Effect of Dietary Interventions on Body Weight, Body Composition and Cardiovascular Risk Factors After Varenicline-assisted Smoking Cessation

A Randomized Controlled Trial

Master Thesis by
Thea Amalie Bergvatn

Department of Nutrition
Faculty of Medicine
University of Oslo

August 2012
Effect of Dietary Interventions on Body Weight, Body Composition and Cardiovascular Risk Factors After Varenicline-assisted Smoking Cessation

A Randomized Controlled Trial

Master Thesis by
Thea Amalie Martinsen Bergvatn

Supervisors: Mette Svendsen and Bjørn S. Skålhegg

Department of Nutrition
Faculty of Medicine
University of Oslo

August 2012
Acknowledgement

I want to thank both my supervisors, Mette Svendsen and Bjørn S. Skålhegg, for their time and guidance, especially during the last writing process.

I want to thank my classmates for several fantastic years as a student at the University of Oslo – it wouldn’t have been the same without you.

I also want to thank my family, especially my mom, dad and fiancé, who always are there for me, support me and believe in me. And a special thanks to my son, Aron, for making me smile every day – you are my sunshine! I love you all so much.

I wish you all the best!

Love, Thea
**Summary**

**Introduction:** Cigarette smoking is a major risk factor for the development of many lifestyle diseases, including cardiovascular disease. Overweight and obesity have also been shown to be associated with an increased risk for several lifestyle diseases, and co-occurrence of overweight and smoking has substantial consequences for health. Smoking cessation and weight reduction are associated with both immediate and long-term benefits including reduced risk of cardiovascular disease and increased life expectancy. Varenicline is an approved smoking cessation product shown to increase the chances of a successful attempt to quit smoking. However, smoking cessation is associated with weight gain, and it is suggested that this weight gain may offset some of the advantages of giving up smoking. Concern regarding post cessation weight gain seems to be a powerful motivator for continued smoking, and post cessation weight gain is also often the reason for relapsing after cessation. It is therefore necessary to find some interventions that may prevent, or at least reduce, the weight gain associated with smoking cessation so that a larger proportion of weight concerned smokers may successfully quit smoking.

**Aims:** The first aim of this thesis was to compare the efficacy of a low fat diet high in complex carbohydrates (LFHCC; ≤30 energy % fat, ≤20 energy % protein and ≥50 energy % carbohydrate) and a high protein diet moderately reduced in carbohydrates (HPMRC; ≥25 energy % protein, ≤55 energy % fat and ≤20 energy % carbohydrates) in preventing short-term weight gain four and 12 weeks after smoking cessation. The second and third aims were to compare the effects of the two diets on body composition and cardiovascular risk factors, respectively, 12 weeks after smoking cessation. The last aim was to compare dietary changes and examine correlations between the dietary changes and changes in body weight four weeks after smoking cessation.

**Subjects and methods:** A total of 80 healthy overweight or obese men and women who were smoking ≥ 10 cigarettes daily and willing to take varenicline were randomized. Mean age was 50 (SD 9) years and mean BMI was 31 (SD 4) kg/m². Both groups received individual counseling for diet and smoking cessation with a total of 12 visits, the first visit at the date of screening and the last visit 12 weeks after smoking cessation. Continuous abstinence rates were estimated based on self-reported smoking status, confirmed by CO-measurements at every visit. Body weight was measured every week. Body composition (waist circumference, ...
hip circumference, waist-to-hip ratio, body fat % and muscle mass in kg) and cardiovascular risk factors (blood pressure, fasting blood glucose, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) were measured at randomization and 12 weeks after smoking cessation. For measuring of compliance with the intervention diets, 7-days weighed records were conducted at randomization and four weeks after smoking cessation. Statistical analyses were performed twice; once for the participants who were abstinent from smoking all 12 weeks after smoking cessation, and once for all completers regardless of their smoking status.

**Results:** A total of 70 participants met at the last visit, with no difference in completion-rates between the intervention groups. Of the participants randomized, 37.5% managed to be abstinent from cigarette smoking all twelve weeks after smoking cessation, with no significant difference between the dietary intervention groups. Four weeks after smoking cessation the change in body weight was not different between the groups (p>.05), but the HPMRC group had a significant (p<.01) mean weight reduction of -1.7 kg (95% CI -2.6, -.7). Post cessation weight gain 12 weeks after smoking cessation was prevented in both groups, with no significant difference (p=.40) in weight change between the groups. Mean difference in body fat was 1.4 (95% CI .0, 2.7) in favor of the HPMRC group (p=.04). No between-group differences in changes in waist and hip circumference, waist-to-hip ratio, muscle mass, blood pressure, glucose, total cholesterol, HDL, LDL or triglycerides were seen 12 weeks post cessation (all p>.05). However, both groups showed an increase in HDL (p<.05).

Among all completers, we found mean between-group differences in waist circumference reduction (2.3 cm [95% CI 2.2, 4.4], p=.03), fat mass (1.6 kg [95% CI 3.2, 2.9], p=.02) and triglycerides (.32 mmol/L [95% CI .03, .62], p=.03), all in favor of the HPMRC group. Both groups made several significant changes to their dietary composition, but no significant between-group difference in reduction of energy intake. The LFHCC group significantly reduced their intake of fat to ≤ 30 E% while the HPMRC group significantly increased their protein intake to ≥ 25 E%, but neither of the intervention groups met the target level for intake of carbohydrates. Despite this, we found a significant correlation between the change in intake of carbohydrate and change in body weight (r=.51, p=.02) in the HPMRC group among the nonsmokers. When we included the reduced smokers we found a significant correlation between changes in intake of protein and fat and changes in body weight (r=.39, p=.01 and r=.36, p=.02, respectively) in the HPMRC group.

**Conclusion:** Both a moderately energy-reduced diet with decreased intake of fat and increased intake of complex carbohydrate and a moderately energy-reduced diet with increased intake of protein and reduced intake of carbohydrates prevented short-term post cessation weight gain. However, it seems
like a diet with increased intake of protein and reduced intake of carbohydrate may result in more beneficial effects, such as decreased body fat, abdominal fat (waist circumference) and triglyceride levels compared to a diet with decreased intake of fat and increased intake of carbohydrate.
# Contents

## 1 Introduction

- **Smoking** ................................................................................................................................. 1  
  - 1.1.1 Prevalence of smoking ........................................................................................................ 1  
  - 1.1.2 Nicotine addiction ................................................................................................................. 1  
  - 1.1.3 The health consequences of smoking ................................................................................... 3  
  - 1.1.4 Smoking and cardiovascular disease ..................................................................................... 3  

## 1.2 Body weight and body composition

- 1.2.1 Body weight and body composition in smokers ........................................................................ 5

## 1.3 Cardiovascular risk factors

- 1.3.1 Cigarette smoking .................................................................................................................. 7  
- 1.3.2 Overweight and obesity .......................................................................................................... 7  
- 1.3.3 Dyslipidemia ........................................................................................................................... 8  
- 1.3.4 Hypertension .......................................................................................................................... 9  
- 1.3.5 Diabetes mellitus .................................................................................................................... 9  
- 1.3.6 Age .......................................................................................................................................... 9  
- 1.3.7 Physical inactivity .................................................................................................................. 10  
- 1.3.8 Diet ......................................................................................................................................... 10

## 1.4 Smoking cessation

- 1.4.1 Health effects .......................................................................................................................... 11  
- 1.4.2 Unintended health consequences of smoking cessation ......................................................... 11  
- 1.4.3 Smoking cessation treatment .................................................................................................... 13

## 1.5 Changes in body weight

- 1.5.1 Health effects of changes in body weight ............................................................................... 15

## 2 Aims and efficacy outcomes

- 2.1 Main aim ................................................................................................................................. 19  
- 2.2 Efficacy outcomes ..................................................................................................................... 19  
  - 2.2.1 Primary efficacy outcomes .................................................................................................... 19  
  - 2.2.2 Secondary efficacy outcomes .............................................................................................. 19  
  - 2.2.3 Third efficacy outcomes ....................................................................................................... 19
3 Subjects and methods ................................................................. 21

3.1 Subjects ................................................................................. 21
  3.1.1 Inclusion criteria ................................................................. 21
  3.1.2 Exclusion criteria ............................................................... 21
  3.1.3 Number of subjects ............................................................ 22

3.2 Study design ............................................................... 23
  3.2.1 Smoking cessation ................................................................. 24
  3.2.2 Dietary intervention ............................................................. 24

3.3 Study measurements and variables .............................................. 27
  3.3.1 Assessment of smoking status ................................................ 28
  3.3.2 Clinical measurements .......................................................... 29
  3.3.3 Laboratory measurements ....................................................... 30
  3.3.4 Assessment of diet ................................................................. 30
  3.3.5 Measurements conducted but not included in the master thesis ......................................................................................... 31

3.4 Safety and adverse events ......................................................... 32

3.5 Data management, statistical procedures and calculation of dietary intake ................................................................. 32
  3.5.1 Data management ................................................................. 32
  3.5.2 Statistical procedures ........................................................... 32
  3.5.3 Calculation of dietary intake .................................................... 34

3.6 Declaration of Helsinki and ethical review .................................. 35

3.7 The student’s tasks ............................................................... 36

4 Results .............................................................................. 37

4.1 Subject characteristics ............................................................. 37
  4.1.1 Characteristics at the date of screening ....................................... 37
  4.1.2 Characteristics at the date of randomization ................................ 38
  4.1.3 Screening failures ................................................................... 40
  4.1.4 Determination of smoking status .............................................. 40

4.2 Smoking cessation ................................................................. 41
  4.2.1 Continuous abstinence rate and point prevalence ....................... 41
  4.2.2 CO measurements and reported number of cigarettes .................. 42

4.3 Outcome variables ............................................................... 43
  4.3.1 Changes in body weight .......................................................... 43
Figures

Figure 1: Flow diagram of the progress throughout the different phases of the trial.
Figure 2: Abstinence rates in the two intervention groups.
Figure 3: Body weight changes from the date of screening to twelve weeks after smoking cessation among the nonsmokers.
Figure 4: Body weight changes from the date of screening to twelve weeks after smoking cessation among nonsmokers + reduced smokers.
Tables

Table 1: The WHO classification of BMI ................................................................. 7
Table 2: Treatment with varenicline 1-2 weeks before smoking cessation .................. 24
Table 3: Characteristics and smoking status at the date of screening ......................... 38
Table 4: Smoking status for all participants at the date of screening and randomization .... 41
Table 5: Weight changes from the date of randomization to twelve weeks after smoking cessation, both among the completers and among all randomized subjects ......................... 44
Table 6: Mean values and changes from randomization to 12 weeks after smoking cessation for the participants with 12 weeks continuous abstinence ............................................. 47
Table 7: Mean values and changes from randomization to 12 weeks after smoking cessation in nonsmokers plus reduced smokers ................................................................. 49
Table 8: Results from dietary records and indirect calorimetry for the participants with 12 weeks continuous abstinence ................................................................. 52
Table 9: Results from dietary records and indirect calorimetry for the participants who completed at both measurement times (randomization and 4 weeks after smoking cessation). .............................................................................................................. 54
Table 10: Intended and reported intake of macronutrients in the two intervention groups four weeks after smoking cessation (nonsmokers + reduced smokers) ............................................. 55
Table 11: Correlations between changes in mean daily intake of macronutrients and change in body weight from randomization to four weeks after smoking cessation ..................... 57
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Added sugar</td>
<td>Simple sugars that are not found naturally in the food</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CAR</td>
<td>Continuous Abstinence Rate; refers to those participants who quit smoking and maintain abstinence throughout the following period</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>CO</td>
<td>(expired-air) carbon monoxide</td>
</tr>
<tr>
<td>Complex carbohydrates</td>
<td>Oligosaccharides, polysaccharides</td>
</tr>
<tr>
<td>CRF</td>
<td>Case record form</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DBP</td>
<td>Diastolic blood pressure</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>DR</td>
<td>Dietary record</td>
</tr>
<tr>
<td>e.g.</td>
<td><em>Exempli gratia</em>, meaning “for example” or “such as”</td>
</tr>
<tr>
<td>etc.</td>
<td><em>Et cetera</em>, meaning “and other things” or “and so forth”</td>
</tr>
<tr>
<td>E%</td>
<td>Energy %, percentage of energy</td>
</tr>
<tr>
<td>FTND</td>
<td>Fagerström Test for Nicotine Dependence</td>
</tr>
<tr>
<td>GABA</td>
<td>Gamma aminobutyric acid</td>
</tr>
<tr>
<td>HDL</td>
<td>High-density lipoprotein (cholesterol)</td>
</tr>
<tr>
<td>HPMRC</td>
<td>High Protein diet Moderately Reduced in Carbohydrates</td>
</tr>
<tr>
<td>i.e.</td>
<td><em>Id est</em>, meaning “that is” or “in other words”</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>Collective term for myocardial infarction, angina pectoris and coronary atherosclerosis</td>
</tr>
<tr>
<td>LDL</td>
<td>Low-density lipoprotein (cholesterol)</td>
</tr>
<tr>
<td>LFHCC</td>
<td>Low Fat diet High in Complex Carbohydrates</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>XIV</td>
<td></td>
</tr>
</tbody>
</table>
MJ  megajoule (= 1000 kJ or 239 kcal)
N  number of subjects
nAChR  nicotinic acetylcholine receptor
NO  nitric oxide
NYHA  New York Heart Association
Overnight fast  minimum 8 hours fasting
PAL  physical activity level
pp  point prevalence abstinence; refers to smoking (yes vs. no) at a particular follow-up time point
ppm  parts per million
REE  resting energy expenditure
RMR  resting metabolic rate
SBP  systolic blood pressure
SC  smoking cessation
SD  standard deviation
TG  triglycerides
TIA  transient ischemic attack
WHO  World Health Organization
WHR  waist-to-hip ratio
24-EE  24-hours energy expenditure
95% CI  95% confidence interval
%COHb  percentage of carboxyhaemoglobin
1 Introduction

1.1 Smoking

1.1.1 Prevalence of smoking

Worldwide, more than 1 billion adults are regular tobacco smokers, and smoking rates are even higher among adolescents. During the last 15 years the proportion of daily smokers in Norway has been almost halved. Yet, in 2011, 17% of the Norwegian population aged 16-74 years reported to be smoking daily. This equals about 700 000 daily smokers in Norway. In addition, 11% reported to be smoking occasionally. Totally there have been comparable smoking habits in men and women the last 15 years, but there are some differences in different age groups. Among the youngest and among people aged 35-54 years, there are a larger proportion of female daily smokers than males. 9% of the men and 13% of the women aged 16-24 years reported to be smoking daily in 2011. There is also a larger proportion of cigarette smokers in lower compared to higher socioeconomic classes.

1.1.2 Nicotine addiction

Although most of the toxicity of smoking is related to other components of the cigarette, it is the pharmacologic effects of nicotine that produce the addiction to tobacco and maintains smoking behavior. Nicotine meets all of the Surgeon General’s primary criteria for drug addiction, which state that the drug must (1) promote highly controlled or compulsive use, (2) have psychoactive effects, and (3) reinforce its own use. Nicotine is associated with many well-known pleasurable psychoactive effects, such as arousal, relaxation and improved mood.

When a person inhales smoke from a cigarette, nicotine is distilled from the tobacco and carried in the smoke particles into the lungs, where it is absorbed rapidly into the pulmonary venous circulation. It then enters the arterial circulation and moves quickly to the brain. Nicotine diffuses readily into brain tissue, where it binds to nicotinic acetylcholine receptors (nAChRs). The nAChR complex is composed of 5 subunits arranged in a ring around a central channel that opens to admit ions when the receptor is activated. The mix of subunits in each nAChR gives the receptor its distinct pharmacological properties, including its
response to nicotine stimulation. There are several types of α- and β-subunits in the mammalian brain, but the predominant receptor subtype in the human brain is α4β2. This is believed to be the main receptor mediating nicotine dependence. Nicotine interacts with nAChRs on different neurons, including dopaminergic neurons, in the brain’s mesolimbic reward system. The interaction between nicotine and nAChRs on dopaminergic neurons results in release of the neurotransmitter dopamine. Increases in dopamine levels within the mesolimbic system give rise to rewarding effects, like stimulation and pleasure, and reduced stress and anxiety. In addition, smoking may improve concentration, reaction time and performance of certain tasks. Nicotine also stimulates dopamine release indirectly by binding to nAChRs located on excitatory glutamatergic neurons. This interaction results in glutamate release, which in turn stimulates dopaminergic neurons. In contrast, binding of nicotine to nAChRs located on inhibitory gamma aminobutyric acid (GABAergic) neurons lead to the release of gamma aminobutyric acid (GABA), which in turn will inhibit dopaminergic neurons. Both glutamate and GABA neurotransmission play important roles in the development of nicotine dependence.

Persistent nicotine use leads to tolerance that is mediated by neuroadaptations occurring in response to chronic nicotine exposure. Concurrent with this neuroadaptation is an increase of nAChRs in the brain. This increase is believed to represent upregulation in response to nicotine-mediated desensitization. This desensitization may play a role in nicotine tolerance and dependence. When a person stops smoking, nicotine withdrawal symptoms will usually emerge. These include irritability, depressed mood, restlessness, anxiety, difficulty concentrating, increased hunger and eating, insomnia and craving for tobacco.

Measurement of nicotine addiction

The most widely used nicotine dependence measure is the Fagerström tolerance questionnaire, or the modified version, the Fagerström Test for Nicotine Dependence (FTND). The latter is a 6-item questionnaire concerning the replier’s smoking behavior. The questionnaire generates test scores ranging from 0 to 10; the higher the score, the more nicotine dependent the smoker. The six questions are as follows: (1) How soon after you wake do you smoke your first cigarette? (2) Do you find it difficult to refrain from smoking in places where it is forbidden, for example church, library, cinema etc.? (3) Which cigarette would you hate most to give up? (4) How many cigarettes/day do you smoke? (5) Do you
smoke more frequently during the first hours after waking than during the rest of the day? and
(6) Do you smoke if you are so ill that you are in bed most of the day?

The more nicotine dependent a smoker is the less is the probability of successful smoking cessation. It is reported that an increase of one unit in baseline FTND score decreases the odds of abstinence at week 24 after smoking cessation by 11%.

1.1.3 The health consequences of smoking

Cigarette smoking harms nearly every organ in the body, and is widely accepted as a major risk factor for the development of many lifestyle diseases, including cardiovascular disease, different kinds of cancer and respiratory diseases\textsuperscript{10,11}. Tobacco smoking is the single greatest cause of avoidable morbidity and mortality in both the United States\textsuperscript{10} and in Europe\textsuperscript{12} and is one of the most hazardous health threats globally\textsuperscript{13}. Approximately half of all long-term smokers die prematurely as a result of smoking, and the life span of the continuing smoker will be reduced by 10 years on average\textsuperscript{1}. Globally, tobacco smoking accounts for over 5 million deaths annually\textsuperscript{8,13}, and the mortality burden is estimated to increase to over 10 million deaths per year in 2025 if present trends continue\textsuperscript{8}. During 2000-2004, cigarette smoking and exposure to tobacco smoke resulted in at least 443 000 premature deaths and approximately 5.1 million years of potential life lost annually in the United States. Among adults aged $\geq$ 35 years, 41.0\% of smoking-attributable deaths were caused by cancer, 32.7\% by cardiovascular diseases, and 26.3\% by respiratory diseases\textsuperscript{14}. It is also shown that insulin resistance may be dose-dependently related to cigarette smoking\textsuperscript{15}, and that the risk of type 2 diabetes is greater in smokers than in nonsmokers\textsuperscript{16,17}. In addition to the health consequences of smoking, cigarette smoking contributes to economic losses to society and a substantial burden on the health-care system, resulting in 96.8 billion US dollars in productivity losses annually in the United States during 2000-2004\textsuperscript{14}.

1.1.4 Smoking and cardiovascular disease

Cardiovascular disease (CVD) is the leading cause of mortality in both men and women, and in the United States CVD accounts for an average of 1 death every 39 seconds\textsuperscript{18}. In Norway there has been a decrease in the number of deaths from cardiovascular diseases from 1986 to 2010, but in 2010 still 2 out of 5 deaths are due to cardiovascular disease. A total of 6 out of 10 deaths were due to cardiovascular disease or cancer. Among the cardiovascular diseases,
ischemic heart disease was the most common cause of death. Among people younger than 65 years, more men than women die of ischemic heart disease\textsuperscript{19}. The risk of coronary heart disease (CHD) increases with the number of cigarettes smoked and cigarette smoking has been reported to increase the incidence of myocardial infarction (MI) and fatal coronary artery disease in both men and women compared to nonsmokers of both sexes\textsuperscript{20,21}. Even passive smoking (environmental tobacco exposure) is associated with approximately a 30% increase in risk of coronary artery disease, compared with an 80% increase in active smokers\textsuperscript{21}. It is also shown that women who smoke may be at greater cardiovascular risk than men who smoke\textsuperscript{22}.

The pathophysiologic mechanisms underlying the health consequences of smoking are complex. The estimated number of compounds in cigarette smoke exceeds 4000, including many that are pharmacologically active, toxic, mutagenic and carcinogenic\textsuperscript{11}. Increased oxidative stress due to free radicals arising from cigarette smoke\textsuperscript{23} may play a central role in cigarette smoke-mediated diseases. It is hypothesized that cigarette smoking can cause release of excessive vasoactive prostanoids to the circulation\textsuperscript{24}. Nitric oxide (NO) is a free radical primarily responsible for the vasodilatory function of the endothelium\textsuperscript{25} and it’s likely that cigarette smoking is associated with decreased NO availability\textsuperscript{26}. This might be a part of the explanation of why cigarette smoking is associated with a decrease in vasodilatory function with impaired endothelium-dependent vasodilation\textsuperscript{27,28} in both macrovascular beds such as coronary arteries and in microvascular beds\textsuperscript{29,30}. In addition, NO also has other important biological functions, including inhibition of platelet adhesion and aggregation\textsuperscript{31}. It is possible that smoking tobacco has direct effects on activation of platelets by decreasing the availability of platelet-derived NO and decreasing platelet sensitivity to exogenous NO, leading to increased activation and adhesion\textsuperscript{32,33}.

Vasomotor dysfunction, inflammation and modifications of lipids are integral components for the initiation and progression of atherosclerosis. Howard et al.\textsuperscript{34} found that both active smoking and the duration of smoking plays a major role in the progression of atherosclerosis, and that smoking especially increased atherosclerosis progression rates among participants with diabetes and hypertension. Dyslipidemia is a risk factor for CVD\textsuperscript{18}, and smokers have increased total cholesterol, low-density lipoprotein cholesterol (LDL) and triglycerides (TG), together with decreased high-density lipoprotein cholesterol (HDL) compared to non-smokers\textsuperscript{35-37}. The risk of CHD is inversely related to serum HDL, and a decrease in HDL of
0.40 mmol/L is associated with an approximately 70% increased risk of CHD in smokers, compared to 30% in non-smokers\textsuperscript{38}. It is, however, shown that chronic cigarette smoking can enhance the progression of atherosclerotic lesions in carotid bifurcations even without hyperlipidemia\textsuperscript{24}. Cigarette smoking also increases oxidative modification of LDL\textsuperscript{39,40}. Oxidized LDL is more atherogenic than native LDL as it is recognized by the scavenger receptors and can therefore give rise to foam cell formation\textsuperscript{41} and the initiation, or at least acceleration, of the atherosclerotic process. Adiponectin is an adipose-specific gene product shown to have an anti-inflammatory effect on endothelial cells, it inhibits the proliferation of vascular smooth muscle cells and suppresses the conversion of macrophages to foam cells\textsuperscript{42}. It has been reported that cigarette smokers have significantly lower plasma concentrations of adiponectin compared to nonsmokers\textsuperscript{42}. It is shown that smoking a single cigarette or receiving intravenous nicotine increases blood pressure, but smokers have equal or lower blood pressures than nonsmokers, probably due to development of tolerance and lower body weights among smokers\textsuperscript{43}.

\section*{1.2 Body weight and body composition}

The prevalence of overweight and obesity is increasing in all age groups\textsuperscript{44,45}. The worldwide prevalence of obesity almost doubled between 1980 and 2008. Overweight and obesity have been shown to be associated with an increased risk of heart disease, diabetes, arthritis and cancer\textsuperscript{45,46}, and there is a strong association between body mass index (BMI) and mortality in nonsmokers\textsuperscript{47}. In addition to total body fat, there are some evidence that fat distribution may be an important determinant of morbidity and mortality. High amounts of abdominal fat have been shown to be associated with metabolic disease risk\textsuperscript{48} and increased mortality\textsuperscript{49}, independent of overall adiposity and BMI\textsuperscript{50,51}.

\subsection*{1.2.1 Body weight and body composition in smokers}

Smoking is associated with a lower body weight, and smokers have a lower BMI than nonsmokers\textsuperscript{35,52,53}. Smoking’s effect on body weight could lead to weight loss by decreasing metabolic efficiency or decreasing caloric absorption through a reduction in appetite, since both are associated with tobacco use\textsuperscript{53}. The metabolic effect of smoking could also explain the lower body weight found in smokers, since there is evidence that cigarette smoking increases 24-hour energy expenditure by approximately 10\%\textsuperscript{54}. However, even though there
is evidence that smokers have lower body weight than never smokers and former smokers, it is also showed in some previous studies that among smokers, increased amount of smoking tends to be positively associated with BMI, particularly among men\textsuperscript{55-57}. This suggests that the factors associated with smoking counter and overtake the metabolic effect of smoking. One explanation could be that heavy smokers are more likely to adopt behaviors favoring weight gain, and it is shown that smokers eat less fruit and vegetables, adopt unhealthy patterns of nutrient intake, drink more alcohol and engage in less physical activity than nonsmokers do\textsuperscript{53}. However, it is suggested that the lower BMI of smokers compared to nonsmokers reflects personality characteristics of those who choose to smoke\textsuperscript{56}, and it is shown that smoking initiation, especially in women, is associated with weight concern or dieting and overweight\textsuperscript{58}. This may be a contributing reason for the associations seen between heavy smoking and obesity. The co-occurrence of overweight and smoking has substantial consequences for health, and in the Framingham Heart Study\textsuperscript{59}, the life expectancy of obese smokers was found to be 13 years less than that of normal-weight nonsmokers.

Even though smokers have a lower BMI than nonsmokers, smoking is not necessarily associated with a smaller waist circumference\textsuperscript{53,60,61}, and some evidence actually suggests that smoking is related to visceral fat accumulation\textsuperscript{62}. In fact, several studies indicate that waist-to-hip ratio (WHR) is higher in smokers than in nonsmokers\textsuperscript{60,61,63,64}, and that there is a dose-response relation between WHR and the number of cigarettes smoked\textsuperscript{56,61}. Actually, smokers tend to have both a larger waist circumference and a smaller hip circumference than do nonsmokers\textsuperscript{37,64}, which indicates less muscle mass at hip level in addition to greater abdominal fat deposition. This paradox of the combination of a high WHR with a low BMI is more frequent in smokers than in nonsmokers\textsuperscript{65}. Less muscle mass at hip level in smokers may be due to impaired protein muscle synthesis and increased expression of genes associated with inhibition of muscle growth and catabolism caused by smoking cigarettes\textsuperscript{66}.

### 1.3 Cardiovascular risk factors

Cardiometabolic risk is the overall risk of cardiovascular disease resulting from the presence of traditional risk factors such as lipids (LDL and HDL), blood pressure, glucose, age, male gender, smoking and other risk factors (including genetic and inflammatory factors), and the metabolic syndrome\textsuperscript{67}. Metabolic syndrome refers to a cluster of risk factors for CVD and type 2 diabetes mellitus (DM)\textsuperscript{18}. 
1.3.1 Cigarette smoking

Cigarette smoking is a major cause of premature CHD\(^68\), and is highly correlated with an increased incidence of CVD mortality\(^69\). Smoking actually more than doubles the risk of all types of CVD – CHD, ischemic stroke, peripheral arterial disease and abdominal aortic aneurism, and smoking is the strongest independent risk factor for abdominal aortic aneurism\(^70\). The risk of CHD associated with smoking has been shown to be proportionally higher in women than in men\(^70\). As mentioned above, smoking leads to an accumulation of central fat and insulin resistance, and this may represent a major link between cigarette smoking and the risk of cardiovascular disease\(^71\).

1.3.2 Overweight and obesity

One of the most important parameters used to assess body weight is the BMI, which is calculated as the body weight in kg divided by the square of the height in meters. BMI is used to set cut-off limits for normal-weight and body weight that can increase the risk of diseases. The World Health Organization’s (WHO) classification of BMI\(^72\) is given in table 1.

<table>
<thead>
<tr>
<th>BMI classification</th>
<th>BMI range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
</tr>
<tr>
<td>Normal range</td>
<td>18.5 – 24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥ 25.0</td>
</tr>
<tr>
<td>Preobese</td>
<td>25.0 – 29.9</td>
</tr>
<tr>
<td>Obese</td>
<td>≥ 30.0</td>
</tr>
<tr>
<td>Obese class I</td>
<td>30.0 – 34.9</td>
</tr>
<tr>
<td>Obese class II</td>
<td>35.0 – 39.9</td>
</tr>
<tr>
<td>Obese class III</td>
<td>≥ 40.0</td>
</tr>
</tbody>
</table>

WHO: World Health Organization, BMI: Body Mass Index, kg/m\(^2\)

Obesity is one of the most important health issues globally, with about 315 million of the world population having a BMI ≥ 30 kg/m\(^2\)\(^73\). Today, as many as 1 out of 5 Norwegians are obese. This is twice as many as twenty years ago. The prevalence of obesity has increased both in developed and developing countries. Globally, women are obese more often than men, but among high-income nations, the prevalence of obesity is equivalent among women and men\(^69\). Obesity is associated with elevated blood pressure, dyslipidemia, physical inactivity and increased insulin resistance, all adding to an increased risk of CVD\(^69\), including myocardial infarction and stroke\(^74\). As much as 23% of ischemic heart disease is attributable
to overweight and obesity\textsuperscript{72}. Obesity increases not only the risk of cardiovascular diseases, but also the risk of several types of cancer, type 2 diabetes, gout, and infertility\textsuperscript{74}. In fact, overweight and obesity are the reasons for 44\% of diabetes and 7-41\% of certain cancers globally\textsuperscript{72}. Excess weight is an important contributing factor to the development of coronary heart disease in younger compared to older patients\textsuperscript{68}. Having increased waist circumference is part of the metabolic syndrome, which is an independent predictor of major coronary events in patients with CHD\textsuperscript{68}. Mortality from cardiovascular disease is increased in obese individuals with a BMI $> 25$ kg/m$^2$\textsuperscript{75}.

Waist circumference or WHR is an indicator of the amount of visceral adipose tissue, and a greater amount of visceral adipose tissue is related to the metabolic syndrome, diabetes and cardiovascular diseases\textsuperscript{76}. Results from the INTERHEART study indicated that abdominal obesity had higher correlation with risk of myocardial infarction compared with BMI\textsuperscript{77}. De Koning et al.\textsuperscript{78} found that both waist circumference and WHR are significantly associated with the risk of incident CVD events, and suggested that these simple measures of abdominal obesity should be incorporated into CVD risk assessments. Increased waist circumference ($\geq 88$ cm in women and $\geq 102$ cm in men) is associated with 3-4 times increased prevalence of risk factors for CVD\textsuperscript{74}. An elevated risk is also associated with a WHR $> .90$ in women and $>1.0$ in men\textsuperscript{75}.

1.3.3 Dyslipidemia

Dyslipidemia has the highest population-adjusted risk among women, and a continuous increase in CVD risk with worsening dyslipidemia has been noted\textsuperscript{69}. It is estimated that the prevalence of total cholesterol levels $\geq 6$ mmol/L among adults $\geq 20$ years of age is 16.2\%\textsuperscript{18}. LDL-cholesterol levels of $\geq 3.3$ mmol/L are considered borderline high, levels of $\geq 4.1$ mmol/L are classified as high, and levels of $\geq 4.9$ mmol/L are considered very high\textsuperscript{18}. For HDL-cholesterol levels, $<1.0$ mmol/L in adult males and $<1.3$ mmol/L in adult females is considered low and is a risk factor for heart disease and stroke. A fasting TG level $>1.7$ mmol/L in adults is considered elevated and is also a risk factor for heart disease and stroke\textsuperscript{18,79}.
1.3.4 Hypertension

High blood pressure is defined as systolic blood pressure (SBP) $\geq 140$ mmHg or diastolic blood pressure (DBP) $\geq 90$ mmHg or taking antihypertensive medications\textsuperscript{18}. As many as one in 3 US adults has high blood pressure\textsuperscript{18}. Hypertension is associated with increased risk of CVD\textsuperscript{69,79}, and approximately 69% of people who have a first heart attack and 77% of those who have a first stroke have blood pressure $>140/90$ mmHg\textsuperscript{18}. Hypertension is also associated with shorter overall life expectancy, shorter life expectancy free of CVD, and more years lived with CVD\textsuperscript{18}.

1.3.5 Diabetes mellitus

An estimated 18.3 million Americans $\geq 20$ years of age have physician-diagnosed DM. An additional 7.1 million adults have undiagnosed DM, and the prevalence of prediabetes (i.e. fasting blood glucose of 5.6 to $<7.0$ mmol/L) in the US population is nearly 37%\textsuperscript{18}. Globally, there are more women diagnosed with DM than men. In addition, a higher correlation between CVD mortality and diabetes exists among women than men\textsuperscript{69}. DM increases the risk of stroke, with the relative risk ranging from 1.8 to almost 10.0. DM increases ischemic stroke incidence at all ages, but this risk is most prominent before 55 years of age in blacks and before 65 years of age in whites\textsuperscript{18}. All-cause and CVD mortality rates among men and women with and without DM decreased from 1950 to 2005, but all-cause and CVD mortality rates among individuals with DM remain approximately 2-fold higher than for individuals without DM\textsuperscript{18,80}.

1.3.6 Age

Advancing age is a major risk factor for CVD. The average annual rates of first cardiovascular events rise from 3 per 1000 men at 35 to 44 years of age to 74 per 1000 men at 85 to 94 years of age. For women, comparable rates occur 10 years later in life\textsuperscript{18}. In 2008, the leading causes of death in both men and women $\geq 65$ years of age were diseases of the heart\textsuperscript{18}. Ischemic heart disease was the main cause of death among people aged 65 years or older in Norway in 2010\textsuperscript{19}.
1.3.7 Physical inactivity

Physical inactivity is responsible for 12.2% of the global burden of MI after accounting for other CVD risk factors, including cigarette smoking, DM, hypertension, abdominal obesity, and lipid profile\textsuperscript{18}. The relative risk of CHD associated with physical inactivity ranges from 1.5 to 2.4. Subjects participating in $\geq 150$ min of moderate physical activity weekly reduce their chance of ischemic heart disease by 30\%\textsuperscript{69}.

1.3.8 Diet

Worldwide epidemiology studies and transmigration studies indicate a strong role for dietary composition with foods rich in saturated fat, cholesterol, and sugar being related to increased CHD mortality\textsuperscript{81}. Conversely, an increased intake of fruits, grains, vegetables, and vegetable oils, as well as moderate alcohol intake, is associated with reduction in CVD risk factors and protection\textsuperscript{81,82}.

1.4 Smoking cessation

In the USA, although more than 79\% of smokers want to quit every year and 45\% make an attempt to quit, less than 5\% in the general population are successful\textsuperscript{8}. In Europe the percentage of smokers without intention to quit is even higher than in the USA\textsuperscript{42}. Fear of weight gain after quitting smoking is often reported to act as a barrier to smoking cessation, especially among women\textsuperscript{12,42}. Post cessation weight gain is also often the reason for relapsing after cessation\textsuperscript{42,83}. The long-term abstinence rate for a given quit attempt among untreated smokers appears to be 3-5 \%, and it may take as much as 10-14 quit attempts before a smoker is successful in achieving abstinence\textsuperscript{84}.

Most of those who quit cigarette smoking do this on their own, but for many people it would be easier to stop smoking if they got a little help. It is therefore previously recommended that all smokers should be provided with treatment for smoking cessation. In 2010, WHO pointed out that the tobacco cessation offer in Norway is too poor. Based on this, in 2012 Helsedirektoratet came up with a plan for a systematic and evidence based offer for smoking- and snus-cessation, addressing different treatments for tobacco cessation and organization of the work with tobacco in Norway\textsuperscript{3}.  

10
1.4.1 Health effects

Quitting smoking has immediate as well as long-term benefits, reducing risks for diseases caused by smoking and improving health in general\(^{10}\). Smoking cessation quickly reduces the risk of developing diseases, and persons who quit smoking before 40 years of age do not have increased risk of premature mortality\(^{3}\), but studies show that the substantial risks of smoking also can be reduced by successfully quitting at any age\(^{10}\). Smoking cessation reduces the risk of stroke with a marked risk reduction within 2-5 years after quitting, and that the risk approaches, but perhaps never quite reaches, the risk of never-smokers after 10-15 years\(^{70}\). Furthermore, it has been reported that for mortality from any cause and from the cause specific diseases (CVD, ischemic heart disease, stroke and smoking-related cancers), sustained ex-smokers have adjusted relative risks that not differs significantly from those of the never smokers\(^{85}\). The exception was the risk of dying from lung cancer in men, but this risk was significantly lower than the risk in male smokers. Cessation of smoking significantly reduces the increased risk of acute MI associated with cigarette smoking over a one- to three-year period, with an exponential decline approaching the risk in ex-smokers within five years of cessation\(^{21}\). In addition, smoking cessation improves insulin sensitivity and is associated with an increase in HDL cholesterol, also in spite of post cessation weight gain\(^{42}\). Some previous trials have suggested that the risk of diabetes in former smokers decreases progressively as the length of time since smoking cessation increases\(^{17,86}\) and may return to normal after a few years\(^{86}\).

1.4.2 Unintended health consequences of smoking cessation

Smoking cessation is associated with increased body weight, mostly due to increased body fat\(^{66,87}\). In the USA it is estimated that 80% of people who quit smoking gain weight, and studies have found that on average women gain more weight than men\(^{88}\). How much weight gain that is reported to follow smoking cessation is not consistent. O’Hara et al.\(^{89}\) found that women gained 5.2 kg and men gained a mean of 4.9 kg the first year after smoking cessation, and Kleppinger et al.\(^{66}\) reported a mean weight gain of 6.5 kg after 16 months. Moreover, it is also reported that most people will gain less than 4.5 kg after smoking cessation, but that as many as 13% may gain as much as at least 11 kg\(^{42}\). The mechanisms for post cessation weight gain are not completely identified, but smoking cessation has been associated with a decrease in resting metabolic rate (RMR). In some trials the increased body weight was attributable to
a decrease in RMR and/or an increase in caloric intake. However, other trials have not found any changes in RMR after smoking cessation. It is also hypothesized that at least some of the weight gain associated with smoking cessation may be due to reduced fat oxidation, since fat oxidation increases with increasing nicotine uptake in smokers.

The weight gain following smoking cessation may produce undesirable health problems. Several previous studies have showed that smoking cessation also is associated with a substantial increase in waist circumference. In men with a recent (within one year) premature major coronary event, current cigarette smoking and smoking cessation has been found to be associated with a greater prevalence of the metabolic syndrome. A high waist circumference, as an indicator of increased abdominal fat, and dyslipidemia were the components of the metabolic syndrome that were more prevalent in exsmokers than in nonsmokers. Another study also found that smoking cessation may increase the risk of developing metabolic syndrome in women, mainly due to increased waist circumference. In addition, a large study found that the onset of hypertension was higher in those who quit smoking (35%) than in those who continued to smoke (27%). This study found that the weight gain following cessation was largely responsible for the increased incidence of hypertension in quitters. However, another trial found that insulin sensitivity improved 8 weeks after smoking cessation in nonobese men, despite an increase in body weight. It is suggested that the weight gain associated with smoking cessation may offset some of the advantages of giving up smoking, and it is in fact showed an increased risk for type 2 diabetes in people recently quitting smoking compared to both never-smokers and current smokers.

Despite these negative consequences, others indicate that the health problems following post cessation weight gain probably are modest given the large health benefits of quitting smoking. It is in fact estimated that quitting smoking at age 35 will increase life expectancy with approximately 6-8 years, and even among smokers who quit at age 65 life expectancy may increase with almost 4 years. However, concern regarding post cessation weight gain seems to be a powerful motivator for continued smoking, and it appears that concerns or beliefs regarding post cessation weight gain are more important than actual weight gain, and may be associated with continued maintenance of smoking. In accordance with this, it is previously shown that weight-concerned smokers have poorer smoking treatment outcomes compared with smokers with lower levels of weight concerns. It is therefore necessary to
find some interventions that may prevent, or at least reduce, the weight gain associated with smoking cessation, so that a larger proportion of weight concerned smokers may successfully quit smoking.

1.4.3 Smoking cessation treatment

Tobacco dependence is a chronic disease that often requires repeated intervention and multiple attempts to quit. Effective treatments exist that can significantly increase rates of long-term abstinence. Counseling and medication are effective when used by themselves for treating tobacco dependence. It is, however, shown that the combination of counseling and medication is more effective than either alone\textsuperscript{100}. Treatments are targeted towards dealing with the physical addiction to nicotine, the psychological reliance on the effects of nicotine, and the behavioral aspects of tobacco use\textsuperscript{8}. Assistance for cessation includes both counseling (ideally, four or more sessions) and pharmacotherapies. Counseling involves motivating tobacco users to quit by examination of the results from smoking. It includes educating tobacco users about the beneficial health effects from stopping smoking, problem solving, and skills training, such as discussing methods and coping skills to deal with high-risk situations for tobacco use, and providing social support as part of treatment\textsuperscript{8}. Pharmacotherapies for nicotine dependence can enhance quit rates by about two-three-fold. Both the UK and US Public Health Service guidelines therefore recommend that all smokers should be considered for pharmacotherapies\textsuperscript{8}. However, special consideration or exception should be given to smokers with specific medical conditions, to those who smoke less than ten cigarettes daily, to pregnant or breastfeeding women, and to adolescents. Seven smoking cessation pharmacotherapies are currently approved by the US Food and Drug administration\textsuperscript{101}. Five of these are nicotine replacement products (nicotine patch, -gum, -lozenge, -nasal spray and oral inhaler). Each delivers nicotine in a way that allows an individual to reduce nicotine withdrawal symptoms and cravings for cigarettes when quitting smoking, and it has been shown that nicotine replacement medications facilitate smoking cessation\textsuperscript{102}. These products are obtained without prescription. The other smoking cessation products approved by the Food and Drug administration are bupropion (trade name Zyban\textsuperscript{®}), which is hypothesized to aid smoking cessation by inhibiting dopamine reuptake in the mesolimbic dopamine system\textsuperscript{103}, and varenicline (trade name Chantix\textsuperscript{®} in the USA and Champix\textsuperscript{®} in Canada, Europe and other countries). Bupropion have previously been shown to increase smoking cessation rates compared to both placebo and nicotine replacement medications\textsuperscript{104,105}. 

13
Varenicline was added to the limited list of first-line pharmacotherapies for smoking cessation by the 2008 update on smoking cessation issued by the Public Health Service\textsuperscript{100}. Varenicline binds to the $\alpha_4\beta_2$ receptor subunit of nicotinic acetylcholine receptors and exerts effects both as a partial agonist that displays approximately 30-60\% of the in vivo efficacy of nicotine by stimulating dopamine release, and as an antagonist by blocking the binding of nicotine to this site\textsuperscript{106}. Varenicline is typically administered for 1 week prior to quitting and is believed to offer the therapeutic benefit of relieving symptoms of nicotine withdrawal and cigarette craving through its agonist action, and at the same time blocking the reinforcing effects of continued nicotine use through the antagonist action. In theory, varenicline will therefore promote the extinction of smoking behavior. In fact, two identically designed, large randomized controlled trials conducted at two different centers both found that varenicline significantly reduced the urge to smoke, smoking satisfaction, psychological reward, enjoyment of respiratory tract sensations and craving relief compared to placebo, with an effect size larger than that of bupropion\textsuperscript{107,108}. In line with this, varenicline had higher continuous abstinence rates (CAR) and 7-days point prevalence abstinence rates (pp) than placebo at weeks 12 (44.0\% vs. 17.7\% CAR in one and 43.9\% vs. 17.6\% in the other), 24 (29.5\% vs. 10.5\% CAR in one and 29.7\% vs. 13.2\% in the other) and 52 (21.9\% vs 8.4\% CAR in one and 23\% vs. 10.3\% in the other). Both bupropion and varenicline can only be obtained with prescription from a physician. Compared to no treatment can nicotine replacement therapy, bupropion and varenicline be considered cost-effective in Norway, with varenicline being the most cost-effective drug alternative\textsuperscript{3}. With structured counseling in addition to pharmacotherapy up to 40\% can succeed with their smoking cessation attempt. It is shown that the chances to succeed with a smoking cessation attempt is about doubled if the person attend a smoking cessation group compared to quitting all by him/herself\textsuperscript{3}.

**Assessment of smoking status**

An accepted method to confirm self-reported smoking status is measuring of expired-air carbon monoxide (CO). This is performed with a monitor which analyzes the amount of carbon monoxide in a single exhaled breath and use this reading to automatically calculate the percentage of carboxyhaemoglobin (%COHb) in the blood\textsuperscript{109}. Another accepted method is measuring of cotinine, the major metabolite of nicotine, in saliva, blood or urine\textsuperscript{110}. 

Most trials comparing smokers and nonsmokers, or estimating smoking cessation-rates, use continuous abstinence rates (CAR) or point prevalence (pp). Continuous abstinence refers to those participants who quit smoking and maintain abstinence throughout the following period. In contrast, point prevalence abstinence refers to smoking (yes vs. no) at a particular follow-up time point, with no correction for previous or subsequent relapses to smoking.

1.5 Changes in body weight

1.5.1 Health effects of changes in body weight

The risk of cardiovascular disease increases with weight gain and decreases with weight loss\textsuperscript{75}. Increased body weight is associated with increased blood pressure and increased risk of type 2 DM\textsuperscript{79,111}. BMI is strongly related to overall mortality, with increased risk of mortality in subjects with BMI $\geq 27.5$ kg/m\textsuperscript{2}\textsuperscript{112}.

Weight reduction and regular physical activity decrease the risk of type 2 DM. A moderate weight reduction in the range of 5-10\% of the body weight provide significant benefits in terms of blood pressure, insulin resistance, blood lipids and light sleeping problems. A greater weight reduction of 15-20\% of the body weight can reverse the increased mortality risk in overweight subjects with type 2 diabetes\textsuperscript{74}.

1.5.2 Nordic and Norwegian recommendations for nutrition

The physical activity level and the diet composition have direct effects on important risk factors such as blood lipids and blood pressure, on the risk of developing chronic diseases and the risk of premature death. Physical activity level and diet composition also affects the risk of cardiovascular diseases, type 2 diabetes and several types of cancers\textsuperscript{74}. The Nordic and Norwegian recommendations for nutrition and physical activity are based on scientific documentation and aims to provide a basis for planning of a diet and physical activity level to help prevent lifestyle diseases, such as obesity, type 2 DM, CVD and cancer\textsuperscript{113}. In brief, the recommended macronutrient composition should be 25-35 energy\% from fat, 50-60 energy\% from carbohydrate, and 10-20 energy\% from protein. The intake of saturated fat, monounsaturated fat and polyunsaturated fat should be $\leq 10$, 10-15, and 5-10 energy\%, respectively. The intake of added sugar should not contribute to more than 10\% of energy.
intake. The intake of dietary fiber should be 25-35 g/day, equivalent to 3 g/MJ. In terms of physical activity it is recommended that adults exert physical activity at moderate or vigorous intensity for at least 30 minutes every day. To prevent weight gain it is probably necessary with 60 minutes of physical activity daily. In 2011, Helsedirektoratet published national dietary advices to prevent lifestyle diseases\textsuperscript{114}. These advices are based on food groups rather than the macronutrient composition, but a diet in accordance with these advices will also meet the macronutrient composition recommended in the Norwegian recommendations for nutrition and physical activity published in 2004.

### 1.5.3 Dietary interventions for weight reduction

Though obesity is caused by an imbalance between the amount of energy consumed and energy expenditure, the exact mechanisms and their relative importance in explaining this energy imbalance is not clear\textsuperscript{115}. Clinical intervention programs have studied different nutritional treatments in order to improve both weight loss and weight maintenance, and the majority has focused on different macronutrient compositions\textsuperscript{116}. So far, it seems like several diets with different macronutrient composition can successfully reduce body weight as long as they are energy-reduced\textsuperscript{117,118}.

The introduction of low-fat, high-complex carbohydrate diets for the prevention and treatment of obesity was based on the link between dietary fat and body fatness; weight loss is correlated positively to the reduction in dietary fat content. A reduction of 10% fat energy produces an average weight loss in obese persons of 5 kg\textsuperscript{119}. Fat is less satiating than carbohydrate and protein. It is shown that persons who had high hunger levels overate when receiving high-fat foods but not when receiving high-carbohydrate foods. Furthermore, it has been suggested that periodic exposure to high-fat meals, particularly when hunger is high, may be sufficient to lead to an over-consumption of energy from fat that is not compensated by a later reduction in energy intake\textsuperscript{119}. In addition, the Finnish Diabetes Prevention Project randomized over 500 middle-aged overweight and obese subjects with impaired glucose tolerance to usual-care or an intensive lifestyle-intervention group\textsuperscript{120}. The intervention goals were to reduce dietary total (<30 E%) and saturated (<10 E%), and increase physical activity and dietary fiber, and this intervention was highly successful in preventing diabetes. However, a previous meta-analysis concluded that low carbohydrate diets were as effective as low-fat diets in reducing body weight for up to one year\textsuperscript{121}. Several dietary intervention trials
have reported greater short-term (≤ 6 months) weight loss in subjects following a high-protein, low-carbohydrate diet versus a low-fat, high-carbohydrate diet, but with no significant weight loss differences after one year\textsuperscript{122-125}. In addition, the high-protein, low-carbohydrate diet was associated with greater decrease in TG and greater increase in HDL-cholesterol. It is hypothesized that the beneficial effects of high-protein diets on adiposity may be due to increased thermogenesis and satiety\textsuperscript{126,127}. It is, however, suggested that high-protein, low-carbohydrate diets (ketogenic diets) do not offer much advantage over high-protein, moderate-carbohydrate diets in terms of appetite control or metabolic advantage\textsuperscript{128}.

**Calculation of estimated energy requirements**

Dietary interventions for weight reduction usually include energy-reduction in addition specific macronutrient compositions, and an accurate method of assessing overall energy requirements is important in weight management of both normal-weight and obese individuals. The assessment of 24-hours energy expenditure (24-EE, in kcal/day) is a requirement for establishing caloric prescriptions for patients. The best predictor of 24-EE is the resting energy expenditure (REE), or RMR, as determined by indirect calorimetric measurement\textsuperscript{75}. However, measuring of REE or RMR with indirect calorimetry is not always available. For these situations the Mifflin-equations for REE\textsuperscript{75} can be used:

For females: \[ \text{REE} = 10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (years)} - 161 \]

For males: \[ \text{REE} = 10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (years)} + 5 \]

These equations are based on a sample of both normal-weight and obese subjects. Usually an individual’s REE is multiplied by an activity factor to arrive at the 24-EE. The WHO values of physical activity level (PAL) are 1.53 for a sedentary or light activity lifestyle, 1.76 for an active or moderately active lifestyle, and 2.25 for a vigorously active lifestyle\textsuperscript{129}.

**Dietary interventions to prevent post cessation weight gain**

There is some evidence that weight management education with personalized support giving feedback on personal goals and a personal energy prescription can limit post cessation weight gain. However, some evidence also suggests that interventions that limit dietary intake may potentially reduce smoking cessation success, because hunger can undermine quit efforts and increases urges to smoke in current smokers\textsuperscript{88}. Furthermore, others have suggested that
dietary interventions might serve to encourage reluctant quitters to try to stop smoking if they can be reassured that weight gain might be limited. It is therefore necessary to find some dietary interventions that prevents, or at least reduces, post cessation weight gain without decreasing abstinence rates, but to our knowledge, no studies comparing the effects of diets with different macronutrient compositions on weight gain after smoking cessation have been performed.
2  Aims and efficacy outcomes

2.1  Main aim

The main aim of this master thesis was to compare two dietary interventions in efficacy of preventing undesired weight gain after smoking cessation. The master thesis is based on an ongoing study at Oslo Universitetssykehus, Ullevål, and is analyzing the results after 4 and 12 weeks after smoking cessation for the first eighty participants included in the study.

2.2  Efficacy outcomes

2.2.1  Primary efficacy outcomes

The primary objective was to compare the effect of a low fat diet high in complex carbohydrates (≤30 energy % fat, ≤20 energy % protein and ≥50 energy % carbohydrate) or a high protein diet moderately reduced in carbohydrates (≥25 energy % protein, ≤55 energy % fat and ≤20 energy % carbohydrates) on body weight 4 and 12 weeks after smoking cessation.

2.2.2  Secondary efficacy outcomes

The secondary objective was to compare the effect of a low fat diet high in complex carbohydrates (≤30 energy % fat, ≤20 energy % protein and ≥50 energy % carbohydrate) or a high protein diet moderately reduced in carbohydrates (≥25 energy % protein, ≤55 energy % fat and ≤20 energy % carbohydrates) on body composition (body fat, lean body mass, waist circumference, hip circumference, waist-to-hip ratio) 12 weeks after smoking cessation.

2.2.3  Third efficacy outcomes

The third objective was to compare the effect of a low fat diet high in complex carbohydrates (≤30 energy % fat, ≤20 energy % protein and ≥50 energy % carbohydrate) or a high protein diet moderately reduced in carbohydrates (≥25 energy % protein, ≤55 energy % fat and ≤20 energy % carbohydrates) on cardiovascular risk factors (glucose, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides and blood pressure) 12 weeks after smoking cessation.
2.2.4 Fourth efficacy outcomes

Compare dietary changes within the two intervention groups and examine correlations between the dietary changes and changes in body weight four weeks after smoking cessation.
3 Subjects and methods

3.1 Subjects
Participants were recruited by advertisement in newspapers (appendix 1) or referral to the Department of Preventive Cardiology at Oslo University Hospital, Ullevål.

3.1.1 Inclusion criteria

- Men and women aged 20 to 65 years.
- Smoking ≥ 10 cigarettes per day.
- BMI 25-40 kg/m^2.
- No attempt to quit smoking in the previous 3 months.
- Change in weight of 4 kg or less during the previous 3 months.
- No major change in physical activity level in the previous 3 months.
- Willing to use varenicline.

3.1.2 Exclusion criteria

- Smoking < 10 cigarettes per day or using snus or other forms of tobacco than cigarettes daily.
- BMI > 40 kg/m^2 or < 25 kg/m^2.
- CVD within last 2 months (i.e. myocardial infarction, angina pectoris, coronary artery bypass graft, percutaneous transluminal intervention, stroke or transient ischemic attack (TIA)).
- Chronic heart failure classified as symptomatic; New York Heart Association (NYHA) class III-IV^{130}.
- Diabetes type I or type II taking insulin for diabetes.
• History of serious psychiatric disorder (e.g. panic disorder, psychosis, bipolar disorder, suicidal attempt).

• Ongoing major depressive illness or major depressive illness during the last year.

• Ongoing anti-depressive treatment.

• History of alcohol/drug abuse.

• Clinical disorders including gastrointestinal disease impairing compliance with dietary recommendations.

• Participation of a drug trial during the previous 30 days before the baseline visit.

• Use of drugs (Xenecal, Reductil), nutritional supplements or herbs for weight loss within the 4 weeks prior to the baseline visit or participation in an active weight loss program.

• Pregnancy or lactation or planned pregnancy during the study.

• History of obesity surgery.

• Exclusively vegan or vegetarian diet.

• Not willing to be randomized to either diet.

• Individual judged by the clinical investigator to be unable to follow instructions and procedures of the study.

3.1.3 Number of subjects

To be able to detect a difference in weight gain of 3 kg between the groups, the main study will need 58 participants in each group. With this number the trial will meet a 90% power to detect a 3 kg difference with 5% significance assuming that the standard deviation (SD) of the change in weight will be 5 kg.
The number of subjects (N) in each group was calculated according to the equation:

\[
N > \frac{(u + v)^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_0)^2} = \frac{(1.28 + 1.96)^2 (5^2 + 5^2)}{3^2} \approx 58
\]

Where:
- \(\mu_1 - \mu_0\): difference between the means, 3 kg
- \(\sigma_1, \sigma_2\): standard deviations, 5 kg
- \(u\): estimated from the test power (1-\(\beta\))
  \[P(Z \geq u) = 100\% - (1-\beta)\]
  \[u = 1.28 \quad (P(Z \geq 1.28) = 0.10)\]
- \(v\): estimated from the significance level (\(\alpha\))
  \[P(Z \geq v) = \alpha/2\]
  \[P(Z \geq 1.96) = 0.025, \quad v = 1.96\]
- 1-\(\beta\): 90%
- \(\alpha\): 5%

Allowing dropouts the main study will therefore require 60 subjects in the two intervention groups, respectively. Since the main study is ongoing and will include the last participants during the fall 2012, only the first 80 subjects randomized in the trial was included in the master thesis. The first 64 subjects participated in the trial in the period January 2010 to September 2011, while the remaining 16 subjects were included in September and October 2011.

### 3.2 Study design

This was a randomized, controlled, parallel group study. Subjects responding to the advertisement in the newspaper consulted a physician at the first visit. Eligible subjects (i.e. subjects who met all inclusion criteria and had no exclusion criteria present) provided written informed consent. At the next visit all included subjects were randomized to one of the two intervention groups. Randomization was done in blocks. When a new subject was ready for randomization a pre-numbered and sealed envelope was opened and the intervention allocation was entered into the subjects clinical report form. See appendix 2 for flow chart of the study. All consultations with subjects and data collection took place at the Department of Preventive Cardiology at Oslo University Hospital, Ullevål. If a subject did not show up for a planned visit, the subject was contacted by one of the investigators by either telephone or e-mail. Follow-up visits were encouraged regardless of smoking status and dietary adherence.
3.2.1 Smoking cessation

Trained counselors provided motivational support and tips regarding behavioral therapy for smoking cessation. Counseling focused on problem solving and skills training for coping with high-risk situations. Prior to the stop smoking day and for 4 weeks after the target-quit date counseling was given at weekly visits. The next 8 weeks counseling was given in biweekly visits. The target date for smoking cessation was decided at the first counseling session (at the date of screening). To improve smoking cessation rate, the subjects were offered the drug varenicline (trade name Champix®) free of charge. Table 2 shows the administration of varenicline.

Table 2: Treatment with varenicline 1-2 weeks before smoking cessation

<table>
<thead>
<tr>
<th>Days before quitting</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1-3</td>
<td>0.5 mg</td>
<td>Once a day</td>
</tr>
<tr>
<td>Day 4-7</td>
<td>0.5 mg</td>
<td>Twice a day</td>
</tr>
<tr>
<td>Day 8</td>
<td>1 mg</td>
<td>Twice a day</td>
</tr>
</tbody>
</table>

The dose of 1 mg varenicline twice a day was used for up to 12 weeks depending on the choice of the subject. Smoking status was assessed by expired-air carbon monoxide (CO) measurement at every visit. CO values ≤ 5 parts per million (ppm) was assessed as no smoking status.

3.2.2 Dietary intervention

The subjects were randomized to follow one of two intervention diets; a low fat diet high in complex carbohydrates (from now on referred to as LFHCC) or a high protein diet moderately reduced in carbohydrates (from now on referred to as HPMRC). The intention with the LFHCC was to reach a macronutrient composition of ≤30 energy % fat, ≤20 energy % protein and ≥50 energy % carbohydrate. To achieve recommended level of fat, the dietary intake of fat had to be limited to 67 g at a daily energy level of 2000 kcal. Dietary carbohydrates should be the most abundant macronutrient. At an energy level of 2000 kcal per day, almost 250 g per day of mainly complex carbohydrates (i.e. oligosaccharides and polysaccharides) from whole meal bread, oat based-cereals, brown rice, whole meal pasta, legumes, fruits and vegetables should be included in the diet. The subjects in this intervention group were also advised to restrict the intake of fatty snack products and products high in simple
carbohydrates, such as fatty cakes, chocolate, potato chips and sugar containing drinks, as much as possible. A restricted amount of unsaturated fat such as soft margarine, vegetable oil, nuts and fish was recommended to ensure the intake of essential fatty acids.

In the HPMRC group the intention was to reach a macronutrient composition of ≥25 energy % protein, ≤20 energy % carbohydrate and ≤55 energy % fat. In this diet the emphasis was on increasing dietary intake of protein and reducing dietary intake of carbohydrate. To achieve the recommended level of protein, the intake of protein had to be almost 125 g per day at a daily energy level of 2000 kcal. This diet included increased amounts of low fat meat, chicken, fish, shellfish and cheese. The energy % from carbohydrate was planned to be about 20 %, and the amount of carbohydrate should be reduced to 100-120 g per day. This is a moderate carbohydrate reduction allowing for a restricted amount of bread, fruit and vegetables. This diet allowed a higher intake of fat than the low fat diet, but the subjects were recommended to choose unsaturated fat from fish, vegetable oils, soft margarine, avocado and nuts etc. instead of saturated fat from meat and full-fat dairy products. The high protein diet group was advised to choose rye bread and protein rich bread spread for breakfast, increase portions of meat, fish or shellfish for lunch and dinner, and to reduce the intake of potatoes, rice, pasta and fruits. The subjects in this intervention group were also advised to restrict the intake of sugar containing food items such as cakes, ice-cream, deserts and drinks as much as possible.

Approximately 5 energy % from alcohol (equals about 1 alcohol equivalent i.e. 350 mL beer, 135 mL wine and 40 mL 40% spirit at an energy level of 2000 kcal) was allowed in both diets.

Trained nutritionists gave cognitive behavioral therapy for the dietary intervention. Prior to the stop smoking day and for four weeks after smoking cessation counseling was given at weekly visits. The next eight weeks counseling was given in biweekly visits. At the screening visit, participants received a food diary (appendix 3), and were guided in how to implement a 7-days weighed dietary record (DR). All participants were offered to borrow a digital kitchen scale, and were encouraged to weigh all food and beverages to be consumed for the next seven days as far as possible. If they for some reason not were able to weigh the food, they were encouraged to write down what they ate, and use household measures or size and numbers of the food eaten. This was not optimal, but may have led to that a greater proportion of the participants recorded more days, due to a smaller workload. At the second visit,
participants were randomized to either of the two intervention diets. The participants received written information and advices tailored to the intervention diet they were randomized to (appendix 4 and 5). They also received some recipes for lunch- and dinner meals (appendix 6 and 7), and a written list over alternative proposals for a diet plan (appendix 8 and 9). Individualized specific advices, in line with the general advices given in the two intervention groups, were given orally based on their weighed dietary records. These specific advices gave the participants a better opportunity to adapt the intervention diet to their original diet and food preferences. Estimated RMR measured at the beginning of the visit, in addition to reported physical activity, was used to give individualized recommendations for energy intake, approximately 500 kcal less than assumed total energy expenditure (measured RMR multiplied with assumed PAL). Since measured levels of physical activity not were used in this calculation, recommendations for estimated energy intake were not as accurate as they in theory could have been.

In theory, written information made it easier for the participants to estimate and calculate the amount of calories, carbohydrate, fat and protein in different foods and meals. It is, however, always a possibility that written information not will be considered any further by some of the participants. For these participants, the oral information and dietary advices given at each visit were probably of more importance.

The high protein diet moderately reduced in carbohydrate was a little more expensive than the low fat diet high in complex carbohydrate due to the high proportions of pure meat and fish, which is more expensive than carbohydrate rich foods like potatoes and whole meal bread, rice and pasta. It was, however, emphasized that the participants anyway would save more money by quitting smoking than they would spend extra on the changes they had to make to their diet, and financial expenses should therefore not be an obstacle for any of the dietary interventions.

At the visit three weeks after their smoking cessation date, participants received a second food diary, and the instructions on how to implement the weighed DR was repeated. They were then asked to record all their consumed foods and beverages for the next consecutive week. The DRs were collected at the visit four weeks after smoking cessation. No dietary records were implemented and collected at the visit twelve weeks after smoking cessation, and it is therefore impossible to say anything about the participants’ adherence to the diet interventions at this time point of the study.
One main meal (lunch) and one snack meal was provided for the first four days after smoking cessation and for the first three days of the second week after smoking cessation. This was primarily done to increase the compliance during the most acute effects of nicotine withdrawal\textsuperscript{132}, but these meals also served as practical examples to give the participants an impression of the amounts of foods rich in carbohydrate, fat and protein. Three different lunch meals were offered in both intervention groups and the subjects were free to choose the ones they preferred. Appendix 10 and 11 shows the lunch meals and the macronutrient composition of the meals that were offered in both groups. The lunches had energy contents in the range of 345 kcal to 410 kcal. In the LFHCC group the content of fat was in the range of 9 g to 13 g and was about half the amount served in the HPMRC group diet. The content of protein in the lunch meals in the HPMRC group was in the range 40 g to 43 g and this amount was almost twice as much as the amount served in the LFHCC group. Likewise the carbohydrate content was in the range of 41 g to 51 g in the LFHCC group and in the range of only 3 g to 5 g in the HPMRC group.

Emphasize was also given to the snack meals, given that nicotine deprivation has been associated with increased reward value of appealing snack foods\textsuperscript{133}. Both intervention groups were offered 4 snack meals the first week after smoking cessation and 3 snack meals the second week after smoking cessation. The LFHCC group was offered pre-packed yoghurt with muesli. Other recommendations for snack meals in the low fat group included fruits, vegetables, oat porridge with milk and hard bread with smooth brown cheese (prim). The HPMRC group was offered high protein yoghurt (SKYR). Other dietary recommendations for the snack meals in the high protein group included natural yoghurt with almonds, egg, cheese, chicken wings, shellfish and fish.

Subjects in both intervention groups were advised to reduce daily coffee drinking to 2 cups for women and 3 cups for men due to increased effects of caffeine during nicotine withdrawal\textsuperscript{134}.

### 3.3 Study measurements and variables

Characteristic variables included sex, age, weight, height, body composition, resting metabolic rate, BMI in kg/m\(^2\), waist circumference, hip circumference, waist-to-hip ratio, systolic and diastolic blood pressure, serum lipids and serum glucose and number of cigarettes
smoked daily. The resting metabolic rate was included in the master thesis in order to estimate the individual energy level for energy restriction in the dietary intervention and to estimate misreporting of energy intake reported in the dietary records.

### 3.3.1 Assessment of smoking status

Participants were encouraged to write a smoking diary (appendix 12), and were asked at each visit how many cigarettes they had smoked since the last visit. Measurement of expired-air CO was performed at every visit using a breath carbon monoxide monitor (piCO+™ Smokerlyzer®, Bedfont Scientific Ltd., Kent, United Kingdom). Abstinence at each visit was defined as a self-report of no smoking of any kind, not even a puff, since the previous visit, confirmed by an expired carbon monoxide level of \( \leq 5 \) ppm in exhaled air. CAR for all 12 weeks of treatment after smoking cessation has been used, and the group of all participants that were continuous abstinent for all twelve weeks is from this point forward defined as nonsmokers, unless otherwise stated. In addition, CAR for the first four weeks (weeks 1-4) was calculated, and nonsmokers during these four weeks have been in the correlation analyses performed in accordance with the fourth efficacy outcome. CAR for the last four weeks (weeks 9-12) were also calculated to compare CAR in the current study with CARs from previous trials, since this measurement of smoking cessation rates has been used in several smoking cessation trials\(^{107,108,135,136}\). Another often used measurement of smoking cessation rates is point prevalence. In most studies using point prevalence, participants self-report their smoking status in the previous 7 days\(^{107,137-139}\). This was not done in this trial, but 14-days point prevalence for week 12 was calculated to be able to compare smoking cessation rates in the current study with point prevalence rates in other trials. The 14-days point prevalence in the current thesis was defined as a self-report of no smoking in the previous 14 days (since the last visit), confirmed with an expired carbon monoxide level of \( \leq 5 \) ppm. Any participant claiming to be abstinent from smoking, but having a level of CO \( > 5 \) ppm, was considered smoking. Participants who have been abstinent for the first 10-11 weeks, but then have failed to meet for counseling, were also considered smoking again unless otherwise stated.
Assessment of nicotine dependence

Technically, nicotine dependence was measured with Fagerström Test for Nicotine Dependence\textsuperscript{140} for every person at the time of the screening visit. This is a recommended tool for assessment of nicotine dependence\textsuperscript{8}. In this study a Norwegian version of FTND (appendix 13), translated and published by Helsedirektoratet, was used\textsuperscript{141}.

In accordance to the FTND, nicotine dependence was divided into three categories, low, medium and high nicotine dependence, in this master thesis. Low nicotine dependence is defined as a total score of 0-3 points, medium nicotine dependence as a total score of 4-6 points, and high nicotine dependence as a total score of 7-10 points\textsuperscript{141}.

3.3.2 Clinical measurements

Anthropometrics

Body weight was measured at every visit by a digital scale. Body weight was measured in light indoor clothing without shoes. Height was measured once at the screening visit using a standard scale, without shoes. BMI was calculated as the ratio of weight in kilograms divided by the square of the height in meters. Waist circumference was measured midway between lower costa and crista while the subject was unclothed and standing\textsuperscript{74}. Hip circumference was measured at the level of the greater trochanter. BMI, waist and hip were measured at randomization and four and 12 weeks after smoking cessation. Body composition was measured after an overnight fast (minimum eight hours) by impedance (InBody720®, Biospace Co Ltd., Seoul, Korea) at randomization and four and 12 weeks after smoking cessation. Measurements were performed in light indoor clothing without shoes and socks. The participants were standing on the electrodes embedded in the scale platform of the analyzer. After their body weight was measured they were instructed to stand upright and to grasp the handles of the analyzer, thereby providing contact with a total of eight electrodes (two for each foot and hand). The participants’ screening number, height, age, and sex were entered into the analyzer, and the participants were instructed to slightly abduct their arms and remain still during the assessment\textsuperscript{142}.
Blood pressure

Blood pressure was measured at the screening visit, at randomization and four and 12 weeks after smoking cessation. Measurements were conducted after at least five minutes of rest using an electronic blood pressure monitor (Omron 5 Series™, Omron Healthcare, Kyoto, Japan) with an appropriately sized cuff with the patient sitting in the upright position. Three measurements were recorded, and the average of the three measurements was used in the analyses.

Resting metabolic rate

RMR was measured indirectly with a standard portable ventilated hood system (Vmax Spectra 229, Sensormedics®, Sensormedics Corporation, Yorba Linda, California) at randomization and four weeks post-cessation. The measurements and calculations were done after standardized procedures\textsuperscript{143}. The last five minutes in steady state was used for the calculations of RMR. Participants who not were fasting when they met at the date of randomization, four weeks after smoking cessation and/or 12 weeks after smoking cessation, were asked to come back for fasting impedance measurement, indirect calorimetry and blood samples the following day.

3.3.3 Laboratory measurements

Eligibility laboratory measurements (hemoglobin, white blood cells, ASAT/ALAT, creatinine and TSH) were done at the screening visit. Blood samples obtained after an overnight fast (minimum eight hours) were collected for analysis of blood lipids (total cholesterol, LDL-cholesterol, HDL-cholesterol and TG) and glucose at the date of randomization and four weeks and 12 weeks post-cessation. The blood measurements were analyzed by conventional laboratory methods at Department of Clinical Chemistry, Oslo University Hospital Ullevål.

3.3.4 Assessment of diet

In this study, weighed DR was used to assess compliance with the dietary interventions for 7 consecutive days. The DR was performed twice; the first week after the screening visit, and during the fourth week after smoking cessation. Participants received a blank food diary and were provided with food scales. They were instructed to weigh each individual food item using the digital scaled weight and provide notes on ingredients of composite dishes with
approximate quantities. When weighing was not appropriate, portion sizes were estimated with the use of household measures and an photographic atlas with photographs of food items\textsuperscript{144}. Days that were very poorly recorded were excluded. These were days where food items not were specified (e.g. “tapas”) and/or portion sizes or numbers not were recorded at all, and the atlas not had been used. The term “sugar” in the chapters of results and discussion, refers to added sugar (i.e. simple sugars that are not found naturally in the food). Mono- and disaccharides naturally occurring in the food items, like in milk and fruits, are included in the term “carbohydrate”. In studies done here there is a chance of misreporting. To estimate errors like over- or under-reporting, the Goldberg equation\textsuperscript{145} (ratio of estimated intake to measured RMR) was used.

3.3.5 Measurements conducted but not included in the master thesis

Several other measurements were conducted in the main study, including HbA\textsubscript{1c}, insulin, urine creatinine, albumin, CRP, ASAT/ALAT, inflammatory markers (TNF\textalpha, IL-6, MCP-1, PAI-1), adipokines (ghrelin, adiponectin, leptin, resistin, visfatin), eating behavior (dietary restraint, disinhibition, binge eating, hunger), food cravings and assessment of total withdrawal discomfort or craving after smoking cessation (Minnesota nicotine withdrawal symptoms questionnaire). Physical activity was measured for 7 consecutive days by an accelerometric device (ActiGraph GT3X+, ActiGraph\textsuperscript{TM}, Pensacola, Florida) the first week after the screening visit and the fourth week after smoking cessation.

These measurements were not included in the master thesis to prevent the workload being too comprehensive, and because some of the measurements not will be analyzed before the main study has completed acquisition of data.
3.4 Safety and adverse events

An adverse event was:

- Any unintended unfavorable laboratory or clinical sign or symptom.
- Any new illness or disease or deterioration of existing illness or disease.
- Any clinical relevant deterioration in a laboratory variable or other clinical test whether or not considered intervention related.

Planned hospital admission and surgical procedures for illness or disease that existed before the start of the trial were not considered to be adverse events. Date of onset, duration and intensity was recorded on the adverse event form in the case record form (CRF). All adverse events not resolved were followed up.

3.5 Data management, statistical procedures and calculation of dietary intake

3.5.1 Data management

Data were collected and recorded in case record forms, and entered, coded and edited into a protected database system (Epi Info™) of Oslo University Hospital, Ullevål to provide data protection.

3.5.2 Statistical procedures

All statistical analyses were performed using IBM SPSS Statistics 19 for Windows. Descriptive statistics were performed for anthropometric characteristics and efficacy variables. The primary efficacy outcome was differences in body weight change between the dietary intervention groups from the date of randomization to four weeks after smoking cessation and 12 weeks after smoking cessation. Other outcomes were between-group differences in the change in body composition (waist circumference, hip circumference, WHR, body fat, lean body mass) and cardiovascular risk factors (glucose, lipids, blood pressure) from randomization to 12 weeks after smoking cessation. Estimates for the main efficacy variables are mean ± standard deviation (SD), between-group differences are mean
(95% confidence interval). However, median (1\textsuperscript{st} and 3\textsuperscript{rd} quartile) are given in addition for triglycerides due to a non-normal distribution. Changes (from randomization to (four) 12 weeks after smoking cessation) in all of these variables were tested for differences between the dietary intervention groups by independent-samples t-test. Mean differences between the groups are the mean change in the HPMRC group subtracted from the mean change in the LFHCC group. The difference in TG from randomization to 12 weeks after smoking cessation was normally distributed in both groups, and independent-samples t-test was used to test the difference between the groups. Changes from randomization to 12 weeks after smoking cessation within groups were tested by paired-samples t-test in each of the two intervention groups. Dietary changes within and between the intervention groups from the date of randomization to four weeks after smoking cessation have been tested with paired-samples t-test and independent-samples t-test, respectively. For all t-tests listwise excluding of missing values have been performed. This means that if a subject has missed one of the visits included in the analyses, this subject has been excluded from the analyses. Chi-square test was used in comparisons of categorical variables. Pearson correlation analyses were performed to test for correlations between the changes in intake of macronutrients (fat, protein and carbohydrate) and changes in body weight from randomization to four weeks after smoking cessation. Other regression analyses have not been performed. All tests were two-tailed and a p-value of <.05 was regarded as the level for statistical significance.

All statistical analyses were performed twice for the participants who met at both the fasting visits at randomization and 12 weeks after smoking cessation. Once regardless of their smoking status (referred to as “nonsmokers + reduced smokers”), and once for the proportion of participants who succeeded to be abstinent from smoking all continuous twelve weeks following their smoking cessation dates (referred to as “nonsmokers”). Statistical analyses on changes in body weight were performed for participants who met at all three fasting visits (randomization, and four and 12 weeks after smoking cessation). Analyses on body weight were also done on an intention-to-treat basis, with a last-measurement-moving-forward approach for non-completers. Intention-to-treat analyses for other efficacy outcomes have not been performed in this master thesis. In addition to these analyses, tables showing mean values for all participants met at any of the three time points for measurements (randomization and four and 12 weeks after smoking cessation) have been made. Due to rounding, all estimates may not match.
3.5.3 Calculation of dietary intake

The dietary records were coded manually for the calculation of energy intake, energy yielding nutrients and food items using a software program (Mat på data 5.0, Mattilsynet, Oslo, Norway, 2007) based on the Norwegian food composition table\textsuperscript{146}. For food products where several different types exists, like soft margarine and bread, one type has been used for all dietary records failing to specify which type the participant has been eating. Food items recorded, but not included in the Norwegian food composition table, were searched for in the Swedish food composition table\textsuperscript{147} or the USDA National Nutrient Database for Standard Reference\textsuperscript{148}. The food items and their nutrient contents were then added to the Mat på data software program through the Reorg-function. For composite dishes recipes were applied for on the internet and then added to Mat på Data. For some composite dishes ordered in restaurants or fast food outlets, the chef weighed the ingredients or the amounts have been obtained from the restaurant’s recipe. For kebab especially, the meat producer has been contacted to find out what the meat mixture used in kebabs usually consist of, and then all the ingredients in a regular kebab, purchased from the largest kebab outlet (Bislett Kebab House) in Oslo, have been weighed separately. This was done because Bislett Kebab House refused to give any information concerning their products. Recipes were also added for mixed drinks, such as Caffè Latte, Caffè Mocca and Irish Coffee, after getting information about the proportions of the various ingredients used in different coffee shops in Oslo.

For Norwegian food items not included in Mat på data, the producers of the food items have been contacted to get a more detailed nutritional content than enlightened on the products. All obtained information about the nutritional content in different products has been added to the software program. If the producers didn’t have more information about the nutritional content of the product, a similar product was used instead. For food items with a different composition of macronutrients than other similar products, such as Vita hjertego’-products, the food items have been added with a limited nutritional content.

For minced meat and some types of pure meat, only the nutrition contents in the raw meat were available in Mat på Data 5.0. Since the participants always ate these food products prepared, minced meat and some types of pure meat have been prepared several times and the food has been weighed at every step of the preparation to be able to calculate the nutrition content in 100 grams of prepared meat. For meat dishes, e.g. meat sauce and taco meat, the meat dishes have been prepared several times, and in each step of preparation the food has...
been weighed. It has then been calculated how much of the water content in the food that has evaporated, and how much of the finished dish that is meat and how much that are other ingredients, such as spices or vegetables. The nutritional content of raw ingredients has then been used to calculate the total nutritional content of the finished dish, and this has been added to the software program. For other types of meat, like grilled chicken, chicken wings and chops with bone, the food item has been weighed in one piece and the meat, bone and skin or fat rim have been weighed separately, and the % of the total weight has been calculated for each part. This has been used to calculate the amount eaten when only the total weight or number has been recorded.

In the dietary records fruits and vegetables were often not weighed, rather only indicated by number and sometimes an estimated size, e.g. “two clementines” or “one large apple”. In these occasions average weights, obtained by weighing several examples of a fruit or a vegetable, have been used. This was not exactly correct, but it was better than using randomly chosen weights for every dietary record not completed correctly. The fruits and vegetables used to get estimated averages have been acquired from different grocery stores in and nearby Oslo during a time period of three months (October 2011 to January 2012). See appendix 14 for averages used in the coding of the dietary records. For other types of food products and dishes, a picture book has been used to estimate the portion sizes.

All these efforts were made to be able to calculate the nutrient contents recorded in the best possible way. Despite this, some food products are missing values for the content of several of the micronutrients, and a good estimate of the intake of micronutrients can never be calculated using this software program. In addition many of the participants failed to record beverages, especially water, and the intake of fluids can therefore not be calculated accurately.

3.6 Declaration of Helsinki and ethical review

The study was conducted in compliance with the ethical principles of the Declaration of Helsinki. At the screening visit the subjects were given full and adequate verbal and written information (appendix 15) about the nature, purpose, possible risks and benefit of the study. The subjects had the opportunity to ask questions, and were given time for consideration. All subjects provided written informed consent before enrollment (appendix 15).
3.7 The student’s tasks

In this study, the master student had the following tasks:

- Dietary counseling and measuring of body weight for the last 16 participants randomized in the main study (the participants screened in September and October 2011).

- Coding of dietary records and calculation of reported energy intake and intake of energy yielding nutrients for all participants randomized in the main study during 2011 (a total of 49 participants).

- Contacting restaurants and producers of different food items, in addition to preparing and weighing several food products to obtain as accurate information about the nutritional content as possible.

- Entering and coding of the case record forms into the EpiInfo software program for all participants randomized in the main study during 2011.

- Performing statistical analyses.

Coding of dietary records and case record forms for the first 31 participants randomized in the main study were performed by two former master students, Åshild Margrethe Lode and Edith Berntzen, in 2010.
4 Results

In this chapter there is first a brief description of the subject characteristics, screening failures and smoking cessation rates before the description of the outcomes on body weight, body composition and cardiovascular risk factors. Results from the dietary interventions and correlation analyses are described in the last part. All statistical analyses are performed with listwise exclusion of missing values unless otherwise stated.

4.1 Subject characteristics

4.1.1 Characteristics at the date of screening

The characteristics of the subjects in the study, at the date of screening, are given in table 3. A female predominance was seen, 58 women (72.5 %) and 22 men (27.5 %). On average, both men and women were 50 (SD 9) years of age, obese with a mean BMI of 31 (SD 4) kg/m$^2$, reported smoking 18 cigarettes per day, and were moderately nicotine-dependent (mean score of FTND was 4.8). However, compared with men, women had a lower mean height (mean difference -12.9 cm [95% CI -15.9, -9.9]), weight (mean difference -13.8 kg [95% CI -20.4, -7.1]) and waist circumference (mean difference -9.4 cm [95% CI -14.4, -4.3]). There were no other statistically significant differences for the rest of the characteristics at the date of screening.
Table 3: Characteristics and smoking status at the date of screening.

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>58 (72.5)</td>
<td>22 (27.5)</td>
</tr>
<tr>
<td>Age, years</td>
<td>50 ± 9</td>
<td>51 ± 9</td>
</tr>
<tr>
<td>Height, cm</td>
<td>167.7 ± 5.5</td>
<td>180.6 ± 7.2***</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>87.8 ± 13.0</td>
<td>101.6 ± 14.1***</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>31.1 ± 3.8</td>
<td>31.1 ± 3.2</td>
</tr>
<tr>
<td>Waist, cm&lt;sup&gt;a&lt;/sup&gt;</td>
<td>98.7 ± 9.8</td>
<td>108.1 ± 10.8***</td>
</tr>
<tr>
<td>Hip, cm&lt;sup&gt;b&lt;/sup&gt;</td>
<td>112.9 ± 9.0</td>
<td>110.8 ± 6.8</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>126 ± 18</td>
<td>132 ± 15</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>80 ± 9</td>
<td>84 ± 10</td>
</tr>
</tbody>
</table>

**Smoking status**

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarettes/day&lt;sup&gt;c&lt;/sup&gt;</td>
<td>18 ± 6</td>
<td>20 ± 7</td>
</tr>
<tr>
<td>Nicotine dependence&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.9 ± 1.9</td>
<td>4.5 ± 1.5</td>
</tr>
</tbody>
</table>

Values are means ± SD (standard deviation) or numbers (%) where specified. Statistically significant differences between males and females are indicated.

*** p<.001, Independent Samples T-Test

<sup>a</sup> Missing values for 1 female

<sup>b</sup> Missing values for 1 female and 1 male

<sup>c</sup> Missing values for 5 females and 1 male

<sup>d</sup> Estimated with Fagerström Test for Nicotine Dependence (FTND). Scores range from 1 to 10, with higher scores indicating greater nicotine dependence.

4.1.2 Characteristics at the date of randomization

Eighty participants were randomly assigned to the two intervention groups (see figure 1 for participant flow). After randomization, the gender distribution between the intervention groups was comparable with 12 (34.3%) males in the LFHCC group and 10 (22.2%) males in the HPMRC group (p=.23). There were no significant differences between the two intervention groups in any of the variables measured at randomization. A total of 71 (88.8%) participants were contacted and reached at the visit 12 weeks after their smoking cessation date. One of the participants was, unable to attend the visit, hence, measurements are missing for this person. However, since this person was reached by telephone and confirmed that she still wanted to participate in the study, she was not considered a drop out. There was no apparent difference in the relative number of participation (in percent) between the LFHCC and HPMRC groups (31 (88.6%) in the LFHCC group vs 40 (88.9%) in the HPMRC group, p=.67).
Responded to advertisement in newspapers or referred to the Department of Preventive Cardiology at Oslo University Hospital, Ullevål (N = 94)

Excluded (N = 11)
- Not meeting inclusion criteria (N = 1)
- Exclusion criteria present (N = 3)
- Not met/withdraw from the study (N = 7)

Screened at the screening visit (N = 83)

Excluded (N = 3)
- Exclusion criteria present (N = 1)
- Other reasons (N = 2)

Randomized (N = 80)

Allocated to the low fat diet (N = 35)

Met at the visit 4 weeks after smoking cessation (N = 33)
- Withdrew from the study, cause not stated (N = 2)

Met at the visit 12 weeks after smoking cessation (N = 30)
- Not met, cause not stated (N = 1)
- Withdrew from the study, cause not stated (N = 2)

Allocated to the high protein diet (N = 45)

Met at the visit 4 weeks after smoking cessation (N = 44)
- Withdrew from the study on account of illness (N = 1)

Met at the visit 12 weeks after smoking cessation (N = 40)
- Withdrew from the study, cause not stated (N = 4)

Figure 1: Flow diagram of the progress throughout the different phases of the trial.
4.1.3 Screening failures

One of the subjects included in the study had a BMI>40 (41.6 kg/m$^2$). Two of the included subjects were more than 65 years of age (66 and 68 years) at the time of the screening visit. One of the participants was not willing to take varenicline. Two of these 4 subjects were randomized to the LFHCC group, and the other two to the HPMRC group. Even though these 4 subjects did not meet all the inclusion criteria, they were still included in the analyses to not influence the randomization or restrict the sample size any further. The participant who did not wish to take varenicline informed that she did not smoke during the 12 weeks after smoking cessation, and this was supported by low CO-measurements at every visit post cessation.

4.1.4 Determination of smoking status

Mean score with Fagerström Test for Nicotine Dependence was 4.7 (SD 1.9) and 4.8 (SD 1.7) in the LFHCC group and the HPMRC group, respectively (p=.89). As a part of the inclusion criteria, at the screening visit all participants reported that they smoked at least 10 cigarettes per day. Furthermore, there was a significant decrease in mean cigarettes smoked daily from the date of screening to the date of randomization (mean difference -1 cigarette/day [95% CI -2, -0], p<.05). See table 4 for changes in number of daily cigarettes and measured CO from screening to randomization. In addition, at randomization the mean CO-measurements in the LFHCC group and the HPMRC group were comparable 16 ppm (SD 10) and 16 ppm (SD 8), respectively (p=.78). Moreover, at the randomization visit a total of 7 participants reported that they were smoking less than 10 cigarettes per day. Furthermore, at the date of randomization the mean number of cigarettes smoked daily were reported to be 18 (SD 8) in the LFHCC group, and 17 (SD 5) in the HPMRC group (p=.55).
Table 4: Smoking status for all participants at the date of screening and randomization

<table>
<thead>
<tr>
<th></th>
<th>Screening</th>
<th>Randomization</th>
<th>Difference from screening to randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>CO, ppm (N = 45)</td>
<td>16 ± 8</td>
<td>16 ± 10</td>
<td>-0.3 (-3.0, 2.4)</td>
</tr>
<tr>
<td>Cigarettes, number (N = 74)</td>
<td>18 ± 6</td>
<td>17 ± 6</td>
<td>-1 (-2, -0)</td>
</tr>
</tbody>
</table>

Mean (95% confidence interval) differences from the date of screening to the date of randomization in CO-measurements and number of daily cigarettes. Analyses are performed with paired-samples t-test. For 35 of the participants CO-measurements were not performed at the screening visit. For 6 of the participants information about number of daily cigarettes is missing at the date of screening. Missing values are excluded listwise. SD: standard deviation

4.2 Smoking cessation

4.2.1 Continuous abstinence rate and point prevalence

Drop-out participants were assumed smoking in all analyses. The one participant not able to physically meet at the 12 weeks visit reported to have been continuous abstinent from her smoking from the date of cessation, and was considered a non-smoker in all analyses. Of the 80 participants included in the study, 30 (37.5%) managed to be continuous abstinent all 12 weeks. There was no significant (p=.60) difference in the proportion of participants who were abstinent continuously for 12 weeks between the intervention groups, with 12 (34.3%) participants in the LFHCC group and 18 (40%) participants in the HPMRC group (figure 2).

Irrespective of intervention groups CAR for the first 4 weeks (weeks 1-4) was 47.5% (38 participants), while 48 participants (60%) were continuous abstinent the last 4 weeks (weeks 9-12). The 14-days point prevalence measured twelve weeks after smoking cessation was almost 69% (55 participants). The continuous abstinence rates at weeks 1-4, weeks 9-12 or weeks 1-12 were not significantly different between the intervention groups (figure 2). We found a significant higher proportion non-smokers among the participants with low nicotine-dependence (FTND score <4) than among the medium (FTND score 4-7) and high nicotine-dependent participants (FTND score ≥7) (12 weeks CAR 66.7%, 25.5% and 40.0%, respectively, p<.01).
Figure 2: Abstinence rates in the two intervention groups.
Continuous abstinence rates (CAR) of the two dietary intervention groups, LFHCC (dark purple) and HPMRC (light purple) for the first four weeks (Weeks 1-4), for the last four weeks (Weeks 9-12) and for all twelve weeks (Weeks 1-12) after smoking cessation, and the 14-days point prevalence (14-days pp) of abstinence measured twelve weeks after smoking cessation. All values are percent nonsmokers in the different periods.

LFHCC: Low Fat diet High in Complex Carbohydrates
HPMRC: High Protein diet Moderately Reduced in Carbohydrates

4.2.2 CO measurements and reported number of cigarettes

Non-smokers

Among the participants that reported not smoking at all during the last 12 weeks from their smoking cessation date, mean CO measurements at randomization were 15 (SD 8) ppm and 16 (SD 9) ppm in the LFHCC and the HPMRC groups, respectively. Twelve weeks after smoking cessation, the mean CO measurements were 2 (SD 1) ppm in the LFHCC group and 3 (SD 1) ppm in the HPMRC group.

Non-smokers + reduced smokers

Regardless if the participants were abstinent or not, mean CO measurements in both the LFHCC group and the HPMRC group were 4 (SD 3) ppm at the 12 weeks visit. Mean number of cigarettes smoked during the last 14 days was less than 1 in the LFHCC group, and slightly higher than 4 in the HPMRC group (p=.09).
4.3 Outcome variables

4.3.1 Changes in body weight

Nonsmokers

As can be seen from table 5, the HPMRC group had a significant (p<.01) mean weight reduction of -1.7 kg (95% CI -2.6, -.7) four weeks after smoking cessation, but there was no significant between-group difference. There was no significant difference in change in body weight between the food intervention groups from randomization to 12 weeks after smoking cessation among the nonsmokers, or from four to twelve weeks after smoking cessation. A last measurement moved forward analysis was performed to include the participant in the LFHCC group as the participant was unable to meet at the last visit. There was no significant difference (p=.48) between the dietary intervention groups in change in body weight 12 weeks post cessation after imputing missing values. An overview over the changes in body weight from the date of screening to twelve weeks after smoking cessation is given in figure 3. Among the nonsmokers there were no significant within-group changes in body weight in either of the two dietary intervention groups.

![Body weight changes among nonsmokers, intention-to-treat analysis](image)

Figure 3: Body weight changes from the date of screening to twelve weeks after smoking cessation among the nonsmokers.
Mean body weight at every visit among the nonsmokers in the two dietary intervention groups, LFHCC (dark purple, N = 12) and HPMRC (light purple, N = 18), from the date of screening to twelve weeks after smoking cessation. Imputation of missing values with a last measurement moved forward method has been performed. LFHCC: Low Fat diet High in Complex Carbohydrates.
HPMRC: High Protein diet Moderately Reduced in Carbohydrates.
Scr.: date of screening, Rand.: date of randomization, SC: date of smoking cessation.
### Table 5: Weight changes from the date of randomization to twelve weeks after smoking cessation, both among the completers and among all randomized subjects.

<table>
<thead>
<tr>
<th></th>
<th>LFHCC</th>
<th>HPMRC</th>
<th>Between-group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization</td>
<td>4 weeks</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>N</td>
<td>Mean ± SD</td>
<td>N</td>
</tr>
<tr>
<td>Body weight,</td>
<td>11</td>
<td>88.5 ± 10.6</td>
<td>88.2 ± 10.5</td>
</tr>
<tr>
<td>completers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>87.8 ± 10.1</td>
<td>86.1 ± 9.3**</td>
</tr>
<tr>
<td>Body weight,</td>
<td>12</td>
<td>89.4 ± 10.6</td>
<td>89.0 ± 10.4</td>
</tr>
<tr>
<td>Intention-to-treat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>91.7 ± 17.4</td>
<td>91.3 ± 17.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>89.5 ± 12.1</td>
<td>89.1 ± 11.8**</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>92.2 ± 16.8</td>
<td>92.0 ± 17.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-smokers + reduced smokers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mean between-group differences in body weight change from randomization to 4 weeks after smoking cessation, from 4 weeks to 12 weeks after smoking cessation and from randomization to 12 weeks after smoking cessation, all with p-values, are given. Independent-samples t-test is used on the within-group differences to test differences between groups.

The upper line for both nonsmokers and nonsmokers + reduced smokers shows the changes in body weight among the completers (those met at both the randomization visit and at the visit 12 weeks after smoking cessation), while the lower line, for both nonsmokers and nonsmokers + reduced smokers, shows an intention-to-treat analysis of changes in body weight, using a last measurement moved forward-approach for the non-completers.

** Significant within-group change from randomization, p<0.01 (paired-samples t-test)

*** Significant within-group change from randomization, p<0.001 (paired-samples t-test)

LFHCC: Low Fat diet High in Complex Carbohydrates
HPMRC: High Protein diet Moderately Reduced in Carbohydrates
SD: standard deviation
CI: confidence interval
Non-smokers + reduced smokers

Among both non-smokers and reduced smokers the HPMRC group had a significant (p=.03) greater reduction in body weight from the date of randomization to four weeks after smoking cessation (mean difference 1.1 [95% CI .1, 2.1]). Only the HPMRC group had a significant (p<.001) reduction in body weight from randomization to four weeks after smoking cessation (mean change -1.3 kg [95% CI -2.0, -.6]). No significant differences in body weight change were seen from randomization to 12 weeks, or from four to 12 weeks after smoking cessation. A last measurement moved forward-analysis was performed to include participants who had missed one or more of the visits. As can be observed from table 5, this analysis had a borderline p-value of .05 for the difference in body weight change between the groups (mean difference 1.4 kg [95% CI -.0, 2.7]) from the date of randomization to twelve weeks after smoking cessation. There was a significant (p=.03) difference in body weight change between the two groups from the date of randomization to four weeks after smoking cessation, but no significant difference from four to twelve weeks after smoking cessation. An overview over the changes in body weight from the date of screening to twelve weeks after smoking cessation is given in figure 4. Neither of the two intervention groups showed a significant within-group change in body weight from randomization to 12 weeks after smoking cessation. In the LFHCC group, mean difference in body weight from randomization to 12 weeks after smoking cessation was .6 kg (95% CI -.5, 1.7), p=.29. In the HPMRC group, the corresponding mean difference in body weight was -.8 kg (95% CI -1.8, .2), p=.13.
Figure 4: Body weight changes from the date of randomization to twelve weeks after smoking cessation among nonsmokers + reduced smokers. Mean body weight at every visit among all participants in the two dietary intervention groups, LFHCC (dark purple, N = 35) and HPMRC (light purple, N = 45), from the date of screening to twelve weeks after smoking cessation. Imputation of missing values with a last measurement moved forward method has been performed.

LFHCC: Low Fat diet High in Complex Carbohydrates
HPMRC: High Protein diet Moderately Reduced in Carbohydrates
Scr.: date of screening, Rand.: date of randomization, SC: date of smoking cessation

4.3.2 Changes in body composition

Nonsmokers

As seen from table 6, the body fat % increased in the LFHCC group compared to the HPMRC group (mean difference 1.4 [95% CI .0, 2.7], p=.04). There were no other significant differences in changes in body composition between the LFHCC group and the HPMRC group from the date of randomization to 12 weeks post cessation. Within the HPMRC group there was a mean decrease in waist circumference of -4.2 cm (95% CI -6.0, -2.4), p<.001, from randomization to 12 weeks after smoking cessation. In addition, this group had a mean decrease in waist/hip-ratio of -.04 (95% CI -.06, -.02), p<.01. There were no significant changes in the LFHCC group.
Table 6: Mean values and changes from randomization to 12 weeks after smoking cessation for the participants with 12 weeks continuous abstinence

<table>
<thead>
<tr>
<th></th>
<th>LFHCC (N = 11)</th>
<th>HPMRC (N = 18)</th>
<th>Between-group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization</td>
<td>12 weeks</td>
<td>Randomization</td>
</tr>
<tr>
<td><strong>BMI, kg/m²</strong></td>
<td>29.9 (27.9, 31.9)</td>
<td>29.9 (28.3, 31.5)</td>
<td>30.4 (28.9, 31.9)</td>
</tr>
<tr>
<td>Waist, cm a</td>
<td>100.8 (94.2, 107.4)</td>
<td>97.9 (91.7, 104.1)</td>
<td>101.4 (97.9, 104.9)</td>
</tr>
<tr>
<td>Hip, cm a</td>
<td>110.5 (104.5, 116.4)</td>
<td>109.4 (104.8, 113.9)</td>
<td>107.5 (104.0, 111.0)</td>
</tr>
<tr>
<td>Waist/hip-ratio a</td>
<td>.92 (.85, .98)</td>
<td>.90 (.84, .95)</td>
<td>.94 (.91, .98)</td>
</tr>
<tr>
<td>Body Fat, %</td>
<td>34.6 (30.1, 39.0)</td>
<td>35.3 (31.4, 39.2)</td>
<td>36.9 (32.8, 41.1)</td>
</tr>
<tr>
<td>Muscle Mass, kg</td>
<td>32.2 (28.9, 35.4)</td>
<td>31.9 (28.8, 35.0)</td>
<td>31.0 (27.8, 34.1)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>109 (100, 117)</td>
<td>109 (99, 118)</td>
<td>116 (110, 121)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>74 (68, 79)</td>
<td>72 (67, 76)</td>
<td>77 (73, 82)</td>
</tr>
<tr>
<td>Biochemical measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>5.3 (4.8, 5.7)</td>
<td>5.3 (5.1, 5.6)</td>
<td>5.5 (5.2, 5.7)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>4.7 (4.0, 5.4)</td>
<td>4.8 (4.3, 5.3)</td>
<td>5.8 (5.3, 6.3)</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.27 (.96, 1.57)</td>
<td>1.41 (1.04, 1.77)*</td>
<td>1.49 (1.26, 1.72)</td>
</tr>
<tr>
<td>LDL, mmol/L a</td>
<td>2.80 (2.11, 3.49)</td>
<td>2.65 (2.17, 3.13)</td>
<td>3.54 (3.08, 4.00)</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.38 (.90, 1.86)</td>
<td>1.64 (.85, 2.43)</td>
<td>1.97 (.75, 3.18)</td>
</tr>
<tr>
<td>Median (Q₁, Q₃)</td>
<td>1.24 (.52, 2.13)</td>
<td>1.12 (.73, 2.69)</td>
<td>1.13 (.92, 2.31)</td>
</tr>
</tbody>
</table>

Estimates are mean (95% confidence interval) unless otherwise stated.

Mean between-group differences in change from randomization to 12 weeks after smoking cessation (LFHCC group – HPMRC group) with p-values are given. Independent-samples t-test is used on the within-group differences to test differences between groups.

LFHCC: Low Fat diet High in Complex Carbohydrates
HPMRC: High Protein diet Moderately Reduced in Carbohydrates

* Significant change from randomization to 12 weeks after smoking cessation. p<.05, paired-samples t-test

** Significant change from randomization to 12 weeks after smoking cessation. p<.01, paired-samples t-test

*** Significant change from randomization to 12 weeks after smoking cessation. p<.001, paired-samples t-test

N = 17 in the high protein group. Missing values are excluded listwise.
**Non-smokers + reduced smokers**

Table 7 shows that when smoking status is not taken into account, waist circumference was more reduced in the HPMRC group compared to the LFHCC group (mean between-group difference 2.3 cm [95% CI .2, 4.4], p=.03) from randomization to 12 weeks after smoking cessation. In addition, there was a significant difference (p=.04) in the change in body fat % (mean difference .9 [95% CI .0, 1.9]) between the groups. Within the HPMRC group there was a mean decrease in waist circumference of -3.6 cm (95% CI -4.9, -2.2), p<.001, from the date of randomization to 12 weeks after smoking cessation.

### 4.3.3 Changes in cardiovascular risk factors

**Non-smokers**

Table 6 also shows that there were no significant differences between the two groups of non-smokers in the change in cardiovascular risk factors. Both groups had a significant within-group increase in mean HDL cholesterol, from 1.27 mmol/L (95% CI .96, 1.57) to 1.41 (95% CI 1.04, 1.77), p<.05 for the LFHCC group, and from 1.49 (95% CI 1.26, 1.72) to 1.68 (1.42, 1.94), p<.01 for the HPMRC group. There were no significant within-group changes in the other cardiovascular risk factors.

**Non-smokers + reduced smokers**

When including all participants, regardless if they were abstinent from smoking or not, there was a significant (p=.03) difference between the groups in change in TG with a mean difference of .32 mmol/L (95% CI .03, .62) from the date of randomization to 12 weeks after smoking cessation. There were no other between-group differences in cardiovascular risk factors.
Table 7: Mean values and changes from randomization to 12 weeks after smoking cessation in nonsmokers plus reduced smokers.

<table>
<thead>
<tr>
<th></th>
<th>LFHCC (N = 30)</th>
<th></th>
<th>HPMRC (N = 40)</th>
<th></th>
<th>Between-group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization</td>
<td>12 weeks</td>
<td>Randomization</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>Mean (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30.7 (29.4, 32.1)</td>
<td>30.9 (29.6, 32.3)</td>
<td>30.6 (29.5, 31.7)</td>
<td>30.3 (29.2, 31.3)</td>
<td>.5 (-.1, 1.0)</td>
</tr>
<tr>
<td>Waist, cm</td>
<td>104.4 (99.5, 109.3)</td>
<td>103.1 (98.1, 108.2)</td>
<td>101.1 (97.9, 104.2)</td>
<td>97.5 (94.6, 100.4)</td>
<td>.05 (-1.8, 2.9)</td>
</tr>
<tr>
<td>Hip, cm</td>
<td>110.6 (107.2, 114.0)</td>
<td>109.6 (106.6, 112.7)</td>
<td>109.7 (107.1, 112.4)</td>
<td>108.2 (105.5, 111.0)</td>
<td>.5 (-.1, 1.0)</td>
</tr>
<tr>
<td>Waist/hip-ratio</td>
<td>.95 (.91, .98)</td>
<td>.94 (.90, .98)</td>
<td>.92 (.90, .95)</td>
<td>.90 (.88, .93)</td>
<td>.02 (-.01, .04)</td>
</tr>
<tr>
<td>Body Fat, %</td>
<td>35.5 (33.2, 37.8)</td>
<td>36.1 (33.9, 38.3)</td>
<td>36.3 (33.4, 39.1)</td>
<td>35.9 (33.1, 38.7)</td>
<td>.9 (.0, 1.9)</td>
</tr>
<tr>
<td>Muscle Mass, kg</td>
<td>33.0 (30.3, 35.8)</td>
<td>32.8 (30.1, 35.6)</td>
<td>32.0 (29.8, 34.2)</td>
<td>32.1 (29.9, 34.3)</td>
<td>-.3 (-1.1, .5)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>115 (109, 121)</td>
<td>114 (108, 120)</td>
<td>117 (112, 122)</td>
<td>116 (112, 120)</td>
<td>0 (-5, 5)</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>79 (76, 83)</td>
<td>78 (74, 82)</td>
<td>79 (76, 82)</td>
<td>78 (75, 81)</td>
<td>0 (-3, 3)</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>6.0 (5.4, 6.7)</td>
<td>6.1 (5.5, 6.7)</td>
<td>5.4 (5.3, 5.6)</td>
<td>5.6 (5.4, 5.7)</td>
<td>-.2 (-.5, .2)</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.3 (4.9, 5.8)</td>
<td>5.5 (5.1, 6.0)</td>
<td>5.5 (5.1, 5.9)</td>
<td>5.4 (5.1, 5.8)</td>
<td>.3 (-1, 1.6)</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>1.24 (1.10, 1.38)</td>
<td>1.37 (1.22, 1.52)</td>
<td>1.42 (1.28, 1.56)</td>
<td>1.58 (1.43, 1.73)</td>
<td>-.03 (-1.2, .06)</td>
</tr>
<tr>
<td>LDL, mmol/L</td>
<td>3.38 (2.95, 3.81)</td>
<td>3.35 (2.93, 3.77)</td>
<td>3.38 (3.03, 3.73)</td>
<td>3.20 (2.90, 3.51)</td>
<td>.14 (-.21, .49)</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.58 (1.24, 1.91)</td>
<td>1.75 (1.34, 2.16)</td>
<td>1.63 (1.09, 2.17)</td>
<td>1.49 (1.02, 1.96)</td>
<td>.32 (.03, .62)</td>
</tr>
<tr>
<td></td>
<td>Median (Q₁, Q₃)</td>
<td>1.37 (.99, 1.90)</td>
<td>1.27 (1.01, 2.55)</td>
<td>1.19 (.92, 1.76)</td>
<td>1.16 (.82, 1.60)</td>
</tr>
</tbody>
</table>

Estimates are mean (95% confidence interval) unless otherwise stated. Missing values are excluded listwise.

Mean between-group differences in change from randomization to 12 weeks after smoking cessation (LFHCC group – HPMRC group) with p-values are given. Independent-samples t-test is used on the within-group differences to test differences between groups.

LFHCC: Low Fat diet High in Complex Carbohydrates

HPMRC: High Protein diet Moderately Reduced in Carbohydrates

* Significant change from randomization to 12 weeks after smoking cessation. p<.05, paired-samples t-test

** Significant change from randomization to 12 weeks after smoking cessation. p<.001, paired-samples t-test

a Missing values for 1 participant in the high protein group (N = 39)

b Missing values for 2 participants in the high protein group (N = 38)

c Missing values for 3 participants in the high protein group (N = 37)

d Missing values for 1 participant in the low fat group (N = 29)

e Missing values for 1 participant in the low fat group (N = 29) and 1 participant in the high protein group (N = 39)
4.4 Dietary intervention

A total of 9 participants were not included in the dietary intervention analysis. This was due to at least one missing dietary record for these participants; one participant did not deliver any of the two records, one participant did not deliver the first record, three participants withdrew from the study before the second recording, and four records were missing from the journals.

4.4.1 Dietary changes

Nonsmokers

Among the 30 participants who were 12 weeks continuous abstinent from smoking, 28 turned in dietary records both at randomization and 4 weeks after their date of smoking cessation.

The HPMRC group had a greater reduction in carbohydrate intake than the LFHCC group (mean difference 52 g [95% CI 6, 98], p=.03). There were no significant differences between the within-group changes in daily intake of protein (mean difference -9 g [95% CI -30, 13], p=.42) or fat (mean difference -9 g [95% CI -29, 12], p=.39). As seen from table 8, there were several significant between-group differences in the changes in energy %.

The dietary records conducted before randomization and four weeks after smoking cessation in the LFHCC group, showed that this group had several significant within-group changes in their diet (see table 8). This intervention group had a significant mean reduction in daily intake of fat, with a mean difference of -24 g (95% CI -37, -11), p<.01. The mean differences in daily intake of carbohydrate and protein were -7 g (95% CI -43, 28), p=.66, and 5 g (95% CI -21, 30), p=.70, respectively. The LFHCC group had a significant increase in fiber from randomization to four weeks after smoking cessation, and the mean intake of fiber was equivalent to an increase from 2.3 g/MJ (SD .8) to 3.4 g/MJ (SD 1.3).

Table 8 also shows that the HPMRC group had several significant within-group changes in their reported diet, including a significant reduction in reported energy intake from 1814 kcal to 1475 kcal. This group had a mean increase in daily protein intake of 13 g (95% CI 3, 23), p<.05. Mean difference in daily intake of carbohydrates was -60 g (95% CI -89, -30), p<.01. Mean reduction in intake of fat was -15 g (95% CI -29, -2), p<.05. The intake of fiber did not
change significant in this intervention group from the date of randomization to 4 weeks after smoking cessation (2.4 g/MJ [SD .7] and 2.4 g/MJ [SD .6], respectively, p=.91).
Table 8: Results from dietary records and indirect calorimetry for the participants with 12 weeks continuous abstinence

<table>
<thead>
<tr>
<th></th>
<th>LFHCC (N = 10)</th>
<th>HPMRC (N = 18)</th>
<th>Difference between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization</td>
<td>4 weeks</td>
<td>Randomization</td>
</tr>
<tr>
<td>Days</td>
<td>Mean ± SD</td>
<td></td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Kcal</td>
<td>6.0 ± 1.7</td>
<td>6.4 ± 0.8</td>
<td>6.3 ± 1.7</td>
</tr>
<tr>
<td></td>
<td>1860 ± 389</td>
<td>1671 ± 685</td>
<td>1814 ± 697</td>
</tr>
<tr>
<td>Energy %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>17.1 ± 1.9</td>
<td>20.2 ± 3.3*</td>
<td>19.2 ± 3.7</td>
</tr>
<tr>
<td>Fat</td>
<td>37.5 ± 4.9</td>
<td>27.4 ± 5.6**</td>
<td>38.2 ± 5.0</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>16.2 ± 3.0</td>
<td>10.2 ± 2.9***</td>
<td>15.0 ± 2.0</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>12.9 ± 2.1</td>
<td>9.5 ± 2.3****</td>
<td>13.3 ± 2.5</td>
</tr>
<tr>
<td>Polysaturated fat</td>
<td>5.6 ± 1.3</td>
<td>5.2 ± 1.2</td>
<td>6.8 ± 2.1</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>41.0 ± 6.3</td>
<td>45.8 ± 7.3</td>
<td>36.4 ± 4.8</td>
</tr>
<tr>
<td>Fiber</td>
<td>1.9 ± 0.6</td>
<td>2.7 ± 1.0*</td>
<td>1.9 ± 0.6</td>
</tr>
<tr>
<td>Added sugar</td>
<td>7.8 ± 5.1</td>
<td>5.6 ± 3.7</td>
<td>5.7 ± 3.7</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2.5 ± 3.9</td>
<td>4.4 ± 5.6</td>
<td>4.3 ± 3.0</td>
</tr>
<tr>
<td>RMR</td>
<td>1683 ± 240</td>
<td>1672 ± 253</td>
<td>1983 ± 521</td>
</tr>
<tr>
<td>Kcal/RMR</td>
<td>1.14 ± .25</td>
<td>1.02 ± .34</td>
<td>.92 ± .30</td>
</tr>
</tbody>
</table>

Estimates are mean ± SD (standard deviation). Differences are mean (95% confidence interval).

Difference between groups in change from randomization to 4 weeks after smoking cessation (LFHCC group – HPMRC group). Independent-samples t-test is used on the within-group differences to test differences between groups.

LFHCC: Low Fat diet High in Complex Carbohydrates

HPMRC: High Protein diet Moderately Reduced in Carbohydrates

RMR: Resting metabolic rate

* Significant change from randomization to 4 weeks after smoking cessation. p<.05, paired-samples t-test

** Significant change from randomization to 4 weeks after smoking cessation. p<.01, paired-samples t-test

*** Significant change from randomization to 4 weeks after smoking cessation. p<.001, paired-samples t-test
Non-smokers + reduced smokers

Dietary intake data and RMR for all participants, regardless of their smoking status, are shown in Table 9. A significant difference between the LFHCC group and the HPMRC group in the mean within-group change in intake of carbohydrate (mean difference 73 g [95% CI 46, 100], p<.001) was seen. The LFHCC group had a significantly larger increase in mean daily protein intake than the HPMRC group, with a mean difference of -12 g (95% CI -24, -1), p=.03. The reduction in daily fat intake in the LFHCC group was not significantly larger than the reduction in the HPMRC group (mean difference -8 g [95% CI -20, 4], p=.20).

The dietary records conducted before randomization and four weeks after smoking cessation in the LFHCC group, showed that this group significantly (p<.001) reduced the mean intake of fat, with a mean difference of -26 g (95% CI -35, -17). The LFHCC group had no significant within-group changes in mean daily intakes of carbohydrate (mean difference 3 g [95% CI -17, 24], p=.75), or protein (mean difference 4 g [95% CI -5, 14], p=.36). The increased mean daily intake of fiber was equivalent to an increase from 2.4 g/MJ (SD .9) to 3.4 g/MJ (SD 1.3), p<.001.

The dietary records conducted in the HPMRC group showed that this group had a significant (p<.001) mean increase in daily intake of protein, with a mean difference of 17 g (95% CI 10, 24). There was a mean reduction in the daily intake of fat of -18 g (95% CI -27, -10), p<.001. This was also the case for daily intake of carbohydrates, with a mean difference of -70 g (95% CI -88, -51), p<.001. Mean daily intake of fiber in g/MJ changed from 2.4 (SD .6) to 2.7 (SD .9) in the HPMRC group, p<.05.

The reported and intended intake of macronutrients among non-smokers plus reduced smokers in both dietary intervention groups are shown in Table 10.
Table 9: Results from dietary records and indirect calorimetry for the participants who completed at both measurement times (randomization and 4 weeks after smoking cessation).

<table>
<thead>
<tr>
<th></th>
<th>LFHCC (N = 29)</th>
<th>HPMRC (N = 42)</th>
<th>Difference between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization</td>
<td>4 weeks</td>
<td>Randomization</td>
</tr>
<tr>
<td>Days</td>
<td>5.7 ± 2.0</td>
<td>6.1 ± 1.1</td>
<td>6.1 ± 1.4</td>
</tr>
<tr>
<td>Kcal</td>
<td>1838 ± 511</td>
<td>1644 ± 561*</td>
<td>1851 ± 639</td>
</tr>
<tr>
<td><strong>Energy %</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>17.7 ± 2.6</td>
<td>20.8 ± 3.2***</td>
<td>18.6 ± 3.9</td>
</tr>
<tr>
<td>Fat</td>
<td>38.3 ± 5.6</td>
<td>28.1 ± 6.3***</td>
<td>37.9 ± 6.0</td>
</tr>
<tr>
<td>Saturated fat</td>
<td>15.6 ± 3.3</td>
<td>10.4 ± 3.3***</td>
<td>15.2 ± 3.1</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>13.4 ± 3.2</td>
<td>9.5 ± 2.5***</td>
<td>13.3 ± 3.3</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>6.0 ± 1.5</td>
<td>5.5 ± 1.7</td>
<td>6.4 ± 1.7</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>38.4 ± 7.5</td>
<td>44.7 ± 6.5***</td>
<td>38.6 ± 6.8</td>
</tr>
<tr>
<td>Fiber</td>
<td>1.9 ± .7</td>
<td>2.8 ± 1.0***</td>
<td>1.9 ± .5</td>
</tr>
<tr>
<td>Added sugar</td>
<td>6.8 ± 5.2</td>
<td>5.7 ± 4.1</td>
<td>6.8 ± 5.2</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3.7 ± 4.9</td>
<td>3.9 ± 4.9</td>
<td>2.9 ± 3.2</td>
</tr>
</tbody>
</table>

Resting metabolic rate (RMR) and under reporting

|                      |                |                |                          |               |              |             |
|----------------------|----------------|----------------|--------------------------|               |              |             |
| RMR *                | 1889 ± 560     | 1815 ± 423     | 1891 ± 401               | 1752 ± 287** | 65 (-98, 228) | .43         |
| Kcal/RMR             | 1.03 ± .33     | .93 ± .27      | .99 ± .33                | .84 ± .27**  | .04 (-.10, .19) | .54         |

Estimates are mean ± SD (standard deviation). Differences between groups are mean (95% confidence interval).

Difference between groups in change from randomization to 4 weeks after smoking cessation (LFHCC group – HPMRC group). Independent-samples t-test is used on the within-group differences to test differences between groups.

LFHCC: Low Fat diet High in Complex Carbohydrates
HPMRC: High Protein diet Moderately Reduced in Carbohydrates

RMR: Resting metabolic rate

* Significant change from randomization to 4 weeks after smoking cessation. p<.05, paired-samples t-test
** Significant change from randomization to 4 weeks after smoking cessation. p<.01, paired-samples t-test
*** Significant change from randomization to 4 weeks after smoking cessation. p<.001, paired-samples t-test

* N = 31 in the LFHCC group, and N = 43 in the HPMRC group
Table 10: Intended and reported intake of macronutrients in the two intervention groups four weeks after smoking cessation (nonsmokers + reduced smokers).

<table>
<thead>
<tr>
<th></th>
<th>LFHCC Intended (g (E%))</th>
<th>LFHCC Reported (g (E%))</th>
<th>HPMRC Intended (g (E%))</th>
<th>HPMRC Reported (g (E%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>≤55 (≤30)</td>
<td>54 (28)</td>
<td>≤91 (≤55)</td>
<td>62 (37)</td>
</tr>
<tr>
<td>Protein</td>
<td>≤82 (≤20)</td>
<td>83 (21)</td>
<td>≥93 (≥25)</td>
<td>99 (28)</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>≥206 (≥50)</td>
<td>179 (45)</td>
<td>≤74 (≤20)</td>
<td>106 (29)</td>
</tr>
</tbody>
</table>

Intended and reported intake of macronutrients in grams and energy % among nonsmokers plus reduced smokers. Intended intake has been calculated from reported energy intake and planned composition of macronutrients in energy %.

LFHCC: Low Fat diet High in Complex Carbohydrates

HHPMRC: High Protein diet Moderately Reduced in Carbohydrates.

g: gram, E%: energy %

4.4.2 Misreporting

Non-smokers

Among the non-smokers there was no significant difference between the two intervention groups in misreporting at the date of randomization (data not shown). Table 8 shows that the change in misreporting of energy intake from the date of randomization to four weeks after smoking cessation not was significant different between the LFHCC and the HPMRC groups. However, the HPMRC group had a significant (p=.03) greater reduction in RMR from the date of randomization to four weeks after smoking cessation than the LFHCC group (mean difference 272 kcal [95% CI 31, 513]).

In the LFHCC group there were no significant changes in either misreporting or RMR. There was no significant change in misreporting in the HPMRC group, but this group had a significant (p<.05) decrease in measured RMR (from 1983 kcal to 1699 kcal).

Non-smokers + reduced smokers

There was no significant difference in misreporting between the LFHCC and the HPMRC group at randomization (data not shown). Table 9 shows that there were no significant differences between the two intervention groups in mean change from randomization to 4 weeks after smoking cessation, neither in misreporting nor in measured RMR.

Furthermore, within the LFHCC group there were no significant changes in misreporting or measured RMR from randomization to 4 weeks after smoking cessation. In the HPMRC
group there was a significant (p<.01) change in misreporting, with a change in estimated intake/measured RMR-rate from .99 (95% CI .89, 1.10) at the date of randomization to .84 (95% CI .76, .93) four weeks after smoking cessation. The HPMRC group also had a significant (p<.05) decrease in measured RMR from before to after smoking cessation (from 1891 kcal to 1752 kcal).

4.4.3 Correlations between changes in body weight and dietary changes

Nonsmokers (weeks 1-4)

Among the participants who managed to be abstinent from their smoking the first four weeks after smoking cessation (weeks 1-4), there was a positive correlation between change in body weight and the reported change in daily intake of carbohydrate (r = .51, p=.02) in the HPMRC group four weeks after smoking cessation. There were no significant correlations between the change in body weight and the reported changes in dietary intake in the LFHCC group (see table 11). There were no correlations between changes in energy % and change in body weight in any of the dietary intervention groups (data not shown).

Nonsmokers + reduced smokers

Among all participants, regardless of their smoking status, there was a positive correlation between the change in body weight from randomization to four weeks after smoking cessation and the reported change in daily intake of protein (r = .36, p=.02) in the HPMRC group. In this intervention group there was also a positive correlation between the change in body weight and the reported change in daily intake of fat (r = .39, p=.01) four weeks after smoking cessation. There were no correlations between the change in body weight and the reported changes in dietary intake in the LFHCC group four weeks after smoking cessation (see table 11). There were no correlations between changes in energy % and change in body weight in any of the dietary intervention groups (data not shown).
<table>
<thead>
<tr>
<th></th>
<th>LFHCC</th>
<th>HPMRC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
</tr>
<tr>
<td><strong>Nonsmokers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate, g</td>
<td>.01</td>
<td>.98</td>
</tr>
<tr>
<td>Fat, g</td>
<td>.19</td>
<td>.46</td>
</tr>
<tr>
<td>Protein, g</td>
<td>-.09</td>
<td>.74</td>
</tr>
<tr>
<td><strong>Nonsmokers + reduced smokers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate, g</td>
<td>.11</td>
<td>.59</td>
</tr>
<tr>
<td>Fat, g</td>
<td>.15</td>
<td>.44</td>
</tr>
<tr>
<td>Protein, g</td>
<td>-.11</td>
<td>.56</td>
</tr>
</tbody>
</table>

r: Pearson correlation  

p: p-value  

LFHCC: Low Fat diet High in Complex Carbohydrates  

HPMRC: High Protein diet Moderately Reduced in Carbohydrates
5 Discussion

In this chapter the discussion of subjects and methods will precede the discussion of the results.

5.1 Discussion of subjects and methods

5.1.1 Subjects

Gender

In this study there was a female predominance (72.5 % women). One reason for this may be that women are more concerned than men about gaining weight after quitting smoking\textsuperscript{149,150}, and that they were therefore more willing to participate in a smoking cessation trial with intention to prevent undesired weight gain. All subjects in the current study were randomized to the intervention groups. Proper randomization reduces selection bias at trial entry and is the crucial component of high quality randomized controlled trials\textsuperscript{151}. Randomization has therefore minimized the chances that any significant differences at the date of screening have affected any of the outcomes.

Screening failures

Despite that four of the eighty subjects randomized did not meet all the inclusion criteria and of these, only three completed the trial and one managed to be continuous abstinent, they were all included in the analyses. This was done since any analysis which omits patients is open to bias because it no longer compares the groups as randomized\textsuperscript{152}. The one participant who did not wish to take varenicline was moderately nicotine dependent with a FTND score of 4, and at the screening visit she reported to be smoking 13 cigarettes daily. Twelve weeks after smoking cessation, her body weight was increased by 3.9 kg since the date of randomization. She managed to be continuous abstinent from her smoking all twelve weeks without taking varenicline. This may be due to a high motivation to quit cigarette smoking, and it is also possible that she was prepared for and accepted some weight gain during the first post cessation period, and therefore did not relapse despite an increase in body weight. One of the two participants over the age of 65 years at the screening visit was randomized to
the LFHCC group, while the other was randomized to the HPMRC group. Neither of them managed to stop smoking, and both were included as smokers in all analyses of abstinence rates. The fact that these participants not managed to be abstinent is not likely to be due to their age, since it has previously been shown that abstinence rates for people ≥ 60 years are not different from abstinence rates for people < 60 years\textsuperscript{153}. It is also shown that sarcopenia, defined as the gradual reduction in skeletal muscle mass and strength observed with advancing age, increases with age and current smoking\textsuperscript{154}. In addition, it is known that blood pressure and the prevalence of hypertension tends to increase with advancing age\textsuperscript{155}.

However, the two participants older than 65 years in the current study did not have any outlier values for muscle mass or blood pressure, and it is therefore not likely that the higher age of the two participants have influenced the data. There was also a female participant with BMI > 40 kg/m\textsuperscript{2} included in the current study. She was not continuous abstinent all 12 weeks, only the last four weeks (weeks 9-12). Despite this, 12 weeks after smoking cessation she had lost 4.3 kg since the date of randomization. It is previously reported that blood pressure, fasting blood glucose and lipids, in addition to underreporting of energy intake, increases with increasing BMI\textsuperscript{156,157}. The participant with the highest BMI in the current study had normal blood pressure (<120/80 mmHG), glucose and lipids, and underreported less than the mean level of underreporting in the current study. We therefore concluded that including this participant would have affected outcomes only marginally.

\textbf{Study completion and drop-outs}

Eight women and two men did not meet at the visit 12 weeks after smoking cessation. One of the women met at the 6 months visit (this visit was not included in the current master thesis), and hence she was not considered a drop-out. In addition to these well-defined factors that could influence the results, other and to us unknown factors may also exist that may have influenced the results.

Almost 90\% of the participants completed the study for 12 weeks, with no difference in completion-rate between the intervention groups. Previous smoking cessation trials have study-completion rates ranging from approximately 50 to 90 percent in trials with study duration of three months up to one year\textsuperscript{107,108,135,137,138}. These trials included a significant higher number of subjects than the current study, ranging from almost 400 to over 1200 randomized participants.
Study-completion rates in previous dietary intervention trials range from 58 to almost 100 percent in trials with study duration of three months up to one year.\textsuperscript{115,117,118,158,159} The number of participants in these trials ranged from 65 to over 800. The trials with shortest duration (3 months) included approximately 200 and 800 participants, and had a study-completion of 94% and almost 100%, respectively.\textsuperscript{115,159} Compared to these trials, the current study had a lower completion rate. A possible reason for this is that the current study combined a dietary intervention with a smoking cessation intervention, which contributed to a greater burden on the participants. It must also be considered that random outliers will have greater impact on the results in studies with small size, as we have here.

5.1.2 Study design and measurements

**Assessment of smoking status**

The main purpose of this study was to assess the effect of two different dietary interventions on preventing undesired weight gain 12 weeks after smoking cessation. Since it is shown that the combination of counseling and medication is more effective than either alone\textsuperscript{100}, conditions in the current study were therefore set for increasing the participants’ opportunities to be able to stop smoking.

Smoking diaries concern normally self-reported smoking status, and it is previously shown that accurate estimates of the prevalence of cigarette smoking can be derived from self-reported data on smoking status\textsuperscript{160}. Different variants of smoking diaries have been used in previous trials assessing smoking status\textsuperscript{161,162}. To assess smoking status, we calculated CAR and point prevalence based on smoking diaries and CO-measurements. CAR, defined as no smoking at all based on self-reported cigarettes per day and CO-measurements, has been calculated for all twelve consecutive weeks. All participants who reported to be abstinent the first 12 weeks after their smoking cessation dates, confirmed by CO-measurements, have been included in the analyses as nonsmokers. Using a combination of self-report and an objective biochemical measurement to assess smoking status has minimized the chances of misclassification of participants as nonsmokers.

Another method often used to confirm smoking status is cotinine. Cotinine is the major metabolite of nicotine and have a higher sensitivity and specificity than CO, and can be measured in plasma, urine or saliva. It also has a longer half-life than CO, and can be detected
up to 3-4 days after exposure\textsuperscript{163}. Measurement of cotinine has been used in several previous trials to assess smoking status\textsuperscript{164-166}, and may have been a more accurate method to determine smoking status and should probably be applied in future studies as conducted here. In addition, cotinine can be measured in saliva, and would certainly not have constituted a greater burden on the participants than the measurements of CO in exhaled air.

With regard to the CO-measurement, a level of \( \leq 5 \) ppm was assumed as a no smoking status. In other smoking cessation trials, this level has been set at 8-10 ppm\textsuperscript{107,108,135,167,168}. These studies are multicenter trials, and the CO-level may have been set as high as \( \leq 10 \) ppm due to a higher level of air pollution, which may influence the expired CO-level in nonsmokers. It is, however, demonstrated that the optimal cut-off level of exhaled carbon monoxide to discriminate between nonsmokers and smokers should be 5.5 ppm\textsuperscript{131}. Taking this into account, we decided a CO-level of \( \leq 5 \) ppm to be a reasonable number to confirm reported abstinence from smoking. This was decided since measurements of carbon monoxide in exhaled air is an accepted method for detection of smoking status\textsuperscript{169}, and since this is a method that measure short-time abstinence. It should however be noted that this method of measuring CO has a low specificity and sensitivity\textsuperscript{163}, as there are several environmental sources of CO in addition to cigarette smoke that may influence the results, such as CO from combustion of coal, petrol and inhaling air in rooms where other people are smoking. In addition, the participants may have failed to report single events of smoking, such as a puff. If such events did not occurred immediately before measuring CO-levels, they may not have influenced the measurements despite that these events could have influenced the participants’ physiology and hence weight etc. To what extent this has influenced the measurements here is unknown.

As some participants missed one or more visits, self-reported smoking status is the only available documentation of smoking status. Participants were tested for CO-levels at the visits before and after a missing visit. If low levels of CO were confirmed, the participants were considered nonsmokers. Participants who, in contrast, reported to be smokers at other visits or dropped out, were considered smokers at missing visits. Similar assumptions are supported as they have been made in other trials\textsuperscript{108,168}. Failure to classify smokers from nonsmokers may have influenced CARs. The use of CAR instead of point prevalence to define the participants as nonsmokers have strengthen the analyses of changes in post cessation weight gain, since using the point prevalence abstinence to define abstainers is likely to underestimate actual
weight gain because of smoking cessation. Misclassification may also have influenced other parameters such as changes in HDL and body weight. The latter is expected as continued smokers are expected not to gain weight during a relatively short period of time. To this end smoking cessation has also been shown to influence HDL levels as quitting smoking is associated with an increase in HDL-levels. Furthermore, it should also be considered that misclassification of nonsmokers as smokers may also lead to fewer nonsmokers, which may certainly influence the test power. Finally, as the participants were randomized, different degree of nicotine dependence may not have influenced the results reported here. Proper randomization is considered the best and most reliable method to ensure comparable distribution between the two intervention groups.

Smoking cessation

In this thesis 37.5% of the participants who were randomized to follow either of the two intervention diets managed to be continuous abstinent all twelve weeks starting at their planned smoking cessation date. Few, if any, other smoking cessation trials have reported continuous abstinence rates for the continuous first twelve weeks. It is therefore difficult to say whether this was a high or low CAR compared to other trials. Klesges et al. did, however, measure CAR at one month and at six months after smoking cessation, and found CARs of 30% and 26%, respectively. CARs for the first four weeks (weeks 1-4) and for the last four weeks (weeks 9-12) in the current study were 47.5% and 60%, respectively. For comparison, previous smoking cessation trials using varenicline had a CAR (weeks 9-12) ranging from 35% to 54%. One of these trials, Hawk et al., compared an extended pre-quit varenicline treatment period of four weeks with a standard pre-quit varenicline treatment period of one week. They found that CAR during the final four weeks (weeks 9-12) of treatment was higher in the extended group than in the standard group (67% vs 35%, respectively). Except from Hawk et al., these trials included about 600-1000 subjects, which are markedly larger trials than the current study. However, in the Hawk et al. study, only 60 subjects were included and had the lowest CAR (in the standard group) of all these trials. This suggests that low numbers of subjects not necessarily results in high abstinence rates. Seven-days point prevalence abstinence at week 12 has been approximately 40-50% in other trials looking at varenicline-assisted smoking cessation rates. In the current study 7-days point prevalence was not measured, but abstinence rate for the last 14 days, confirmed with CO-measurements at week 12, was almost 69%. Compared to previous trials,
the current study has a high rate of continuous abstinence among the participants. Considering our efforts to minimize the risk of misclassification of smokers, we assume that the CAR found here was not overestimated. Participants claiming to be abstinent, but were measured with CO-level above 5 ppm, were considered smoking. This was done despite that CO-levels of 6 ppm may be caused by passive smoking or passing traffic dense areas before the visit. Based on this it may be that the limit of CO ≤ 5 ppm can actually have led to a lower CAR than what really is the case. All participants apart from one received varenicline. Several trials have shown that the use of varenicline increases smoking cessation rates\textsuperscript{107,108,135,137,168}. However, varenicline adherence has not been analyzed in this master thesis. It is therefore difficult to say if the high CAR was due to good compliance with the medication, the dietary intervention focusing on prevention of post cessation weight gain, or both. Indeed, a previous pilot study showed that offering a weight management program to overweight and obese weight-concerned smokers increased the probability of the participants to be 6 months abstinent\textsuperscript{171}. In contrast, there is some evidence suggesting that combining diet and smoke cessation, in attempt to prevent weight gain, may undermine the attempt to quit smoking\textsuperscript{42,172}. Temporary smoking cessation rates in the current study do not support this, since we reached a CAR comparable with CARs in large trials assessing efficacy of varenicline for smoking cessation\textsuperscript{107,108,138}.

It is possible that the subjects participating in this study were highly motivated as they were recruited through an advertisement in the newspaper and had to make their own initiative to sign on. Another aspect is the fact that all visits were at daytime, meaning that many of the participants had to take time off from work. All participants reported to smoke at least 10 cigarettes daily when they met at the screening visit, but seven of them reported to be smoking less than 10 cigarettes/day when they met at the next visit (the randomization visit). This may indicate that some of the participants started to reduce the number of daily cigarettes already after the first visit, probably to prepare themselves for smoking cessation, which may suggest a high motivation. Another possibility is that these participants did not smoke an average of as much as 10 cigarettes daily at the beginning, and hence were over-reporting in order to be included in the study. If this is the case, these participants did not meet all the inclusion criteria, and the subjects included in the analyses were not be representative for the population meant to be included.
Clinical and biochemical measurements

Any measurement found to be clearly incorrect, e.g. a blank print from the impedance measurement, was repeated if discovered immediately, or excluded if it first was detected after the participant had finished the visit. Any excluded measurement would appear as a missing value in the statistical analyses. Several missing values in statistical tests would have weakened the power of the tests to detect any differences between the intervention groups. To ensure comparable measurements, participants who were not fasting when they met at visit 2, 8 or 12 (randomization and 4 and 12 weeks post-cessation, respectively), were asked to come back for fasting impedance measurement, indirect calorimetry (at visit 2 and 8), and blood samples the following day.

Body weight was measured with impedance at randomization and four and 12 weeks after smoking cessation and with a digital scale at the remaining visits. This has most likely not influenced the measurement of body weight since all scales used in the current study are tared once every year. We have also sought to minimize measurement errors due to slightly different method executions by limiting the number of study personnel doing the tests. Two nutritionists were responsible for measuring waist and hip circumference. Hence, any measurement errors due to different performance of the nutritionists are most likely equally distributed between the intervention groups and over time, and may therefore not have affected the outcome results markedly. Measurements were, however, not performed blinded and, in theory, this may have influenced the measurements. Despite this, to further minimize biased measurements in favor of either of the two diet groups, we suggest that such measurements should be performed blinded in future studies.

The blood measurements were taken after one overnight fast (at least 8 hours fasting), and were analyzed by conventional laboratory methods at Department of Clinical Chemistry, Oslo University Hospital Ullevål. If the amount of TG was higher than 4.5 mmol/L, LDL could not be analyzed, and LDL values are therefore missing for two participants, one in each group, with high TG both at randomization and 12 weeks after smoking cessation. However, as LDL values are only missing for one participant in each group, we assume that this has minor effect on the results for LDL levels.
Statistics

Since all statistical tests performed have been done on only 70 participants, which is a considerably lower number of subjects than originally estimated to be required, the power of the tests are less than optimal. According to Altman’s nomogram for calculating sample size or power\textsuperscript{173} these analyses only had, approximately, a 70% power to detect a 3 kg difference with 5% significance assuming that the SD of the change in weight was 5 kg. Analyses performed on the group of participants who were 12 weeks continuous abstinent had significantly lower power than this and cannot be used to draw any absolute conclusions. This because a low test power increases the risk of type II errors (not detecting an existing difference between the groups).

Paired-samples t-test was performed to assess within-group changes, while between-group differences were analyzed with independent-samples t-test for continuous variables, and chi-squared test for categorical variables. These tests have been used for similar assessments in other trials with normally distributed variables\textsuperscript{117,174,175}. However, a one-way analysis of variance (ANOVA) is another often used method to test for differences between two or more independent groups, and could have been a good alternative to the independent-samples t-test\textsuperscript{117,176}. The chi-squared test is an accepted method of analyzing categorical variables, such as differences in proportion of drop-outs\textsuperscript{158,175}. In the current thesis, Pearson correlation was used to assess correlations between changes in body weight and changes in dietary intake of macronutrients. Pearson correlation has been used in previous trials\textsuperscript{37,117}. However, due to the small sample size, multiple linear regression analyses were not performed. This makes it difficult to identify any other possible relationships between the outcomes and dietary changes, or if there are any interactions or confounders present (e.g. age, gender, education level etc). This can be considered a weakness in the current thesis.

Intention-to-treat is a strategy for the analysis of randomized controlled trials that compares participants in the groups to which they were originally randomly assigned, i.e. includes all participants regardless of whether they actually satisfied the entry criteria, the treatment actually received, and subsequent withdrawal or deviation from the protocol\textsuperscript{152,177}. The intention-to-treat approach has two main purposes. Firstly, the approach maintains treatment groups that are similar apart from random variation. This is the reason for randomization, and the feature may be lost if analysis is not performed on the groups produced by the randomization process. Secondly, intention-to-treat analysis allows for non-compliance and
deviations from policy by clinicians\textsuperscript{177}. However, no consensus exists about how missing responses should be handled in intention-to-treat analyses, and different approaches are used. In the current thesis a last-measurement-moved-forward analysis was performed for body weight, since this was the only effect variable measured at every visit. This intention-to-treat approach to implement missing values has been used in some previous trials\textsuperscript{176,178}. However, even though intention-to-treat analyses are necessary to keep the randomization intact, there is some controversy about using intention-to-treat approaches in analyses of body weight in smoking cessation trials. As mentioned above, cigarette smokers have lower body weight than nonsmokers\textsuperscript{52,53}, and quitting is associated with weight gain\textsuperscript{170,179}. Moreover, those who return to smoking tend not attend clinics for follow-up\textsuperscript{88}. Including those who were not abstinent can reduce the mean weight gain, since it is likely that the body weight will depend on time since relapse. People who try to become abstinent but fail after a few days do not gain weight, while those who relapse to smoking seem to lose the weight they gained previously\textsuperscript{88}. A last-measurement-moved-forward analysis may therefore be slightly misleading. In accordance with this and in order to evaluate the effect of smoking status on body weight, the analysis both with and without missing values were performed to detect potential changes, both among nonsmokers and among all participants randomized to the intervention diets. The last-measurement-moved-forward analysis on body weight among the nonsmokers in the current study did not differ from the analysis performed only on the completers (those met at both randomization and twelve weeks post-cessation). This strengthens the results we found for changes in body weight. For analyses in most randomized controlled trials intention-to-treat is a recommended approach, and almost half the reports of randomized controlled trials includes an analysis described as intention-to-treat\textsuperscript{177}. For the other efficacy outcomes in the current thesis an intention-to-treat approach would probably have been closer to the effects likely to be encountered in subsequent clinical use\textsuperscript{152}, since it is rather rare that all patients will be able to follow a diet exactly as prescribed all the time, and since most cigarette smokers need several attempts before, if at all, they manage to quit smoking\textsuperscript{84}. The fact that intention-to-treat analyses not have been performed for the other efficacy outcomes in this master thesis may therefore be considered a weakness.
Dietary intervention and assessment of diet

In this study a total of seven intervention meals were handed out at two time points, four and three meals, respectively. In some previous trials of compared different intervention diets all meals for the whole intervention period were provided at the same time\textsuperscript{158,175}. In the present study, providing all meals would probably have resulted in a better adherence to the intervention diets. It is, however, not likely that this ever will be done in future practice, and we assume that not providing all meals most likely resulted in a more realistic effect of the intervention.

Both over- and underreporting of food intake are documented, although underreporting is the most regular event\textsuperscript{180-183}. Furthermore, it is previously shown in postmenopausal women that a 7-day dietary record captures changes in dietary intake after smoking cessation\textsuperscript{184}. Nelson et al.\textsuperscript{185} have suggested that in order to be able to estimate daily energy intake, considering between- and within-subject variation, a total of 4 and 6 days of recording is necessary for men and women, respectively. In the present study weighed DRs were used to measure compliance to the intervention diets. However, due to some customization of number of days between the visits, it was impossible for some of the participants to conduct more than 5-6 days. Despite that this might have weakened the chance of detecting the daily variation in dietary intake, it was well in line with previous studies where food records were conducted for 3-5 days\textsuperscript{117,118,174-176,186,187} or only as 24-hour recalls\textsuperscript{188-190} or food frequency questionnaires\textsuperscript{189,191}. Measurements of food intake are often prone to misreporting, especially when it comes to self-administered tools. To this end, validation of different methods of dietary assessment has shown that weighed records, compared to 24 hours recall and food-frequency questionnaires, is the most accurate method of dietary assessment, despite problems of underreporting\textsuperscript{192}. To use the method of weighed DR to measure compliance in the current study may therefore not have resulted in poorer estimation of dietary intake than other used methods. Furthermore, here the Goldberg equation which is commonly used to identify misreporters\textsuperscript{145} was used. Moreover, Tooze et al.\textsuperscript{193} compared the classification of underreporters using the Goldberg method with underreporters classified using doubly labeled water, and concluded that the Goldberg method is a reasonable approach to characterize underreporting. Goldberg et al. made cut-off limits to recognize underreporting at the group level\textsuperscript{180}, and unless a person has a very inactive lifestyle, a physical activity level (PAL) <1.35 is not very likely. A PAL value of 1.55 is the WHO value for a sedentary lifestyle\textsuperscript{129}. In our study we report that the LFHCC and the HPMRC groups had a mean PAL <1.35, both before
and after smoking cessation. This may indicate underreporting in both groups. In the current study all participants were overweight or obese, and it is shown that people with high BMI often underreport more than lean people\textsuperscript{157,192,194}. Moreover, there is some evidence that women and smokers may underreport more than males and nonsmokers, respectively\textsuperscript{157,194}. Since the participants in the current study were smokers, and predominantly women in addition to all being overweight or obese, this may support that underreporting was present. Also eating behaviors like eating restraint and eating disinhibition are associated with misreporting, and this may be contributing factors to underreporting here. It has been suggested that eating disinhibition may affect a person’s ability or motivation to accurately report energy intake, while eating restraint directly reduces “normal” intake, thereby contributing to underreporting\textsuperscript{195}.

The possible underreporting of energy intake in both groups provides a great uncertainty about the participants’ actual diet, since it is impossible to know what kind of food items they underreported. It has previously been reported that energy and energy-yielding nutrients like fat and sucrose\textsuperscript{119}, in addition to cakes, were underreported, while vegetables, potatoes and meat, amongst others, were not underreported\textsuperscript{192}. If this is the case in the current study, the macronutrient composition of the diets consumed in the two intervention groups would have been somewhat different than reported. In addition, it has previously been suggested that the number of days of diet records required to estimate the intake of protein, fat and carbohydrate are up to 8, 7 and 6 days, respectively\textsuperscript{185}. This indicates that the number of days recorded in the current study, may not have been enough to estimate the true daily intake of macronutrients in the first place. However, more days of dietary recording would have been a greater burden on the participants, and would probably have led to less motivation among the subjects and poorer recording.

The software program Mat på data 5.0 was used to calculate the reported intake of calories, carbohydrate, fat and protein. Since this program not has been updated for several years, it is incomplete when it comes to the number of food items. The Mat på Data 5.0 software program do not have options for getting results of intake of different food items, only different food groups, which makes it difficult to evaluate if any decrease or increase in a nutrient might be due to a reduced or increased intake of a specific type of food. One previous trial comparing a low glycemic load diet high in protein and a low-fat diet, found that the group following the diet high in protein significantly reduced their intake of bread, potatoes
and rice, in addition to increase their total intake of meat. It is possible that the HPMRC group in the current study have made similar changes to their diet. The Mat på Data 5.0 software program is well suited to estimate energy intake and energy percent from the different macronutrients recorded in the dietary records. Even though we are not able to differentiate between different food groups, the use of this program has most likely given a good estimate of the reported macronutrient composition in the current study.

5.1.3 Can the results be generalized?

This thesis is based on a relatively small sample size. In addition, a relative smaller number of men compared to women were included in the study group. This makes it difficult to generalize the results to the Norwegian cigarette smoking population, considering the low power of statistical tests and the fact that there are at least as many male smokers as female smokers in Norway. Furthermore, due to the inclusion and exclusion criteria, results cannot be generalized to normal-weighted smokers or smokers with obesity class III, smokers taking insulin for diabetes or smokers who have history of serious psychiatric disorder or depressive illness. Finally, the current study only shows results after a few months duration, and any long-term effects of the interventions are thus far unknown.

5.2 Discussion of results

5.2.1 Outcome variables

Body weight

Twelve weeks post cessation both dietary interventions seem to be equally successful in preventing undesired weight gain. Previous smoking cessation trials without dietary interventions have found a significant increase in body weight following smoking cessation, although most of these trials have looked at weight gain during the first year or longer after smoking cessation. Klesges et al. found an average increase in body weight of 3 kg after one month and 5.5 kg after 6 months among continuous abstinent participants, and it is shown that the weight gain is greatest the first 1-2 months following smoking cessation. Compared to these findings, the lack of any within- or between-group
difference in body weight 12 weeks after smoking cessation in this thesis suggests that both dietary interventions successfully prevented short-term post cessation weight gain.

However, since changes in physical activity were not considered here, we do not know whether the relatively stable body weight in the current study was due to an increase in physical activity among the participants or other factors. There are some evidence that exercise interventions may reduce body weight after smoking cessation, but the results from different trials are inconsistent, and increased physical activity seems to be most effective in the long term and if it is of vigorous intensity. Since participants in the current study only were encouraged to increase physical activity and no exercise interventions were performed, and, in addition, body weight was measured after only four and 12 weeks after smoking cessation, it is not likely that a change in physical activity is the whole explanation. In addition, previous studies have either shown no change in physical activity or a decrease in physical activity after smoking cessation. It is previously shown that post cessation weight gain is inversely associated with socioeconomic status, but this has not been included in the statistical analyses in this master thesis, and whether a high economic status among the participants can explain some of the reason for the absence of weight gain or not is not known.

There is evidence for varenicline reducing post cessation weight gain at the end of the treatment period, and the use of varenicline might therefore be some of the reason for the stable body weight seen in the current study. How much of the effect varenicline is responsible for is not known since analyses of varenicline adherence and regression analyses not have been performed. It is also possible that the close follow-up with regular recording of body weight and counseling has made the participants more aware of their dietary habits, like snacking between meals. Snacking is a common displacement activity after smoking cessation, and the delivery of recommended snack foods and the nutritional counseling may have prevented post cessation weight gain. The prevented weight gain in the current study may have contributed to the relatively high smoking cessation rates, since weight gain after smoking cessation is associated with relapse.

In the current study, we failed to show any difference between a low fat diet high in complex carbohydrates and a high protein diet moderately reduced in carbohydrates in preventing post cessation weight gain. This is in accordance with previous findings supporting that both low fat diets and diets high in protein and low in carbohydrate can reduce body weight.
However, when including the reduced smokers, we did find a greater weight reduction in the group following the diet with highest protein content six weeks after initiation of the diet. Twelve weeks post cessation we did no longer find a significant difference between the intervention groups. However, the difference in weight between groups was greater when reduced smokers were included than among nonsmokers only. This may indicate a true difference between diets in favor of the diet with highest protein content. Some previous trials have shown that higher protein diets may increase total weight loss. Furthermore, there is evidence that modestly increasing the proportion of protein in the diet, while controlling energy intake, may improve body weight maintenance after weight loss. The greater effect on weight loss of high protein diets compared to lower-protein diets is probably due to a lower spontaneous energy intake brought about by enhanced satiety and a greater thermogenic effect.

**Body composition**

In this study a decrease in body fat % was seen in the HPMRC group compared to the LFHCC group. Even though the 95% confidence interval contained 0, and a possibility for a random finding exists, this finding together with the changes in waist circumference within the HPMRC group is in line with previous trials that have found decreased total body fat and waist circumference with a high protein diet. Wycherley et al. found, however, greatest effect for body weight, fat mass and waist circumference in the high protein group following a progressive resistance exercise training program. Exercise is associated with improved body composition, and it is demonstrated that a diet with higher protein and reduced carbohydrates combined with exercise additively improves body composition during weight loss. Since the current study not included any kind of exercise interventions, it is not likely that one of the intervention groups would have increased their physical activity significant more than the other and the significant difference between the groups in mean change in waist circumference and body fat may indicate a beneficial effect of the high protein diet. There is some evidence that diets high in protein and low in carbohydrate favorably affect body mass and composition independently of energy intake. Several studies have suggested that higher protein diets not only may increase total weight loss, but also may increase the percentage of fat loss. A previous study found that a high-protein diet (E% 25) experienced a 10% greater reduction in intra-abdominal adipose tissue than a medium-protein diet (E% 12). This is in accordance with the reduction in waist.
circumference observed in the group with highest protein intake in the current study. Parker et al.\textsuperscript{208} found that women on a high protein diet (E\% 28) lost significantly more total and abdominal fat compared with women on a low protein diet (E\% 16), but that there was no difference in men. Since women and men not have been analyzed separately in this master thesis, it is not known whether this also is the case in the current study. However, since the gender distribution in the two intervention groups in the current study was comparable, this should not have any influence on the outcomes. Even though we found a significant reduction in waist circumference only in the diet with the highest content of protein, both interventions prevented the increase in waist circumference previously associated with smoking cessation\textsuperscript{91,96,212}. It has also previously been found that a higher intake of protein is associated with maintenance or accretion of fat-free mass\textsuperscript{174,205,213}, although there was no significant difference in the change in muscle mass between the LFHCC and the HPMRC groups in the current study. This may in part be due to the relative short follow-up period, or the lack of exercise intervention since Josse et al.\textsuperscript{214} found lean mass gain during diet- and exercise-induce weight-loss.

**Cardiovascular risk factors**

Among the nonsmokers, there were no significant differences between the LFHCC group and the HPMRC group when it comes to changes in cardiovascular risk factors 12 weeks post cessation, but both groups had a significant increase in HDL cholesterol. The effects of diets low in carbohydrate on HDL reported in previous trials are inconsistent\textsuperscript{205,215}, while low fat diets have been shown to decrease HDL\textsuperscript{119,216}. We found increases in HDL in both groups in the current study, which suggests that the effect on HDL was due to quitting cigarette smoking rather than the dietary interventions as it has previously been shown that smoking cessation is associated with an increase in HDL\textsuperscript{94,217,218}. If not considering smoking status, there was a significant between-group difference in the change in TG when analyzing all participants. We did not find any significant within-group alterations in TG from randomization to 12 weeks after smoking cessation. Low-fat diets have previously been shown to increase TG, at least under weight-maintenance conditions\textsuperscript{219}. In contrast did one previous trial found that a diet low in carbohydrate gave a greater decrease in triglyceride levels compared with a low-fat diet in severely obese subjects\textsuperscript{122}. Evidence from other trials also shows that high-protein diets decrease fasting plasma TG\textsuperscript{158,187,205}. Most of these trials had study duration of four to six months, and the short duration of only three months in the
current study may explain some of the reason for why we failed to observe a significant reduction in TG. However, Layman et al.\textsuperscript{205} found a significant decrease in TG after only 10 weeks on a high protein diet. Although there was no significant decrease in TG in the current study, mechanisms for the changes in TG exists and may relate to a lower daily blood glucose concentration and lower daily insulin which primary functions as a hormone are to promote storage of blood glucose in skeletal muscle and adipose tissue and to inhibit lipolysis and promote triglyceride synthesis and storage rather than release\textsuperscript{220}. The significant increase in fasting blood glucose from the date of randomization to 12 weeks post cessation seen in the HPMRC group is, however, not in accordance with this theory. Previous trials studying the effects of a high-protein diet usually have found no effect\textsuperscript{117,118,175} or a decrease in blood glucose\textsuperscript{208,221}. Moreover, some previous studies have found an increase in blood glucose after decreasing cigarette smoking\textsuperscript{96,166,212}. Increased glucose may be a contributor to the increased risk for type 2 diabetes the first years after smoking cessation, since post cessation weight gain only partially explains this increased risk\textsuperscript{96}. However, we did only find increased blood glucose when we included the reduced smokers, and we suggest that this result was mainly caused by the reduced smokers who were least compliant to the intervention diet (i.e. those who gained most body weight). This may indicate that successful prevention of post cessation weight gain and following increased blood glucose may prevent the increased risk for type 2 diabetes associated with smoking cessation.

In the current study, we did not find any changes in systolic or diastolic blood pressure. A recent meta-analysis showed a greater mean decrease in both systolic and diastolic blood pressure after 3 months with higher- compared to lower-protein diets\textsuperscript{222}. Furthermore, there is some evidence suggesting that the dietary content of fat not has a large impact on blood pressure\textsuperscript{223,224}, while others have found that a diet rich in fruits, vegetables and low-fat dairy products and with reduced saturated and total fat (the DASH-diet) can lower blood pressure\textsuperscript{225}. Moreover, epidemiologic data support a positive association between body weight and blood pressure, and randomized controlled trials have demonstrated that a reduction in weight is associated with a reduction in blood pressure\textsuperscript{226}. Our participants were normotensive at randomization in addition to maintaining a stable body weight during the follow-up period, and a decrease in blood pressure would therefore not be expected. However, smoking cessation has been associated with increased blood pressure and incidence of hypertension, mainly due to post cessation weight gain\textsuperscript{94,227}. Our findings suggests that by preventing weight gain after smoking cessation, an increase in blood pressure will also be prevented.
Among weight-reduction diets, low-fat diets have been reported to decrease total cholesterol and LDL more than high-protein, low-carbohydrate diets\(^{117,118,219}\). We did not find any changes in LDL or total cholesterol, which may be due to the stable body weight.

### 5.2.2 Dietary interventions

#### Compliance with the dietary interventions

To achieve the planned macronutrient compositions at a daily energy level of 2000 kcal, the study protocol estimated limits for intake of fat and carbohydrate in the LFHCC group and for intake of protein and carbohydrate in the HPMRC group. In this dietary intervention study the reported dietary intake showed that the intended intake in the intervention groups was not achieved with regard to carbohydrates. The reported intake of carbohydrates was too low in the LFHCC group and too high in the HPMRC group. Previous trials have also shown too low compliance with the dietary interventions\(^{115,117}\), with the greatest discrepancy from target level for carbohydrates\(^{118}\). Other trials have reported a good correspondence between reported intake and planned intake of macronutrients, but in these trials all food for the intervention groups were provided\(^{158,175,228}\). This suggests that it may be difficult for free-living subjects to comply with the macronutrient composition of specific diets. This was probably even harder for the participants included in the current study considering simultaneously smoking cessation.

Some of the participants in the LFHCC group reported that they thought it was difficult to choose sweet toppings like prim and jam when they were supposed to reduce their intake of added/refined sugars. Together with their attempt to reduce their intake of fat, this may have resulted in a greater use of ham and low-fat cheese than intended in this intervention group. This may be a reason for the low carbohydrate intake and high protein intake reported four weeks after smoking cessation in the LFHCC group. The HPMRC group managed to reach a reported intake of protein greater than 25 energy %, but they did not report a large enough reduction in carbohydrates. In accordance with this, they did not report an increased intake of fat, but rather a decrease in the intake of fat in grams, especially of saturated fat. This indicates that this group reduced the intake of sources to saturated fat, like whole fat dairy products and minced meat, in addition to increase the intake of unsaturated fat, like vegetable oils, fish and nuts. The fact that the HPMRC group reduced the reported intake of carbohydrate, but not the intake of fiber, suggests that these participants altered their food choices to more whole grain
products in addition to decreasing the total intake of food products rich in carbohydrate. They did, however, not reduce the intake of carbohydrate as much as intended, which may be due to increased cravings for sweet foods associated with smoking cessation. It seems therefore that the dietary composition has improved, and is more in accordance with the Norwegian recommendations, especially regarding to the distribution of fatty acids.

Since neither the LFHCC group nor the HPMRC group managed to implement all the intended dietary changes, we have no data on the effects of the planned intervention diets. Hence there is a possibility that both the planned intervention diets would have given greater effects on body weight, body composition or cardiovascular risk factors, or that there would have been a greater difference between the intervention diets when it comes to changes in one or several of the efficacy outcome measures. It does, however, seem like the two groups have eaten diets with significant different macronutrient composition, and that these intervention diets are different enough to compare the effects. One previous trial found a significant difference on body weight between two groups with 15 and 18 energy % from protein, respectively, and in the current study there was a greater difference in reported energy % from protein between the dietary intervention groups than this. Since all data based on dietary records only are modestly reliable in assessing the true dietary intake over time, for instance due to underreporting and undereating, it must be considered that the clinical results in this master thesis may be consequences of exposing the participants to different dietary advices, and not as a direct consequence of the estimated macronutrient consumption in the two dietary intervention groups.

**Correlations between changes in body weight and dietary changes**

Both intervention groups tended to have a weight loss during the first six weeks of the dietary intervention, and then started to gain some weight again. This is in accordance with previous findings, which have suggested that the greatest effect of dietary interventions often can be seen during the first period of time, most likely partly due to a decrease of dietary adherence with time. However, since no dietary records were conducted 12 weeks after smoking cessation here, it is not possible to say whether the dietary compliance decreased or not during the last eight weeks of treatment and follow-up.

Among the nonsmokers, there was a positive correlation between the change in intake of carbohydrate and the change in body weight four weeks after smoking cessation in the
HPMRC group. This suggests that those who followed the intervention diet best (i.e. reduced the carbohydrate intake the most) were those who had the best effect on changes in body weight (had the greatest reduction). This is in accordance with findings in a previous trial, where it was suggested that increased adherence was associated with greater weight loss, even though overall dietary adherence rates were low\textsuperscript{117}. Considering that no other correlations between the dietary changes and the change in body weight were observed in any of the two intervention groups, it is possible that the positive correlation between changes in intake of carbohydrate and changes in body weight in the HPMRC group was due to a larger variation in the changes in carbohydrate intake than in intake of protein or fat.

When including the reduced smokers there were positive correlations between the changes in body weight and the changes in intake of fat and protein in the HPMRC group. If the participants who had the greatest increase in intake of fat and protein not reduced the carbohydrate enough, this would lead to an increase in body weight. This might be the reason for the positive correlations seen in the HPMRC group. The absence of any other correlations may be due to a small sample size, especially among the nonsmokers.

It must also be considered that weight loss predominantly results from reduced energy intake, not the macronutrient composition, as previously suggested\textsuperscript{124}. This is also supported by the POUNDS LOST trial, which found no differences in weight loss between four energy-reduced diets with different macronutrient compositions\textsuperscript{229}. 
6 Conclusion

Our results show that intervention of combined smoking cessation and restricted diet can successfully prevent short-term post cessation weight gain. However, close follow-up with personal counseling and medication may be necessary to obtain good results. The prevention of post cessation weight gain may prevent unintended health consequences of smoking cessation such as increased blood pressure and increased blood glucose. This may be of great clinical significance. Even though we did not find any significant difference between diets containing high carbohydrate or high protein in efficacy of prevention weight gain after smoking cessation, a diet high in protein and reduced in carbohydrates may have a better effect on body composition and some cardiovascular risk factors, especially waist circumference and triglycerides, compared to a low fat diet high in carbohydrates. It should however be stressed that the analysis reported here should be interpreted with caution due to the low statistical power, and the fact that neither the high carbohydrate group nor the high protein group reached the intended macronutrient composition of their reported diets. In addition, any long-term effects of the two dietary interventions cannot be estimated.
7 Future perspectives

This master thesis only included 12 weeks of treatment and follow-up after smoking cessation, and it is therefore not possible to say anything about the long-term effect on body weight of the two intervention diets used in the current study. It is first of all necessary to look at the effects after 6 months, which will be accomplished in a later and larger study, before it is possible to recommend any of the two dietary interventions for prevention of long-term weight gain after smoking cessation. Results after 6 months may indicate more beneficial effects of one of the diets over the other, and if so, effects after one year or longer should be included in future research. It is also necessary to adjust for all possible interacting or confounding factors, such as age, socioeconomic status and physical activity.
References


171. Love SJ, Sheffer CE, Bursac Z, Prewitt TE, Krukowski RA, West DS. Offer of a weight management program to overweight and obese weight-concerned smokers


success of breast-cancer survivors. *Breast cancer research : BCR.* Jan 6


Appendices

Appendix 1: Advertisement

Appendix 2: Flow chart of the study

Appendix 3: Food diary

Appendix 4: Written information to the participants randomized to the low fat diet high in complex carbohydrates.

Appendix 5: Written information to the participants randomized to the high protein diet moderately reduced in carbohydrates.

Appendix 6: Recipes for the low fat diet high in complex carbohydrates.

Appendix 7: Recipes for the high protein diet moderately reduced in carbohydrates.

Appendix 8: Alternative proposals for a diet plan for the low fat diet high in complex carbohydrates.

Appendix 9: Alternative proposals for a diet plan for the high protein diet moderately reduced in carbohydrates.

Appendix 10: The lunches and snack meals offered in both intervention groups.

Appendix 11: Macronutrient composition of the three lunches and snack meals.

Appendix 12: Smoking diary

Appendix 13: Fagerström Test for Nicotine Dependence (Norwegian version).

Appendix 14: Averages used in the coding of the dietary records.

Appendix 15: Written information and informed consent.
Lyst til å slutte å røyke, men redd for vektoppgang?

Hvis du røyker mer enn 10 sigaretter daglig, er mellom 20 og 65 år, er overvektig (kroppsmasseindeks 25-40 kg/m²) og bor i Oslo og omegn, kan du sende en e-post med navn, adresse og mobil nummer til: mette.svendsen@uus.no.

Du kan også ringe på tlf. 23 01 66 53 eller sende faks til 22 11 99 75.

Du melder deg på studien nå, men oppstart av studien og røykeslutt er i januar.
**Appendix 2: Flow chart of the study**

<table>
<thead>
<tr>
<th>Weeks</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>I----</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>II--</td>
</tr>
<tr>
<td>S*</td>
<td>R*</td>
<td>SC*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Study end</td>
</tr>
<tr>
<td>Physical examination</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body composition</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist/hip-ratio</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory measurements</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine test</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting metabolic rate</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity registration</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO measurement</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Counseling for SC*</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Determination of SC*</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varenicline treatment</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking diary</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>(X)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTND*</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MNWS*</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>EBQ*</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary records (start)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietary counseling</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

* S: Screening, R: Randomization, SC: Smoking cessation, FTND: Fagerström Test for Nicotine Dependence, MNWS: Minnesota Nicotine Withdrawal Questionnaire, EBQ: Eating behavior questionnaire. Everything marked with blue is not included in the master thesis.
Appendix 3: Food diary (2 pages)

Dag/dato: ____________ Screeningnr: ____________

Informasjon

Som deltager i denne studien ved Avdeling for preventiv kardiologi ved Oslo universitetssykehus Ullevål skal du nå skrive ned alt det du spiser og drikker i 7 dager.


- Start med å skrive ned det første du drikker/utter i munnen den dagen registreringen starter. Skriv på ny linje for hver matvare. Spesifiser så nøyaktig du kan (f.eks: Gulost, lettere)
- Husk å føre opp om du bruker smør på brødskiven, olje til steking, dressing, saus etc.

Tips:

- Når du har veid noe en gang, kan denne vekten kan du brukes hvis du spiser det samme ved en annen anledning (for eksempel ved lik frokost hver dag).
- Dersom det du skal spise har emballasje hvor det står oppført vekt på maten/drikken fører du opp dette i skjemaet.
- Dersom det av ulike grunner er vanskelig å få veid, skriver du ca størrelse; 1 glass, stk, 1 skive, osv. Husk uansett å skrive så detaljert som mulig.
- Ha med deg skjema der du er slik at du fortløpende kan føre opp;– lett å glemme underveis i løpet av dagen. Husk å føre opp drikke.

**NB:** Bein, skall osv, veies for seg etterpå og trekkes fra vekten på den totale matvaren. Dersom dette blir vanskelig- husk å notere at vekten på matvaren inkluderer bein osv.
Dag/dato: __________________  Screeningnr: __________________

<table>
<thead>
<tr>
<th>Tidspunkt</th>
<th>Spist/drukket</th>
<th>Mengde</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4: Information about the low fat diet high in complex carbohydrates (3 pages).

Til deg på lav-fett kost

Bakgrunn for lav-fettkosten
De offentlige anbefalinger sier mindre enn 30 prosent av energien vi får fra maten vi spiser skal komme fra fett. Siden fett inneholder mer enn dobbelt så mye energi per gram sammenlignet med karbohydrater og proteiner vil man ved å redusere på mengden fett i kosten lettere kunne redusere det totale inntaket av energi (kilokalorier). Videre er det anbefalt at rundt 50-60 prosent av den energien vi spiser skal komme fra karbohydrat, og da fortrinnsvis fra grove kornprodukter, frukt og grønnsaker. Dette er matvarer som bidrar til å øke mettheten, samtidig som de bidrar til et kosthold som inneholder mindre energi.

Hva innebærer denne lavfett kosten?
I denne kosten vil det fokuseres på å redusere inntaket av fett.

Først og fremst vil du reducere:

- Mettet fettet fra fete meieriprodukter (for eksempel ost, fløte, rømme)
- Smøer på brødet (erstatt med lettre varianter)
- Sjokolade, kakker og snacks, samt fra friterte matvarer (for eksempel potetchips, pommes frites og panert fisk)

Det umettede fettet fra olje, myk margarin, majones, avocado, oliven og nøtter, trenger vi i kosten. Hvis du bruker mer enn 1 ss av disse matvarene i måltidene vil du bli bedt om å redusere mengden til ca 1 ts per måltid. Fet fisk inneholder også fett som kroppen trenger å få tilført gjennom maten vi spiser. I denne kosten anbefaler vi å spise fet fisk som pålegg og til middag, men hvis du spiser doble porsjoner må du reducere litt på porjsjonsstørrelsen.

En annen god måte å redusere inntaket av fett på er ved å sørge for at det er mye grønnsaker og frukt i kosten. Da spiser du deg mett på matvarer som inneholder veldig lite fett. Sørg derfor for at det er rikelig med grønnsaker både til middag og andre måltider, både som tillegg i måltidet, som snacks og som pålegg.


Matvarer som inneholder mye fiber gir mettethetsfølelse. Derfor anbefaler vi grove komprodukter. Vi anbefaler deg å du velger det groveste brødet slik som merket under viser.
Til middag er det fint å velge fullkorns pasta, grov naturreis eller andre gryn som bulgur. Kok gjerne opp store porsjoner av dette, og bruk i salater til lunsj.

Du deltar nå i en studie der vi skal undersøke forskjellen mellom to ulike dietter. Diettene må være så ulike som mulig. Siden den andre kosten inneholder mye protein, er det viktig at du begrenser proteininnmatet så mye som mulig i denne perioden du er med i studien. Proteiner finnes i de fleste matvarer, men i ulik grad. Matvarer som kjøtt, kylling, fisk, skalldyr og egg, og pålegg av kjøtt og fisk inneholder mye proteiner. Siden denne kosten skal ha et moderat innhold av proteiner er det et tips å spare store proteinkilder til middagsmåltidet.

Middagsmåltidet bør bestå av godt med grønnsaker. Ta utgangspunkt i at halve tallerkenen din skal være dekket med grønnsaker, og bruk gjerne flere forskjellige typer samtidig. Lag gjerne store porsjoner med middag, slik at du kan bruke som lunsj eller middag dagen etter. For forslag til middags- og lunsjretter se de vedlagte oppskriftene.

Gode pålegg alternativer kan være lettsyltetøy, mager smøreost med ekstra grønnsaker på toppen, lettere brunost, mager prim, banan. Siden kosten ikke skal inneholde for mye proteiner er det viktig at du ikke spiser for mye proteinrike pålegg hvis du ønsker kjøtt eller fisk til middagen. Pålegg som kokt skinke, reker, cottage cheese, mager leverpostei og gulost er rike på proteiner og bør derfor ikke spises på mer enn 1-2 skiver per dag.

**Kaffe**

Etter røykeslutt vil kroppen tåle kaffe dårligere enn den gjorde mens du røkte. Det betyr at du kan oppleve symptomer som røstløshet, søvnløshet og konsentrationsvansker.

Du kan også få problemer som diaré og kvalme om du drikker for mye kaffe. Det vil derfor være en fordel for deg om du reducerer innmatet av kaffe, og maksimalt drikker 2-3 kopper per dag.

**Tips:**

- Planlegg gjerne flere dager frem i tid, og sett opp handleliste når du skal i butikken.
- Bruk grønnsaker til alle måltider, som pålegg og snacks og ved siden av matpakke.
- Du vil få oppskrift på lunsmåltidene som deles ut i uken etter røykeslutt. Bruk gjerne disse som lunsj også etter den første uken.
- Les varedeklarasjoner, og pass på innhold av fett. Vi anbefaler kjøttprodukter med mindre enn 10% fett og ost med mindre enn 20% fett.

**Appendix 5:** Information about the high protein diet moderately reduced in carbohydrates (3 pages).

**Til deg på høyprotein kost**

**Bakgrunn for høyprotein kosten**
Proteiner er en viktig bestanddel i maten vi spiser, sammen med karbohydrater og fett. Bakgrunn for denne kosten er studier som har vist at økt inntak av protein kan være gunstig i forhold til vektsregulering, knyttet til en rekke fysiologiske mekanismer.

**Hva innebærer en høyprotein kost?**
Høyprotein kost innebærer at du øker inntaket av fisk, skalldyr, renn kjøtt, kylling, egg og magre meieriprodukter til alle måltider. **Ved å:**

- Spise større porsjon med renn kjøtt (for eksempel filé av kylling, kalkun og svin, samt bifkjet) til middag og lunsj.
- Velge proteinrike pålegg som skalldyr, skinke, roastbiff, egg og fisk (tunfisk, makrell i tomat, fiskepudding, laksepostei).
- Velge lettere gulost, lettere smøreoster og cottage cheese.
- Velge proteinrik yoghurt som Skyr og Yoplait yoghurt, 0,1%.

Når du spiser mer av en matvaregruppe, vil du måtte spise mindre av en annen når du samtidig ønsker å gå ned i vekt. I denne studien skal du **spise mindre av karbohydratrike matvarer som inneholder mye sukker, samt brød, kornprodukter, ris, pasta og poteter.**

- Redusere tidligere mengde ris/potet til middag.
- Redusere antall brødskiver, spise mer pålegg.
- Forsøke å unngå sokerrike matvarer som is, kaker, boller, muffins, kjeks, sjokolade og godteri.
- Velg vann, farris eller kunstig søtet drikke i stedet for å drikke sukkerholdig brus og saft, nektar og juice.

Når det gjelder fett, anbefaler vi at du først og fremst spiser matvarer som inneholder det fettet kroppen trenger å få tilført gjennom maten du spiser. Derfor kan du ha opp til 1 ss fett fra olje, majones, nøtter og oliven i hvert måltid.

<table>
<thead>
<tr>
<th>Øk inntak</th>
<th>Reduser inntak</th>
<th>Unngå</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Magre proteinrike</strong></td>
<td><strong>Bred</strong></td>
<td>Søte drikker: brus, saft, nektar og juice</td>
</tr>
<tr>
<td>pålegg/hovedingrediens i salater:</td>
<td>Pasta, ris, poteter og couscous*</td>
<td>Is, kaker, boller, muffins, kjeks</td>
</tr>
<tr>
<td>○ Kjøtt guler</td>
<td>Kornblanding</td>
<td>Sjokolade og godteri</td>
</tr>
<tr>
<td>○ Kalkun pålegg, roastbiff</td>
<td>Frukt*</td>
<td>Pålegg med mye sukker</td>
</tr>
<tr>
<td>○ Egg</td>
<td>Kaffe</td>
<td>(syltetø, honning, sjokolade pålegg, brunost, prim)</td>
</tr>
<tr>
<td>○ Reker, krabbe,</td>
<td></td>
<td>Potetchips og pommes frites</td>
</tr>
</tbody>
</table>

*Se karbohydratkvote under.*
Når det gjelder grønnsaker kan disse spises i den mengden du orker etter at du har spist anbefalt mengde proteinrike matvarer.

**Kaffe**

**Karbohydratkvote**
I uten med matutdeling vil lunsj og snacks måltidet gjennomsnittlig innholde litt over 10 g karbohydrat. Total må du redusere karbohydratinnøkkelen ditt til rundt 110 g karbohydrat per dag for å få spist nok protein uten å samtidig gå opp i vekt. Listen under viser brød og pasta/ris alternativer som naturlig innholder mindre karbohydrater og som er gode valg på høyprotein kost. Mengden karbohydrat må likevel begrenses; Finn ut når du har mest behov for slike matvarer, og ha kontroll på hvor mye du kan spise i løpet av en dag

<table>
<thead>
<tr>
<th>Matvare</th>
<th>Mengde</th>
<th>Karbohydrat (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brødskive/ knekkebrød</td>
<td>1 brødske/2 knekkebrød</td>
<td>15-20g</td>
</tr>
<tr>
<td>Tørr pasta/ris</td>
<td>50g</td>
<td>35g</td>
</tr>
<tr>
<td>Grønnsaker</td>
<td>150g</td>
<td>5-15g</td>
</tr>
<tr>
<td>Frukt</td>
<td>150g</td>
<td>15-25</td>
</tr>
<tr>
<td>Sjokolade</td>
<td>100g</td>
<td>50-60</td>
</tr>
<tr>
<td>Potetgull</td>
<td>100g</td>
<td>25-30</td>
</tr>
</tbody>
</table>

*Brod: Havrebrød, 100% sammet, pumpenrikkelbrød. Se etter brødkvalmærking
*Knekkebrød: Fiber pluss, husmann, rugspør

Matvarer som inneholder mye fiber gir mettadvækkelse. Derfor anbefaler vi grove kornprodukter. Vi anbefaler deg at du velger det groveste brødet slik som merket under viser.

**Tips**
- Ha gjerne dobbelt lag med proteinrikt pålegg og skjær tynne brødskiver
- Middagsmåltidet er det måltidet der er enklest å spise størst mengde protein; bruk lunsj og middagsoppskrifter utdelt som utgangspunkt.
- Ha som en regel at halvparten av talleren skal være dekket av kjøtt/fisk. Spis deretter grønnsaker til du er forsynt. Bruk middagsrester av kjøtt og fisk til lunsj dagen etter.
- Stek kjøtt/fisk i folie i ovnen så beholder det saftighet og blir lettere å spise
- Bruk krydder, urter og sauser (se oppskrifter) slik at kjøttet og fisken blir mer smakfullt
- Lag måltidssarter og gjør forberedelser. Planlegg dagen med tanke hva du skal spise, når du skal spise og om du trenger å ta med deg mat/matpakke
- Sett opp handleliste før du går i butikken
**Generelle tiltak ved røykesug**  
Ved røykeslutt er det viktig å ha alternative ting å gjøre når suget melder seg:

- Ring en telefon; snakk  
- Gjør noe: Les, gå en tur  
- Gjør avspенноningsøvelser  
- Dersom du må putte noe i munnen, sør for å ha gode alternativer tilgjengelig:

*Forlag til snacks*

<table>
<thead>
<tr>
<th>Snacks når du er hjemme:</th>
<th>Snacks på farten</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 fiberpluss med lett-gulost/egnet pålegg</td>
<td>Skyr, yoghurt</td>
</tr>
<tr>
<td>2 husmann med egnet pålegg</td>
<td>Kyllingvinger</td>
</tr>
<tr>
<td>Knekkebrød med lett-gulost og skinke</td>
<td></td>
</tr>
<tr>
<td>Rutsprø med egnet pålegg (se over)</td>
<td>Snacksposer med friske grønnsaker:</td>
</tr>
<tr>
<td>Rett i koppen med kocht egg</td>
<td>- <em>cherrytomater</em></td>
</tr>
<tr>
<td>Roastbeef, kocht skinke</td>
<td>- <em>babygulrøtter</em></td>
</tr>
<tr>
<td>Reker (med avocado og majones)</td>
<td>- <em>sukkereter</em></td>
</tr>
</tbody>
</table>
Forslag til oppskrifter, lavfettkost

Lunchoppskrifter:

**Pastasalat med skinke:**

Isbergsalat, agurk, vårløk og mais 150g
Fullkornspasta 150 g
Kokt skinke 50 g
Grønn pesto 15g/1ss

*Skjer skinken i strimer*
*Bland med salat og rør pestoen inn i den kokte og avkjølte pastaen.*

**Kylling i rataouille:**

Fullkornspasta 100 g
Kyllingfilet 50g

*Ratatouille av:
Håkede tomater 50g
Løk 25g
Kikerter 50 g
Paprika 25g
Squash 50g

*Stek kyllingen i strimer og la surre sammen med grønnsakene i noen minutter. Tilsett krydder etter smak.*

**Roastbeef med wraps**

Fullkornswrap 80 g
Bønner 50 g
Roastbeef 50 g
Sukkererter
Salat
Tomater 75g
Dressing, fettredusert, 15 g/1ss

*Skjær tomatene og sukkerertene i biter, og salaten i strimer. Varm opp wraps og legg på kjøtt, bønner og grønnsaker sammen med dressing.*
Bulgursalat

Bulgur 140 g
Fetaost 30 g
Salat 100 g
Tomat 50 g
Oliven 20 g
Olje og sitrondressing 1 ss.

Kok opp bulgur eller spelt helkorn og la dette avkjøles. Skjær fetaosten i terninger og kutt opp salaten. Bland med oliven og bulgur og hell over dressingen.

Curry med svin

Mager svinefilet 50 g
Bønner 50 g
Brun ris 100 g
Løk 50 g
Erter 50 g
Rosiner 10 g
Ananas 50 g
Olivenolje 5 g
Krydder

Kutt kjøttet i strimler og stek i oljen.
Skjær løken i hiter og la surre sammen med kjøttet. Ha i erter, rosiner, bønner og ananas mot slutten.

- Bruk middagsrester fra dagen før
- Kok gjerne opp store porsjoner med pasta, bulgur, helkorn etc og bruk dette til lunnsj dagen etter
- Bruk gjerne lunjsalternativene som middag
**Kyllingfilet på grønnsakseng**

(2 porsjoner)

2 kyllingfileter  
1/2 rød løk  
100 g purre  
1 rød chili  
2 tomater  
1/2 grønn squash  
1/2 aubergine  
1 ss olivenolje  
1 ss frisk hakket rosmarin

I stekeovn ved 180 °C

Hell over litt ekstra vann m/buljong, og bruk dette som saus.

Serveres sammen med grov ris eller bulgur, og kokt brokkoli.
Ovnsbakt kyllingfilet m/sennep og tomat
(2 persjoner)

2 kyllingfileter
1 ss dijonsemenp
4 tomater
salt og kvernet pepper
1 ss griljermel/vanlig mel
1/2 ss mandelflak


Serveres med grov ris, fullkornspasta, spelt helkorn eller bulgur.

Kylling- og grønnsakwok
(2 persjoner)

2 kyllingfileter, strimlet
1 ss olje
400 g blandede grønnsaker (paprika, vårlokk, brokkoli, gulerøt)
1/2 rød chili, finhakket
1 hvitløk, finhakket
1/2 tommerstør bit ingefær, finhakket
1 ss soyasaus
Frisk koriander eller vårlokk, hakket

Varm litt av oljen i en wokpanne eller en dyp stekepanne og stek kyllingbitene på høy temperatur til de er nesten gjennomstekt.
Ta dem ut av pannen og hold dem varme. Varm opp pannen igjen med resten av oljen og frems grønnsakene raskt sammen med chili, hvitløk, ingefær og cashewnøtter. Tilsett kjøtt og soyasaus, og stek det hele til det er gjennomvarmt. Dryss over hakkede urter.
**Kyllingfilet med hvitvin**  
(1 porsjon)

1 kyllingfilet  
2-3 champignoner  
½ løk  
litt hvitvin

Legg kyllingfilet sammen med sopp og løk i aluminiumsfolie. Dryss over salt og pepper, og hell over litt hvitvin. Stekes på 230 grader i cirka 30 minutter.  

**Steinbifflet med hvitvin**  
(1 porsjon)

1 steinbifflet, ca 130 g  
2-3 champignoner  
2 små solterkede tomater  
½ løk  
litt hvitvin

Samme oppskriften som for kyllingfilet :)

Snitt opp de tørre tomatene og legg i bunnen. Legg fiskens sammen med sopp og løk i aluminiumsfolien oppå tomatene. Dryss over salt og pepper, og hell over litt hvitvin. Stekes på 230 grader i cirka 30 minutter.  

Smaker godt sammen med kokt brokkoli, grov ris eller bulgur.
Ovnsbakt fisk
Legg laks, ørret eller steinbitfilet i folie.
Smør over pesto eller olje med krykker.

Pakk sammen og stek i ovnen. Fileter ca 20 min på 200 grader. Prøv deg frem.

Ha gjerne også tomater, løk, sopp, paprika etc i folien, og kok opp gulrøtter og brokkoli ved siden av. Serveres sammen med kokte poteter eller grov ris.
Appendix 7: Recipes for the high protein diet moderately reduced in carbohydrates (4 pages).

Forslag til oppskrifter, høyproteinkost

Lunchoppskrifter:

Ost og skinkesalat:
Kokt skinke, 125g. Lettgulost, 50g. Isbergsalat 100g. Grønn pesto, 30g
-Skjær skinken i strioler og riv osten. Bland med salat og bruk pesto som dressing.

Kylling i rataouille:
Kyllingsfilet, 175g. Hakkede tomater, 50g. Løk, 25g. Paprika, 25g. Squash, 50g. Olivenolje, 1 ss.
-Stek kyllingen i strioler med oljen og la suerre sammen med grønnsakene i noen minutter. Tilsett krydder etter smak.

Roastbeef og grønnsaker
Roastbeef, 175g. Sukkererter, Salat, Tomater. Olivenolje, 1 ss.
-Skjær tomatene i biter og skjær salaten i strioler. Bland med kjøttet og vend inn oljen.
Tunfisksalat

Tunfisk, 135g. Fetaost, 50g. Salat, 100g. Oliven, 20g. Olje og sitrondressing, 30g.

-Skjær opp feta i terninger og kutt opp salaten. Bland med oliven og tunfisk og hell over dressingen.

Curry med svin

Mager svinfilet, 175 g. Løk, 50g. Erter, 50g. Melk, 50g. Olje, 1ss.

-Kutt kjøttet i strimler og stek i oljen. Skjær løken i biter og la surre sammen med kjøttet og melken. Ha i erter mot slutten.

Middagsoppskrifter (til 2 pers):

Kyllingfilet på grønnsaksseng

400g kyllingfilet (4 små kyllingfileter) 
1 rød løk 
1 rød chili 
3 tomater 
1 grønn squash 
1/2 aubergine 
4 ss olivenolje 
1 ss frisk hakket rosmarin

Del grønnsakene i passe biter og legg dem i en ildfast form sammen med kyllingfiletene. Hell over olje og dryss på krydder, salt og pepper. Stek retten 15-20 minutter, 180 °C
Ovnshakte kyllingfileter med sennep og tomat

400g kyllingfilet
2 ss dijonsemenep
2 tomater
salt og kvernet pepper
1 ss griljermel/vanlig mel
1 ss mandelflak


Kylling- og grønnsakwok

400g kyllingfileter, strimlet (eller 1 pakke strimlet kyllingkjøtt)
2 ss solsikkcolje
200 g blandede grønnsaker (paprika, vårlokk, brokkoli, gulrot,
1 rød chili, finhakket
2 hvitløk, finhakket
1 tommelstor bit ingefær, finhakket
50 g cashewnøtter
1 ss soyaasaus
1 ½ dl ferdig wok-saus
Frisk koriander eller vårlokk, hakket

Varm 1 ss av oljen i en wokpanne eller en dyp stekepanne og stek kyllingbitene på høy temperatur til de er nesten gjennomstekt. Ta dem ut av panen og hold dem varme. Varm opp panen igjen med resten av oljen og fres grønnsakene raskt sammen med chili, hvitlek, ingefær og cashewnøtter. Tilsett kjøttet, sojaasaus og wok-sausen, og stek det hele til det er gjennomvarmt. Dryss over hakked urter.
**Laks i folie**

Legg laks, ørret eller steinbitfilet i folie. Smør over pesto eller olje med krydder/ha i sopp, grønnsaker, urter osv.

Pakk sammen og stek i ovnen. Fileter ca 20 min på 200 grader. Prøv deg frem.

---

**Omelett med ost og skinke**

4 egg
4ss vann
litt salt
litt smør til steking

Visp sammen egg, vann og salt og hell røren i en stekepanne. Pannen må være så varm at en smørklutt friser når den slippes i. Trekk røren inn mot midten. Omeletten vil være ferdig på noen minutter. Hakk opp skinke og gulost og legg på den ene halvdelen, den andre halvdelen brettes over
Appendix 8: Alternative proposals for a diet plan for the low fat diet high in complex carbohydrates (2 pages).

Alternative forslag til kostplan fettredusert diett

Frokost-alternativer (300-400 kcal)
1. Grovbønd, 2 skiver (ca 120 g), med en banan og lettsyltetøy (2 ss)
2. Grovbønd, 2 skiver (ca 120 g), en skive med lettsyltetøy (2 ss) og en skive med lettere brunost (2 høvelskiver)
3. Grovt knekkebrød (3 stk, grovt, type Husman), tynt lag med lettmargarin. Et knekkebrød med magerost (bacon, skinke etc), et med lettsyltetøy (1 ss), et med kakt skinke (1 skive). Pynt med tomat og agurk
4. Kornblanding (feks 4korn, 1,5 dl) med 2 dl lettyoghurt

Lunsj-alternativer (250-500 kcal)
- Grovbønd, 2 skiver (ca 120 g), en med makrell-i-tomat (25 g) og agurk, og en med lettere brunost (2 skiver)
- Grovt rundstykke (ca 80 g), med lettmargarin og kakt skinke (2 skiver). Salat ved siden av, med isbergsalat, tomat, agurk og mais, og litt dressing.
- Rett-i-koppen-suppe med en skive grovbønd med lettmargarin og kakt skinke
- Alternativer fra oppskriftsheftet

Middags-alternativer
- Kyllingfilet (150 g) stekt i olje (10 g), med kakt ris (150 g) og grønnsaker
- Laksefilet (125 g) stekt i olje (10 g), med kakt potet (150 g) og grønnsaker
- Pasta (150 g kakt), med tomataus: karbonadedeg (100 g) stekt i olje (10 g), hermetiske tomater (2 dl), lak og sopp
- Fiskeburger (ca 150 g), stekt i olivenolje (10 g) med lak og sopp, med grønnsaker og kakt potet (150 g)

Mellommåltider under 100 kcal
- 200 g frukt
- en stor pose knaskerøtter (300 g)
- 1 beger sukkererter (150 g)
- Rett-i-koppen suppe (tomat, kylling etc)
- Salat med pasta (40 g), uten dressing
- 1 knekkebrød med pålegg (feks 1 ss lettsyltetøy, ½ banan, magerost, lettere prim)

Mellommåltider under 200 kcal
- Lettere Go’ morgen/YT
- 2 grove knekkebrød med lettere brunost (2 skiver) og kakt skinke (2 skiver)
- 1 knekkebrød med banan og lettsyltetøy
- 1 eple i biter med 1,5 dl lettere vaniljeyoghurt over

Drikke, ca 100 kcal
- Skummetmelk (2 dl)
- Appelsinjuice (2 dl)
- Sukkerholdig brus (2 dl)
- 1 glass vin (1,5 dl)
- 1 flaske pils (3,3 dl)
- Brennevin, 4 cl
Energitette måltider (250-500 kcal)

- 1 liten hamburger
- 1 pølse med pølsebrød
- 1 stor hvetebolle
- 1 skolebrød
- 1 wienerbrød
- 1 muffins
- 1 vaflerplate med syltetøy
- 1 iskrem i kjeks
- 1 liten sjokolade
- 4 salte kjeks med ost
- 1 pakke nudler
- ½ liter sjokolademelk
- 1 flaske vin
- 1 liter brus

Energitette måltider (1000-1500 kcal)

- 1 pizza (580 g)
- 1 stor hamburger med pommes frites
- 1 pose boller
- 1 pakke kjeks
- 1 stor plate (200 g) sjokolade
- 1 pose (180 g) peanøtter
- 1 pakke (250 g) saltstenger
- 1 pose (300 g) smågodt
- 1 six-pack pils

Energitette måltider (ca 2000 kcal)

- 2 liter is
- 1 stor pose potetchips
- 1 eske konfekt
Appendix 9: Alternative proposals for a diet plan for the high protein diet moderately reduced in carbohydrates (2 pages).

Alternative forslag til kostplan Proteinrik diett

Frokost alternativ (300-400 kcal)

- To knekkebrød med myk lettmargin; ett med to skiver med lettere gulost (40g), ett med to skiver med kalkunpallegg, pluss salatgrønnsaker ved behov.
- En skive grovt brød til stekt egg, røkt skinke, tomater og oliven (15g).
- To knekkebrød med myk lettmargin; ett med smøreost, og ett medrostbiff og majones (lettere), pluss salatgrønnsaker.

Lunsjalternativer (300-400 kcal)

- Et grovt rundstykke med myk lettmargin. Salat med 100g kyllingfilet/tunfisk/rostabiff. Dressing, 1ss.
- 3 knekkebrød med myk lettmargin; ett med makrell i tomat (30g), ett med lettere gulost (3 skiver), ett med kokt skinke (2 skiver) pluss paprika/agurk/salat
- En skive grovt brød med lettere margarin og ett kokt egg. Ett knekkebrød med rostabiff (50g) og majones (lettere)
- Ett grovt rundstykke med lettere margarin. Salat med reker (100g) og avocado (50g) og 1 ss lettere majones.
- Omelett (150g) med 2 skiver lettere gulost, 2 skiver kokt skinke og salat ved siden av.
- Alternativer fra oppskrifthefte.

Middagsalternativer (400-500 kcal)

- Kyllingfilet (200g = 2 store fileter) stekt i olje (maks 1ss) og wokkede grønnsaker (løk, paprika, sukkererter)
- Laks 150g/ hvitfisk (200g) stekt i olje (maks 1ss) og kokte grønnsaker (blomkål, brokkoli, guorreter)
- Karbonadedeig (200g) i tomatasus + salat.
- Indrefilet/rent kjøtt stekt i smør (1ss) med tyttebær (1ss) og 1 ss kesam og egne grønnsaker

Mellommåltider < 200 kcal

- 1 knekkebrød med roastbeef 50g og majones 10g
- 2 knekkebrød med ost og skinke; lettere gulost (1 skive) og kokt skinke (1 skive)
- ½ avocado med 100g reker og 10 g lettere majones
- Knekkebrød med røkelaks (30g) lettere majones og grov sennep (20g)

Mellommåltider < 100 kcal

- Skyr yoghurt
- Yoghurt Yoplait, 0,1%
- Knekkebrød med cottage cheese, 20g og lettsyltetøy 10g
- 1 pose knaskeglørretter
- Sukkererter (200g)
Drikke ca 100 kcal
• 1 glass (2 dl) skummet melk
• 1 glass (2 dl) appelsinjuice
• 1 glass (2 dl) sukkerholdig brus
• 1 flaske (3.3) pils
• 1 glass (1.5 dl) vin
• 4 cl brennevin

Energitette måltider 250-500 kcal
• 1 liten hamburger
• 1 pølse med pølsebrød
• 1 stor hvetebolle
• 1 skolebrød
• 1 wienerbrød
• 1 muffins
• 1 vaffelplate med syltetøy
• 1 iskrem i kjeks
• 1 liten sjokolade
• 4 salte kjeks med ost
• 1 pakke nudler
• 0.5 liter sjokolademelk
• 1 flaske vin
• 1 liter brus

Energitette måltider 1000-1500 kcal
• 1 pizza (580g)
• 1 stor hamburger med pommes frites
• 1 pose bolier
• 1 pakke kjeks
• 1 stor plate (200g) sjokolade
• 1 pose (180g) peanøtter
• 1 pakke (250g) saltstenger
• 1 pose smågodt (300g)
• 1 "6-pack" pils

Energitette måltider ca 2000 kcal
• 2 liter is
• 1 stor pose potetchips
• 1 eske konfekt
**Appendix 10**: The lunches and snack meals offered in both dietary intervention groups.

<table>
<thead>
<tr>
<th></th>
<th>Low fat diet high in complex carbohydrates</th>
<th>High protein diet moderately reduced in carbohydrates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lunch 1</strong></td>
<td>Iceberg salad, cucumber spring onion and maize (150 g) with pasta (150 g) and ham (50 g). Salad dressing (15 g).</td>
<td>Ham (125 g) and low fat cheese (50 g) with iceberg salad (100 g). Salad dressing (30 g).</td>
</tr>
<tr>
<td><strong>Lunch 2</strong></td>
<td>Whole meal pasta (100 g), and ratatouille (tomato sauce 50 g, garbanzo beans 50 g, onions 50, squash 50, peppers 50 g and chicken (50 g).</td>
<td>Chicken (175 g) and ratatouille (tomato sauce 50 g, onion 25 g, peppers (25 g) squash (50 g). Olive oil (15g)</td>
</tr>
<tr>
<td><strong>Lunch 3</strong></td>
<td>Whole meal wrap (80 g) with beans (50 g) and beef (50 g) with sugar snaps (75 g) and tomatoes (75 g). Low fat dressing (15 g).</td>
<td>Beef (175 g) with sugar snaps (50 g) and tomatoes (50 g). Olive oil (15 g).</td>
</tr>
<tr>
<td><strong>Snack meal 1</strong></td>
<td>YT yoghurt including müsli (25 g)</td>
<td>SKYR yoghurt and sun flower seeds (20 g)</td>
</tr>
<tr>
<td><strong>Snack meal 2</strong></td>
<td>Go´morgen yoghurt including müsli (25 g)</td>
<td>SKYR yoghurt and sun flower seeds (30 g)</td>
</tr>
</tbody>
</table>
Appendix 11: Macronutrient composition of the three lunches and snack meals.

<table>
<thead>
<tr>
<th></th>
<th>Low fat diet high in complex carbohydrates</th>
<th>High protein diet moderately reduced in carbohydrate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Energy, kcal</td>
<td>Protein, g</td>
</tr>
<tr>
<td>Lunch 1</td>
<td>405</td>
<td>18</td>
</tr>
<tr>
<td>Lunch 2</td>
<td>350</td>
<td>22</td>
</tr>
<tr>
<td>Lunch 3</td>
<td>375</td>
<td>23</td>
</tr>
<tr>
<td>Snack meal 1*</td>
<td>204</td>
<td>11</td>
</tr>
<tr>
<td>Snack meal 2*</td>
<td>260</td>
<td>9</td>
</tr>
</tbody>
</table>
**Appendix 12: Smoking diary**

<table>
<thead>
<tr>
<th>Dag 1</th>
<th>Dato</th>
<th>Hvor mange sigaretter har du røkt de siste 24 timer?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dag 2</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 3</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 4</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 5</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 6</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 7</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 8</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 9</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 10</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 11</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 12</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 13</td>
<td>Dato</td>
<td></td>
</tr>
<tr>
<td>Dag 14</td>
<td>Dato</td>
<td></td>
</tr>
</tbody>
</table>
**Appendix 13: Fagerström test for nicotine dependence**

1. How long after you wake do you smoke your first cigarette?
   - In less than 5 minutes: 3
   - 6-30 minutes: 2
   - 31-60 minutes: 1
   - After 60 minutes: 0

2. Is it difficult for you to not smoke in places where smoking is prohibited, for example at a cinema or on a plane?
   - Yes: 1
   - No: 0

3. Which cigarette do you least want to give up?
   - First thing in the morning: 1
   - One of the others: 0

4. How many cigarettes do you smoke per day?
   - 10 or less: 0
   - 11-20: 1
   - 21-30: 2
   - 30 or more: 3

5. Do you smoke more in the first hour after waking than the rest of the day?
   - Yes: 1
   - No: 0

Do you feel sick even though you are the only one smoking the majority of the day?
   - Yes: 1
   - No: 0
**Appendix 14: Averages used in the coding of the dietary records (2 pages).**

<table>
<thead>
<tr>
<th>Vegetable/fruit</th>
<th>Small</th>
<th>Medium</th>
<th>Large</th>
<th>Edible percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edible part (whole fruit/vegetable)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apple</td>
<td>174g (190g)</td>
<td></td>
<td></td>
<td>92</td>
</tr>
<tr>
<td>Avocado</td>
<td>104g (146g)</td>
<td>127g (191g)</td>
<td></td>
<td>69</td>
</tr>
<tr>
<td>Baby corn</td>
<td>8g</td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Banana</td>
<td>83g (134g)</td>
<td>131g (213g)</td>
<td>177g (291g)</td>
<td>61</td>
</tr>
<tr>
<td>Bell pepper</td>
<td>92g (99g)</td>
<td>168g (188g)</td>
<td>203g (233g)</td>
<td>90</td>
</tr>
<tr>
<td>Broccoli (without stem)</td>
<td></td>
<td>298g</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Carrot</td>
<td>42g (56g)</td>
<td>85g (110g)</td>
<td>122g (153g)</td>
<td>77</td>
</tr>
<tr>
<td>Cauliflower</td>
<td></td>
<td>595g</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Celery, one stalk</td>
<td></td>
<td>50g</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Champignon</td>
<td></td>
<td>46g</td>
<td>68g</td>
<td>100</td>
</tr>
<tr>
<td>Clementine</td>
<td>52g (64g)</td>
<td>80g (105g)</td>
<td>98g (120g)</td>
<td>80</td>
</tr>
<tr>
<td>Corn cob</td>
<td>181g (279g)</td>
<td></td>
<td></td>
<td>65</td>
</tr>
<tr>
<td>Cucumber</td>
<td></td>
<td>382g</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Grapefruit</td>
<td>323g (456g)</td>
<td></td>
<td></td>
<td>71</td>
</tr>
<tr>
<td>Grapes, seedless</td>
<td></td>
<td>5g</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Iceberg lettuce</td>
<td>463g (489g)</td>
<td></td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>Kiwi</td>
<td>58g (75g)</td>
<td>83g (114g)</td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>Nectarine</td>
<td>146g (157g)</td>
<td></td>
<td></td>
<td>93</td>
</tr>
<tr>
<td>Onion, red</td>
<td>158g (165g)</td>
<td></td>
<td></td>
<td>96</td>
</tr>
<tr>
<td>Onion, yellow</td>
<td>177g (185g)</td>
<td></td>
<td></td>
<td>96</td>
</tr>
<tr>
<td>Orange</td>
<td>165g (242g)</td>
<td>190g (311g)</td>
<td>234g (365g)</td>
<td>64</td>
</tr>
<tr>
<td>Pear</td>
<td>195g (203g)</td>
<td></td>
<td></td>
<td>96</td>
</tr>
<tr>
<td>Plum</td>
<td>79g (81g)</td>
<td></td>
<td></td>
<td>98</td>
</tr>
<tr>
<td>Radish</td>
<td>26g</td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Raspberries</td>
<td></td>
<td>5g</td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Squash</td>
<td>375g (393g)</td>
<td></td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>Spring onion</td>
<td>18g (19g)</td>
<td></td>
<td></td>
<td>95</td>
</tr>
<tr>
<td>Sugar snaps</td>
<td>4g</td>
<td></td>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Tomato,</td>
<td></td>
<td>95g</td>
<td>112g</td>
<td>166g</td>
</tr>
<tr>
<td>Tomato, beef</td>
<td></td>
<td>203g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tomato, cherry</td>
<td>11g</td>
<td>16g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tomato, taste-</td>
<td></td>
<td>40g</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Meat</th>
<th>Grilled chicken</th>
<th>Chicken (leg)</th>
<th>Chicken (wing)</th>
<th>Pork chop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (1 piece)</td>
<td>695 g</td>
<td>173 g</td>
<td>17 g</td>
<td>158 g</td>
</tr>
<tr>
<td>Bone/cartilage</td>
<td>164 g</td>
<td>40 g</td>
<td>5 g</td>
<td>41.5 g</td>
</tr>
<tr>
<td>Skin/fat rim</td>
<td>39 g</td>
<td>27 g</td>
<td>4 g</td>
<td>54 g</td>
</tr>
<tr>
<td>Meat</td>
<td>492 g (~71%)</td>
<td>106 g (~61%)</td>
<td>8 g (~47%)</td>
<td>62.5 g (~40%)</td>
</tr>
<tr>
<td>Total edible portion</td>
<td>531 g (~76%)</td>
<td>133 g (~77%)</td>
<td>12 g (~71%)</td>
<td>116.5 g (~74%)</td>
</tr>
</tbody>
</table>
Weight losses during preparation of meat:

- Pure meat/filet: ~31% weight loss during preparation/cooking in a frying pan.
  - One piece chicken filet (prepared) weigh approximately 112 g.
- Ground beef: ~26% weight loss during preparation/cooking in a frying pan.
  - Ground beef w/Dolmio: ~47% is cooked ground beef.
  - Ground beef for taco: ~89% is cooked ground beef.
    ~7.5% is spices
    ~3.5% is added water
Appendix 15: Written information and informed consent (8 pages).

Proteinrik versus fettredusert diett ved røykeslutt – Hoveddel 07.01.2010

Forespørsel om deltakelse i forskningsprosjektet: "Effekten av proteinrik versus fettredusert diett i forhold til vekttab, kroppssammensetning, energiforbruk, metaboliske risikofaktorer og spiseadferd etter røykeslutt"  

Bakgrunn og hensikt
Dette er en forespørsel til deg om å delta i en studie som skal undersøke effekten av to ulike dietter for å forebygge vektoppgang etter røykeslutt. Ved Avdeling for preventiv kardiologi ønsker vi å undersøke effekten av proteinrik diett sammenliknet med fettredusert diett. Vi vil undersøke kroppsvekt og kroppssammensetning, forbruk av kalorier, risikofaktorer for hjerte- og karsyndrom (blodtrykk, kolesterol, blodsukker) og svar på et spørreskjema angående forhold til mat. Friske personer som røyker minst 10 sigaretter daglig og er mellom 20 og 65 år og som ikke har hatt alvorlig psykisk sykdom og ikke får behandling for depression kan delta i studien. I alt vil 120 personer delta i studien som varer i 6 måneder. Du er blitt spurt om å delta i studien fordi du er overvektig og er villig til å slutte å røyke, og følge en av de to diettene (tilfeldig valgt ved trekning). Oslo universitetssykehus, Ullevål er ansvarlig for studien.

Hva innebærer studien?
Dersom du er villig til det, vil du først få en legeundersøkelse for å sjekke om du kan være med i studien. Legeundersøkelsen innebærer blant annet sykehistorie, blodprøver, måling av blodtrykk og vekt før studiestart. Hvis du ikke blir med i studien, blir dine medisinske opplysninger kun registrert i din journal ved Avdeling for preventiv kardiologi, Oslo universitetssykehus Ullevål.

Deltagelse i studien innebærer at

1. du vil gjøre et forsøk på å slutte å røyke og
2. du spiser den dietten som du blir trukket ut til å spise i 6 måneder etter røykeslutt.


For å undersøke om du har sluttet å røyke, vil du bli bedt om å avgjøre en puste prøve ved hver visitt. Du skal også skrive en røykedagbok og svarer på spørreskjema. Selv om du ikke klarer å slutte å røyke...
Proteinrik versus fettredusert diett ved røykeslutt – Hoveddel 07.01.2010

under studien, vil du bli fulgt opp i forhold til studieprotokollen i den tiden studien varer. Dette innebærer at du møter opp til avtalte visitter og spiser den maten du har fått råd om.

Relevant informasjon fra din pasientjournal vil også bli samlet inn.

**Mulige fordeler og ulemper**
Det er ikke tidligere blitt gjort en undersøkelse der to ulike dietter sammenlignes ved røykeslutt. Vi kan derfor ikke si om den ene dietten vil være bedre enn den andre.

Alle prøver, undersøkelser og mat som blir utdelt er gratis. Blod- og urinprøver vil bli tatt både før og etter studien for å sjekke eventuelle bivirkninger.

**Hva skjer med prøvene og informasjonen om deg**

**Frivillig deltakelse**

**Annen informasjon**
Har du spørsmål til studien, ta kontakt med klinisk ernæringsfysiolog Mette Svendsen telefon 23016653 eller mobil 45212344. Du kan også sende e-post til: mette.svendsen@uus.no eller: mettsven@online.no

Ved spørsmål som trenger svar fra lege, kan du kontakte:
Lege Eli Heggen telefon 22119982 eller Dr. med Tor Ole Klemsdal telefon 22119453

- Ytterligere informasjon om studien finner du i kapittel A – Utdypende forklaring om hva studien innebærer
- Ytterligere informasjon om personvern, biobank, økonomi og forskning finner du i kapittel B
- Samtykkeerklæring finner du etter kapittel B
Kapittel A- utdypende forklaring om hva studien innebærer

Kriterier for å delta

Bakgrunnsinformasjon om studien
For mange er redsel for vektoppgang i forbindelse med røykeslutt et hinder til å slutte å røyke. Røykeslutt gir mindre risiko for sykdom og død, men stor vektoppgang i forbindelse med røykeslutt kan redusere helseeffekten. Hva som er årsak til vektoppgangen i forbindelse med røykeslutt er ikke avklart, men studier har vist at økt energinntak, redusert hvilestoffskifte og totalt energiforbruk, samt redusert fettforbrenning kan være medvirkende årsaker. En studie der man sammenligner effekten av to ulike dietter i forhold til vekt, kroppssammensetning, energiforbruk og spiseadferd er tidligere ikke blitt gjennomført.

De to diettene i studien
Begge diettene vil være moderat energireduiserte og tilpasset deg ut i fra målinger av hvilestoffskifte og fysisk aktivitet.


Den andre dietten er fettredusert. Det vil si at når du velger magre meieri- og kjøttprodukter, kan du spise omtrent 1 ss med oljerike produkter per dag. I denne dietten vil du først og fremst øke porsjonen av frukt, grønnsaker og komprodukter som grovt brød, fullkornspasta, brun ris, bulgur eller eventuelt grovt brød til middag og lunsj. For å få forskjell mellom diettene vil vi anbefale at du reduserer på porsjonen kjøtt og fisk til middag og velger mindre mengde proteinrike pålegg.

Mulige ubehag, bivirkninger og risiko
Endring av kostsammensetning kan medføre ubehag fra mage og tarm. Ubehaget er som regel forbigående.
Medikamentet varenicline som reduserer abstinenssymptomene ved røykeslutt, kan ha bivirkninger som søvnløshet, uvanlige drømmer og hodepine. Det er rapportert få alvorlige bivirkninger, men det er rapportert en mulig økt forekomst av økt risiko for adferdsendring, nedsenhet, selvmdrddystone og selvmord.
Du er fri til å trekke deg fra studien når du måtte ønske. Hvis du trekker deg fra studien vil du få tilbud om ordinær oppfølging for røykeslutt ved Avdeling for preventiv kardiolog.

Ubehag i forbindelse med studieprosedyr
Blodprøven krever nålestikk og du kan oppleve følgende ubehag: Smerter, blåmerke, svimmelhet og noen kan besvime.
Kroppssammensetning vil bli målt ved omkrets av liv og hofte og ved impedans vekt. Målingene er ikke forbundet med ubehag.

Studiedeltagerens ansvar

Avbrutt studiedeltagelse
Legen eller studieansvarlig kan stoppe din deltagelse i studien hvis:
1. Du ikke følger opp studieprotokollen som avtalt.
2. Du får en alvorlig sykdom.
3. Studielegen mener at deltagelse i studien ikke er til ditt beste.
Informasjon til kvinner

## Oversikt over studiebesøkene

<table>
<thead>
<tr>
<th>Uker</th>
<th>-3</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>---</td>
</tr>
<tr>
<td>Lege undersøkelse</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kroppsvekt</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Kroppssammensetning</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liv/hofte omkrets</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hvilestoffsflukter</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aktivitetsregistrering</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CO måling</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Veiledning for røykeslutt</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Bestemme dato for røykeslutt</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start varenicline</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stopp varenicline</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Røykedagbok</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Spørre skjema røyk</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spørreskjema spiseadferd</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Registrering av mat</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kostveiledning</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Oppstilling av mat</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blodtrykk</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blodprover</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinprov</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gruppmøte</td>
<td>(x)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(x) - Ikke relevant
Proteinrik versus fettredusert diett ved røykeslutt – Kapittel B 07.01.2010

Kapittel B – Ytterligere informasjon om personvern, biobank, økonomi og forskring

Personvern
All informasjon vil bli behandlet konfidensielt. Fastlegen din blir vanligvis informert om din deltagelse hvis du ikke har noe i mot det. Personlige opplysninger om deg som kan være sensitive (for eksempel sykehistorie og medisinbruk), vil bli samlet inn og behandlet, men kun til forskningsformål i forbindelse med studien. Du vil ikke bli referert til ved navn eller bli identifisert i noen publikasjon, så dataene kan ikke spores tilbake til deg.

Oslo universitetssykehus er databehandlingsansvarlig for studien.

Forskningsbiobank

Innynsrett og oppbevaring av materiale
Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Finansiering
Denne studien er finansiert ved hjelp av opptjente forskningsmidler ved Avdeling for preventiv kardiologi.

Forsikring
Vi forventer ikke at du skal få noen helseproblemer ved å delta i denne studien, men dersom din helse forverres som et resultat av deltagelse vil du kunne få erstatning. Du må ikke bevise at det var noen sin skyld. Dersom det viser seg at problemene oppstod som følge av studien, vil du få erstatning. Du er forsinkret i henhold til Oslo Universitetssykehus Ullevål sine egne forsinkringer.

Informasjon om resultatet av studien
Du har rett til å få informasjon om resultatet av studien. Studielegen vil kunne fortelle deg dette når resultatene er klare.
Samtykke for deltagelse i studien

Jeg er villig til å delta i studien

(Signert og datert av deltager)

Deltagers navn med blokkbokstaver

Deltagers fødselsdato

Bekreftelse på at informasjon er gitt deltageren i studien

Jeg bekrefter å ha gitt skriftlig og muntlig informasjon om studien

(Signert og datert av lege)

Legens navn med blokkbokstaver/stempel