Diet and lifestyle factors in individuals with a large reduction in non-HDL-cholesterol after a lifestyle intervention

An observational study of individuals at moderately elevated risk of cardiovascular disease

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Abstract

Background: Cardiovascular disease (CVD) is the main cause of death worldwide. Prevalence of CVD is increasing globally. Atherosclerosis is the pathophysiological process driving CVD and is often asymptomatic, with risk factors exacerbating this process. Major risk factors include high age, high blood pressure, diabetes, dyslipidemia, tobacco smoking, poor diet, and lack of physical activity. Diet and lifestyle factors (tobacco smoking, poor diet, and low physical activity) could both reduce the risk for developing CVD and other lifestyle-related diseases. However, the effect of lifestyle intervention in population groups to reduce CVD risk is not certain. Much is still unclear when it comes to which diet and lifestyle factors have the most effect in reducing CVD risk, and therefore should be prioritized in these lifestyle interventions.

Aim: Identify diet and lifestyle factors in individuals with a large reduction in non-high-density lipoprotein cholesterol (non-HDL-C) after a lifestyle intervention.

Method: A sample of 325 participants who completed an 8-week lifestyle intervention and returned for a 52-week follow-up visit was analyzed. Anthropometric, biochemical, diet, and lifestyle data related to CVD risk factors was collected during this intervention. Total, low-density lipoprotein (LDL), high-density lipoprotein (HDL) -cholesterol, and triglycerides (TG) concentrations were measured. Non-HDL-C was calculated as HDL-C subtracted from total cholesterol (TC). Participants were split into quartiles (Q) according to change in non-HDL- C from end of the 8-week intervention to the 52-week follow-up, which equals a change over a period of 44 weeks (ten months). Next, we compared diet and lifestyle factors between individuals in the lower (Q1=non-HDL-C: ≤-0.57 mmol/L) and top (Q4=non-HDL-C: ≥0.49 mmol/L) quartiles of non-HDL-C change.

Results: There were 77 participants in both Q1 and Q4. There was a significant difference in six risk factors between individuals in Q1 and Q4: TC (P<0.001), HDL-C (P<0.001), LDL-C (P<0.001), non-HDL-C (P<0.001), TG (P<0.001), and diastolic blood pressure (P=0.002). Individuals in Q1 had a healthy diet consisting of nuts, whole grains, fruits, berries, and lean protein sources, such as lean meats and lean dairy products, while their lifestyle included more daily physical activity and less smoking when compared to individuals in Q4.

Conclusion: We identified some key diet and lifestyle factors in the individuals with the largest reduction in non-HDL-C over a ten-month period.

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Table of Contents

1. Introduction *1*

2. Background *4*

2.1. Cardiovascular disease *4*

2.1.1. Atherosclerosis 4

2.2. Risk factors **5**

2.3. Lipids and lipoproteins **6**

2.4. Diet and lifestyle **7**

2.5. Current research on diet and lifestyle interventions **8**

3. Aim of the study *11*

4. Method *12*

4.1. Design **12**

4.2. Population **13**

4.3. Data collection **14**

4.3.1. Anthropometric and biochemical measures 15

4.3.2. Baseline questionnaire 15

4.3.3. VISA-FFQ 16

4.4. Statistical analysis **16**

4.4.1. Principal component analysis 17

4.5. Ethical considerations **19**

4.6. Financial considerations **19**

5. Results *20*

5.1. Descriptive statistics **20**

5.1.1. Sex differences in the study sample 20

5.1.2. Comparison of mean reduction between women and men 22

5.1.3. Comparison of quartiles 23

5.1.4. Comparison of mean reduction between quartiles 25

5.2. Dietary patterns **26**

6. Discussion *29*

6.1. Methodical evaluations **31**

6.1.1. Non-HDL-C as biomarker for CVD 32

7. Conclusion *34*

Bibliography *35*

Tables

Table 1: Background characteristics of study sample at V1 and V2 21

Table 2: Reduction in risk factors for women and men from V1 to V2 22

Table 3: Background characteristics of Q1 and Q2 at V1 and V2 24

Table 4: Reduction in risk factors for Q1 and Q4 from V1 to V2.....26

Figures

Figure 1: Selection sample eligible for analysis from total sample with data collection and visit points from the VISA-study 14
Figure 2: Scree plot of principal components (PCA) and inflection point 18
Figure 3: Loading plot showing differences in dietary patterns between quartiles 28
Figure 4: Box plots showing differences in dietary patterns between quartiles 28

Attachments

Attachment 1: Baseline questionnaire 42

Attachment 2: VISA-FFQ 46

Attachment 3: REK applications 49

Attachment 4: Prosjektplan 52

Abbreviations

Apo	Apolipoprotein
ApoB	Apolipoprotein B
BMI (kg/m^2)	Body mass index
BP	Blood pressure
CAC	Coronary artery calcification
CAD	Coronary artery disease
CHD	Coronary heart disease
CI	Confidence interval
CVD	Cardiovascular disease
HbA1c	Hemoglobin A1c (glycosylated hemoglobin)
HDL	High-density lipoprotein
HDL-C	High-density lipoprotein cholesterol
IDL	Intermediate density lipoprotein
IHD	Ischemic heart disease
LDL	Low-density lipoprotein
LDL-C	Low-density lipoprotein cholesterol
MI	Myocardial infarction
NSD	Norsk senter for Forskningsdata (Norwegian Centre for Research Data)
P1	Percentile 1 (lowest)
P10	Percentile 10 (top)
PAD	Peripheral arterial disease
PC	Principal component
PCA	Principal component analysis
Q1	Quartile 1 (lowest)
Q10	Quartile 10 (top)
RCT	Randomized controlled trial
REK	Regional Etisk Komité Helse Sør-Øst (Regional Ethical Comittee Health South-East)
SD	Standard deviation
TC	Total cholesterol
TSD	Tjenester for Sensitive Data (Services for Sensitive Data)
UiO	University of Oslo
V0	Start of VISA-intervention
V1	Visit 1
V2	Visit 2
VLDL	Very low-density lipoprotein
WHO	World Health Organization

1. Introduction

Cardiovascular disease (CVD) is a group of non-communicable diseases affecting the heart and blood vessels through the pathophysiological process of atherosclerosis (American Heart Association, 2017; World Health Organization, 2021) Fatal outcomes of CVD include heart attack and stroke. CVD are the leading cause of death globally, with an estimated 17.9 million people dying from CVD during 2019 (World Health Organization, 2021). This represents 32% of all deaths globally. The majority (85%) of these deaths were due to heart attack or stroke. In Norway, 21% of the entire population currently lives with an established CVD or are at a high risk for developing CVD (Folkehelseinstituttet, 2020). It is estimated that the proportion of people living with CVD and the global burden will increase in the future as the general population grows older and lives longer (Roth et al., 2020).

Major risk factors include age, genes, diet, and lifestyle. Age and genes are non-modifiable risk factors and thus not in the scope of lifestyle interventions. Diet and lifestyle factors which can be subject to behavioral change include physical activity, body weight, tobacco smoking, alcohol consumption, and diet (World Health Organization, 2021).

Measuring lipid concentrations and other biomarkers in blood is the main method of predicting CVD risk. Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) concentrations are used as predictive risk factors for CVD development (El Harchaoui et al., 2007). Emerging evidence has shown more accurate predictive risk factors for CVD. One such is non-high-density lipoprotein cholesterol (non-HDL-C) (Carr, Hooper, Sullivan, & Burnett, 2019).

A change in diet and lifestyle can influence the risk of developing CVD. In recent years, it has become evident that focus on single foods or nutrients do not provide a uniform picture (Calabrese & Riccardi, 2019; Lichtenstein et al., 2021). Food is a mixture of nutrients and other bioactive components, so the emphasis should be put on dietary patterns rather than single foods or nutrients (Svendsen, Vinknes, Retterstol, & Olsen, 2020).
Dietary patterns high in saturated fats and cholesterol may increase blood pressure and LDL-C. Recent systematic reviews show elevated levels of lipids as a risk factor in CVD and

lowering of blood pressure and LDL-C could halve the risk for CVD (Alloubani, Nimer, & Samara, 2020; Wang, Huffman, Sundstrom, & Rodgers, 2021). LDL-C is a known risk factor in CVD (Ference et al., 2017). Dietary patterns high in fruits, vegetables, low-fat dairy products, and fiber, like the Mediterranean diet and various plant-based diets, have shown to reduce LDL-C (Appel et al., 1997; Toh, Koh, & Kim, 2020). Physical activity is also known to reduce the risk for developing CVD through several mechanisms (Ahmed, Blaha, Nasir, Rivera, & Blumenthal, 2012; Blair & Jackson, 2001; Lee, Paffenbarger, & Hennekens, 1997; P. D. Thompson et al., 2003).
Not smoking tobacco and cessation of tobacco smoking is another known factor in reducing the risk for developing CVD (Bullen, 2008; Chelland, Moffatt, & Stamford, 2008; Duncan et al., 2019).

Eating a healthy dietary pattern consisting of more fibrous fruits and vegetables, whole grains, lean protein sources, and a reduction in saturated fat, and having a lifestyle focusing on daily physical activity, maintaining a healthy body weight, not smoking tobacco, and moderation of alcohol consumption have been shown to reduce the risk of developing CVD (Toh et al., 2020). These diet and lifestyle factors can affect risk factors such as blood pressure, blood glucose, blood lipids and body weight. These are the general guidelines lifestyle interventions follow to reduce CVD risk (Khanji et al., 2018).

There are some successful lifestyle interventions that have been shown to reduce the risk of CVD, including the PREDIMED study (Mediterranean diet on CVD risk), LOOK-AHEAD (weight reduction by physical activity), and the Oslo Diet and Heart study (advice to stop smoking and reduce saturated fat intake) (Estruch et al., 2018; Leren, 1970; Salvia, 2017). However, besides the Oslo Diet and Heart study, conducted in the 1970s, there have not been many randomized controlled trial (RCT) lifestyle interventions conducted in Norway in the recent years.

The VISA-study was a recent RCT lifestyle intervention recently conducted in Norway (Svendsen, Telle-Hansen, et al., 2018). The participants were randomly divided into three groups: a risk alert and advice group, an advice-only group, and a control group. The alert and advice were pertaining to CVD risk factors. Results from the lifestyle intervention in the VISA-study showed no significant effect for either of the three groups in reducing CVD risk

score (composite of CVD risk factors). However, there were certain individuals in this lifestyle intervention who managed to reduce their CVD risk by a significant reduction in non-HDL-C one year after intervention (Svendsen, Telle-Hansen, et al., 2018). We wanted to dig into the diet and lifestyle patterns of these individuals to study what diet and lifestyle factors.

2. Background

2.1. Cardiovascular disease

CVD is the leading cause of death in the world (World Health Organization, 2021). CVD is a class of diseases affecting the heart and blood vessels. These diseases are non-communicable, meaning they are not infectious and can be prevented. This group of diseases include four main types: coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease (PAD) and aortic disease (National Health Services, 2018). For simplicity, the definition of CVD from here on will include ischemic heart disease (IHD), CHD, coronary artery disease (CAD), myocardial infarction (MI), PAD, coronary artery calcification (CAC), stroke, and aneurysms. The major cause of CVD is atherosclerosis (Scott, 2004). The prevalence is ever increasing, and more people are affected by CVD than ever before. However, this is mostly due to the population getting older (Folkehelseinstituttet, 2020; Roth et al., 2020).

The global estimate of deaths from CVD was 17.9 million in 2019. This represents a total of 32% of deaths globally. 85% of these deaths were due to stroke or heart attack (World Health Organization, 2021). In 2019, WHO estimated that out of 17 million premature deaths (defined as death before age 70), 38% were due to CVD. The prevalence of CVD cases on a global scale has nearly doubled from 271 million cases in 1990 to 523 million cases in 2019 (Roth et al., 2020).

Atherosclerosis seems to be an important underlying pathophysiological mechanism for many types of CVD (Falk, 2006; Scott, 2004). Upon further research of the atherosclerotic processes in the human body, several important risk factors have been identified that affect this cascade (Ference et al., 2017; Libby, 2021; Nordestgaard et al., 2010).

2.1.1. Atherosclerosis

Atherosclerosis is one of the main biological processes driving the development of CVD. This process starts early in life (Hong, 2010). The atherosclerotic process involves accumulation of plaque particles inside the walls of the arteries (Falk, 2006). These plaque particles consist of various substances, mainly cholesterol and lipoproteins (Scott, 2004).

This was recognized decades ago (Onitiri et al., 1976). Part of this process is endothelial dysfunction (Berenji et al., 2020). Lipoproteins are carrier proteins that transport triglycerides and cholesterol in the blood vessels throughout the body. If these lipoproteins stay circulating in the blood stream, they may aggravate the atherosclerotic process (Badimón, Vilahur, & Padró, 2009). While the exact molecular mechanism behind the pathophysiology of atherosclerosis is under extensive scientific research, there is evidence that some lipoproteins and associated particles are pro-atherogenic, hence elevated concentrations can accelerate atherosclerosis (Ference et al., 2017).

The consequence of plaque accumulation in the endothelium of arteries causes a gradual narrowing of arteries, which can reduce blood flow to organs and cause IHD and CHD (Bentzon, Otsuka, Virmani, & Falk, 2014). As these plaques build up inside the arteries, they are susceptible to rupture. This may cause the aggregation of blood platelets, forming a blood clot (Mehta & Tzima, 2016). Ultimately, this can cause a sudden fatal cardiac event, such as MI or stroke. The dysfunction of the endothelium in arteries is gradual process which takes place over the course of years in humans (Berenji et al., 2020).

2.2. Risk factors

Risk factors are defined as factors influencing the development of CVD. Some of these risk factors are not subject to change, such as genes and age (Tyrrell & Goldstein, 2021). Findings from the INTERHEART study suggest that potentially modifiable risk factors affecting the development of CVD include abnormal concentrations of blood lipids (dyslipidemia), tobacco smoking, elevated blood pressure (hypertension), elevated blood glucose, abdominal obesity, psychosocial factors, an increased consumption of fruit & vegetables, a moderation of alcohol intake, and regular physical activity (Yusuf et al., 2004).

Tobacco smoking is highly associated with poor health and negative outcomes regarding CVD (Chelland et al., 2008). A systematic review and meta-analysis regarding smoking reduction & cessation found complete cessation among smokers to be the most effective prevention for CVD (Chang, Anic, Rostron, Tanwar, & Chang, 2021).
Smoking is shown to affect triglycerides, cholesterol, and lipoprotein metabolism in a negative manner. Smoking is an independent risk factor which is modifiable. Smoking

cessation at any time and age is considered a favorable choice to prevent future CVD (Bullen, 2008).

Elevated blood pressure is positively associated with IHD (Morkedal, Romundstad, & Vatten, 2011). Elevated blood pressure in age groups under 65 years is a more severe risk factor. Elevated blood pressure is often asymptomatic and can persist for long periods.

Obesity, overweight, and high BMI (≥25) is associated with increased risk for CVD (Bogers et al., 2007; Poirier et al., 2006). A paradox in medical research has been noted, as being obese and overweight has shown a decrease in all-cause mortality and certain cardioprotective qualities (Brodsky et al., 2016; Oreopoulos et al., 2008). However, the consensus is that obesity and overweight can lead to elevated blood pressure, dyslipidemia, and an increase in atherosclerosis & cardiovascular events(Klein et al., 2004; Lau, Dhillon, Yan, Szmitko, & Verma, 2005; Lavie, Milani, & Ventura, 2009). Maintaining a healthy body weight and weight reduction is therefore considered beneficial to reduce risk for CVD.

2.3. Lipids and lipoproteins

Lipids are fatty substances which serve as an energy source for cells and building material for cellular membranes and hormones. These lipids include cholesterol and triglycerides and cannot travel freely in the blood stream. Therefore, their associated transport molecules are lipoproteins with various apolipoproteins (apo) attached. Lipoproteins have varying size and density depending on the amount of cholesterol and triglycerides they transport (Kenneth R. Feingold, 2021). Main types of lipoproteins include very low-density (VLDL), LDL (low-density), intermediate-density (IDL), and high-density lipoprotein (HDL). VLDL, LDL, and IDL are pro-atherogenic, in association with apolipoprotein B (apoB) (Carmena, Duriez, & Fruchart, 2004). HDL is considered anti-atherogenic (Fernandez-Hernando, 2014; Murphy, Westerterp, Yvan-Charvet, & Tall, 2012).

TC and LDL-C are important CVD risk factors and has been for many years (Brown & Goldstein, 1981). Although a reduction in TC gives a decrease in CVD-related mortality, the ranges of TC in which large populations reside makes it harder to predict individuals at high risk for CVD (Jousilahti et al., 1998). TG also have the same association to CVD risk as TC

but are dependent on established risk factors to predict CVD risk (Sarwar et al., 2007). Normal food intake affects concentrations of TG and to some degree TC, LDL-C, HDL-C (Langsted, Freiberg, & Nordestgaard, 2008).

Although LDL-C serves as a well-established risk factor for CVD, non-HDL-C and apoB is suggested to be a more accurate way of predicting risk for CVD (Brea et al., 2019; A. Thompson & Danesh, 2006). Non-HDL-C (calculated as HDL-C subtracted from TC) has an advantage over LDL-C as risk factor since it is independent on TG concentration, not affected by normal food intake and is possible to measure in individuals with very low LDL-C concentration (Carr et al., 2019). While the measuring of apoB concentrations includes all pro-atherogenic lipoprotein (Wilkins, Li, Sniderman, Chan, & Lloyd-Jones, 2016). Non-HDL-C and ApoB are superior to LDL-C in predicting risk for CVD. Measuring apoB can come at a slightly higher financial cost than non-HDL-C.

Novel findings suggest that elevated concentration of non-HDL-C is associated with increase in CVD- across the lifespan (Armstrong et al., 2021). Elevated concentration in adolescences is strongly associated with CVD in mid-adulthood, which is likely to continue if not monitored (Pencina et al., 2019). Low levels of non-HDL-C is shown to reduce CVDs (Nayor, Murthy, & Shah, 2020).

2.4. Diet and lifestyle

Primary prevention to reduce CVD includes lifestyle interventions (Chapman et al., 2011; Liu et al., 2012). Adherence to a healthy diet and lifestyle can have remarkable results on CVDs for both men and women across all stages of life (Akesson, Larsson, Discacciati, & Wolk, 2014; Akesson, Weismayer, Newby, & Wolk, 2007; Stampfer, Hu, Manson, Rimm, & Willett, 2000). Adopting a low-risk diet and lifestyle early in life can be an effective in reducing CVD. The Norwegian Directorate of Health has 12 advice in their National Nutritional Advice guidelines for a healthy diet and lifestyle (Helsedirektoratet, 2016). These guidelines include a varied diet consisting of fruits, vegetables, berries, whole grains, lean dairy products, lean protein sources, and regular physical activity.

Several dietary patterns can affect the risk for CVD (Calabrese & Riccardi, 2019; Siervo et

al., 2015). Both low-fat and low-carbohydrate diets are seen to reduce CVD risk factors, such as body weight and blood pressure (Brehm, Seeley, Daniels, & D'Alessio, 2003; Meckling, O'Sullivan, & Saari, 2004).

Whereas the effects on lipids showed to be positive in the low-fat diet groups only, by a reduction in LDL. There is strong evidence for a Mediterranean-style diet to be effective in reducing CVD risk (Estruch et al., 2018). However, much remains unclear concerning which factors in dietary patterns to reduce CVD risk in different population groups.

Of specific foods and nutrients, limiting saturated fat & salt intake, avoiding transaturated-fats, and added sugar, moderating alcohol consumption, and increasing intakes of fruits, vegetables, fish, and wholegrains are key to prevention of CVD (Khanji et al., 2018).

Replacing saturated fats with unsaturated fats is one important dietary factor to change for a reduction in CVD risk (Hooper et al., 2020; Mensink, Zock, Kester, & Katan, 2003; Mozaffarian, Micha, & Wallace, 2010). Long-term follow up of the Oslo intervention study showed that smoking cessation in addition to replacing fats from butter and dairy with fats from fish in addition to increasing the intake of vegetables reduced the risk of CVD mortality even after 40 years of follow-up (Holme, Retterstol, Norum, & Hjermann, 2016).
Lately, there has also been emerging evidence that ultra-processed foods significantly increase the risk of CVDs, and thus, the new American Heart Association guidelines on healthy diet and lifestyle now endorses lowering ultra-processed foods as one of their 10 "heart-healthy advice" (Juul, Vaidean, & Parekh, 2021; Lichtenstein et al., 2021).

Lifestyle interventions could also include increasing physical activity level, as this is a major factor in a healthy lifestyle to prevent a host of non-communicable disease, such as diabetes and CVD, and reduce all-cause mortality (Ahmed et al., 2012; Schnohr, O'Keefe, Lange, Jensen, & Marott, 2017). Recommendations for physical activity to reduce CVD risk are at the least 30 minutes of moderate-intensity physical activity, such as a brisk walk, on most, if not all, days of the week (Helsedirektoratet, 2016; P. D. Thompson et al., 2003). Being physically active daily can be an effective component of lifestyle interventions (Khanji et al., 2018). Effective lifestyle interventions should also focus on smoking cessation (Khanji et al., 2018).

2.5. Current research on diet and lifestyle interventions

When looking in the PUBMED database from 2020-2022 for meta-analyses and systematic overviews on the subject of diet and lifestyle interventions and their effect, we found some interesting articles. There is evidence for certain foods and beverages as well as nutrients affecting the risk for CVD in either a positive or a negative fashion (Miller et al., 2022). The quality of evidence for these foods, beverages and nutrients were considered at least probable in association to CVD risk. Risk ratios ranged from 0.87 to 0.96 pr daily serving change for protective associations, and 1.06 to 1.15 per daily serving change for harmful associations. However, the authors discuss that well-conducted observational studies on dietary patterns and lifestyle factors can provide valid and reliable risk estimates for association between diet and disease (Miller et al., 2022).

When observing selected population groups, a dietary transition towards replacing saturated fats with more refined carbohydrates leading to negative health outcomes related to cardiometabolic diseases (diabetes, CVD) (Pressler et al., 2022). It is clear that the current research focus should be on establishing clinically relevant dietary patterns to promote in lifestyle interventions for CVD prevention. Predominantly plant-based diets are effective at reducing several risk factors associated with CVD such as blood lipids, body weight, blood pressure and HbA1c (Remde, DeTurk, Almardini, Steiner, & Wojda, 2022). This systematic review also found in some cases that a plant-based diet may be better than the usual health-oriented diets suggested by the American Heart Association and Mediterranean diet.
The long-standing idea of dietary cholesterol as a specific important nutrient to eliminate in recent guidelines is now being less emphasized, and instead guidance should be put on dietary patterns (Carson et al., 2020).

Limbachia et. al. suggests that evidence for lifestyle interventions is assumed to be of moderate-to-high quality (Limbachia, Ajmeri, Keating, de Souza, & Anand, 2022). Adopting a healthy lifestyle is associated with lowering risk for CVD and other negative health outcomes consistently among populations from different continents, racial groups and socioeconomic backgrounds (Zhang et al., 2021). A systematic review and meta-analysis published in 2021 found that even simple caloric restriction for 1-4 weeks could reduce blood pressure similar to what is expected of medications, and even larger effect than lifestyle interventions could produce (Kirkham, Beka, & Prado, 2021). However, the long-term (>24 months) effect of lifestyle interventions on CVD risk factors is still uncertain (Bergum, Sandven, & Klemsdal, 2021). The TANSNIP-PESA trial showed that in a low-

intermediate CVD risk population, a lifestyle intervention reached a peak effect of reducing CVD risk after 1 year but attenuated after the 3 years (Garcia-Lunar et al., 2022).

3. Aim of the study

The main goal of this study was to identify dietary patterns and lifestyle factors that contributes to large reduction in non-HDL-C concentration in a population of individuals at a moderately elevated risk of CVD ten months after participating in a lifestyle intervention.

4. Method

4.1. Design

A parallel three-group 8-week RCT lifestyle intervention was conducted from September 2014. This study was the Vascular Lifestyle-Intervention and Screening in Pharmacy (VISA) (Svendsen, Telle-Hansen, et al., 2018). Pharmacy staff screened volunteers for eligibility during September 8.-13. 2014 in 48 community pharmacies (Boots™ Norge AS) countrywide in Norway.

At the first visit (V0) and end of intervention (V1) volunteers had their anthropometric (body weight, height, blood pressure) and biochemical (TC, TG, LDL-C, HDL-C, HbA1c) measures assessed by pharmacy staff. Information gathered from these measurements resulted in calculation of an ad hoc CVD risk score. Screening-results were recorded in an electronic program created by LINK medical Research AS Oslo. The program calculated CVD risk score using the variables from Table 1 in the VISA-study (Svendsen, Telle-Hansen, et al., 2018). CVD risk score was a summarization of scores ranging from zero (favorable) to four (very unfavorable) assigned for TC, HDL-C, HbA1c, BP, BMI, and age. A CVD risk score ≥4 served as inclusion criteria, indicating a moderately elevated risk of CVD.

Individuals at a moderately elevated risk for CVD were invited to participate in the lifestyle intervention. Verbal and written informed consent were obtained at this point. The participants also completed a baseline questionnaire regarding demographics at V0. Diet and lifestyle factors (intake in grams of different food groups) was assessed by the VISA-Food Frequency Questionnaire (VISA-FFQ) at V0 and V1 (Svendsen, Henriksen, et al., 2018). At V0, the study sample was randomized and placed into 3 groups: two differing intervention groups or control group in the ratio 1:1:1.

At the end of the 8-week intervention, participants were invited to do a follow-up 52-weeks after V0 (V2). The participants were then again assessed with anthropometric and biochemical measures, and VISA-FFQ at the follow-up.

Data used in this study includes data collected from V0, V1, and V2. We wanted to identify important dietary patterns and lifestyle factors in individuals that had a large reduction in non-HDL-C concentration over the 10-month period between V1 and V2.

4.2. Population

Criteria for inclusion and exclusion were as follows:

- Inclusion: Age ≥18 years, Norwegian speaking, moderate CVD risk
- Exclusion: Pregnant, lactating, using medication (lipid- and BP-lowering, anti-diabetic), history of CVD, diabetes mellitus (type 1 or 2)

In total 542 participants completed the 8-week intervention and were measured at V1. At V2, 377 participants returned and were measured according to protocol. 165 participants were excluded for not showing up for both V1 and V2. Out of the 377 who attended both V1 and V2, 52 participants had to be excluded due to missing data. 325 participants were the final number of participants that could be included in statistical analysis in this master thesis (*Figure 1*).

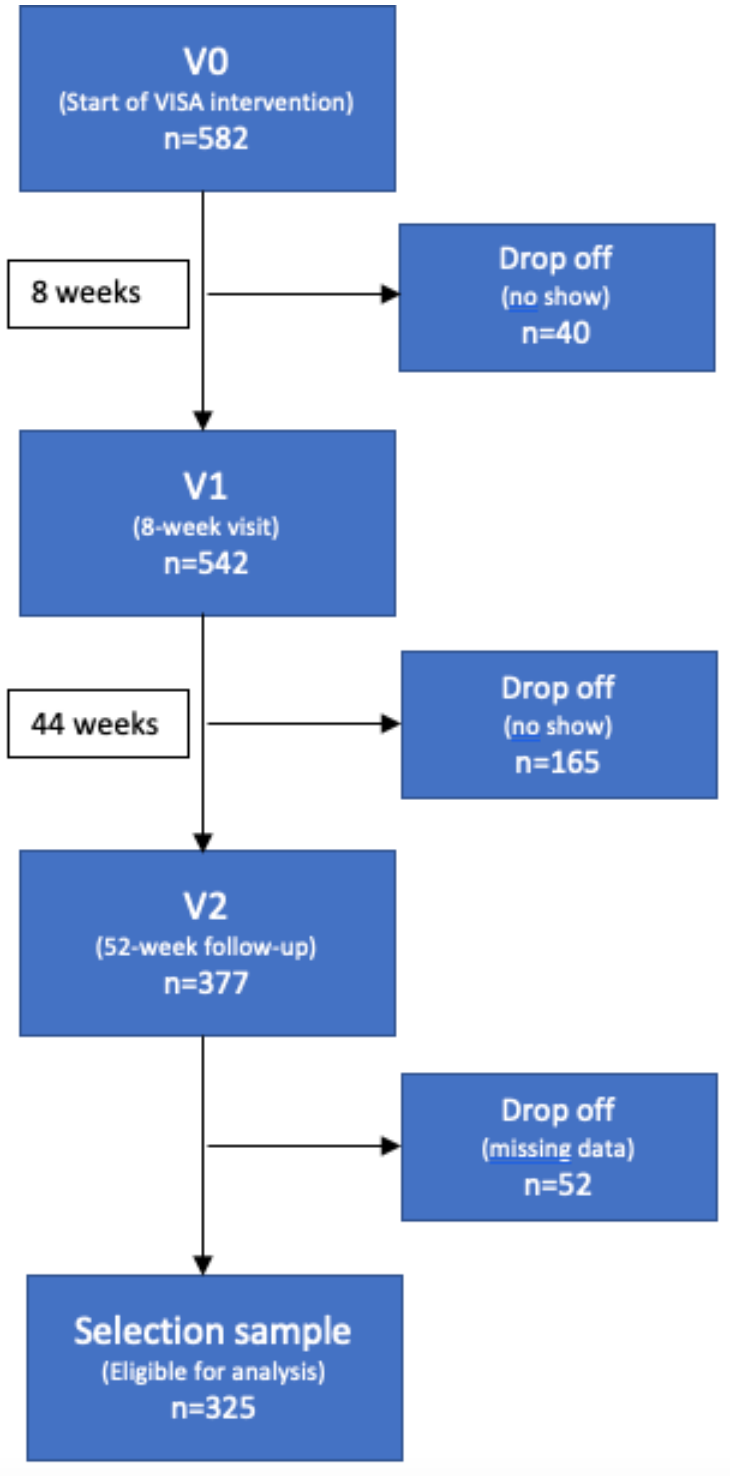

Figure 1: Selection sample eligible for analysis from total sample with data collection and visit points from the VISA-study

4.3. Data collection

All the data was collected by pharmacy staff (pharmacists, technicians, nurses) at the various pharmacies. Two questionnaires were used to obtain self-reported information from the participants. To ensure standardization of screening protocol, pharmacy staff were instructed and trained prior to the screening process in accordance with screening protocol. Pharmacy staff conducted the screening in separate private rooms in the respective pharmacies. Each screening session took about 20 minutes to complete.

4.3.1. Anthropometric and biochemical measures

The VISA-study used a screening protocol for anthropometric and biochemical measures (Svendsen, Telle-Hansen, et al., 2018). The screening protocol included measurements of height, body weight, blood pressure, blood lipids (TC, HDL-C, LDL-C, TG) and HbA1c. Body weight was measured in kilograms using a digital scale and with participants wearing light clothing. Height was measured in centimeters with an erect standing posture and bare feet against a wall mounted board. BMI was calculated using the formula body weight in kg divided by height in meters squared (kg/m^2). A finger prick-measurement was done to measure blood lipids and HbA1c by the measurement device Alere Afinion^{TM} AS 100. Blood lipids and HbA1c were measured in intervals where values outside the stated intervals were recorded as error and were not included in the data file. The intervals were the following: total cholesterol: 2.59-12.95 mmol/L; HDL-C: 0.39-2.59 mmol/L; LDL-C: 0.5-12.0 mmol/L; triglycerides: 0.51-7.34 mmol/L; HbA1c: 4-15%. Non-HDL-C was calculated by subtracting total cholesterol with HDL-C. LDL-C was calculated by the device with Friedewald´s formula. At triglycerides >4.52 mmol/L, LDL-C was not calculated, whereas for triglycerides >7.32 mmol/L, HDL-C was not calculated. Two consecutive blood pressure measurements were done by A&D Medical blood pressure Monitor^{TM} Model UA-767Plus30. An average of the two measurements were recorded.

4.3.2. Baseline questionnaire

At V0 a self-reported baseline questionnaire was filled out that included age, sex, highest attained education level, medical history, smoking status, and daily physical activity. Education level was measured and divided into two categories: higher and lower. Higher education was equal to at least 1 year of university level education, whereas lower education ≤13 years of formal school education. Physical activity was measured as total minutes per day spent at moderate- intensity, such as brisk walking. (Attachment 1)

4.3.3. VISA-FFQ

At V2 the VISA-FFQ was issued to obtain information on intakes during the last 1-2 months. VISA-FFQ is a validated 62-item questionnaire that covers dietary intake (grams per day) of food and drink items and frequency of consumption (Svendsen, Henriksen, et al., 2018). VISA-FFQ is adopted from the NORDIET-FFQ, with slight changes to focus more on dietary fat quality (Henriksen et al., 2018). In addition to dietary intake, the VISA-FFQ also includes questions about numbers of cigarettes per day and time spent doing moderate-intensity (brisk walking) and high-intensity (exercising) physical activity per day. In the final analyses, the physical activity parameter was estimated from self-reported levels in the VISA-FFQ and both moderate-intensity and high-intensity physical activity was merged to produce the response variable. Estimating nutrients and total energy intake is not possible with the VISA-FFQ. (Attachment 2)

4.4. Statistical analysis

Descriptive statistical analysis and t-tests were computed with the software IBM Statistical Package for Social Sciences (SPSS, version 27). For the principal component analysis, the statistical software R (version 4.0.0) was used.

Continuous variables were presented with mean and one standard deviation (SD). Categorical variables were presented with total number of cases. Differences were reported with mean, SD, 95% confidence interval (CI) and a 2-tailed significance value (*P*-value). Significance level was set to $P < 0.05$. Distribution of the continuous variables were assessed to be normally distributed through histogram visualization with Gaussian curve and mean/median differences. All continuous variables were normally distributed. Due to the explorative nature of this project, none of the *P*-values were adjusted for multiple comparisons.

The selection sample (n=325) at V1 and V2 were assessed with descriptive statistics. The mean change between V1 and V2 for the group was analyzed with Independent Sample t-tests for continuous variables or Whitney-Mann U test for categorical variables.

The sample was split into quartiles according to reduction in non-HDL-C from V1 to V2. 15 participants were lacking non-HDL-C data from either V1 or V2, and thus could not be included in quartiles of non-HDL-C change. Sum of individuals in all quartiles was n=310. The lower quartile (Q1) included individuals (n=77) with the largest reduction in non-HDL-C at ≤0.57 (max. 3.99) mmol/L. The top quartile (Q4) included individuals (n=77) with the largest increase in non-HDL-C at ≥0.49 (max. 4.8) mmol/L.

Preliminary analyses split the total sample (n=325) by sex. This was done to see if there were any significant differences between the sexes in the sample, and if this had to be considered when pursuing further analyses. After looking at the sample split by sex, individuals in Q1 and Q4 were compared to each other at 10 risk factor for CVD. These risk factors are body weight, BMI, TC, HDL-C, LDL-C, non-HDL-C, triglycerides, HbA1c, systolic and diastolic BP. Mean reduction was calculated as variable at V2 subtracted from variable at V1, then reported with mean. The purpose of this was to statistically assess if there was a significant difference in the favorable and unfavorable responders of this lifestyle intervention study. This was done using descriptive statistics, Independent Samples t- test, and Whitney-Mann U test.

4.4.1. Principal component analysis

To identify dietary patterns, we opted to use a principal component analysis (PCA). This is a method of reducing the total number of variables in a dataset to a smaller subset of components. These principal components (PC) consist of the variables that explain most of the total variance in the dataset.

In this section, we modify the dataset, so it adheres to standards for PCA. This was done by z-transforming all diet and lifestyle variables. A simple factor analysis was performed with no rotation of the coordinate system for simplicity. The scree plot reveals an inflection point around component 3. (*Figure 2*)
We extracted the first (PC1) and second (PC2) principal components as these explained a total variance in the dataset by 14% and 9%, respectively. (*Attachment 3*)

PC1 is associated with high intakes of whole grains (bread), dairy (milk, half-fat dairy products), fish (fatty, lean), and lean meats. PC2 is associated with high intakes of dairy (milk, half-fat dairy products) and low intakes of fish (fatty, lean).

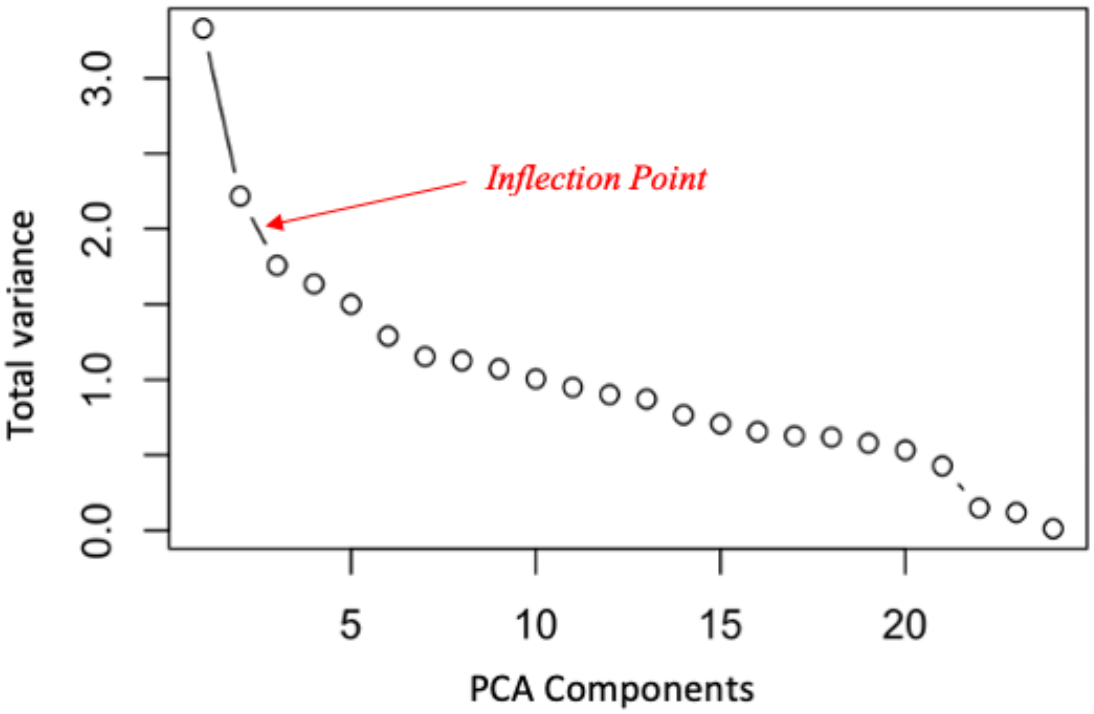

Figure 2: Scree plot of principal components (PCA) and inflection point

4.5. Ethical considerations

The participants were given a unique ID-number and the information related to them could not produce a possibility to identify personal traits. All personal sensitive data is kept stored in TSD at UiO, without the student having access to the data. The study was approved by REK (ClinicalTrials.gov Identifier: NCT02223793).

All participants volunteered by free will and gave a verbal and written consent before the screening protocol. At any given time during the intervention, the participants had the opportunity to withdraw consent without reason. During the screening protocol, the participants were allocated to a private room in the pharmacy and supervised by trained authorized pharmacy staff.

Screening protocols in lifestyle interventions for CVD risk, involving risk alerts and blood sampling, are not associated with an increase in mental distress (Jorgensen et al., 2009). Making people aware of their risk factors and behavior, alongside counseling and advice, should not produce any particular stress-response in the general population (Christensen, Engberg, & Lauritzen, 2004).

4.6. Financial considerations

Boots™ Norge AS covered all expenses related to training and employment of staff, and the necessary equipment for anthropometric and biochemical screening. Mills AS and Wendel Jarlsbergs fund contributed with funding for the administration of questionnaires. No other expenses were related to the completion of the study.

5. Results

The results are separated into two parts.

1. Part one (5.1) is descriptive statistics of anthropometric and biochemical measurements in risk factors and reduction in these risk factors from V1 to V2 for the study sample stratified first by sex, and secondly by quartiles.
2. Part two (5.2) is the results of a PCA used to examine dietary patterns and lifestyle factors for individuals in the quartiles.

5.1. Descriptive statistics

5.1.1. Sex differences in the study sample

Background information on the included sample is shown in **Table 1**. In total, there were 243 women with mean age 60.44 ± 12.99 years, and 82 men with mean age 56.06 ± 14.08 years. 39.9% (97 of 243) of the women in the sample had completed higher education, whereas 56% (46 of 82) of the men in the sample had similar educational level. Both women and men had self-reported above 30 mean minutes of physical activity per day, which is in accordance with guidelines for daily physical activity. 10.6% (26 of 243) of the women were smokers and 8.5% (7 of 82) of the men were smokers.

Overall, both women and men in the study sample had a total reduction in many risk factors from V1 to V2 (except HDL-C, which is favorable with increases). Body weight and BMI were reduced in both women and men. This was true for total cholesterol also, although only slight reduction was seen in the women. Women had a small increase in HDL-C between V1 and V2, which is considered beneficial. However, the women also had a small increase in LDL-C, thus not changing that ratio between HDL/LDL-C. The men had only a small reduction in HDL-C, but a greater reduction in LDL-C. The major risk factor non-HDL-C was reduced in both women and men from V1 and V2. Interestingly, triglycerides were reduced for women but not for men, where it was increased. HbA1c in women had no change, but a small increase in men. Systolic BP was reduced in both women and men. Diastolic BP was reduced in women but not in men.

Sex differences with regards to absolute reduction or increase in the study sample was seen

in HDL-C, LDL-C, triglycerides, HbA1c and diastolic BP. Women had 0.03 mmol/L increase in HDL-C, but also 0.02 mmol/L increase in LDL-C. Men had a 0.01 mmol/L decrease in HDL-C and 0.18 mmol/L decrease in LDL-C. Triglycerides decreased by 0.12 mmol/L in women. In men, triglycerides increased by 0.06 mmol/L. HbA1c was unchanged in women and increased by 0.04% in the men. Diastolic BP was lowered in women by 0.55 mmHg, whereas it was increased by 0.97 mmHg in men.

Table 1: Demographics and cardiovascular risk factors of study sample (n=325) at visit 1 and visit 2

		Women (n=243)		**Men** (n=82)	
Age, years		60.44 (12.99)		56.06 (14.08)	
Education[1]	lower, n	134		34	
	higher, n	97		46	
Physical activity[2], min. pr. day		32.58 (27.82)		35.53 (30.53)	
Smokers, n		26		7	
		V1	**V2**	**V1**	**V2**
Body weight, kg		73.77 (13.54)	73.58 (13.92)	83.62 (11.64)	83.32 (11.48)
BMI, kg/m^2		27.13 (4.66)	27.07 (4.79)	26.89 (3.52)	26.78 (3.59)
Total cholesterol, mmol/L		6.66 (1.21)	6.64 (1.12)	6.26 (1.19)	6.09 (1.21)
HDL-C, mmol/L		1.80 (0.45)	1.83 (0.43)	1.59 (0.58)	1.58 (0.54)
LDL-C, mmol/L		3.98 (1.03)	4.00 (0.99)	3.86 (0.91)	3.68 (0.88)
Non-HDL-C, mmol/L		4.85 (1.12)	4.80 (1.05)	4.66 (1.11)	4.50 (1.05)
Triglycerides, mmol/L		1.98 (1.08)	1.86 (0.98)	1.96 (1.23)	2.02 (1.22)
HbA1c, %		5.53 (0.32)	5.53 (0.29)	5.48 (0.39)	5.52 (0.38)
Systolic BP, mmHg		129.57 (17.28)	127.40 (16.31)	135.10 (15.16)	134.42 (16.72)
Diastolic BP, mmHg		79.70 (9.85)	79.15 (9.68)	81.98 (8.59)	82.95 (10.20)

BMI; body mass index, non-HDL-C; non-high-density lipoprotein cholesterol, BP; blood pressure
HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol
HbA1c; glycosylated hemoglobin, SD; standard deviation, V1; visit 1, V2; visit 2

[1] Highest level of education completed, higher equals >13 years and lower equals ≤13 years
[2] Measured as moderate-to-strenous physical activity
Anthropometric and biochemical measurements are presented with mean (SD)
Education level and smoking status is presented in total number of cases

5.1.2. Comparison of mean reduction between women and men

Mean reduction from V1 to V2 in the sample was observed and compared between women and men in **Table 2**. These values show mean reduction for men and women from V1 and V2, not total or absolute reduction that was reported in **Table 1**.

T-tests were used to compare the mean reduction of women and men, although not adjusted for multiple comparisons. Only significant reduction in a risk factor was found at systolic BP between women and men (*P*=0.036). These findings allowed us to see that there was no significant reduction in response variable between women and men (except for systolic BP). This way, we could conclude that differences in sex did not impact most of the risk factors in the study sample.

Table 2: Mean reduction in cardiovascular risk factors of study sample (n=325) from visit 1 to visit 2, negative values indicate an increase in the given cardivascular risk factor

	Women (n=243)	**Men** (n=82)		
	Mean reduction		**95% CI**	***P*-value***
Body weight, kg	0.32 (3.28)	0.29 (3.50)	-0.80, 0.86	.944
BMI, kg/m^2	0.11 (1.22)	0.07 (1.12)	-0.22, 0.30	.768
Total cholesterol, mmol/L	0.01 (1.04)	0.16 (1.18)	-0.42, 0.12	.276
HDL-C, mmol/L	0.03 (0.29)	-0.01 (0.42)	-0.10, 0.06	.633
LDL-C, mmol/L	-0.02 (0.88)	0.18 (0.90)	-0.42, 0.22	.078
Non-HDL-C, mmol/L	0.05 (0.89)	0.17 (1.20)	-0.36, 0.12	.337
Triglycerides, mmol/L	0.11 (1.07)	-0.07 (1.27)	-0.10, 0.46	.211
HbA1c, %	0.00 (0.20)	-0.03 (0.21)	-0.02, 0.08	.247
Systolic BP, mmHg	**4.43 (13.87)**	**0.67 (14.42)**	**0.24, 7.28**	**.036**
Diastolic BP, mmHg	0.63 (7.14)	-0.96 (8.31)	-0.28, 3.46	.096

BMI; body mass index, non-HDL-C; non-high-density lipoprotein cholesterol, BP; blood pressure
HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol
HbA1c; glycosylated hemoglobin, SD; standard deviation, V1; visit 1, V2; visit 2
CI; confidence interval, P-value; 2-tailed significance level

Anthropometric and biochemical measurements are presented with mean (SD)
**P-values were not adjusted for multiple comparisons*

5.1.3. Comparison of quartiles

Individuals in the sample was divided into quartiles of reduction in non-HDL-C between V1 to V2, from largest reduction in Q1 (≤0.57 mmol/L) to largest increase in Q4 (≥0.49 mmol/L), as shown in **Table 3**. Therefore, it would be most beneficial to have all participants in Q1 to reduce CVD risk.

Both quartiles had 77 individuals. In Q1, roughly 70% were women and 30% were men. In Q4, 80% were women and 20% were men, rounded to nearest whole. The mean age for Q1 was 59.18 ± 13.31 years. In Q4, the mean years for individuals were 60.00 ± 13.23. Both quartiles had similar distribution of educational level (48% and 46.75% in Q1 and Q4, respectively). There were 9 smokers in total in Q4, contrary to the 6 in Q1.
Interestingly, the individuals in Q1 had self-reported above 30 mean minutes of physical activity per day, whereas the individuals Q4 had self-reported less than 30 mean minutes of physical activity per day.

Overall, the individuals in Q1 had a total reduction in all but one risk factors from V1 to V2, also HDL-C where a reduction is seen as negative for CVD risk. Q1 saw a minor increase in HbA1c.
Individuals in Q4 had an increase in all risk factors but one from V1 to V2. HDL-C was increased, but LDL-C and non-HDL-C was also increased. Q4 saw a reduction in systolic BP.

Table 3: Demographics and cardiovascular risk factors of individuals divided by quartiles of non-HDL-C reduction from visit 1 to visit 2

		Q1 (n=77)		**Q4** (n=77)	
Men, n		23		15	
Women, n		54		62	
Age, years		59.18 (13.31)		60.00 (13.23)	
Education[1]	lower, n	40		41	
	higher, n	37		36	
Physical activity[2], min. pr. day		33.34 (29.21)		29.55 (27.46)	
Smokers, n		6		9	
		V1	**V2**	**V1**	**V2**
Body weight, kg		78.09 (14.52)	77.32 (14.21)	73.17 (12.67)	73.22 (12.70)
BMI, kg/m^2		27.38 (4.95)	27.06 (4.91)	26.64 (4.08)	26.67 (4.14)
Total cholesterol, mmol/L		7.33 (1.29)	5.93 (1.19)	6.01 (1.08)	7.12 (1.12)
HDL-C, mmol/L		1.73 (0.44)	1.63 (0.46)	1.72 (0.58)	1.82 (0.48)
LDL-C, mmol/L		4.66 (1.00)	3.56 (0.89)	3.54 (0.89)	4.41 (0.96)
Non-HDL-C, mmol/L		5.59 (1.13)	4.30 (1.03)	4.28 (1.06)	5.30 (1.07)
Triglycerides, mmol/L		2.24 (1.25)	1.70 (0.89)	1.75 (0.76)	2.09 (0.99)
HbA1c, %		5.58 (0.38)	5.59 (0.30)	5.48 (0.29)	5.50 (0.30)
Systolic BP, mmHg		130.14 (17.91)	126.14 (19.31)	129.09 (18.54)	126.00 (15.77)
Diastolic BP, mmHg		79.94 (10.25)	78.11 (11.01)	78.92 (9.40)	80.46 (8.97)

BMI; body mass index, non-HDL-C; non-high-density lipoprotein cholesterol, BP; blood pressure
HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol
HbA1c; glycosylated hemoglobin, SD; standard deviation, Q1; quartile 1, Q4; quartile 4
V1; visit 1, V2; visit 2

Individuals in Q1 had non-HDL-C reduction by ≤0.57 mmol/L
Individuals in Q4 had non-HDL-C increase by ≥0.49 mmol/L
[1] Highest level of education completed, higher equals >13 years and lower equals ≤13 years
[2] Measured as moderate-to-strenous physical activity
Anthropometric and biochemical measurements are presented with mean (SD)
Education level and smoking status is presented in total number of cases

5.1.4. Comparison of mean reduction between quartiles

As seen in **Table 4**, mean reduction in Q1 and Q4 between V1 and V2 saw significant differences in reduction at several risk factors. Six risk factors had a significant reduction when comparing mean reduction between Q1 and Q4.

Total cholesterol, HDL-C, LDL-C, non-HDL-C, and triglycerides was all significantly (***P*<.001**) different when compared. Diastolic BP was also significantly different with a value of ***P*=.002.**

All the individuals in Q1 enjoyed beneficial changes in all six of the significant risk factors associated with CVD, whereas all the individuals in Q4 saw a negative change of significant risk factors, giving an increase for CVD risk.

Table 4: Mean reduction in cardiovascular risk factors of individuals divided by quartiles of non-HDL-C reduction from visit 1 to visit 2, negative values indicate an increase in the given risk factor

	Q1 (n=77)	**Q4** (n=77)		
	Mean reduction		**95% CI**	***P*-value***
Body weight, kg	0.84 (4.02)	-0.04 (2.71)	-1.96, 0.20	.113
BMI, kg/m^2	0.28 (1.40)	-0.03 (1.00)	-0.69, 0.07	.116
Total cholesterol, mmol/L	**1.39 (0.90)**	**-1.11 (0.60)**	**-2.74, -2.25**	**<.001**
HDL-C, mmol/L	**0.10 (0.27)**	**-0.10 (0.46)**	**-0.31, -0.08**	**<.001**
LDL-C, mmol/L	**1.06 (0.78)**	**-0.86 (0.58)**	**-2.13, -1.70**	**<.001**
Non-HDL-C, mmol/L	**1.29 (0.79)**	**-1.01 (0.62)**	**-2.52, -2.07**	**<.001**
Triglycerides, mmol/L	**0.54 (1.20)**	**-0.33 (0.94)**	**-1.21, -0.53**	**<.001**
HbA1c, %	0.00 (0.23)	0.01 (0.16)	-0.07, 0.05	.755
Systolic BP, mmHg	4.00 (14.33)	3.08 (16.51)	-5.91, 3.91	.691
Diastolic BP, mmHg	**1.83 (7.93)**	**-1.53 (7.68)**	**-6.52, -1.47**	**.002**

BMI; body mass index, non-HDL-C; non-high-density lipoprotein cholesterol, BP; blood pressure
HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol
HbA1c; glycosylated hemoglobin, SD; standard deviation, Q1; quartile 1, Q4; quartile 4
CI; confidence interval, P-value; 2-tailed significance level

Individuals in Q1 had non-HDL-C reduction by ≤0.57 mmol/L
Individuals in Q4 had non-HDL-C increase by ≥0.49 mmol/L
Anthropometric and biochemical measurements are presented with mean (SD)
**P-values were not adjusted for multiple comparisons*

5.2. Dietary patterns

As a way of exploring dietary patterns, we used a PCA to reduce food intake variables into principal components (PC). Food groups positively associated with PC1 were intakes of fish, dairy, whole grains, and lean meats. For PC2 a positive association was observed for intakes of dairy products but inverse association for fish intakes. This indicates that individuals with high PC1 scores have high intakes of fish, dairy, whole grains, and lean meats. Individuals with high PC2 scores would be expected to have high intakes of dairy but low intakes of fish.

We plotted the PC1 and PC2 scores for all individuals in Q1 and Q4 into a loading plot (*Figure 3*). The individual points were colored according to quartiles of non-HDL-C

reduction. No clear separation between the points was seen, and thus the two groups could not be separated by PC1 and PC2 and the dietary factors therein.

As another means of assessing the dietary patterns, we also plotted the PC1 and PC2 as box plots (*Figure 4*). The individuals were grouped according to quartiles of non-HDL-C reduction. There was no dispersion between PC1 and PC2 according to quartiles of non-HDL-C reduction. PC1 and PC2 box plots showed that there was no difference in dietary patterns for individuals in Q1 and Q4.

Individuals in Q1 had the highest consumption of nuts, cereals, fruits, berries, juice, fish, and beer. They consumed the least of full fat dairy, fatty meats, and meat in general. Individuals in Q4 had the highest consumption of crispbread, whole grain bread, fatty meats, and coffee, and had the least consumption of nuts, cereals, fruit, berries, juice, lean dairy, milk (low fat, skim and in total), dairy products in total, water, and beer.

Some differences in the specific dietary items were observed. Individuals in Q1 had higher dietary intakes of nuts, cereals, fruits, berries, juice, fish, dairy products (particularly milk and lean dairy), beer, and water than individuals in Q4. On the other hand, individuals in Q4 had higher dietary intakes of breads, fatty meats, diet drinks, and coffee than individuals in Q1.

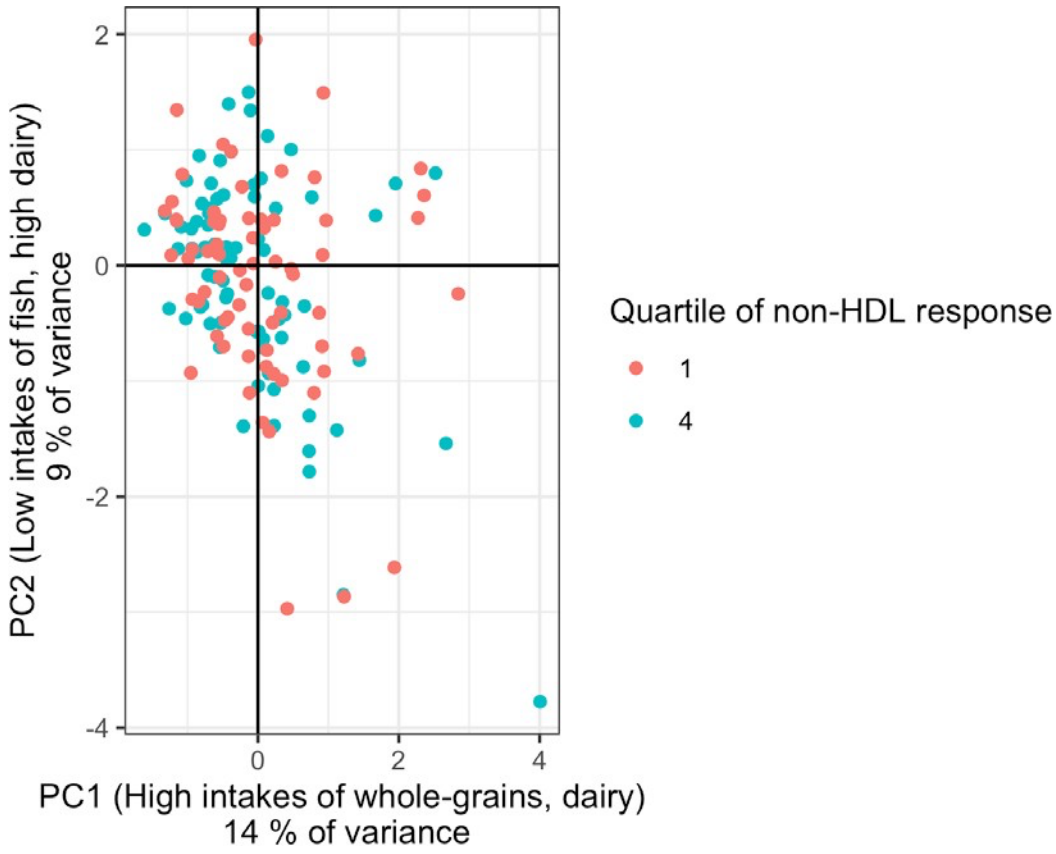

***Figure 3**:* Loading plot showing differences in dietary patterns between quartiles

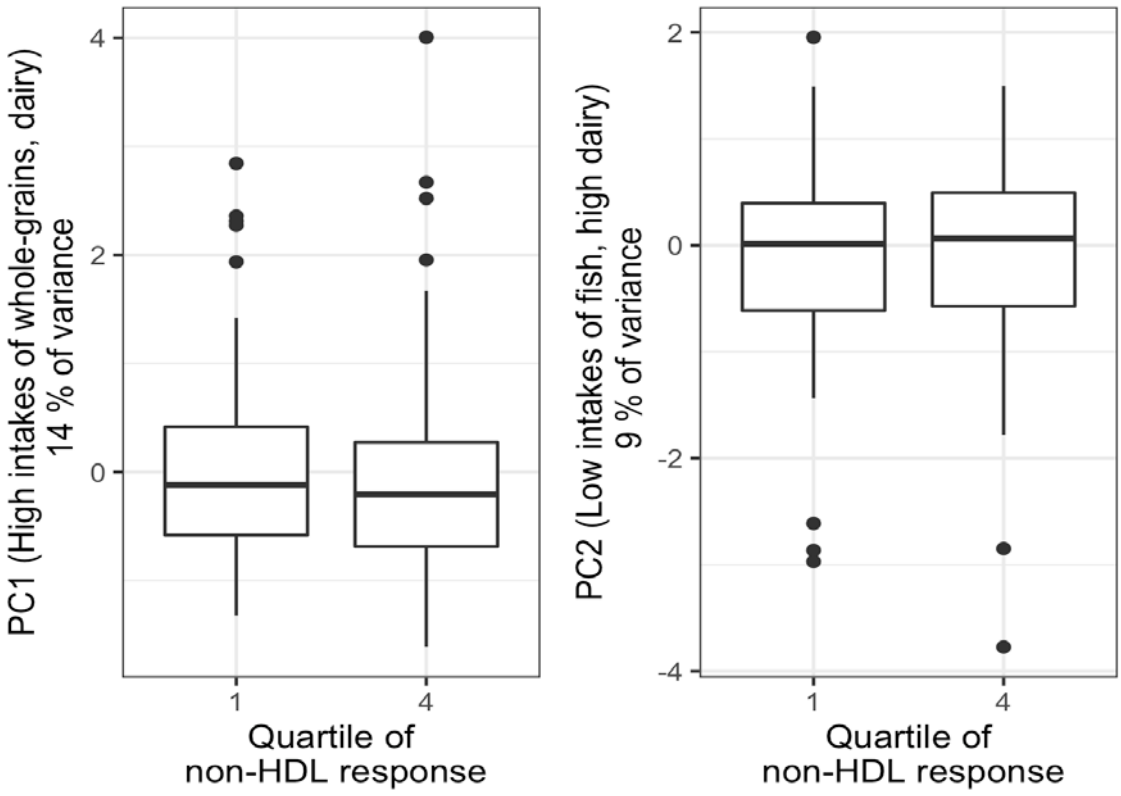

***Figure 4**:* Box plots showing differences in dietary patterns between quartiles

6. Discussion

In summary, our findings suggest that the individuals who had a large reduction in non-HDL-C ten months after a lifestyle intervention adhered to current guidelines for diet and physical activity. Being physically active for 30 minutes pr. day and choosing a diet high in fruits, vegetables, lean protein sources, low-fat dairy and whole-grains is an excellent strategy to stabilize, minimize and even reduce CVD risk.

Lifestyle interventions are considered an important first step of primary prevention for CVD, but there are large individual differences between individuals and the long-term effects still need more research. The aim for this study was therefore to find out more about the individuals who do see a benefit from lifestyle interventions by looking at diet and lifestyle factors. With longer follow-up, a meta-analysis looking at high-risk subjects 24 months or more after a lifestyle intervention found only modest effects on blood pressure (Bergum et al., 2021).

As we saw in **Table 1**, there were no big differences between the sexes at V1 and at V2 in terms of demographic, anthropometric and biochemical measures. Looking at the change in risk factors for both women and men, in **Table 2**, we could still not see many significant changes. Only at systolic BP did we see a significant difference in mean reduction between the sexes. Therefore, we decided to split our sample into quartiles of non- HDL-C change to look for what differentiated these individuals with a narrower scope.

When we examine our findings looking at **Table 3**, demographics for the individuals in Q1 and Q4, there was a slight difference between individuals with regards to sex (70% versus 80% females). Age (59 versus 60 years) and level of education (48% versus 47% of individuals in higher education) was similar in both Q1 and Q4. Hence, these factors do not seem to determine which individuals had a beneficial outcome of the lifestyle intervention in our study.

A difference between the quartiles was observed at physical activity levels. Individuals in Q1 spent slightly more time every day being physically active than individuals in Q4. However, we refrain from drawing a too robust conclusion from out data as the spread in this variable

was very large. We could also not say anything about how this physical activity was exercised, whether anaerobic or aerobic activity. Physical activity is known to reduce CVD risk, contrary to sedentary lifestyles (Liang, Zhang, Wang, Yuan, & Liang, 2022). The mean average and 1 standard deviation were almost identical. This means we had several individuals in both quartiles who spent close to zero or very little time being physically active. What we can say is that Q1 had slightly above 30 minutes of physical activity, whereas Q4 had slightly below 30 minutes on average. The updated 2018 guidelines from American Heart Association on Managing Blood Cholesterol for CVD prevention recommends up to and about 40 minutes of moderate-to-vigorous aerobic physical activity 3-4 times per week (Grundy et al., 2019).

The results presented in **Table 4** show us that the Q1 group did indeed have significant reduction in six risk factors associated with CVD. In all likelihood, this was a true beneficial reduction in CVD risk for these individuals. Positive outcome ten months after a lifestyle intervention is also indicated by other studies, but we do not know the if the individuals continued to see benefits at a later stage (Garcia-Lunar et al., 2022).

We wanted to see if there was a special dietary pattern or other variables that differed from the individuals with a large reduction in non-HDL-C and those who had not. Therefore, we chose to do a PCA, as there were many variables of specific food components in the dataset. By reducing these specific food components into broader components, we were hoping to identify a dietary pattern that could identify the individuals with a large reduction in non-HDL-C. By extracting the two most prominent components (PC1 and PC2) of the PCA and looking if there was a difference between individuals in Q1 and Q4, we could determine a dietary pattern that would identify these individuals, as shown in *Figure 3*.

While we could not observe any dietary pattern that could explain the large reduction in non-HDL-C, the individuals in the large reduction group (Q1) showed some variation in the amounts of specific dietary components consumed. Individuals in the large reduction groups (Q1) of non-HDL-C consumed more nuts, cereals, fruits, berries, juice, lean meats, lean dairy, water, and beer. They also consumed less bread, fatty meats, and coffee than the individuals (Q4) who had an increase in non-HDL-C.

The diet and lifestyle of these individuals are in line with current knowledge and guidelines

(Helsedirektoratet, 2016). This is further supporting the idea of a heart-healthy diet, which is a major primary preventative method for reducing CVD (Khanji et al., 2018).

Current guidelines on diet and lifestyle reflects what we found in the group of individuals with a large reduction in non-HDL-C, as these findings match the very recent & updated 2021 Dietary Guidelines to Improve Cardiovascular Health from the American Heart Association (Lichtenstein et al., 2021). These guidelines suggest a dietary pattern which include a variety of fruits and vegetables, healthy sources of protein, such as nuts, legumes, fish and lean meats, fat-free and lean dairy products, choosing foods with whole grains over refined grains, avoiding drinks with added sugar, and if drinking alcohol, limiting intake (Lichtenstein et al., 2021).

Alcohol consumption still has an unclear association with CVD risk. Observational studies see an inverse U-shaped relationship in alcohol and CVD, where non-drinkers and heavy drinkers are at a higher risk than moderate drinkers (Ding, O'Neill, Bell, Stamatakis, & Britton, 2021). We found that individuals with a large reduction in non-HDL-C consumed more alcohol than the individuals who had an increase in non-HDL- C.

Furthermore, we saw a correlation with lower coffee consumption and having lower concertation of non-HDL-C. Coffee consumption may be associated with an increase in LDL-C and triglyceride concentration (Du, Lv, Zha, Hong, & Luo, 2020). We saw a correlation with lower coffee consumption having lower concentration of non-HDL-C. However, there might be many confounding factors unaccounted for, such as individuals consuming coffee may be having a higher workload in daily life.

6.1. Methodical evaluations

Strengths of the study include a similarity in the groups being compared with respect to demographic and anthropometric measures. Although this study has an exploratory nature and the groups compared (Q1 to Q4) are not randomized, similarities in the groups can increase the likelihood of variation in non-HDL-C are explained by diet and lifestyle factors. However, there are several unmeasured factors that should be considered when interpreting the findings. Another strength includes the size of the sample (n=325) and time span between

measuring points (10 months) in addition to multiple risk factors measured (body weight, blood pressure, TC, TG, LDL, HDL, HbA1c).

Limitations of the study include the drop off from the 8-week intervention and the 52-week follow-up (about 35% were lost follow-up) (Svendsen, Telle-Hansen, et al., 2018). There could be a selection bias in the sample as the individuals returning at the 52-week follow-up might be the ones performing better in the 8-week intervention, and therefore more health conscious. Also, we recognize that people who actually come to pharmacies in the first place are already more health-oriented in their lifestyle than those who do not go to pharmacies.

In the VISA-FFQ, participants are asked to recall last 1-2 months of their diet and lifestyle habits. However, when we compared V1 with V2 there are 10 months between them. This could have impacted the results due to recall bias. Diet and lifestyle factors were also self-reported, which is associated with information bias (Althubaiti, 2016). Data collection and measurements at various pharmacies were done by different employees, which could lead to variation in procedure. An attempt to standardize by training was done, but it will be recognized as a limitation.

6.1.1. Non-HDL-C as biomarker for CVD

Which of the risk factors for CVD that are most appropriate to use and in what circumstances is still being debated. Outcome variable in this study was non-HDL-C as main risk factor for CVD. This choice was made based on available information in the datasets and that non-HDL-C is certainly a better factor for CVD risk than LDL-C or total cholesterol (Carr et al., 2019). There might be potential for other markers serving as more accurate measure of CVD risk. Emerging evidence suggest remnant cholesterol as a better predictive marker for CVD risk than LDL-C and ApoB (Quispe et al., 2021). A recent publication in the Journal of American Medical Association calls for an end to the debate, suggesting ApoB as primary marker for CVD risk (Sniderman, Navar, & Thanassoulis, 2021). While the jury is still out on most accurate markers for CVD risk, we recognize the strengths and limitations of non-HDL-C as outcome variable for CVD risk and continue to follow the debate closely.

7. Conclusion

Our findings suggests that the individuals in our sample at a moderately elevated risk for CVD with a large reductions in non-HDL-C ten months after a lifestyle intervention is adhering to the current guidelines for dietary pattern and lifestyle aiming at lowering CVD risk (Helsedirektoratet, 2016; Lichtenstein et al., 2021). These guidelines on dietary patterns and lifestyle include not smoking, being moderately physically active daily, eating a varied diet including vegetables, fruits, berries, nuts, lean protein sources, lean dairy products, choosing whole grain foods and products, and moderating alcohol intake.

When we compared the intakes of specific dietary components between the individuals with a large reduction in non-HDL-C versus the individuals with a large increase in non-HDL-C over a ten-month period, we found some differences in dietary intakes. Individuals with a reduction in non-HDL-C had a high consumption of nuts, fruits, berries, juice, cereals, dairy, fish, and lean meats. They drank more water and beer than the individuals with an increase in non- HDL-C, but less coffee. Individuals with an increase in non-HDL-C had higher intakes of bread and fatty meats. They drank more diet drinks and coffee than the individuals with a reduction in non-HDL-C, while drinking less water and beer.

Our findings in the dietary pattern and lifestyle of individuals with a reduction in non-HDL-C supports the current guidelines on a heart-healthy diet. Implementing these in future lifestyle interventions is crucial to reduce the growing prevalence of CVD.

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Attachment 1: Baseline questionnaire

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

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11 Fikk du beskjed om at blodsukkeret 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, *ikke* 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)

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 2

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+ ☐

61883

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+		½	1	2	3	4	5+
Fete kjøttprodukter (f.eks. familiedeig, vanlig grillpølser/wienerpølser, stek med fettrand, bacon, flesk o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =150g)	☐	☐	☐	☐	☐	☐
Halvfete kjøttprodukter (f.eks. kjøttdeig (okse,lam), kyllingpølse, lettpølse, hamburger, kylling med skinn o.l)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =150g)	☐	☐	☐	☐	☐	☐
Magre kjøttprodukter (f.eks. karbonadedeig, kjøttdeig (svin,kylling), biff, filet (kylling, svin, okse, lam), viltkjøtt, "Go' og mager pølser" o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =150g)	☐	☐	☐	☐	☐	☐

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+		1	2	3	4+
Polert, hvit ris	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Upolert, naturris	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Vanlig pasta	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Fullkornspasta	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐

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+		1	2	3	4	5+
Kaker, hvetebakst, vafler, søt kjeks	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐	☐
Dessert (f.eks. is, hermetisk frukt, pudding)	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Sjokolade, godteri	☐	☐	☐	☐	☐	☐	☐	☐	(porsjon =100g)	1/4 ☐	1/2 ☐	1 ☐	11/2 ☐	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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Attachment 3: REK applications

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Gjøril Bergva	22845529	01.07.2014	2013/1660/REK sør-øst D
			Deres dato:	**Deres referanse:**
			17.06.2014	

Vår referanse må oppgis ved alle henvendelser

Kjetil Retterstøl
PB 1046 Blindern
0317 Oslo

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

Forskningsansvarlig: Universitet i Oslo
Prosjektleder: Kjetil Retterstøl

Vi viser til søknad om prosjektendring datert 17.06.2014 for ovennevnte forskningsprosjekt. Søknaden er behandlet av leder for REK sør-øst D på fullmakt, med hjemmel i helseforskningsloven § 11.

Endringene innebærer:
-Endring i inklusjons- og eksklusjonskriterier: Hba1c >7,0 % og totalkolesterol >12,00 mmol/L tas inn som eksklusjonskriterer. I tabellen for kalkulering av risikoscore, er HDL inkludert, kjønn tatt ut og poengscoren for nivåer av blodtrykk, HbA1c, totalkolesterol har økt, slik at mindre nivåer nå gir høyere score.
-Kontrollgruppe 3 (som får utsatt kjennskap til nivåer og ikke får brosjyre om tips og råd til redusere risikonivåene), skal inkluderes fra de med høy risiko.
-LINK medical benyttes til å kalkulere hvilke deltagere som tilfredsstiller inklusjonskriteriene til høyrisikogruppene og for å sikre riktig randomisering og kjønns/alder/risikoscore fordeling.
-Antallet deltagere i intervensjon- og kontrollgruppene er redusert fra 700 deltagere i både intervensjon og kontrollgruppen til 200 i intervensjonsgruppen, og 200 i hver av de to kontrollgruppene. Det er derfor gjort en ny

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

styrkeberegning.
-Bioindex skal likevel ikke måles på visitt 1.
-Revidert forespørsel om deltakelse og samtykkeerklæring: Mindre endringer.
-Reviderte spørreskjema: i spørreskjema 1 inkluderes spørsmål om hvor lenge det er siden deltageren har spist eller drukket noe annet enn vann. Det er utviklet et nytt spørreskjema om kosthold og fysisk aktivitet (spørreskjema 2).
-Det er utformet kundekort.

Vurdering
REK har vurdert endringssøknaden og har ingen forskningsetiske innvendinger mot endringen av prosjektet.

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

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

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 med 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

Søknadsinformasjon

Utlysning	Prosjektsøknad
Søknad	Vaskulær livsstils-Intervensjon og Screening i Apotek: VISA studien
Søknadsld	7 791
Søkerorganisasjon	Universitetet i Oslo

Oppgave: Endring og/eller henvendelse

Oppgaveid	232432
Utført	14.01.2021
Sist oppdatert	14.01.2021

Hva gjelder endringen/prosjekthenvendelsen?

- Endring i prosjektmedarbeidere
- Annen endring

CRISTIN ID medarbeider

Name	Bård Lorentzen
Degree	Mastergrad
Position/Appointment	Masterstudent på prosjektet
Institution	Universitetet i Oslo
Research project role	Masterstudent på prosjektet

Beskriv annen endring:

Bård Loretzen er masterstudent som skal jobbe med innsamlede data i intervensjonsstudien i VISA. Resultatene av intervensjonen er publisert (Svendsen, 2018. PMCID: PMC6125803) og de viste ingen effekt av intervensjonen. Samtidig var det store individuelle forskjeller i effekt; noen fikk god effekt av reduksjonen definert som reduksjon i risikofaktorer for hjerte- og karsykdom, mens andre fikk en økning. Vi ønsker dermed med Bård sin masteroppgave å bruke innsamlede data på kosthold, livsstil, demografiske variabler og andre risikofaktorer til å finne ut hvilke faktorer som forklarer i størst mulig grad hvorfor noen individer har stor effekt/ suksess av livsstilsintervensjoner mens andre ikke har det. Denne informasjonen vil bli nyttig for planlegging og gjennomføring av fremtidige livsstilsintervensjoner. "Suksess" eller effekt er her definert som størst versus minst reduksjon i non-HDL som er et mål på negativ sammensetning av fettstoffer i blodet.

Andre nødvendige vedlegg 1 attachment (Prosjektskisse.pdf)

Beskrivelse av og begrunnelse for endringen

Det er stor nytte for samfunnet at vi utnytter innsamlede data i størst mulig grad til å utforske problemstillinger som kan komme folkehelsa til gode. Denne prosjektendringen, som går ut på å inkludere en masterstudent i prosjektet som vil jobbe med av-identifiserbare data fra livsstilsintervensjoner har potensielle til å få resultater som kan legge grunnlag for hvordan vi implementerer livsstilsintervensjoner i fremtiden for å påvirke til redusert hjerte- kar risiko.

Prosjektskisse vedlagt.

Attachment 4: Prosjektplan

1. **Tittel**

   Hvilke kosthold- og livsstilsfaktorer kjennetegner personer med stor reduksjon i non-HDL-kolesterol etter livsstilsintervensjon

2. **Introduksjon/bakgrunn**

   Omfanget av hjerte- og karsykdom er økende i verden. Omtrent 30% av alle dødsårsaker er knyttet til hjerte og karsykdom (Institute of Medicine, 2010; Townsend et al., 2016). Det ikke bare den vestlige verden som lider av hjerte- og karsykdom, utviklingsland har også en økende forekomst av hjerte- og karsykdom. Estimater viser at hjerte- og karsykdom vil dominere som dødsårsak i fremtiden (WHO, 2017). Livsstil er en viktig faktor for å kunne predikere risiko i utviklingen av hjerte- og karsykdom (Yusuf et al., 2004). Faktorer som er mulige å endre innenfor livsstil er fysisk aktivitet, kosthold og røyking (Vasan et al., 2005). Høyt nivå av total kolesterol, høye verdier av LDL-kolesterol og lave verdier av HDL-kolesterol er sterkt assosiert med risiko for utviklingen av hjerte- og karsykdom (Ference et al., 2017; Wilson, 1994). Måling av non-HDL-kolesterol (definert som total kolesterol minus HDL-kolesterol) kan være en bedre predikator for risiko knyttet utviklingen av hjerte- og karsykdom siden man tar hensyn til alle lipoproteinene i motsetning til å kun måle LDL-kolesterol eller HDL-kolesterol (F. J. Brunner et al., 2019; Lu et al., 2003). Endring av kosthold, økning av fysisk aktivitet og røykeslutt er forebyggende tiltak som kan redusere risiko for utvikling av hjerte- og karsykdom (Chomistek et al., 2015; Record et al., 2015). Livsstilsintervensjoner, med formålet om å endre kosthold, oppmuntre til mer fysisk aktivitet og redusere røyking, har potensielt en kraftig virkning for reduksjon av hjerte- og karsykdom (Akesson, Larsson, Discacciati, & Wolk, 2014; E. J. Brunner, Rees, Ward, Burke, & Thorogood, 2007).

   Denne studien baserer seg på en intervensjonsstudie fra Norge gjennomført i 2014 og 2015. (Svendsen, Telle-Hansen, et al., 2018) Denne studien gjorde en kartlegging av personer med risiko for utvikling av hjerte- og karsykdom. Formålet var å se om

livsstilsintervensjon og advarsel ved apotek kunne redusere risiko for utvikling av hjerte- og karsykdom. Personene ble randomisert i 3 grupper; intervensjon med advarsel, kun advarsel og kontroll. Intervensjonen omhandlet kosthold- og livsstilsråd, som reduksjon av salt, mettet fett, sukker, røyk og økning av fysisk aktivitet. Advarselen innebar at personen ble informert om at de hadde en økt risiko for utvikling av hjerte- og karsykdom. Det ble gjort 2 screeninger med 8-ukers mellomrom og 1 års oppfølging. Funnen fra studien viste ingen signifikante forskjeller mellom gruppene. Enkelte individer hadde stor endring i kolesterol-verdier og dette er hva denne studien skal forsøke å se nærmere på.

Det er lite man vet om hvilke faktorer som predikere en gunstig virkning av livsstilsintervensjoner. Hva er det som kjennetegner individer som har en god virkning på reduksjon av risiko for hjerte- og karsykdom som målt ved non-HDL-kolesterol (uten bruk av medisiner)?

Hvilke kosthold og livsstilsråd fulgte de? Bedre kunnskap om de faktorene som ligger til grunn for reduksjon av risiko for utvikling av hjerte- og karsykdom hos enkelt individer er nødvendig for å kunne forebygge forekomsten av livsstilssykdommer og skreddersy en mer målrettet intervensjon for enkelt individene som er i risikogruppen.

3. Formål/problemstilling

Formålet med denne studien er å kartlegge kosthold- og livsstilsfaktorer som påvirker risiko for utviklingen av hjerte- og karsykdom ved å bruke non-HDL-kolesterol som et mål for risiko. Det vil bli brukt to grupper fra utvalget til sammenligning. Den ene gruppen vil inkludere de forsøkspersonene som hadde størst reduksjon i non-HDL-kolesterol og den andre gruppen vil inkludere de forsøkspersonene som hadde minst reduksjon i non-HDL-kolesterol. Problemstillingen som studien skal forsøke å besvare: «*Hvilke kosthold- og livsstilsfaktorer kjennetegner personer med størst reduksjon i non-HDL-kolesterol sammenlignet med personer med minst reduksjon i non-HDL-kolesterol 52 uker etter en gjennomført intervensjonsstudie?»*

4. Metode

a. Design

Designet er en observasjonsstudie som benytter seg av det som var en tidligere 8-ukers intervensjonsstudie med 1 års oppfølging.

b. Utvalg

Utvalget består av 377 individer. Kriteriene for inklusjon er: ≥18 år og bosatt i Norge. Kriteriene for eksklusjon er: gravide/ammende, brukere av lipidsenkende, blodtrykkssenkende og/eller antidiabetiske medikamenter, personer som har/har hatt hjerte- og karsykdom eller diabetes mellitus type 1 & 2.

c. Variabler

Variablene som er nødvendige for å besvare denne problemstillingen er alder(skalanivå), kjønn(nominalnivå), høyde(skalanivå), vekt(skalanivå), total kolesterol(skala), HDL-kolesterol(skala), triglycerider(skala) og kalkulert non-HDL-kolesterol(skalanivå) samt utvalgte kosthold variabler og fysisk aktivitet målt med VISA-Food Frequency Questionnaire (VISA-FFQ)(Svendsen, Henriksen, et al., 2018). Måleskala for de enkelte variablene er angitt i parentes bak nevnte variabel. De uavhengige variablene er alle variablene som inneholder kostholdsvalg. De avhengige variablene er non-HDL-kolesterol.

d. Datainnsamling

Datainnsamling ble gjort av (Svendsen, Telle-Hansen, et al., 2018) på 48 forskjellige Boots apotek i 2014 og 2015. Forsøkspersonene ble kartlagt ved bruk av spørreskjema, kliniske undersøkelser og blodprøver. Det ble brukt 2 spørreskjema; ett hvor kosthold- og spisevaner ble registrert (VISA-FFQ) og ett hvor antropometriske og demografiske mål ble registrert, i tillegg til tidligere sykehistorie, bruk av medikamenter og sykdom i nærmeste familie relatert til hjerte- og karsykdom. Forsøkspersonene ble spurt om kosthold- og spisevaner i løpet av en gjennomsnittlig uke og basert på de 2 siste månedene. Antropometriske mål inkluderer alder, høyde, vekt og kjønn. Demografiske mål

inkluderer lønn, utdanning, bosted og etnisitet. I tillegg ble røykevaner og fysisk aktivitet kartlagt. Det ble også gjort måling av blodtrykk og tatt blodprøver. Blodtrykksmålingene ble gjort to ganger og basert på en gjennomsnittsverdi av disse. Blodprøvene kartla total kolesterol, triglyserider, LDL-kolesterol, HDL-kolesterol og HbA1c.

e. Analyse

Analysen av datamateriale blir gjort i statistikkprogrammet SPSS. Deskriptiv statistikk og regresjonsanalyser vil bli brukt for å svare på problemstillingen, eventuelt andre analysemetoder som kan benyttes i besvarelsen.

f. Prosjektorganisasjon/veileder, utstyr, ressurser

Prosjektet er tilknyttet avdeling for ernæringsvitenskap på UiO. Prosjektet gjennomføres av Bård Lorentzen (UiO). Hovedveiledere er Karianne Svendsen (UiO og OUS) og Hanne Solveig Dagfinrud (UiO). Andre veiledere er Kjetil Retterstøl, Kathrine J. Vinknes og Thomas Olsen (alle UiO). Prosjektet gjennomføres ved bruk av statistikk programmet SPSS og skriveprogram Word. Det er ingen økonomiske kostnader ved gjennomføringen av prosjektet.

g. Tidsplan

Juni, juli og august 2020: Lære SPSS og bli fortrolig med programmet og mulighetene med analyser av statistikk og databehandling. Finne relevante forskningsartikler, teoretiske arbeider og lignende tidligere prosjekter.

September, oktober og november 2020: Lese og gjennomgang av forskningsartikler, teoretiske arbeider og prosjekter. Gjøre analyser av dataene fra prosjektet i SPSS. Alle statistiske analyser planlagt ferdig innen slutten av november.

Desember, januar og februar 2020-21: Skriving av oppgaven, basert på tidligere arbeid gjort av andre og analysene av data gjort i SPSS. Ferdig med 1. utkast i slutten av februar.

Mars og april 2021: Sendte 1. utkast til veiledere for gjennomgang, korrekturlesing og tilbakemelding. Forbedring og ferdigstilling av oppgaven til 2. utkast. 2. utkast til veiledere for godkjenning.

April og mai 2021: Innlevering av ferdig prosjekt innen 1. mai 2021.

h. Etikk/personvern

Prosjektet er godkjent for gjennomføring av REK Sør-Øst (ref:2013/1660). Det er ingen ytterlige etiske betraktninger tilknyttet gjennomføringen av prosjektet. Alle forsøkspersoner avidentifisert ved hjelp av ID-nummer.

5. Referanseliste

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