Reported food and energy intake among morbidly obese women, and the effect of a low-calorie-diet among obese women with PCOS

- with regard to markers for cardiovascular disease

Master Thesis in Clinical Nutrition

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Summary

Background: Obesity is associated with increased risk for cardiovascular disease, type 2 diabetes mellitus, sleep apnea and some cancer types. In women, obesity may play a role in the development of polycystic ovary syndrome (PCOS). Obesity develops when a human's energy intake exceeds its energy expenditure, and choice of food is an important factor in the development of excessive fat tissue. However, the actual diet composition to obese compared to normal weight women are difficult to obtain. Reported information about food habits and dietary pattern, tend to be misreported, both among lean and obese women. Furthermore, diet, physical activity and adipositas status affect risk markers for cardiovascular disease; as dyslipidemia and adipokine profile. A common metabolic abnormality in women with PCOS is dyslipidemia, and these women also tend to have a more abdominal fat distribution than other women, making them more vulnerable for cardiovascular disease. Weight reduction and thereby improved body composition, improve the risk factors for cardiovascular disease, and might be induced by low-calorie-diets, which consist of either traditional food items or meal replacements.

Method: Part one: Dietary interview, from 116 morbidly obese women and 20 normal weight control women, based on a FFQ, were utilised in the MOBIL-study. The reported food and energy intake among obese women were compared to normal weight women, with regard to dietary composition, food choices and accuracy in energy intake reporting. Part two: Preliminary results from a randomized controlled prospective diet intervention study (FEMIN), including 9 morbidly obese women diagnosed with PCOS, where the effect of eight weeks intake of two different low-calorie-diets; the crisp bread diet and the powder diet, on anthropometric measures, body composition, blood pressure, lipid and adipokine profile were investigated.

Results: Part one: Morbidly obese women had a more unfavourable lipid profile, body composition and expression of adipokines compared to the control women. Obese women reported almost the same energy and macronutrient intake as normal weight women. The intake of fat and saturated fat tended to be higher, while the

consumption of alcohol was lower among the obese women than among the control women. There were more under-reporters among obese than the normal weight women, and the amount of underreported kcal was higher. Part two: Eight weeks on a low-calorie-diet lead to significant improvement in anthropometric measures together with an improved body composition among women with PCOS.

Conclusion: Obese women and normal weight controls reported the same energy and macronutrients intake; however the intake of fat and saturated fat tended to be higher among the obese. Our results may suggest that obese women have a diet consisting of more fat containing food items compared to the normal weight women, whose fat intake is restricted to fewer particularly fatty food items. Obese women with pre-PCOS status consumed more potatoes, meat products and forcemeat, butter, margarine and oil, light squash/soft drinks and artificially sweetened soft drinks than women with lower FTI score. However, since the obese women underreported more than normal weight controls, it is difficult to state what the actual differences between the diets of obese and normal weight women are. Furthermore, morbidly obese women with PCOS have favourable effects of low-calorie-diets, improving several of their enhanced cardiovascular risk factors.

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Abbreviations

ApoA-I	Apolipoprotein A-I
ApoB	Apolipoprotein B
ApoB/ApoA-I	Apolipoprotein B and Apolipoprotein A-I ratio
BEE	Basal Energy Expenditure
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
BMR	Basal Metabolic Rate
CHD	Coronary Heart Disease
CI	Confidence Interval (95 %)
CRP	C-Reactive Protein
CVD	Cardiovascular Disease
DLW	Doubly Labelled Water
DR	Dietary Record
ED	Energy Density
EI	Energy Intake
eTEE	estimated Total Energy Expenditure
FAO	Food and Agriculture Organization
FEMIN	the Female health dietary intervention study

FFM	Fat Free Mass
FFQ	Food Frequency Questionnaire
FM	Fat Mass
FTI	Free Testosterone Index
HDL-C	High Density Lipoprotein Cholesterol
H.C.	Hip Circumference
LCD	Low-Calorie-Diet
LDL-C	Low Density Lipoprotein Cholesterol
MOBIL study	Morbid Obesity treatment, Bariatric surgery versus Intensive Lifestyle intervention study.
N	Numbers
NCEP	National Cholesterol Education Program
NNR	Nordic Nutrition Recommendations from 2004
PAL	Physical Activity Level
PCOS	PolyCystic Ovary Syndrome
rEI	reported Energy Intake
RMR	Resting Metabolic Rate
SHBG	Sex Hormone-Binding Globulin
TEE	Total Energy Expenditure
VLCD	Very-Low-Calorie-Diet
VLDL	Very Low Density Lipoprotein

W.C.	Waist Circumference
WHO	World Health Organization
WHR	Waist-to-Hip Ratio

1. Introduction

1.1 Overweight and obesity

Obesity is accumulation of body fat tissue, which interferes with a human beings physical and psychosocial health. The World Health Organization (WHO) defines overweight as a body mass index (BMI) equal to or greater than 25, while obesity is defined as a BMI equal to or more than 30 (weight (kg) / height (m^2)=BMI).Globally, overweight and obesity are an increasing problem. There are today more than one billion adults who are overweight. At least 300 millions of these are obese. This increase is attributed to the changes of the society. People are adapting to a more sedentary lifestyle, with less physical activity, and easily access to more energy dense food. (1). Data from Svensson et al showed that the proportion of obese men and women in some parts of Norway have increased from 5 % and 4 % respectively, in 1990, to 12 % (men) and 11 percent (women) in 2001. At the same time, the proportions of people with overweight were increased from 37 % of men and 20 % of women in 1990 to 48 % of men and 27 % of women in 2001(2). In 2007 a meta-analysis was published on the prevalence of obesity in Norway. The proportion of obese men (BMI> 30) in the Norwegian studies from 2000-03 was 11-29% (median 19.5%), and for women; 9-38% (median 20%). Data from this study also indicates that there has been, and still is, an increasing proportion of obese people in Norway (3). Obesity is associated with increased risk for cardiovascular disease (CVD), type 2 diabetes mellitus, sleep apnea and some cancer types (endometrial, breast, and colon) (1). Obesity, together with insulin resistance and lipid disorder are factors in the metabolic syndrome (4). In women obesity may play a role in the development of polycystic ovary syndrome (PCOS) (5).

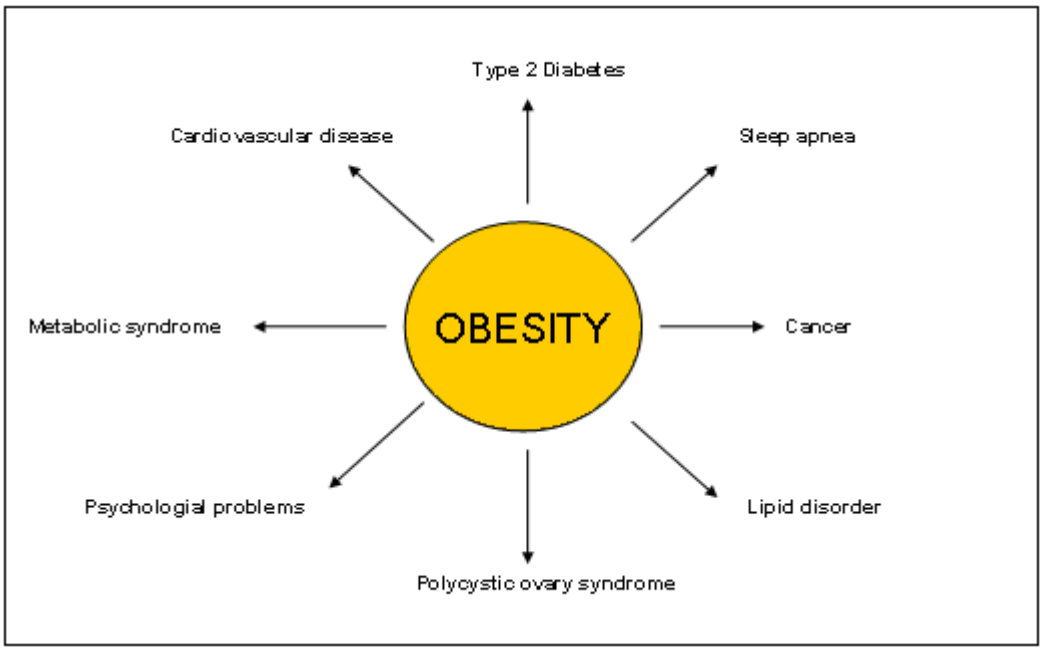

Figure 1. *Possible consequences of obesity*

1.2 Diet and development of overweight/obesity

Overweight and obesity develop when a human's energy intake exceeds its energy expenditure. Lifestyle, environment and genes are all also related to obesity, making a complex interaction. However, choice of food is an important factor in the development of excessive fat tissue. A report of the joint WHO/FAO expert consultation, "Diet, nutrition and the prevention of chronic diseases" from 2003 gives recommendations for preventing excessive weight gain and obesity. The report focuses on a diet rich in dietary fibre, as well as avoiding intake of high energy-dense food. Such foods often contain a lot of fat and sugar and are low in micronutrients content (6), just like sugar-sweetened beverages. A greater consumption of sugar-sweetened beverages is associated with weight gain and obesity (7).

1.2.1 Diet among Norwegian men and women

In 1999 a report from a nationwide dietary assessment from 1997 among a representative selection of Norwegian men and women aged 16-79 years was

published (the Norkost Survey). The mean energy intake (EI) among men and women were 2600 kcal and 1920 kcal respectively. Women had a higher energy percent from protein and carbohydrate than men. Men had higher energy percent from total fat, monounsaturated fat and polyunsaturated fat and alcohol than women. According to the official recommendations in Norway, the intake of both fat and sugar in men and women were close to the maximal recommended level. The recommended intake of maximum ten energy percent from saturated fat were exceeded in both groups(8). The intake of dietary fibre was lower than recommended (as in the Nordic Nutrition Recommendations 2004 (9)), among the women.

Table 1. *Data from the Norkost Survey 1997, describing the general intake of energy and macronutrients in the Norwegian population, and among men and women, aged 16-79 years. Bold numbers indicate statistically significant difference in intake between men and women, compared with t-test ($p<0.05$) (modified) (8).*

	Total (n=2672)	Men (n=1298)	Women (n=1374)
Energy intake (kcal)	2250	**2600**	1920
Protein intake (g)	86	**99**	74
Fat intake (g)	79	**93**	66
-saturated fat (g)	31	**36**	27
-monounsaturated fat (g)	28	**33**	23
-polyunsaturated fat (g)	14	**17**	12
Carbohydrate intake (g)	284	**327**	244
-sugar intake (g)	56	**66**	46
Alcohol consumption (g)	6	**8**	4
Dietary Fibre intake (g)	23	**25**	21
Share of energy intake			
Protein intake (%)	15.9	15.7	**16.2**
Fat intake (%)	30.6	**30.9**	30.4
-saturated fat (%)	12.1	12.1	12.2
-monounsaturated fat (%)	10.8	**11**	10.7
-polyunsaturated fat (%)	5.4	**5.6**	5.2
Carbohydrate intake (%)	51.6	51.1	**52.1**
-sugar intake (%)	9.3	9.5	9.1
Alcohol consumption (%)	1.8	**2.2**	1.4

Men ate more of most of the food items, while women had a significant higher intake of vegetables, fruits and berries, skimmed milk, tea and wine than men. Among the 1319 participating women in this assessment, 549 women were aged between 20-39 years, having a mean BMI of 23.1. Of the women aged 20-29 (n=263) 13 % and 4%

were overweight and obese respectively, while in the group of women aged 30-39 (n=286) 20 % were overweight, while 7 % were obese (8).

1.2.2 Diet among obese women

Recently, Savage et al investigated the energy density (ED) and food choices among 186 white women in Pennsylvania, USA. They grouped the participants into three groups based on the energy density in their diet. Women having a low energy density diet ate more water-rich foods as fruits and vegetables, while they had lower intake of grains. They had fewer servings of bread, baked desserts and refined products compared to the high energy density group, which again consumed less whole grains than the low energy density group. Women in the high ED group reported higher consumption of French fries and potato chips compared to the low energy density group which reported higher intake of dark green, yellow and red vegetables. Women in the low ED group gained less weight than in women in the high ED group over six years (10). Schulze et al examined women in the Nurses' Health Study II and their dietary patterns over a period of time. Findings from this cohort suggested that a diet characterized by high intakes of red and processed meats, refined grains, sweets, desserts and potatoes may contribute to a greater weight gain than a dietary pattern consisting of a lot of fruits and vegetables, whole grains, poultry, fish and salad dressing (based on oil and vinegar). The latter diet may result in weight maintenance (11).

1.3 Cardiovascular disease

Cardiovascular disease is a collective term which includes coronary heart disease (CHD), hypertension, cerebrovascular disease, peripheral artery disease, rheumatic heart disease, congenital heart disease and heart failure. In 2005 approximately 17.5 million people died from cardiovascular disease globally, making CVD the number one cause of death (12). The largest epidemiologic study of cardiovascular disease in the world is the Framingham Heart Study. There are seven major risk factors for

CVD identified by the Framingham study; age, sex, blood pressure, total and high-density lipoprotein cholesterol (HDL-C), smoking, glucose intolerance, and left-ventricular hypertrophy. However in the Framingham studies, obesity has not been identified as a risk factor for CVD (13-16). Environmental risk factors predisposing to CVD are among others physical inactivity, obesity and unhealthy diet (12;17;18). The INTERHEART study identified nine important risk factors for myocardial infarction; abnormal lipids, abdominal obesity, diabetes, smoking, hypertension, psychosocial factors, intake of fruit, vegetables and alcohol and regular physical activity. The same risk factors were identified for both sexes and at all ages (19).

1.3.1 Lipids and lipoproteins

Cholesterol is a lipid with several physiologically functions. It is a precursor for bile acids and steroid hormones, as well as an important constituent of the cell membrane. In the blood, cholesterol is transported in particles consisting of lipids and proteins, called lipoproteins. There are three main lipoprotein particles in serum – very low density lipoproteins (VLDL) (secreted by the liver), low density lipoproteins (LDL) and high density lipoproteins. Lipids travel in the blood as triglycerides incorporated in the lipoproteins. A proportion of the triglycerides are also free in serum. Heritage, diet, physical (in)activity, obesity and smoking are some of the factors which affect the levels of cholesterol in the body (20-22). The recommended concentration of total cholesterol and LDL-C in plasma in persons without disease is below 5.0 mmol/l and 2.5 mmol/l respectively. Triglyceride values below 1.7 mmol/l are recommended. For both men and women, the National Cholesterol Education Program (NCEP) in USA, defines a categorical low HDL-C as less than 1.0 mmol/l. High levels of HDL-C is classified as more than 1.55 mmol/l (17;20).

Subclasses of lipoproteins and apolipoproteins

Low density lipoproteins

There are different subclasses of the lipoproteins. There are several subspecies of low density lipoproteins, based on the size and density. The main fractions are the large

and more buoyant, and the small and more dense particles. The last mentioned has more atherogenic properties than the large LDL particles (23;24). LDL particles contain a protein; apolipoprotein B 100 (apoB), and it serves as a receptor ligand. Apolipoprotein B 100 is produced in the liver and incorporated into VLDL, which is then transformed to LDL during the metabolism (22).

High density lipoproteins

Reverse cholesterol transport is one of the main tasks for HDL particles, making it the "good cholesterol". They transport excess cholesterol from peripheral cells to the liver for excretion (25). HDL particles have other properties as well, contributing to its antiatherogenic effect. It serves as an antioxidant and an anti-thrombotic molecule. (26). HDL-particles are also associated with apolipoproteins; apoA-I and/or apoA-II (20).

1.3.2 Atherosclerosis

Atherosclerosis is an inflammatory disease in the arteries, causing cardiovascular disease. This is a formation of lesions in the arteries that is characterized by inflammation, lipid accumulation, cell death and fibrosis. At the initiation these plaque are called fatty streaks (27). The major cellular events contributing to these fatty streaks are the diffusion of LDL-cholesterol through dysfunctional endothelium into the subendothelial space, and the subsequent recruitment of macrophages (28;29). Subsequent LDL oxidation and enzymatic modifying in the intima layer, form new molecules of LDL, like oxidized LDL. The macrophages have scavenger receptors which mediate the uptake of oxidized LDL. The accumulation of lipid droplets inside the macrophage turns it into a foam cell. With time the lesions can disappear, or they can mature and gain new characteristics. They are then called atherosclerotic plaques. (27). An intact endothelium covers the plaque. Progressive development of the atherosclerotic plaque narrows the vessel lumen and results in ischemic symptoms. Major complications occur if the endothelium ruptures. Exposure of subendothelial material to the vascular lumen promotes blood platelet

aggregation and thrombus formation. A thrombus might occlude the artery, leading to acute ischemia (27-29).

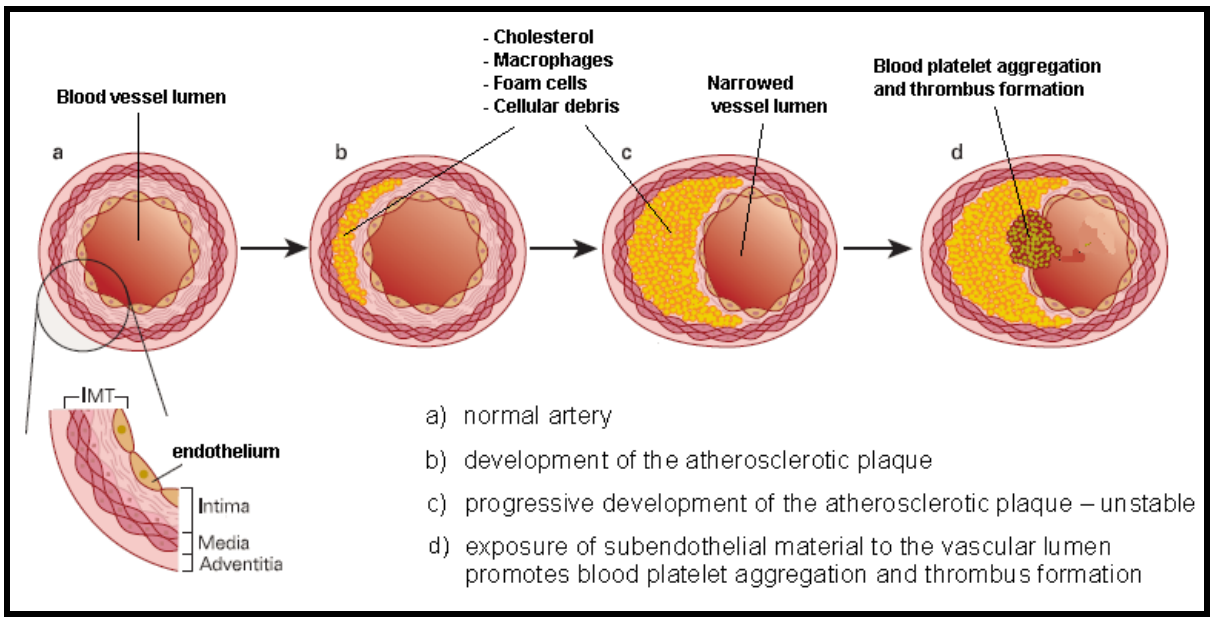

Figure 2. *The development of the atherosclerotic plaque, modified from Dahl et al (30).*

1.3.3 Risk factors for atherosclerosis and cardiovascular disease

Dyslipidemia

Dyslipidemia is characterized by increased levels of VLDL- and LDL cholesterol in the blood. The triglycerides are often raised and the HDL-C is decreased. Hypercholesterolemia, hypertriglyceridemia together with low levels of HDL-C can occur one by one or all together. Obesity, diabetes mellitus type 2, high intake of saturated fat and alcohol, and physical inactivity may lead to increase in plasma cholesterol and triglycerides (21). Atherosclerotic vascular disease is linked to elevated levels of cholesterol in the blood. A reduction of LDL-C by 1 mmol/l has been estimated to give a 23 % reduction in first major coronary events. Furthermore, a 10 percent reduction of total cholesterol is accompanied by a 25 % reduction of incidence of cardiovascular disease after 5 years (31;32). HDL-C less than 1.0 mmol/l for men and 1.2 mmol/l for women ,and fasting triglycerides over 1.7 mmol/l may also serve as markers of increased cardiovascular risk (32). The Framingham

study found that decreased levels of HDL-C increases the risk for coronary heart disease (33). Higher levels of HDL-C are associated with reduced risk (20).

Subclasses of lipoproteins

The presence of small, dense LDL particles together with decreased HDL-C and increased triglycerides have been associated with a three-fold increased risk for coronary heart disease (34).

Ratio between the apolipoproteins

There is growing evidence that the ratio between apolipoprotein B and apolipoprotein A-I can be predictive in the estimation of cardiac risk. Walldius et al showed that the values for apoB and apoB/apoA-I were positively and strongly related to increased risk of fatal myocardial infarction in both men and women. In multivariate analysis, apoB was a stronger predictor of risk than LDL-C in both sexes (35).

C-Reactive Protein (CRP)

This is as acute phase protein which is synthesised in the liver and released in response to inflammation. CRP is a potential inflammatory marker for cardiovascular risk, and CRP levels may predict CVD in apparently healthy individuals. Since atherogenesis (the process of development of atherosclerosis) is an inflammatory response to many different risk factors (as raised LDL-C), CRP has been shown to be elevated, independently of other risk factors. Subjects with concentrations of CRP above 3.0 mg/L are regarded as having a higher risk for subsequent cardiovascular disease. Obesity, which also is an inflammatory state, produce elevations in CRP, but weight loss have been shown to lower the CRP level in blood (17;36).

Obesity

Adipose tissue serves as an energy depot, located in the body. The distribution of body fat is important in the development of different diseases, like diabetes, atherosclerosis and coronary heart disease. Upper-body obesity (android) is more likely to be associated with these diseases than lower-body obesity (gynoid). Upper-

body fat, as abdominal fat distribution, includes both the visceral fat, which encircle the internal organs, and the subcutaneous depots. The latter depot is situated below the skin in the abdominal region. Lower-body fat consists only of subcutaneous adipose depots, lying immediately under the skin, especially in the gluteal and femoral regions (37).

Visceral fat is metabolically very active, having high rates of lipogenesis and lipolysis. These processes result in release of free fatty acids to the circulation, which again may cause increased lipid synthesis in liver and insulin resistance. This may result in hyperlipidemia, glucose intolerance and hypertension, all of which are risk factors for atherosclerosis. Suggested factors for visceral fat accumulation are aging, disturbances of sex hormones, overconsumption of sucrose and physical inactivity. (38). A simple way to predict the amount of visceral fat is to use the anthropometric measure of waist circumference (W.C.), which has been shown to be positive correlated to the visceral fat mass (FM) (39). The waist circumference is not enough to diagnose visceral obesity, but together with raised levels of fasting triglycerides, may represent a simple marker of excess visceral fat (40). Excessive upper-body fat can be measured by an increase in waist-to-hip ratio (WHR). The cut off value for the waist-to-hip ratio is 0.85 in women and 1.0 in men, where higher ratios indicates increased upper-body fat (41).

To detect a subject's body composition, the use of Bioelectrical Impedance Analysis (BIA) is an applicable method. Different tissue in the body differ in their way to conduct bioelectrical impedance, and in this way the BIA can analyse the percentage of fat mass, fat free mass (FFM) and body water in the body. Ozenolgu et al have recently described that increasing BMI is associated with higher percentage of body fat, while the amount of lean body mass and body water decrease (42). In normal weight women, 21-35 % of the body weight is contributed by fat tissue (43). In obese and morbidly obese women the fat mass have been shown to constitute 35 and 40 % respectively, of the body weight (42).

The adipose tissue is also a secretory organ. Increase of adipose tissue lead to altered production and secretion of adipokines which is a collective term for chemokines, cytokines and hormone-like proteins. These substances affect virtually all organ systems in the body. The adipokines have either systemic or local effect, and they are implicated in metabolic and inflammatory processes. Energy homeostasis, adipocyte differentiation, insulin sensitivity, control of inflammation, vascular inflammation and neo-angionesis are all affected by these substances (44;45). The abdominal visceral adipose tissue seems to be the most unfavourable, due to the great secretion of these substances, especially affecting the cardiovascular system (40;45).

Metabolic syndrome

The metabolic syndrome includes a cluster of metabolic disturbances, and was defined by the WHO in 1998. Later, new criteria have been proposed. The International Diabetes Federation released in 2006 a new consensus statement on the definition of the syndrome. In the new definition, central obesity is important. For a person to be defined as having the metabolic syndrome, he/she must have a waist circumference over a specific value (for Europeans; males > 94 cm, females > 80 cm) plus any two of four additional factors; raised blood pressure (systolic: ≥ 130 mmHg or diastolic: ≥ 85 mmHg, or treatment of previously diagnosed hypertension), increased values of triglycerides (≥1.7 mmol/l), reduced HDL-C (< 1.03 mmol/l in males and < 1.29 mmol/ l in females) and/or raised fasting plasma glucose (fasting plasma glucose ≥ 5.6 mmol/l or previously diagnosed type 2 diabetes) (4). The International Diabetes Federation criteria lowered the cut off values for the waist circumference and made this parameter essential in the definition of the metabolic syndrome compared to the previous definition of the syndrome made by the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). In this definition the criteria of waist circumference were higher (males > 102 cm, females > 88 cm) and equalised with the other criteria, where having three out of the five criteria was enough to be defined with the metabolic syndrome (20).

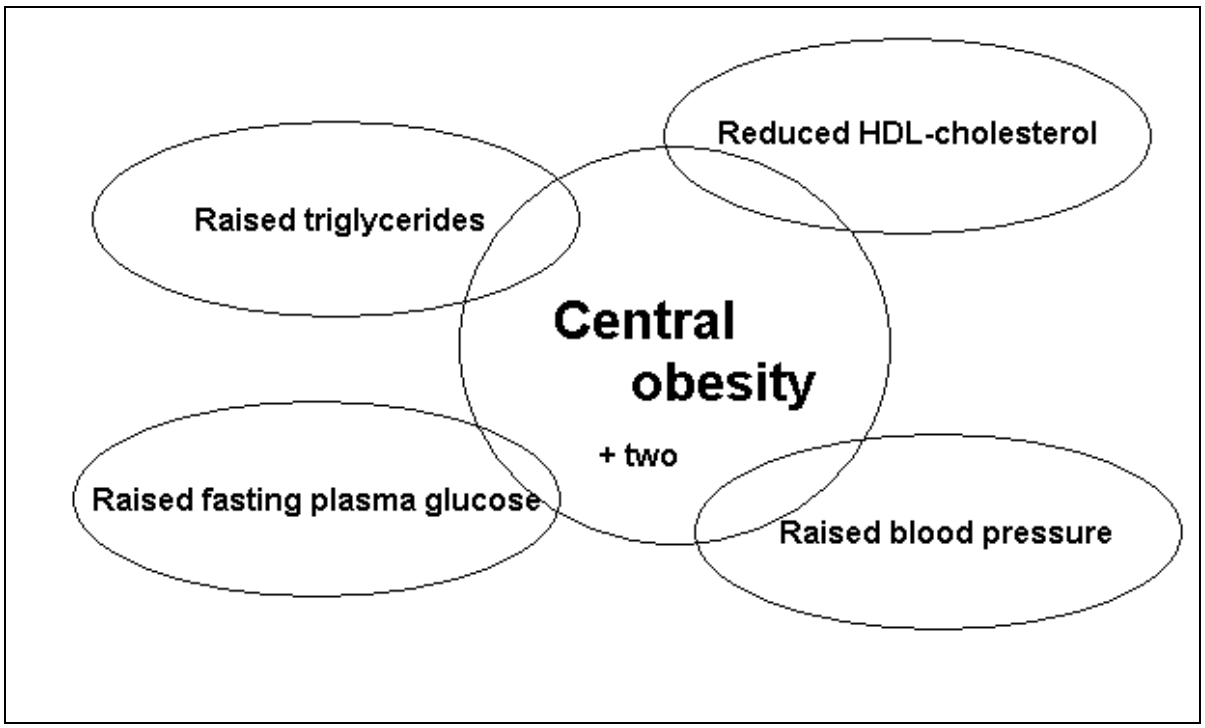

Figure 3. *Definition of the metabolic syndrome from the International Diabetes Federation (2006)(4), see details in text.*

Adipokines – Leptin and adiponectin

Leptin

Adipokines are secreted by the adipose tissue, and they are involved in the regulation of metabolic homeostasis. Leptin circulates in the body influencing the regulation of energy stores and energy balance. One site of action is the central nervous system where it affects the expression of molecules that influence the feeling of hunger and satiety. Leptin inhibits orexigenic peptides, thereby reducing appetite and subsequent food intake, and hamper peptides which decrease energy expenditure (46-48). The concentration of plasma leptin is dependent of the amount of energy stored as fat and also the energy balance. Obese persons have increased levels of leptin, but the mechanism behind this is debated. It is not evident if this increase are due to the increased adipose tissue itself and thereby increased release, or if the body develops a central leptin resistance, which leads to increased levels of leptin in plasma (46;47).

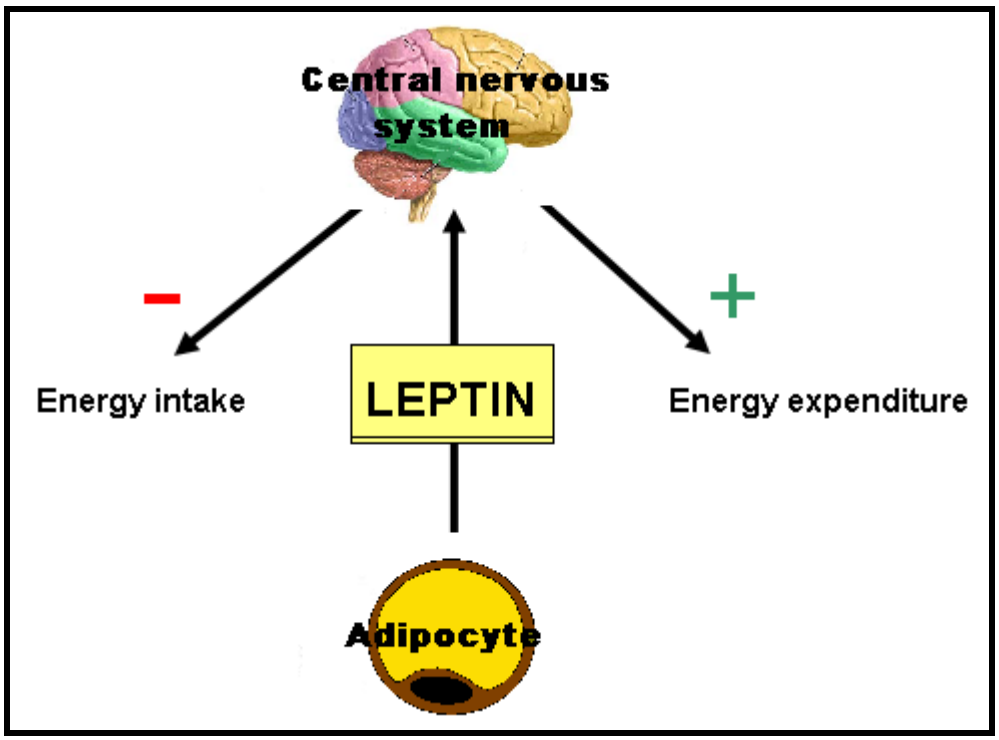

Figure 4. *Action of leptin in the regulation of energy balance.*

Adiponectin

Adiponectin is also secreted by adipose tissue, and it plays a role in the lipid and glucose homeostasis. In the liver, adiponectin decreases glucose production and lipid synthesis (49). In other tissues, this circulating protein influences the basal glucose level, decreasing it transiently (50). In addition, adiponectin affects muscle tissues, increasing tissue fat oxidation and reducing triglyceride production, thereby lowering the triglyceride concentration in tissues. Decreased levels of triglycerides may enhance insulin sensitivity, or adiponectin may increase the insulin sensitivity of the hepatocytes by the direct action on the liver (49). Thus, adiponectin may have a role in preventing or counteracting the development of insulin resistance. Although adiponectin is secreted from adipose tissue, obese persons have lower concentrations of this parameter in plasma than normal weight persons (49;51). Adiponectin have further been associated with dyslipidemia; and is negatively correlated with triglycerides and apolipoprotein B-100, and a positively correlated with HDL-C (51). Weight loss in obese persons has been shown to increase the concentration of adiponectin in plasma (52). Adiponectin may also have an anti-inflammatory and

anti-atherogenic function (49;51). Recent studies have reported that different adipose tissues have unequal capacity to secrete adipokines. Subcutaneous adipose tissue has been shown to produce leptin, while visceral fat is the major production site of adiponectin (53).

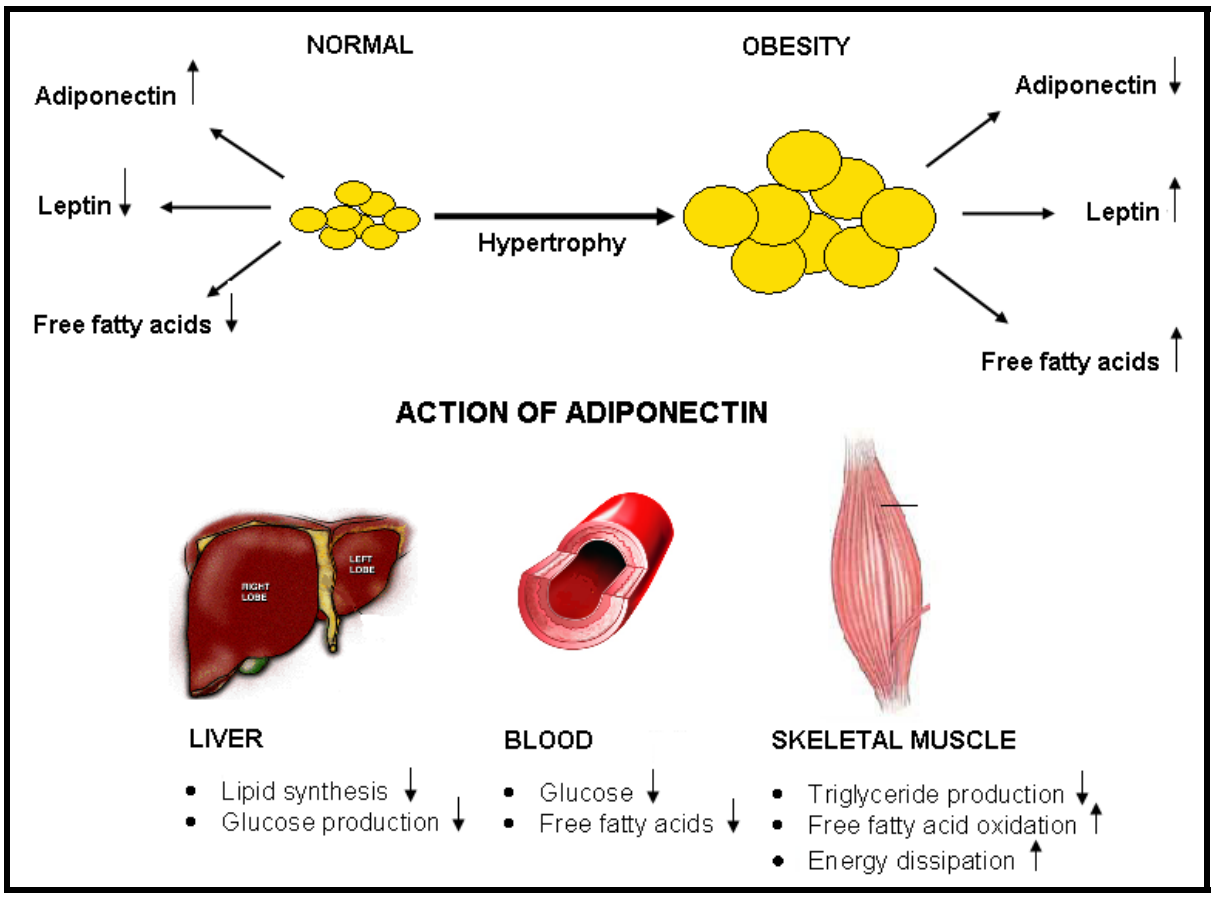

Figure 5. *Action of adiponectin on adipose tissue and peripheral organs (liver, blood and skeletal muscle). Adapted from Meier et al (49).*

Insulin resistance

Raised fasting plasma glucose can be caused by resistance to the effects of insulin on glucose uptake, metabolism or storage (54). Insulin is secreted from the islet β-cells in pancreas due to increasing concentrations of glucose in the blood. Insulin is essential in the process where glucose is transported into the cells. Some people are lacking production of insulin. They have diabetes mellitus type 1. Other people show resistance and low sensitivity to the insulin which is produced in their body and become insulin resistant. When this development starts, the pancreas will increase the

production of insulin and thereby overcome the reduced efficacy of insulin action. Normal glucose tolerance is maintained. When the tissues are getting more insulin insensitive and pancreatic insulin production no longer can overcome this, the person becomes insulin resistant and will develop hyperglycaemia. Adipocytes also express insulin resistance, and as a consequence lipolysis is enhanced, increasing the concentration of free fatty acids in plasma (55). Insulin sensitivity is affected by several factors like obesity, physical activity and fitness (56)

1.4 Polycystic ovary syndrome

1.4.1 Diagnosis

Polycystic ovary syndrome is a syndrome of ovarian dysfunction, characterized by hyperandrogenism, polycystic ovaries, and chronic oligo-anovulation. Clinical manifestations may be infertility, menstrual irregularities, signs of androgen excess and obesity. The diagnostic criteria for PCOS, which were revised in 2003, are (two out of three of the following criteria) 1) oligo- and/or anovulation 2) clinical and/or biochemical signs of hyperandrogenism and 3) polycystic ovaries. Other medical conditions that may cause irregular menstrual cycles and androgen excess must be excluded (57).

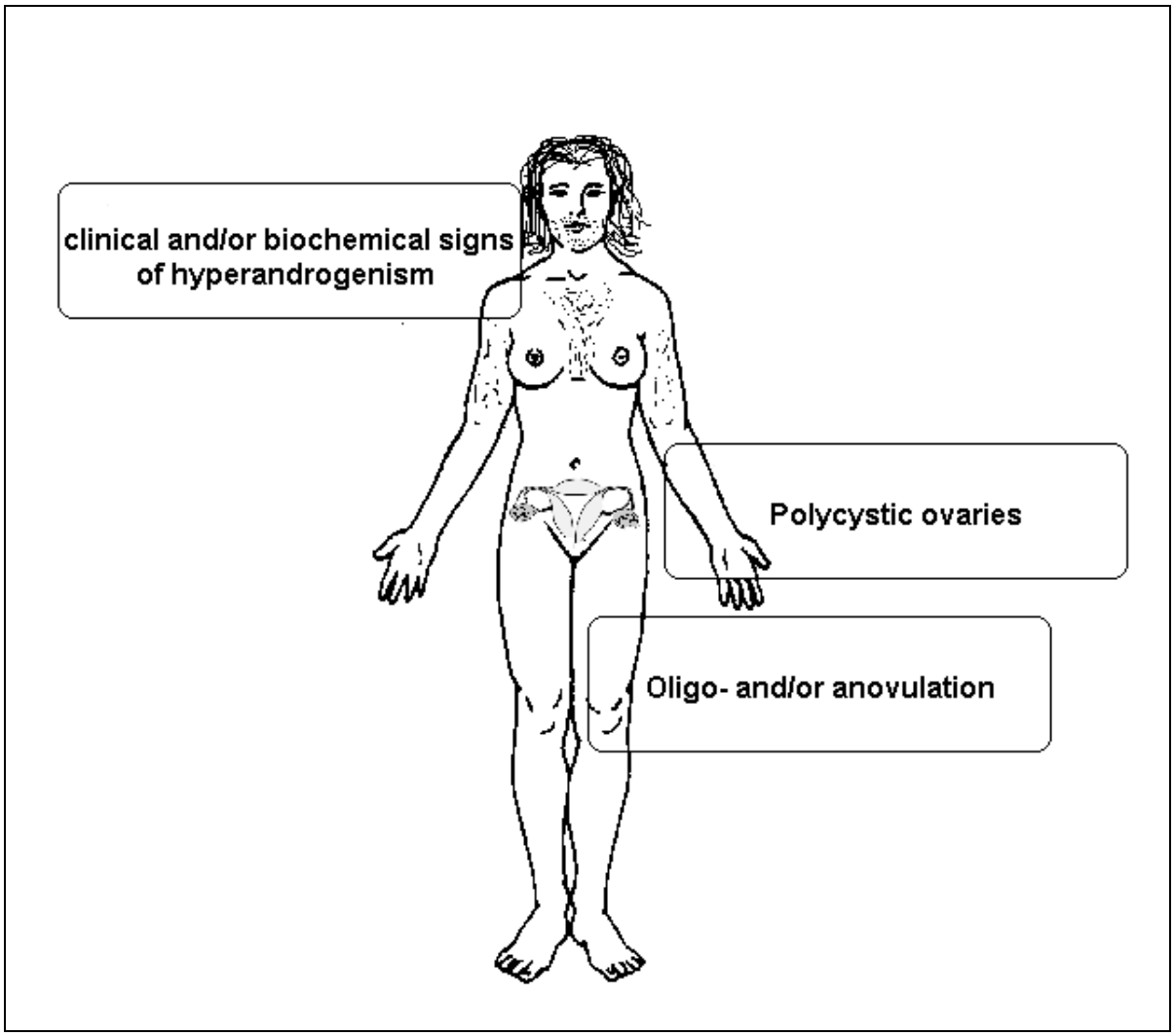

***Figure 6**. The diagnostic criteria for PCOS are (two out of three) 1) oligo- and/or anovulation 2) clinical and/or biochemical signs of hyperandrogenism and 3) polycystic ovaries.*

1.4.2 Prevalence of polycystic ovary syndrome

Polycystic ovary syndrome is a common endocrine disorder among reproductive-aged women. Though the data is scarce on the prevalence of PCOS among overweight or obese women, there seems to be a trend that many women with PCOS tend to be overweight or obese (5) . A study of overweight and obese Spanish women demonstrated a prevalence of PCOS of 28 percent (58). Recently Yildiz et al described the prevalence of PCOS among overweight and obese premenopausal females in Birmingham, Alabama to be 9.9% and 29.2%, respectively. By using the obesity classes (class 1: BMI 30-35, class 2: BMI 35-40, class 3: BMI>40) they

reported an increasing proportion of women diagnosed with PCOS in relation to higher obesity classes. The researchers further described the prevalence of obesity among PCOS patients diagnosed between 1987 and 2002. In 1987-1990 the prevalence of obesity in PCOS patients was 51%, and increasing to 74% in 2000-2002. However, they indicated that the risk for PCOS is only slightly increased in obese women, although the proportion of obese women with PCOS has increased. This increase in PCOS may be similar to the increase of obesity seen in the general population (59). On the other hand, PCOS has also been shown in normal weight women, where the prevalence of PCOS is estimated to be between 4 and 10 percent (59-62).

1.4.3 Clinical features of PCOS

Ultrasound is used to diagnose polycystic ovaries by assessing follicle number and/or ovarian volume. The polycystic ovary should have 12 or more follicles, each measuring 2-9 mm in diameter, or increased ovarian volume (>10cm^3) (63).

Clinical signs of chronic anovulation are either oligomenorrhoea or amenorrhoea. Oligomenorrhoea is defined as less than eight menstruations per year, or cycles that are longer than 35 days. Amenorrhoea is absence of periods for more than three months, without pregnancy (64).

Hyperandrogenism has cutaneous manifestations like hirsutism, acne and female-pattern alopecia. Hyperandrogenemia can be proven biochemically by measuring serum total testosterone (T) and sex hormone binding globulin (SHBG), with subsequent calculation of the free testosterone index (FTI). The reference value for FTI among women is 0.1 – 0.6. Women with PCOS have FTI scores around 1 (65;66). Since the reference value is up to 0.6, a FTI score above 0.6 may indicate the beginning of a PCOS diagnosis. Women with FTI > 0.6 can be classified as pre-PCOS subjects.

Women with PCOS have increased risk of developing dyslipidemia, cardiovascular disease, endometrial carcinoma and also type 2 diabetes, due to insulin resistance and hyperinsulinemia (66-69).

1.4.4 Adipose tissue distribution in women with PCOS

There is increasing evidence that the distribution of body fat among women with PCOS is abnormal, and that these women tend to have a more abdominal fat distribution than women without PCOS (70;71). Furthermore, visceral fat have been shown to be the most significant variable to correlate with metabolic disturbances seen in women with PCOS (5;39). Carmina et al reported that overweight and normal weight women with PCOS had similar amounts of total and trunk fat, but they had a higher proportion of central abdominal fat, compared to normal age-and-weight-matched controls. However, obese women with PCOS did not show this difference compared to obese controls, all the fat parameters were the same, though increased. PCOS patients with increased central abdominal fat had significantly higher concentrations of insulin levels and lower insulin sensitivity. Also the PCOS women without excessive central abdominal fat had the same disturbance in the insulin balance compared to matched controls (72). Another study comparing non-obese (BMI < 25) PCOS women with lean control women found that the women with PCOS had significantly higher proportions of preperitoneal and visceral fat than the control women, while the distribution of subcutaneous fat was similar for both groups. The HDL-concentration was inverse correlated with the intra-abdominal fat, while the triglyceride levels correlated positively (73). Excess central fat accumulation in PCOS women have been shown to be associated with the low-grade inflammation and the insulin resistance in these women, independent of the PCOS diagnosis (74).

Cussons et al investigated the prevalence of metabolic syndrome in women with PCOS and found that there is an approximately four times increase in the incidence of the metabolic syndrome in women with PCOS compared to the general population.

The estimate will vary according to different diagnostic criteria of PCOS and the metabolic syndrome, as well as different ethnicity (75).

1.4.5 Dyslipidemia in PCOS women

Dyslipidemia is appointed as a common metabolic abnormality in women with PCOS, but the extent of and type of dyslipidemia are reported differently. Dyslipidemia characterised by elevated triglyceride levels and small, dense LDL particles as well as lower concentration of HDL-C have been reported (68;76). A cross sectional study from Glasgow found that women diagnosed with PCOS had higher concentrations of triglycerides and VLDL-cholesterol. The same women also had higher concentrations and proportion of the atherogenic, small and dense LDL compared to BMI-matched controls. They found no differences in total cholesterol, LDL-C and HDL-C between the groups (77). Talbott et al demonstrated that women with PCOS, under the years of 45, had higher LDL-C compared to controls, after adjustment for insulin levels, BMI and hormone use. Little difference was however detected between PCOS-cases and controls over the age of 40 years (78). Contrary to this, Holte et al did not find any significant differences in serum concentrations of the major serum lipoprotein lipids when comparing lean and obese patients with PCOS with lean and obese controls. Obese cases with PCOS showed similar abnormal lipid profile as obese women without PCOS, even though the PCOS women had significantly reduced insulin sensitivity and glucose tolerance (79). However, Legro et al observed that both obese and non-obese women with PCOS had significantly higher levels of total cholesterol and LDL-C compared with BMI-matched controls. The obese PCOS women also had significantly greater HDL-cholesterol and triglyceride levels than the obese control women. When they adjusted for age and BMI, the levels of HDL-C were higher among all the women with PCOS compared to controls. Furthermore, when the researchers adjusted for age, BMI, waist-to-hip ratio and fasting insulin and glucose levels, the levels of LDL-C were still significantly higher in the PCOS women, while the levels of HDL-C and triglyceride were still increased, but no longer significantly increased compared to the controls

(80). Recently, a study comparing thirty overweight PCOS women with twenty-four matched control subjects found higher concentrations of plasma triglycerides and lower levels of HDL-C among the women with PCOS. In this study there were no difference in total cholesterol and LDL-C, but fourteen of the patients with PCOS had smaller and more atherogenic LDL particles than the controls. This was the second most common lipid alteration after the decreased HDL-C (81). In conclusion, a majority of studies indicate that women with PCOS have an atherogenic lipoprotein profile, characterized by elevated levels of triglycerides, increased levels of small dense LDLs and depressed concentration of HDL-C.

1.4.6 Expression of adipokines in women with PCOS

Leptin levels have been investigated in women with PCOS and have been related to BMI rather than other metabolic or hormonal disturbances in PCOS (82). Leptin levels increases with increasing BMI for obese women both with and without PCOS (83). Studies of obese women with polycystic ovary syndrome have reported significantly lower levels of adiponectin in these women compared to weight-matched controls (83;84). Increasing BMI and waist circumference have been shown to be negatively correlated to adiponectin levels for obese women both with and without PCOS (83;85). In addition, Spranger et al explored that circulating levels of adiponectin was independently correlated to the degree of insulin resistance in PCOS women, and may contribute to the development and/or maintenance of insulin resistance independently from adiposity (85).

1.4.7 PCOS and cardiovascular disease

Women with polycystic ovary syndrome tend to hold shares of many of the cardiovascular risk factors, like obesity, insulin resistance and dyslipidemia (67;86). Studies of PCOS women have discovered altered function and structure of the cardiovascular system in these women, which mainly have been described as a consequence of the risk factors mentioned earlier, rather than to the presence of

PCOS per se (76). Recently, asymptomatic coronary atherosclerosis (using coronary artery calcium as a marker) was detected in young obese women with PCOS, and this group had a significantly higher prevalence of coronary atherosclerosis compared to young, obese controls. The risk for subclinical coronary atherosclerosis was independent of other known risk factors for cardiovascular disease (87). Furthermore, the increased distribution of visceral fat in PCOS women is shown to be correlated with elevated carotid artery intima-media thickness, and reduced flow-mediated dilation. These two parameters are predictors of vascular health (71). Young normal weight and overweight girls with PCOS have been examined, and increased carotid intima-media thickness and reduced flow-mediated dilation are common features, suggesting that the vascular wall is affected, leading to premature subclinical atherosclerosis and vulnerability to cardiovascular disease later on in life (88;89).

A retrospective cohort study of women diagnosed with PCOS before 1979 was conducted in United Kingdom in 1999, where they wanted to explore the prevalence of cardiovascular disease. Despite elevated prevalence of several cardiovascular risk factors in the PCOS women, the researchers did not find increased history of coronary heart disease in these PCOS women compared to the controls (90). Solomon et al used material from the Nurses' Health Study, and examined the relationship between irregular menstrual cycles and coronary heart disease. Fourteen years after they had stated their menstruation pattern, women with usually irregular or very irregular menses (a reasonable surrogate for the presence of PCOS) were compared to women with regular menstrual cycles. Adjusted for age, those who had had usually irregular and very irregular menstruations had increased relative risk (RR 1.25 and 1.67) for nonfatal and fatal coronary heart disease. Adjusting for BMI; higher BMI was associated with greater risk for the development of CHD (91). However, there are too few good epidemiological studies about PCOS and cardiovascular disease, thus definitive evidence for an increased incidence of CVD among women with PCOS is lacking (76).

CRP in PCOS women

The levels of CRP in women with PCOS are reported to be increased compared to age- and weight-matched controls (71). However, some studies also report that obese women with PCOS have similar concentrations compared to obese controls. It has been shown that obese PCOS women have CRP values above 3 mg/L, which indicates a higher risk of cardiovascular disease in these women (67). The association of increased CRP levels in PCOS women may be dependent upon the co-existent obesity, rather than the PCOS diagnosis per se (76). A recently published study concluded that both PCOS and obesity contribute to a proatherogenic state (with increased CRP among other factors), but in women with PCOS, abdominal adiposity and hyperandrogenism may exacerbate the risk for atherosclerosis (92).

1.5 Weight reduction

Obesity and its complications are, as mentioned, associated with increased risk to develop different diseases. Thus, there is evidence that weight loss reduces the risk factors for both cardiovascular disease and diabetes (93), and can prevent the development of different cancers (94). Weight reduction leads to lowered levels of triglycerides, higher concentrations of HDL-C and some reduction in total cholesterol and LDL-C. Weight loss also results in reduced blood pressure and lower levels of blood glucose (41;93). Furthermore, the "Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults" recommends that the initial goal of weight loss therapy should be to reduce the body weight by approximately 10 percent from the weight at baseline (93). A successful weight loss is defined as loosing at least 10 percent of the initial body weight and maintain this weight reduction for at least one year (95).

Weight loss and diet

One way to achieve weight loss is to reduce the intake of energy from the diet to a lower level than the body needs to keep the machinery going. Diets with an extremely

low calorie intake are called very-low-calorie diets, while diets with higher calorie content, though they are still low in energy, are named low-calorie diets. Today, there is not enough evidence to conclude what kind of diet regimen a person should use to loose weight. There are many different regimens, and there is an ongoing debate discussing which one of them will make the greatest weight loss, improve the body composition in the most favourable way and lead to a better health status generally. The different diet regimens differ in the amount of carbohydrate, fat and protein, some being low in one macronutrient and very high in another (96-98). Recently, Sacks et al published a study on the effect on weight reduction of four different weight-loss diets composited of different amounts of fat, protein and carbohydrates. 645 participants completed the two years study. The nutrient goals for the four diet groups were: #1: 20% fat, 15% protein and 65% carbohydrates (low-fat, average-protein), #2: 20% fat, 25% protein and 55% carbohydrates (low-fat, high-protein), #3: 40% fat, 15% protein and 45 % carbohydrates (high-fat, average-protein) and #4: 40% fat, 25% protein and 35% carbohydrates (high-fat, high-protein). Each participant was instructed to eat 750 kcal less than their estimated total energy expenditure (eTEE). The participants were followed-up by regularly group- and individual sessions. All diets were successful in causing weight loss regardless of which macronutrients they emphasized. The degree of weight loss was strongly associated with the attendance to the group- and individual sessions (99).

Body composition after weight loss

During a period of weight reduction, the body utilize energy from its stored energy compartments, due to the insufficient energy intake. The body uses energy stored in the fat compartments, but may also utilize energy stored in muscle tissue. Loss of fat free mass (muscle mass) is unfavourable, since these tissues are responsible for the majority of the resting metabolic rate (RMR) (see section 1.6.3), regulation of core body temperature and maintenance of function in the body (100). A review over dietary weight interventions revealed that weight loss induced by low-calorie-diets (LCD) or very-low-calorie-diet (VLCD) alones, led to weight losses where 14% and

23.4 % of these weight losses were constituted by fat free mass. Among subjects on LCD without exercise, a higher proportion of their weight loss were fat free mass, compared to the subjects who had engaged in exercise (100). Recently, Chaston et al reviewed the literature with regard to different weight loss interventions and the percentual decrease in visceral versus subcutaneous adipose tissue in the abdominal region. Since the visceral fat has known unfavourable characteristics, a weight reduction program addressing particular loss of this fat depot will be of interest. The researchers did not find any compelling evidence for a diet preferentially targeting the visceral fat. However, they found that there are signs of an association between preferential loss of visceral fat with modest weight loss, and that the effect is attenuated with greater weight loss (101).

Janssen et al investigated the effect of an energy-restricted diet on adipose tissue and skeletal muscle tissue, together with or without exercise among obese women. After a weight reduction period they found significant reduction in total body weight, total adipose tissue and reduced waist circumferences among the participants. The groups who had diet and exercise together did not lose skeletal muscle, while the group who had diet intervention alone lost skeletal muscle (102). Furthermore, the same researchers detected that the weight loss among obese women were associated with reductions in the levels of total cholesterol, LDL-C and apolipoprotein B (103).

Weight loss in women with PCOS

Andersen et al showed in 1995 that among women with PCOS eating a very-low-calorie diet (~ 420 kcal/day) for four weeks reduced their weight significantly (median 9%), and improved their insulin sensitivity (104). Moran et al studied the difference in weight reduction between two diets with approximately 1400 kcal/day, one with high protein content (30% protein, 40 % carbohydrate), and the other with low protein content (15% protein, 55% carbohydrate). Women with PCOS followed one of these diets for 12 weeks. Mean weight loss for both groups was 7.7 kg, with a total reduction of 14 % in total fat mass, and 12.5% decrease in abdominal fat mass. Independently of the diets, total cholesterol, triglycerides and LDL-C decreased.

HDL-C decreased on the low protein diet, but remained unaltered on the high protein diet (105). A study in Jordanian PCOS woman found that an energy-restricted diet lead to improved clinical and hormonal characteristics of these women (106). A recent published study examined the difference in weight loss among women with PCOS after an energy-reduced diet supplemented with powder supplements, providing 240 kcal, either containing sugar-free whey protein isolate or simple sugars. The group consuming the extra protein lost more weight than the "simple sugar group". Fat mass reduction was also greater in the "protein group", and a greater decrease in adiponectin concentrations was also observed. Total cholesterol, apo B and HDL-C levels were significantly reduced after two months in the "protein group", but these parameters did not change significantly in the "simple sugar group". There was significant difference in these parameters between the "protein group" compared to the "simple sugar group" (107).

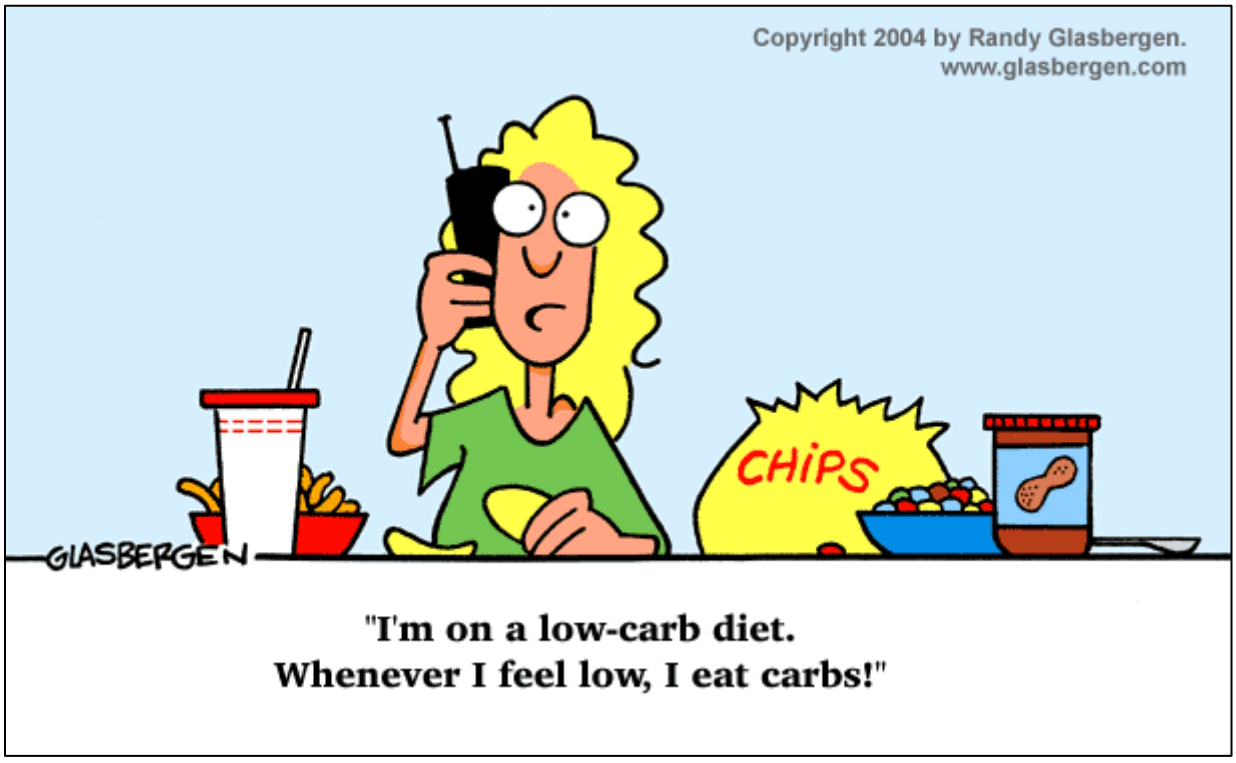

Figure 7. *Cartoon from www.glasbergen.com*

Meal replacements and fructose

One way to accomplish a VLCD or a LCD is to use meal replacements, and replace either all or some of the meals during the day with these products. There are different

meal replacements available on the market, ranging from bars, soups and shakes. Some replace one or two meals during the day with such products, while others only use these meal replacements during a certain period of time. Many of the available products consist of a considerably amount of mono- and disaccharides, where fructose is one of the main ingredients. High intake of fructose has been suggested to have an important participatory role in the expansion of the global obesity epidemic, and the development of hypertension, diabetes, metabolic syndrome and cardiovascular disease among others (108). Teff et al discovered in 2004 that high intake of fructose influences negatively the levels of insulin and leptin, which may therefore interfere with appetite regulation and calorie intake, and may affect the long term regulation of energy homeostasis, thus leading to increased weight. Furthermore, fructose intake may give prolonged elevation of triglycerides in plasma compared to similar intake of glucose (109). Recently, Stanhope et al assessed the relative effects of consuming either glucose- or fructose-sweetened beverages, providing 25 % of the energy requirements for ten weeks, in overweight and obese persons. The results suggested that a high intake of fructose may lead to increased hepatic de novo lipogenesis, promote dyslipidemia, decrease insulin sensitivity and enhance the visceral adiposity in overweight or obese subjects (110).

Meal replacements and soy protein

The source of protein in meal replacements differ between the available products. Many of these products use soy protein as the protein source. Soy protein intake may have effects on serum lipids, as shown by a meta-analysis done by Anderson et al. They found that ingestion of soy protein was associated with lower levels of total cholesterol, decreased LDL-cholesterol, and a decrease in triglyceride concentration compared to control diets (111). In an intervention study comparing the weight loss and lipid changes after a 12 weeks low-calorie diet consisting of either five soy-based meal replacements or two milk-based meal replacements and two servings of lean meat, the researchers reported a slightly higher weight loss in the “soy group”. The reduction in levels of total cholesterol, LDL-cholesterol and triglycerides were higher

at six weeks than 12 weeks with both diets. The group using soy-based meal replacements was associated with lower values of all these three lipid parameters after both six and 12 weeks, compared to the group who consumed milk-based meal replacements (112).

Whole grain food and dietary fibre

Whole grain products with their high content of dietary fibre are associated with a better health profile. An abundant intake of dietary fibre reduces the risk for developing several diseases; coronary heart disease, stroke, hypertension, diabetes, obesity and certain gastrointestinal disorders. In addition, higher intake of dietary fibre improves serum lipid concentrations, lowers blood pressure, improves blood glucose control in diabetes, aids in weight loss and appears to improve immune function. The dietary fibre sources are whole-grain products, vegetables, fruits, legumes and nuts, and products having dietary fibre as a supplement. Dietary fibre is classified as soluble fibre (viscous or fermentable fibres), which are fermented in the colon, and insoluble fibres, that to a limited extent get fermented in the colon and serve as bulking agents (113).

A review of current studies demonstrated that intake of whole grain food reduced the risk for cardiovascular disease. The exact mechanisms remain unclear, and the effect may be due to the high content of cereal fibre, but also valuable nutrients found in whole grains, as vitamin E, magnesium, folate, vitamin B6 and phytochemicals. Flight et al summarises the reported effects of cereal fibre on coronary heart disease events as to not have an independent effect alone, but is probably best obtained from whole grain sources (114).

1.6 Energy intake and energy expenditure

1.6.1 Dietary assessment

Information about people's dietary habits and food pattern can be obtained using several methods. The methods differ in design, structure and performance. An important part of the collecting procedure is that the technique chosen is not to intensely applied as well as comprehensive, making the subject changes his/hers dietary patterns and habits. Two frequently used methods are the food frequency questionnaire (FFQ) and dietary record (DR).

Food frequency questionnaire (FFQ)

This is a retrospective review of the food intake, based on the frequency of consumption of different food groups. Food items are organized into groups, according to their nutrient content. The obtained information is about the frequency of ingested food groups, and grouped like "eaten each day", "twice per week", "once per month" etc, giving general information about ingested nutrients, and not specific information for each nutrient alone. FFQ gives estimates of the usual or habitual diet and dietary patterns at a group level. The FFQ can be administered as a questionnaire which the patients will fill in themselves, or a dietician can use it as a template in a dietary interview.

Dietary record (DR)

When DR is used, the person itself document dietary intake as it occurs during the day, by recording the food eaten, usually in household measures like spoons and cups. This is done for a given time interval, usually consisting of 3 – 7 days. After the recorded period, the nutrient intake is calculated and then averaged, and can be compared to dietary references and recommendations (115).

1.6.2 Reporting of food intake

When energy derived from food exceeds the energy used by the body, the net result will be weight gain. On the other hand, if energy expenditure (EE) exceeds energy intake, net weight reduction will occur. EI and EE are equal during periods of stable body weight. When people are asked to give information about their food habits and dietary pattern, they tend to misreport the actual food intake. Physical and psychological characteristics influence on the reporting. A relationship between under-reporting and increasing adiposity in subjects have been suggested. Poor body image and weight consciousness may also affect the inaccurate reports of EI, or the misreporting of energy intake can be due to dieting and dietary restraint, low social class and educational level (116).

There are several methods to validate the reported food intake, like doubly labelled water (DLW), total water loss, resting metabolic rate and physical activity. Studies using the DLW technique have been revised, and in the majority of the studies a lower value of reported energy intake (rEI) compared to measured total energy expenditure (TEE) were reported. For normal-weight individuals the average underreporting of energy intake were 16 % less than the estimated energy expenditure (kcal), ranging from 0-25 %. In obese subjects the average underreporting values were in the 25-50 % range, averaging of 41 %. Obese persons generally under-reported twice as much as normal-weights. A difference between the genders has not been reported (117). A study of a representative sample of Norwegians aged 16 – 79 with a BMI of 24.6 and 23.4 for men and women respectively, showed an underreporting of 38 % among men and 45 % among women (118).

Reported food intakes among obese persons tend to be less than estimated total energy expenditure. Svendsen et al examined 50 obese persons, using a dietary interview based on a food-frequency questionnaire, and the participants also completed a recorded diary. Energy intakes were compared to energy expenditures measured by the doubly labelled water method. They indentified 28 subjects (12

males and 16 females) as under-reporters and 22 persons (11 males and 11 females) as non-under-reporters of energy intake by the FFQ. The same amount of under-reporters and non-under-reporters of energy intake were estimated by using dietary records as well. According to the FFQ, energy intake was underreported by 14.1 % among all the men and by 20.6 % among all the women. Dietary records revealed an underreporting of 27.9 % and 31 % for men and women respectively (119).

Misreporting of specific food items is linked to the experience of what is "good and bad" for health. Among under-reporters, energy derived from protein tends to be higher, while a lower contribution of energy from carbohydrates and fat are also common. The absolute intakes of these nutrients are all lower in under-reporters than non-under-reporters (118;120).

1.6.3 Estimating energy expenditure

Total energy expenditure is the total energy expended by a person during 24 hours. Energy costs are basal energy expenditure (BEE), active exercise and nonexercise activity thermogenesis, and the thermic effect of food. To estimate the total energy expenditure among humans, the doubly labelled water is the gold standard. However, it is limited in use because of its expensiveness. Another method, called indirect calorimetry, measures the resting metabolic rate, which is the amount of energy expended for the maintenance of normal body functions and homeostasis. RMR is 10-20 % higher than the basal metabolic rate (BMR), which is the energy needed to maintain the metabolic activities of cells and tissues; all the physiological functions in the body (121). There are several predictive equations for estimating the resting metabolic rate in humans. The American Dietetic Association reviewed the validity of different predictive equations, in both non-obese and obese people. They concluded that the Mifflin-St Jeor equation "is more likely than the other equations tested to estimate RMR to within 10 % of that measured" (122). The equation for resting metabolic rate designed by Mifflin and St Jeor is as follow: RMR (kcal/d) = 9.99 x weight (kg) + 6.25 x height (cm) – 4.92 x age + 166 x sex (males = 1, females

= 0) -161 (123). By knowing the RMR, the TEE can be estimated by multiplying the RMR with an activity factor. The Nordic Nutrition Recommendations (NNR) from 2004 has different estimates of physical activity level (PAL) as indicated in table 2.

***Table 2**. Estimates of physical activity levels expressed as multiplies of resting energy expenditure according to different levels of occupational and leisure activity. Adapted from Nordic Nutrition Recommendations 2004, page 122 (9).*

	PAL
Bed-bound or chair-bound (not wheelchair)	1.1 – 1.2
Seated work with no option of moving around and little or no leisure activity	1.3 – 1.5
Seated work with some requirement to move around but little leisure activity	1.6 – 1.7
Work including both standing and moving around (e.g. housework, shop assistant)	1.8 – 1.9
Very strenuous work or daily, competitive training	2.0 – 2.4

Energy expenditure increases with weight or the fat free mass. Estimating of RMR by the equations is based on the individual's weight, making the calculated RMR greater with increasing weight. Obese persons are comprehended as sedentary, but weight-bearing activities in a large body require more energy than in a lean individual (124). A study from 2008 demonstrated an average PAL factor of 1.71 for healthy Danish men and women. PAL for the women alone were 1.68 (125). Hustvedt et al measured energy expenditure and physical activity using ActiReg and doubly labelled water in Norwegian, obese persons. Comparing the TEE, measured by DLW, with the measured RMR by indirect calorimetry, they discovered an average PAL among the obese of 1.8. These were fifty obese, non-smoking men and women with mean BMI 34.9 and 36.6, respectively (126). Das et al examined 30 extremely obese women with a BMI between 37.5 and 77 using DLW and indirect calorimetry. The subjects were placed into three groups based on their BMI. TEE and RMR were significantly greater in the highest BMI tertile compared to the lowest BMI tertile, but when adjusting for FFM, no significant differences were observed. There was no difference between the groups according to PAL, which were in average 1.63 (1,61, 1,67, 1,62) (127). Johannesen et al investigated the energy expenditure among ten lean and ten

obese women (average BMI 23 and 32.7 respectively), and discovered PAL-values of 1.75 and 1.59, respectively. Adjusting the TEE for fat free mass, TEE was significantly lower among the obese women. Absolute RMR was greater in the obese women, but after controlling for FFM and FM the significant difference disappeared. Furthermore they discovered that the obese women expended almost 400 kcal less in activity per day than the lean individuals. The obese women spent significantly more time with sedentary activities and rest each day. The obese and the lean women reported the same intake of total kilocalories, carbohydrate, protein and fat. By allowing for the actual weight change during the period, both groups underreported their caloric intake by about 300 kcal. Seven of the ten obese and eight of the ten lean women underreported their intake (128).

2. Aims and hypothesis

The master thesis consist of two separately parts, where part one includes analyses of reported food intake among morbidly obese women compared to normal weight control women in the MOBIL-study (Morbid Obesity treatment, Bariatric surgery versus Intensive Lifestyle intervention). Part two is a preliminary report of a weight reduction study on two different low calorie diets in morbidly obese women with PCOS. The main objective was to assess the effects of low-calorie-diet, and to compare the effects of two different low-calorie-diets, on anthropometric measures, body composition, lipid profile and adipokines.

My master thesis focuses on markers for cardiovascular disease as blood lipids, body composition as well as adipokines, while the master thesis of Linn Mari Gunnarsrud Bjørnådal puts emphasis on blood glucose, insulin resistance and the hormone profile due to PCOS among these women.

2.1 Part one – Analyses of reported food intake in the MOBIL-study

2.1.1 Aim of the master thesis

The objective was to explore the reported food and energy intake among morbidly obese women referred to a regional tertiary care centre (Morbid Obesity Centre) at Vestfold Hospital Trust, comparing the obtained information to the reported food and energy intakes among healthy lean control women. In addition, among the morbidly obese women the associations between reported food intake and anthropometric measures and blood parameters were investigated.

2.1.2 Hypotheses

- Morbidly obese women have a more unfavourable lipid profile and expression of the adipokines, leptin and adiponectin, than healthy normal weight control women
- Morbidly obese women have a different composition of their diet with regard to energy and macronutrient intake and choices of food items compared to healthy normal weight control women
- Morbidly obese women underreport their energy intake to a larger degree than healthy normal weight control women
- Morbidly obese women with a free testosterone index (FTI) score > 0.6 (pre-PCOS) have a more unfavourable anthropometry, lipid profile, adipokine profile and reported food, energy and macronutrient intake than morbidly obese women with an FTI score ≤ 0.6

2.2 Part two – PCOS women and effect of weight loss – preliminary results of the FEMIN study

2.2.1 Aim of the master thesis

The objective was to explore the effects of eight weeks with low-calorie-diet, and to compare the effects of two different low calorie diets, one based on crisp bread, the other based on flavoured powder solved in water, on different parameters, for instance weight loss and lipid profile, among obese women with PCOS recruited to "Kvinnehelsesenteret", "Kvinneklinikken" at Rikshospitalet. These women were part of the Female Health Dietary Intervention study – the FEMIN study. However, due to delayed accept from the safety delegate on the inclusion of women from Aker University Hospital HF, only a small number (n=10) of obese women with PCOS were included in the study.

2.2.2 Hypotheses

- Eight weeks on a low-calorie-diet leads to significant improvement in markers for cardiovascular disease
    - Improved body composition
    - Improved lipid profile, CRP and blood pressure
    - Improved adipokine profile (adiponectin and leptin)
- Achieved improvements in markers for cardiovascular disease are different between the crisp bread diet and the powder diet of eight weeks duration leading to different improvement in body composition, lipid profile, CRP, blood pressure and adipokine profile.

3. Methods

3.1 Analyses of reported food intake in the MOBIL-study

3.1.1 Case recruitments

Between December 2005 and May 2006, 228 morbidly obese patients (BMI ≥ 40 or ≥ 35 kg/m2 with weight-related co morbidity) were consecutive screened at a regional tertiary care centre for participation in the MOBIL Study. Exclusion criteria were lacking of informed consents, patients in need of nursing and patients who could not go through an intensive lifestyle intervention due to health related reasons. A total of 181 patients were found eligible for either bariatric surgery or intensive lifestyle intervention, and included in the non randomized study. The two groups were matched with regard of sex, age and BMI. Normal weight employees at the Vestfold Hospital Trust entered the study as controls after advertisement at the hospital. We received baseline data from 189 subjects, of which 159 were morbidly obese patients and 30 were normal weight controls. One-hundred-and-sixteen of the morbidly obese patients, and 20 of the 30 controls, were women. Baseline data from these 136 women were used in our analysis of diet history, diet composition and underreporting of energy. In our study the term “obese women” is frequently used, meaning the 116 morbidly obese women. The primary aim of the MOBIL-study was to compare the effects of bariatric surgery and intensive lifestyle intervention on various co morbidities, food intake and quality of life.

A total of 116 obese women aged 18-65 years with a median BMI of 44; together with 20 normal weight controls (median BMI 23) aged 30-54 years were included in our study.

3.1.2 Data collection

Clinical and biochemical characteristics

All participants underwent a medical examination by a physician, and demographic data and medical history were recorded on standardized forms. Weight and height were measured in patients wearing light clothing without shoes. BMI was calculated as weight in kilograms divided by the square of the height in meters. Waist circumference was measured at the level midway between the lowest rib margin and the iliac crest. Hip circumference (H.C.) was measured over the widest part of the hip. Blood was collected by venipuncture following an overnight fast. Fasting sera were analysed for markers of interest; triglycerides, total cholesterol, LDL-C, HDL-C, glucose, insulin, HbA1C, leptin, adiponectin, testosterone and SHBG. Data on apolipoprotein A and apolipoprotein B were not available in the MOBIL-study. Markers of the glucose metabolism were analysed and discussed by master thesis student Linn Mari Bjørnådal.

Food frequency questionnaire

Information about diet and dietary pattern were obtained by dietary interview based on an optical readable FFQ, developed by the Department of Nutrition, University of Oslo (for FFQ, see Appendix 1). The interviews were performed by trained clinical nutritionists at the regional tertiary care centre (Morbid Obesity Centre) at Vestfold Hospital Trust, lasting between one and two hours. The FFQ contained approximately 180 food items and courses. Subjects were asked to describe their diet during the last year, and describe how often the food items and courses were used (pr day, week or month) and in what quantity (units or household measures). Questions about food supplements, physical activity and medical history were also a part of the FFQ. The FFQs were scanned, optical read and controlled. Daily intakes of foods, energy and nutrients were computed using a computation program which has linkage to the Norwegian food composition table, and further analyzed in the computer program SPSS.

Because of low average intake of specific foods, some food items were grouped into the same food group. Other food items where the average intake was higher, the food item constitute the group itself. Following are the used food items and food groups based on the food item database IE96 (boldfaced words are the main groups):

Table 3. *Food items and food groups used in the analyses of reported food intake from the dietary interview based on the food frequency questionnaire. Boldfaced words are the main groups, words below are subgroups.*

• **Bread** - white bread - whole-grain bread	• **Egg**
• **Cereal products**	• **Milk/cream/ice cream** - whole milk - partly-skimmed milk - skimmed milk - yogurt - ice cream
• **Cakes**	• **Cheese**
• **Potatoes**, - fresh potatoes - pommes frites	• **Butter/margarine/oil** - oil/other fat
• **Vegetables**	• **Sugar/sweet stuff** - chocolate - sweets
• **Fruits/berries**	• **Drinks** o Coffee o Tea o squash/soft drink (with sugar) - soft drink with sugar - squash with sugar o squash/soft drink (light) - soft drink (artificially sweetened) o water, mineral water o beer o wine, liquor
• **Meat/blood/entrails/pluck** - whole meat/minced meat - forcemeat	• **Various** - potato chips - other snacks - fat fruit/seeds
• **Fish/shellfish** - fish spreads	

Selected PAL values

Former studies reporting physical activity levels among obese subjects have reported different values. Hustvedt et al measured energy expenditure and physical activity using ActiReg and doubly labelled water in Norwegian, obese persons. Comparing the TEE, measured by DLW, with the measured RMR by indirect calorimetry, they discovered an average PAL among the obese of 1.8. These were fifty obese, non-smoking men and women with mean BMI 34.9 and 36.6, respectively (126). With regard to our obese women these persons had lower body mass indexes and they were equipped with ActiReg for a period of time, which might have influenced their activity level. On the other hand, Johannsen et al reported a PAL value of 1.59 among obese women (mean BMI 32.7) (128). Furthermore, Das et al, who examined women with a BMI between 37.5 and 77 using DLW and indirect calorimetry, found an average PAL value for the whole group to be 1.63. They also split the women into BMI tertiles, and women with BMI between 37.5 – 45 (mean 40.8) had PAL 1.61, while women with BMI between 45.1 – 52 (mean 49.47) and BMI between 52.1 – 77 (mean 60.3) had PAL values of 1.67 and 1.62 respectively (127). According to this, we decided to use a PAL value of 1.6 when estimating the total energy expenditure among our obese women. The PAL value selected to the healthy lean controls was 1.8, according to NNR and based on the information about their work (9). This level is higher than demonstrated in a Danish healthy population (125), but we assumed that our control women were more physical active due to their work and health occupation, as they are health workers.

Definition of under-reporters and non-under-reporters of energy

Subjects were identified as under-reporters or non-under-reporters based on calculation of the reported energy intake (rEI) and the estimated total energy expenditure (eTEE):

$rEI - eTEE = < 0 \geq$

According to this calculation, subjects who reported an intake that was less than the estimated TEE were classified as under-reporters. Subjects defined as non-under-reporters had a reported energy intake higher than the estimated TEE.

Definition of pre-PCOS women

We were interested in studying if there was a difference in anthropometry, lipid and adipokine profile, diet composition and underreporting of energy between the obese women with PCOS versus the obese women without PCOS. In lack of PCOS diagnosis in the MOBIL-study, a surrogate marker for PCOS was chosen; free testosterone index score. FTI was calculated by using measured serum total testosterone and SHBG, parameters which indicates hyperandrogenemia. The reference value for FTI among women is 0.1 – 0.6. Women with PCOS have FTI scores around 1 (65;66). Since the reference value is up to 0.6, a FTI score above 0.6 may indicate the beginning of a PCOS diagnosis. We therefore decided to classify women with FTI > 0.6 as pre-PCOS subjects.

3.1.3 Statistical methods

The computing program SPSS for windows (version 16.0) was used to perform the statistical analysis in the study. The data were evaluated in regard to normal distribution by means of Shapiro-Wilk test of normality, histograms and Q-Q plots. The principal data were non-normally distributed, and the control group of women was small. Therefore, non-parametric tests were used. The results are presented as medians, point estimates and 95 % confidence intervals (CI) for the point estimates. Median differences were tested with the non-parametric test Mann-Whitney U test. The results were considered significant at $p< 0.05$. After consultation with the statistician Petter Laake, we agreed that p-values between 0.05 and 0.1 were interpreted as a *tendency* toward significance. Furthermore, after advice from Petter Laake, normally distributed data which almost reached significant differences between the groups were further investigated with a parametric test, independent-samples t-test. Statistically significant correlation between different variables was

calculated with the non-parametric Spearman rank order correlation (rho). Significant correlation was considered at $p< 0.05$, and the significant correlations are expressed as rho-values.

3.2 PCOS women and effect of weight loss – preliminary results of the FEMIN study

3.2.1 Case recruitments

Women attending "Kvinnehelsesenteret", "Kvinneklinikken" at Rikshospitalet University Hospital HF in Oslo diagnosed with PCOS, aged 19 to 38 years, having a BMI > 35 kg/m^2 were invited to participate in the FEMIN study (information letter given to the women, see Appendix 2). Obese females with possible PCOS diagnosis coming to Aker University Hospital HF were also asked if they wanted to participate in the study. If interested, they were sent to Rikshospitalet to get the PCOS diagnosis confirmed by ultrasound. Subjects were excluded if they had a BMI < 35 kg/m^2, were pregnant or breastfeeding, had other medical conditions as Cushing's syndrome and androgen producing cysts/ tumours, used oral or parenteral contraceptives, used medicaments to improve insulin sensitivity (metformin) or had anovulation due to hyperprolactinemia. Participants had to quit using oral contraceptive or other hormone treatment four weeks or two weeks respectively, before the study start. The women who agreed to participate were block randomized, in blocks of six. Three were placed in the powder diet group, and the last three to the crisp bread diet group. The time of randomization was at the same time as the women were summoned to Rikshospitalet for the first meeting (second information letter sent to the women together with the summons, see Appendix 3).

A total of ten women aged 19-37 years, were included in our study. Five women were randomized to the crisp bread diet, while the other five women were randomized to the powder diet. Due to heavily problems drinking the powder shakes, one woman dropped out from the powder diet after few days on the diet. She had great desire to

accomplish an eight weeks diet, and she asked to be transferred to the crisp bread diet. According to the protocol she was no longer part of the FEMIN study, but due to our small selection of women, we decided to let her continue on the crisp bread diet in our study. Furthermore, one of the women in the crisp bread diet group did not attend the second visit, then becoming a "drop out". Therefore, we had nine participating women in our study, five on the crisp bread diet and four women in the powder diet group.

3.2.2 Data collection – visit 1

Anthropometry, blood pressure and blood samples

The women's standing body height (cm) were measured to nearest cm. Body weight (kg) was assessed using a computerized Bioelectrical impedance analysis (BIA) (Tanita BC-418MA), and was measured to the nearest 0.1 kg. The subjects were barefoot and lightly clothed, and one kilogram was subtracted for the clothes. Body composition as fat free body mass, total fat mass and percent body water were estimated by the BIA. Waist circumference was measured between the lowest rib and the iliac crest using a non-elastic tape measure. Hip circumference was measured over the widest part of the hip. A newly accepted marker for insulin resistance/central obesity is the neck circumference, which was also measured at the same time (129). We calculated body mass index as a measure for overall body composition and waist-to-hip-ratio as measure of abdominal fat distribution. The blood pressure was measured by an automated device, while the subjects were in a seated position. Blood samples were collected from all patients by trained nurses between 0800 and 1100 hours, after an overnight fast. They were centrifuged immediately and stored at - 80 ºC until assayed. Anthropometric measures and blood pressure were performed by a clinical nutritionist, Line Kristin Johnson, or by the two master thesis students, Linn Mari Bjørnådal and Hanne Lessner, following standardized procedures. Data collection was done at baseline and after 8 weeks with one of the diets. Fasting sera were analyzed for markers of interest; triglycerides, total cholesterol, LDL-C, HDL-

C, apolipoprotein A, apolipoprotein B, glucose, insulin, c-peptide, HbA1C, Hs CRP, leptin, adiponectin, SHBG, LH and FSH. Markers for the glucose metabolism and PCOS status were analysed and discussed in the master thesis by Linn Mari Bjørnådal.

Questionnaires and hirsutisme score

During visit one, at baseline, the obese women were asked to fill in four questionnaires; a food frequency questionnaire (the same as was used in the MOBIL-study, see Appendix 1), a questionnaire about life quality and PCOS, the gastrointestinal symptom rating scale (GSRS) and a questionnaire about personally experienced health/life quality (SF 36). Hirsutism was classified according to the Ferriman-Gallwey score(130). Data obtained from these questionnaires and from the Ferriman-Gallwey score were not a part of my master thesis, and therefore the results are not referred to in my master thesis. However, data on hirsutism score and the GSRS are described in the master thesis by Linn Mari Bjørnådal.

3.2.3 Weight reduction period

The included PCOS women were randomized to either of the low-calorie diets; the "crisp bread diet" or the "powder diet" (meal replacement shakes). Both diets consisted of less than 1000 kcal per day. The participants got thorough information about the diet they were randomized to, and they received enough crisp breads or meal replacement shakes for eight weeks duration. The PCOS women started as soon as possible on the intensive weight reduction period lasting for eight weeks. During the weight loss phase, the clinical nutritionist, Line Kristin Johnson, or the master thesis students called the women once a week, to give them moral support, as well as the participants were given the opportunity to ask questions and reel off their frustrations.

The crisp bread diet

The crisp bread diet was based on easily accessible Norwegian food items, dispersed on four meals, where crisp bread was used in three of these four meals. Crisp bread from Wasa, Ideal Wasa A/S, was used, mainly "Wasa Husman", "Wasa Fibre Plus" and "Wasa Sport". These crisp breads are made of whole grain rye, and have a high content of dietary fibre. During the day, the women were supposed to eat six crisp breads dispersed on breakfast, lunch and supper, and they had to select from three groups of different spreads. One crisp bread should have a spread of fatty fish, another with a sparingly amount of cottage cheese or another low-fat (3%) cheese. The spreads for the last four crisp breads were lean meat (e.g. ham, turkey, lean liver pate) or fish (e.g. crabsticks, fish pudding). One glass of skimmed milk was included in each of these meals. The dinner was composed of a certain amount of lean meat, fish or poultry, or fatty fish, and a small amount of potato, rice or pasta. In addition there were no restrictions on the intake of vegetables (raw or boiled). Furthermore, one fruit per day was allowed, and the participants were recommended to take a multivitamin pill daily, and use one teaspoon soy margarine during cooking. The women were encouraged to drink a lot of water and other drinks without calories. See Appendix 4 for the nutrient composition of the crisp bread diet, and Appendix 5 for further description of the diet.

The powder diet - meal replacement shakes

Flavoured powders from Nutrilett, Axellus AS, were utilized by the women who used

this diet. The shakes were solved in water to generate shakes with either chocolate or strawberry flavour. Each day, the women had to drink eight such shakes supplying a total of 888 kcal. The flavoured powders contained mainly soy protein, fructose and soy fibres, and as well vitamins and minerals. Five of these shakes (providing 555 kcal) would provide enough of the essential nutrients that the body need per day. In addition to the shakes, the women were allowed to eat a few vegetables low in dietary fibre, like different types of salad, cucumber, tomato, onion, garlic, paprika and mushrooms, and also 150 grams of root vegetables (carrots, turnip cabbage, broccoli etc.) and one fruit per day. The women were encouraged to drink a lot of water and other drinks without calories. See Appendix 4 for nutrient content of the powder diet, and Appendix 6 for the description of the diet.

3.2.4 Data collection – visit 2

After eight weeks, the participating women were summoned to visit number two. The same procedure regarding anthropometric measures, blood samples and blood pressure were used, as described earlier. During the second visit they completed three of the same questionnaires they filled in at visit 1 (not the FFQ). At the end of the visit they got instructions to increase the calorie content of their diets to 1300 kcal, and they received a pedometer as reward for completing the eight weeks of diet.

3.2.5 Statistical methods

The computing program SPSS for windows (version 16.0) was used to perform the statistical analysis in the study. The data were evaluated in regard to normal distribution by means of Shapiro-Wilk test of normality, histograms and Q-Q plots. The achieved differences ((Δ), baseline data – eight weeks data) in different parameters after the low-calorie-diet (both together) at eight weeks from baseline were normally distributed. Therefore a parametric test were used; one-sample t-test, to assess whether these differences (Δ) were significant from baseline. Furthermore, to assess possible differences between the two diet groups with regard to the achieved

changes (Δ) in the different parameters within each group, we used independent-samples t-test after advice from the statistician Petter Laake. The results are presented as means ± standard deviations (SD), achieved mean differences (Δ) and 95 % confidence intervals for the mean differences. The results were considered significant at $p< 0.05$. After advice from Petter Laake, p-values between 0.05 and 0.1 were interpreted as a *tendency* toward significance. Statistically significant correlation between different variables was calculated with the non-parametric Spearman rank order correlation (rho). Significant correlation was considered at $p< 0.05$, and the significant correlations are expressed as rho-values. Comparison of baseline characteristics and also after eight weeks measurements, were done by a non-parametric test, due to a small number of women in each diet group and thereby impossibility to predict the distribution of the data. Median differences were tested with the non-parametric test Mann-Whitney U test.

4. Results

4.1 Analyses of reported food intake in the MOBIL-study

4.1.1 Characterization of the morbidly obese women and the normal weight control women

Anthropometric measures

A characterization, by anthropometric measures, of the 116 morbidly obese women and the 20 healthy normal weight controls who participated in the present study is summarized in table 4. As expected, all anthropometric measures (except height) were significantly higher among obese women than among the lean control women.

Table 4**. Anthropometric measures of the morbidly obese women and the normal weight control women (median values, point estimates for difference with 95 % confidence interval are given when significant difference between the groups were observed)* **

ANTHROPOMETRY	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Age (y)	42.0	44.1	-	-	0.825
Weight (kg)	**120.0**	**64.9**	**57.5**	**(51.0 ; 65.0)**	**< 0.001**
Height (cm)	167.0	167.5	-	-	0.863
Body Mass Index (kg/m²)	**43.9**	**22.9**	**21.0**	**(19.0 ; 23.0)**	**<0.001**
Waist circumference (cm)	**128.0**	**77.0**	**52.0**	**(47.0 ; 58.0)**	**<0.001**
Hip circumference (cm)	**137.0**	**98.0**	**38.0**	**(34.0 ; 43.0)**	**<0.001**
Waist-to-hip ratio	**0.95**	**0.76**	**0.17**	**(0.13 ; 0.20)**	**<0.001**

***** *Differences between the obese and control women were tested with the Mann-Whitney U test.*

Lipid profile

Characteristics of the obese women and the control subjects according to their lipid profile are shown in table 5. Analyses of the blood samples demonstrated that there were statistically significant differences in the median concentrations of total cholesterol, LDL-C, HDL-C and triglycerides between the obese women and the lean control women.

Table 5**. Lipid profile of the morbidly obese women and the normal weight control women (median values and point estimates for difference with 95 % confidence interval) **

LIPID PROFILE	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Total cholesterol (mmol/L)	**5.2**	**4.4**	**0.7**	**(0.1 ; 1.1)**	**0.014**
LDL-cholesterol (mmol/L)	**3.2**	**2.4**	**0.8**	**(0.4 ; 1.1)**	**<0.001**
HDL-cholesterol (mmol/L)	**1.2**	**1.8**	**-0.5**	**(-0.7 ; -0.4)**	**<0.001**
Triglycerides (mmol/L)	**1.5**	**0.6**	**0.8**	**(0.6 ; 1.1)**	**<0.001**

***** *Differences between the obese and control women were tested with the Mann-Whitney U test*

The relationships between the anthropometric measures and the lipid profile were investigated using Spearman rank order correlation (rho). For both groups, the total cholesterol level was correlated to age. Among the obese, triglyceride level were correlated to age, waist circumference and the waist-to-hip ratio. In the control women, total cholesterol level and the concentrations of LDL-C and HDL-C were correlated to the waist circumference. The LDL-C and HDL-C levels were also correlated to the waist-to-hip ratio. Furthermore, the HDL-C concentration correlated to age, while the triglyceride level was negatively correlated to height (table 6 & 7).

***Table 6**. The relationships between the lipid profile and anthropometric measurements among the obese women (Spearman's correlation coefficient rho). Negative rho indicates negative correlation. Only significant correlations are stated.*

OBESE WOMEN (n=116)	**Age**	**Weight**	**Height**	**BMI**	**W. C.**	**H. C.**	**WHR**
Total cholesterol	0.27**	-	-	-	-	-	-
LDL-cholesterol	-	-	-	-	-	-	-
HDL-cholesterol	-	-	-	-	-	-	-
Triglycerides	0.18*	-	-	-	0.21*	-	0.24*

BMI = body mass index. W.C. = waist circumference. H.C. = hip circumference. WHR = waist-to-hip ratio.
***** *Correlation was significant at the 0.05 level.*
****** *Correlation was significant at the 0.01 level*
- = not significant correlation

***Table 7.** The relationships between the lipid profile and anthropometric measurements among the normal weight control women (Spearman's correlation coefficient rho). Negative rho indicates negative correlation. Only significant correlations are stated.*

CONTROL WOMEN (n=20)	**Age**	**Weight**	**Height**	**BMI**	**W. C.**	**H. C.**	**WHR**
Total cholesterol	0.52*	-	-	-	0.54*	-	-
LDL-cholesterol	-	-	-	-	0.55*	-	0.50*
HDL-cholesterol	0.51*	-	-	-	0.45*	-	0.49*
Triglycerides	-	-	-0.46*	-	-	-	-

BMI = body mass index. W.C. = waist circumference. H.C. = hip circumference. WHR = waist-to-hip ratio
** Correlation was significant at the 0.05 level.*
*** Correlation was significant at the 0.01 level.*
- = not significant correlation

4.1.2 Adipokines

The levels of the adipokines leptin and adiponectin were investigated, and the obese women had significantly elevated concentrations of leptin and lower levels of adiponectin compared to the healthy, lean control women (table 8).

Table 8**. The adipokine profile of the morbidly obese women and the normal weight control women (median values and point estimates for difference with 95 % confidence interval)* **

ADIPOKINE PROFILE	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Leptin (ng/ml)	**60.1**	**14.9**	**46.1**	**(39.5 ; 53.1)**	**<0.001**
Adiponectin (ng/ml)	**5452**	**8017**	**-2488**	**(-4246 ; -937)**	**0.002**

***** *Differences between the obese and control women were tested with the Mann-Whitney U test.*

Furthermore, we investigated the correlation between the adipokines and different anthropometric parameters and lipid values using Spearman rank order correlation (rho). Among the obese, leptin was positively correlated to weight, BMI and waist- and hip circumference. With regard to the levels of adiponectin, which was significantly lower among the obese women, adiponectin was negatively correlated to weight, BMI and waist circumference among the obese subjects, while the levels of HDL-C were positively correlated with adiponectin (table 9). Among the control women, significant positive correlation ($p<0.05$) between the level of leptin and waist circumference (rho = 0.51), LDL-C concentration (rho = 0.51) and triglyceride level (rho = 0.24) were observed.

Table 9. *The relationships between the adipokines and anthropometric measurements and among the obese women (Spearman's correlation coefficient rho). Negative rho indicates negative correlation. Only significant correlations are stated*

OBESE WOMEN (n=116)	Age	Weight	Height	BMI	W. C.	H. C.	HDL-C
Leptin	-	0.44**	-	0.48**	0.33**	0.48**	-
Adiponectin	-	-0.26*	-	-0.22*	-0.27**	-	0.24*

BMI = body mass index. W.C. = waist circumference. H.C. = hip circumference. WHR = waist-to-hip ratio
***** *Correlation was significant at the 0.05 level.*
****** *Correlation was significant at the 0.01 level.*
- *= not significant correlation*

4.1.3 Energy intake and macro nutrients

The two groups were compared in order to explore differences in the reported energy intake and/or the macro nutrient composition (table 10). The obese women had a median intake of energy of 2603 kcal, while the control women had 2301 kcal as the median. This difference in 300 kcal was not statistically significant. The reported intake of protein, carbohydrate, sugar and fibre separately were not significant different between the two groups. The fat intake tended to be higher among the obese women compared to the control subjects (p-value 0.087). When analyzing for differences in the intake of the different types of fat, we observed a trend among the obese women to have a higher intake of saturated fat compared to the control women (p-value 0.077). Ingestion of monounsaturated fat and polyunsaturated fat were not significantly different between the groups. Finally, the data showed that the control women drank significantly more alcohol than the obese women (p-value <0.001).

Table 10. *Intake of macronutrients among the morbidly obese women and the normal weight control women (median values, point estimates for difference with 95 % confidence interval are given when significant difference between the groups were observed)* *******

MACRONUTRIENTS	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Energy intake (kcal)	2603	2301	-	-	0.124
Protein intake (g)	105	103	-	-	0.527
Fat intake (g)	***111***	***91***	***16.2***	***(-2.5 ; 34.5)***	***0.087*****
-saturated fat (g)	***43***	***36***	***6.6***	***(-1.0 ; 15.2)***	***0.077*****
-monounsaturated fat (g)	37	31	-	-	0.131
-polyunsaturated fat (g)	20	18	-	-	0.176
Cholesterol (mg)	327	285	-	-	0.424
Carbohydrate intake (g)	287	254	-	-	0.107
-sugar intake (g)	40	34	-	-	0.839
Dietary fibre intake (g)	26	27	-	-	0.619
Alcohol consumption (g)	**1**	**4**	**-2.6**	**(-3.9 ; -1.8)**	**<0.001**

******* *Differences between the obese and control women were tested with the Mann-Whitney U test.*

******** *The difference tended to be significantly different (0.05 < p > 0.1)*

In Norway we have nationwide dietary assessments; the latest updated information about the diet among men and women was published in 1999 (data from 1997) (8). We wanted to compare the diet composition among our participating women compared to the Norkost Survey women, who represent a nationwide selection of women aged 16-79 years. The obese women in the MOBIL-study and the control women had approximately the same contribution of energy from the different macronutrients. Compared to the Norkost Survey women, our women, both the lean and the obese, had more of the total energy from fat and less from carbohydrate. The Norkost Survey women and our control women had the same energy contribution from alcohol; a minor energy percentage from alcohol was seen among the obese women. Furthermore, we compared the diet composition to our participating women to the Nordic Nutrition Recommendations (9). With regard to the NNR, both the

obese and the control subjects had slightly elevated energy percentages from fat and saturated fat compared to the recommendations. Due to the enhanced contribution of energy from fat, the energy percentages from carbohydrate were lower than recommended for both groups (table 11).

Table 11. *Intake of macronutrients as percentages of total energy intake (E%) among the morbidly obese women, the normal weight control women and the Norkost Survey women, together with the recommendations for E % from macronutrients for adults and children from 2 years of age.*

ENERGY PERCENTAGES	Obese women (n=116)	Control women (n=20)	Norkost women (n=1374) *	NNR **
Energy percent from				
Protein (%)	16.6	17.5	16.2	10-20
Fat (%)	36.7	36.1	30.4	25-35
-saturated fat (%)	14.6	14.9	12.2	< 10
-monounsaturated fat (%)	12.2	12.0	10.7	10-15
-polyunsaturated fat (%)	7.1	6.4	5.2	5-10
Carbohydrate (%)	45.0	45.1	52.1	50-60
-sugar (%)	6.0	6.2	9.1	< 10
Alcohol consumption (%)	0.2 ‡	1.3 ‡	1.4	-

Energy percentages from the different macronutrients were not significantly different between the obese women and the control women in our study, except from E % from alcohol (‡), which was significantly higher among the control women.
***** *data from the Norkost Study (8)*
****** *Recommendations from the Nordic Nutrition Recommendations 2004 (9).*

4.1.4 Intake of food items

Table 12 summarizes the median intake of food items, reported by the obese women and the control subjects. Total intake of food was greater among the obese than the control women. The obese women reported a higher intake of meat and especially processed meat, like sausages and meat loafs. Statistically significant variations in the use of butter, margarine and oils were also observed between the groups, the obese women using a greater proportion of these food items. The drinking pattern was

different in the two groups. The obese women seemed to report overall more drinks than the control women, especially were the consumption of light squash as well as artificially sweetened soft drinks greater among the obese. On the other hand, the control group reported a higher intake of alcoholic beverages.

Table 12. *Reported daily intake of food (g/day) in morbidly obese women and normal weight control women according to dietary interviews based on a FFQ (median values, point estimates for difference with 95 % confidence interval are given where statistically significant differences were observed)* *

FOOD ITEMS (gram/day)	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Total intake	**3632**	**3045**	**561.6**	**(81.1 ; 1074.4)**	**0.022**
Bread	186	172	-	-	0.452
White bread†	-	-	-	-	
Whole-grain bread	80	140	-	-	0.433
Cereal products	58	61	-	-	0.634
Cakes	23	21	-	-	0.980
Potato	64	61	-	-	0.768
Fresh potatoes	51	50	-	-	0.768
Pommes frites	5	6	-	-	0.725
Vegetables	247	281	-	-	0.419
Fruits, berries	189	195	-	-	0.610
Meat, blood, entrails/pluck	**171**	**120**	**45.7**	**(10.3 ; 77.3)**	**0.01**
Whole meat, minced meat	65	57	-	-	0.951
Forcemeat	**76**	**48**	**29.1**	**(8.0 ; 53.1)**	**0.007**
Fish, shellfish	54	64	-	-	0.246
Fish spreads	9	4	-	-	0.512
Egg	16	16	-	-	0.412
Milk, cream, ice cream	294	246	-	-	0.946
Whole milk	0	0	-	-	0.265

FOOD ITEMS (gram/day)	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Partly-skimmed milk	27	16	-	-	0.687
Skimmed milk	0	0	-	-	0.639
Yogurt	15	25	-	-	0.520
Ice cream	7	7	-	-	0.643
Cheese	39	46	-	-	0.640
Butter, margarine, oil	**45**	**26**	**18.4**	**(5.4 ; 30.8)**	**0,003**
Oil, other fat	1	1	-	-	0.276
Sugar, sweet stuff	27	20	-	-	0.665
Chocolate	13	10	-	-	0.824
Sweets	4	6	-	-	0.880
Drinks	***1713***	***1483***	***312.5***	***(-14.0 ; 668.1)***	***0.058*****
Coffee	240	420	-	-	0.356
Tea	0	0	-	-	0.336
Squash, soft drink, with sugar	0	5	-	-	0.211
Soft drink with sugar	0	3	-	-	0.103
Squash with sugar	0	0	-	-	0.165
Squash, soft drink, light	**250**	**0**	**210.0**	**(90.0 ; 465.0)**	**<0.001**
Soft drink, artificially sweetened	**180**	**0**	**180**	**(70.0 ; 465.0)**	**<0.001**
Water, mineral water	649	488	-	-	0.770
Beer	**4**	**51**	**-35.0**	**(-53.0 ; -14.0)**	**<0.001**
Wine, liquor	**3**	**29**	**-19.5**	**(-28.0 ; -12.0)**	**<0.001**
Various	162	125	-	-	0.400
Potato chips	4	2	-	-	0.321
Other snacks	***0 (8 ‡)***	***0 (0.9‡)***	***0***	***(0.0 ; 1.0)***	***0.095 *****
Fatty fruit, seeds	**1**	**5**	**-3.0**	**(-5.0 ; -1.0)**	**0.007**

***** *Differences in reported intake of food among the obese and control women were tested with the Mann-Whitney U test.*

****** *The difference tended to be significantly different*

† data on reported intake was not available
‡ mean intake

4.1.5 Intake of fat and saturated fat and choice of food

Since the consumption of fat among the obese women tended to be higher than among the control subjects, we wanted to investigate the relationships between fat intake and different food items, using Spearman rank order correlation (rho). Ingestion of fat was positively correlated ($p<0.05$) to the intake of these food items among the obese women: bread, white bread, cereals, cakes, potatoes, meat, minced meat, forcemeat, fish, partly skimmed milk, ice cream, cheese, butter, margarine and oil, sugar and sweet stuff, chocolate, sweets, light squash and soft drink and artificially sweetened soft drinks, potato chips, snacks and fatty fruits. Ingestion of saturated fat was positively correlated ($p<0.05$) to the same food items as total fat intake, except from fish. In addition, intake of saturated fat was positively correlated with squash and soft drinks with sugar, in the obesity group.

In the normal weight group, the fat intake was positively correlated ($p<0.05$) to the intake of fewer food items; bread, whole grain bread, meat, mince meat, sugar, sweet stuff, sweets, and was negatively correlated with the consumption of tea. Ingestion of saturated fat was positively correlated ($p<0.05$) to the intake of cakes, pommes frites, meat, sugar, sweet stuff and sweets in the control group (for correlation coefficients, see Appendix 7).

The higher number of positive correlations between the intake of total fat and saturated fat and different food items among the obese women compared to the lean control subjects may suggest that the obese women ate more fat containing food items whereas the fat intakes among the control subjects were restricted to fewer, particularly fatty food items.

4.1.6 Plasma cholesterol level and food items

In the group of obese women, statistically significant ($p<0.05$) negative correlations were found between the plasma level of total cholesterol and intake of cereals and

oils, and between the level of LDL-cholesterol and the intake of alcohol, cereals and snacks (not potato chips).

Among the controls the level of total cholesterol and LDL-C were correlated positively ($p=0.019$) to the intake of potato chips. Plasma level of HDL-C was negatively correlated ($p=0.044$) to reported intake of cheese. The levels of triglycerides and the reported intakes of pommes frites, ice cream and cheese correlated positively ($p<0.05$); while the intakes of butter, margarine and drinks and water gave negative correlation ($p<0.05$) with the triglyceride levels (for correlation coefficients, see Appendix 8).

4.1.7 Adipokines and food items

We investigated the statistically significant correlation ($p < 0.05$) between levels of leptin and adiponectin with the reported intake of different food items (table 13 & 14). In the obese group, the concentration of leptin had a positive relationship to the intake of cereals ($p=0.004$) and ice cream ($p=0.029$), while the reported intake of alcohol (wine and liquor) ($p=0.008$), fish ($p=0.033$) and water ($p=0.007$) correlated negatively with the levels of leptin. In the control women, a positive relationship between levels of leptin and the reported intake of partly skimmed milk, wine and liquor was shown, while the intake of bread was negatively correlated with leptin levels (all p-values < 0.05).

Among the obese, reported intake of water ($p<0.01$) and vegetables ($p=0.022$) was positively related to the levels of adiponectin. Another finding was that among the obese women the levels of adiponectin were correlated negatively to the intake of light squash and artificially sweetened soft drinks (p-values < 0.01) whereas in the control subjects, a negative correlation between levels of adiponectin and the reported intake of sugar containing squash and soft drinks ($p=0.047$) was found.

***Table 13**. The relationships between the adipokines, leptin and adiponectin, and the reported intake of different food items among the obese women (Spearman's correlation coefficient rho). Negative rho indicates negative correlation. Only significant correlations are stated.*

OBESE WOMEN (n=116)	**Alcohol**	**Cereals**	**Vegetables**	**Fish**	**Ice cream**
Leptin	-0.27**	0.26**	-	-0.20*	0.23*
Adiponectin	-	-	0.21*	-	-

OBESE WOMEN (n=116)	**Light squash/ soft drinks**	**Artificially sweetened soft drinks**	**Water**	**Wine/beer**
Leptin	-	-	-0.25**	-0.25
Adiponectin	-0.28**	-0.26**	0.34**	-

***** *Correlation was significant at the 0.05 level*
****** *Correlation was significant at the 0.01 level*
- *= not significant correlation*

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***Table 14.** The relationships between the adipokines, leptin and adiponectin, and the reported intake of different food items among the normal weight control women (Spearman's correlation coefficient rho). Negative rho indicates negative correlation. Only significant correlations are stated.*

CONTROL WOMEN (n=20)	**Bread**	**Partly skimmed milk**	**Squash/soft drinks with sugar**	**Fatty fruit**	**Wine/beer**
Leptin	-0.48*	0.45*	-	-	0.49*
Adiponectin	-	-	-0.45*	-0.59**	-

***** *Correlation was significant at the 0.05 level*
****** *Correlation was significant at the 0.01 level*
- *= not significant correlation*

4.1.8 Accuracy of reported energy intake

The estimated total energy expenditure is predicted by resting metabolic rate multiplied by an activity factor. Since the physical activity level differ between subjects, and between obese and lean women, we decided to calculate the TEE based

on two different PAL values for the obese women and the control subjects. According to the Nordic Nutrition Recommendations (9) and previous literature (127;128), we choose a PAL factor of 1.6 among the obese subjects and 1.8 among the control women.

PAL 1,6 in obese women and PAL 1,8 among the controls

Using a PAL value of 1.6 to estimate the TEE among the obese women yielded an energy expenditure of 2981 kcal (median) per day. Calculating the TEE for the control women with a PAL value of 1.8 gave an energy expenditure of 2362 kcal, which is significantly lower than in the obesity group. Extracting the estimated TEE from the reported energy intake demonstrated a median under-reporting of about 570 kcal (17.4 %) per day for the obese women, while the energy intake matched the energy expenditure among the control subjects (median) (table 15).

***Table 15**. Accuracy of reported food intake among the morbidly obese women and the normal weight control women (median, point estimate for difference with 95 % confidence interval are given where statistically significant differences were observed)* *

ACCURACY OF REPORTED ENERGY INTAKE	Obese women (n=116)	Control women (n=20)	Point estimate for difference	95 % CI	p-value *
Reported EI (kcal)	2603	2301	-	-	0.124
RMR (kcal)	**1863**	**1312**	**571.0**	**(493.4 ; 661.3)**	**< 0.001**
PAL	1.6	1.8	-	-	-
eTEE (kcal)	**2981**	**2362**	**653.4**	**(530.8 ; 797.9)**	**< 0.001**
EI - eTEE (kcal)	**-570**	**5**	**-456.9**	**(-856.4 ; -16.8)**	**0.044**
EI - eTEE (%)	**-17.4**	**0.3**	**-13.6**	**(-28.4 ;-0.4)**	**0.047**

***** *Differences in reported intake of food among the obese and control women were tested with the Mann-Whitney U test.*
EI = energy intake. RMR = resting metabolic rate. PAL = physical activity level. eTEE = estimated total energy expenditure.

Splitting the group of obese women into under-reporters (rEI – eTEE < 0) and non-under-reporters (rEI – eTEE ≥ 0), 70 % (n=81) of the obese women underreported their energy intake. In the control group, 10 (50%) of the lean women underreported

their energy intake (table 16). The obese under-reporters underreported approximately 848 kcal per day, which constituted 25.3 % of the total estimated energy requirement. The controls underreported in median 17.6 % (median 428 kcal), and this was significantly lesser than among the obese women. On the other hand, the obese women who did not underreport had a median over-report of 624 kcal, 18.7 % more than the estimated requirement. Among the non-underreporting control women; 479 kcal, constituting 20.3 %, was the extra intake reported by these women compared to the estimated total energy requirement.

Table 16. *Number of under-reporters and non-under-reporters among the morbidly obese women and the normal weight control women. Amount of misreported energy intake compared to the estimated total energy expenditure (rEI-eTEE) are given in absolute values and percentages (median)* ***

UNDER-REPORTERS VERSUS NON-UNDER-REPORTERS	**Obese women (n=116)**		**Control women (n=20)**	
	Under-reporters	Non-under-reporters	Under-reporters	Non-under-reporters
Number (n)	81	35	10	10
Number (%)	69.8	30.2	50.0	50.0
Misreported value (kcal)	-848**	624‡	-428**	479‡
Misreported value (%)	-25.3	18.7	-17.6	20.3

***** *Differences between under-reporters and between the non-under-reporters were tested with the Mann-Whitney U test.*
****** *Significant difference (p=0.037) was seen between the two groups using Mann-Whitney U test*
‡ *The difference in misreported value tended to be different between the two groups (p=0.078)*

To illustrate the misreporting of energy intake compared to the estimated energy expenditure, we designed a histogram (see figure 8 and 9). The number of subjects who misreported the energy intake is illustrated by the bars. Each bar represents 200 kcal. The zero on the x-axis represents correct reporting of energy intake; the reported energy intake is equal to the estimated energy expenditure. The bars to the left of zero represent underreporting, while the bars to the right represent over reporting.

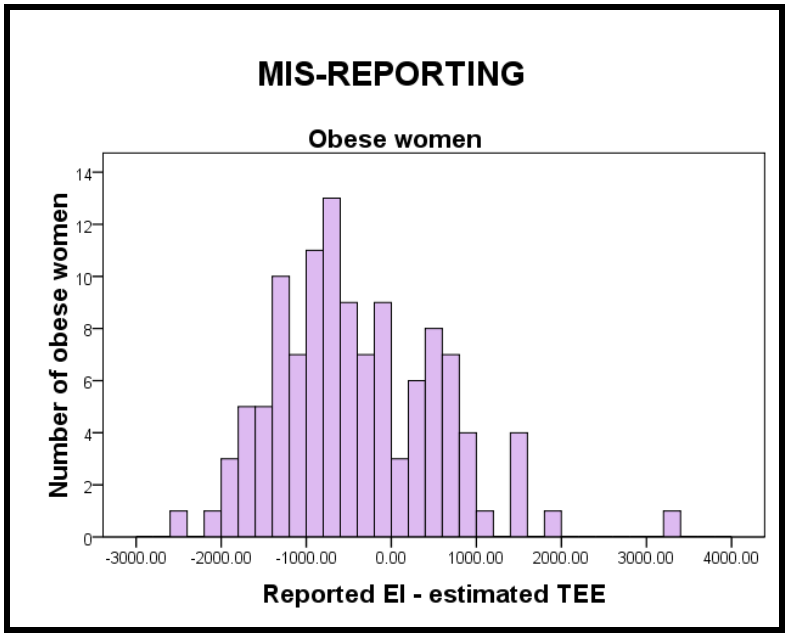

Figure 8*.Estimated TEE from a PAL value of 1.6 among obese women. The mis-report of energy intake was expressed by the reported intake minus the TEE. The bars indicate number of subjects who misreported within that 200 kilocalorie range. The bars to the left of "0" (EI-TEE = 0 = energy balance) represent the number of subjects who underreported their energy intake, while the bars to the right of "0" represent over reporting. The histogram is slightly shifted to the left, indicating a higher proportion of under-reporters.*

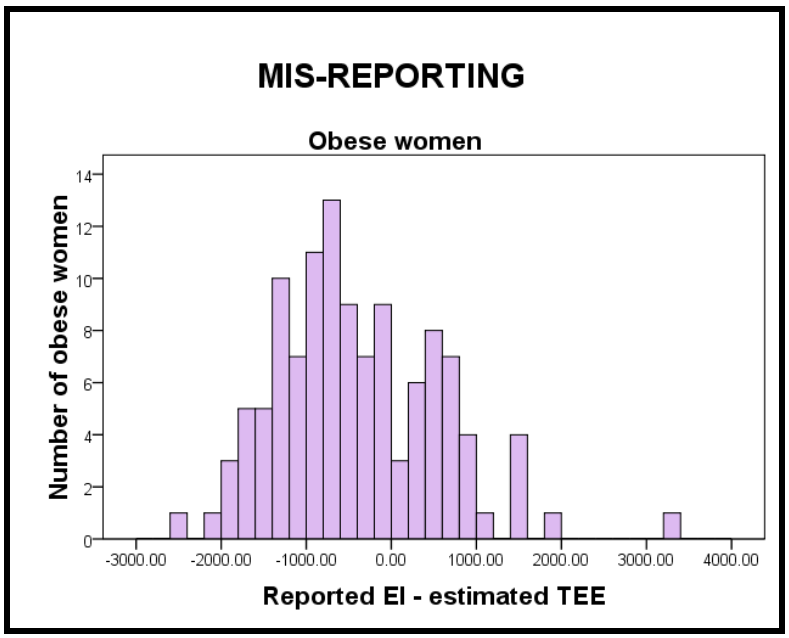

Figure 9*.Estimated TEE from a PAL value of 1.8 among control women. The mis-report of energy intake was expressed by the reported intake minus the TEE. The bars indicate number of subjects who misreported within that 200 kilocalorie range. The bars to the left of "0" (EI-TEE = 0 = energy balance) represent the number of subjects who underreported their energy intake, while the bars to the right of "0" represent over reporting.*

We found a significant inverse correlation between BMI and the amount of misreporting in the obese women (rho= -0.23, p= 0.015). With increasing BMI, the amount of underreported kilocalories enhanced (figure 10).

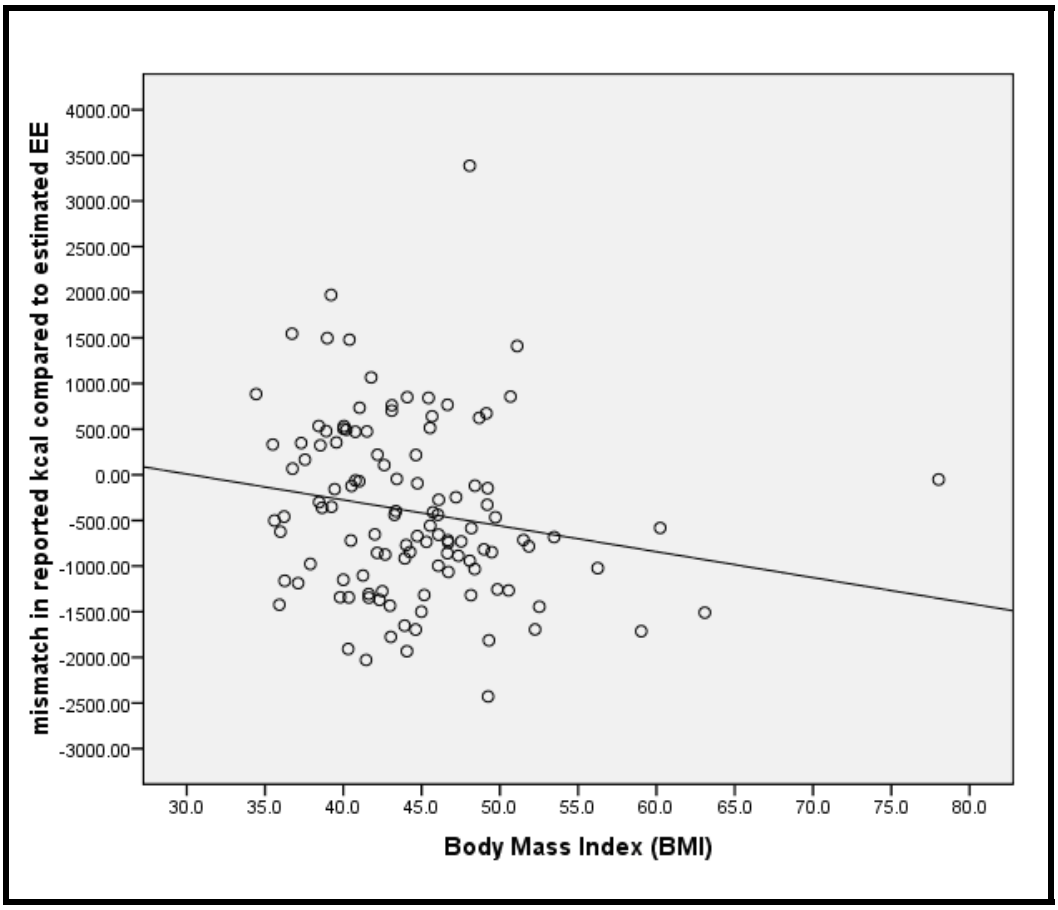

Figure 10. *The significant (p=0.015) inverse correlation between BMI and the mismatch in reported kilocalories compared to estimated energy expenditure (rho=-0.23) among the obese women (n=116) is illustrated. By removing the two most outliers the correlation was further enhanced to -0.26 (p<0.01).*

4.2 Women with FTI ≤ 0,6 versus women with pre-PCOS

We were interested in studying if there was a difference in anthropometric measurements, lipid and adipokine profile and dietary intake between the obese women with pre-PCOS versus the obese women without PCOS. In lack of PCOS diagnosis a surrogate marker for PCOS (free testosterone index score) was chosen.

We therefore divided the 116 obese women into two groups. The women having an FTI score below or equal to 0.6 were compared to women with an FTI score above 0.6 (pre PCOS). There were 68 women in the first group and 46 in the latter. Two women were excluded because information on testosterone level or SHBG was lacking. Forty-six out of 116 women had pre-PCOS status, constituting 39.7 % of the group of obese women

4.2.1 Anthropometric measures and blood samples

Women with pre-PCOS had significantly higher body weight and height ($p< 0.05$), and waist circumference ($p< 0.01$) than women with FTI ≤ 0.6. The concentration of triglycerides tended to be higher in the pre-PCOS group ($p=0.073$) (table 17).

***Table 17**. Characteristics of the obese pre-PCOS (FTI>0.6) women and the obese women with lower FTI (≤ 0.6). Anthropometric measures and lipid profile, (median values, point estimates for difference with 95 % confidence interval are given where statistically significant differences were observed)**

CHARACTERISTICS	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Age (y)	41.8	41.9	-	-	0.402
Weight (kg)	**118.0**	**128.9**	**-7.7**	**(-15.0 : -0.5)**	**0.034**
Height (cm)	**166.0**	**169.5**	**-0.03**	**(-0.1 ; 0.0)**	**0.034**
Body Mass Index (kg/m²)	43.1	44.1	-	-	0.212
Waist circumference (cm)	**125.5**	**133.0**	**-6.0**	**(-11.0 ; -1.0)**	**0.011**
Hip circumference (cm)	135.0	139.5	-	-	0.106
Waist-to-hip ratio	0.93	0.95	-	-	0.120
Total cholesterol (mmol/L)	5.1	5.3	-	-	0.540
LDL-cholesterol (mmol/L)	3.2	3.3	-	-	0.612
HDL-cholesterol (mmol/L)	1.2	1.1	-	-	0.121
Triglycerides (mmol/L)	***1.4 (1.56‡)***	***1.5 (1.67‡)***	***-0.2***	***(-0.4 ; -0.0)***	***0.073 *****

** Differences between the obese pre-PCOS women and the obese women with lower FTI were tested with the Mann-Whitney U test.*
*** The difference tended to be significantly different*
‡ mean values

4.2.2 Adipokines

The serum concentrations of adiponectin in plasma tended to be lower (p= 0.069) in the group of females with pre-PCOS, whereas there was no statistically significant difference in the levels of leptin (table 18).

***Table 18**. Adipokine profile among the obese pre-PCOS (FTI>0.6) women and the obese women with lower FTI (≤ 0.6) (median values, point estimates for difference with 95 % confidence interval are given where statistically significant differences were observed)**

ADIPOKINE PROFILE	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Leptin (ng/ml)	59.9	60.9	-	-	0.666
Adiponectin (ng/ml)	***5615***	***4926***	***1040***	***(-91 ; 2226)***	***0.069 *****

** Differences between the obese pre-PCOS women and the obese women with lower FTI were tested with the Mann-Whitney U test.*
*** The difference tended to be significantly different.*

4.2.3 Energy intake and macronutrients

The obese pre-PCOS women reported significantly higher intake of polyunsaturated fat compared to the obese women with lower FTI score. The reported energy intake was similar between the groups (not significantly different), but the intake of protein and total fat tended to be higher among the women with pre-PCOS status (table 19).

Table 19. *Intake of macronutrients among the obese pre-PCOS (FTI>0.6) women and the obese women with lower FTI (≤ 0.6) (median, point estimate for difference with 95 % confidence interval are given when significant difference between the groups were observed) **

MACRONUTRIENTS	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Energy intake (kcal)	2577	2612	-	-	0.167
Protein intake (g)	***102***	***107***	***-11.1***	***(-23.0 ; 0.6)***	***0.068****
Fat intake (g)	***104***	***114***	***-16.9***	***(-34.4 ; -2.6)***	***0.091****
-saturated fat (g)	41	45	-	-	0.125
-monounsaturated fat (g)	37	38	-	-	0.132
-polyunsaturated fat (g)	**19**	**23**	**-4.7**	**(-8.4 ; -0.9)**	**0.019**
Cholesterol (mg)	327	328	-	-	0.178
Carbohydrate intake (g)	281	290	-	-	0.333
-sugar intake (g)	41	39	-	-	0.851
Dietary fibre intake (g)	26	25	-	-	0.782
Alcohol consumption (g)	1	1	-	-	0.626

***** *Differences between the obese pre-PCOS women and the obese women with lower FTI were tested with the Mann-Whitney U test.*
****** *The difference tended to be significantly different*

4.2.4 Intake of food items

The pre-PCOS women reported a significantly higher consumption of potatoes (also fresh potatoes), meat products and forcemeat, butter, margarine and oil than women with lower FTI score. The pre-PCOS women tended to drink more light squash and soft drinks (p= 0.097), and the intake of artificially sweetened soft drinks was significantly higher compared to the women with FTI ≤ 0.6 ($p < 0.05$). Table 20 summarizes the median intake of food items, reported by the obese pre-PCOS women and the obese women with lower FTI score.

***Table 20**. Reported daily intake of food items (g/day) among the pre-PCOS (FTI>0.6) women and the women with lower FTI (≤ 0.6) according to dietary interview based on a FFQ (median values, point estimates for difference with 95 % confidence interval are given where statistically significant difference were observed) **

FOOD ITEMS (gram/day)	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Total intake	3611	3751	-	-	0.307
Bread	181	194	-	-	0.174
White bread	0	0	-	-	0.509
Whole-grain bread	80	80	-	-	0.93
Cereal products	59	54	-	-	0.824
Cakes	20	25	-	-	0.343
Potato	**57 (62.3‡)**	**79 (85.3‡)**	**-24.7**	**(-39.4 ; -6.4)**	**0.006**
Fresh potatoes	**50 (47.4‡)**	**52 (68.6‡)**	**-24.8**	**(-35.2 ; -0.8)**	**0.011**
Pommes frites	4	5	-	-	0.727
Vegetables	250	235	-	-	0.917
Fruits, berries	186	192	-	-	0.733
Meat, blood, entrails/pluck	**161**	**203**	**-49.3**	**(-81.7 ; -14.9)**	**0.003**
Whole meat, minced meat	65	66	-	-	0.479
Forcemeat	**63**	**95**	**-29.0**	**(-48.9 ; -8.0)**	**0.007**
Fish, shellfish	52	56	-	-	0.699
Fish spreads	9	9	-	-	0.508
Egg	16	16	-	-	0.437
Milk, cream, ice cream	270	328	-	-	0.114

FOOD ITEMS (gram/day)	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Whole milk	0	0	-	-	0.345
Partly-skimmed milk	58	25	-	-	0.833
Skimmed milk	**0 (23.2 ‡)**	**0 (62‡)**	**0**	**(-0.0 ; -0.0)**	**0.003**
Yogurt	14	20	-		0.448
Ice cream	7	11	-	-	0.319
Cheese	38	38	-	-	0.593
Butter, margarine, oil	**35**	**47**	**-15.4**	**(-26.1; -3.2)**	**0.014**
Oil, other fat	1	1	-	-	0.174
Sugar, sweet stuff	25	31	-	-	0.669
Chocolate	13	17	-	-	0.677
Sweets	4	6	-	-	0.271
Drinks	1709	1744	-	-	0.838
Coffee	150	240	-	-	0.947
Tea	0	0	-	-	0.379
Squash/ soft drink, with sugar	0	0	-	-	0.982
Soft drink with sugar	0	0	-	-	0.952
Squash with sugar	0	0	-	-	0.123
Squash/ soft drink, light	***210***	***423***	***-116.0***	***(-289.9 ; 1.1)***	***0.097*****
Soft drink, artificially sweetened	**133**	**323**	**-98.0**	**(-235.2 ; -0.1)**	**0.044**
Water, mineral water	698	576	-	-	0.226

FOOD ITEMS (gram/day)	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Beer	4	0	-	-	0.401
Wine, liquor	3	3	-	-	0.465
Various	148	174	-	-	0.68
Potato chips	4	7	-	-	0.216
Other snacks	0	0	-	-	0.603
Fatty fruit, seeds	***3***	***1***	***0.0***	***(0.0 ; 3.0)***	***0.062*****

****** Differences in reported intake of food in obese and control women were tested with the Mann-Whitney U test*
******* The difference tended to be significantly different*
‡ mean intake

4.2.5 Accuracy of reported food intake

We presumed that the obese women had a sedentary lifestyle; however, since they are obese, they have increased energy cost due to weight bearing activities. Therefore we decided to use a PAL value of 1.6 to predict the total energy expenditure among the obese women with and without pre-PCOS status.

Energy reporting among obese pre-PCOS women versus obese women

The estimated resting metabolic rate multiplied with a PAL factor of 1.6 resulted in estimated total energy expenditures, which were significant different between the obese pre-PCOS women and the other obese women. The energy requirements among women with FTI ≤ 0.6 and the pre PCOS women, to maintain stable body weight, were 2926 and 3105 kcal, respectively. When subtracting the estimated TEE from the reported energy intake, the women with low FTI under-reported 584 kcal (median) versus the pre-PCOS women who under-reported approximately 531 kcal per day (median) (table 21).

Table 21. *Accuracy of reported food intake among the obese pre-PCOS (FTI>0.6) women and the obese women with lower FTI (≤ 0.6) (median, point estimate for difference with 95 % confidence interval are given where statistically significant differences were observed).*

ACCURACY OF REPORTED ENERGY INTAKE	Obese women FTI ≤ 0.6 (n=68)	pre-PCOS Obese women FTI > 0.6 (n=46)	Point estimate for difference	95 % CI	p-value *
Reported EI (kcal)	2577	2612	-	-	0.167
RMR (kcal)	**1828**	**1940**	**-100.5**	**(-173.4 ; -21.3)**	**0.012**
PAL	1.6	1.6	-	-	-
eTEE (kcal)	**2926**	**3105**	**-160.9**	**(-277.4 ; -34.1)**	**0.012**
EI - eTEE (kcal)	-584	-531	-	-	0.439

***** *Differences between the pre-PCOS women and the women with lower FTI were tested with the Mann-Whitney U test.*
EI = energy intake. RMR = resting metabolic rate. PAL = physical activity level. e TEE = estimated total energy expenditure.

The number of under-reporters (rEI – eTEE < 0) among women with lower FTI was 49 (72 %), and they underreported in median 874 kcal, constituting 29 % of the total estimated energy requirement (table 22). Among the obese pre-PCOS women the number of under-reporters was 30 (65%). The underreported value constituted 851 kcal; 26 % of the total estimated energy expenditure. On the other hand, 19 women with low FTI non-underreported (27.9%) and the misreported value was 534 kcal above the estimated requirement (18.7 %). Sixteen of the pre-PCOS women misreported median 632 kcal; 19 % extra energy compared to the estimated total requirement. All in all, we did not find any difference between the obese pre-PCOS women and the obese women in regard to under- and over reporting.

Table 22. *Number of under-reporters and non-under-reporters among the pre-PCOS (FTI>0.6) women and the women with lower FTI (≤ 0.6) (median). Amount of misreporting energy intake compared to the estimated total energy expenditure (rEI-eTEE) are given in absolute values and percentages (median)**

UNDER-REPORTERS VERSUS NON-UNDER-REPORTERS	Obese women FTI ≤ 0.6 (n=68)		pre-PCOS Obese women FTI > 0.6 (n=46)	
	Under-reporters	Non-under-reporters	Under-reporters	Non-under-reporters
Number (n)	49	19	30	16
Number (%)	72.1	27.9	65.2	34.8
Misreported value (kcal)	-874	534	-851	632
Misreported value (%)	-29.2	18.7	-26.1	19.0

** Differences between the under-reporters and non-under-reporters among the pre-PCOS women and the women with lower FTI were tested with the Mann-Whitney U test. We did not find any significant differences.*

4.3 PCOS women and effect of weight loss – preliminary results of the FEMIN study

4.3.1 Effects of a low-calorie-diet on different parameters among PCOS women

To achieve weight reduction in the women participating in the FEMIN study, two different low-calorie-diets were used, however the total calorie intake were similar in the two diets. Therefore, we first wanted to investigate the effects of low-calorie-diets on different parameters among the nine PCOS women in our study, independently of which diet they were randomized to.

Effect of a LCD on anthropometric measures, body composition and blood pressure

After eight weeks consuming a low-calorie-diet, the obese PCOS women significantly reduced their weight, BMI, waist-, hip- and neck circumferences, as expected. The participating women reduced their weight on average with 7.4 ± 6.2

kg, and this constitutes a mean percentage weight loss of 6.3 % of total body weight at baseline. Furthermore, the weight alteration among the obese women ranged from -14.4 kg (-10.9 %) to +4.4 kg (+4.2 %). In accordance with the weight reduction, the women's body compositions were altered. The PCOS women lost significant amounts of both fat mass and fat free mass. At baseline the analysis of body composition detected a mean fat mass percentage of 49.0 % among the PCOS women, and after eight weeks on diet the fat percentage was reduced to 47.4 %, which tended to be significant. The women had a decrease of 9.7 % in total fat mass. The loss of fat free mass constituted 25.1 % of the total body weight loss. Even though the women significantly lost muscle mass (in kg) during the low-calorie-diet period, their percentage of muscle mass, after the eight weeks, tended to be increased compared to baseline. Baseline data and measurements after eight weeks on LCD are summarized, together with the achieved differences ([Δ], baseline data – eight weeks data) between these two measurements in table 23.

Table 23. *Effect of LCD on anthropometric measures, body composition and blood pressure among obese PCOS women. Data from baseline and after eight weeks on LCD are given (mean values), together with the achieved differences ([Δ], baseline data – eight weeks data) (mean values) between these two measurements (95 % confidence interval for the difference). **

ANTHROPOMETRY, BODY COMPOSITION AND BLOOD PRESSURE	Baseline (n=9)	After 8 wks (n=9)	Mean difference (Δ)	95 % CI	p-value *
Age (years)	28.7 ± 6.3	28.7 ± 6.3	-	-	-
Weight (kg)	**116.9 ± 11.5**	**109.5 ± 9.2**	**7.4**	**(2.7 ; 12.2)**	**0.007**
Height (cm)	169.8 ± 4.5	169.8 ± 4.5	-	-	-
BMI (kg/m²)	**40.6 ± 4.7**	**38.0 ± 3.2**	**2.6**	**(0.9 ; 4.3)**	**0.008**
Waist circumference (cm)	**120.9 ± 6.4**	**114.9 ± 5.9**	**5.9**	**(2.8 ; 9.0)**	**0.002**
Hip circumference (cm)	**130.5 ± 8.6**	**125.3 ± 8.4**	**5.2**	**(0.8 ; 9.6)**	**0.025**
Waist to hip ratio	0.93 ± 0.06	0.92 ± 0.06	0.01	(-0.01 ; 0.02)	0.233
Neck circumference (cm)	**40.3 ± 2.6**	**38.8 ± 1.9**	**1.5**	**(0.6 ; 2.4)**	**0.005**
Fat mass (kg)	**57.5 ± 8.9**	**51.9 ± 5.5**	**5.6**	**(1.2 ; 10.0)**	**0.019**
Fat percent (%)	***49.0 ± 4.2***	***47.4 ± 2.9***	***1.6***	***(-0.3 ; 3.5)***	***0.081 *****
Fat free mass (kg)	**59.4 ± 6.0**	**57.5 ± 5.8**	**1.9**	**(0.6 ; 3.1)**	**0.008**
Muscle mass (kg)	**56.4 ± 5.6**	**54.6 ± 5.4**	**1.8**	**(0.7 ; 2.9)**	**0.006**
Muscle percent (%)	***48.4 ± 4.0***	***49.9 ± 2.7***	***-1.5***	***(-3.3 ; 0.3)***	***0.085 *****
Systolic blood pressure (mmHG)	130 ± 16.4	125 ± 8.6	5.2	(-6.0 ; 16.4)	0.313
Diastolic blood pressure (mmHG)	91 ± 8.0	86 ± 7.7	4.9	(-2.8 ; 12.6)	0.181

***** *The achieved differences ([Δ] baseline measurements - eight weeks measurements) were investigated with the One Sample t-test.*
****** *The achieved difference tended to be significant*

Effect of LCD on lipid profile, CRP and adipokines

The participating PCOS women had increased level of LDL cholesterol (mean) at baseline, whereas the other lipid parameters (mean values) were within the recommended range. The mean concentrations of apolipoprotein B and apolipoprotein A-I were within their reference values (0.5-1.3 g/L and 1.2-2.3 g/L), while the level of CRP was above the reference value (<4 mg/L) (131). After eight

weeks on low-calorie-diet, the level of apolipoprotein A-I was significantly lowered, while the level of triglycerides tended to be reduced. Furthermore, the leptin concentration was significantly lowered after the diet period. The achieved difference in leptin concentration was statistically positively correlated to the leptin concentration at baseline (rho=0.83, p=0.005) and the achieved difference in body weight from baseline to eight weeks measurement (rho= 0.67, p=0.05). Baseline data and measurements after eight weeks on LCD are summarized, together with the achieved differences ([Δ], baseline data – eight weeks data) between these two measurements in table 24.

***Table 24**. Effect of LCD on lipid profile, CRP and adipokines among obese PCOS women. . Data from baseline and after eight weeks on LCD are given (mean values), together with the achieved differences ([Δ], baseline data – eight weeks data) (mean values) between these two measurements (95 % confidence interval for the difference) **

BLOOD PROFILE	Baseline (n=9)	After 8 wks (n=9)	Mean difference (Δ)	95 % CI	p-value *
Total cholesterol (mmol/l)	5.0 ± 0.9	4.8 ± 1.0	0.3	(-0.4 ;0.9)	0.362
HDL cholesterol (mmol/l)	1.2 ± 0.3	1.2 ± 0.3	0.1	(-0.1 ; 0.2)	0.397
LDL cholesterol (mmol/L)	3.23 ± 0.6	3.0 ± 0.8	0.2	(-0.3 ; 0.8)	0.371
Triglycerides (mmol/l)	***1.2 ± 0.7***	***1.0 ± 0.7***	***0.2***	***(-0.0 ; 0.4)***	***0.057 *****
Apolipoprotein B (g/L)	0.9 ± 0.2	0.8 ± 0.2	0.1	(-0.0 ; 0.2)	0.174
Apolipoprotein A-I (g/L)	**1.5 ± 0.3**	**1.3 ± 0.2**	**0.3**	**(0.0 ; 0.5)**	**0.025**
ApoB/ApoA-I	0.59 ± 0.2	0.65 ± 0.27	-0.1	(-0.2 ; 0.1)	0.271
CRP (mg/L)	9.3 ± 8.0	8.5 ± 6.7	0.8	(-1.2 ; 2.8)	0.384
Adiponectin (ng/ml)	2233 ± 840	2306 ± 714	-73.1	(-282.6 ; 136.4)	0.444
Leptin (ng/ml)	**77.7 ± 18.2**	**51.2 ± 12.5**	**26.4**	**(13.7 ; 39.2)**	**0.001**

***** *The achieved differences ([Δ] baseline measurements - eight weeks measurements) were investigated with the One Sample t-test.*
****** *The achieved difference tended to be significant*

4.3.2 Effects of *two different* low-calorie-diets on different parameters among PCOS women

We wanted to investigate if the low-calorie-diets; the crisp bread diet and the powder diet, induced different changes (Δ) on the parameters among the nine PCOS women after completion of the eight weeks with diet. At baseline, the women in the two different low-calorie-diet groups did not differ with regard to anthropometric measures, body composition, lipid profile and blood pressure. A significant difference in leptin levels ($p = 0.05$) was detected between the two groups. The women in the powder diet group had lower levels of leptin at baseline.

Effects of two different LCDs on anthropometric measures, body composition and blood pressure

The achieved differences ([Δ], baseline data – eight weeks data) in anthropometry and body composition from baseline to the eight weeks measurements were not significant different between the two low-calorie-diet groups (table 25). However, there tended to be a difference in systolic blood pressure from baseline to the eight weeks measurement where a reduction tended to be more pronounced in the powder diet group than in the crisp bread diet group.

Table 25. *Effects of two different LCDs on anthropometric measures, body composition and blood pressure among obese women with PCOS. Data from baseline and after eight weeks on the diets are shown (mean values and standard deviation)**

COMPARISON BETWEEN THE TWO DIETS	**Crisp bread diet**		**Powder diet**		
	Baseline (n=5)	**After 8 wks (n=5)**	**Baseline (n=4)**	**After 8 wks (n=4)**	**p-value ***
Age (years)	27.6 ± 8.4	27.6 ± 8.4	30 ± 2.9	30 ± 2.9	-
Weight (kg)	118.9 ± 10	111.4 ± 6.5	114.4 ± 14.3	107.0 ± 12.4	0.993
Height (cm)	169 ± 6.0	169 ± 6.0	170.8 ± 2.2	170.8 ± 2.2	-
BMI (kg/m²)	41.8 ± 5.2	39.1 ± 2.7	39.2 ± 4.2	36.7 ± 3.6	0.895
Waist circumference (cm)	123.2 ± 6.2	117.9 ± 5.0	118 ± 6.2	111.3 ± 5.2	0.625
Hip circumference (cm)	131.9 ± 11.1	126.9 ± 9.1	128.8 ± 4.9	123.3 ± 8.3	0.906
Waist to hip ratio	0.94 ± 0.06	0.93 ± 0.04	0.92 ± 0.07	0.91 ± 0.08	0.686
Neck circumference (cm)	41.1 ± 3.0	39.7 ± 2.2	39.3 ± 1.7	37.6 ± 0.5	0.796
Fat mass (kg)	59.3 ± 10.3	54 ± 4.6	55.3 ± 7.5	49.4 ± 6.1	0.879
Fat percent (%)	49.6 ± 5.3	48.4 ± 2.5	48.3 ± 3	46.2 ± 3.2	0.585
Fat free mass (kg)	59.6 ± 4.5	57.5 ± 3.9	59.1 ± 8.2	57.6 ± 8.2	0.556
Muscle mass (kg)	56.6 ± 4.2	54.5 ± 3.7	56.1 ± 7.8	54.7 ± 7.7	0.527
Muscle percent (%)	47.9 ± 5.0	48.9 ± 2.3	49.0 ± 2.9	51.1 ± 3.01	0.577
Systolic blood pressure (mmHG)	***123 ± 15.2***	***125 ± 11.5***	***139 ± 14.9***	***125 ± 4.3***	***0.095 *****
Diastolic blood pressure (mmHG)	92 ± 8.2	87 ± 10.2	91 ± 9.0	86 ± 4.4	0.930

***** *The achieved differences ([Δ] baseline measurements - eight weeks measurements) were compared between the two diet groups, using the Independent Samples t-test.*

****** *The achieved difference between the groups tended to be significant.*

Effects of two different LCDs on lipid profile, CRP and adipokines

Furthermore, we investigated the difference between two different dietary groups with regard to lipids, CRP and adipokines. The achieved differences ([Δ], baseline data – eight weeks data) for the parameters were however not significantly different between the two diet groups (table 26).

***Table 26**. Effects of two different LCDs on lipid profile, CRP and adipokines. Data from baseline and after eight weeks on the diets (mean and standard deviation)**

COMPARISON BETWEEN THE TWO DIETS	Crisp bread diet		Powder diet		
	Baseline (n=5)	After 8 wks (n=5)	Baseline (n=4)	After 8 wks (n=4)	p-value *
Total cholesterol (mmol/l)	5.3 ± 0.8	5.3 ± 0.8 #	4.6 ± 0.9	4.0 ± 0.7 #	0.270
HDL cholesterol (mmol/l)	1.2 ± 0.4	1.2 ± 0.3	1.3 ± 0.3	1.2 ± 0.2	0.928
LDL cholesterol (mmol/L)	3.5 ± 0.5	3.5 ± 0.7 #	3.0 ± 0.7	2.4 ± 0.5 #	0.195
Triglycerides (mmol/l)	1.3 ± 0.9	1.1 ± 0.9	1 ± 0.3	0.8 ± 0.4	0.906
Apolipoprotein B (g/L)	0.9 ± 0.2	0.9 ± 0.2 #	0.8 ± 0.2	0.6 ± 0.1 #	0.238
Apolipoprotein AI (g/L)	1.5 ± 0.3	1.2 ± 0.3	1.6 ± 0.4	1.3 ± 0.2	0.625
ApoB/ApoAI	0.7 ± 0.2	0.8 ± 0.3 #	0.5 ± 0.1	0.5 ± 0.1 #	0.282
CRP (mg/L)	12.1 ± 10.0	11.0 ± 8.5	5.9 ± 2.6	5.5 ± 1.5	0.744
Adiponectin (ng/ml)	2093 ± 487	2154 ± 404	2408 ± 1221	2497 ± 1028	0.886
Leptin (ng/ml)	88.0 ± 9.6 †	58.7 ± 10.1 ‡	64.9 ± 19.0 †	41.9 ± 8.6 ‡	0.604

****** The achieved differences ([Δ], baseline measurements - eight weeks measurements) were compared between the two diet groups, using Independent Samples t-test.*
***†** p=0.05, difference in this parameter between the two diet groups at baseline (tested with Mann Whitney U test)*
***‡** p=0.05, difference in this parameter between the two diet groups at eight weeks measurement (tested with Mann Whitney U test)*
***#** Significant difference (p<0.05) in the parameters between the two diet groups at eight weeks measurement (tested with Mann Whitney U test)*

When comparing the eight weeks measurements between the two groups, we found significant differences between the two low-calorie-diet groups. The eight weeks measurements of total cholesterol (p = 0,049), LDL-C (p = 0,027), ApoB (p = 0,035), ApoB/ApoA1 (p = 0,014) and leptin (p = 0,050) were significantly different between these two diet groups. All the mentioned parameters were lower among the women in the powder diet group, compared to the crisp bread diet group

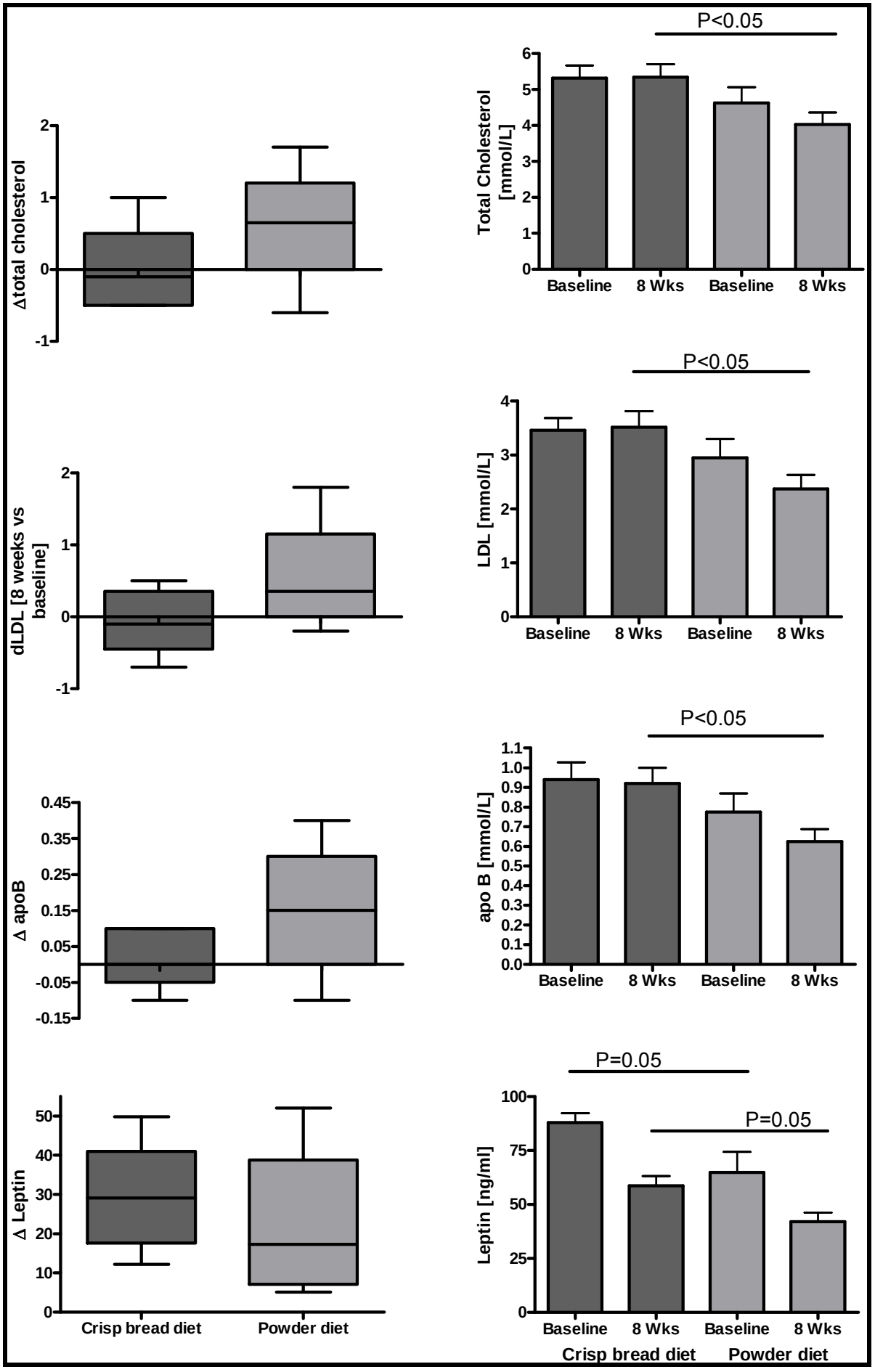
Δtotal cholesterol
2
1
0
-1
P<0.05
Total Cholesterol [mmol/L]
6
5
4
3
2
1
0
Baseline
8 Wks
Baseline
8 Wks
dLDL [8 weeks vs baseline]
2
1
0
-1
P<0.05
LDL [mmol/L]
4
3
2
1
0
Baseline
8 Wks
Baseline
8 Wks
Δ apoB
0.45
0.35
0.25
0.15
0.05
-0.05
-0.15
P<0.05
apo B [mmol/L]
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Baseline
8 Wks
Baseline
8 Wks
Δ Leptin
50
40
30
20
10
0
Crisp bread diet
Powder diet
P=0.05
P=0.05
Leptin [ng/ml]
100
75
50
25
0
Baseline
8 Wks
Baseline
8 Wks
Crisp bread diet
Powder diet

Figure 11. *The box plots to the left illustrate the achieved differences (Δ) in total cholesterol, LDL-C, apo B and leptin from the measurement at baseline to the measurement after eight weeks on the crisp bread diet and the powder diet. The delta differences in the parameters were not significantly different between the diets. The histograms to the right illustrate the measurements of these parameters at baseline and after eight weeks for the two low-calorie-diets. At the eight weeks measurement the concentration of total cholesterol, LDL-C and apo B were significantly different between the two diet groups (not significantly different at baseline). At baseline and at the eight weeks measurement the concentration of leptin was significantly different between the two diet groups.*

5. Discussion

5.1 Analyses of reported food intake in the MOBIL-study

5.1.1 The morbidly obese women versus the normal weight control women

Lipid profile and expression of adipokines

Lipid profile

As expected, the lipid profile among the obese women was more unfavourable than the lipid profile observed in the lean control women. According to the National Cholesterol Education Program (ATP III) and the recommended concentrations of the different lipid parameters, total cholesterol and LDL-C (median values) were higher in the obese women. The median levels of triglycerides and HDL-C were within the cut off values. The control women had lipid values within the recommended range. Among our morbidly obese women, the increase in plasma cholesterol and levels of triglycerides may be a result of the observed higher intake of saturated fat as well as physical inactivity and obesity (21). Obese persons tend to have higher levels of triglycerides and LDL-C and reduced HDL-C concentrations (18); a tendency we also observed among the obese women in the present study compared to the lean control women. Raised levels of cholesterol in the blood are linked to atherosclerotic vascular disease, because elevated LDL cholesterol plays a role in the development of the vascular plaque (31). Our obese women also had raised levels of triglycerides compared to the controls, and elevated serum triglycerides are also associated with increased risk for coronary heart disease (20). Furthermore, the levels of triglycerides correlated to the waist circumference among the obese women in the present study. Waist circumference is a measurement of visceral adipose tissue, which again is associated with elevated levels of triglycerides (132).

Expression of adipokines

We found significant higher levels of leptin and lower levels of adiponectin among the obese women compared to the control women.

Leptin reduces appetite and enhances the energy expenditure in the body, but like others, we observed increased levels of leptin among the obese women compared to the controls. Our results correspond to previous published findings, and may be caused by; the increase in fat mass or support the idea about leptin resistance in obese subjects. In addition, higher concentrations of this parameter in obese subjects may not have the assumed enhanced effect in reducing appetite (46;47). Leptin levels were positively correlated to weight, BMI, waist- and hip circumference among our obese women, which may explain the significant difference in this parameter between the two groups. In the control group, positive correlation was seen between this parameter and waist circumference, LDL-C and triglycerides.

Lower plasma concentrations of adiponectin among obese subjects have previously been described (49;51). They also reported a negative correlation between levels of adiponectin in plasma and BMI in both men and women. We found lower levels of adiponectin and the same negative correlation to BMI among our obese women, together with a negative correlation between plasma adiponectin levels and weight and waist circumference. The synthesis and secretion of this adipokine are decreased during periods of caloric excess, presumably associated with leptin deficiency or resistance (49). Regarding the levels of adiponectin and the association to dyslipidemia, we observed a significant positive correlation between this parameter and levels of HDL-C, while we did not find any correlation with triglycerides or LDL-C, as demonstrated by Matsuzawa et al (51). The lower levels of adiponectin among the obese women may also partly be accounted by adiponectin's positive correlation with HDL-C, since the concentration of HDL-C was significantly lower in the obese women compared to the control subjects.

Former studies on the association between diet and total adiponectin levels have demonstrated a negative correlation between total adiponectin and refined cereals,

while whole-grain cereals, dietary cereal fibre intake, and moderate alcohol consumption have been positively associated with higher levels of adiponectin (133). We found positive correlation between adiponectin levels and vegetables, which is a source for fibre, and also positive association to the intake of water; two "food groups" which represent healthy dietary choices. Recently Yannakoulia et al reported a higher percentage of energy from carbohydrates among women who had the lowest concentration of adiponectin (133), which supports the finding among the control subjects who had a negative correlation between levels of adiponectin and the reported intake of sugar containing squash and soft drinks. We did not find any correlation between alcohol and adiponectin, neither among the obese nor the controls.

Energy and macronutrients intake and food choices

Energy and macronutrients intake

The obese women had a median intake of energy of 2603 kcal, while the control women had 2301 kcal as the median. This difference in 300 kcal was not statistically significant, using a non-parametric test. However, investigating the data with a parametric test, since the data were normally distributed, resulted in an almost significant difference in total energy intake. This indicates that the obese women tended to report a higher energy intake than the lean control women. Compared to the results from Johannsen et al (128), we saw a tendency to difference in intake of energy between obese and lean women, which Johannsen et al did not detect in their data of lean and obese women. However, the obese women in the former study had lower mean BMI than our obese women, while the BMI among the lean women were similar. Heavier women have to consume more food to maintain their weight due to higher RMR, and might therefore report higher intake.

In the present study, the total intake of fat tended to be higher in the obese group compared to the control women; and more specifically it was the saturated fat which tended to be more consumed by the obese women. Higher fat intake among obese women compared to normal weight women have been described earlier, together with

an higher intake of protein and carbohydrate (134). However, we did not find any difference between the two groups regarding protein and carbohydrate intake. Previously Davis et al did not report any difference in protein intake between overweight/obese women (mean BMI 34) and matched normal weight women (mean BMI 21.2) either. However, they reported that overweight/obese women had a larger portion of total energy from fat, and the intake of saturated fat was significantly higher than among normal weight subjects. Furthermore, overweight/obese women had a smaller portion of total energy from carbohydrate, and especially dietary fibre and complex carbohydrates than normal weight women (135). In our study, the obese and the control women had the same intake of carbohydrates, including dietary fibre. Intake of the latter was satisfactory, according to the Nordic Nutrition Recommendations (9), and compared to the data from the Norkost Survey, our women, both the obese and the controls consumed more dietary fibre than the Norkost women (8). Our control women reported significant greater alcohol consumption than the obese subjects. Alcohol consumption was also higher in non-obese subjects (BMI< 30) compared to obese subjects (BMI > 30) studied by Berg et al (136) and by Berteus et al (obese women mean BMI 41 and reference women mean BMI 23.8) (134). Compared to the Norkost Survey women, our control women had approximately the same intake of alcohol (8).

Food choices

In our study, the total intake of food (in gram) was significantly higher among the obese, than the control women. The obese women reported a significantly higher intake of meat, forcemeat and butter/margarine/oil compared to the control women, and these food items may be contributing factors to the tendency of higher fat intake among the obese compared to the control women. Higher consumption of meat among overweight/obese is previously described by Davis et al (135). Schulze et al suggested that a diet characterized by high intakes of red and processed meats (and also refined grains, sweets, desserts and potatoes) may contribute to weight gain (11). Furthermore, the obese women had significantly increased consumption of snacks (others than potato chips) compared to the control women. Previously, Berteus et al

reported a trend between reported snacking frequency and increased proportions of fat intake and decreased proportions of protein intake in obese women (and men)(137). In the present study, the correlations between fat intake and different food items suggested that the obese women ate more fat containing food items, whereas the fat intakes among the control subjects were restricted to fewer particularly fatty food items.

Davis et al reported lower consumption of fruits among overweight/obese women compared to normal weight controls (daily servings of vegetables were almost identical) (135), but in our study the intake of both fruits and vegetables were reported equally between the two groups. Reported intakes of bread and diary products did not differ between the groups, and this coincidence with previous published data comparing food intake (135).

The consumption of light soft drinks and squash were significantly increased among the obese women. A recent published study describing the different characteristics of people consuming either soft drinks with and without sugar, described that intake of artificially sweetened soft drinks was associated with a higher body weight for adults. Consumption of light soft drinks was also related to higher restrained eating, whereas sugar containing soft drinks were related to less restrained eating. This may imply that persons with higher body weight tried to avoid calories by choosing light products (138), and this interpretation can be conveyed to our data material as well. The relationship between artificial sweeteners and control over body weight is an issue in dispute. Whether these sugar replacements are used by the overweight/obese to control the intake of calories and by that body weight, or if these substitutes could be a leading cause to the increasing weight problem in the population. An epidemiological study from 2008 questioned whether the use of artificially sweetened soft drinks might “fuel the obesity epidemic rather than fighting it”. They reported a positive dose-response relationship between the use of artificially sweetened soft drinks at baseline and the prevalence of overweight and obesity after seven to eight years (adjusted for BMI at baseline) (139). On the other hand, review of the literature

is inconsistent in the evaluation of the use of artificial sweeteners in soft drinks with regard to body weight control. Some, but not all findings support that the replacement of sugar by low-energy sweeteners may result in lower energy intake and better weight control (140). On the other hand, there are discussions about how sugar replacements affect satiety, metabolic mechanisms in the body, and by that energy intake. One view is that sweetness supplied without calories results in equivocal psychobiological signals that confuse the regulatory mechanisms in the body, leading to loss of appetite control and overeating (141).

Selection of physical activity level

Physical activity level in obese subjects and as well in normal weight persons is very subjective and difficult to state. Our obese women reported a sedentary lifestyle and in proportion to the defined PAL values extracted from the Nordic Nutrition, a person described as *having a seated work with no option of moving around and little or no leisure activity* has a PAL factor of 1.4 (9). However, NNR do not distinguish between normal weight subjects and morbidly obese persons. They report values for the population as a whole. According to other studies exploring obese subjects, the PAL values varies, and Hustvedt et al estimated a PAL of 1.8, due to increased energy expenditure during weight bearing activities. This finding was demonstrated among obese men and women with an average BMI of 36 using DLW and ActiReg (126). However, Johannesen et al found a PAL value of 1.6 among obese women (BMI 33), while Das et al examined morbidly obese women and found an average PAL of 1.6 (127;128). Based on this data, we decided to use PAL 1.6 in our group of obese women.

The healthy controls were doctors, nurses and physiotherapists, indicating works with standing, some moving around as well as seated paper work. From NNR the PAL value to a person who has *work including both standing and moving around,* is between 1.8 and 1.9. However, the controls also had seated work, but they probably had higher physical activity in the leisure time than the “normal” population, due to occupancy of own health. Because of this assumption, we choose PAL of 1.8 among

the control women, even though this physical activity level is slightly higher than demonstrated in healthy normal weight Danish adults (125). According to the control women's working positions and health attitude, a higher PAL value than this may be expected.

In the present study we found, when using PAL 1.6 among the morbidly obese women and PAL 1.8 among the control subjects, an underreported amount of 570 kcal (17 %) among the obese women, while the median reported food intake among the controls matched the estimated energy expenditure for this group.

Comparing the TEE with the reported energy intake for the obese women, they underreported approximately 17 %, which is consistent with findings from other studies. Svendsen et al demonstrated an underreporting of 20.6 % of energy intake compared to the estimated EE when using FFQ (119). However, in the OPEN study they found among women (normal weight and obese) an underreporting of energy compared to total EE as high as 34-38 % when compared to reported intake obtained by FFQs, and 16-20 % underreporting when compared with 24-hour dietary recall. (142). The obese women in the OPEN study reported an energy intake of 80 % of their energy requirement according to FFQ, and 71 % of the energy requirement based on 24-hour dietary recall (143).

In the present study (using PAL 1.6 for the obese women), investigating the under-reporters separately, we found 69.8 % of the obese women to be under-reporters, which is a higher percentage of under-reporters than previously described. Svendsen et al reported that 59 % of the obese women underreported, using a FFQ (119), while in the OPEN study they demonstrated 57 % underreporting among obese men and women (n=142) when using a FFQ. For all the women (n=223), 49 % underreported, while 46.7 % of the *obese* women (n=65) underreported their energy intake (142). Since the amount of under-reporters in our study was higher than previous findings, we also calculated the TEE based on a lower PAL value; 1.4, in accordance with the definition of PAL 1.4 in NNR (*seated work with no option of moving around and little or no leisure activity*). When using PAL 1.4 in the calculation of TEE we

achieved a better correlation to previous published findings of the estimation of under-reporters. By “lowering” the energy expenditure, fewer women became under-reporters, now constituting 59.5 % (results not shown), very close to what Svendsen et al reported (119). However, the definition of under-reporters plays a major role in the calculation of under-reporters (see next section). On the other hand, the results obtained with the use of a PAL value of 1.4, lead to a median underreported value among all the obese women which was much smaller (5.6 %) and very different, compared to previous published findings (117;119). This further supported our choice of PAL 1.6 among the obese women. However, another point of view, is that several of the obese women in the MOBIL-study might have been in a weight reduction phase (no information was obtained on this topic), thereby reporting a lower energy intake than the estimated expenditure (EI < EE = weight loss), without actually underreporting their food intake. We might have misclassified these women as under-reporters

One may discuss whether the control women reported correctly, or if our estimation of physical activity level was too low. Other studies indicate that underestimation to some extent of food intake is common, independently of adiposity (117;118;144). If the control subjects underreported and the energy account were “break even”, the controls might have a PAL greater than 1.8. This is not unlikely due to the control women’s work and the high assumed activity level in their leisure time. However, the controls were highly motivated health workers, instructed to be specifically accurate during the food frequency questionnaire interview, so the measurements may be valid, resulting in a match between the estimated energy expenditure and the reported food intake, giving energy balance and stable weight. Compared to the mean intake among women aged 30 – 54 years in the Norkost Survey, which was 1864 kcal, our control women reported a higher median energy intake (8). But our control group did not represent a normal, healthy and lean control group. They were all health workers which have more active jobs. As health workers they are probably more occupied with their own health and lifestyle, including eating more healthy food and exercise more than average.

Definition of under-reporters

The definition of under-reporters can be discussed. We used a simple calculation to estimate the number of under-reporters and the number of non-under-reporters, calculated as the reported energy intake minus the estimated total energy expenditure. Subjects with negative outcome of this calculation were classified as under-reporters, while positive outcome resulted in non-under-reporters. In other words, all subjects having only a slightly lower energy intake compared to estimated TEE were classified as under-reporters, even though the difference only constituted a few kilocalories. Svendsen et al. identified under-reporters based on the 95 % confidence limits of the expected EI: TEE ratio of 1.0. Subjects with a ratio below this limit were classified as under-reporters. They also identified accurate-reporters who had their EI: TEE ratio in between the limits. Taken this into consideration, a simple and appropriate definition of accurate-reporters in our study could be the energy intake minus energy expenditure is zero plus/minus 200 kcal (equivalent to two slices of bread, one with ham, the other with cheese). The amount of accurate-reporters in our data material will then be 12 of the obese women. Nine of these 12 accurate-reporters were originally classified as under-reporters, and the "new" percent of under-reporters will be 62 %, compared to 69.8 % originally. This is more consistent with the reported percent of under-reporters (59.3 %) among obese women in the study by Svendsen et al (119). If we used PAL 1.4 among the obese women and extracted the accurate-reporters from the underreporting group, percent under-reporters among the obese would be 48.3 %, which is very consistent with the findings among women in the OPEN study (143).

Another and frequently used method to define under reporters is to calculate the EI: BMR ratio. According to Goldberg et al, the cut off value representing a reported energy intake that may be representative of long-term energy intake, and which is compatible with a normal lifestyle (not bedbound) is 1.35. EI: BMR lower than 1.35 is regarded as underreporting (118;145). This cut off value represent almost the same value as we used when we stated that the obese women reporting energy intake lower than the estimated BMR multiplied with 1.4, were under-reporters. If we had used

Goldberg's cut off (using RMR predicted by Mifflin St-Jeor, in lack of BMR), 61 (52.6 %) of the obese women would have been under-reporters.

Estimating the resting metabolic rate

To estimate the resting metabolic rate, we used the Mifflin-St Jeor equation, both for the obese and the control women. This predictive equation is based on a data set that included normal weight, overweight, obese and severely obese subjects, making the equation more valid for obese persons, than other equations which are based predominantly on normal weight subjects. These equations, as the Harris Benedict equation, are more commonly used to estimate EE among normal weight persons. We used the same equation (Mifflin St-Jeor) for both the lean and the obese women. It is discussable whether this is a source for wrong estimation of RMR, since other equations as the Harris Benedict may be a better equation for the lean, control group. However, in 2005, the American Dietetic Association analyzed different predictive equations for resting metabolic rate. The Mifflin-St Jeor equation performed best with regard of accurately measurement of RMR, both among obese and normal weight subjects. Based on the systematic review of the literature, they recommended the Mifflin-St Jeor equation to estimate RMR (122). The difference between the calculated RMRs from the two equations is minor. When using the median data of the control women in the two equations, Mifflin St-Jeor yielded 70 kcal less in estimated RMR compared to Harris Benedict (weight 65 kg, height 168 cm, age 44 years [medians] estimating RMR of 1321.9 kcal for Mifflin and 1390.1 kcal for Harris). We estimated RMR by both Mifflin St-Jeor and Harris Benedict equation for the obese and the control women, and subtracting the estimated RMR amount of Harris Benedict from the estimated RMR amount of Mifflin St-Jeor. The median difference between these two equations was 44 kcal for the obese women, whereas among the controls the Harris Benedict estimated 71 kcal more in RMR than Mifflin St-Jeor. It is unlikely that this would influence our results, but if we had used the Harris Benedict equation the estimated amount of underreported kcal would be slightly different. With Harris Benedict predicting RMR calculated with PAL 1.8 among the

control women, the estimated TEE would exceed the reported energy intake, stating more underreporting than the Mifflin St-Jeor equation among the control women. With regard to previously reported findings that normal weights also underreport their food intake (118;144), this calculation might be more accurate, but there are only small differences in the estimation of energy expenditure compared to the reported energy intake. Furthermore, our control women are not a representative selection of women, and we think they may be more accurate in their reporting, and the accurate estimation of EI versus EE using Mifflin St-Jeor and PAL 1.8 might be right for this control group. Using Harris Benedict for the obese women would increase the underreported amount of kcal.

Reasons for under-reporting

Our control women reported accurately when we used a PAL value of 1.8, while the obese women (PAL 1.6) underreported approximately 570 kcal (median). Previous studies have supported the assumption that underreporting becomes more common as body weight increases. Still, underestimation of energy intake is also common among non-obese subjects (116). Even though the obese women underreported the EI, they simultaneously reported an intake of energy of 300 kcal more than the control women. This difference of 300 kcal tended to be significantly different. Significant difference between the reported EI among obese women and controls was found in a study by Berteus et al. The Swedish obese women (BMI 38.1 ± 4.5 kg/m²) had an energy intake which were approximately the same as in our study, but it was significant different from the reference group of lean women (it is likely that our control women had an higher EI due to higher physical activity level) (137).

Since the estimated TEE was significantly higher among the obese than the control women, an accurately reported EI could be expected to be significant different between the two groups as well. This non significant difference between the obese and the controls, and why underreporting is an issue, can be explained by several factors. Hill et al have summarized characteristics of under-reporters and proposed mechanisms for underreporting. Higher educational level and social class has been

associated with better correlation between reported EI and the estimated TEE (116). Our controls were health workers; doctors, nurses and physiotherapists, and were all subjects with higher educational achievement and thereby presumable a higher social class. Furthermore, Hill et al characterizes under-reporting persons as possible restrained eaters who have increased concerns about their body weight and poor body image (116). In obese subjects the reported intake may actually be lower in periods due to dieting (dietary restraint) and an attempt to weight reduction. On the other hand, other periods may be filled with binge eating and perhaps compulsive eating contributing to the weight gain. During these periods, most likely the obese subject will not seek medical centres, due to bad self efficacy. It is not unlikely that the interception of this dietary pattern and food choices not will be included in a study seeking information about dietary history in obese persons. FFQs often focus on the diet during the last year, but intakes during the last months may be easier to remember, than recalling the food intake eight months ago. In a period with dietary restraint an obese person diet report may actually be precisely and describe the actual intake, but the periods of binge eating which has brought this person to the obesity scale is forgotten, and comes off the record. Furthermore, there might be great differences between weekdays and weekends. The diet through the week might be reasonable healthy, while during the weekends the intake may include very calorie dense food (such as sweets, cakes, junk foods and alcohol). Most likely the diet through weekdays may be easier to recall and generalize because of more routines and rhythm these days than weekends. Subjects visiting a nutritionist to give a dietary interview may have a deliberate or subconscious intention to report a healthier diet than normally consumed. Underreporting may be manifested by failure to report eating occasions or to report eating occasions incorrectly, misreport in the quantity eaten, or maybe a combination of these together, or denial of food consumption (116;146). All put together, diet among obese subjects may be difficult to define, and to detect the representative normal diet during a period of time.

Previous published findings have tried to detect the difference in food intakes between under-reporters and non-under-reporters. Lafay et al demonstrated a higher

contribution of snacks to the total energy intake among normal weight, middle aged non-under-reporters compared to the ones who underreported. Lunch and dinner, for underreporting men and women respectively, contributed to a higher extent to the total energy intake. Food items such as butter, dairy desserts, sugars and confectionery, cakes/pastry/biscuits, French fries and to a lesser extent fruit were significantly less frequently reported by the underreporting men and women. Food items reported equally between non-under-reporters and under-reporters were vegetables, green vegetables, fish and meat (120). By looking at the diet history of 50 obese persons studied by Svendsen et al, the researchers revealed by the dietary record a lower intake of "sweets, desserts and snacks" and drinks with sugar among the under-reporters compared to the non-under-reporters. The under-reporters also had a higher energy percent from protein, and a lower energy percent from sugar compared to non-under-reporters. However, the reported absolute intake of protein was lower in the under-reporting group. According to both FFQ and DR, sweets, desserts and snacks was inversely related to energy percent from protein. Diet history obtained by FFQ revealed that accuracy in food intake reporting was inversely correlated to the percentage energy from protein and positively correlated to energy percent from sugar (119).

5.1.2 Obese pre-PCOS women versus obese women

In our lack of a PCOS diagnosis among the obese women in the MOBIL-study, we used a surrogate marker, the free testosterone index, and classified women having a FTI score above 0.6 to be pre-PCOS subjects. In the real diagnosis of PCOS, hyperandrogenemia is one out of the three diagnostic criteria; and the women have to satisfy two of the criteria to be diagnosed. By using only the FTI score as a "diagnostic criteria", we classified 46 out of the 116 obese women to have pre-PCOS status. This is almost 40 % of the obese women, which is a higher prevalence of PCOS in a obese population compared to previously published studies on PCOS among overweight and obese women (58;59).

Anthropometry

The obese women with pre-PCOS diagnosis were significant heavier than the obese women with free testosterone index below 0.6, and the waist circumferences were also significantly higher, suggesting a more android fat distribution among the pre-PCOS women. Carmina et al investigated the abdominal fat among women with PCOS compared to weight matched controls. They found similar quantity of total fat and trunk fat in these two groups, but only the normoweight and overweight women with PCOS had increased central abdominal fat compared to the controls, not the obese women with PCOS (72). On the other hand, Cascella et al examined overweight PCOS women and reported larger waist circumference among these women compared to age- and BMI-matched controls (71). Furthermore, measurement of waist circumference is valuable to identify people who are at increased risk to develop obesity-related illness, due to accumulation of abdominal fat tissue. The pre-PCOS women who had elevated waist circumference compared to the women with lower FTI score, may possess more risk factors for cardiovascular disease (41).

Lipid profile

Dyslipidemia is reported to be common among women with PCOS, characterized by increased levels of triglycerides and small, dense LDL particles and decreased concentration of HDL-C (68;76).With regard to levels of LDL-C and HDL-C, we did not find a more unfavourable status among the obese pre-PCOS women compared to the obese women. However, the levels of triglycerides tended to be greater in the pre-PCOS women. Enhanced levels of triglycerides in women with PCOS have been described previously. Pirwany et al found significant difference from BMI matched controls (77), and Legro et al reported significant higher triglyceride values in PCOS women compared to BMI matched controls, but after adjusting for age, BMI, waist-to-hip ratio, and fasting insulin and glucose levels, the difference was present but not significantly different (80).

Adipokines

Previous studies done on women diagnosed with PCOS, have reported significantly lower levels of adiponectin in these women compared to weight-matched controls (147). Among our obese pre-PCOS women, the adiponectin levels, tended to be lower compared to the obese women with FTI below 0.6. Leptin levels were equally between the groups, and this result correspond to previous published findings that leptin levels have been related to BMI rather than other metabolic or hormonal disturbances in women with PCOS (82).

Reported food intake

The pre-PCOS women tended to have a higher intake of protein and fat compared to women with lower FTI score, the intake of polyunsaturated fat was significant higher. There are limited data on the dietary history of women with PCOS. Douglas et al compared the dietary profile to overweight women with PCOS with age-, race- and BMI-matched controls. They did not find any significant difference between the groups in total energy, macronutrient and micronutrient intake. However, the PCOS women had significant more servings of white bread (including white hamburger and hot dog buns, muffins and biscuits) and the intake of fried potatoes tended to be higher in the PCOS group (148). Our obese pre-PCOS women reported higher intake of potatoes and also of the under group fresh potatoes, than the obese women with lower FTI score. Another study done on women with PCOS and dietary intake reported a higher intake of meat, fish, poultry and eggs among obese PCOS women compared to obese women without PCOS (149). We found significant higher reported intake among the pre-PCOS of meat and the under group forcemeat, as well as the food group consisting of butter, margarine and oils. This may be contributing factors to the total fat intake, which tended to be higher among the pre-PCOS women, together with a significantly higher intake of polyunsaturated fat. Perhaps the higher fat intake is a factor which plays a role in the development of greater body weight of the obese pre-PCOS women compared to the obese women with FTI < 0.6. Interestingly, the pre-PCOS reported a higher intake of the same food items (except potatoes) which constituted a difference between the diets of morbidly obese women

and normal weight women. Carefully, we might assume that the intake of these particularly food items might be a contributing factor to the development of obesity and perhaps PCOS. Previously, dietary histories from American women with PCOS were compared to dietary histories from Italian women with PCOS. The American women had an average BMI 40.3, while the Italian women had a mean BMI of 29.7. The total reported caloric intakes, as well as the proportions of the main dietary constituents were similar in the two groups. However, the amount of saturated fat was significantly higher among the American women than the Italian. Together with genetic and lifestyle factors, the researches concluded that this higher consumption of saturated fat may have played a role in the development of excessive weight among the American PCOS women (150).

5.2 PCOS women and effect of weight loss – preliminary results of the FEMIN study

5.2.1 Effects of low-calorie-diet among PCOS women

The crisp bread diet and the powder diet were high-protein diets, yielding 32.4 % and 42 %, respectively, of the total energy intake from protein. Furthermore, they were low in fat, having an energy percent from fat of 13.5 % and 18.9 %, respectively of the total energy intake. With these contributions of energy from protein and fat, the powder diet was low in carbohydrate as well (38.8 E %), while the crisp bread diet had a carbohydrate content in a more "normal" range (53.1 %). However, such composition of low-calorie-diets have previously demonstrated weight reduction among obese persons (99;105).

Effect of LCD on anthropometric measurements

At baseline, nine women diagnosed with PCOS had a mean BMI of 40, waist circumference of 121 cm, hip circumference of 131 cm and a waist-to-hip ratio of 0.93. Compared to anthropometric measures of morbidly obese women (mean BMI

47) reported by Ozenoglu et al, our PCOS women had wider waist circumference, lower hip circumference and a more unfavourable waist-to-hip ratio (42). Interestingly, our PCOS women had lower mean BMI than the other morbidly obese women, still they had wider waist circumference. Among the pre-PCOS women in the MOBIL-study we also detected a significant higher waist circumference compared to the non-pre-PCOS women. This is accordance with findings from Cascella et al, who reported significant higher waist circumference and amount of visceral fat among overweight women with PCOS, compared to BMI-matched controls (71).

After the weight reduction intervention period, the participating PCOS women significantly reduced their weight, BMI, waist- and hip circumferences. The extent of the reductions is in accordance with a previous report on a low-calorie-diet lasting for eight weeks among PCOS women (151).

König et al reported a reduction in waist circumference per kilogram loss of body weight to be 0.96 cm/kg in a group of pre-obese/obese women who used a diet consisting of meal replacements (ca 1000 kcal/day) in six weeks (152). Our women lost an average of 7.4 kg during the weight reduction period, and the waist circumferences were lowered by an average of 5.9 cm. This gives a reduction of 0.80 cm in waist circumference per one lost kilogram body weight.

Neck circumference is a new risk factor that may reflect risk of the metabolic and PCOS syndromes in premenopausal obese women. A neck circumference below 39 cm indicates a low risk; while a circumference above 42 cm reflect a higher risk. Our PCOS women had at baseline a mean neck circumference of 40.3, which indicated that they had a intermediate risk to develop the metabolic syndrome (129). However, after the low-calorie-diet period, our PCOS women significantly reduced their neck circumference with 1.5 cm, to 38.8 cm. According to reference values given by Dixon et al, our PCOS women may therefore have reduced their risk of metabolic syndrome from intermediate to low (129).

Effect of LCD on body composition

After eight weeks on the low-calorie-diet the PCOS women lost in average 7.4 kg of the total body weight, representing a 6.3 % reduction. Loss of fat mass was 5.6 kg, representing a 9.7 % reduction in the total fat mass. The women lost 1.9 kg (3.1%) of fat free mass, constituting 25.1 % of the total weight loss. Our findings are in accordance with a previous study by Moran et al who explored the effect of meal replacements, where PCOS patients followed an energy-restricted diet (1100-1200 kcal/day) for eight weeks, in which two meals per day were replaced by a meal replacement. These women lost in average six kg, reduced their total fat mass with approximately 12.3 % and lost about 2.5 % of the total fat-free body mass after eight weeks intervention (151).

The observed reduction in fat free mass (25.1 % of total weight loss) is also consistent with the findings of Janssen et al, who reported a percentage loss of fat free mass of 25.2 of the total weight loss in obese women after LCD (-1000 kcal/day, 16 weeks), without additional exercise (102). Chaston et al referred to three randomized clinical trials which used low-calorie-diets (restricted calorie intake by 1000 kcal/day) for 16 weeks, and these subjects lost 27.8 % of the total weight loss as fat free mass (approximately 23 % for women). However, participants who participated in exercise lost less fat free mass (100). Our results showing that PCOS women lost muscle mass (mean 1.8 kg), are in accordance with former studies using low-calorie-diets without additional exercise (100;102). Some of the women reported physical activity during the weight reduction phase, while others expressed that they did not have the energy and drive to perform physical activity together with the diet. To induce weight loss, former studies have shown that diet alone, diet with aerobic exercise and diet with resistance exercise lead to the same weight loss. However, the loss of muscle mass was decreased in groups who engaged in physical activity, and thereby having a better body composition after the weight reduction period (102;153).

Effect of LCD on lipid profile

At baseline in the present study, the participating PCOS women had a mean level of total cholesterol of 5.0 mmol/l and mean concentrations of LDL-C, HDL-C and triglycerides of 3.2, 1.2 and 1.2 mmol/l respectively. According to the recommendations from the National Cholesterol Education Program in USA, our women had a borderline value of total cholesterol, the levels of LDL-C were elevated, while the concentrations of HDL-C and triglycerides were within the recommended range (20). Former studies have stated that women with PCOS are characterized by elevated levels of triglycerides, and small, dense LDL particles together with lower levels of HDL-C (68;76). Our women did not have unfavourable triglyceride values, and the concentration of HDL-C was not (yet) to low. According to former reported effects of weight loss (41;93), we did not significantly detect the expected decrease in levels of total cholesterol and LDL-C, but the levels of triglycerides tended to be reduced after the weight reduction period. Recently, Thomsen et al investigated the effect of a low-calorie-diet (1200-1400 kcal) among obese women with PCOS. After ten weeks on the diet, the women lost weight and significantly reduced their levels of total cholesterol, LDL-C and HDL-C compared to the concentrations analysed at baseline (153). The same observation was reported by Moran et al together with lowered levels of triglycerides (151). We observed not significant reductions in the levels of total cholesterol, LDL-C and HDL-C after the low-calorie-diet period. However, we might have detected a significant reduction in these parameters if our sample of women had been larger.

Compared to the 52 overweight PCOS women in a study by Pirwany et al, our women had approximately the same values of total cholesterol, triglycerides, LDL-C and HDL-C as these women (mean age 28.2, mean BMI 29.4). These overweight women were compared to BMI-matched controls, and the PCOS women had higher concentrations of triglycerides, but the other parameters were not significantly different to the values from the controls. However, as our participants were young women below the age of 40, the raised levels of LDL-cholesterol were in accordance to the findings from Talbott et al, who detected that young women with PCOS have

higher LDL-C concentration than controls (78). Elevated levels of LDL-C are also reported by Legro et al, who demonstrated a mean value of LDL-C among 144 obese PCOS women to be 3.4 mmol/l. Furthermore, these women had higher HDL-C concentration than their obese control women, still the absolute value (0.9 mmol/l) was below the recommended cut off value, and lower than the HDL-C level observed in our women. Furthermore, the triglyceride values to these women were increased compared to the levels we detected in our women, 2.2 mmol/l versus 1.2 (80).

Effect of LCD on cardiovascular disease risk

According to the Framingham and the INTERHEART study, some risk factors for cardiovascular disease are abnormal lipids, abdominal obesity, hypertension, intake of fruit and vegetables together with low physical activity. Our PCOS women tended to have an unfavourable lipid profile. According to the recommendations from the National Cholesterol Education Program, the level of LDL-C was elevated, while the concentration of triglycerides was below the recommended value. The level of HDL-C was tilting around the lower acceptable concentration of this parameter, which again has been shown to be a marker of increased cardiovascular risk (32). Furthermore, the PCOS women had increased waist circumferences, which were higher than the recommended cut off values for metabolic syndrome (4;20). The PCOS women also had slightly raised blood pressure. If we assume that these women had the same food intake as the obese women from the MOBIL-study, we know that they might have an unsatisfactory intake of fruit and vegetables. Furthermore, none of the women did report own high physical activity, during the visits at Rikshospitalet. Taken all this into consideration the participating PCOS women possessed several of the identified risk factors for cardiovascular disease.

Former studies are inconsequent in whether women with PCOS have increased risk of developing cardiovascular disease than women without this syndrome or not (90;91). Cussons et al reported that studies of women with PCOS have detected that these women have altered function and structure of the cardiovascular system, addressing the risk factors to be the consequence, rather than the PCOS diagnosis

alone (76). Lo et al have identified such risk factors for CVD among women with PCOS (86), and we have consisting findings among our PCOS women. However, Shroff et al investigated asymptomatic coronary atherosclerosis among young obese women with PCOS, and found elevated occurrence of atherosclerosis in these women compared to obese controls, independent of other known risk factors for CVD (154). Furthermore, increased carotid intima-media thickness and reduced flow-mediated dilatation are demonstrated in young girls with PCOS, factors which lead to premature subclinical atherosclerosis (88;89). If women with PCOS tend to have more subclinical atherosclerosis due to this syndrome, together with the occurrence of other risk factors for cardiovascular disease, the outbreak of these diseases may occur earlier than among other women without the syndrome (67).

Due to the small number of PCOS women we may not have detected significant reductions in some of the risk factors for cardiovascular disease (abnormal lipids, abdominal obesity, and hypertension) as we might have seen in a larger selection of women. However, we observed reductions in total cholesterol, LDL-C, triglycerides and systolic- and diastolic blood pressure, together with a significant reduction in waist circumference, which may play an important part in development of better cardiovascular health among the PCOS women. Furthermore, during the low-calorie-diet period the women were urged to consume a considerable amount of fruit and vegetables, which may further protect against CVD.

Effect of LCD on CRP

Another potential marker for cardiovascular risk; CRP, was elevated among the PCOS women. At baseline they had a mean concentration of CRP of 9.3, which is far above the cut off level which indicates increased risk for subsequent cardiovascular disease (17;36). Reduction in CRP levels have been shown after weight reduction (17), however we only observed a slight decrease in this parameter after the low-calorie-diet. However, Moran et al reported from a group of obese women with PCOS and their BMI-matched controls that a weight loss of 4-5 % lead to a decrease in CRP levels among the non-PCOS women, but not for the women with PCOS. The

researchers suggested that in order to see an improved effect in CRP level and achieve equivalent cardiovascular benefit as non-PCOS women, a larger weight loss is required in women with PCOS compared to women without PCOS. We observed a mean weight loss of 6.3 %, but we did not detect a significantly reduction in CRP levels (may be type II error). Future research (for instance the FEMIN study) with a larger selection of women may detect improved CRP levels according to this percentage of weight reduction.

Apolipoproteins and risk for cardiovascular disease

Low-calorie-diet lasting for eight weeks did not reduce the concentration of apoB among our PCOS women. However, their concentration of apoB was lower than previously described among 64 464 females in a Swedish population (155). Elevated levels of apoB have been reported to cause an increase in risk for fatal myocardial infarction. With apoB levels around 0.8 g/L, our women had a risk ratio of 1 (35). Furthermore, the level of apoA-I was significantly lowered after the low-calorie-diet. At baseline our PCOS women had the same concentration of this parameter as the Swedish women, reported by Jungner et al (155). Walldius et al described that an ApoA-I concentration around 1.5 reduces the relative risk for fatal myocardial infarction to approximately 0.55 (45 % reduction). However, after the eight weeks on diet, our women reduced their concentration of this parameter to 1.3 g/L. A reduction in apoA-I diminishes the protective effect of this parameter (relative risk for fatal myocardial infarction closer to 1) (35). The ratio of apoB/apoA-I among the PCOS women predicted a relative risk for myocardial infarction to be around 1 (35), and the ratio was slightly lower than the observed value in the study of the Swedish population (155).

Effect of LCD on the expression of adipokines

Compared to the pre-PCOS women from the MOBIL-study, the women in the FEMIN-study had lower levels of adiponectin and higher concentration of leptin at baseline. Previous research has reported significantly lower levels of adiponectin in PCOS women (83;147), together with an inverse correlation of this parameter with

BMI and waist circumference (83;85), which may explain the lowered levels of this parameter among the PCOS women. After the low-calorie-diet the PCOS women improved their leptin concentration significantly which is consistent with de Luis et al, who reported a decrease in leptin concentrations even after modest weight reduction among obese men and women (156). Glintborg et al reported an increase in leptin concentration with increasing BMI (83), and by reducing the BMI among the PCOS women we observed a reduction in the leptin levels. With regard to the concentration of adiponectin we only observed a small increase in this parameter. Weight reduction have been associated with an increase in adiponectin levels, however this was described in patients without PCOS (52;83).

5.2.2 Effect of two different low-calorie-diets among PCOS women

As expected, we did not observe any significant difference between the achieved differences ([Δ], baseline measurements – eight weeks measurements), from the baseline measurement to the eight weeks control, between the crisp bread diet and the powder diet.

However, when we compared the eight weeks measurement between the groups, we detected differences between the groups, which were not present at baseline, see figure 11. The women in the powder diet group had significantly lower concentrations of total cholesterol, LDL-C, apoB, and leptin, and the apoB/apoA-I ratio was more favourable. Furthermore, the waist circumference tended to be lower in the powder diet group at the eight weeks control (data not shown). Statistically these results can not be used to predict that the powder diet was more effective than the crisp bread diet; it is the delta changes which can indicate such a finding. As stated before; the achieved differences (Δ) in the two diet groups were not significantly different from each other. However, the significant differences between the two groups after eight weeks may indicate a difference, which might have been demonstrated, with a larger sample of women in each diet group. These results may be regarded as hypothesis-generating for the FEMIN study.

Different low-calorie-diets and effects on body composition

Deibert et al compared weight loss and the body composition between three groups following three different weight reduction regimens. They showed that a high-soy-protein, low-fat diet consisting of meal replacements to some of the meals during the day, resulted in a greater weight loss and decrease in fat mass compared to a conventional moderate-fat diet. The same diet with high-soy-protein and low fat content together with physical activity two times during the week did not create a higher weight reduction than the diet alone. The researchers assume that the high intake of soy-protein may induce a greater loss of fat mass than reduction of muscle mass compared to a standard diet, and may minimize the benefit of physical activity by preventing the loss of muscle mass (157). Unfortunately, due to our small sample of women, we did not detect any difference in loss of fat free mass between the two diet groups. However, in both diets, the protein content was high.

As we compared the women in the two diet groups after eight weeks, we observed a tendency to lower waist circumference among the women in the powder diet group. This is not in accordance with a recently published study by Katcher et al. They studied both women and men with the metabolic syndrome eating an energy-restricted diet, high in whole grains compared to the same hypo caloric diet, but with refined grain products. Both groups lost weight, but the “whole grain group” had greater decrease in percentage abdominal fat and CRP, compared to the “refined-grain group” (158).

In the powder diet, 34.4 % of the total energy came from added sugar, compared to 9.8 % in the crisp bread diet. The second main ingredient in the meal replacements shakes was fructose, suggesting that the energy derived from fructose was at least 17 energy percent. Recently focus has been drawn to the potential unfavourably effects of high intake of fructose, which according to recent findings of Stanhope et al, may lead to a more unfavourable distribution of abdominal fat (viscerally vs. subcutaneous) compared to intake of glucose, together with a decreased insulin sensitivity and promotion of dyslipidemia(110).

Total cholesterol and LDL-C; effects of soy protein and dietary fibre?

The achieved differences (Δ) in levels of total cholesterol and LDL-C were not significant different between the two diet groups. However, it seemed like the powder diet group women reduced their levels of total cholesterol and LDL-C more, and their eight weeks measurements were significantly lower than the eight weeks measurements for the crisp bread diet women. The powder diet consisted of meal replacements shakes, which contained soy as the source of protein. Anderson et al described a better improvement in total cholesterol and LDL-C after a weight reduction period consisting of meal replacements based on soy, compared to milk-based meal replacements (112). In a meta-analysis of the effects of soy protein intake on serum lipids, they concluded that the ingestion of soy protein rather than animal protein significantly decreased levels of total cholesterol, LDL-C and triglycerides (111). Furthermore, from this analyse of 29 studies, they reported that consumption of soy protein was associated with a net change (change during the soy diet minus change during the control diet) of -0.60 mmol/L in total cholesterol. After ingestion of Nutrilett powder, the mean value of total cholesterol, among our four PCOS women on this diet, were changed with -0.57 mmol/L. For the concentration of LDL-C, in the meta-analysis the reported reduction was 0.56 mmol/L, and we observed an equal reduction of 0.62 mmol/L among our powder diet women. Interestingly, approximately similar reduction in triglyceride values was also reported in the meta-analysis (-0.15 mmol/L) as we detected in our powder diet women; -0.25 mmol/L. These results may indicate that the content of soy protein in the powder diet may have importance for achieving a better lipid profile, in addition to the weight loss induced by these low-calorie meal replacements.

However, there is not enough evidence to suggest that the content of soy protein in meal replacements alone were responsible for what may as an assumed better lipid profile. Former studies have described the potential role of dietary fibre in the improvement of serum lipids. The meal replacements as we used, contained a considerable proportion of dietary fibre, and in the Nutrilett powder, the dietary fibre source is soy fibre. Soy beans consist of both insoluble and soluble fibres (10g and 7g

respectively, per 100 g dry weight soy bean), and we assume that the shakes have a mixture of both these fibre types. In the crisp bread diet, the dietary fibre content was also high, allowing for more fibre-rich vegetables. Rye and vegetables have a varying content of soluble and insoluble fibre. However, soluble fibres have been investigated in regard to the effect on serum cholesterol levels, and soluble fibres have significant hypocholesterolemic effects. RCTs have been reviewed, and consumption of soluble fibres is associated with reduction in LDL-cholesterol, without significant changes in HDL-cholesterol or triglyceride concentrations (113).

5.2.3 Low-calorie-diets in clinical practice

Pros and cons for the crisp bread diet

The strength with the crisp bread diet is the dietary composition and its proximity to healthy food choices, portion sizes and meal pattern, all of which are important factors in weight reduction. These factors are of equivocal importance in further weight reduction or weight maintenance after the end of the low-calorie-diet. In addition, dietary fibre, which is a prominent part of crisp breads and vegetables, has bulking action, and increase the satiety due to the "fill effect" in the gastrointestinal tractus of this dietary component. In this way consumption of dietary fibre can decrease the intake of other food items during a meal, and still lead to satiety. Some of the women in the crisp bread diet claimed that they actually thought they were "allowed" to eat quite a large amount of food, which probably is caused by the bulking action. In addition, vegetables are low in calorie content compared to their size and amount eaten. Furthermore, using normal food items in a restricted diet may enhance the compliance to diet, due to enhanced palatability and plenty of food items options. However, what a person might find challenging with the crisp bread diet is to restrict their intake of food within the limits given for the diet. Two crisp breads for each meal is a much smaller amount of food for a meal, compared to what morbidly obese persons might be used to ingest.

The crisp bread diet is also easier to incorporate into everyday life, since it is based upon common food items and Norwegian food traditions, and therefore might reduce the amount of questions and attention given the "slimming" woman. In this way her low-calorie-diet period may progress without interfering too much with her social life. This may act relieving for some women; others might want the attention and "feed back" to get the drive to progress with the diet.

Pros and cons for the powder diet

Meal replacements are an effective, nutritionally adequate short-term strategy for reducing weight and improving body composition, quality of life, and metabolic and reproductive variables. Meal replacements may be a preferred weight-loss strategy for some persons, because they can aid in compliance with and adherence to a low-calorie- diet. However, what might be very essential is the subject's attitude to the meal replacement at the beginning, together with her former experience with such shakes and the taste of these. These are some of the factors which might be predictive of the participant's compliance to the powder diet. Some women were disgusted just of the thought of the shakes. However, those who completed the eight weeks period with meal replacements were positively surprised by how well this worked out. Furthermore, powder diet is easy to manage; you know exactly what you are allowed to consume each day. However, it might be experienced as boring and monotonous, and unfortunately the participants do not get the practice to choose healthy food, learn about right portion sizes and meal pattern as they do with the crisp bread diet. However the powder diet may give a "kick-start" to weight reduction, leading to the a feeling of "master and command", which again may promote enhanced motivation to proceed with further lifestyle modifications and thereby further weight reduction/weight maintenance.

Which low-calorie-diet should we recommend?

As experienced during this year with ten women participating in, and nine women completing an eight weeks period of two different low-calorie-diets, we would

indulge our experience to previous published findings (99), that a diet is followed with best compliance and results if the person itself is motivated and positively directed to the diet in question. Until the results from the FEMIN study is available, and until we know if any of the diets give better results among women with PCOS, we would recommend and practise both diets, letting the patient itself choose which diet she thinks may be most advantageous for her. Both the weight reduction phase and the kilocalorie-escalation-phase afterwards must be considered and discussed. As a clinical nutritionist, our main task will be to ensure nutritionally adequate intakes, as former researchers have concluded that while following energy-restricted diets to induce weight loss, the incorporation of fortified foods and/ or dietary supplements may be needed (159). Furthermore, of similar importance, is to be a fellow-being, giving a lot of support, motivation and care.

5.2.4 Methodological issues

Part one - Analyses of reported food intake in the MOBIL-study

Collecting of data

When using dietary interviews as a measure of energy intake, we do not know whether this person is in a weight stable period, in a weight reduction period or in a weight gaining period. The estimated food intake may reflect the actual food intake for that period, but not the actual food habits the person has during the whole year. The strength with a dietary interview based on a FFQ which was used in the MOBIL study is that the interviewer follows the FFQ, making the interviews alike. Furthermore, the interviewer may help the interviewed subject to remember forgotten food intake occasions etc, which may be forgotten or left out, when the subjects fill in the FFQ themselves. A disadvantage of the interviewed FFQ is that the interviewer may affect the subject in such way that he/she reports a healthier dietary composition than actually consumed. Filling in the FFQ by themselves may result in a more honest reporting.

Another problem in the measurement of food intake in humans is the conversion of the information obtained about the everyday food consumption to nutrient and energy intake. Errors may come into being, but this error will most likely be alike for all the participants.

Part two - PCOS women and effect of weight loss – preliminary results of the FEMIN study

Sample size

A limitation with the present study is the reduced/ non-exciting power to detect differences between the two low-calorie-diets. In the FEMIN study the inclusion of 180 women are calculated to give statistically power. However, due to delayed approval to recruit PCOS women from Aker University Hospital, together with a more slowly recruitment of PCOS women from "Kvinnehelsesenteret", "Kvinneklinikken" at Rikshospitalet University Hospital HF than expected, we ended up with a very small selection of women. A total of ten women were included in our study, however one of the women did not attend the second visit, so we had one "drop out", and thereby nine participating women. Due to this small sample size our study became a preliminary report of the FEMIN study, where we investigated the effect on different body and blood parameters of a low-calorie-diet, rather than comparing the effects of the two different diets. Drawing a comparison between the crisp bread diet and powder diet group became impossible due to the small number of women participating, making statistically analyses almost powerless. However, our results may indicate trends that might be detected in the FEMIN study.

Collecting of data

Anthropometric data were collected by three different persons (Line Kristin Johnson, Linn Mari Bjørnådal and myself) in the present study, which may lead to measurement errors. Furthermore, the PCOS women were summoned to Rikshospitalet after eight weeks on the low-calorie-diet, but not all the women met to this arranged meeting. In addition, some of the blood samplings went wrong and the woman had to come back for a new sampling. Therefore, some of the women met a

couple of weeks later than planned, to be anthropometrically measured and giving blood samples. At this point these women had ended their low-calorie-diet and had carried forward with "normal food" and a higher energy intake. This might have given effect on the registered blood parameters and the weight losses, resulting in incorrect values of the effects of LCD. This may be especially relevant for the powder diet women, where a switch from meal replacements to "normal food" may interfere on the results of the powder diet.

Statistics

Part one

We consulted a statistician, Petter Laake, who advised us to use non-parametric test for all of the data, since the principal data were non-normally distributed. Further on, he recommended us to investigate the normally distributed data which almost reached significant differences with a parametric test as well, to find statistic support to the tendency we had detected by the non-parametric test. The control group consisted only of 20 women, and with such a small group, it is difficult to detect statistically significant differences between groups. The power to correctly identify whether or not there was a difference between our groups was weakened/impaired due to for one thing the use of non-parametric tests, and also the small size of the control group. We may have found some non-significant results due to insufficient power.

Part two

Since the achieved differences resulting from the low-calorie-diet were normally distributed; we used a parametric test to detect any significant changes at eight weeks from baseline. When comparing the two diets against each other, the sample size in each group became very small. However, still we were recommended by the statistician Petter Laake to perform a parametric test on this material. His argumentation for this was based on the fact that our number of women in each group was small, and therefore impossible to predict the distribution of the data. In addition he assumed that we most likely would not detect any significant differences, so we could use the parametric test in any case. Laake also supported the non-parametric

comparison of the eight weeks measurements between the two LCD groups, to see if we could detect small dissimilarities between them, which were not present at baseline.

6. Conclusion

6.1 Part one – Analyses of reported food intake in the MOBIL-study

In the present study we found that

- Morbidly obese women have a more unfavourable lipid profile and expression of the adipokines, leptin and adiponectin, compared to healthy normal weight control women

- There was no significant difference in the composition of their diet with regard to energy and macronutrient intake between morbidly obese women and healthy normal weight control women. The intake of fat and saturated fat tended to be higher among the obese women, while the consumption of alcohol (beer, wine, and liquor) was significantly lower than among the control women. Total intake of food was greater among the obese than the control women. Furthermore, the obese women reported a higher intake of meat and forcemeat, butter/margarine/oil; light squash and artificially sweetened soft drinks compared to the control women.

- Morbidly obese women underreport their energy intake more than healthy normal weight control women, when using PAL of 1.6 among the obese women and PAL 1.8 among the control women.

- Morbidly obese women with free testosterone index score > 0.6 (pre-PCOS) have higher weight, height and waist circumference, and a trend to more unfavourable concentration of triglycerides and adiponectin, than morbidly obese women with an FTI score ≤ 0.6. The reported energy and macronutrient intake were equal between the two groups; however, the consumption of total

fat tended to be higher in the pre-PCOS group, and the intake of polyunsaturated fat was significantly higher.

6.2 Part two – PCOS women and effect of weight loss – preliminary results of the FEMIN study

The results in the present study indicate that

- Eight weeks on a low-calorie-diet lead to significant improvement in weight, BMI, waist-, hip-, and neck circumferences, together with reduction in fat mass and fat free mass (and muscle mass), leading to an improved body composition.

- Eight weeks on a low-calorie-diet tended to improve the triglyceride concentration, however it did not lead to significant improvements in levels of total cholesterol, LDL-C, HDL-C and apolipoprotein B, but lead to an unfavourable significant decrease in apolipoprotein A-I. Eight weeks on LCD did not improve CRP level, systolic and diastolic blood pressure significantly.

- Eight weeks on a low-calorie-diet lead to significant improvement in leptin concentrations, however no effect was observed on adiponectin levels.

- Changes in markers for cardiovascular disease were not different between subjects consuming the crisp bread diet and the powder diet of eight weeks duration.

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8. Appendix

8.1 Appendix 1: Food Frequency Questionnaire used in the MOBIL study

1. Hvor mye brød pleier du å spise?

Legg sammen det du bruker til alle måltider i løpet av en dag.
(1/2 rundstykke = 1 skive, 1 baguett = 5 skiver, 1 ciabatta = 4 skiver)

	Antall skiver pr. dag													
	0	1/2	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød (loff, baguetter, fine rundstykker o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mellomgrovt brød (lys helkorn, lys kneipp, lys hj.bakt o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grovt brød (fiberkneipp, mørk kneipp, mørkt hj. bakt o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Knekkebrød (kavring, grov skonrok o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sum skiver pr. dag = ___
Antall skiver pr. uke: ___ x 7 = ___. Tallet brukes i spørsmål 5.

2. Hva pleier du å smøre på brødet?

Merk av både for hverdag og helg, selv om du bruker det samme.

Hverdager		Lørdager, søndager
☐	Bruker ikke noe	☐
☐	Smør (meierismør)	☐
☐	Bremykt, Smøregod	☐
☐	Brelett	☐
☐	Soft-, soyamargarin (pakke, beger)	☐
☐	Solsikke	☐
☐	Oliven	☐
☐	Vita	☐
☐	Olivero	☐
☐	Omega	☐
☐	Soft light	☐
☐	Vita lett	☐
☐	Annen margarin	☐

3. Om du bruker fett på brød, hvor mye bruker du?

En porsjonspakning på 12 g rekker til antall skiver	
1	☐
2	☐
3	☐
4	☐
5	☐
6 eller flere	☐

4. Melk (Husk å ta med melk du bruker på frokostgryn, grøt og dessert)

(1 glass = 1,5 dl)

	Drikker sjelden/ ikke	Antall glass pr. dag								
		1/2	1	2	3	4	5	6	7	8+
Helmelk, søt, sur (kefir/kultur)...	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettmelk, søt, sur (kefir/kultur)..	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lettmelk, ekstra lett	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Skummet melk, søt, sur (kultur)..	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Cultura naturell/bær/frukt.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Biola naturell/bær/frukt.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Drikker du vanligvis Cultura eller Biola (sett kryss) ☐ med bær/frukt ☐ uten bær/frukt

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5. Påleggssorter

Bruk sum skiver pr. uke fra spørsmål 1.

	Til antall skiver pr. uke									
	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29+
Brun ost, prim	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hvit ost, helfet, 27% fett (Jarlsberg, Norvegia o.l., smøreost; eske, tube)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Hvit ost, halvfet, 16% fett (Jarlsberg, Norvegia o.l. smøreost; eske, tube)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ost med mer enn 27% fett (kremoster, Normanna, Ridderost)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29+
Leverpostei, vanlig	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Leverpostei, mager	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Servelat, vanlig	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Lett servelat, kalverull, kokt skinke, okserull o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Salt pølse, spekepølse (fårepølse, salami o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29+
Kaviar	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Makrell i tomat, røkt makrell	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Sardiner, sursild, ansjos o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Laks, ørret	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Reker, krabbe	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29+
Syltetøy, marmelade, frysetøy	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Honning, sirup, sjokolade-, nøttepålegg	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

	0	1/2	1	2-3	4-5	6-7	8-14	15-21	22-28	29+
Grønnsaker som pålegg (agurk, tomat o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Frukt som pålegg (banan, eple o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Salater med majones	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Majones på smørbrød	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

6. Egg

	Antall pr. uke							
	0	Mindre enn 1	1	2	3-4	5-6	7	8+
(kokt, stekt, eggerøre, omelett)	☐	☐	☐	☐	☐	☐	☐	☐

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7. Frokostgryn, grøt og yoghurt

Svar enten pr. måned eller pr. uke. <1 betyr sjeldnere enn 1 gang.

	Gang pr. måned					eller	Gang pr. uke					Mengde pr. gang			
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1	1 1/2	2	3+
Havregryn	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
4-korn	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Müsli, søtet (müsli, Solfrokost o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Müsli, usøtet (Go´Dag, Fruktmüsli)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Cornflakes, puffet ris, havrenøtter o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Havregrøt.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7 ☐
Sukker til frokostgryn, grøt.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ts)	☐	☐	☐	☐
Syltetøy til frokostgryn, grøt.....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ts)	☐	☐	☐	☐
Yoghurt, naturell	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	☐	☐	☐	☐
Fruktyoghurt, vanlig	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	☐	☐	☐	☐
Fruktyoghurt lett/mager	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	☐	☐	☐	☐
Go'morgen yoghurt, inkl. müsli	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(beger)	☐	☐	☐	☐

8. Kaffe og te

(1 kopp kaffe = 1,2 dl, 1 kopp te = 2 dl, 1 kopp caffe latte/cappucino = 4dl, 1 kopp espresso = 1 dl)

	Drikker ikke daglig	Antall kopper pr. dag 1/2	1	2	3-4	5-6	7-8	9-10	11+
Kaffe, kokt (eks. presskanne), espresso	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe, traktet, filter	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kaffe, pulver (instant)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Caffe latte, cappucino	☐	☐	☐	☐	☐	☐	☐	☐	☐
Te, vanlig (f. eks. Earl Grey, Solbær)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Nypete, urtete, (f. eks. kamille)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Grønn te, (med/uten sitron)	☐	☐	☐	☐	☐	☐	☐	☐	☐

	Antall teskjeer eller biter pr. kopp 0	1/2	1	2	3	4+
Sukker til kaffe	☐	☐	☐	☐	☐	☐
Sukker til te	☐	☐	☐	☐	☐	☐

9. Andre drikker

Svar enten pr. måned eller pr. uke. < 1 betyr sjeldnere enn 1 gang. Merk at porsjonsenhetene er forskjellige. 0,33 liter tilsvarer en halvflaske øl og 0,66 liter tilsvarer en helflaske.

	Gang pr. måned				eller	Gang pr. uke						Mengde pr. gang					
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1/2	1	2	3	4	5+
Vann	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	☐	☐	☐	☐	☐	☐
Appelsinjuice	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	1/2 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Annen juice, most, nektar	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	1/2 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Saft, solbærsirup m. sukker	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	1/2 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Saft, kunstig søtet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	1/2 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Brus, Cola, Solo o.l. med sukker	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	1/4 ☐	1/3 ☐	1/2 ☐	2/3 ☐	1 ☐	1 1/2+ ☐
Brus, Cola, Solo o.l. kunstig søtet	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	1/4 ☐	1/3 ☐	1/2 ☐	2/3 ☐	1 ☐	1 1/2+ ☐
Farris, Selters, Soda o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	1/4 ☐	1/3 ☐	1/2 ☐	2/3 ☐	1 ☐	1 1/2+ ☐
Alkoholfritt øl, vørterøl, lettøl	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	1/4 ☐	1/3 ☐	1/2 ☐	2/3 ☐	1 ☐	1 1/2+ ☐
Pilsnerøl	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(liter)	1/4 ☐	1/3 ☐	1/2 ☐	2/3 ☐	1 ☐	1 1/2+ ☐
Rødvin	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐
Hvitvin	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(glass)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐
Brennevin, likør	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(1 dram =4cl)	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6+ ☐

10. Middagsretter

Vi spør både om middagsmåltidene og det du spiser til andre måltider. Tell til slutt sammen antall retter du har merket av for å se om summen virker sannsynlig.

	Gang pr. måned										Mengde pr. gang					
	0	<1	1	2	3	4	5-6	7-8	9+		1/2	2/3	1	1 1/2	2+	
Kjøttpølse, medisterpølse	☐	☐	☐	☐	☐	☐	☐	☐	☐	(kjøttpølse)	☐	☐	☐	☐	☐	
Hamburger, karbonader o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Grill- og wienerpølse	☐	☐	☐	☐	☐	☐	☐	☐	☐	(pølse)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Hamburger-, pølsebrød, lomper	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Kjøttkaker, medisterkaker, kjøttpudding	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Kjøttdeigretter (saus eller gryte med kjøttdeig, lasagne o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Taco (med kjøtt og salat)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	
Pastaretter	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐	

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	Gang pr. måned										Mengde pr. gang				
	0	<1	1	2	3	4	5-6	7-8	9+		1/8	1/4	1/2	3/4	1+
Pizza (500-600 g)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(pizza)	☐	☐	☐	☐	☐
Biff (alle typer kjøtt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	11/2 ☐	2 ☐	21/2+ ☐
Koteletter (lam, okse, svin)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	11/2 ☐	2 ☐	21/2+ ☐
Stek (lam, okse, svin)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Stek (elg, hjort, reinsdyr o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Gryterett med helt kjøtt, frikassè, fårikål o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Lapskaus, suppelapskaus, betasuppe .	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Bacon, stekt flesk	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Kylling, høne	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/4 ☐	1/3 ☐	1/2 ☐	3/4 ☐	1+ ☐
	0	<1	1	2	3	4	5-6	7-8	9+		1	2	3	4	5+
Fiskekaker, fiskepudding, fiskeboller	☐	☐	☐	☐	☐	☐	☐	☐	☐	(kake)	☐	☐	☐	☐	☐
Fiskepinner	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7-9 ☐	10+ ☐
Torsk, sei, hyse, steinbit, uer (kokt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Torsk, sei, hyse, steinbit, uer (stekt, panert)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Sild (fersk, speket, røkt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(filet)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Makrell (fersk, røkt)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(filet)	1/2 ☐	1 ☐	11/2 ☐	2 ☐	3+ ☐
Laks, ørret (sjø, oppdrett)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Laks, ørret (røkt, gravet)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Fiskegryte, -grateng, suppe med fisk	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Reker, krabbe	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl, renset)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
	0	<1	1	2	3	4	5-6	7-8	9+		1-2	3-4	5-6	7-8	9+
Risgrøt, annen melkegrøt	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Pannekaker	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Suppe (tomat, blomkål, ertesuppe o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Vegetarrett, vegetarpizza, grønnsaksgrateng, -pai	☐	☐	☐	☐	☐	☐	☐	☐	☐	(bit/dl)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
	0	<1	1	2	3	4	5-6	7-8	9+		1/2	1	11/2	2	21/2
Brun/hvit saus	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐	☐
Smeltet margarin, smør til fisk	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Bearnaisesaus o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Majones, remulade	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Ketchup	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)	1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐

11. Poteter, ris, spagetti, grønnsaker

Svar enten pr. måned eller pr. uke. < 1 betyr sjeldnere enn 1 gang.
Disse spørsmålene dreier seg først og fremst om tilbehør til middagsretter, men spiser du for eksempel en rå gulrot eller salat til lunsj, skal det tas med her.

	Gang pr. måned					eller	Gang pr. uke						Mengde pr. gang				
	0	<1	1	2	3	1	2-3	4-5	6-7	8+			1	2	3	4	5+
Poteter, kokte	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)		☐	☐	☐	☐	☐
Pommes frites, stekte poteter	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Potetmos, -stuing, gratinerte poteter	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Ris	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Spaghetti, makaroni, pasta	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Gulrot	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)		1/2 ☐	1 ☐	11/2 ☐	2 ☐	3+ ☐
Hodekål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skalk)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Kålrot	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(skive)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Blomkål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(bukett)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Brokkoli	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(bukett)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Rosenkål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Grønnkål	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
	0	<1	1	2	3	1	2-3	4-5	6-7	8+			1	2	3	4	5+
Løk	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)		☐	☐	☐	☐	☐
Spinat, andre bladgrønns.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Sopp	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Avocado	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)		1/4 ☐	1/2 ☐	3/4 ☐	1 ☐	11/4+ ☐
Paprika	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(strimmel)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Tomat	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)		1/2 ☐	1 ☐	11/2 ☐	2 ☐	3+ ☐
Tomatbønner, bønner/linser	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Mais	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)		1-2 ☐	3-4 ☐	5-6 ☐	7-8 ☐	9+ ☐
Erter, frosne grønnsak-blandinger	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Salat/salatblandinger	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)		1 ☐	2 ☐	3 ☐	4 ☐	5+ ☐
Dressing	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)		1/2 ☐	1 ☐	2 ☐	3 ☐	4+ ☐
Rømme	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(ss)		1/2 ☐	1 ☐	2 ☐	3 ☐	4+ ☐

Hvor mange ganger om dagen spiser du vanligvis grønnsaker utenom grønnsakene du spiser til middag?

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+ ☐

12. Type fett til matlaging.
Hva steker du mest med? (Velg en eller to)

	Smør/margarin		Oljer
☐	Smør (meierismør)	☐	Olivenolje
☐	Bremykt	☐	Soyaolje
☐	Melange, Per	☐	Maisolje
☐	Soft-, soyamargarin (pakke, beger)	☐	Solsikkeolje
☐	Solsikke	☐	Valnøttolje
☐	Oliven	☐	Rapsolje
☐	Annen margarin	☐	Andre oljer

13. Frukt
Svar enten pr. måned eller pr. uke. < 1 betyr sjeldnere enn 1 gang.

	Gang pr. måned					Gang pr. uke						Mengde pr. gang			
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1/2	1	2	3+
Eple	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Pære	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Banan	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Appelsin, mandarin, grapefrukt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Druer	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(klase)	☐	☐	☐	☐
Kivi	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Fersken, nektarin	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Annen frukt (mango, melonskiver) ..	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	☐	☐	☐	☐
Jordbær, bringebær (friske, frosne) ..	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Blåbær	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Bjørnebær	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Multer	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐

	0	1	2	3	4	5	6	7	8	9+
Hvor mange frukter spiser du vanligvis pr. dag?	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

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14. Desserter, kaker, godteri

Svar enten pr. måned eller pr. uke. < 1 betyr sjeldnere enn 1 gang.

	Gang pr. måned					Gang pr. uke					Mengde pr. gang				
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1/2	1	2	3+
Hermetisk frukt, fruktgrøt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Puddinger (sjokolade, karamell o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Is (1 dl=1 pinne=1 kremmerhus)....	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1 ☐	2 ☐	3 ☐	4+ ☐
Boller, julekake, kringle	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Skolebrød, skillingsbolle	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Wienerbrød, -kringle o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Smultring, formkake	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1 ☐	2 ☐	3 ☐	4+ ☐
Vafler	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(plate)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Sjokoladekake, bløtkake, annen fylt kake	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Søt kjeks, kakekjeks (Cookies, Bixit, Hob Nobs)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Sjokolade (60 g)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(plate)	1/2 ☐	1 ☐	2 ☐	3+ ☐
Drops, lakris, seigmenn o.l.	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(stk)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Smågodt (1 hg = 100g)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(hg)	1/2 ☐	3/4 ☐	1 ☐	11/2+ ☐
Potetgull (1 pose 100g=7 dl)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Annen snacks (skruer, crisp, saltstenger, lettsnacks o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Peanøtter, andre nøtter (1 pose 100g = 4 never)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(neve)	1 ☐	2 ☐	3 ☐	4+ ☐

15. Kosttilskudd (bs = barneskje, ts = teskje)

	Hele året	Bare vinter-halvåret	Gang pr. uke							Mengde pr. gang			
			0	<1	1	2-3	4-5	6-7		1 ts	1 bs	1 ss	
Tran	☐	☐	☐	☐	☐	☐	☐	☐		☐	☐	☐	
Trankapsler	☐	☐	☐	☐	☐	☐	☐	☐	kapsler	1 ☐	2+ ☐		
Fiskeoljekapsler	☐	☐	☐	☐	☐	☐	☐	☐	kapsler	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐
Seloljekapsler	☐	☐	☐	☐	☐	☐	☐	☐	kapsler	1-2 ☐	3-4 ☐	5-6 ☐	7+ ☐

Multipreparater	Hele året	Bare vinter-halvåret	Gang pr. uke 0	<1	1	2-3	4-5	6-7		Mengde pr. gang 1	2	3	4+
Sanasol	☐	☐	☐	☐	☐	☐	☐	☐	bs	☐	☐	☐	☐
Biovit	☐	☐	☐	☐	☐	☐	☐	☐	bs	☐	☐	☐	☐
Vitaplex	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Kostpluss	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Vitamineral	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
		Hvis annet, hvilket?.....											
Jernpreparater			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Ferro C	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Hemofer	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Duroferon, Duretter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
		Hvis annet, hvilket?.....											
Annet			0	<1	1	2-3	4-5	6-7		1	2	3	4+
B-vitaminer	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
C-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
D-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
E-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Folat (folsyre)	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Kalktabletter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Fluortabletter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

Annet (inkludert helsekostpreparater): .....
.....

16. Medisiner

Har du brukt noen medisiner de siste 3 månedene? (Ta med medisiner du har brukt sammenhengende (daglig) i 3 dager eller mer. Husk også medisiner kjøpt uten resept, men ikke ta med helsekostpreparater)

☐ Ja ☐ Nei

HVIS JA, fyll ut:

NAVN på medisinene du bruker/har brukt de siste 3 mnd (en bokstav i hver rute, de første 14 bokstavene holder)	Kryss av hvis du bruker dette nå	Antall dager du har brukt medisinene de siste 3 mnd (90 dager)				
		3-14	15-30	31-60	61-80	81+ dager
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐
	☐	☐	☐	☐	☐	☐

Dersom du ikke husker navnet, skriv for eksempel: Antibiotika, Betennelsesdempende, Smertestillende

Bruker du avføringsmidler? (F.eks. Pursennid, Laktulose, linfrø, loppefrø). ☐ Ja ☐ Nei

HVIS JA: Hvor ofte bruker du avføringsmidler?

sjelden/aldri	1 - 2 ganger/uke	3 - 6 ganger/uke	daglig
☐	☐	☐	☐

Hvor ofte har du avføring?

2 eller flere daglig	1 gang daglig	4 - 6 ganger/uke	2 - 3 ganger/uke	1 gang/uke eller sjeldnere
☐	☐	☐	☐	☐

Er avføringen som oftest: ☐ løs ☐ formet, men ikke hard ☐ hard

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17. Fysisk aktivitet

Har du noen kroniske sykdommer eller tilstander som gjør at du ikke kan utføre fysisk aktivitet?

☐ Nei ☐ Ja, angi grunn

☐ asthma ☐ hjertesykdom ☐ annen lungesykdom
☐ leddgikt ☐ hofte/kneplager ☐ ryggplager
☐ annet: _____

Tenk gjennom hvor lang tid du i løpet av en vanlig uke tilbringer med fysisk aktivitet. Ta bare med episoder som varer i alle fall 10 minutter. Hvor lang tid tilbringer du hver uke på:

Turgåing (og rolig skigåing)	Middels anstrengende aktiviteter (aktiviteter som krever moderat innsats og får deg til å puste litt mer enn vanlig som å sykle i moderat tempo, svømme i moderat tempo, jogge rolig, gå relativt raskt på ski, dans, golf):	Meget anstrengende aktiviteter (aktiviteter som krever hard innsats og får deg til å puste mye mer enn vanlig som aerobics, løpe eller sykle fort, svømme fort, gå raskt på ski, ballspill):
minutter/timer per uke	minutter/timer per uke	minutter/timer per uke
☐ ingenting	☐ ingenting	☐ ingenting
☐ mindre enn 30 min	☐ mindre enn 30 min	☐ mindre enn 30 min
☐ 1/2 til 1 time	☐ 1/2 til 1 time	☐ 1/2 til 1 time
☐ 1 1/2 - 2 timer	☐ 1 1/2 - 2 timer	☐ 1 1/2 - 2 timer
☐ 2 1/2 -3 1/2 timer	☐ 2 1/2 -3 1/2 timer	☐ 2 1/2 -3 1/2 timer
☐ 4-6 timer	☐ 4-6 timer	☐ 4-6 timer
☐ 7-10 timer	☐ 7-10 timer	☐ 7-10 timer
☐ 11 eller flere timer	☐ 11 eller flere timer	☐ 11 eller flere timer

18. Eventuelle andre matvarer

Bruker du regelmessig matvarer, drikker eller andre produkter (feks. kosttilskudd) som ikke er nevnt i spørreskjemaet? Skriv ned dette så detaljert som mulig. Ta med produktnavn og produsent hvis mulig. Skriv også hvor ofte du spiser/drikker dette (ganger per måned eller uke) og hvor mye du spiser av dette per gang. BRUK BLOKKBOKSTAVER.

19. Har du noen kommentarer til skjemaet kan du skrive det her.

Tusen takk for innsatsen!

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8.2 Appendix 2: Information letter to the PCOS women

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Forespørsel om deltakelse i forskningsprosjektet

"Behandling av PCOS (polycystisk ovariesyndrom) ved sykelig overvekt – en randomisert kontrollert prospektiv kostintervensjonsstudie – FEMIN studien"

Bakgrunn og hensikt
Dette er et spørsmål til deg om å delta i en forskningsstudie for å sammenlikne effekten av to ulike typer lavkaloridietter (pulverkur og knekkebrøddiett) på helseproblemer ved PCOS. Eksempler på slike helseproblemer er hormonelle forstyrrelser som gjør at man ikke menstruerer, eller svært sjelden har menstruasjon, har uønsket hårvekst, ufrivillig barnløshet, uren hud, for høyt blodsukker, for høyt blodtrykk og/eller for høye nivåer av fettstoffer i blodet. Vektreduksjon gir bedring av PCOS og lavkaloridietter gir rask og effektiv vektreduksjon. I tillegg vil vi vurdere effekten av to ulike oppfølgingsprogram for å vedlikeholde vekttapet. For å delta i studien må man være kvinne 19-38 år, ha PCOS og sykelig overvekt (BMI > 35).
Vekttap i seg selv er god behandling for de helseproblemene som er nevnt over. Formålet med denne studien er å finne ut om en av lavkaloridiettene gir bedre helsegevinst enn den andre, og om de ulike oppfølgingsprogrammene gir utslag på hvor varige vekttapet vil være. Studien går over ett år og er knyttet til Kvinneklinikken ved Rikshospitalet og gjennomføres i samarbeid med Overvektsenheten ved Aker Universitetssykehus i Oslo og Senter for sykelig overvekt i Helse Sør-Øst ved sykehuset i Tønsberg.

Hva innebærer studien?
Deltakelse i studien innebærer følgende: Det vil bli gjennomført en grundig legeundersøkelse for å kunne stille korrekt PCOS-diagnose (blodprøver og en gynekologisk ultralydundersøkelse). Vi ønsker også å måle kjente risikofaktorer for utvikling av type 2 diabetes og hjerte- og karsykdommer (blant annet vekt, livmål, blodtrykk, blodfett, blodsukker og måling av mengde fett og muskulatur i kroppen). I tillegg ønsker vi å undersøke effekt av vektreduksjon på livskvalitet og kost- og mosjonsvaner gjennom ulike spørreskjemaer.
Du vil få skriftlig beskjed om når og hvor du skal møte til de ulike undersøkelsene.

Studien har 2 faser.

Fase 1
Den første fasen består av en 8 ukers diett som innebærer en meget stor reduksjon i det daglige energi-inntaket, hvor du vil gå ned mellom 1 og 2 kg per uke. Du vil tilfeldig trekkes til å gjennomføre en lavenergidiett på ca. 900 kcal per dag ved hjelp av enten pulverkur (Nutrilett) eller en såkalt "knekkebrøddiett" hvor grove knekkebrød inngår i 3 av dagens 4 måltider. Du vil få pulver eller knekkebrød til bruk for hele 8 ukers perioden, og følges opp med jevnlige samtaler med studiesykepleier og/eller ernæringsfysiolog i denne fasen.

Fase 2
Etter gjennomføring av fase 1, vil du motta et kostforslag for opptrapping av matinntak. Deretter vil du på ny trekkes tilfeldig til å følges opp i de neste 44 ukene, (fase 2), enten med jevnlige samtaler med studiesykepleier og/eller ernæringsfysiolog hver 14. dag (gruppe 1), eller et gruppemøte i løpet av perioden (gruppe 2). Enten du trekkes til gruppe 1 eller 2, vil du motta kostforslag for opptrapping av matinntak i til sammen 3 etapper. Hensikten med dette er at du skal opprettholde vekttapet og de gunstige helseeffektene fremover, og for noen vil det være aktuelt med fortsatt vekttap.

Undersøkelser i form av blodprøver og spørreskjemaer vil finne sted ved oppstart av studien, etter 8 uker og ett år. Gynekologisk undersøkelse vil finne sted ved oppstart og etter ett år.

Mulige fordeler og ulemper
Du vil gjennom deltakelse i studien bidra til viktig kunnskap om behandling av overvekt og PCOS, samt forebygging av alvorlige sykdommer som diabetes type 2 og hjerte- og karsykdommer. Du vil øke din egen kunnskap om PCOS, vektreduksjon og sunn livsstil, og gjennomgå viktige og grundige helseundersøkelser.
Du vil ikke ha noen spesielle fordeler av studien, men erfaringer fra studien vil senere kunne hjelpe andre med samme diagnose.

Hva skjer med prøvene og informasjonen om deg?
Blodprøvene som blir tatt og informasjonen utledet av dette materialet vil bli lagret i en forskningsbiobank ved Kvinneklinikken på Rikshospitalet. Hvis du sier ja til å delta i studien, gir du også samtykke til at det biologiske materialet og analyseresultater inngår i biobanken. Professor dr. med. Tom Tanbo ved Kvinneklinikken er ansvarlig for biobanken. Biobanken planlegges å vare til 2023. Etter dette vil materiale og opplysninger bli ødelagt etter interne retningslinjer.

Prøvene tatt av deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene og prøvene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste.

Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg

Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

Frivillig deltakelse
Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte prosjektleder Line Kristin Johnson, tlf: 33 34 23 20.

Ytterligere informasjon om studien finnes i kapittel *A – utdypende forklaring av hva studien innebærer.*
Ytterligere informasjon om biobank, personvern og forsikring finnes i kapittel B – *Personvern, biobank og økonomi.*
Samtykkeerklæring følger etter kapittel B.

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Kapittel A- utdypende forklaring av hva studien innebærer

Å delta i denne studien krever tid, motivasjon og egeninnsats.
For å delta i studien må du ha vært stabil i vekt (+/- 5 kg) de siste 2 månedene. I tillegg må du være villig til å hverken bruke p-piller, p-sprøyte eller minipiller i studieperioden. Du vil være mer fruktbar etter vektreduksjon, så husk annen prevensjon i denne tiden. Du kan heller ikke bruke medikamenter for å bedre insulinfølsomhet i studieperioden (f. eks. metformin/Glucophage®).

Mulige bivirkninger lavkaloribehandling:
Forventet vektnedgang i løpet av behandlingsperioden er 1-2 kg/uke. Forbigående bivirkninger kan forekomme. Mange beskriver tretthet og sult den første uken. Etter en uke vil det føles bedre, og gleden over vektnedgangen vil overstige ubehaget. De hyppigste bivirkningene er:

- Hodepine og svimmelhet. Det hjelper da å drikke mye.
- Følelse av å fryse kan forekomme.
- Forstoppelse kan forekomme

I sjeldne tilfeller kan rask vektnedgang forårsake gallestensanfall.

Kapittel B - Personvern, biobank og økonomi

Personvern
All informasjon som innhentes om deg i forbindelse med denne studien vil bli behandlet konfidensielt. Denne informasjonen vil foreligge i din journal. Resultatene fra forsøket vil bli publisert i vitenskapelige tidsskrifter på en slik måte at enkeltdata ikke kan tilbakeføres til enkeltpersoner. Alt involvert personale som håndterer opplysninger om deg har taushetsplikt.
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.

Du vil etter hvert kunne få informasjon om studiens resultater ved henvendelse til prosjektleder for denne studien, Line Kristin Johnson, cand. scient. i klinisk ernæring og stipendiat ved Kvinneklinikken, Rikshospitalet.
Datamaterialet anonymiseres i 2023.

Prosjektet er tilrådd av Regional komité for medisinsk forskningsetikk Sør-Norge og Personvernombudet for forskning ved Rikshospitalet. Prosjektet finansieres av Helse Sør-Øst.

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Samtykke til deltakelse i studien

Jeg er villig til å delta i FEMIN studien

(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

8.3 Appendix 3: Information letter to the participating PCOS women in the FEMIN study

Sykehuset i Vestfold | HELSE SØR-ØST

RIKSHOSPITALET KVINNEKLINIKKEN

Vedrørende deltakelse i FEMIN-studien for kvinner med PCOS og overvektsproblematikk.
(The Female Health Dietary Intervention study).

Viser til hyggelig samtale med deg for en tid tilbake hvor du sa deg interessert i å delta i denne studien. Vedlagt følger som avtalt nærmere informasjon om hva studien innebærer for deg.

Du innkalles med dette til første undersøkelse på Kvinnehelsesenteret ved Rikshospitalet. (Se eget brev med oversikt over tid og sted hvor du skal møte).

HUSK:

1. **Møt fastende** (ikke spis de siste 8 timene før konsultasjonen – drikk kun vann)
2. Det kan være lurt å ta med en stor bag med hjul, trillekoffert el.l. for transport av pulverkur eller knekkebrød hjem
3. Ta med samtykkeerklæringen som ligger vedlagt i underskrevet stand

Undersøkelsen vil ta ca. 2 timer og omfatter:

- Blodprøver og blodtrykksmåling
- Veiing på vekt som viser kroppens sammensetning av muskler og fett (Lurt å ha sokker og ikke strømpebukser på)
- Utfylling av ulike spørreskjemaer

Dersom du etter å ha lest informasjonen likevel ikke ønsker å delta, ber vi deg ta kontakt med Kvinnehelsesenteret på telefon 23072683 eller sende –post til: kvinnehelsesenteret@rikshospitalet.no så snart som mulig slik at vi kan tilby din plass til en annen.

Med vennlig hilsen

Line Kristin Johnson
cand. scient. i klinisk ernæring, stipendiat og prosjektleder
Nasjonalt kompetansesenter for kvinnehelse
Rikshospitalet

8.4 Appendix 4: Nutrient composition in the crisp bread diet and the powder diet

Næringsinnhold per 1000 kcal

Næringsstoff	Ref. kvinner 19-30 år	Knekkebrød-dietten	Pulverkur (Nutrilett) – jordbær
Energi (kcal)	1000	1000	1000
Protein (g)	30,9	81	105
E %	12,4	32,4	42
Karbohydrat (g)	142	132,7	97
E %	56,7	53,1	38,8
Mono+disakk. (g)	-	62,4	9,9
E %	-	25	4
Tilsatt sukker (g)	24,5	1,4	86
E %	9,8	0,6	34,4
Fiber (g)	12,7	30,8	35,5 (soyafiber)
Fett (g)	34	15	21
E %	30,7	13,5	18,9
Mettet fett (g)	10,5	4,1	7,9
E %	9,4	3,7	7,1

8.5 Appendix 5: The crisp bread diet

Knekkebrødkuren – tilsvarende ca 900 kcal / dag

Frokost

- 1-2 grove knekkebrød med valgfritt pålegg fra påleggsoversikten (neste side)
- 1 glass skummet melk (søt eller sur)
- Vann og grønnsaker
- Evt. kaffe/te uten melk/sukker

Lunsj

- 2 grove knekkebrød med valgfritt pålegg som i oversikten
- 1 glass skummet melk (søt eller sur)
- Vann og grønnsaker
- Evt. kaffe/te uten melk/sukker

Middag

- 150 gram kokt torsk, sei eller annen mager fisk

eller

- 70 gram kokt laks, makrell eller annen fet fisk

eller

- 1 kyllingbryst, bakt i ovn eller stekt i teflonpanne uten steikefett

eller

- 100 gram magert rent kjøtt tilberedt uten steikefett

- 1 liten potet *eller* 2 ss kokt ris *eller* 2 ss pasta
- Vann og grønnsaker i fri mengde

Kveldsmat

- 2 grove knekkebrød med valgfritt pålegg fra "påleggsboksen"
- 1 glass skummet melk (søt eller sur)
- Vann og grønnsaker
- Evt. kaffe/te uten melk/sukker

I tillegg

- 1.5 l væske i form av vann, mineralvann (Farris, Bonaqua etc), sukkerfri saft (eks. FUN light), kaffe eller te (uten sukker), buljong. Maks ½ liter sukkerfri brus per dag (Pepsi Max, TaB extra el.l.)
- 1 multivitamintablett, for eksempel Vitamineral eller Kostpluss
- 1 ts soyamargarin eller Vita – brukt til knekkebrødene og/eller steking

Påleggsoversikt:

På ***ett*** av knekkebrødene per dag:

- 1 ss av makrell i tomat, røkelaks, peppermakrell, sardiner, sild eller tunfisk.

På ***ett*** av knekkebrødene per dag:

- Cottage cheese m/grønnsaker (paprika, tomat, agurk, reddik etc) eller magerost med 3 % fett.

På ***de fire andre*** knekkebrødene kan du ***velge mellom***:

- Kokt skinke, pastramiskinke, kalkunpålegg, mager leverpostei (9 % fett), servelat med 3 % fett, bankekjøtt, reker, crabsticks, fiskepudding, fiskekaker, egg i skiver, og/eller grønnsakspålegg.

Obs! Drikk ikke juice, verken kjøpt eller hjemmelaget, ettersom juice inneholder store mengder energi (="kalorier").

Utenom kostplanen kan du spise kokte eller rå grønnsaker og 1 frukt per dag. Spis ingenting utover dette. Alt annet som spises i tillegg vil redusere vektnedgangen. Dersom du ønsker å tygge på noe, er sukkerfri tyggegummi et godt alternativ. Unngå drops, karameller etc.

♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦

Bivirkninger lavkaloribehandling:
Forventet vektnedgang i løpet av behandlingsperioden er 1-2 kg/uke. Forbigående bivirkninger kan forekomme. Mange beskriver tretthet og sult den første uken. Erfaringsmessig er den tredje og fjerde dagen vanskeligst. **Ta en dag om gangen! Etter en uke vil det føles bedre, og gleden over vektnedgangen vil overstige ubehaget.**

De hyppigste bivirkningene er:

- Hodepine og svimmelhet. Drikk mye! Kroppen trenger kontinuerlig tilførsel av væske!
- Følelse av å fryse – kan forekomme i løpet av lavkaloriperioden. Kle deg varmt og drikk varme drikker.
- Forstoppelse (gjelder spesielt lavkaloripulver) – drikk mye! Det er normalt at toalettbesøkene blir færre, men det skal ikke gjøre vondt å gå på toalettet. Følgende råd kan hjelpe:
  - 2 ts linfrø i ½ glass vann, la det stå en stund og drikk/spis det.
  - Laktulose, fås kjøpt på apotek.

I sjeldne tilfeller kan rask vektnedgang forårsake gallestensanfall. Rådfør deg med din lege dersom du har gallesykdom.

Lykke til!

8.6 Appendix 6: The powder diet

Pulverkur – tilsvarende ca 900 kcal/dag

Lavkaloripulveret skal i 8 uker erstatte *alle* måltider.
Det finnes flere lavkaloripulver på markedet, vi har valgt å bruke Nutrilett som er lett tilgjengelig og av de mest kjente. Alle pulverdietter som selges i Norge følger kravene i Statens næringsmiddeltilsyns forskrift i "Forskrift om næringsmidler beregnet til bruk i energibegrenset kost for vektreduksjon 1998.10.01 nr 949". Du skal imidlertid passe på at du tar tilstrekkelig antall poser lavkaloripulver per dag slik at du kommer opp i et energiinntak rundt 800-900 kcal per dag. Dette tilsvarer:

- ***Åtte poser Nutrilett hver dag - 880 kcal/d***

Fordel posene jevnt utover dagen – frokost, lunsj, middag og kvelds. Det betyr i praksis at du må ta en shake ca. hver 2. time.
For å dekke ditt daglige behov for proteiner og andre næringsstoff, er det viktig at du tar det korrekte antall poser. Hopp ikke over noen poser, da vil du ikke få dekket behovet ditt. Posene blandes med vann (2-2.5 dl) og ristes i et glass med tett lokk eller mikses med en stavmikser.

Drikk 2- 2.5 liter væske per døgn i tillegg til væsken du får fra pulverkuren. Velg mellom følgende drikker:

- Vann
- Mineralvann (Farris, Bonaqua etc)
- Sukkerfri saft (f.eks. FUN light)
- Maks ½ liter sukkerfri brus per dag (Pepsi Max, Cola light/Zero, TaB x-tra og lignende)
- Kaffe eller te uten sukker – ha gjerne flere gode te-sorter i hus, og evt. kaffe tilsatt smak (IKKE Latte, Cappucino og lignende)
- Buljong

For noen er det enklere å drikke pulvershaken dersom man vekselvis drikker litt kaffe/te/saft og shake.

Obs! Drikk ikke juice, verken kjøpt eller hjemmelaget, ettersom juice inneholder store mengder energi.

Utenom pulveret kan du spise enkelte grønnsaker; alle typer salat, tomat (også hermetiske), slangeagurk, squash, purre, ulike typer løk (rødløk, sjalottløk, hvitløk, vårløk m.m.), paprika – alle farger, også chili og sopp. Du kan bruke alle krydder og urter, og f.eks balsamico-eddik over salaten. Litt taco-saus kan også gi god smak som "dressing".
Et tips er å lage en liten "tomatsuppe" av 1 boks hermetiske tomater med hakket løk, hvitløk og sopp. Smaksett med hvitløk, krydder og urter slik du liker det. Suppen varmer og metter. I stedet for hermetiske tomater kan tilsvarende suppe lages av buljong.

Du kan også spise inntil 150 gram av følgende grønnsaker daglig: brokkoli, blomkål, gulrot, kålrot, samt 1 frukt per dag. Spis ingenting utover dette. Alt annet som spises i tillegg vil

redusere vektnedgangen. Dersom du ønsker å tygge på noe, er sukkerfri tyggegummi et godt alternativ.

♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦♦

Bivirkninger lavkaloribehandling:
Forventet vektnedgang i løpet av behandlingsperioden er 1-2 kg/uke. Forbigående bivirkninger kan forekomme. Mange beskriver tretthet og sult den første uken. Erfaringsmessig er den tredje og fjerde dagen vanskeligst. **Ta en dag om gangen! Etter en uke vil det føles bedre, og gleden over vektnedgangen vil overstige ubehaget.**

De hyppigste bivirkningene er:

- Hodepine og svimmelhet. Drikk mye! Kroppen trenger kontinuerlig tilførsel av væske!
- Følelse av å fryse – kan forekomme i løpet av pulverperioden. Kle deg varmt og drikk varme drikker.
- Forstoppelse (gjelder spesielt lavkaloripulver) – drikk mye! Det er normalt at toalettbesøkene blir færre, men det skal ikke gjøre vondt å gå på toalettet. Følgende råd kan hjelpe:
    - 2 ts linfrø i ½ glass vann, la det stå en stund og drikk/spis det.
    - Laktulose, fås kjøpt på apotek.

I sjeldne tilfeller kan rask vektnedgang forårsake gallestensanfall. Rådfør deg med din lege dersom du har gallesykdom.

Lykke til!

8.7 Appendix 7: Correlation table; between intake of fat and saturated fat and different food items

Appendix 7

The relationships between the intake of total fat (g) and saturated fat (G) with the ingestion of different food items among the obese women (Spearman's correlation coefficient rho). Only food items which were significantly correlated to the fat intake are stated.

Spearman's rho		bread	white bread	cereals	cakes	potatoes	meat	whole meat, minced meat	forcemeat	fish	milk, cream, ice cream	partly-skimmed milk	ice cream	cheese
Total fat intake (g)	Correlation-Coefficient	.424**	.316**	.515**	.389**	.277**	.601**	.381**	.514**	.208*	.384**	.255**	.284**	.255**
	p-value	,000	,001	,000	,000	,003	,000	,000	,000	,025	,000	,006	,002	,006
	N	116	116	116	116	116	116	116	116	116	116	116	116	116
Saturated fat intake (g)	Correlation-Coefficient	.360**	.333**	.534**	.409**	.239**	.561**	.318**	.524**		.395**	.268**	.298**	.291**
	p-value	,000	,000	,000	,000	,010	,000	,001	,000	ns	,000	,004	,001	,002
	N	116	116	116	116	116	116	116	116		116	116	116	116

Spearman's rho		cheese	butter, margarine, oil	sugar, sweet stuff	chocolate	sweets	drinks	squash, soft drink, w/sugar	squash, soft drink, light	soft drink, artificially sweetened	various	potato chips	other snacks	fatty fruit
Total fat intake (g)	Correlation-Coefficient	.255**	.770**	.541**	.508**	.342**	.423**		.363**	.373**	.516**	.418**	.250**	.264**
	p-value	,006	,000	,000	,000	,000	,000	ns	,000	,000	,000	,000	,007	,004
	N	116	116	116	116	116	116		116	116	116	116	116	116
Saturated fat intake (g)	Correlation-Coefficient	.291**	.704**	.608**	.570**	.352**	.378**	.189*	.357**	.362**	.494**	.435**	.222*	.186*
	p-value	,002	,000	,000	,000	,000	,000	,042	,000	,000	,000	,000	,017	,045
	N	116	116	116	116	116	116	116	116	116	116	116	116	116

The relationships between the intake of total fat (g) and saturated fat (g) with the ingestion of different food items among the normal weight control women (Spearman's correlation coefficient rho). Only food items which were significantly correlated to the fat intake are stated

Spearman's rho		bread	whole grain bread	cakes	pommes frites	meat	whole meat, minced meat	sugar, sweet stuff	sweets	tea
Total fat intake (g)	Correlation-coefficient	.493*	.467*	,279		.457*	.487*	.449*	.616**	-.472*
	p-value	,027	,038	,234	n.s	,043	,030	,047	,004	,036
	N	20	20	20		20	20	20	20	20
Saturated fat intake (g)	Correlation-coefficient			.447*	.534*	.445*		.472*	.512*	
	p-value	n.s	n.s	,048	,015	,049	n.s	,036	,021	n.s
	N			20	20	20		20	20	

8.8 Appendix 8: Correlation table, between lipid parameters and different food items

Appendix 8

The relationships between plasma levels of total cholesterol, LDL-C, HDL-C and triglycerides with the ingestion of different food items among the obese women (n=116) (Spearman's correlation coefficient rho). Only food items which were significantly correlated to the fat intake are stated.

Spearman's rho		cereals	potatoes	oil	alcohol	snacks
Total cholesterol	Correlation Coefficient	-.218*		-.200*		
	p-value	,019	n.s	,031	n.s	n.s
	N	116		116		
HDL cholesterol	Correlation Coefficient			-.200*		
	p-value	n.s	n.s	,031	n.s	n.s
	N			116		
LDL cholesterol	Correlation Coefficient	-.249**			-.206*	-.215*
	p-value	,008	n.s	n.s	,029	,023
	N	116			116	116
Triglycerides	Correlation Coefficient		.186*			
	p-value	n.s	,046	n.s	n.s	n.s
	N		116			

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