsker å måle kolesterolet sitt motta ett lite hefte som inneholder informasjon om studien, samtykkeskjema (2 eks) og et spørreskjema. På denne måten kan de lese om studien og vurdere om de kun ønsker kolesterolmålinger, eller om de ønsker flere målinger. Ved sistnevnte må deltagerne samtykke skriftlig.	Beskriv hvordan førstegangskontakten opprettes og oppgi hvem som foretar den. Les mer om dette på våre temasider.
Alder på utvalget	□ Barn (0-15 år) □ Ungdom (16-17 år) ■ Voksne (over 18 år)	
Antall personer som inngår i utvalget	10-15 000: kun kolesterolmålinger av dem (det vi kaller screeningen) 4000: studien, måle mer enn kolesterol (det vi kaller intervensjonsstudien).	
Inkluderes det myndige personer med redusert eller manglende samtykkekompetanse?	Ja ○ Nei ●	Begrunn hvorfor det er nødvendig å inkludere myndige personer med redusert eller manglende samtykkekompetanse. Les mer om Pasienter, brukere og personer med redusert eller manglende samtykkekompetanse
Hvis ja, begrunn		
8. Metode for innsamling av personopplysninger		
Kryss av for hvilke datainnsamlingsmetoder og datakilder som vil benyttes	■ Spørreskjema □ Personlig intervju □ Gruppeintervju □ Observasjon □ Psykologiske/pedagogiske tester ■ Medisinske undersøkelser/tester □ Journaldata ■ Registerdata □ Annen innsamlingsmetode	Personopplysninger kan innhentes direkte fra den registrerte f.eks. gjennom spørreskjema, intervju, tester, og/eller ulike journaler (f.eks. elevmapper, NAV, PPT, sykehus) og/eller registre (f.eks. Statistisk sentralbyrå, sentrale helseregistre).
Annen innsamlingsmetode, oppgi hvilken		
Kommentar	Det skal samles registerdata etter 2 og 5 år av dem som blir stratifisert til høy risikogruppen. Koblingene vil bli til reseptregisteret, pasientregisteret og dødsårsaksregisteret.	
9. Datamaterialets innhold		

Redegjør for hvilke opplysninger som samles inn	Alle deltagerne skal svare på et spørreskjema med ulike demografiske og sosioøkonomiske variabler. Det vil også være spørsmål om blant annet tidligere målinger og verdier av blodsukker, blodtrykk og kolesterol, samt forekomst av hjerte- og karsykdommer, behandlinger og medikamenter tilknyttet disse sykdommene.	Spørreskjema, intervju-/temaguide, observasjonsbeskrivelse m.m. sendes inn sammen med meldeskjemaet. NB! Vedleggene lastes opp til sist i meldeskjema, se punkt 16 Vedlegg.
Samles det inn direkte personidentifiserende opplysninger?	Ja ● Nei ○	Dersom det krysses av for ja her, se nærmere under punkt 11 Informasjonssikkerhet. Les mer om hva personopplysninger er NB! Selv om opplysningene er anonymiserte i oppgave/rapport, må det krysses av dersom direkte og/eller indirekte personidentifiserende opplysninger innhentes/registreres i forbindelse med prosjektet.
Hvis ja, hvilke?	■ 11-sifret fødselsnummer ■ Navn, fødselsdato, adresse, e-postadresse og/eller telefonnummer	
Spesifiser hvilke	Navn, fødselsnummer, adresse, e-post, telefonnummer	
Samles det inn indirekte personidentifiserende opplysninger?	Ja ● Nei ○	En person vil være indirekte identifiserbar dersom det er mulig å identifisere vedkommende gjennom bakgrunnsopplysninger som for eksempel bostedskommune eller arbeidsplass/skole kombinert med opplysninger som alder, kjønn, yrke, diagnose, etc. Kryss også av dersom ip-adresse registreres.
Hvis ja, hvilke?	Fylke, hvilket land er dine foreldre født i (ikke spesifisert mor/far), har du hatt tidligere hjerte- og karsykdommer, og om noen i familien har hatt det (spør kun indirekte om det er første- og andregradsslekninger). Disse opplysningene blir kombinert med alder, kjønn.	
Samles det inn sensitive personopplysninger?	Ja ● Nei ○	
Hvis ja, hvilke?	■ Rasemessig eller etnisk bakgrunn, eller politisk, filosofisk eller religiøs oppfatning □ At en person har vært mistenkt, siktet, tiltalt eller dømt for en straffbar handling ■ Helseforhold □ Seksuelle forhold □ Medlemskap i fagforeninger	
Samles det inn opplysninger om tredjeperson?	Ja ● Nei ○	Med opplysninger om tredjeperson menes opplysninger som kan spores tilbake til personer som ikke inngår i utvalget. Eksempler på tredjeperson er kollega, elev, klient, familiemedlem.
Hvis ja, hvem er tredjeperson og hvilke opplysninger registreres?	Vi spør om foreldrenes fødeland og hjerte- og karsykdommer i familien. Men istedenfor å samle inn spesifikk informasjon om hvem det gjelder, spør vi heller om fødeland for mor eller far og hjertekarsykdommer hos første (mor/far/søsken) eller andregradssslekninger (onkel/tante/besteforeldre) i disse spørsmålene.	
Hvordan informeres tredjeperson om behandlingen?	□ Skriftlig □ Muntlig ■ Informeres ikke	
Informeres ikke, begrunn	Fordi vi deler inn i første- og andregradsslektninger og spør ikke spesifikt om det er mor, far, søster osv, og innhenter heller ikke opplysninger som navn eller fødselsdato.	
10. Informasjon og samtykke		
Oppgi hvordan utvalget informeres	■ Skriftlig ■ Muntlig □ Informeres ikke	Vennligst send inn informasjonsskrivet eller mal for muntlig informasjon sammen med meldeskjema. NB! Vedlegg lastes opp til sist i meldeskjemaet, se punkt 16 Vedlegg. Dersom utvalget ikke skal informeres om behandlingen av personopplysninger må det begrunnes. Last ned vår veiledende mal til informasjonsskriv
Begrunn		

Oppgi hvordan samtykke fra utvalget innhentes	■ Skriftlig □ Muntlig □ Innhentes ikke	Dersom det innhentes skriftlig samtykke anbefales det at samtykkeerklæringen utformes som en svarslipp eller på eget ark. Dersom det ikke skal innhentes samtykke, må det begrunnes.
Innhentes ikke, begrunn		
11. Informasjonssikkerhet		
Direkte personidentifiserende opplysninger erstattes med et referansenummer som viser til en atskilt navneliste (koblingsnøkkel)	Ja ● Nei ○	Har du krysset av for ja under punkt 9 Datamaterialets innhold må det merkes av for hvordan direkte personidentifiserende opplysninger registreres. NB! Som hovedregel bør ikke direkte personidentifiserende opplysninger registreres sammen med det øvrige datamaterialet.
Hvordan oppbevares navnelisten/ koblingsnøkkelen og hvem har tilgang til den?	Under studien skal koblingslisten med ID-nummer og personopplysninger oppbevares innelåst i safe på ulike Boots apotek. Hvert apotek har en koblingsliste (dette gjelder kun de 50 studie-apotekene). Etter studien sendes koblingslisten til UiO, hvor den oppbevares innelåst på kontor. På apotek har helsepersonell tilgang til navnelisten mens studien pågår, men etter dette skal den sendes til UiO og da vil kun prosjektleder og daglig ansvarlig (stipendiaten) ha tilgang til denne.	
Direkte personidentifiserende opplysninger oppbevares sammen med det øvrige materialet	Ja ○ Nei ●	
Hvorfor oppbevares direkte personidentifiserende opplysninger sammen med det øvrige datamaterialet?		
Oppbevares direkte personidentifiserbare opplysninger på andre måter?	Ja ○ Nei ●	
Spesifiser		
Hvordan registreres og oppbevares datamaterialet?	□ Fysisk isolert datamaskin tilhørende virksomheten ■ Datamaskin i nettverkssystem tilhørende virksomheten □ Datamaskin i nettverkssystem tilknyttet Internett tilhørende virksomheten □ Fysisk isolert privat datamaskin □ Privat datamaskin tilknyttet Internett □ Videoopptak/fotografi □ Lydopptak ■ Notater/papir □ Annen registreringsmetode	Merk av for hvilke hjelpemidler som benyttes for registrering og analyse av opplysninger. Sett flere kryss dersom opplysningene registreres på flere måter.
Annen registreringsmetode beskriv		
Behandles lyd-/videoopptak og/eller fotografi ved hjelp av datamaskinbasert utstyr?	Ja ○ Nei ●	Kryss av for ja dersom opptak eller foto behandles som lyd-/bildefil. Les mer om behandling av lyd og bilde.
Hvordan er datamaterialet beskyttet mot at uvedkommende får innsyn?	Datamaskintilgangen beskyttes med brukernavn og passord, og lagres på egen forskningsserver på UiO. Koblingslisten oppbevares innelåst. Utfylte spørreskjemaer med ID-nummer oppbevares innelåst på kontoret til prosjektleder og avskilt fra koblingslisten.	Er f.eks. datamaskintilgangen beskyttet med brukernavn og passord, står datamaskinen i et låsbart rom, og hvordan sikres bærbare enheter, utskrifter og opptak?
Dersom det benyttes mobile lagringsenheter (bærbar datamaskin, minnepenn, minnekort, cd, ekstern harddisk, mobiltelefon), oppgi hvilke		NB! Mobile lagringsenheter bør ha mulighet for kryptering.
Vil medarbeidere ha tilgang til datamaterialet på lik linje med daglig ansvarlig/student?	Ja ○ Nei ●	
Hvis ja, hvem?		

Overføres personopplysninger ved hjelp av e-post/Internett?	Ja ○ Nei ●	F.eks. ved bruk av elektronisk spørreskjema, overføring av data til samarbeidspartner/databehandler mm.
Hvis ja, hvilke?		
Vil personopplysninger bli utlevert til andre enn prosjektgruppen?	Ja ● Nei ○	
Hvis ja, til hvem?	Kun evt. når registerkoblinger skal utføres.	
Samles opplysningene inn/behandles av en databehandler?	Ja ○ Nei ●	Dersom det benyttes eksterne til helt eller delvis å behandle personopplysninger, f.eks. Questback, Synovate MMI, Norfakta eller transkriberingsassistent eller tolk, er dette å betrakte som en databehandler. Slike oppdrag må kontraktsreguleres Les mer om databehandleravtaler her
Hvis ja, hvilken?		
12. Vurdering/godkjenning fra andre instanser		
Søkes det om dispensasjon fra taushetsplikten for å få tilgang til data?	Ja ○ Nei ●	For å få tilgang til taushetsbelagte opplysninger fra f.eks. NAV, PPT, sykehus, må det søkes om dispensasjon fra taushetsplikten. Dispensasjon søkes vanligvis fra aktuelt departement. Dispensasjon fra taushetsplikten for helseopplysninger skal for alle typer forskning søkes Regional komité for medisinsk og helsefaglig forskningsetikk
Kommentar		
Søkes det godkjenning fra andre instanser?	Ja ● Nei ○	F.eks. søke registereier om tilgang til data, en ledelse om tilgang til forskning i virksomhet, skole, etc.
Hvis ja, hvilke?	Universitetet i Oslo, REK (godkjent)	
13. Prosjektperiode		
Prosjektperiode	Prosjektstart:08.09.2014 Prosjektslutt:01.02.2022	Prosjektstart Vennligst oppgi tidspunktet for når førstegangskontakten med utvalget opprettes og/eller datainnsamlingen starter. Prosjektslutt Vennligst oppgi tidspunktet for når datamaterialet enten skal anonymiseres/slettes, eller arkiveres i påvente av oppfølgingsstudier eller annet. Prosjektet anses vanligvis som avsluttet når de oppgitte analyser er ferdigstilt og resultatene publisert, eller oppgave/avhandling er innlevert og sensurert.
Hva skal skje med datamaterialet ved prosjektslutt?	□ Datamaterialet anonymiseres ■ Datamaterialet oppbevares med personidentifikasjon	Med anonymisering menes at datamaterialet bearbeides slik at det ikke lenger er mulig å føre opplysningene tilbake til enkeltpersoner.NB! Merk at dette omfatter både oppgave/publikasjon og rådata. Les mer om anonymisering
Hvordan skal datamaterialet anonymiseres?		Hovedregelen for videre oppbevaring av data med personidentifikasjon er samtykke fra den registrerte. Årsaker til oppbevaring kan være planlagte oppfølgningsstudier, undervisningsformål eller annet. Datamaterialet kan oppbevares ved egen institusjon, offentlig arkiv eller annet. Les om arkivering hos NSD
Hvorfor skal datamaterialet oppbevares med personidentifikasjon?	Fordi det skal utføres koblinger til sentrale helseregistre etter 2 og 5 år. Datamaterialet er derimot avidentifisert og koblingslitsten oppbevares avskilt.	
Hvor skal datamaterialet oppbevares, og hvor lenge?	Navnlister eller koblingslister skal oppbevares innelåst på Universitetet i Oslo helt til alle eventuelle registerkoblinger er utført og data publisert, innen utgangen av 2022.	

14. Finansiering		
Hvordan finansieres prosjektet?	Doktorgradsprosjektet finansieres av Universitetet i Oslo, Boots apotek Norge, Mills DA sponser markedsføringen og alle målingene som skal utføres.	
15. Tilleggsopplysninger		
Tilleggsopplysninger	Prosjektet er godkjent av REK sør-øst	
16. Vedlegg		
Antall vedlegg	4	

Attachment 4

Norsk samfunnsvitenskapelig datatjeneste AS
NORWEGIAN SOCIAL SCIENCE DATA SERVICES

Harald Hårfagres gate 29
N-5007 Bergen
Norway
Tel: +47-55 58 21 17
Fax: +47-55 58 96 50
nsd@nsd.uib.no
www.nsd.uib.no
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Karianne Svendsen
Institutt for medisinske basalfag Universitetet i Oslo
Postboks 1110 Blindern
0317 OSLO

Vår dato: 03.09.2014 Vår ref: 39255 / 4 / JSL Deres dato: Deres ref:

TILBAKEMELDING PÅ MELDING OM BEHANDLING AV PERSONOPPLYSNINGER

Vi viser til melding om behandling av personopplysninger, mottatt 04.08.2014. Meldingen gjelder prosjektet:

39255	*Vaskulære helseundersøkelser i apotek. En randomisert, kontrollert studie av effekten av risikoidentifisering i apotek, og en studie for å monitorere endringer i risikofaktorer i populasjonen fra 2012-2014*
Behandlingsansvarlig	*Universitetet i Oslo, ved institusjonens øverste leder*
Daglig ansvarlig	*Karianne Svendsen*

Personvernombudet har vurdert prosjektet og finner at behandlingen av personopplysninger utløser konsesjonsplikt i henhold til personopplysningsloven § 33 1. ledd.

I henhold til avtalen med Universitetet i Oslo er meldingen behandlet og innstilling sendt til Datatilsynet for vurdering av konsesjonsspørsmålet. Det er anbefalt at prosjektet gis konsesjon. Kopi av vår innstilling til Datatilsynet følger vedlagt.

Det gjøres oppmerksom på at det skal gis ny melding dersom behandlingen endres i forhold til de opplysninger som ligger til grunn for personvernombudets vurdering. Endringsmeldinger gis via et eget skjema, http://www.nsd.uib.no/personvern/meldeplikt/skjema.html. Det skal også gis melding etter tre år dersom prosjektet fortsatt pågår. Meldinger skal skje skriftlig til ombudet.

Personvernombudet har lagt ut opplysninger om prosjektet i en offentlig database, http://pvo.nsd.no/prosjekt.

Personvernombudet vil ved prosjektets avslutning, 01.02.2022, rette en henvendelse angående status for behandlingen av personopplysninger.

Dersom noe er uklart ta gjerne kontakt over telefon.

Vennlig hilsen

Katrine Utaaker Segadal

Juni Skjold Lexau

Kontaktperson: Juni Skjold Lexau tlf: 55 58 36 01

Dokumentet er elektronisk produsert og godkjent ved NSDs rutiner for elektronisk godkjenning.

Avdelingskontorer / *District Offices*:
OSLO: NSD. Universitetet i Oslo, Postboks 1055 Blindern, 0316 Oslo. Tel: +47-22 85 52 11. nsd@uio.no
TRONDHEIM: NSD. Norges teknisk-naturvitenskapelige universitet, 7491 Trondheim. Tel: +47-73 59 19 07. kyrre.svarva@svt.ntnu.no
TROMSØ: NSD. SVF, Universitetet i Tromsø, 9037 Tromsø. Tel: +47-77 64 43 36. nsdmaa@sv.uit.no

Vedlegg: Prosjektvurdering

Personvernombudet for forskning

Prosjektvurdering - Kommentar

Prosjektnr: 39255

BAKGRUNN
Det skal gjennomføres en randomisert kontrollert studie av effekten av risikoidentifisering av ukjent høy risiko for hjerte-karsykdommer i apotek. Etter 2 og 5 år vil data fra studien kobles mot Reseptregisteret, Pasientregisteret og Dødsårsaksregisteret for å se på langtidseffekten av kunnskap om egen risiko.

Prosjektet omfattes av helseforskningsloven og er, etter klage og et par endringer, godkjent av Regional komité for medisinsk og helsefaglig forskningsetikk (se vedlagte dokumenter).

Søknaden her gjelder kun koblingen til registrene, da den øvrige studien er vurdert og godkjent av REK. Koblingen mot Reseptregisteret utløser konsesjonsplikt til Datatilsynet, jf. helseregisterloven § 5, jf. Reseptregisterforskriften § 5-3, jf. personopplysningsloven § 33.

Personvernombudet vurderer at prosjektets formål faller inn under formålet til Reseptregisteret, jf. Reseptregisterforskriften § 1-3.

FORMÅL
Det overordnede målet med prosjektet er å bidra med ny kunnskap om helseundersøkelser (screening) i apotek. Vi ønsker å vurdere om det å få kunnskap om ukjent høy risiko for hjerte-kar sykdommer vil føre til positive endringer i verdier av risikofaktorene, kosthold, livsstil, og fysisk aktivitet etter 8 og 52 uker. Videre vil langtidseffekten av kunnskap om egen risiko vurderes i ett langtidsperspektiv ved å utføre koblinger til sentrale helseregistre etter 2 og 5 år.

Hovedhensikten med koblingen til registrene er å se på langtidseffekter av intervensjonen. Dvs se om deltagerne har fått ulike sykdommer og om de overlever eller dør, samt om de har startet på relevante medikamenter etter intervensjonen.

Se for øvrig vedlagt prosjektbeskrivelse.

UTVALG
Det skal gjennomføres gratis kolesterolmålinger i apotek i 150 Boots apotek. I 50 av Boots apotekene kan man samtykke til å måle blodtrykk, HbA1c (langtidsblodsukker) , LDL- og HDL-kolesterol, triglyserider, vekt og høyde i tillegg til målingen av totalkolesterol. Alle i Norge som har mulighet og ønsker det kan måle kolesterolet sitt gratis i apotek i studieuken. Basert på tidligere erfaringer, og det at 50 av apotekene skal tilby flere målinger enn bare totalkolesterol, estimeres det at 10-15000 personer vil måle kolesterolet. Omtrent 4000 av dem skal rekrutteres til studien. Disse skal deles i to grupper - høyrisiko og lavrisikogruppen. I høy risikogruppen skal deltagerne blokk-randomiseres til 3 grupper; 1 intervensjon og 2 kontrollgrupper.

METODE OG DATAINNSAMLING

Data fra undersøkelsen samles inn ved hjelp av følgende metoder:

Målinger av kolesterol m.m. i apotek (anonymt for dem som ikke skal delta videre i studien).

I apotekene vil deltagerne som kommer for å måle kolesterolet sitt, motta informasjon om den videre studien, spørreskjema og samtykkeerklæring for videre deltakelse. De som tilfredsstiller kriteriene for videre deltakelse, blir spurt om å delta. Intervensjonsgruppen får vite sin skår (sine verdier) umiddelbart etter målingen, mens kontrollgruppen først får vite sin skår (sine verdier) etter 8 uker. Like etter det første besøket denne første testen, vil deltakerne bli bedt om å besvare et kostholdsspørreskjema.

De som tilfredsstiller kriteriene for videre deltakelse, blir spurt om å delta i en studie. Intervensjonsgruppen får vite sin skår umiddelbart etter målingen, mens kontrollgruppen først får vite sin skår etter 8 uker. Like etter denne første testen, vil deltakerne bli bedt om å besvare et kostholdsspørreskjema.

Deltakerne inviteres til nye prøvetakinger etter 8 uker, samt å besvare et spørreskjema.

Etter ca 1 år kan det tenkes at deltakerne inviteres på nytt til å ta nye prøver og besvare nye spørreskjema.

Etter 2 og 5 år vil det innhentes opplysninger fra Reseptregisteret, Norsk pasientregister og Dødsårsaksregisteret for å se på langtidseffekten av intervensjonen. Målet er å se om målgruppen endrer adferd i forhold til resultatene fra målingene, kostholds- og livsstilsendringer eller endringer i medisinbruk, legekontakt o.l.

Variabellistene (se vedlegg) viser fullstendig oversikt over de opplysninger som er nødvendig å inkludere fra registrene for å oppfylle formålet med studien.

PERSONOPPLYSNINGER
Det registreres en rekke personopplysninger om deltakerne. Personnummer, navn og kontaktopplysninger. Alder, kjønn, fylke, foreldres landbakgrunn/verdensdel, vekt, høyde, helsetilstand m.m.

Datamaterialet vil inneholde sensitive opplysninger om helseforhold.

DATASIKKERHET
Under datainnsamlingsperioden (8 uker) skal koblingslisten med ID-nummer oppbevares innelåst i safe på ulike Boots apotek til andre måling er gjennomført. Deretter skal denne sendes til UiO, hvor den skal oppbevares på innelåst kontor. Kun prosjektleder og daglig ansvarlig (stipendiaten) skal ha tilgang til denne ved UiO. Helsepersonell vil ha tilgang til listen i datainnsamlingsperioden.

Datasettet oppbevares på pc i nettverkssystem tilhørende virksomheten (UiO).

Boots apotekene og Reseptregisteret er databehandlere for prosjektet. UiO skal inngå skriftlig avtale med databehandlerne om hvordan personopplysninger skal behandles, jf. personopplysningsloven § 15.

Det er oppgitt at studien er et samarbeidsprosjekt med Boots apotek, Mills DA, Universitetet i Tromsø og Universitetet i Minnesota. Det er imidlertid UiO som er behandlingsansvarlig institusjon og som har ansvar for

studien og behandlingen av personopplysninger.

KOBLINGSPROSEDYRE
Datamaterialet skal kobles med Dødsårsaksregisteret (DR), Pasientregisteret (PR), og reseptregisteret (RP). SSB forvalter nøkkelfilen. Det inngår ingen SSB-variabler i koblingen.

Koblingen vil foregå slik:
1 SSB får en fil fra Universitetet i Oslo (UiO) med fødselsnummer og data. Fødselsnummer fjernes og erstattes med et nytt SSB-løpenummer
2. SSB påfører ID for DR, PR og RP for å kunne koble mot disse registrene
3. Registrene kobler sine data på ID-filen og sender den til SSB
4. SSB erstatter ID for registrene med nytt SSB-løpenummer på ID-filen og sender denne filen til prosjektansvarlig sammen med den opprinnelige datafilen fra UiO (uten fødselsnummer, med SSB-løpenummer). Begge filene vil ha samme løpenummerserie.
5. Prosjektleder kobler sammen datafilene ved hjelp av PID, og kontrollerer/kvalitetssikrer den sammenstilte datafilen. Prosjektleder sender deretter filen med PID til FHI som kobler på reseptregisterdata i tråd med registerets retningslinjer (vedlegg 6): http://www.fhi.no/dokumenter/60b07a1072.pdf

BEHANDLINGSGRUNNLAG
Behandlingen av personopplysninger hjemles i personopplysningsloven §§ 8 første alternativ og 9 a).

Utvalget informeres skriftlig og muntlig om studien, og samtykker skriftlig til deltakelse. Det er i informasjonsskrivet oppgitt at materialet etter 2 og 5 år skal kobles mot Reseptregisteret, Pasientregisteret og Dødsårsaksregisteret.

ANDRE GODKJENNINGER
Prosjektet er godkjent av Regional komite for medisinsk og helsefaglig forskningsetikk (ref.: 2013/1660/REK sør-øst) . Registereiere søkes om tilgang til data.

PROSJEKTSLUTT
Prosjektet er planlagt avsluttet innen 01.02.2022. På grunn av REKs krav til kontroll og etterprøvbarhet av resultatene, må datamaterialet oppbevares i fem år etter prosjektslutt. Det søkes derfor om konsesjon frem til 01.09.2025.

Datamaterialet skal da anonymiseres, ved at koblingsnøkkel slettes og eventuelle indirekte identifiserende opplysninger slettes eller grovkategoriseres/omskrives, slik at opplysningene ikke lenger kan tilbakeføres til enkeltpersoner.

ANBEFALING
Personvernombudet anbefaler at det gis konsesjon for behandling av person- og helseopplysninger i henhold til helseregisterloven § 5, jf. Reseptregisterforskriften
§ 5-3, jf. personopplysningsloven § 33, jf. § 34.

VEDLEGG

1) Prosjektbeskrivelse + diverse spørreskjema o.l

2) Søknader til REK og godkjenninger fra REK

3) Meldeskjema til NSD

4) Variabelliste Reseptregisteret, Pasientregisteret og Dødsårsaksregisteret

5) Koblingsbeskrivelse Reseptregisteret: http://www.fhi.no/dokumenter/60b07a1072.pdf

UiO : Universitetet i Oslo

SPØRRESKJEMA

1 Kjønn:
Merk: Sett ett kryss

- ☐ Mann
- ☐ Kvinne

2 Alder - Fyll inn antall år

☐☐ År (ett tall i hver rute)

3 Hvilket fylke bor du i?
Merk: Sett ett kryss

- ☐ Akershus
- ☐ Aust Agder
- ☐ Buskerud
- ☐ Finnmark
- ☐ Hedmark
- ☐ Hordaland
- ☐ Møre og Romsdal
- ☐ Nord- Trøndelag
- ☐ Nordland
- ☐ Oppland
- ☐ Oslo
- ☐ Rogaland
- ☐ Sogn og Fjordane
- ☐ Sør-Trøndelag
- ☐ Telemark
- ☐ Troms
- ☐ Vest Agder
- ☐ Vestfold
- ☐ Østfold

4 Hvilket land/verdensdel er dine foreldre født i?
Merk: Flere kryss mulig

- ☐ Norge
- ☐ Norden unntatt Norge
- ☐ Vest-Europa
- ☐ EU-land i Øst-Europa
- ☐ Øst-Europa ellers og Russland
- ☐ Afrika
- ☐ Asia med Tyrkia
- ☐ Sør- og Mellom-Amerika
- ☐ Nord-Amerika og Oseania

5 Har du målt kolesterolet ditt før?
Merk: Sett ett kryss

- ☐ Ja → Gå til 6
- ☐ Nei → Gå til 8
- ☐ Vet ikke/husker ikke → Gå til 8

6 Hvor målte du kolesterolet ditt?
Merk: Flere kryss mulig

- ☐ Apotek
- ☐ Fastlegen
- ☐ Bedriftshelsetjenesten
- ☐ Sykehus
- ☐ Annet

7 Fikk du beskjed om at kolesterolverdien din ved *siste* måling var:
Merk: Sett ett kryss

- ☐ Under 5
- ☐ 5-6
- ☐ 6-7
- ☐ 7-8
- ☐ Over 8
- ☐ Husker ikke
- ☐ Fikk ikke vite svaret

8 Har du målt blodtrykket ditt tidligere?
Merk: Sett ett kryss

- ☐ Ja → Gå til 9
- ☐ Nei → Gå til 10
- ☐ Vet ikke → Gå til 10

9 Fikk du beskjed om at blodtrykket ditt ved *siste* måling var:
Merk: Sett ett kryss

- ☐ Lavt
- ☐ Normalt
- ☐ Litt forhøyet
- ☐ Høyt
- ☐ Husker ikke
- ☐ Fikk ikke vite svaret

10 Har du målt blodsukkeret ditt tidligere?
Merk: Sett ett kryss

- ☐ Ja → Gå til 11
- ☐ Nei → Gå til 12
- ☐ Vet ikke → Gå til 12

11 **Fikk du beskjed om at <u>blodsukkeret</u> ditt ved *siste* måling var:**

Merk: Sett ett kryss

- ☐ Lavt
- ☐ Normalt
- ☐ Litt forhøyet
- ☐ Høyt
- ☐ Husker ikke
- ☐ Fikk ikke vite svaret

12 **Hva er din høyeste oppnådde utdanning?**

Merk: Sett ett kryss

- ☐ Grunnskole
- ☐ Videregående (allmennfag, yrkesskole, realskole, husmorskole)
- ☐ Høgskole/universitet 1-3 år
- ☐ Høgskole/universitet 4 år eller mer

13 **Omtrent hvor ofte mosjonerer du i minst 30 minutter slik at du blir lett andpusten eller svett?**

(Eks: Rask gange, løping, skigåing, sykling, svømming o.l.)

Merk: Sett ett kryss

- ☐ Aldri
- ☐ Sjeldnere enn 1 gang i uka
- ☐ 1-2 ganger i uka
- ☐ 3-4 ganger i uka
- ☐ 5 ganger eller flere i uka

14 **Hvor høy var husstandens samlede bruttoinntekt det siste året?**

(Ta med alle inntekter fra arbeid, trygder, sosialhjelp og lignende. Sett kryss ved det mest passende alternativet)

Merk: Sett ett kryss

- ☐ Under 150 000 kr
- ☐ 151 000 – 300 000 kr
- ☐ 301 000 – 450 000 kr
- ☐ 451 000 – 600 000 kr
- ☐ 601 000 – 750 000 kr
- ☐ 751 000 – 900 000 kr
- ☐ Over 900 000 kr
- ☐ Ønsker ikke å svare

15 **Hva er din sivilstatus?**

Merk: Sett ett kryss

- ☐ Gift/registrert partner
- ☐ Samboende
- ☐ Ugift/ikke samboende
- ☐ Tidligere gift (enke/enkemann/skilt)

16 **Røyker du?**

Merk: Sett ett kryss

- ☐ Nei, jeg har aldri røykt
- ☐ Nei, jeg har sluttet å røyke
- ☐ Ja, daglig
- ☐ Ja, av og til (fest, ferie, <u>*ikke*</u> daglig)

17 **Har noen i din slekt fått hjerteinfarkt, angina/hjertekrampe eller slag i ung alder?**

(Ung alder er under 55 år for menn og under 65 år for kvinner)

Merk: Flere kryss mulig

- ☐ Ja, mor/far/søsken
- ☐ Ja, onkel/tante/besteforeldre
- ☐ Nei
- ☐ Vet ikke

18 **Har du hatt noen av disse sykdommene/ behandlingene?**

Merk: Flere kryss mulig

- ☐ Hjerteinfarkt
- ☐ Hjerneslag
- ☐ Hjertekrampe/angina pectoris
- ☐ Utblokking i hjertets blodårer
- ☐ By-pas operasjon på hjerte
- ☐ Utposing av hovedpulsåra
- ☐ Nei, ingen

19 **Bruker du noen av medisinene nevnt nedenfor nå?**

Merk: Flere kryss mulig

- ☐ Ja, blodtrykksenkende
- ☐ Ja, kolesterolsenkende
- ☐ Ja, mot sukkersyke/diabetes
- ☐ Ja, blodfortynnende
- ☐ Nei, ingen

20 **Omtrent hvor lenge er det siden du har spist og/eller drukket noe annet enn *vann* i dag?**

Merk: Sett ett kryss

- ☐ Under 1 time
- ☐ 1-3 timer
- ☐ Mer enn 3, men mindre enn 8 timer
- ☐ 8 timer eller mer

Fylles ut av apotekpersonell:

TABELL 1 FOR BESØK 1:

Dato i dag:

☐☐☐☐ ddmm

Referanseområdet
(Målingene utenfor referanseområdet oppgis med henholdsvis laveste eller høyeste mulig verdi)

Blodtrykk 1.gang (SYS) (mmHg)

☐☐☐ *20-280 (0 hvis ikke mulig å måle)*

Blodtrykk 1.gang (DIA) (mmHg)

☐☐☐ *20-280 (0 hvis ikke mulig å måle)*

Blodtrykk 2.gang (SYS) (mmHg)

☐☐☐ *20-280 (0 hvis ikke mulig å måle)*

Blodtrykk 2.gang (DIA) (mmHg)

☐☐☐ *20-280 (0 hvis ikke mulig å måle)*

Hba1c (%)

☐☐,☐ *4,0-15,0*

Totalkolesterol (chol) (mmol/L)

☐☐,☐☐ *2,59-12,95*

LDL (mmol/L)

☐☐,☐☐

HDL (mmol/L)

☐☐,☐☐ *0,39-2,59*

Triglyserider (trig) (mmol/L)

☐☐,☐☐ *0,51-7,34*

Vekt (kg)

☐☐☐,☐

Høyde (cm)

☐☐☐,☐

BMI (beregnes i LINK)

☐☐,☐

Gruppe:
Merk: Sett ett kryss

- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4
- ☐ 5

ID-nummer festes her:

TABELL 2 FOR BESØK 2:

Dato i dag:

				ddmm

Referanseområdet
(Målingene utenfor referanseområdet oppgis med henholdsvis laveste eller høyeste mulig verdi)

Blodtrykk 1.gang (SYS) (mmHg)

			20-280 (0 hvis ikke mulig å måle)

Blodtrykk 1.gang (DIA) (mmHg)

			20-280 (0 hvis ikke mulig å måle)

Blodtrykk 2.gang (SYS) (mmHg)

			20-280 (0 hvis ikke mulig å måle)

Blodtrykk 2.gang (DIA) (mmHg)

			20-280 (0 hvis ikke mulig å måle)

Hba1c (%)

		,		*4,0-15,0*

Totalkolesterol (chol) (mmol/L)

		,			*2,59-12,95*

LDL (mmol/L)

		,		

HDL (mmol/L)

		,			*0,39-2,59*

Triglyserider (trig) (mmol/L)

		,			*0,51-7,34*

Vekt (kg)

			,	

Høyde (cm)

			,	

BMI (beregnes med formel)

		,	

Attachment 6

Samtykke til å innhente flere opplysninger

Da du var i apotek i september i fjor, samtykket du til å delta i forskningsprosjektet *"Effekt av vaskulær screening i apotek"*

Med bakgrunn i av at du har møtt opp på 52-ukers oppfølgingsbesøk, er dette en forespørsel om du samtykker til at det samles inn flere opplysninger fra deg:

Hva innebærer det i dag?

Du vil ta en ekstra fingerstikk-blodprøve og får med deg materiell for ny blodprøve hjem.

Hva innebærer det om ca. 4 uker?

Du tar fingerstikk-blodprøven du har fått med deg ved å følge prosedyren som ble vist i apotek og som står i pakningsvedlegget. Prøven tørkes og returneres.

Du vil få et kostholdsspørreskjema i posten som fylles ut og returneres i konvolutten du får med.

Du vil motta en påminnelse når dette skal gjøres

Fordelene er at du vil få ekstra informasjon om ditt nivå av fettstoffer som omega 3 og omega 6 i forhold til anbefalingene pr post når resultatene foreligger

---

Ulempene er at du får en ekstra blodprøve i dag, og får med deg utstyr hjem til å ta blodprøven og svare på kostholdsspørreskjemaet på nytt

Du kan velge å være med på alt eller bare noe. Vennligst kryss av ja eller nei på hva du er villig til:

Jeg er villig til å ta en ekstra blodprøve i dag:
ja / nei
Jeg er villig til å få med meg utstyr hjem og etter beste evne ta blodprøven på nytt hjemme:
Ja / nei
Jeg er villig til å få kostholdsspørreskjemaet i posten og etter beste evne fylle det ut og returnere det: ja / nei

---

(Signert av prosjektdeltaker, sted, dato)

Ved spørsmål, vennligst kontakt: Karianne Svendsen
22 85 12 10/ karianne.svendsen@medisin.uio.no

* Helsepersonell: Husk å registrere ID-nummer med svar

SPØRRESKJEMA KOSTHOLD OG FYSISK AKTIVITET

Vi ønsker opplysninger om ditt vanlige kosthold for en gjennomsnittlig uke.
Ha de siste 2 månedene i tankene når du fyller ut.

Skjemaet skal leses av en maskin og det er derfor viktig at du setter tydelige kryss i rutene. Bruk blå eller sort kulepenn. Alle svar vil behandles fortrolig.

Riktig markering i rutene er slik: [X]
Ved feil markering, fyll hele ruten slik: ■

Av hensyn til den maskinelle lesningen - pass på at arkene ikke brettes.
Har du spørsmål angående utfyllingen av skjemaet kan du ringe:
Karianne Svendsen på prosjekttelefon: 22 85 12 10

ID ☐☐☐☐☐ **Besøk 1**

1. FRUKT

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr.gang				
	0	1	2	3	4	5	6-7	8+					
Stor frukt (f.eks. et helt eple, nektarin, banan, appelsin, en skive melon o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Mellomstor frukt (f.eks. klementiner, kiwi, plommer o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐

2. NØTTER

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr.gang				
	0	1	2	3	4	5	6-7	8+					
Usaltede nøtter (f.eks. mandler, peanøtter, valnøtter, cashew, ferdig blandinger o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(neve= 25g)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Saltede nøtter (f.eks. peanøtter, valnøtter, ferdige blandinger, chilinøtter, pekannøtter, mandler o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(neve= 25g)	1/2 ☐	1 ☐	2 ☐	3+ ☐

3. GRØNNSAKER (ikke potet)

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr.gang					
	0	1	2	3	4	5	6-7	8+						
Hvitløk (friske, hermetiske)	☐	☐	☐	☐	☐	☐	☐	☐	(fedd=båt)	1/4 ☐	1/2 ☐	1 ☐	2 ☐	3+ ☐
Løk, vårløk og purre	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Tomat (friske, 6 cherry= 1 vanlig tomat)	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(liten bolle=100g)	1/4 ☐	1/2 ☐	1 ☐	2 ☐	3+ ☐
Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål, frosne blandinger o.l)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐

4. KORN

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr. gang				
	0	1	2	3	4	5	6-7	8+					
Søtet frokostblanding (f.eks.Corn Flakes, Chocofrokost o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Usøtet frokostblanding eller grøt (f.eks. havregrøt, 4-Korn o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1/2 ☐	1 ☐	2 ☐	3+ ☐

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5. DRIKKE

	Hvor mange ganger pr. uke drakk du								Hvor mye drakk du pr.gang						
	0	1	2	3	4	5	6-7	8+		1/2	1	2	3-4	5-6	7+
Vann (springvann, flaskevann)	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Annen drikke uten tilsatt sukker (f.eks. farris, lettsaft, lettbrus o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Juice (f.eks. eplejuice, appelsinjuice, Manajuice o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Annen drikke tilsatt sukker (f.eks. brus, saft, nektar o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Helmelk, kulturmelk, kefir o.l.	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Lettmelk, ekstra lettmelk, cultura, biola naturell o.l.	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Skummet melk, skummet kulturmelk, biola bærdrikk 0,1 % fett o.l.	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Øl med alkohol	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Vin med alkohol	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Brennevin	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Kaffe (filtermalt)	☐	☐	☐	☐	☐	☐	☐	☐	(kopp)	☐	☐	☐	☐	☐	☐
Annen type kaffe (espresso,presskanne,kapsel, kokmalt o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(kopp)	☐	☐	☐	☐	☐	☐

6. MEIERIPRODUKTER

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr. gang						
	0	1	2	3	4	5	6-7	8+		1/4	1/2	1	1 1/2	2	3+
Fete produkter (f.eks. kremfløte, creme fraiche, seterrømme o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐	☐
Halvfete produkter (f.eks. matfløte, lettrømme, yoghurt med sukker, lett creme fraiche o.l)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐	☐
Magre produkter (f.eks. kaffefløte, ekstra lett rømme, kesam, matyoghurt yoghurt naturell/Dobbel 0% o.l)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐	☐

7. BRØD (f.eks. 1/2 rundstykke = 1 skive, 1 baguett = 4 skiver, 1 ciabatta = 2 skiver)

	Hvor mange skiver spiste du pr. DAG													
	0	1/2	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød, 0-25% sammalt mel (f.eks. loff, baguetter, fine rundstykker, ciabatta)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Halvgrovt brød, 25-50% sammalt mel (f.eks. helkornbrød, kneipp, grove rundstykker)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt brød, 50-75% sammalt mel (f.eks. havrebrød)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ekstra grovt brød, 75-100% sammalt mel (f.eks. mørkt rugbrød)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fint knekkebrød (f.eks. kavring, frokost knekkebrød)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt knekkebrød (f.eks. Husmann, Sport, Solruta o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sum skiver pr.dag=_____ Antall skiver pr.uke:_____x 7=_____. Tallet brukes i spørsmål 8.
(sum skiver pr.dag)

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8. REGISTRER PÅLEGGET DU VANLIGVIS SPISER PÅ DISSE SKIVENE I LØPET AV EN UKE:

	Antall skiver pr. UKE									
	0	1	2-3	4-5	6-7	8-12	13-18	19-24	25-30	31+
Fete oster som pålegg (f.eks. hvitost, nøkkelost, Gudbrandsdalsost, brie o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Halvfete oster som pålegg (f.eks. lettere hvitost,lettere Gudbrandsdalsost, lettere smørbare oster, prim o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Andre oster som pålegg (f.eks. Vita gulost, cottage cheese, lettere prim, "lett gulost" med 10 % fett o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fete kjøttpålegg (f.eks. salami, servelat, falukorv, vanlig leverpostei o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Magre kjøttpålegg (f.eks. kokt/røkt skinke, kylling/kalkunpålegg, lett servelat, mager eller oljebaserte leverposteier o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Pålegg med sukker (f.eks. honning, syltetøy, nøttepålegg o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grønnsaker og frukt som pålegg (f.eks. paprika, agurk, avokado, banan, eple o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fiskepålegg (f.eks. makrell i tomat, røket/gravet laks, sild o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

9. EGG

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

10. Hvilken type smør/margarin/olje brukte du oftest til:

NB! Sett **ETT** kryss på hver linje	Bruker ikke	Mykt margarin (Soft Flora, Vita, Soft oliven)	Hardt smør (meierismør, Bremykt, Melange)	Oljer (olivenolje, soyaolje, rapsolje, Vita hjertego)
Matlaging, steking, baking	☐	☐	☐	☐
På brød, baguette, rundstykke	☐	☐	☐	☐

11. KOLESTEROLSENKENDE MARGARIN

	Nei	Ja, daglig	Ja, av og til	Vet ikke
Bruker du Vita Pro-Aktiv eller Becel Pro-Activ?	☐	☐	☐	☐

12. FISK TIL MIDDAG/VARM LUNSJ

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr. gang						
	0	1	2	3	4	5	6-7	8+		½	1	2	3	4	5+
Fet fisk (f.eks. laks, ørret, sild, kveite o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon= 145g)	☐	☐	☐	☐	☐	☐
Mager fisk (f.eks. torsk, sei, hyse, rødspette, breiflabb o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon= 145g)	☐	☐	☐	☐	☐	☐
Bearbeidet fisk (f.eks.fiskegrateng, fiskepudding, fiskeboller, fiskegryte o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon= 180g)	☐	☐	☐	☐	☐	☐

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13. KJØTT TIL MIDDAG/VARM LUNSJ

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr.gang						
	0	1	2	3	4	5	6-7	8+							
Fete kjøttprodukter (f.eks. familiedeig, vanlig grillpølser/wienerpølser, stek med fettrand, bacon, flesk o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =150g)	½ ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Halvfete kjøttprodukter (f.eks. kjøttdeig (okse,lam), kyllingpølse, lettpølse, hamburger, kylling med skinn o.l)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =150g)	½ ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Magre kjøttprodukter (f.eks. karbonadedeig, kjøttdeig (svin,kylling), biff, filet (kylling, svin, okse, lam), viltkjøtt, "Go' og mager pølser" o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =150g)	½ ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐

14. RIS OG PASTA

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr.gang				
	0	1	2	3	4	5	6-7	8+					
Polert, hvit ris	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Upolert, naturris	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Vanlig pasta	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Fullkornspasta	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐

15. KAKER, DESSERT, GODTERI

	Hvor mange ganger pr. uke spiste du								Hvor mye spiste du pr.gang					
	0	1	2	3	4	5	6-7	8+						
Kaker, hvetebakst, vafler, søt kjeks	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Dessert (f.eks. is, hermetisk frukt, pudding)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Sjokolade, godteri	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =100g)	1/4 ☐	1/2 ☐	1 ☐	1 1/2 ☐	2+ ☐
Potetgull, chips	☐	☐	☐	☐	☐	☐	☐	☐	(neve)	1-2 ☐	3-5 ☐	6-8 ☐	9-11 ☐	12+ ☐

16. RØYKING

	Nei	Ja, av og til	Ja, daglig
Røyker du?	☐	☐	☐
Hvis ja, hvor mange sigaretter/piper røyker du i gjenomsnitt *pr. dag*? Antall:	☐☐		

17. DAGLIG FYSISK AKTIVITET (Registrer hele treningsøkter og vanlig fysisk aktivitet i dagliglivet)

	Hvor mange ganger pr. uke var du fysisk aktiv								Hvor lenge var du fysisk aktiv pr. gang (minutter)							
	0	1	2	3	4	5	6-7	8+	1-4	5-9	10-15	16-20	21-30	31-45	46-60	60+
Moderat intensitet (f.eks. hurtig gange, fysisk aktivitet i arbeid, hardt husarbeid, annen aktivitet der du blir lett andpusten)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Høy intensitet (f.eks. jogging, skigåing, hard fysisk aktivitet i arbeid, driver trening/idrett, annen aktivitet der du blir veldig andpusten)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

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