Polycystic ovary syndrome

Diet, micronutrient status and eating behaviour

Master thesis in Clinical Nutrition

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October 2008

Acknowledgements

I would like to thank:

Professor Serena Tonstad, for inspiration, useful comments and proofreading. You are unique, and your help and knowledge has proven decisive for both the writing process and the final results. Thank you for believing in me!

Dr. Med. Svein Skeie, for useful comments, advice and great response all the way.

Professor Andrew Collins, for support. Thank you for always taking time to help!

Torbjørn Aarsland and the other health care personnel from Stavanger Health Research for helping me with the biochemical part.

Jannicke Fredriksen, for helping me with the food diaries.

Alieu S.C.Cham, for always taking time to help me.

All the nutritionists from Stavanger University Hospital, for supporting me.

Mette Svendsen, for helping me with advice.

All the participants, for accepting to join the study.

My family and friends, for love and support.

Especially to my dear son, Edward and my husband, Olaviu, thank you for your love and patience!

Marioara Covrig

October 2008

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Abbreviations

PCOS Polycystic ovary syndrome

BMI Body mass index

BES Binge eating scale

TFEQ Three factor eating questionnaire

UE Uncontrolled eating

CR Cognitive restraint

EE Emotional eating

LH Luteinizing hormone

FSH Follicle-stimulating hormone

SHBG Sex-hormone-binding-protein

IMT Intima media thickness

ROS Reactive oxygen species

WHO World Health Organization

ICD 10 International Classification of Disease and Related Health Problems 10th Revision

TSH Thyroid-stimulating hormone

WHR Waist to hip ratio

cm Centimetre

PFD Pre-coded food diaries

TINIA Turbidimetric inhibition immunoassay

ECLIA Electrochemiluminescence immunoassay

HBA1c Glycated haemoglobin

HPLC High performance liquid chromatography

EI Energy intake

BMR Basal metabolic rate

NNR Nordic Nutrition Recommendations

PAL Physical activity level

PUFA Polyunsaturated fatty acids

g Gram

mg Milligram

MJ Mega joule

E% Energy percent

αTe Tocopherol equivalenter

FFQ Food frequencies questionnaire

MMA Methyl-malonic acid

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Sammendrag

Bakgrunn: Polycystisk ovariesyndrom (PCOS) er en kompleks endokrin forstyrrelse hos kvinner og har viktige helsekonsekvenser. Pasienter med PCOS har høy forekomst av risikofaktorer for kardiovaskulær sykdom, høyere risiko for utvikling av diabetes type 2 og opp til 30-70 % av PCOS pasientene er overvektige. Oksidativ stress kan ha en sentral rolle i utvikling av alle disse sykdommene og det ble vist at økt oksidativ stress og nedsatt antioksidant kapasitet kan gi økt risiko for kardiovaskulær sykdom i kvinner med PCOS. Basert på foreliggende kunnskap, riktig kost kan korrigere hormonell og metabolsk balanse, og redusere risikoen for diabetes type 2. Individualisert vektnedgang kunne ha en viktig plass i livsstil intervensjon i PCOS.

Flere studier har også foreslått en link mellom spiseforstyrrelser, spesielt bulimia nervosa, og PCOS. Hensikten med denne studien, derfor, var å sammenligne kost og antioksidant konsentrasjoner mellom kvinner med PCOS og BMI-matched kontroller for å få kunnskap om mulige kost intervensjoner i denne pasient gruppen og å sammenligne spise atferden mellom gruppene.

Vi studerte også assosiasjoner mellom plasma antioksidanter og serum ferritin nivåer, og antropometriske målinger.

Sted: Stavanger Universitetssykehus

Deltakere: Til sammen 25 kvinner diagnostisert med PCOS og 24 BMI-matched friske kvinner.

Metode: Deltakernes matinntak ble registrert ved bruk av prekodet matdagbok. Deltakernes spise atferd var studert ved bruk av to spørreskjema (binge eating scale (BES) og three-factor eating questionnaire (TFEQ).

Resultater: Det ble ikke påvist statistisk signifikant forskjell i mikro- og makronæring inntak mellom gruppene. Begge gruppene underapporterte deres

energiinntak og hadde en kost med høy energiandel fra mettet fett og lav innhold av fiber, enkelte vitaminer (som folat, tiamin, riboflavin og vitamin D) og jern. Det ble ikke påvist statistisk signifikant forskjell i plasma antioksidant, vitamin og jern konsentrasjoner mellom gruppene. Kvinnene med PCOS hadde høyere serum ferritin nivåer men forskjellen var ikke statistisk signifikant.

Både BMI og mageomkrets korrelerte signifikant og negativ med plasma konsentrasjoner av flere antioksidanter som lycopen, xanthophyll, beta-karoten og vitamin C. Sterk positiv korrelasjon mellom mageomkrets, BMI og serum ferritin nivåer var påvist i PCOS gruppen men ikke i kontroll gruppen.

Kvinnene med PCOS rapporterte høyere BES and TFEQ score, men forskjellen var ikke statistisk signifikant.

Konklusjon: Når matched i forhold til BMI, ble det ikke påvist signifikant forskjeller i kost og plasma antioksidant og vitamin nivåer mellom kvinner med PCOS rapporterte og friske kontroller. Høyere BMI var assosiert med lavere nivåer av flere antioksidanter og med emosjonell spising.

Et balansert kosthold bør anbefales til kvinner med PCOS, spesielt i forhold til de negative helsekonsekvensene disse pasientene er utsatt for. Man bør ha ekstra fokus på kvinner med høy BMI.

Summary

Background: PCOS is a complex endocrine disease with important health implications. PCOS patients have a higher prevalence of cardiovascular risk factors and higher risk for type 2 diabetes and up to 30-70 % of women affected with PCOS are obese. Oxidative stress may play a central role in the pathophysiology of these disorders and it has been shown that increased oxidative stress and decreased antioxidant capacity may contribute to the increased risk of cardiovascular disease in women with PCOS. Evidence suggest that diet not only ameliorate many of the features of the metabolic syndrome present in these women, but also could reduce risk for type 2 diabetes mellitus. Weight loss and maintenance may play an important role to lifestyle intervention in PCOS. Furthermore, a link between PCOS and eating disorders, specifically bulimia nervosa, was suggested by several studies.

Thus, the aim of this study was to compare the diet and antioxidant levels of women with PCOS to matched controls, in order to understand the potential of dietary intervention in this group of patients and further to compare eating behaviour in the two groups. We also studied the association between plasma antioxidants and ferritin levels with anthropometric measures.

Setting : Stavanger University Hospital**.**

Subjects: A total of 25 women diagnosed with PCOS and 24 BMI- matched healthy women.

Methods: Participants dietary intake was recorded using pre-coded food diaries.

Participants' eating behaviour was assed by using two questionnaires (binge eating scale (BES) and three-factor eating questionnaire (TFEQ).

Results: No statistical significant difference in macro- and micronutrient intake between the PCOS and control group was demonstrated. Both groups underreported their food intake and reported diets with a high energy percentage from saturated fat

and low content of fiber, certain vitamins (e.g. folate, thiamine, riboflavin and vitamin D) and iron. No statistical significant difference in antioxidants and micronutrient plasma levels between the two groups was found. Women with PCOS had higher serum ferritin levels, but the difference was not statistically significant.

Both BMI and waist circumference correlated negatively with plasma concentrations of several antioxidants such as lycopene, xanthophyll, beta-carotene and vitamin C. Strong positive correlation between waist circumference, BMI and serum ferritin levels were demonstrated in the PCOS group, but not in BMI-matched controls.

Women with PCOS presented higher BES and TFEQ scores, but the difference was not statistically significant.

Conclusion: When matched for BMI, women with PCOS had similar diets and antioxidant blood levels as well as eating behaviour to controls. However, increased BMI was associated with emotional eating and binge eating as well as with low levels of several antioxidants. The importance of an adequate diet in attention of the negative health outcomes women with PCOS are at risk of seems evident and a balanced diet within the present recommended levels should be advised. An extra attention should be given to those with a BMI not within the normal range.

1. Polycystic ovary syndrome: a complex endocrine disease

Polycystic ovary syndrome (PCOS) is a prevalent and frequently encountered endocrine disorder that was first described by Stein Leventhal in 1935. It has been suggested that this disorder occurs in 5% of women at reproductive age (1).

Svein Leventhal described PCOS as a syndrome with pathognomonic findings and the clinical triad of hirsutism, amenorrhea, and obesity. Since then there has been some debate as to whether the syndrome represents a single disorder or multiple associated pathologic conditions. PCOS is primarily characterized by hyperandrogenism, insulin resistance, and chronic anovulation. Hyperandrogenism and insulin were linked as early as 1921, when Achard and Thiers published a classic description of bearded women with diabetes (1).

PCOS is considered, today, a common endocrine condition in premenopausal women with reproductive and metabolic consequences, including anovulation, infertility and an increased prevalence of diabetes mellitus. Obesity, particularly central obesity, and insulin resistance are considered now as strongly implicated in its aetiology (2). The syndrome has been also associated with dyslipidemia, hypertension, non-alcoholic fatty liver disease, sleep apnea, with increased risk of cardiovascular disease and hyperestrogen-related cancers (i.e. endometrial and breast cancer). Therefore, the syndrome is considered not only a reproductive problem but a complex endocrine disease with important health implications.

Three main hypotheses have been proposed as implicated in PCOS aetiology (3):

1. hypothalamic-pituitary axis abnormalities that cause increased ovarian androgen production.
2. an enzymatic defect of ovarian steroidogenesis that favours excess androgen production.

3. insulin resistance driving the metabolic and reproductive abnormalities in PCOS women. This hypothesis will be discussed in more detail below.

1.1 Diagnostic criteria for PCOS

According to the National Institutes of Health, basic diagnostic criteria for PCOS include the presence of chronic oligo-anovulation and signs of hyperandrogenism such as hirsutism or male-pattern hair loss, with the exclusion of other causes of hyperandrogenism.

An international consensus group revised the diagnostic criteria at a consensus conference held in Rotterdam and broadened the definition by also including ovarian morphology (3-7). The diagnostic criterion proposed by this international consensus requires two of following three criteria: menstrual irregularity, such as oligo- or anovulation, biochemical or clinical signs of hyperandrogensim and polycystic ovaries on ultrasound. In both definitions, hyperandrogenism has to be documented either by biochemical data or clinical signs. Laboratory abnormalities in PCOS can be expressed by elevated levels of testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and low sex hormone-binding protein (SHBG) concentrations.

Table 1: Diagnostic Criteria for PCOS (1):

Clinical Features:
Menstrual irregularity: amenorrhea oligomenorrhea menorrhagia
Anovulatory infertility
Hirsutism and/or acne
Central obesity

Endocrine abnormalities on Laboratory Tests:
Elevated androgen levels (testosterone) Elevated LH concentration Elevated FSH level Insulin resistance with hyperinsulinemia
Ultrasound examination:
Multiple subcortical follicular cysts Increased ovarian stromal density and/or volume

The clinical features of PCOS are heterogeneous and may change throughout the lifespan. Hyperandrogenism and menstrual irregularities represent the major complaints in young women with the PCOS; oligorrhoea or amenorrhoea and, particularly, infertility are the main complaints of adult women with PCOS during the reproductive age. The rate of spontaneous abortions is increased as well.

There are also other causes of menstrual irregularity and hyperandrogenism such as androgen-secreting neoplasms, late-onset congenital adrenal hyperplasia, Cushing syndrome, hyperprolactinemia, hypo- and hyperthyroidism(1;3;4). The diagnostic criteria for PCOS require for all these diseases to be evaluated and excluded through a detailed medical history, medical examination and biochemical tests.

1.1.1 Medical history and physical examination

A detailed medical history, focused primarily on symptoms related to pubertal development and menstrual regularity, is very important in the diagnosis of PCOS, as precocious puberty can be associated with hyperandrogenism (1;8). The pathophysiology of PCOS may have a genetic component (1;4;5;9) and performing a complete family medical history is relevant.

Physical examination should focus on establishing the presence of clinical components, especially the presents of hirsutism and acne. Gynaecologic examination should assess the cysts by palpation of ovaries and ultrasound examination. The presence of eight or more follicle less than 10 mm in diameter, at ultrasound, classifies the ovary as polycystic. These modifications are found in 90% of the women with PCOS but can also be present in about 25% of women without PCOS (10;11). Ultrasonography thus is though not sufficient to diagnosis PCOS but is a very important tool to confirm the ovarian findings.

2. Background of the current study

Cardiovascular disease remains the leading cause of death in women, and there are a number of modifiable and non-modifiable risk factors for cardiovascular disease. According to prospective studies, PCOS patients have a higher prevalence of cardiovascular risk factors such as hypertension, type 2 diabetes and dyslipidaemia (12). Insulin resistance is implicated in PCOS aetiology and up to 30-70% of women affected with PCOS are obese (3), a condition that has been found to increase the magnitude of underlying insulin resistance.

2.1 PCOS and Obesity

Obesity has existed in the population throughout recorded history, but only in recent generations it has increased to an extent that public health experts are calling it an epidemic. Since the mid-1980s, the prevalence of obesity has increased steadily and markedly in both Westernized and non-Westernized countries, and there are no indications that this trends is abating. Overweight and obesity are strongly associated with the PCOS (13-15). Although the cause of this association remains unknown, obesity is present in at least 30% of cases and, in some populations, the percentage may be as high as 75%. Obesity, especially central obesity, has an important impact on the severity of all manifestations in PCOS (16). Studies in early adolescence support the role of obesity in the expression of PCOS features (14;17-19).

The increasing prevalence of obesity among adolescent and young women with PCOS may partly be due to the increasing worldwide epidemic of obesity. The prevalence of PCOS seems to increase and it can be suggested that the main factors responsible for this increasing are related to the influence of the environment, including dietary habits, behaviour and other still undefined factors (14).

2.1.1 Obesity represents a functional hyperandrogenic state.

There is now consistent evidence that the increase in body weight may favour a more severe hyperandrogenism in women with PCOS. Moreover, one of the clinical and laboratory features of PCOS is hyperandrogenism. Normally, less than three percent of testosterone circulates freely in serum. Most circulating androgens (e.g. testosterone) are bound, primarily to SHBG and any condition that decreases the levels of SHBG or other binding proteins can lead to a relative excess of circulating androgens. The major conditions that are linked with decreased SHBG are PCOS and obesity, independently (1).

2.1.2 Central obesity, insulin and SHBG

Central obesity in PCOS is associated with more pronounced hyperandrogenism and insulin resistance than the peripheral body fat phenotype. Several studies concluded that, compared with normal weight women with PCOS, obese women are characterized by a worsened hyperandrogenic and metabolic state, irregular menses and ovulatory performance and poorer pregnancy rates. Levels of the SHBG tend to linearly decrease with increasing body fat. It is well established that, in women, the abdominal obesity phenotype is associated with a marked decrease of SHBG levels and some increase in total and free testosterone (20-23), which is consistent with a state of relative hyperandrogenism. Women with central obesity usually have lower SHBG concentrations compared with women with peripheral obesity (24). Increased visceral fat development may occur much earlier than general fat excess in the natural history of PCOS, leading in turn to the development of insulin resistance and associated hyperinsulinaemia and to a hyperandrogenic state (5;15). However, the role of obesity in the development of hyperandrogenism is still being debated.

2.1.3 Hyperandrogenism, a link between obesity and PCOS

SHBG levels are regulated by a complex of factors (estrogens, iodothyronines and growth hormone (GH) are stimulating factors; androgens and insulin are inhibiting

factors). The network of this regulation, with the dominant role of insulin, which inhibits SHBG synthesis in the liver, may be responsible for the decrease of SHBG concentrations observed in obesity. Obesity, in fact, is associated with hyperinsulinaemia that compensates for the presence of insulin resistance. All these conditions could explain lowered SHBG concentrations. This is what occurs particularly in the presence of the abdominal phenotype of obesity. Women with central obesity usually have lower SHBG concentrations compared with age- and weight-matched women with peripheral obesity (25). In addition, women with central obesity have higher testosterone and dihydrotestosterone production rates which may exceed their metabolic clearance rates. Moreover, an increased production rate occurs even for androgens not bound to SHBG, such as dehydroepiandrosterone and androstenedione. Therefore, the abdominal phenotype of obesity can be defined as a condition of relative functional hyperandrogenic state. Abdominal obesity per se may play a key role in determining both altered androgen metabolism and insulin resistance (5).

Overall, obesity in PCOS significantly changes the reproductive and endocrine environment of PCOS. Obesity in combination with PCOS is associated with worse androgenic profile, increases the rate of menstrual disturbance and the risk of endometrial cancer as well.

The importance of obesity in the pathogenesis of PCOS is emphasised by the efficacy of lifestyle intervention and weight loss, not only on metabolic alterations but also on hyperandrogenism, ovulation and fertility (discussed in detail below). This may have great relevance in preventive medicine and offer the opportunity to expand our still limited knowledge of the genetic and environmental background favouring the development of the PCOS.

2.2 PCOS, Insulin Resistance and Type 2 Diabetes

The metabolic profile noted in women with PCOS is similar to the insulin resistance syndrome, a clustering within an individual of hyperinsulinemia, mild glucose intolerance, dyslipidemia, and hypertension (26;27). PCOS may be considered a component of the metabolic syndrome. On the other hand, the most significant metabolic complication of PCOS is insulin resistance, accompanied by compensatory hyperinsulinemia, which places women with PCOS at an increased risk for the development of hypertension, dyslipidemia, type 2 diabetes mellitus (28-30).

The insulin resistance syndrome has been identified as both a risk factor for developing type 2 diabetes and a major cardiovascular risk factor (31). Furthermore, evidence shows that both lean and obese women with PCOS have increased insulin resistance and impaired beta-cell function and are at a markedly increased risk of type 2 diabetes (3;32).

Cibula et al. showed that despite the identical risk for the development of type 2 diabetes and cardiovascular disease, the prevalence of type 2 diabetes was significantly higher in PCOS women compared with healthy women. These results confirmed that women with markedly expressed clinical symptoms of PCOS make up a subgroup in the general population, at high risk for the development of diabetes and heart disease. Subjects with PCOS appear to have a greater risk for developing type 2 diabetes, regardless of ethnicity, compared with age- and weight-matched healthy controls (33).

2.3 PCOS and Cardiovascular Disease Risk Factors

After several decades of research there is general agreement that there is an association of increased cardiovascular risk factors with PCOS (32). These risk factors are increased by obesity and place obese women with PCOS at potentially

higher risk for cardiovascular disease in part because of lipid disturbance that accompany PCOS.

2.3.1 Serum lipid profile in PCOS

Hypertriglyceridemia and decreased high-density lipoprotein are relatively common in women with polycystic ovary syndrome. Elevations in low-density lipoprotein have also been noted. Results showed that elevated insulin resistance and plasma homocysteine levels, and changes in serum lipid profile, which are possible risk factors for cardiovascular disorders, play important roles in the development of cardiovascular disease in both obese and non-obese patients with PCOS (34;35). Women with obesity and PCOS demonstrated increased insulin resistance when compared with controls and it is postulated that insulin resistance is the mediating factor in cardiovascular risk (36).

Obese women with PCOS in their 30s were compared with weight-matched women without PCOS. Lipid profiles indicated higher total cholesterol and triglycerides in PCOS women (36).

Another study showed that plasma free fatty acid correlations were markedly increased in obese women with PCOS, closely associated with the lower insulin sensitivity and lower glucose tolerance in these women. In spite of these profound metabolic aberrations, the lipoprotein lipid profile was not significantly more abnormal in obese women with PCOS than in their weight-matched controls (37).

2.3.2 Subclinical signs of cardiovascular disease in PCOS

Subclinical measures of cardiovascular disease include carotid intima media thickness (IMT) and brachial artery flow-mediated vasodilatation and may be predictive of cardiovascular mortality. The existing data suggest that PCOS may adversely affect or accelerate the development of an adverse cardiovascular risk profile, and even of subclinical signs of atherosclerosis. Surrogate markers for cardiovascular disease (i.e.

carotid artery intima-media thickness, coronary artery calcification, and C-reactive protein) are found to be abnormal in these patients (3). Women with PCOS had increased arterial stiffness and decreased flow-mediated vasodilatation (36). This study did not demonstrate an increase in carotid IMT, although other studies have demonstrated increased IMT in obese women with PCOS (38;39).

2.4 PCOS and Oxidative stress

Oxidative stress is an imbalance between tissue oxidants and antioxidants and may be a unifying mechanism in the development of major diseases such as cardiovascular disease and diabetes type 2. There is considerable evidence that hyperglycaemia, hyperinsulinemia and insulin resistance result in greater reactive oxygen species (ROS) production that contributes to oxidative stress and that this greater oxygen species production may be beyond the capacity of the antioxidant defence mechanisms. Antioxidant defences, both intrinsic and of dietary origin are very important in neutralizing excessive and inappropriate ROS formation (40-42). High intakes of fruit and vegetables or, high circulating levels of their biomarkers (carotenoids, vitamin E, C) have been associated with a relative low incidence of cardiovascular disease (43).

2.4.1 Antioxidants of dietary origin

Several clinical studies have pointed to the protective effect of antioxidant nutrient such as beta-carotene, vitamin C, vitamin E, selenium and zinc, for cardiovascular disease, type 2 diabetes and cancer (44). Extensive studies have shown an inverse association between carotenoids, vitamin E and C intake from the diet and lifestyle diseases. Fruit and vegetables are known to be important sources of vitamins (e.g. vitamin C, and folate), fiber and, also of a wide variety of phytochemicals (e.g. carotenoids). There is a large body of epidemiological evidence that supports the hypothesis that vegetables and fruit are protective against type 2 diabetes (45) and

cardiovascular disease (46). Numerous epidemiological studies have also demonstrated that individuals with higher dietary consumption of foods rich in carotenoids have lower risk of cardiovascular diseases (43).

A high and varied consumption of fruit and vegetables is desirable because it provides a range of nutrients and, additionally, could play an important role in improving the dietary patterns by replacing other, less favourable foods in the diet.

2.4.2 Plasma antioxidants

Increased oxidative stress and decreased antioxidant capacity has been show to contribute to the increased risk of cardiovascular disease in women with PCOS, in addition to known risk factors such as insulin resistance, hypertension, central obesity, and dyslipidemia (43). Lower antioxidant concentrations among patients with metabolic syndrome (47) and diabetes (48) were observed and these findings could be explained by a lower intake of antioxidants, increased use of antioxidants, or both.

Some studies have provided evidence that obesity could contribute to oxidative stress, but the exact mechanisms are still not understood. Several studies suggested that abdominal adiposity is an independent risk factor for cardiovascular disease (43), possible through increased oxidative stress. Thus, there may be a difference in oxidative stress between individuals with or without increased abdominal obesity.

There is, however, unclear whether blood concentrations of antioxidants are lower in obese people and there are several studies that investigated the determinants of serum levels of antioxidants in both men and women. It has been suggested that different obesity measures such as BMI, waist circumference and waist to hip ratio are important predictors of plasma concentrations of different antioxidants, but the results have been inconsistent (49). Moreover, serum levels of carotenoids and vitamin C have been demonstrated to be influenced by other factors, especially smoking. These aspects are shortly presented below.

Predictors of carotenoids and retinol levels

Serum levels of carotenoids and retinol have been shown to be influenced by sex, smoking, alcohol use, BMI and oral contraceptive use (50). The population-based data from NHANES 3 suggested that carotenoid concentrations are associated with insulin resistance, glucose tolerance status (47), conditions women with PCOS are shown to be at risk of.

It was shown that women with abdominal obesity as determined by high waist circumference and waist hip ratio are significantly and independently associated with oxidative stress as determined by decreased serum levels of several carotenoids (i.e. alpha-, beta-carotene, lycopene, lutein) (43). In an article published recently it was shown that BMI is inversely associated with plasma concentration of carotenoids (51).

Most of the studies pointed that beta-carotene concentrations are associated with obesity. Accordingly, BMI has been reported to be independently related to beta carotene concentrations in obese subjects of both gender (44) and several reports among females consistently showed that serum beta-carotene was negatively associated with BMI and with other measures of obesity (52-54). There are, however, reports that showed that plasma alpha- and beta-carotene were not correlated with any anthropometric variable (55) and no association of BMI with beta-cryptoxanthin and lutein + zeaxanthin was found (56;57).

Predictors of Vitamin C levels

Reports consistently showed that plasma vitamin C levels are negatively correlated with BMI and other measures of obesity in women, even after correcting for age, body mass and vitamin C supplement use (44). Another study conducted among participants from both gender showed that higher waist to hip ratio was associated with lower vitamin C levels (49). On the other hand, there are published reports that found no relation of obesity, assessed by BMI, with plasma vitamin C (51;58).

Predictors of alpha- and gamma-tocopherol levels

Gamma tocopherol was shown to be positively associated with BMI in several studies (54;59).

On the other hand, negative association between serum alpha-tocopherol and both general and central obesity (60;61) were observed, whereas no associations were found in two other studies (55;62).

Smoking, plasma carotenoid and vitamin C concentrations

Several studies reported that serum carotenoid and vitamin C levels are affected by various factors, such as smoking and drinking habits, physical exercise and age. Especially smoking is known to generate reactive oxygen species in vivo and it has been reported that serum levels of carotenoids and vitamin C are lower in smokers compared to non-smokers (63). Current smokers of both sexes were shown to have significantly lower concentrations of beta-carotene and vitamin C (44).

2.5 PCOS and Lifestyle

Research consistently demonstrates that lifestyle interventions such as diet and exercise should be the primary goal of treatment in PCOS patients, particularly if they are overweight. Among several other mechanisms, hyperinsulinaemia plays a fundamental role in PCOS, which has been demonstrated both in vitro and in vivo (28;64;65). Menstrual cycles and fertility rate are negatively affected by the presence of insulin resistance, hyperinsulinaemia and obesity. There are several trials, all with relatively small sample sizes, that consistently show improvement in reproductive parameters with weight reduction in PCOS.

2.5.1 Weight loss

There has been much discussion in recent years on the role of specific dietary components on weight reduction in PCOS. Currently, a diet low in saturated fats with

an increase in dietary fiber with predominantly low glycemic-index carbohydrates is recommended.

Glycemic index is a classification of carbohydrates based on their effects on blood glucose response over 2 hours. Low glycemic index foods include bran cereals, mixed grain breads, lentils, and soy. High glycemic index foods include white rice and bread, potatoes, and sweets containing simple sugars.

Several studies have looked at a comparison of low carbohydrate to standard dietary intervention regimens in both amount of weight lost as well as specific metabolic and endocrine features of PCOS. Douglas CC et al. showed that a eucaloric low CHO diet, which was relatively low in carbohydrate (43%) and cholesterol, high in fiber, and comprised of 45% fat (18% monounsaturated fat and <8% saturated fat), improved the metabolic profile of women with PCOS within 16 days (28).

Body weight loss and dietary changes is associated with beneficial effects on clinical, endocrinological and metabolic features of obese women presenting both PCOS and hyperinsulinemia (28;66). Dietary weight loss is usually followed by reduced hyperandrogenism and hyperinsulinemia and improved clinical status (menstrual regularity, less hirsutism, and increased fertility rate) in many obese women with PCOS (67-70). The central role of improved insulin concentrations and insulin-resistant state is emphasized by the fact that similar effects can be achieved by both short- and long-term administration of metformin (an insulin-lowering drug which ameliorates peripheral insulin action in non-diabetic insulin resistant states) (14).

Studies of obese women with menstrual abnormalities have demonstrated that cycles can potentially normalize and fertility been re-established following weight loss (1). The most frequent measure of restoration of reproductive function is menstrual cycling or return of ovulation. It has been shown that even short term treatment of obese PCOS women lead to fall in serum insulin and improvement in hormone levels and restore regular ovulatory menstrual cycles and fertility (69;71). Lifestyle

modification with modest weight loss goals of 5-10% appear to be equally effective in restoring fertility and may be more compatible with long-term success (14).

Long-term treatment with metformin added to hypocaloric diet induced, in PCOS women with abdominal obesity, a greater reduction of body weight and abdominal fat, more decrease of serum insulin and testosterone compared with placebo. These changes were associated with a significant improvement of hirsutism and menses abnormalities (72).

The Journal of the Norwegian Medical Association and Norwegian Society of Gynaecology and Obstetrics highlighted that lifestyle factors, especially diet and weight loss, are important factors in the development and treatment of polycystic ovary syndrome. Lifestyle modification with modest weight loss goals of 5-10 % appear to be equally effective in restoring fertility in 20% of cases (73).

2.5.2 Diet

Diet, Heart Diseases and Diabetes

Epidemiological and clinical research have identified physical activity, excess calorie consumption and excess weight as common risk factors for both cardiovascular disease and diabetes type 2. A substantial body of research have been pointed that a diet with about 30 E% fat, less than 10 E% saturated fat, and rich in fruit, vegetables and wholegrain cereal in combination with physical activity can reduce the risk of diabetes and heart disease (74;75) in the general population, conditions which PCOS women are at high risk to develop.

Experimental evidence has indicated that typical western diet, which is high in fat and refined carbohydrate and low in fiber, induces insulin resistance and precedes obesity. Evidence, from epidemiological studies, suggests an association between consumption of fruits, vegetables, and high fiber complex carbohydrates and a reduced risk of cardiovascular disease (76;77). It is not known for certain which

active dietary constituents or combination of constituents and what are the mechanisms that contribute to these protective effects (78).

The components of diet currently recommended as "healthy" are likely also protective against metabolic syndrome, including low saturated and trans fat, balanced carbohydrate intake rich in dietary fiber, as well as high fruit and vegetable intake and the inclusion of low-fat dairy foods. Extensive studies have shown an inverse association between cardiovascular disease and vitamin E and carotenoids from the diet and based on these data high intake of fruits and vegetables has been included in guidelines against cardiovascular disease (79). Replacing refined grain products with minimally processed plant-based foods such as fruits, vegetables, whole grains and reducing the intakes of high glycaemic index beverages may offer a simple strategy in for reducing the incidence of heart diseases (80). The health benefits of dietary fiber in reducing the risk of chronic diseases have been well-established. Several lines of evidence also suggest that dietary fiber may play a key role in the regulation of circulating insulin levels (81;82). Fiber reduces insulin secretion by slowing the rate of nutrient absorption following a meal and several studies showed that insulin sensitivity increases and body weight decreases in people on high fiber diets (83;84).

Diet and PCOS

Compared with matched control women, women with PCOS exhibited a dietary pattern that was marked by consumption of a greater amount of specific foods with a high glycemic index; however, diet composition was not associated with the greater fasting insulin concentration or with lower glucose-to-insulin ratio that was observed in the PCOS group (64).

In an article published recently, Moran LJ et al. emphasized that a moderate fat intake or carbohydrate restriction is equally effective in improving reproductive and metabolic variables in women with PCOS (85). Results from a clinical trial also showed that increased dietary polyunsaturated fatty acids (PUFA) intake can exert significant metabolic and endocrine effects in women with PCOS (86).

Moreover, Farshchi H et al. made recommendations on macronutrient intake that could improve endocrine features, reproductive function and cardio metabolic risk profile. They pointed that a restriction of fat intake to 30 E% or below 30 E% of total energy intake, with a low proportion of saturated fat, distributed between several meals per day could be beneficial even when marked weight loss is not achieved. They also emphasized that both diet and exercise need to be tailored to the women's need and preferences (87).

Evidence suggest also that diet not only ameliorate many of the features of the metabolic syndrome, present in women with PCOS, but also could reduce risk for atherothrombosis and type 2 diabetes mellitus in these patients (88)**.** Individualized pharmacological support aimed at favouring weight loss and maintenance and improving insulin resistance may play a complementary role to lifestyle intervention in PCOS women (89)**.**

2.6 PCOS and Micronutrient status

2.6.1 Iron

There is now increasing evidence that moderately elevated body iron stores, below levels commonly found in genetic hemochromatosis, may be associated with adverse health outcomes. Elevated serum ferritin levels independently predicted type 2 diabetes and several cross-sectional studies showed that elevated serum ferritin is associated with hypertension, dyslipidemi and metabolic syndrome (90). There is evidence that iron stores, measured by serum ferritin concentration, are related to the degree of insulin resistance in women and with increased prevalence of metabolic syndrome (90). However, not much is known about the association between iron stores and polycystic ovary syndrome.

Indeed, increased serum ferritin levels, indicating increased body iron stores, have been found in overweight and obese women with PCOS (91).

2.6.2 B vitamins and folate

There are published several studies that investigated vitamin B12 and folate levels in women treated with metformin. In nonpregnant women both serum folate and vitamin B12 levels decreased with metformin treatment but serum homocysteine levels did not increase (92). In contrast, a study that compared two medical treatments in PCOS patients (metformin and rosiglitazone) showed that treatment with either of these medicines may lead to increases in homocysteine levels (93). Moreover, women with insulin resistance have higher homocysteine levels than those who are not insulin resistant (94).

Results from a study in PCOS women on metformin treatment suggest that B-group vitamins and folic acid administration counteract the homocysteine - increasing effect seen with metformin therapy (95). In patients with type 2 diabetes, metformin reduces levels of folate and vitamin B12 and increases homocysteine concentrations. Conversely, rosiglitazone decreases homocysteine levels in this time period. The clinical significance of these findings remains to be investigated (96).

There is now consistent evidence that there is a strong association between diet, vitamin and antioxidant intake, nutritional status and prevention and treatment of several lifestyle diseases. Furthermore, oxidative stress may play a central role in the pathophysiology of diabetes and cardiovascular disease. Still, little is known about macronutrient and micronutrient intake and vitamin and mineral status among women with PCOS who are at high risk for developing these conditions.

2.7 PCOS and Eating disorders

Body dissatisfaction is widely accepted to play an important causal role in eating disorders and a link between PCOS and eating disorders, specifically bulimia, has been suggested by several studies (97).

McCluskey S et al. reported that one third of women with PCOS at an outpatient endocrine clinic scored in the abnormal range on a standardized test of eating behaviour with 6% in the bulimic range (98). On the other hand several studies found that bulimia may lead to polycystic ovaries (99).

Compared with healthy women, PCOS patients have reduced secretion of cholecystokinin (a satiety peptide) causing abnormal appetite regulation and possibly leading to the tendency to binge (100). Binging and starving cycles may create changes in insulin sensitivity and androgen levels, in turn affecting ovarian morphology (99;101).

In order to assess eating attitudes two questionnaires have been widely used and validated: the binge eating scale, developed by Gormally J et al. (102) and three-factor eating questionnaire, developed by Stunkard and Messik (103).

3. Aims and Hypothesis

The main aim of this master thesis was to examine dietary intake, nutritional status in regard to selected vitamins and minerals and eating behaviour in PCOS patients.

3.1 Aims

- To examine macro-, micronutrient, and fiber intake in a group of women with PCOS group and a control group and compare these intakes in the two groups.

- To measure micronutrient status in both groups using biochemical analysis and to identify potential deficiencies, and compare the results from the two groups.

- To examine whether there is an association between antioxidant status and obesity measures in both groups.

- To examine eating behaviour in both groups using BES and TFEQ and to examine whether there is an association between BMI and the scores of these questionnaires.

3.2 Hypothesis

H01: Dietary consumption of total energy, macronutrients, micronutrients and fiber is similar in women with PCOS and controls.

H02: Women with PCOS do not have lower blood vitamin and mineral concentrations compared with healthy age- and BMI matched controls.

H03: There is not an association between obesity measures and plasma levels of antioxidants

H04: BES and TFEQ scores are similar in women with PCOS and controls. There is not an positive association between BMI and these scores.

HA1: Consumption of total energy, macronutrients, micronutrients, and fiber is not similar between the groups.

HA2: Women with PCOS have lower vitamin and mineral levels compared with healthy age matched controls.

HA3: There is an association between obesity measures and plasma levels of antioxidants

HA4: BES and TFEQ scores are not similar in women with PCOS and controls. There is a positive association between BMI and these scores.

4. Subjects and Methods

This pilot study was conducted at Stavanger University Hospital between the months of September and December 2007. In summary, demographic, anthropometric, dietary, eating behaviour and laboratory data from women with polycystic ovary syndrome were compared to age- and body mass index matched controls. We used standardised questionnaires and a detailed seven-day food diary. Weight, height, waist to hip ratio, relevant medical history and pharmaceutical therapy were recorded in a personal interview.

4.1 Patient and Control Selection

Twenty five women with PCOS were recruited from the Stavanger University Hospital, Department of Medicine, Section of Endocrinology, Outpatient Clinic and other units at the Stavanger University Hospital. At the beginning of the study the student searched on in the internet (World Health Organization, WHO) for the ICD-10 code for polycystic ovary syndrome in the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). The List of ICD-10 codes is a coding of diseases, symptoms, signs, social circumstances and external causes of injury or diseases, as classified by WHO. The code for PCOS is E28.2, from ICD-10 chapter IV, block E00-E90, title Endocrine, nutritional and metabolic diseases, subtitle Disorders of other endocrine glands (E20-E25), Ovarian dysfunction (E28) (104).

There were 74 women that had been diagnosed with PCOS, as the first or second diagnosis, at Stavanger University Hospital. Potential participants with one or more of the following conditions were excluded:

- A history of type 2 diabetes mellitus.
- Pregnancy.

- Any known condition with impact on the nutritional status such as cystic fibrosis, malabsorption, celiac disease, inflammatory bowel disease (Crohns disease and ulcerative colitis), known eating disorders.
- Ongoing diet program such as weight loss dietary program.

All the questions regarding diagnoses and other medical conditions of potential subjects were discussed with the internal and external supervisors of the project, Professor Serena Tonstad and Dr. Med. Svein Skeie.

Diagnostic criteria for inclusion in the study required two of the three following criteria: oligo- or anovulation, biochemical or clinical signs of hyperandrogenism, and polycystic ovaries on ultrasound. The participants with other diagnosed endocrinological disorders, e.g. hypothyroidism, could enter the study as long they were treated and the condition was stable.

Based on diagnostic criteria, inclusion and exclusion criteria, 56 patients were invited to take part in the project. Every patient received one invitation letter with an attached informed consent form (see appendix B and C). Women who were interested in participating in the study returned the informed consent to the Stavanger University Hospital, addressed to the external supervisor. Eleven potential participants responded positively to the invitation during the first three weeks after they received the invitation. The student telephoned all the patients who had not answered the invitation within three weeks after they received the letters in order to invite them to participate in the project, explain the conduct of the study and to answer any questions. There were 13 patients that responded positive due to conversation on the telephone. Potential participants were invited to call the project staff at any time with questions.

Patients were classified into three groups according to BMI: six had normal weight (BMI 18.5-24.9), overweight (25-29.9) and obese (30 or above). The distribution was as follows: six normal weight, eight overweight and 11 obese patients.

Control subjects were than selected to give the same number of controls in each BMI group. The control group of twenty five healthy, age- and BMI matched control women who were recruited from the hospital staff, excepting healthcare workers; controls were also recruited through Stavanger Lærings og Mestringssenteret and from staff working at two driving schools. Potential controls were invited to participate in the study and informed about the study by e-mail or phone. Women who were interesting in participating in the project could answer either the external supervisor or the student.

All the participants were promised individual nutritional counselling after all the data are gathered and investigated.

4.2 Methods of Data Collection

The student conducted a one hour long interview with every participant and relevant medical history, pharmaceutical therapy, weight, height and waist/hip ratio for every participant were recorded.

4.2.1 Anthropometrical measures

The student measured each participant's weight, height, waist and hip circumferences once before the participant recorded her dietary intake.

Weight was measured with a digital scale (+/-0.1 kg) with subjects dressed in light clothes (i.e. T-shirt/sweater, pants, socks) and without their shoes on. Height was measured to the nearest centimetre (cm). BMI was calculated as body weight (kg) divided by the square of height (kg/m^2) and waist to hip ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm). Waist circumference was measured as the minimum value between the iliac crest and the lateral costal margin, whereas hip circumference was determined as the maximum value over the buttocks, using a 1-cm-wide metal measuring tape.

4.2.2 Dietary Assessment

The dietary monitoring period was seven consecutive days, including two weekend days; the recording of the diet could start any day during the week, any week, except two weeks before Christmas and two weeks after New Year.

Pre–coded food diary

The traditional food record method may provide a detailed dietary assessment, but requires much work by the participants. To simplify the work for both the participants and the project staff, we used a scannable pre-coded food diary (PFD) (see appendix D), that uses household measures and photographs for portion size estimation (105) .

The PFD lists 277 drinks, food items and dishes that are grouped together according to the typical Norwegian meal pattern (105). The PFD includes 28 drinks, 24 dishes and 255 food items grouped into following sections: beverages, bread, spread on bread, yoghurt, breakfast cereals, milk for breakfast cereals, meat dishes, fish dishes, other dishes, mixed salads, potatoes/rice/pasta, vegetables, sauces, dessert, cakes, fruit and berries, snacks, sweets and chocolate, supplements. The design of the PFD lists food, drinks and dishes on the left side of the page and time span across the top. One day is divided in five time spans: four time spans covered 4 hours (e.g. 06.00–10.00, 10.00–14.00, 14.00-18.00 and 18.00-22.00) and one time span covered 8 hours (22.00–06.00) (106). The amount of food is recorded in different household units, depending on the food item (e.g. beverages are recorded in glasses, sauces in tablespoons, pizza in slices) and as portion sizes estimated from a portion size booklet (see appendix E). The participants were asked to fill inn what they had eaten, how many units of that drink/food item they have eaten. The student explained that is also important to fill inn the information in the actual time span in order to assess the meal pattern. Furthermore, each food group is supplemented with open spaces for drinks, food items and dishes not in the PFD list. If the participants had eaten a food item that is not in the PFD list, she had to write in the open spaces the name for the drink/food

item she had eaten, amount (e.g. what portion size and how many portion sizes), and time for the actual meal.

The participants were asked to record food intake during seven consecutive days and they received one pre-coded food diary for each day. They also had to record any dietary supplements they used.

Along with the food diary each participant was handed a photographic booklet that includes 15 color photograph series (107). Every page in the photographic booklet includes four different portion sizes. The portion sizes range from small (A) to large (D) portion sizes.

The student carefully instructed every participant how to fill out the food diary. First she explained how the PFD is designed and than she gave examples on how the PFD had to be filled inn. Furthermore, the student went through one specific example and every participant received that paper example. Written instructions on how to fill out the food diary were handed to every participant at the end of the meeting. The student emphasized that the participants should not make any alterations to their normal diets during the recording period. The participants could also call the master student at any time with questions.

To ensure that all participants were familiar with the inclusion criteria, all participants had to read the informational letter at the beginning of the meeting and sign an informed consent stating that they are familiar with the conduct of the study, and volunteer to participate.

Nutrition Calculation database

The completed food diaries were computed - scanned and manually checked for errors, using the Teleform programme 6.0. Daily food intake, energy and nutrients content of the participant's reported food intake were calculated by using a food database and software program developed at the Institute of Nutrition Research, University of Oslo, Norway (KBS, 2004). The same person conducted the scanning

and verifying. Moreover, a supplementary manually check of the food diaries was conducted in SPSS. The database is based on the Food table from 1995 (108). Dietary supplements are included in the calculations (cod liver oil, multivitamin – mineral supplements, vitamin B-, C, D-, E- supplements, iron, calcium and fluoride).

4.2.3 Eating behavior assessment

Binge Eating Score

In order to assess participants' eating pattern we used the binge eating scale (BES) (see appendix F) that describes both behavioural manifestations (e.g., eating large amounts of food) and feeling/cognitions surrounding a binge episode (e.g., guilt, fear of being unable to stop eating) (102).

Binge eating is a key feature of the binge eating disorders bulimia nervosa and binge-eating disorder. Binge eating score is an 16-item scale that assesses binge eating severity and includes items that describes feeling (e.g. guilt, preoccupation with eating restriction) and behavioural manifestations (e.g. eating in secret) (109). Binge Eating Scale is a self-reported instrument that measures the severity of binge eating and consists of 16 items. For research purpose, investigators have classified subjects based on total score into three groups: nonbingers, moderate bingers, or severe bingers or set a cut-off point of 27 or higher to identify only the severe binge eaters.

Three Factor Eating Questionnaire

The three-factor eating questionnaire TFEQ-R21(see appendix G) used in this master project is a revised TFEQ instrument and aggregates three separate scale scores: eating behaviour, cognitive restraint and emotional eating scale. The Uncontrolled eating scale assesses the tendency to lose control over eating when feeling hungry or when exposed to external stimuli. The Cognitive restraint scale assesses the tendency to control food intake in order to influence body weight and body shape. The Emotional eating scale measures the propensity to overeat in relation to negative mood states, e.g., when feeling lonely, anxious, or depressed (110). The student

carefully instructed every participant how to fill out the questionnaires which were completed by the participants at home.

4.2.4 Biochemical Measurements

Requisitions for blood tests were given to all 49 participants about two months after the beginning of the study. All the blood samples were taken at Stavanger Helseforskning by two trained venipuncturists at the Clinical Chemistry Laboratory.

Serum levels of nutritional biomarkers of interest, including serum levels of iron, vitamin B12. folate, total carotenoids and tocopherols were obtained.

Table 2 Biochemical measurements

Nutrient	**Blood tests**
Iron	Haemoglobin, hematocrit, s-iron, ferritin, transferrin
Vitamin B12	Cobalamin
Folate	Folate
Antioxidant vitamins	Retinol, alpha-, gamma -tocopherol, vitamin C
Carotenoids	Beta-carotene, lycopene, xanthophyll

Blood values for cholesterol, triglycerides and fasting blood glucose were also measured.

Blood collection

Early morning venous blood samples were drawn for biochemical screening tests, following a 12-hour overnight fast. All the patients that were on Metfomin treatment were asked to stop taking the medication 24 hours before the blood samples were taken.

A biobank was established and all the blood samples were identified with a participant number. The samples were either analyzed at the Stavanger University Hospital or sent to The Slovak Medical University Nutrition Laboratory, Bratislava, Slovakia, for analyses.

All the blood samples shall be destroyed either when the analyses are completed or at the completion of the project.

The blood was collected first in two serum aliquot tubes, 5 ml blood in each tube, and centrifuged. Blood was then collected in two tubes containing ethylenediaminotetraacetic acid as anticoagulant, 3 ml blood in each tube. Those four aliquots were transferred immediately to the Biochemical Laboratory of the Stavanger University Hospital and used for blood analysis of haemoglobin, haematocrit, glucose, glycated haemoglobin (HbA1c), triglycerides, total cholesterol, serum-iron, ferritin, transferrin, vitamin B12, folate. Analyses were performed on the same day of collection.

Biochemical screening tests

Serum glucose concentrations were measured using heksokinase method based on the work of Schmidt, Peterson and Young, on Roche automated clinical chemistry analyzers (111). The glycated haemoglobin determination was based on the turbidimetric inhibition immunoassay (TINIA) for hemolyzed whole blood (112). HbA1c (%) values were obtained on a Cobas Integra 800 analyzer using Cobas Integra Hemolyzing Reagent Gen.2.

The quantitative determination of serum iron levels was based on the FerroZine method without deproteinizaion and serum ferritin was measured by using the "ECLIA" method (electrochemiluminescence immunoassay), on Elecsys immunoassay analyzer (113). For the determination of transferrin, the Roche transferring assay, based on the immunological agglutination principle, was used (114). Triglycerides and Cholesterol levels were measured by an enzymatic colorimetric test; the colour intensity of the end product is directly proportional to the triglycerides and cholesterol concentrations, that were determined photometrically (115).

Vitamin B12 and Folate serum levels were measured with the Elecsys vitamin B12, respectively Elecsys Folate assay. The assay employs a competitive test principle using natural intrinsic factor specific for vitamin B12 for the determination of vitamin B12 levels, respectively, a natural folate binding protein specific for folate for the determination of folate levels (116).

Serum samples for determination of antioxidant vitamins and carotenoids serum levels were collected. About 10 ml blood was collected in a Vacutainer (Beckton Dickinson) containing heparin as anticoagulant. As soon as possible, the samples were centrifuged at 2000 x g for 15 minutes at 4ºC. The plasma was removed by pipette, and aliquots distributed (0.5-1 ml) in micro centrifuge tubes. Samples for vitamin C were acidified at this stage, so two tubes were labeled separately and an equal volume of 10% (v/v) metaphosphoric acid was added to each of them. The tubes was kept on ice while all this was done, and then as soon as all the tubes were prepared, they were dropped into a flask containing liquid nitrogen to 'snap freeze' them. The samples were then stored at - 76ºC.

Serum samples were sent in dry ice to The Slovak Medical University Nutrition Laboratory, Bratislava, for analyses. A,C,E vitamin and alpha-, beta-carotene, lycopene, lutein, and tocopherols serum concentrations were measured. Ascorbic acid

concentrations were measured using high performance liquid chromatography (HPLC) by the method of Ross MA (117). Vitamins A and E as well as carotenes and lycopene in plasma were measured by reverse-phase HPLC using the method of Hess et al. (118).

4.3 Data Analysis

All analyses were conducted using The Statistical Package of Social Science (SPSS, Inc., Chicago, IL, USA) version 13.0. The level of statistical significance was set at the 0.05-level, thus any p-value at this level or lower was considered a significant result.

4.3.1 Descriptive statistics

Differences between means in groups were compared with T-test. The non-parametric alternative Mann Whitney was used to compare groups when data in the groups were not normally distributed.

Comparative statistics

Macronutrient and micronutrient intake

Differences in macronutrient and micronutrient intake between the PCOS group and their age- and BMI-matched controls were examined. Groups were tested to see if they were coming from a normally distributed sample. The paired sample T-test was used when the dietary variables met this assumption of normality; otherwise the non-parametric alternative Wilcoxon Signed Rank test was conducted.

Serum levels of vitamins and minerals

Differences between serum levels of measured vitamins and minerals between the groups were examined by using the paired sample T-test if the data was normally distributed; otherwise the non-parametric test Wilcoxon Signed Rank test was conducted.

4.3.2 Analyses of correlations

The correlation is defined as the influence one independent variable (e.g. waist circumference) has on one dependent variable (e.g. plasma antioxidant concentration). Adjusted correlation is the effect one independent variable has on serum antioxidant concentration after adjustment for the other possible cofounding variables, such as age and smoking.

Pearson's correlation analysis was conducted to look at patterns between body mass index, waist circumference, waist to hip ratio and serum levels of antioxidants and serum ferritin. This was investigated in our population sample (both PCOS patients and controls) and than, in the patient and control group, separately. To check if the assumption of normal distribution and linearity were violated, we looked at the shape of the scatter plots and the descriptive statistics. Spearman's correlation analysis was used when the assumption of Pearson's were violated. Any p-value at the 0.01-level or lower was considered a significant result.

4.3.3 Regression analyses

Univariate analyses

Univariate analyses were conducted prior to the multivariate analyses. Serum antioxidant level was the independent continuous variable. The different independent variables were age and measures of obesity, such as body mass index, waist circumference and waist to hip ratio.

Linear multiple regression

Three different models were created in order to investigate the effect of different obesity measures on different antioxidant levels in the two groups.

Serum antioxidant level was the dependent variables like in the univariate analyses. Independent variables were included in the models based on knowledge from former

research on factors that influence serum antioxidant levels, independently of their level of significance in this study.

In the multiple regressions analysis when age, smoking and each of the obesity measures were included separately, we tested the effect of body mass index, waist circumference and waist to hip ratio on variation of plasma antioxidants concentrations.

The assumption of normality and linearity was checked by looking at the descriptive statistics and scatter plots.

4.4 Ethics

The study was evaluated and approved by the Regional Committee for Medical Research Ethics, Western Norway (see appendix A). To ensure that everyone is familiar with the inclusion criteria, all participants had to read and sign an informed consent stating that they are familiar with the conduct of the study, and volunteer to participate. The identity of all participants was protected; none of them can be identified from the report that was used for the master thesis.

5. Results

5.1 Subject characteristics

Initially there were a total of 27 potential participants with PCOS and the initial control sample consisted of 25 women. Two recruited patients decided not to participate in the study due to personal reasons and one control was lost because she started a special diet before she could start to complete the food diary. This left 49 subjects, 25 patients, ages between 20 and 42 years old and 24 BMI matched controls, ages between 21 and 44 years old. All the participants were, by chance, of Norwegian ethnicity.

Two women in the PCOS group and three women in the control group had hypothyroidism but all of them were adequately treated and had normal tyroid stimulating hormone (TSH) levels. One patient was diagnosed with celiac disease by the time we took the blood samples but this was after she completed the food diary, so she had a normal diet. This patient was excluded when we investigated and compared micronutrient and antioxidant status from the two groups.

Twelve participants from the patient group and 15 from the control group reported that they took dietary supplements such as multivitamin, B12 vitamin and folate supplement, during the registration period. Three participants, two from the PCOS, and one from the control group, were taking vitamin B12 injections. One patient and two controls were taking folic acid supplement, 0.4 mg/day.

Nine subjects reported smoking, three from the patient group (12%) and six from the control group (25%). The patients and controls were well matched in regard to BMI, as shown in table 3.

Table 3 Participants categorized according to BMI

	Group		
	All	**PCOS group**	**Control group**
BMI	**N=49**	**N=25**	**N=24**
18.5-24.9 kg/m^2	N=12 (24%)	N=6 (24%)	N=6 (25%)
25-29.9 kg/m^2	N=16 (33%)	N=8 (32%)	N=8 (33%)
> 30 kg/m^2	N=21 (43%)	N=11(44%)	N=10 (42%)

Table 4 describes the age and anthropometric characteristics of the subjects participating in the study. The patient and control groups were in the same age group as well. Data are presented as mean and standard deviation (SD).

Table 4 Age and anthropometric characteristics of the participating women

	Group			
	All	**PCOS group**	**Control group**	
Continuous characteristics	**N=49**	**N=25**	**N=24**	**p-value**
Age (years)	33 (7)	31 (7)	35 (7)	0.05
Weight (kg)	88.6 (24.9)	89.9 (25.6)	87.8 (25)	0.7
Height (cm)	169 (6)	169 (6)	169 (6)	0.8
Waist (cm)	95 (20)	98 (21)	92 (18)	0.3
Hip (cm)	102 (17)	1 04 (18)	101 (18)	0.6
Waist to hip ratio	0.91 (0.06)	0.93 (0.06)	0.90(0.06)	0.07

5.2 Nutrient intake

5.2.1 Under-reporters

Energy intake (EI) divided by basal metabolic rate (BMR) gives an estimate whether or not subjects are having an EI that is consistent with life over time. Under-reporters are subjects with values EI:BMR<1.35, whereas <1.14 is not consistent with life (119).

Table 5 shows the proportion of the participants that were categorised as under - reporters.

Table 5 Proportion of subjects categorised as under-reporters

	PCOS group N=25		**Control group N=24**	
	%	**N**	**%**	**N**
EI:BMR < 1.35	100	25	80	19
EI:BMR < 1.14	64	16	58	14

5.2.2 Macronutrient intake among patients and controls

Table 6 shows values for energy and energy providing nutrients intake among patients and controls. There were no statistical significant differences when comparing the self-reported energy and macronutrient intake between the patient group and control group. Both groups reported energy provided by fat and saturated fat that was over the recommended limits and the dietary fibre intake was under the recommended limits (120).

Table 6 Macronutrient intake in PCOS and control group

	PCOS group (N=25)					**Control group (N=24)**					
	Mean	SD	Median	Q1	Q2	**Mean**	SD	Median	Q1	Q2	P-value
Energy (Kj)	8259	1720	7935	7519	9216	8694	1759	8890	7296	9567	0.4
Protein (E%)	17	3	16	15	18	16	3	16	15	18	0.5
Fat (E%)	36	6	35	32	40	37	6	37	32	40	0.6
Saturated fat (E%)	16	3	15	13	17	15	2	15	13	16	0.7
Monounsaturated fat (E%)	12	2	12	10	13	12	2	12	10	13	0.7
Polyunsaturated fat (E%)	7	2	6	6	8	7	2	7	5	8	0.5
Carbohydrate* (E%)	45	5	44	42	48	45	6	45	41	50	0.4
Added sugar ** (E%)	7	4	6	4	10	10	7	9	5	13	0.09
Fiber (g)	18	6	18	14	23	19	7	16	13	23	0.8
Fiber (g/MJ)	0.02	0.008	0.02	0.01	0.02	0.02	0.006	0.019	0.01	0.02	0.5

***** Carbohydrate minus fiber

****** Added, refined sugars include sucrose, fructose, glucose or starch hydrolysates added during food manufacturing.

5.2.3 Micronutrient intake among patients and controls

Micronutrient intake among patients and controls, dietary supplements included

Table 7 shows values for micronutrient intake, including dietary supplements. There were no statistical significant differences when comparing the self-reported micronutrient intake between the patient group and control group. There was a trend toward a difference in tocopherol intake between the groups (mean intake of 10 mg/day, SD = 5 in PCOS group and 14 mg/day, SD = 10 in the control group) but this did not achieve statistical significance (p = 0.08).

Table 7 Micronutrient intake in PCOS and control group, dietary supplements included

	PCOS group (N=25)					**Control group (N=24)**					
	Mean	SD	Median	Q1	Q2	**Mean**	SD	Median	Q1	Q2	P-value
Iron (mg)	12	6	10	9	12	12	5	11	9	15	0.7
Folate (mcg) *	279	206	212	168	334	252	130	235	153	293	0.8
Thiamin (mg)	1.5	0.7	1.3	1	1.8	1.4	0.6	1.3	0.9	1.6	0.7
Riboflavin (mg)	1.9	0.9	1.6	1.3	2.6	1.7	0.9	1.4	1.1	2.1	0.2
Vitamin A (mcg)	1013	546	795	616	1252	1039	412	1027	653	1332	0.4
Vitamin C (mg)	100	55	87	66	114	113	59	101	71	154	0.4
Tocopherol (mg)	10	5	9	7	15	14	10	11	7	18	0.08
Vitamin D (mcg)	5.3	3.7	4.1	2.3	8.1	6.5	5.2	4.8	2.1	9	0.49
Calcium (mg)	867	237	857	729	1002	820	295	763	595	974	0.34

* corrected for cooking losses

The mean values for the reported intakes in both groups was within recommended limits for the most of the nutrients, except for iron, folate and vitamin D, where the mean values were below recommended limits for both groups (120).

Micronutrient intake among patients and controls, dietary supplements not included

Table 8 presents the values for self-reported micronutrient intake, with no dietary supplements included. There are no statistically significant differences when comparing nutrient intake between the two groups. Participants' nutrient intake is less in accordance with NNR 2004 after excluding dietary supplements. We observed low intakes of folate and iron in both groups. Iron intake in PCOS group presented a mean value for the reported intake of 10 mg/day (SD=3). Vitamin D intake is also below recommended levels (120).

Table 8 Micronutrient intake in PCOS and control group, dietary supplements not included

	PCOS group (N=25)					**Control group (N=24)**					
	Mean	SD	Median	Q1	Q2	**Mean**	SD	Median	Q1	Q2	P-value
Iron (mg)	10	3	10	9	11	11	3	11	9	13	0.51
Folate (mcg) *	176	39	185	148	209	187	60	190	137	236	0.45
Thiamin (mg)	1.1	0.2	1.1	0.9	1.3	1.1	0.3	1.2	0.8	1.5	0.60
Riboflavin (mg)	1.5	0.4	1.4	1.2	1.6	1.5	0.6	1.2	1.1	1.8	0.31
Vitamin A (mcg)	878	417	715	595	1036	859	327	813	578	1196	0.74
Vitamin C (mg)	89	40	78	65	108	93	41	81	61	133	0.69
Tocopherol (mg)	8	3	7	6	9	9	4	7	6	10	0.72
Vitamin D (mcg)	3.7	2.2	3.9	2.1	5.2	4.4	3.7	3.3	1.7	6.1	0.9

Calcium (mg)	864	297	763	729	1002	816	296.8	763	594	974	0.34

*corrected for cooking losses

5.2.4 Proportion of subjects in the project not eating within recommended limits (NNR 2004)

Macronutrient intake

In table 9 we show proportion of subjects that were not eating within recommended limits, according to NNR 2004. All (100 %) of each group ate too little dietary fiber, and 24 % (n = 6) in the PCOS group and 38 % (n = 9) in the control group ate too much added sugar. We found that 92 % (n = 23) from the patient group and 83 % (n = 20) from the control group, reported a diet high in total fats (i.e. > 30E %/day). Moreover, 96 % (n = 24) from the patient group and 100 % (n = 25) of the healthy women reported a diet with too much saturated fat intake compared to the recommended levels in NNR 2004.

Table 9 Proportion of participants not eating within recommended limits, macronutrient intake

	PCOS group N=25		**Control group N=24**	
	%	**N**	**%**	**N**
Low dietary fiber (<3g/MJ/day)	100	25	100	24
High added sugars, (>10E%/day)	24	6	38	9
Low in carbohydrates, (<50E%/day)	88	22	79	19
High in carbohydrates, (>60E%/day)	0	0	0	0

High in total fats, (>30E%/day)	92	23	83	20
Higher in total fats, (>35E%/day)	56	14	63	15
High in saturated fat, (>10E%/day)	96	24	100	24
High in PUFA (>10E%/day)	8	2	4	1
Low in protein (<15E%/day)*	20	5	21	5
High in protein (>20E%/day)	12	3	8	2

* **Low protein** was set at a level that lies within the recommended level according to NNR. A level of protein intake less than 10E%, which would below recommended level, it's difficult to find in the Norwegian population. A national dietary survey showed that a level below 10E% is found among few Norwegian women, thus the 'low protein' intake was defined to 15E% or lower.

Micronutrient intake

Micronutrient intake, dietary supplements included

Table 10 shows proportion of participants from each group with a dietary intake that is not in accordance with NNR 2004. Contributions to intakes of vitamins and minerals from supplements are included.

We observed that most of the participants reported a diet poor in iron, B vitamins, and vitamin D. For example, 84 % (n = 21) from the patient group and 75 % (n = 18) from the healthy women group ate a diet with iron content below recommended levels. Twenty one women from each group (i.e. 84 % from the PCOS group and 88 % from the control group) ate too little folate compared to the recommended levels in NNR 2004. The majority of the participants had also calcium and vitamin D intake below recommendations.

Table 10 Proportion of participants not eating recommended limits; micronutrient intake, dietary supplements are included

	PCOS group N=25		**Control group N=24**	
	%	**N**	**%**	**N**
Low iron (<15mg/day)	84	21	75	18
Low folate (<400mcg/day)	84	21	88	21
Low thiamin (< 1.1g/day)	28	7	25	6
Lower thiamin (< 0.05 mg/ MJ)	100	25	100	24
Low riboflavin (<1.3mg/day)	32	8	46	11
Low vitamin A (<700mcg/day)	44	11	25	6
Lower vitamin A intake (<400mcg/day)	0	0	0	0
Low vitamin C intake (<75mg/day)	36	9	25	6
Low tocopherol (<8 mg/day)	36	9	25	6
Low vitamin D (<7,5mcg/day)	76	19	67	16
Low calcium (<800mg/day)	40	10	54	13

Micronutrient intake, dietary supplements not included

Participants' nutrient intake is, as expected, less in accordance with recommendations after excluding dietary supplements. Table 11 shows proportion of subjects that reported a diet with vitamins and minerals content below recommended levels (120). All the participants had a folate intake below recommended level and 96 % (n = 24) from the PCOS patient and 88 % (n = 21) of healthy women reported a diet with iron

values below recommendations. Over half part of the patients 56%, (n = 14) and half part of the controls 50%, (n = 12) ate less tocopherol than recommended. Vitamin D intake was below recommendations in most of the participants, as well.

Table 11 Proportion of participants not eating within recommended limits; micronutrient intake, dietary supplements not included

	PCOS group N=25		**Control group N=24**	
	%	**N**	**%**	**N**
Low iron (<15mg/day)	96	24	88	21
Low folate (<400mcg/day)	100	25	100	24
Low thiamin (< 1.1g/day)	44	11	33	8
Lower thiamin (< 0.05 mg/ MJ)	100	25	100	24
Low riboflavin (<1.3mg/day)	36	9	54	13
Low vitamin A (<700mcg/day)	48	12	38	9
Lower vitamin A intake (<400mcg/day)	0	0	4	1
Low vitamin C intake (<75mg/day)	40	10	42	10
Low tocopherol (<8 mg/day)	56	14	50	12
Low vitamin D (<7,5mcg/day)	96	24	79	19
Low calcium (<800mg/day)	44	11	54	13

5.3 Plasma vitamins, antioxidants and iron

Plasma levels of folate, cobalamins, antioxidant vitamins and carotenoids and serum ferritin were measured in all forty nine participants. One patient was diagnosed with celiac disease after we collected the blood samples; therefore she was excluded from these analyses.

5.3.1 Plasma micronutrient levels, comparing the groups

We found no statistical significant differences when comparing plasma antioxidant concentrations between the patient and control group, nor when comparing the other measured plasma micronutrient levels. Previous studies showed that serum alpha- and beta- tocopherol concentrations are strongly correlated with serum cholesterol. In addition there was demonstrated an association with triacylglycerol and between serum triacylglycerol and central obesity concentrations (121). In order to eliminate a possible confounding effect by cholesterol and triglycerider on serum levels of these antioxidants, alpha- and gama-tocopherol levels were corrected for cholesterol and triglycerider before statistical analysis.

The results are presented as mean, SD, median and 25, 75 percentiles.

Table 12 Serum ferritin, folate and cobalamins in PCOS and control group

	PCOS group (N=25)					**Control group 2 (N=24)**					
	Mean	SD	Median	Q1	Q2	**Mean**	SD	Median	Q1	Q2	P-value
Folate	17	9	14	11	20	15	5	14	12	17	0.7
Cobalamins	324.8	175.7	288	212.7	374.2	384.4	253.4	303	258	452.7	0.2
Serum ferritin	66.2	46.6	46.5	31.2	97.7	62.2	45.4	47	31.5	94.5	0.8

Table 13 Plasma antioxidant levels in PCOS group and control group

	PCOS group (N=25)					Control group (N=24)					
	Mean	SD	Median	Q1	Q2	**Mean**	SD	Median	Q1	Q2	P-value
Retinol	2.7	0.5	2.6	2.4	3.1	2.6	0.4	2.6	2.3	2.9	0.4
Lycopene	0.8	0.3	0.7	0.6	0.9	0.7	0.3	0.6	0.5	0.8	0.2
Xantophyll	0.3	0.1	0.3	0.2	0.4	0.3	0.1	0.3	0.3	0.4	0.9
Beta carorotene	0.8	0.5	0.6	0.3	1.1	0.9	1.0	0.6	0.4	1.0	0.7
Alpha tocopherol *	4.2	1.2	4.4	3.7	4.8	4.7	1.1	4.7	3.9	5.2	0.2
Gamma tocopherol *	0.3	0.2	0.3	0.2	0.4	0.4	0.1	0.3	0.3	0.5	0.4
Vitamin C	73	28.6	71.2	48.8	93	66.6	23.2	66.0	49.1	86.4	0.4

* corrected for cholesterol and triglyceride

5.3.2 Predictors of plasma antioxidant levels in the PCOS and control group

Correlations between obesity measures (e.g. body mass index, waist circumference and waist to hip ratio) and plasma antioxidant levels were conducted in the entire population sample and then separately in the patient and control group.

The relationships between the different antioxidants and various variables in the entire population sample are shown as correlations factor Pearson, adjusted correlation and p-value. The present study indicated different associations between different antioxidant levels and obesity measures. Apart from waist to hip ratio, the other obesity measures were significant related to different antioxidant levels, before and after adjustment for the potential confounders. Most of the correlations were stronger in the PCOS women, compared to their BMI-matched controls.

Predictors of plasma retinol and carotenoid levels

Predictors of plasma retinol and carotenoid levels are shown in table 14. We found that waist circumference (r=-0.31) and BMI (r=-0.30) are significant predictors of serum lycopene levels in the entire population sample. Waist circumference (r=-0.49) and BMI (r=-0.45) showed significant negative correlations with beta-carotene levels, independent of other considered disturbing factors.

Table 14 Predictors of plasma retinol and carotenoid levels

		N=48			
	Variable	Unadjusted correlation	p-value	Adjusted correlation*	p-value
Retinol	Age	0.12	0.4	0.09	0.5
	Smoking	0.23	0.1	0.22	0.1
	BMI	0.03	0.8	-0.01	0.9
	Age	0.12	0.4	0.07	0.6
	Smoking	0.23	0.1	0.22	0.1
	Waist	0.13	0.3	0.10	0.4
	Age	0.12	0.4	0.08	0.5
	Smoking	0.23	0.1	0.22	0.1
	Waist to hip ratio	0.22	0.1	0.21	0.1
Lycopene	Age	-0.11	0.4	-0.06	0.6
	Smoking	0.09	0.5	0.12	0.4
	BMI	-0.32	0.02	-0.31	0.03
	Age	-0.11	0.4	-0.05	0.6
	Smoking	0.09	0.5	0.11	0.4

	Waist	-0.32	0.02	-0.30	0.04
	Age	-0.11	0.4	-0.12	0.4
	Smoking	0.09	0.5	0.10	0.4
	Waist to hip ratio	0.18	0.2	-0.18	0.2
Beta - carotene	Age	0.25	0.07	0.36	0.07
	Smoking	-0.03	0.8	-0.03	0.7
	BMI	-0.41	0.04	-0.49	0.000
	Age	0.25	0.07	0.36	0.008
	Smoking	-0.03	0.8	-0.05	0.6
	Waist	-0.37	0.009	-0.45	0.001
	Age	0.25	0.07	0.27	0.06
	Smoking	-0.03	0.8	-0.06	0.6
	Waist to hip ratio	-0.2	0.2	-0.22	0.1
Xanthophyll	Age	-0.02	0.8	0.09	0.4
	Smoking	-0.18	0.2	-0.15	0.2
	BMI	-0.46	0.001	-0.46	0.001
	Age	-0.02	0.8	0.10	0.4
	Smoking	-0.18	0.2	-0.17	0.2
	Waist	-0.46	0.001	-0.48	0.001
	Age	-0.02	0.8	0.009	0.9
	Smoking	-0.18	0.2	-0.18	0.2
	Waist to hip ratio	-0.26	0.06	-0.26	0.07

* corrected for the other variables from the table.

Predictors of plasma vitamin C levels

Predictors of plasma vitamin C levels are shown in table 15.

Waist circumference (r=-0.45) and BMI (r=-0.43) were significantly correlated with plasma vitamin C concentrations.

Table 15 Predictors of plasma vitamin C levels

		N=48			
	Variable	unadjusted correlation	p-value	Adjusted correlation*	p-value
Vitamin C	Age	-0.10	0.5	0.01	0.9
	Smoking	-0.21	0.2	-0.17	0.2
	BMI	-0.46	0.001	-0.45	0.001
	Age	-0.10	0.5	0.01	0.9
	Smoking	-0.21	0.2	-0.19	0.2
	Waist	-0.43	0.002	-0.43	0.003
	Age	-0.10	0.5	-0.07	0.6
	Smoking	-0.21	0.2	-0.19	0.2
	Waist to hip ratio	-0.19	0.2	-0.18	0.2

* corrected for the other variables from the table.

Furthermore, when analyzing correlations in the two groups, results from linear multiple regressions showed that BMI and waist circumference were stronger predictors of vitamin C levels in the control group compared with the PCOS group (results not shown).

Predictors of plasma alpha- og gamma tocopherol levels

Predictors of plasma alpha- and gamma-tocopherol levels in the entire population sample are shown in table 16. We found that body mass index (r=-0.31) and waist circumference (r=-0.35) were significant predictors of plasma alpha-tocopherol levels and their influence on alpha-tocopherol concentration were equally strong.

Table 16 Predictors of plasma alpha- and gamma-tocopherol levels

		N=48			
	Variable	Unadjusted correlation	p-value	Adjusted correlation*	p- value
Alpha-tocopherol	Age	0.19	0.2	0.26	0.07
	Smoking	0.02	0.9	0.02	0.9
	BMI	-0.25	0.07	-0.31	0.03
	Age	0.19	0.2	0.27	0.05
	Smoking	0.02	0.9	0.003	0.9
	Waist	-0.28	0.04	-0.35	0.01
	Age	0.19	0.2	0.2	0.2
	Smoking	0.02	0.9	0.00	0.9
	Waist to hip ratio	-0.14	0.3	-0.15	0.3
Gamma-tocopherol	Age	0.1	0.4	0.08	0.6
	Smoking	-0.06	0.6	-0.09	0.5
	BMI	0.18	0.2	0.17	0.2
	Age	0.1	0.4	0.08	0.6
	Smoking	-0.06	0.6	-0.08	0.6
	Waist	0.16	0.2	0.14	0.3

	Age	0.1	0.4	0.10	0.4
	Smoking	-0.06	0.6	-0.08	0.6
	Waist to hip ratio	0.17	0.2	0.17	0.2

* corrected for the other variables from the table.

When analyzing the groups separately, no statistical significant correlations were found with plasma gamma-tocopherol, nor with alpha-tocopherol levels, except for a significant association of alpha tocopherol with waist circumference in the control group after correcting for possible cofounders (r=-0.43, p=0.04).

5.4 Binge Eating Score and Three Factor Eating Questionnaire

Patients with polycystic ovary syndrome showed higher BES and TFEQ scores, but the differences between the PCOS and the healthy women group were not statistical significant. The most representative difference between the groups was when investigated the emotional eating scale, but we could not demonstrate significant difference (p=0.09).

In table 17 we show the values for the BES and TFEQ scores in the patient and control group. The results are presented as mean, SD, median and 25, 75 percentiles.

Table 17 BES and TFEQ scores

	PCOS group (N=25)					**Control group (N=24)**					
	Mean	SD	Median	Q1	Q2	**Mean**	SD	Median	Q1	Q2	P-value
BES score	10.8	7.8	10.00	4.00	16.00	8.7	5.6	8.00	5.2	10.7	0.4
TFEQ score:											
UE scale*	44.5	20.8	44.44	29.6	57.4	38.5	15.6	37.04	26.8	50.9	0.2
CR scale**	44.6	20.5	44.44	30.5	61.1	40.5	19.2	38.8	27.7	55.5	0.4
EE scale***	42.8	26.7	44.44	25.0	63.8	30.7	23.1	27.7	12.5	54.1	0.09

* Uncontrolled eating

** Cognitive restraint

*** Emotional eating

Proportion of subjects characterized as non bingers, moderate or severe bingers, according to BES score, are shown in table 18.

Table 18 Classification according to BES score

	PCOS group N=25		**Control group N=24**	
	%	**N**	**%**	**N**
Non bingers	80	20	92	22
Moderate bingers	16	4	8	2
Severe bingers	4	1	0	0

Correlations of BMI with BES and TFEQ scores in both groups are shown in table 19.

A strong positive correlation for BES scores and the BMI was observed with univariate analysis in both our patients (r=0.50) and controls (r=0.53).

We demonstrated also a medium strong correlation between BMI and emotional eating scale in the PCOS group (r=0.46, p=0.02) and a stronger correlation was found between these two variables among controls (r=0.72, p=0.000).

Table 19 Correlations of BMI with BES and TFEQ scores

	Group 1 (N=25)		**Group 2 (N=24)**	
	BMI		BMI	
	r	p-value	r	p-value
BES score	0.50	0.009	0.53	0.008
TFEQ score:				
UE scale	0.20	0.33	0.13	0.52
CR scale	0.19	0.35	-0.09	0.65
EE scale	0.46	0.02	0.72	0.00

6. DISCUSSION

Analyses of this data showed no statistical significant difference in macro- and micronutrient intake between the PCOS and control group. Both groups reported a diet with a high energy from saturated fat and low content of fiber, certain vitamins (e.g. folate, thiamine, riboflavin and vitamin D) and iron.

We found no statistical significant difference in micronutrient plasma levels between the two groups. We demonstrated that both BMI and waist circumference are significant negative predictors for plasma concentrations of several antioxidants such as lycopene, xanthophyll, beta-carotene and vitamin C. Our results showed also a positive correlation between waist circumference and BMI and serum ferritin levels in the PCOS group but not in their BMI-matched controls.

According to our data, PCOS patients reported a higher BES and TFEQ scores compared to the controls, but this difference did not reach statistical significance. We noted also that participants with a higher degree of overweight presented higher BES and TFEQ scores.

6.1 General methodological considerations

6.1.1 Study population

All the participants in the project were recruited through Stavanger University Hospital.

This master thesis is a pilot study with a small number of participants, which could give insufficient statistical power. Thus, it is difficult to come to definite conclusions about diet in the PCOS. We included 25 patients in the PCOS group and planned to include the same number participants in the control group. We managed to recruit 24 controls. More time and resources to plan and recruit a larger number of participants

in the PCOS and control group, could give more statistical power and the results could be of more clinical importance. In addition, several statistical analyses were conducted on correlations between plasma antioxidants levels and obesity measures, and this could influence our results.

6.2 Dietary intake

Analyses of this thesis showed that there is no significant statistical difference at 0.05 - level when comparing the self reported energy, macro- and micronutrient intake between the patient and control group. We were surprised to observe that both groups reported a diet with an energy content that did not meet their needs and, at the same time, was high in saturated fat and poor in vitamins and minerals.

6.2.1 Methodological limitations of the dietary method

Recruitment period

We began recruiting the PCOS group in the month of September 2007 and we interviewed the first patients in the month of October. Those patients began to complete the food diary already that month. Because we planned to include BMI matched controls, we could not begin recruiting the control group before after we had recruited most of the patients. It could have been better if we had the possibility to recruit both groups at the same time. In that way the participants from the two groups could complete the food diary during the same time period.

Methods of dietary assessment

We did not record participants physical activity level (PAL) during the registration period. If we had been doing that we could than get a more representative picture of the energy needs and energy expenditure for every participant, and at the group level.

As a dietary assessment, seven days pre-coded food diary was chosen as the best available way to collect dietary data from the participants. It is possible that other dietary assessment methods would have provided a more accurate report of the food intake. It is possible that traditional method like the weighted record could reflect the true intake more accurate than the method we used. In addition it may be a level of inaccuracy when coding the food items/dishes that were written on the open spaces in the food diary, but one must note that the traditional weighted method has this disadvantage too.

Compared to food frequencies questionnaire and a 24 hour recall, a pre-coded food diary requires more work from the participants and nutritionist than a food frequencies questionnaire and a 24 hour recall but it also gives a better estimate of the nutrient intake of the participants. Anyway, dietary analyses were limited o the contents of the nutrition database.

However, the advantage of the pre-coded food diary method is that it is less time – consuming for the participants and researchers to conduct. Data from focus group interviews including adolescents showed that the daily time needed to complete the food diary was 10-15 minutes, which can be considered as acceptable (107).

Along with the food diary the participants received a portion size booklet. A study conducted among adolescents showed that a large variability may exist in an individual level when choosing a photograph that correctly depicts a food portion size, but the error at the group level is quite small (107).

Overall, in order to give the best possible data to our study it was important to choose this dietary assessment method because it gives a very good estimate of the food intake from our participants and, at the same time, is little time-consuming and easy to fill inn.

Under-reporting

Under-reporting food intake is a well known phenomenon in dietary surveys and is caused by a variety of factors (122). Under- reporting can be divided in two subtypes: "Under-eating" and "under-registration". When subjects "under-eat", they eat less than they normally do due to the fact that they are conscious of what they are eating when reporting. When subjects are "under-registering", they omit reporting what they actually are consuming.

Energy intake divided by basal metabolic rate will give an estimate whether or not subjects are having an EI that is consistent with life over time. Under-reporters are subjects with values EI:BMR<1.35, whereas <1.14 is not consistent with life (119). We calculated basal metabolic rate for every participant by using a regression equation based on age, sex and body weight (123). Accordingly, 100% of the patients (n = 25) and 80 % of the controls (n= 19) were under-reporters. Moreover, there were 64% of the patients (n = 16) and 58 % of the controls (n= 14) that had values of EI : BMR < 1.14, aspects that could influence our final results.

6.2.2 Discussion of dietary results

The main objective of the current study was to examine whether women with PCOS consume a diet higher in total energy; fat and lower in vitamins, minerals and fiber, compared to a healthy control group. Based on recommendations for macro- and micronutrient intake for general populations and relevant findings in the literature regarding diet, PCOS and other lifestyle diseases, we gathered and discussed the nutritional factors that seem to play an important role in PCOS.

Energy and nutrient intake

Analyses of this thesis showed that there is no significant statistical difference at 0.05 - level when comparing the self reported energy and macronutrient intake between the

patient and control group (p=0.38). The patient group reported a diet with saturated, mono- and polyunsaturated content similar to the diet reported by the control group.

All the women participating in the PCOS study have good protein intakes at levels thought to be sufficient to meet the needs according to the Nordic recommendation for the general population (10-20 E %). Our results showed that there was no significant statistical difference when comparing protein intake between the groups (p = 0.5), nor when comparing carbohydrate intake (p = 0.4). The lack of statistical difference between the groups could be explained by the small sample size and measurement error. In addition there were subjects that were taking oral contraceptives which could affect their appetite and food choices.

Comparing our data with results from other studies

There are few studies that investigated diet in PCOS patients. Douglas CC et al. studied dietary intake in a group of thirty PCOS women, compared to a group of twenty seven healthy women. Similar to our findings, they demonstrated that women from PCOS group consumed a diet that was similar in total energy and macronutrient content to that of age-, race-, and BMI matched healthy women. In contrast to our results, they concluded that PCOS patients consumed more fat, especially trans fat but, that difference did not reach statistical power (64). Another study conducted by Wild et al. showed that PCOS women exhibited a diet higher in saturated fat than did age-matched control women (124). Moreover, a more recently study that compared two different ethnic, large populations, American and Italian PCOS women, concluded that the US group consumed significantly more saturated fat than did the Italian counterparts, despite having similar energy and macronutrient intake (125). We must note that all these studies used either a three day or four-day food diary, as a dietary assessment tool. Therefore, it is possible that our results are more representative because we used a seven-day food diary that included weekend days, which could be of importance when conducting a dietary survey.

We hypothesized that reported intake of dietary fiber would be significantly lower in women with PCOS compared with age-, and BMI-matched control women. Our analyses showed that the difference between the groups was not statistical significant with a mean reported intake of 18 g/day in the patient group and 19 g/day in the control group, i.e. 0.02 g/MJ in both groups. These results are similar to those from the study conducted by Douglas et al. but in contrast with the results published by Wild et al. that concluded that the dietary fiber intake was lower in the PCOS group compared to age-matched control women (124).

Concerning literature I could not find other studies were micronutrient intake in PCOS patients was investigated. We hypothesized that women with PCOS will have a diet with a lower content of vitamins and minerals compared to our healthy age- and BMI-matched women. Analyses of our data showed that there were no statistical significant differences when comparing the reported micronutrient intake between the groups. However, we found that a large proportion of the women in PCOS and control group are not eating within recommended levels stated in NNR 2004, aspects that are discussed later in this master thesis.

Women not eating within recommended levels stated in NNR 2004

The results from our analyses reveal that a large proportion of the women in PCOS and control group are not eating within recommended levels stated in NNR 2004.

Energy intake

When comparing the mean values for energy intake in our groups with the references values for energy intake for women in the same group of age, there are lower values for energy intake in our groups. The references values for energy intake in NNR are calculated for groups of women with two different physical activity levels. When we look at our results the mean values for reported intake in our groups were lower, regardless of activity level. The mean value for the reported energy intake in the

PCOS group and control group was 8.25 MJ/day and 8.69 MJ/day respectively. The reference values for energy intake for women age 18-30 and 31-60, with a sedentary work and limited physical activity in leisure time, are 9.4 MJ/day and 9.2 MJ/day respectively. We must emphasize that fiber was not included when we calculated energy content. In addition, the values we are referring to were calculated for individuals within the normal range (18.5-24.9) of body mass index (120), while our participants were both normal and overweight women.

Our participant's low energy intake could be explained either by a low physical activity level or by the fact that they under-reported their food intake, or both factors.

Both excessive and insufficient energy intake in relation to requirements leads in the long term to negative consequences for health. A very low energy intake is defined as an energy intake below 6.5 MJ/day as a minimum daily energy intake necessary for providing adequate amounts of micronutrients from the diet, while an energy intake of 6.5-8 MJ/day is considered a low energy intake. At a low energy intake there is an increased risk of an insufficient intake of micronutrients (120;126).

Several studies suggested that normal weight women with PCOS have a lower total energy intake when compared to healthy normal weight women (127). Carmina et al. comments that obesity or overweight could be part of the disorder of PCOS and diet and lifestyle may modify the phenotype (125).

We did not observe among our participants that normal weight PCOS women have a lower energy intake than their BMI-matched controls. The reported energy intake in normal weight PCOS women was actually higher, with a mean value of 9 MJ/day, compared to 8 MJ/day mean intake reported by the healthy normal weight women. However, the normal weight groups have a very small number of participants (six normal weight women in each group) to give sufficient statistical power.

A low energy intake can be related to a low body weight. When looking at our normal weight and overweight patient's energy intake, we observed that their individual energy intake varied largely independent of their body weight (results not shown). However we must note that while in the control group the overweight women (n= 18) reported a mean energy intake higher than normal weight controls (n = 6), i.e. 9 MJ, respectively 8 MJ/day, the overweight PCOS (n = 19) had a mean energy intake that was alike the energy intake reported by the normal weight PCOS (n = 6), i.e. 8 MJ.

Could this mean that our overweight patients are less physical active, thus they need less energy, or that they under-reported their energy intake? There is now evidence that overweight subjects underreport their energy intake (122) and according to our calculations, all our patients under-reported their energy intake.

On the other hand, it is possible that our overweight patients are aware of the negative effects of overweight in PCOS and they consciously restraint their food intake.

Or is that possible that there are two different types of hormonal state in PCOS with different consequences on body weight, regardless energy intake?

Fat intake

Our data showed that the diet reported by our study population had a relatively high fat content, especially saturated fat. The mean value for the total fat intake was above recommended value in both groups, i.e. 36 E% fat, whereas 16 E % from saturated fat in the patient group and 37 E%, whereas 15 E% from saturated fat in the control group. At individual level there were twenty three women in the PCOS and twenty women in the control group that had a total fat intake that exceeded 35E %. Most importantly, twenty four women from each group (i.e. 96% from the PCOS and 100% from the patient group) did not manage to limit their saturated fat intake below recommended level.

However, the reported PUFA intake in our groups was within recommended levels, with a mean intake of 7 E% in both patient group and control group. An intake of

polyunsaturated fatty acids exceeding 10 E% is not recommended, because this may increase the risk of lipid peroxidation. There were just 8% (n = 2) in the patient group and 4% (n=1) in the control group that had a diet with a high PUFA content.

Although there are studies that showed beneficial effects of high fat diets in PCOS (28), on the balance of evidence to date a diet low in saturated fat is recommended in women with polycystic ovary syndrome (128). Thus, women participating in this project should be strongly advised to decrease their saturated fat intake.

Fiber intake

Dietary fiber intake in our population had a reported mean value that was below recommended levels, i.e. 18g fiber/day in PCOS group and 19g fiber/day in the control group. Fiber intake varied among participants but, most importantly, very few (five patients and four controls) reached the minimum recommended level of 25 g fiber/day. Moreover, when adjusted for energy intake (g/MJ), none of them managed to reach recommended level of 3mg/MJ/day. These results could mean that our participants had a very low intake of foods naturally rich in dietary fiber such as wholegrain cereals, vegetables, fruits and berries.

As we mentioned in the introduction part of this master thesis, the health benefits of dietary fiber in reducing the risk of chronic diseases have been well-established. Several lines of evidence suggest that dietary fiber may play a key role in diseases which PCOS patients are at risk of, thus an increasing in fiber intake should be strongly advised.

Added sugar intake

Added sugar intake in our population varied largely. Many of the women from both groups did not manage to limit their intake to the recommended levels. More importantly, most of the women did not exceed 20 E% from added sugar and there were no participants with a sugar intake that exceed 30 E%. Consequently, even though too many participants, especially from the control group, ate too much sugar (four controls exceed 20 E% from added sugar), few had very extreme levels. We

found that no participant from the patient group reported more than 20 E% from added sugar and there were only five of them that had over 10 E% from added sugar. During the personal interviews with the participants, the master student noted that PCOS patients were more interested and aware of the effects of simple carbohydrates intake, (i.e. sugar), than our healthy women. It is, though, possible that the patients were more careful regarding sugar intake. On the other hand it is possible that they under-reported it.

However, there is now ample evidence that a diet high in added sugar is unhealthy contributing only with 'empty- calories' which dilute the quality of the diet (129). In addition it is well proved that a consumption of sugar-containing soft drinks is positively correlated with overweight and obesity (130). Accordingly, there is sufficient basis to assert that a reduced intake of added sugars is recommendable.

Vitamins and minerals intake

Women from both the patient and control group reported a mean intake of A, C, and E vitamin that were within recommended levels, when including dietary supplements.

After excluding dietary supplements, the mean reported intake of vitamin E was 8 mg/day in the PCOS group and 9 mg/day in the control group. However, the levels of antioxidant vitamins intake were still within recommended levels after correcting for cooking losses, except for vitamin E intake from the patient group. The vitamin E requirement is partly related to the PUFA intake, which is generally not a practical problem since most foods rich in PUFA also are rich in vitamin E. The relationship between vitamin E and PUFA intake is related to the general antioxidant effect of vitamin E and, according to NNR, a ratio of 0.6α- TE / g PUFA in adults would be sufficient (120). This means that at an average of 5 E% from PUFA an intake of 7 mg/day vitamin E should be sufficient for women in fertile age. The reported PUFA intake in our patient and control group was 7 E%. Thus, vitamin E intake in our groups should be approximately 9 mg/day in order to satisfy the ratio between vitamin E and PUFA intake, as recommended by NNR.

When looking at the proportion of the patients and controls not eating within recommended limits when excluding dietary supplements, we noted that 40%, respectively 42% reported a vitamin C intake below recommended by NNR. Over half part of the patients and half part of the controls ate less tocopherol than recommended. There was also 48% in the PCOS group and 38% of the healthy women that reported an intake of vitamin A below daily recommended.

Analyses of this thesis showed that most of the women from both groups did not manage to reach the recommended level for iron and folate intake, even when including dietary supplements. Although we did not find a significant statistical difference between the groups, both PCOS and control group reported a diet where the mean values for iron and folate were below recommended values. When excluding contribution from dietary supplements, we noted a reduction in iron intake from 12 to 10 mg/day in the patient and from 12 to 11 mg/day in the control group. There were also a high proportion of the women that had a low iron intake, i.e. 96% from the PCOS and 88% from the control group reported an iron intake below recommendations, after correcting for contribution from iron supplements.

The mean values for folate intake were very low in both groups, especially after excluding folate supplements, when the patient group reported a mean intake of 176 mcg/day and the healthy women had an intake of 187 mcg folate/day. However, one must note that folate values are presented after correction for cooking losses.

Furthermore, our results show that it was a representative proportion of women from both groups that did not follow recommended level for folate intake. We found that 21 women from each group (i.e. 84% from the PCOS and 88% from the control group) ate too little folate compared to the recommended levels, when including folate supplements. Moreover, after correcting for the contribution from folate supplements none of the participants managed to reach the recommended value by NNR.

Comparing the women from PCOS study with Norwegian women at fertile age (results from Norkost 1997)

A national dietary survey from 1997 using food frequencies questionnaires (FFQ) shows that Norwegian women at the age of 20-29, 30-39 and 40 - 49 have a mean intake of 20, 21 and 21 g of dietary fiber/day respectively, 12 and 9.3 E%, 8.1E % added sugar, 12.0, 13, 12 E% from saturated fat, and 5.3, 5.6 and 5.5 E% PUFA (including both omega-3 and omega-6 fatty acids). It is not shown how large percentage of the studied group did not follow the recommended intakes (131). However, when looking at mean values in our PCOS population, the mean fiber intake is lower with a mean intake of 18 g/day, the added sugar intake is also lower with a mean value of 7 E %, but saturated fat and intake of PUFA is higher (mean intake 16 E%, respectively 7 E%) than in the general female population from 1997 aged 20-39. On the other hand when comparing our control group with Norwegian fertile women, we observe that our population has a higher proportion of energy from added sugar (mean value 10 E%).

Regarding iron intake, women from the PCOS study reported a higher mean value for iron intake, with a mean value of 12 mg iron / day while the dietary survey showed that Norwegian women at age of 20-29, 30-39 and 40-49 have a mean intake of 9.7, 9.6, 9.6 mg iron/day respectively.

These results could indicate that participants in this study have an unfavourable diet, and they may not be eating healthier than women of fertile age in the Norwegian population. Yet, one must note that our study is conducted among few participants and we must be aware of the time of difference between 1997 and 2007, which may change the picture.

6.3 Vitamins, iron and antioxidant vitamins

Results of this master project showed no statistical significant difference in folate, cobalamins, iron or antioxidant vitamins levels when comparing PCOS women with healthy women. We found, however, higher levels of serum ferritin and positive correlations of serum ferritin and obesity measures in our patients, which could indicate a higher degree of inflammation and oxidative stress associated with polycystic ovary disease.

Our analyses indicated different associations of waist circumference and body mass index with the different antioxidants, but no statistical significant association of waist to hip ratio with any of the antioxidants.

6.3.1 Methodological limitations of biochemical measurements

Some of our results could be limited because we did not use the most specific method for the assessment of vitamin B12 and folic acid status. The assay of methyl-malonic acid (MMA) is very specific (raised MMA always means impaired B12 status) but this method is, however, very expensive (123). For the determination of folate levels we measured folate level in serum. Red-cell folate, however, reflecting the average intake 120-day life of the red cells is a far superior index (123).

6.3.2 Discussion of biochemical results

Vitamin B12 and folic acid

Women with PCOS have been shown to have lower vitamin B12 levels and higher homocystein levels due to metformin treatment (93). In addition, folic acid and B12 are all co-factors in homocystein metabolism, thus we assumed that women with this disorder could present lower folic acid levels, as well.

Our data showed lower vitamin B12 levels in the PCOS group (mean value 324.8 umol/L) compared with the healthy women group (mean value 384.4 umol/L), but this

difference could not reach statistical significant level. On the other hand, we found higher folate levels in our patients (17.2 nmol/L) compared with our controls (14.7 nmol/L), but again, we could not find a significant difference between the groups.

These results could be explained either by differences in dietary intake, dietary supplement use or other factors. Lower vitamin B12 levels in the patient group could be explained by the effect metformin treatment, as reported by several other studies. However, several patients reported that they took vitamin B supplements and some of them took folic acid supplement due to reduced serum levels of folic acid. There were women from the control group as well, that were on B vitamins and folate supplements. Thus, it is very difficult to conclude which factor has an important role in determining the difference between the groups.

Iron stores

Our results showed that patients with polycystic ovary syndrome have higher serum ferritin levels, compared with their BMI-matched controls (mean value 66.2ug/L, 62.2ug/L respectively), but this difference did not reach statistical significance ($p=0.7$). This could be explained the fact that we had to small population sample to give sufficient statistical power and. In addition, our population sample included both normal- and overweight women and this could influence the outcomes. Higher levels of serum ferritin in PCOS women could be related to chronic inflammation or could indicate that body iron stores are increased in these women in agreement with what has been published for other insulin-resistant conditions (91). Luque RM et al. suggested that insulin resistance and hyperinsulinism, and not the reduced menstrual losses secondary to from oligo- or amenorrhea, are responsible of the increased ferritin levels and body iron stores found in overweight and obese women with PCOS (91).

Increased iron stores in the liver are postulated to induce liver-mediated insulin resistance, with reduced hepatic insulin extraction and hyperinsulinemia and reduced ability of insulin to suppress hepatic glucose production. Serum ferritin levels have

been found to be associated with decreased insulin sensitivity and increased fasting serum insulin and blood glucose. These abnormalities might lead to increased adiposity. In several studies, serum ferritin was correlated with insulin resistance syndrome (132), metabolic syndrome (90) and diabetes (133), all conditions women with PCOS are at risk of. Indeed, it has been reported previously that overweight and obese women with PCOS have increased serum ferritin levels (134) and it has been discussed that the increased body iron stores might contribute to the insulin resistance and beta-cell dysfunction frequently found in PCOS patients (91).

Correlations of iron stores with obesity measures

A strong positive correlation between waist circumference and BMI and serum ferritin levels was found in the PCOS group but not in their BMI-matched controls. Moreover, these two variables were equally strong predictors for serum ferritin concentrations in the PCOS women (r=0.57 for both variables). These observations could indicate a higher degree of oxidation stress associated with the PCOS and, in accordance with results from other studies, these women could be at higher risk for development of diabetes type 2 and cardiovascular disease, compared with the controls.

Few studies have examined the relationship of body iron stores and indices of body fat distribution, despite the relationship postulated for both variables with coronary heart disease and ischemic stroke (135-137). However, like our data, results from two other studies showed a positive correlation between serum ferritin levels and various index of adiposity, such as BMI: data from a study that examined the association between serum ferritin levels and cardiovascular risk factors among Norwegian men reported independent associations of serum ferritin with waist-to-hip ratio and body mass index (138) and, Gillum et al reached similar conclusions in a study conducted among Mexican American men aged 20-49 years (139). On the other hand, in a small study of healthy Spanish volunteers, no association of serum ferritin with waist-to-hip ratio was found (132), results that are consistent with our findings.

Plasma antioxidant levels

Comparing the groups

Our data showed mean values of measured antioxidants vitamins that were lower in the patient group compared with their BMI matched controls, except for retinol, lycopene, and vitamin C. However, we failed to show a statistical significant difference in plasma antioxidant levels between the groups. It is possible that this is due to a too small population sample to give statistical power.

The differences we observed, however, could be a result of dietary differences, increased oxidative stress or dietary supplements, impaired absorption, increased use, or other possible factors. We found no significant differences in vitamin intake between the groups, thus is more likely that the differences could be explained by oxidative stress, increased use and dietary supplements. Our healthy women, for instance, presented lower vitamin C concentrations compared with the PCOS women. It is possible that this result is primarily due to smoking habits and higher oxidative stress and it is plausible to discuss an increased use in of ascorbic acid (and other antioxidants) in smokers in order to scavenge free radicals. Anyway, other factors such as difference in dietary supplements and impaired absorption should be considered.

Correlations between obesity measures and antioxidant plasma levels

Results of this thesis showed different associations between different antioxidant levels and abdominal and general obesity as determined by waist circumference and BMI. We found no significant correlations between waist to hip ratio and measured serum levels of antioxidants. Our observations are presented below.

Predictors of plasma carotenoid and retinol levels

Results from the entire population

We observed that serum beta carotene and xanthophyll levels correlated negatively with waist circumference and BMI before and after adjusting for confounding factors such as age and smoking. The correlations of abdominal and general obesity with

serum beta-carotene and xanthophyll levels were strong. These results could indicate that general and central obesity are more important determinants of serum carotenoid and xanthophyll levels compared to the other considered factors. Furthermore, BMI was an independent significant predictor of lycopene levels (r=-0.32), so was waist circumference. We could note small correlations between waist to hip ratio and plasma levels of measured carotenoids, but the correlations could not reach statistical significance.

Results from each group

Serum beta-carotene levels were negatively associated with general and central obesity in both groups, when controlling for confounding factors. Both the correlation with BMI and with waist circumference was strong. However, the association with both obesity measures was stronger in the patient group compared with the control group, after correcting for considered disturbing factors. This could indicate that obesity is a stronger determinant for beta-carotene levels in PCOS patients compared to other factors and, possible more than in the controls.

Waist circumference (r=-0.55) and BMI (r=-0.56) were significantly associated with decreased serum levels of xanthophyll in patients with polycystic ovary syndrome, whereas it was just central obesity (r=-0.44), after controlling for disturbing factors in the control group. The correlation was, as shown above, not as strong as in the patient group. These observations could overall indicate that central obesity is a stronger predictor of xanthophyll levels compared to other considered factors, in both groups.

On the other hand, when correcting for age and smoking in the patient group, waist circumference (r=-0.39) and BMI (r=-0.38) were still determinants of serum lycopene levels but not statistical significant, as before correcting for disturbing factors. Thus, the correlation PCOS patients presented in univariate analysis could be attributed to the interference of other non considered factors.

No significant correlations between obesity measures and plasma retinol levels were found. We noted, however, that waist circumference (r=0.22) and BMI (r=0.18) were

positively correlated with retinol in the patient group, whereas we noted a negative correlation with BMI (r=-0.2) and no correlation with waist (r=-0.05), in the control group. None of these correlations could reach statistical significance.

Predictors of vitamin C plasma levels

Results from the entire population

Our results showed that waist circumference (r=-0.43) and BMI (r=-0.45) are strong, negative predictors of plasma vitamin C concentrations even after controlling for the potential cofounders, but no significant correlations were found in relation to waist to hip ratio. The oxidative stress associated with obesity and increased use of scavenging antioxidants could be consistent with our findings, lower vitamin C levels in women with higher degree of obesity.

Results from each group

We noted that our healthy women presented stronger association of obesity with plasma vitamin C levels compared with the PCOS patients, which showed no statistical significant correlations after adjustment for confounding factors. It is possible, thus, that the effect of obesity measures on plasma vitamin C levels is stronger than the effect of other factors in our control group but not in the patient group. Could this indicate that there are other factors, no considered here, that influence vitamin C levels in this group of PCOS patients?

Predictors of gamma- and alpha-tocopherol plasma levels

Results from the entire population

No statistical significant correlations between any of the obesity measures and plasma levels of gamma-tocopherol were found. However, both waist circumference (r=-0.35) and BMI (r=-0.31) were significant predictors of alpha-tocopherol levels after adjusting for confounding factors. Waist circumference correlated negatively with alpha-tocopherol concentrations (r=-0.28), before adjustment for confounding factors, as well.

Results from each group

Our results showed that waist circumference is a negative, significant predictor of alpha - tocopherol levels after correcting for age and smoking, in the healthy women group (r=-0.43) but not in the patient group. We noted, anyway that the effect waist circumference had on alpha-tocopherol concentrations was actually not so different between the groups (a increasing in waist circumference by one centimetre could decrease serum alpha - tocopherol levels by 0.02 umol/l among the healthy women and by 0.017umol/l in the patient group).

Our data compared with results from other studies

Concerning literature I was not able to find other studies where correlations of obesity measures with plasma antioxidant concentrations were investigated in women with PCOS.

Several studies showed, however, that women with PCOS have increased oxidative stress and that hyperinsulinemia resulting from insulin resistance is frequently associated with the disorder (140;141), which could give lower antioxidant status in this group of patients compared with age- and BMI-matched healthy women. As presented earlier, we found negative correlations between obesity measures and plasma antioxidant levels in this population. Lower plasma antioxidant levels in women with higher degree of obesity could be interpreted as high degree of oxidative stress, more pronounced inflammation and high use of antioxidants with increasing fat mass.

In accordance with our results, most of the reports among females consistently showed that serum beta-carotene (53;54;142) and vitamin C (49) were negatively associated with BMI and other measures of obesity. A study conducted among both men and women demonstrated that abdominal adiposity is significantly and independently associated with decreased serum levels of several carotenoids in women (43). However, in an article published more recently it was shown that BMI is inversely associated with plasma concentration of carotenoids but not with plasma vitamin C in older women (51).

Virtanen et al. investigated correlations of antioxidant levels in adipose tissue and measures of obesity in both men and women. In women waist circumference was shown to be an independent negative predictor of alpha-carotene level, BMI was a predictor of beta-carotene, results that are consistent with our findings (50).

It has been suggested that the independent negative association between general obesity and serum beta - carotene concentration might have at least two mechanisms. The first is that beta-carotene is distributed differently between plasma and adipose tissue, the former being the dominant storage tissue of beta-carotene in humans. Accordingly, a person with high fat mass would have a larger proportion of ingested beta-carotene absorbed by fat tissue than would a lean person if all other metabolic factors were equal. A second explanation could be that the estimates of beta-carotene intakes among obese individuals fail to detect a lower consumption of foods that would increase serum beta-carotene concentrations (44;143).

Recently it was shown that BMI predicted even the evolution of serum carotenoids during a 7-year follow-up among young non-smoking adults with the exception of lycopene (144). Several other studies have also failed to observe associations between BMI and lycopene (53;145;146). These results are in contrast with our findings; we observed a significant correlation of BMI with plasma lycopene levels.

Consistent with the results from this master thesis, previous studies reported a negative association between serum alpha-tocopherol and both general and central obesity (60;61). It was suggested that the part of the increased incidence of cardiovascular disease associated with central obesity may be caused by low alpha-tocopherol status. Body mass index was shown to influence alpha-tocopherol concentrations in a group of non-smoking Mediterranean population (59) and, in like in our PCOS group, no associations were found in two other studies (55;62). However, the first study mentioned was conducted among younger and older participants (over 60 years) of both gender and the second was conducted among obese children. Thus, the comparison with our results is not optimal primarily because of participant's different metabolic state that could influence the results.

No significant associations of gamma-tocopherol concentrations with obesity measures were found in women participating in this project, but it was positively associated with BMI in several other studies (53;54).

Smoking, carotenoid and vitamin C levels

In this study, smoking was not a significant predictor of different carotenoid levels and, particularly, no significant correlation was found between smoking and beta-carotene concentrations ($r<0.1$) both unadjusted and adjusted for obesity measures and age. This could be explained by the fact that there were few smokers in our population, 9 (18.3%) participants reported that they were smokers. We found no correlation with smoking in the PCOS group and a small negative correlation in our healthy women, when adjusted for age and waist to hip ratio (the difference in beta carotene levels between healthy smokers and non smokers was 0.28 umol/L). Anyway, our analysis in the control group showed that smoking was a negative, medium strong predictor ($r=-0.4$) of plasma vitamin C levels when controlling for age and waist circumference. We found that the difference in plasma vitamin C levels between smokers and non-smokers is 21.2 umol/L. These results are in accordance with reports that indicated adverse effects of smoking on vitamin C metabolism and results that demonstrated lower vitamin C concentrations in smokers compared with non-smokers (63).

6.4 Binge Eating Score and Three Factor Eating Questionnaire

Analysis of the data from this project showed higher BES and TFEQ scores in PCOS women compared with the controls, but the difference was not statistical significant. We observed that women with a higher degree of obesity were more likely to express binge eating episodes and emotional eating. All these aspects are discussed below.

6.4.1 Methodological limitations of the questionnaires

The BES score has been proposed as a screening tool for binge eating disease in obese. It was however proposed that the diagnosis binge eating should be confirmed by a clinical interview (147). A disturbing element when using self-reported questionnaires could be the subjectivity when answering the questions. For example, how much food is actually considered larger than normal amount of food?

Compared to self-reported questionnaires, interviews could provide more accurate information and reliable diagnose, since the interviewer can define the terms and explain questions and help the participants remember. An interview is, however, more time consuming and needs to be performed by specifically trained personnel.

6.4.2 Discussion of results on dietary behaviour

Binge Eating Score

According to our observations, PCOS patients showed a higher BES score compared to their BMI-matched controls (mean score 10.8 point in the PCOS, and 8.7 point in the control group) but the difference was not statistical significant ($p=0.4$).

As in previous studies using BES, subjects scoring 17 or lower were classified as non bingers, those with scores of 18-26 as moderate bingers, and those scoring 27 or higher as severe bingers. Twenty (80%) women from the PCOS population and 22

(92 %) healthy women were classified as nonbingers. Moderate binge eating was diagnosed in four (16%) women in the polycystic ovary group and in two (8 %) women in the control group. One woman from the patient group reached a score of more than 27 and, accordingly, was diagnosed as severe binger. Thus, we observed that, compared to their BMI-matched controls, more than the double of women from the patient group experienced binge eating episodes.

The term binge eating is a term introduced in 1959 to describe a problematic behaviour found in a subgroup of overweight individuals (148). Several research groups described a subset of obese patients who had episodes of binge eating in the absence of compensatory behaviours, distinctive clinical features and high levels of associated psychopathology.

Research showed that women with PCOS are often diagnosed with eating disorders and, moreover, it was postulated that there is a correlation between ovarian morphology and bulimia. Changes in peripheral insulin sensitivity were proposed as the link between PCOS and bulimia (99). This study was, however, conducted on a small population sample, thus the clinical importance of their results could be questionable.

Moreover, there were researchers that proposed another theory in order to explain the link between these two disorders. Fairburn et al. postulated that some symptoms of PCOS such as menstrual irregularity, hirsutism, acne and obesity, may contribute in development of disordered eating habits (149). In this master project we did not investigate the clinical features in the patients and we did not perform pelvic ultrasonography, thus we could not investigate possible associations of these factors with binge eating. We found, however, a higher BES score in the PCOS group compared to their BMI-matched controls. We could, though, assume that women with polycystic ovary disease could be at increased risk of binge eating, maybe due to

clinical signs such as weight gain, hirsutism and acne, in accordance with the theory proposed by Fairburn et al.

Results from a study conducted recently, could not find any significant association between PCOS, or polycystic ovaries with binge eating disorder nor to support the hypothesis that polycystic ovaries predispose towards development of eating disorders (150). This study used eating disorder examination (EDE) as assessment tool, an interviewer-based questionnaire, which is considered "gold standard" diagnostic tool for assessment of eating disorders, and thus the results could be more conclusive.

Three Factor Eating Questionnaire

The PCOS patients presented higher scores on all three TFEQ-R21 scales compared to the controls but we could not demonstrate a statistical significant difference between the groups. These results could, however, indicate that women with polycystic ovary syndrome express a more uncontrolled, restraint and emotional eating. This means that women with this disorder are more likely to lose control over eating and have higher tendency to restraint their food intake in order to control body weight. Especially the emotional eating scale score was higher in our patients compared to controls. Even when we could not demonstrate a significant higher emotional eating scale, a higher score in our patients could indicate that this group of patients is at a higher risk of overeat in relation to negative mood states. This observation is in accordance with the higher BES scores in women with PCOS that places these women at higher risk of developing binge eating.

Correlations of BMI with BES and TFEQ scores

A strong positive correlation for BES scores and the BMI was observed with univariate analysis in both our patients (r=0.50) and controls (r=0.53). Accordingly, when analyzing correlations between TFEQ scales scores an BMI, we found a strong correlation between emotional eating scale and body mass index. Indeed, these results could indicate that participants with a higher degree of overweight are more likely to engage in binge eating behaviour, as previously reported by other studies (151) and to

overeat in relation to negative mood states. Or is it possible that these women are overweight because they are bingers or emotional eaters? In accordance with our findings, BMI was positively correlated with all three TFEQ-R18 factors, a revised the instrument to an 18-item questionnaire based on the original items in a study conducted recently (152). Moreover, the correlation between emotional eating and BMI it was shown to be higher in overweight than in normal-weight subjects (153).

It was suggested that specific eating behaviours may contribute to weight gain through an increase in food intake (154). However, the causal relation between these two variables remains unclear. Further studies are needed to find out whether the weight gain leads to emotional eating or whether persons with a tendency toward emotional eating gain weight more easily than do others.

Further, we found of interest to analyze the relationship of binge eating behaviour with uncontrolled eating and emotional eating in our groups. Strong correlations of BES score with both uncontrolled and emotional eating scales were observed in both groups. According to these findings, women with problems in controlling food intake and in controlling eating in relation to emotions are more likely to engage in binge eating.

Our results showed a higher BES score and TFEQ scale scores in PCOS patients compared with the healthy women, the difference was not statistical significant, possible due to small population sample. Therefore, these results could be of questionable clinical significance. One must note, however, that our observations are in accordance with results from several other studies, regardless of the assessment tool that was used.

7. Conclusion

Results of this master thesis showed that the women with PCOS had similar diets to controls and the majority of women from both groups reported an unbalanced diet that is not within recommended guidelines. Saturated fat from fatty diary products, minced meat and meat products, added sugar from soft drinks, sweets and chocolates, and low intakes of important micronutrients contribute strongly to an unhealthy diet, and were observed in both groups. Women from both groups underreported their food intake. When matched for BMI, women with PCOS had similar antioxidant blood levels as well as eating behaviour to controls. However, increased BMI was associated with emotional eating and binge eating as well as with low levels of several antioxidants.

These observations could indicate that specific dietary interventions may not be needed for women with PCOS. However, a balanced diet within the present recommended levels, rich in mixed greens, whole grains cereals, fat reduced diary products, fish, and lean meats should be consumed, whereas intake of soft drinks, sweets and chocolates, minced meat and meat products should be limited. Extra attention should be given to those with a BMI not within the normal range.

Knowledge of how to advice and reach out to this population with the right information is a challenge, and must be focused on. The importance of an adequate diet in attention of the negative health outcomes women with PCOS are at risk of seems evident. The importance of life style factors, including diet, in managing this disorder needs to be explored further in detail. More research is needed to confirm previous findings or add new information, so we can tailor advice to women with PCOS and women with BMI not within the normal range, and thus prevent negative health outcomes.

A great effect may come from promoting the already existing recommendations. Thus, the question of how to influence women to change their diet and life style should be addressed. Clinical nutritionists and other health workers should guide

women with PCOS and women with BMI not within normal range, in how to achieve healthier life style. However, it is likely that giving information to these women is not enough. Well-designed interventions and studies of how to implement of how to implement the existing recommendations are most likely needed.

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Appendix A Ethical approval for PCOS study

UNIVERSITETET I BERGEN
Regional komité for medisinsk forskningsetikk, Vest-Norge (REK Vest)

Avdelingsoverlege Svein Skeie
Medisinsk klinikk
Stavanger universitetssjukehus
Pb 8100Postterminalen
4068 STAVANGER

Deres ref	Vår ref	Dato
	07/9231- 133.07/ars	29.06.2007.

Ad. prosjekt: Diett og ernæringsmessig status hos kvinner med polycystisk ovarie-syndrom; - en pilot-studie (133.07)

Det vises til din søknad om etisk vurdering datert 04.06.7, inklusiv søknad om opprettelse av forskningsbiobank datert 04.06.07. REK Vest vurderte studien i møte den 21.06.07.

Komiteen mener at studien kan gjennomføres i samsvar med søknad, men vi tror den vitenskapelige verdien kan økes, dersom en knytter til seg gynekologisk ekspertise.

Studien er da endelig klarert fra denne komité sin side

Vi ønsker dere lykke til med gjennomføringen og minner om at komiteen setter pris på en sluttrapport, eventuelt en kopi av trykt publikasjon når dette foreligger.

Med vennlig hilsen

Jon Lekven
leder

Arne Salbu
sekretær

Kopi:
-SHDir

Postadresse
Postboks 7804
5020 Bergen

rek-vest@uib.no
www.etikkom.no/REK
Org no. 874 789 542

Regional komité for medisinsk
forskningsetikk, Vest-Norge
Telefon 55 97 84 97 / 98 / 99

Besøksadresse
Haukeland
Universitetssykehus

Appendix B Invitation letter to the patients

(Til pasient)

September 2007

Jeg har påtatt meg å være medveileder for en masteroppgave som utføres av Marioara Covrig, student i klinisk ernæringsfysiologi ved Universitetet i Oslo med prof. Serena Tonstad som hovedveileder. For å få godkjent utdannelsen sin, må Marioara levere inn en masteroppgave som bidrar med kunnskap om en problemstilling som har interesse for hennes fagfelt.

Denne masteroppgaven vil forsøke å kartlegge kosthold og spisevaner samt vitamin- og mineralstatus hos kvinner med polycystisk ovarie syndrom. Tilstanden er velkjent, men lite studert. Vi vil sammenligne data fra 25 kvinner som har sykdommen med en tilsvarende gruppe friske kvinner. Undersøkelsen er beskrevet ganske detaljert i det vedlagte informasjonsskrivet. Etter fullført datainnsamling vil deltakerne bli tilbudt en konsultasjon for å vurdere eventuelle konsekvenser av observasjonene.

Jeg mener denne masteroppgaven kan bli både interessant og nyttig så vel for fagmiljøet som for deltakerne selv. Jeg håper derfor at du kan tenke deg å delta i denne undersøkelsen. Du må gjerne kontakte meg (tlf 51519828) eller din fastlege for å diskutere dette nærmere.

Informasjonsskrivet som er vedlagt er tilrådd av Regional komite for medisinsk forskningsetikk, Vest-Norge.

Dersom du ønsker å delta, kan du fylle ut og sende inn det vedlagte skjemaet i vanlig post. Så vil vi kontakte deg. Vi tar imot påmeldinger til undersøkelsen frem til utgangen av 2007.

På forhånd takk for samarbeidet.

Med vennlig hilsen

Svein Skeie
Avdelingsoverlege, Medisinsk Klinikk
Stavanger Universitetssjukehus

Appendix C Informational letter to the patients

Forespørsel om å delta i et medisinsk forskningsprosjekt.

Tittel: Diett og ernæringsmessig status hos kvinner med polycystisk ovarie-syndrom; - en pilot-studie.
Prosjektleder: Avdelingsoverlege Svein Skeie, Stavanger Universitetssjukehus

Dette informasjonsskrivet beskriver prosjektet og hvilke praktiske og medisinske konsekvenser det kan ha for deltakerne. Les informasjonen nøye og diskuter gjerne eventuelle spørsmål med prosjektleder, fastlegen eller andre før du bestemmer deg for om du vil delta.

Innledning:

Diagnosen polycystisk ovariesyndrom (PCOS) innebærer at det kan påvises et unormalt stort antall cyster på eggstokkene samtidig som kvinnen også har minst to av følgende forstyrrelser: Menstruasjonsforstyrrelser, sjenerende hårvekst på kroppen, manglende eggløsning, eller unormalt høyt nivå i blodet av visse kjønnshormoner.

Man regner med at ca 5% av kvinner i fruktbar alder lider av PCOS med varierende grad av symptomer. En relativt vanlig følgetilstand er nedsatt respons på insulin, noe som gjør at enkelte næringsmidler ikke opptas og / eller forbrennes normalt. Det eksisterer lite kunnskap om konsekvensene for opptaket av viktige næringsemner og vitaminer.

Hensikt og målsetning.

Dette prosjektet skal samle inn mål på kroppsstørrelse og –fasong samt detaljerte opplysninger om kosthold og ernæring, og analyser av hormoner, vitaminer og andre substanser i blodet som har betydning for hvordan kroppen utnytter næringsemnene. Disse målingene skal sammenlignes med tilsvarende målinger fra en gruppe friske kvinner. Hensikten er å forsøke å vise om kvinner med PCOS har unormalt lave nivåer av viktige vitaminer i blodet, og andre tegn på endret forbrenning.

Aktuelle deltakere.

Målinger skal samles inn fra 25 kvinner i fruktbar alder som har diagnosen PCOS og fra 25 friske kvinner i tilsvarende alder. Mulige deltakere kan ikke være gravide eller ha kjent stoffskiftesykdom, diabetes eller annen sykdom eller behandling som påvirker forbrenningen. Deltakerne må heller ikke delta i et aktivt slankeprogram.

Mulige deltakere skal rekrutteres fra de aktuelle poliklinikkene ved Stavanger Universitetssjukehus, enkelte allmenpraktiserende leger og ved annonsering i lokale aviser.

Gjennomføringen av prosjektet.

Ved den første avtalen vil prosjektlegen eller masterstudenten gjøre et innledende intervju om sykehistorie og gå gjennom sykejournalen for å utelukke deltakere med problemstillinger som kan forstyrre prosjektet. Det vil bli tatt fastende blodprøver enten i tilknytning til dette intervjuet eller en av de første dagene etterpå. Deltakerne vil deretter bli bedt om å fylle ut en dagbok i 7 døgn med detaljere opplysninger om mengde og type av næringsmidler som er inntatt, etterfulgt av 2 standardiserte skjema med totalt 37 spørsmål for å kartlegge diett og spisevaner. Man må dermed regne med 2 eller 3 besøk i forbindelse med prosjektet. Deltakerne skal ikke følges opp over lenger tid.

Mulige fordeler av å delta.

Dette prosjektet skal sammenligne innsamlede observasjoner. Behandling inngår ikke som en del av prosjektet. Deltakerne kan derfor ikke forvente å oppnå noen direkte helsemessige gevinster av prosjektet. Imidlertid vil alle funn som tyder på at det trenges behandlingsmessige eller andre tiltak bli rapportert til fastlegen for videre oppfølging. Hver enkelt deltaker vil få tilbud om veiledning om kosthold med utgangspunkt i de innsamlede observasjonene etter den siste kontrollen i prosjektet.

Biobank.

Dette prosjektet krever at det opprettes en godkjent biobank. Alle blodprøvene som tas vil bli merket med et eget deltakernummer (avidentifisert) og analysert fortløpende ved norske

laboratorier. Resultatene kan ikke koples til person av andre enn prosjektleder. Det vil ikke bli gjort genetikk-analyser. Alle blodprøvene vil bli destruert umiddelbart etter avsluttet analyse, og senest ett år etter avslutningen av prosjektet.

Frivillighet.

Deltakelse i dette prosjektet er helt frivillig. Deltakerne kan når som helst trekke seg fra videre deltakelse uten å måtte oppgi noen grunn for det. Dersom en deltaker trekker seg, kan vedkommende også kreve at de innsamlede blodprøvene blir destruert og / eller at alle innsamlede målinger og observasjoner blir slettet, såfremt de ikke inngår i allerede utførte vitenskapelige analyser.

Konfidensialitet.

Alle opplysninger som samles inn i prosjektet vil bli avidentifisert, dvs at de merkes med et eget deltakernummer og initialer. Det er bare prosjektleder, mastergradsstudent Covrig og sykepleiere ved Stavanger Helseforskning som får kjennskap til personopplysninger. Alt involvert personale er underlagt taushetsplikt. Ingen deltakere vil kunne gjenkjennes i sluttrapporten.

Denne rapporten skal benyttes i en mastergradsoppgave av Marioara Covrig, student i klinisk ernæringsfysiologi ved Universitetet i Oslo. Vitenskapelige veiledere er prof. Serena Tonstad, Universitetet i Oslo, og avdelingsoverlege Svein Skeie, Stavanger Universitetssjukehus. Alle innsamlede målinger vil bli oppbevart i ca 2 år etter offentliggjøring av rapporten, og deretter vil målingene bli anonymisert før videre lagring ved Stavanger Helseforskning AS.

Økonomi.

Dette prosjektet mottar ikke støtte fra noen kommersielle interessenter. Personalet bidrar med gratis arbeid. Analyseutgifter vil måtte dekkes. Det søkes derfor støtte fra interne finansieringskilder ved Stavanger Universitetssjukehus, Universitetet i Oslo og fra andre offentlige organer. Deltakerne kan ikke regne med dekning av reiseutgifter eller andre kostnader. Det skal heller ikke medføre ekstra kostnader å delta i prosjektet.

Prosjektet har ingen forsikringsordning siden deltakelse ikke medfører noen øket risiko for skade eller feilbehandling.

Andre opplysninger.

Denne pilotstudien er vurdert av Regional komite for medisinsk forskningsetikk Vest-Norge, og Sosial- og Helsedirektoratet har godkjent at det opprettes en biobank for undersøkelsen.

Dersom deltakerne har noen spørsmål før, under eller etter undersøkelsen kan de kontakte medisinsk ansvarlig, overlege Svein Skeie, Stavanger Universitetssjukehus, telefon 05151.

Forespurte personer har krav på minst 2 dagers betenkningstid før de bestemmer seg for å delta.

Deltakerne skal få utlevert en signert gjenpart av dette informasjonsskrivet.

Informasjonen om prosjektet er gitt av: _____ _____

Navn Dato

Samtykke-erklæring.

Jeg har lest dette informasjonsskrivet og fått anledning til å diskutere innholdet med prosjektansvarlig. Jeg er villig til å delta i prosjektet.

_____ _____ _____

Navn Dato Deltaker nr.

Dagbok

Fyll inn:

Kjønn ☐ Skriv 1 hvis gutt/mann, 2 hvis jente/kvinne

Alder ☐☐ år

Ukedag ☐ 1=mandag, 2=tirsdag, 3=onsdag, 4=torsdag, 5=fredag, 6=lørdag og 7=søndag

Dato ☐☐.☐☐.☐☐

Var denne dagen en vanlig dag? Skriv ja eller nei i rutene.

☐☐☐

Hvis det var en uvanlig dag, forklar hvorfor denne dagen var uvanlig:

Hvor finner jeg matvarene i dagboken?

HUSK:

Alt du spiser/drikker skal skrives opp

Sett ikke kryss i dagboken

Sett bare bokstaver i de orange rutene

Sett bare tall i de sorte rutene

Drikke

For størrelsen på glasset du drikker av, se bildeserie 1.
Fyll inn bokstaven i den orange ruten.

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Vann	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Helmelk, søt/sur (eks. helmelk, kefir)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Lettmelk, søt/sur (eks. lettmelk, Cultura)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Ekstra lett lettmelk	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Skummet melk	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Drikkeyoghurt	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Sjokolademelk av helmelk (eks. O'boy, Nesquick)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Sjokolademelk av lettmelk (eks. Nesquick, Litago)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Sjokolademelk av ekstra lett lettmelk (eks. O'boy)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Sjokolademelk av skummet melk (eks. O'boy, Nesquick)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Litago sjokolademelk	1/2 liter	☐☐	☐☐	☐☐	☐☐	☐☐
Kakao av helmelk	kopp	☐☐	☐☐	☐☐	☐☐	☐☐
Kakao av lettmelk	kopp	☐☐	☐☐	☐☐	☐☐	☐☐
Kakao av ekstra ett lettmelk	kopp	☐☐	☐☐	☐☐	☐☐	☐☐
Kakao av skummet melk	kopp	☐☐	☐☐	☐☐	☐☐	☐☐
Appelsinjuice	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Eplejuice/eplemost	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Nektar (eks. eple, tropisk frukt, annen frukt)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Brus med sukker (eks. Cola, Solo)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Brus med sukker (eks. Cola, Solo)	1/2 liter	☐☐	☐☐	☐☐	☐☐	☐☐
Brus, kunstig søtet (eks. Cola light, Solo lett)	glass	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Brus, kunstig søtet (eks. Cola light, Solo lett)	1/2 liter	☐☐	☐☐	☐☐	☐☐	☐☐

Drikke forts.

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Saft med sukker (eks. husholdning, appelsin, solbær)	glass					
Saft, kunstig søtet (eks. Fun light)	glass					
Mineralvann (eks. Farris)	glass					
Mineralvann (eks. Farris)	1/2 liter					
Energidrikk (eks. Battery)	boks (330 ml)					
Te, vanlig (eks. Earl Grey, solbær)	kopp					
Fruktte (eks. nype, kamille)	kopp					
Iste/urtete med sukker	glass/pakning (250 ml)					
Kaffe, kokt (eks. presskanne)	kopp					
Kaffe, traktet/filter	kopp					
Kaffe, pulver (instant)	kopp					
Caffe latte, Cappucino	glass/kopp (4dl)					
Espresso	kopp (1dl)					
Sukketter/Natrena/ Canderel	stk					
Sukker til te/kaffe	teskje/ biter					
Melk til te/kaffe	spiseskje					

Annet
beskriv best mulig hva, hvor mye og når:

Øl, vin, brennevin

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Alkoholfritt øl, vørterøl (eks. Clausthaler, Munkholm)	glass					
Lettøl	boks/flaske (330 ml)					
Pilsner	boks/flaske (330 ml)					
Sterkøl	boks/flaske (330 ml)					
Rusbrus (eks. Cider, Bacardi breezer)	boks/flaske (330 ml)					
Hvitvin	glass					
Rødvin	glass					
Brennevin	dram (4 cl)					

Annet
beskriv best mulig hva, hvor mye og når:

Brød m.m.

Skriv antall skiver i sort rute. For tykkelse på brødskiven se bildeserie 2 og fyll inn bokstaven i orange rute.

1 skive = 1/2 rundstykke

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Loff/fint rundstykke	skiver					
Mellomgrovt brød, grovt rundstykke, kneippbrød	skiver					
Grovt brød	skiver					
Dansk rugbrød, Pumpernikkel	skiver					
Baguette/Ciabatta	stk					
Knekkebrød lyst, skonrok, kavring	stk					
Knekkebrød, mørkt	stk					
Lompe, potetlefse	stk					
Pølsebrød, hamburgerbrød	stk					
Pitabrød	stk					
Flatbrød (eks. Mors flatbrød, Ideal)	stk					

Smør eller margarin på brød.

1 skive = 1/2 rundstykke = 1 knekkebrød
= 2 vaffelhjerter = 2 kjeks = 1/2 ciabatta

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl.22-6
Meiersmør	til antall skiver					
Bremykt	til antall skiver					
Brelett	til antall skiver					
Margarin (eks. Soya, Per, Melange)	til antall skiver					
Lettmargarin (eks. Soft light)	til antall skiver					

Annet
beskriv best mulig hva, hvor mye og når:

Hvor mye smurte du på brødet?

Se bildeserie 3 og skriv bokstaven for det bildet som ligger nærmest opp til den smør-/margarinmengden du brukte på brødet. Hvis du hadde forskjellig mengde smør/margarin på de brødskivene du spiste innenfor det angitte tidsrommet, kan du anslå et gjennomsnitt for skivene.

	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Bildeserie 3					

Pålegg

Du skal oppgi mengde pålegg i forhold til brødskiver. Har du spist to typer pålegg på samme brødskive, fører du opp begge (eks. 1 hvitost helfet og 1 skinke). Hvis du bare har spist pålegg og ikke brød, anslå til hvor mange skiver du kunne brukt dette pålegget.

1 skive = 1/2 rundstykke = 1 knekkebrød
= 2 vaffelhjerter = 2 kjeks = 1/2 ciabatta

Kjøttpålegg	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Servelat, vanlig	til antall skiver					
Kokt skinke, spekeskinke, lett servelat	til antall skiver					
Salami, spekepølse, fårepølse	til antall skiver					
Leverpostei, vanlig	til antall skiver					
Leverpostei, mager	til antall skiver					
Kalkun-/ kyllingpålegg	til antall skiver					

Ost	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Hvitost helfet 27% fett (eks. Jarlsberg, Norvegia)	til antall skiver					
Hvitost halvfet 16% fett (eks. Norvegia lettere)	til antall skiver					
Brunost helfet (eks. Geitost, G35, Fløtemysost)	til antall skiver					
Brunost halvfet, prim	til antall skiver					
Smøreost, vanlig (eks. Baconost, Snøfrisk)	til antall skiver					
Smøreost, mager (eks. mager skinkeost)	til antall skiver					
Kremost (eks. Philadelphia, Gourmetoster)	til antall skiver					
Dessertost (eks. Brie, Gräddost, Ridderost)	til antall skiver					

Fiskepålegg	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Kaviar	til antall skiver					
Røkt laks/ørret	til antall skiver					
Makrell i tomat, røkt makrell	til antall skiver					
Sardiner, sursild, ansjos	til antall skiver					

Syltetøy/søtpålegg	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Syltetøy vanlig, gelé, marmelade	til antall skiver					
Syltetøy lett, frysetøy	til antall skiver					
Honning	til antall skiver					
Peanøttsmør	til antall skiver					
Sjokolade-/nøttepålegg	til antall skiver					
Hapå/Litagopålegg	til antall skiver					

Annet
beskriv best mulig hva, hvor mye og når:

Annet pålegg

1 skive= 1/2 rundstykke= 1knekkebrød
=2 vaffelhjerter= 2 kjeks= 1/2 ciabatta

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Egg, kokt/stekt	til antall skiver					
Majonessalat (eks. italiensk salat, rekesalat)	til antall skiver					
Majonessalat, lett (eks. italiensk salat, lett)	til antall skiver					
Tomat som pålegg	til antall skiver					
Banan som pålegg	til antall skiver					

Annet
beskriv best mulig hva, hvor mye og når:

Pynt på brødskiver

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Majones/remulade, vanlig	til antall skiver					
Majones/remulade, lett	til antall skiver					
Agurk (frisk/syltet)	til antall skiver					
Rødbeter (syltet)	til antall skiver					
Paprika	til antall skiver					

Annet
beskriv best mulig hva, hvor mye og når:

Yoghurt

	Antall	kl. 6-10	kl.10-14	kl.14-18	kl.18-22	kl.22-6
Yoghurt med frukt	beger (175 ml)					
Yoghurt 0,1% fett	beger (125 ml)					
Yoplait frukt	beger (125 ml)					
Litago yoghurt	beger (125 ml)					
Litago yoghurt m/müsli	beger inkl. müsli					
Go'morgen yoghurt m/müsli	beger inkl.müsli					
Piano Duo Yoghurt	beger (125 ml)					

Frokostgryn/grøt

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
lavregrøt	bildeserie 5					
lavregryn	bildeserie 4					
irkorn	bildeserie 4					
lüsli, søtet ıks. Crusli, Solfrokost)	bildeserie 4					
lüsli, usøtet ıks. Go'Dag, Frukt müsli)	bildeserie 4					
ornflakes	bildeserie 4					
onnikorn/ rosties/Chocofrokost	bildeserie 4					
uffet ris/ avrenøtter/hvetenøtter	bildeserie 4					

ınnet
eskriv best mulig
ıva, hvor mye og når:

Melk/sukker/syltetøy brukt sammen med frokostgryn og grøt

3 teskjeer=1 spiseskje

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Helmelk, søt/sur	dl					
Lettmelk, søt/sur	dl					
Ekstra lett lettmelk	dl					
Skummet melk, søt/sur	dl					
Syltetøy vanlig, gelé, marmelade	teskjeer					
Syltetøy lett, frysetøy	teskjeer					
Sukker	teskjeer					

Annet
beskriv best mulig
hva, hvor mye og når:

For drikkeyoghurt som tilbehør til frokostgryn og grøt se side 2
For yoghurt som tilbehør til frokostgryn og grøt se side 7

Kjøtt og kjøttretter

Pølse	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Grillpølse/wienerpølse, vanlig	stk					
Grillpølse/wienerpølse, lett	stk					
Kalkun/kyllingpølse	stk					
Middagspølse/ kjøttpølse/medisterpølse	kjøttpølse (15cm)					
Middagspølse/ kjøttpølse, lett	kjøttpølse (15cm)					

Kjøttretter/pizza	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Karbonader	stk					
Kjøttkaker/medisterkaker	stk					
Elg-/reinkarbonader	stk					
Snitzel (eks. ostesnitzel)	stk					
Løvstek	skiver					
Hamburger med brød (eks. vanlig, McDonalds mfl.)	stk					
Tacoskjell med kjøttdeig og salat	fylte skjell					
Pitabrød med kjøtt og salat	fylte pita					
Kebab	fylte pita					
Kjøttdeigsaus/tomatsaus med kjøttdeig	bildeserie 11					
Lasagne	stk (10x8cm)					
Moussaka	stk (10x8cm)					
Pizza, trekantstykker	bildeserie 12					
Pizza, firkantstykker	bildeserie 13					

Annet
beskriv best mulig hva, hvor mye og når:

For lompe, pølsebrød og hamburgerbrød se side 4
For ketchup og sennep se side 14
For kokt pasta (uten saus) se side 13

Kjøtt forts.

ent kjøtt	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
iff (okse, lam, svin)	stykker					
oteletter (svin, lam, okse)	koteletter					
tek (svin, lam, okse)	skiver					
kinke (Bayonne, hermetisk)	skiver					
lg-/hjort-/reinsdyrstek	skiver					
irillet kylling	1/4 kylling					
yllingfilet	fileter					
acon	skiver					

iryteretter	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
isotto	bildeserie 11					
årikål	bildeserie 11					
apskaus	bildeserie 11					
iryterett (basis) med øttdeig/pølser	bildeserie 11					
iryterett med g-/hjort-/reinsdyrkjøtt	bildeserie 11					
iryterett med r-/okse-/svinekjøtt	bildeserie 11					
everretter	bildeserie 11					

nnet
eskriv best mulig hva, hvor mye og når:

For saus se side 14

Fisk og fiskeretter

Fiskefarse

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Fiskeboller	stk					
Fiskekaker/fiskepudding	stk/skiver					

Ren fisk

Torsk/sei, kokt/bakt	stykke					
Torsk/sei, stekt	bildeserie 14					
Laks/ørret, kokt/bakt	stykke					
Laks/ørret, stekt	bildeserie 14					
Makrell, kokt	stykke					
Makrell, stekt	bildeserie 14					
Lyndre/steinbit, kokt	stykke					
Lyndre/steinbit, stekt	bildeserie 14					

Tillagede fiskeretter og fiskepinner

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Fiskepinner	stk					
Panert fisk	stk					
Fiskegryte/suppe med fisk	tallerken (3 dl)					
Fiskegrateng	stk (10x8cm)					

Reker og fiskeinnmat

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Reker (uten skall)	bildeserie 9					
Fiskerogn	skiver					
Fiskelever	spiseskjeer					

Annet
Skriv best mulig hva, hvor mye og når:

Andre retter

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Risengrynsgrøt (For sukker se s. 8 og smørøye s. 5)	bildeserie 5					
Pannekaker (For sukker og syltetøy se s. 8)	stk					
Suppe (eks. blomkål, tomat)	tallerken (3dl)					
Ertesuppe/betasuppe	tallerken (3dl)					
Kjøttsuppe (eks. Trøndersodd)	tallerken (3dl)					
Omelett	antall egg i stykket					
Eggerøre	til antall skiver					
Ostepai	stykke (10x8cm)					
Pasta med tomatsaus uten kjøtt	bildeserie 6					
Pasta med hvit saus (eks. carbonara)	bildeserie 6					

Vegetarrett
beskriv hva (oppskrift), hvor mye og når:

Annet
beskriv best mulig hva, hvor mye og når:

Blandet salat med kjøtt/fisk/skalldyr

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Blandet salat med kjøtt/skinke	bildeserie 10					
Blandet salat med skalldyr/fisk	bildeserie 10					
Blandet salat med tunfisk	bildeserie 10					
Blandet salat med pasta	bildeserie 10					

Annet
beskriv best mulig hva, hvor mye og når:

For dressing se side 14

Potet/ris/pasta

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Potet, kokt	stk					
Potet, bakt	stk					
Potetmos	bildeserie 7					
Gratinerte poteter	bildeserie 7					
Pommes frites	bildeserie 8					
Potetsalat med majones/rømmedressing	spiseskjeer					
Potetsalat med oljedressing	spiseskjeer					
Ris, kokt (eks. parboiled, naturris)	bildeserie 6					
Ris, kokt (eks. jasmin, basmati, hurtigris)	bildeserie 6					
Pasta, kokt (eks. spaghetti, makaroni, tagliatelle)	bildeserie 6					
Nudler (eks Mr.Lee)	pose					

Annet
beskriv best mulig hva, hvor mye og når:

Grønnsaker

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Gulrot	stk					
Kålrot	skive					
Brokkoli	bildeserie 9					
Blomkål	bildeserie 9					
Hodekål	skalk					
Surkål	spiseskjeer					
Råkost (gulrot, blandet av flere grønnsaker)	bildeserie 9					
Grønnsaksblanding, fryst (eks. amerikansk blanding)	bildeserie 9					
Blandet salat (eks. kinakål, mais, tomat og agurk)	bildeserie 10					

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Grønnsaker forts.

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Stekte grønnsaker (eks. wokblanding)	bildeserie 9					
Tomat	skiver/båter					
Paprika	ringer					
Mais	spiseskjeer					
Løk, stekt	spiseskjeer					
Ertestuing	spiseskjeer					

Annet
beskriv best mulig hva, hvor mye og når:

Saus/dressing

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Hvit saus	spseskjeer					
Ostesaus	spseskjeer					
Brun saus	spseskjeer					
Smeltet smør/ margarin	spseskjeer					
Tomatsaus (uten kjøtt)	spiseskjeer					
Ketchup	spiseskjeer					
Sennep	spseskjeer					
Bernaisesaus ol.	spiseskjeer					
Dressing, vanlig (eks. Thousand Islanc)	spseskjeer					
Dressing, lett (eks. Thousand Island light)	spiseskjeer					
Olje- og eddikdressing	spseskjeer					
Seterrømme 35% fett	spiseskjeer					
Lettrømme 20% fett	spiseskjeer					
Majones/remulade, vanlig	spseskjeer					
Majones/remulade, lett	spseskjeer					

Annet
Beskriv best mulig hva, hvor mye og når:

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Is/dessert

Is	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl.22-6
Is (eks. vanilje, krokan, sjokolade)	bildeserie 15					
Yoghurtis (eks. Dream, Living Lite)	bildeserie 15					
Ispinne (eks. Gullpinne, Pinup)	stk					
Kremmerhus (eks. Kroneis, Kronevaffel)	stk					
Saftispinne (eks. Lollipop)	stk					

Gelé, pudding, fromasj						
Gelé (eks. sitron, jordbær)	bildeserie 15					
Pudding (eks. sjokoladepudding)	bildeserie 15					
Riskrem, multekrem, fromasj	bildeserie 5					
Risifrutti med saus	beger					

Hermetisk frukt, fruktgrøt						
Fruktcoctail	bildeserie 5					
Ananas (ring), pære/fersken (halv)	stk					
Fruktgrøt, kompott	bildeserie 5					

Annet
beskriv best mulig hva, hvor mye og når:

Dessertsauser/krem	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Fløte	spiseskjeer					
Krem, pisket	spiseskjeer					
Sjokoladesaus	spiseskjeer					
Karamellsaus	spiseskjeer					
Vaniljesaus	spiseskjeer					

Annet
beskriv best mulig hva, hvor mye og når:

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Kaker, gjærbakst

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Boller	stk					
Julekake, kringle	skive/stykke					
Skolebrød, skillingsbolle	stk					
Wienerbrød, wienerkringle	stk					
Vafler (Se syltetøy s. 6, se rømme s. 14)	hjerter					
Eplekake, pai med frukt/bær	stykker					
Formkake, muffins	skive/stk					
Sjokoladekake	stykker					
Marsipankake, bløtkake	stykker					
Fyrstekake, nøttekake	stykker					
Smultring	stk					
Kokosbolle	stk					

Kjeks	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Kjeks (eks. Mariekjeks, Gjende), småkaker	stk					
Fylte kjeks (eks. Ballerina, Monaco, Pepita)	stk					
Havrekjeks (eks. Bixit, Sibas)	stk					
Smørbrødkjeks (eks. Kornmo, GoldenCrisp)	stk					
Smørbrødkjeks (eks. Kaptein, Start)	stk					
Salte kjeks (eks. Ritz, Salinas)	stk					
Kjeks med sjokolade (eks. Maryland cookies, Bixit med sjokoladetrekk)	stk					

Annet
beskriv best mulig hva, hvor mye og når:

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Frukt/bær	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Eple	stk					
Banan	stk					
Pære	stk					
Appelsin	stk					
Mandarin/klementin	stk					
Druer	stk					
Fersken/nektarin	stk					
Melon, vann	skive					
Melon, eks. cantalup	skive					
Jordbær (friske/frosne)	stk					
Rosiner	neve					
Kiwi	stk					

Annet
beskriv best mulig hva, hvor mye og når:

Snacks	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Potetgull, vanlig (1 neve= 8 flak)	neve					
Potetgull, vanlig	pose (300g)					
Potetgull, lett/ potetskruer (1 neve= 8 flak)	neve					
Potetgull, lett/ potetskruer	pose (300g)					
Ostepop (1 neve= 8 ostebuer)	neve					
Maischips (1 neve= 8 flak)	neve					
Peanøtter	pose (100g)					
Popcorn	neve					
Dip (eks. rømme m/dipmix)	spiseskjeer					

Annet
beskriv best mulig hva, hvor mye og når:

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Godterier

Sjokolade/konfekt	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Melkesjokolade (Melkesjokolade, Firkløver, Helnøtt)	plate (100g)					
Melkesjokolade (Melkesjokolade, Firkløver, Helnøtt)	ruter					
Mørk kokesjokolade	staver/4 ruter					
Marsipan med sjokolade (eks. Gullbrød, marsipangris)	som Gullbrød (65g)					
Sjokoladebiter (eks. Twist, konfekt)	biter					
Kinderegg	stk					
Snickers, Japp	stk (85g)					
Kjekssjokolade (eks. Kvikklunsj, Twix)	som Kvikklunsj (46g)					
Gelesjokolade (eks.Troika)	stk					
New Energy	stk					

Smågodt	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Lakris (eks. "salte sild", lakrisbåter)	stk					
Gelégodt (eks. seigmenn, vingummi, "colaflasker")	stk					
Skumgodt (eks. "viskelær", "sopp", marshmellows)	stk					
Syrlige drops (eks. "bringebær", salte og sure bomber)	stk					
Karamell (eks. Fudge, Smørbukk, Fox)	stk					
Godteripose (Godt & blandet, Søppeldynga, Partymix)	pose (150g)					
Kjærlighet på pinne	stk					

Annet
beskriv best mulig hva, hvor mye og når:

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Drops/pastiller

	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Drops/pastiller med sukker (eks. kamferdrops, Halslinser, Doc)	stk					
Pastiller, kunstig søtet (eks. Dent)	stk					
Tyggegummi med sukker	stk					
Tyggegummi, kunstig søtet (eks. Extra, V6)	stk					

Annet
beskriv best mulig
hva, hvor mye og når:

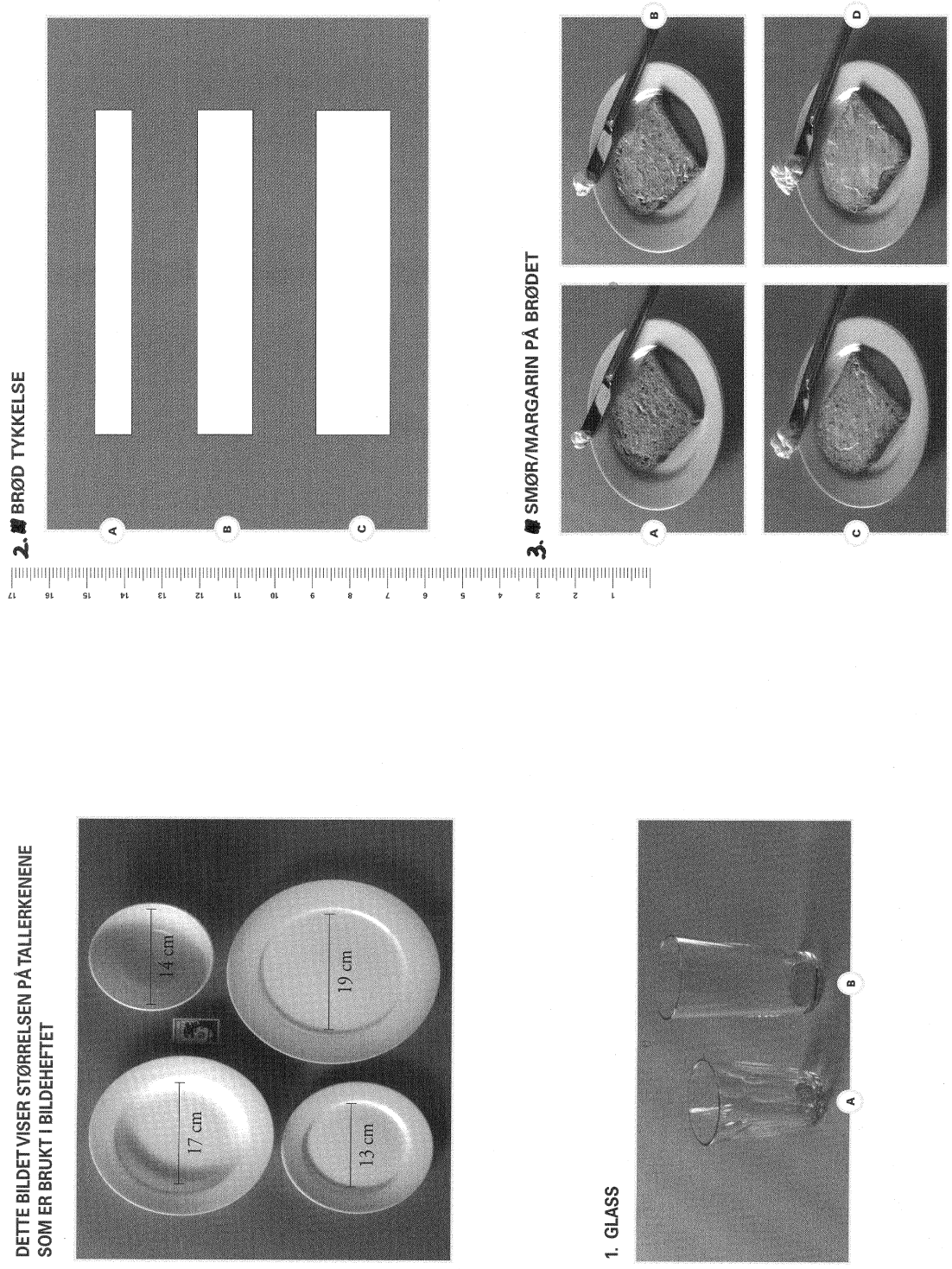
Tran/kosttilskudd

1 barneskje= 5 ml

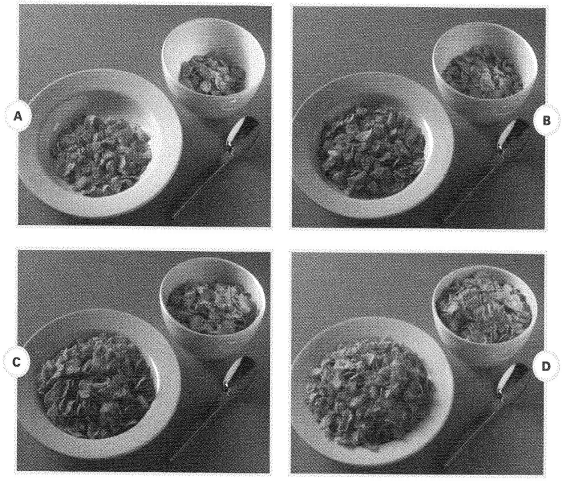
	Antall	kl. 6-10	kl. 10-14	kl. 14-18	kl. 18-22	kl. 22-6
Tran	barneskje					
Trankapsler	stk					
Sanasol	barneskje					
Biovit	barneskje					
Multivitamin (eks. Vitaplex, Vitamineral)	stk					
Fluortabletter	stk					
Jerntabletter (9mg)	stk					
Folat (400 µg)	stk					

Annet
beskriv best mulig
hva, hvor mye og når:

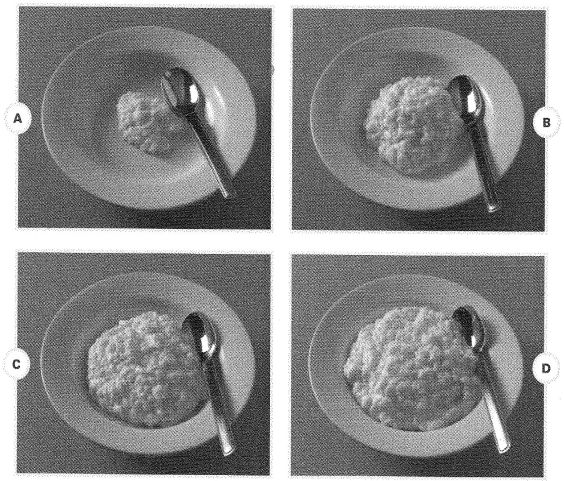
Appendix E Portion size booklet



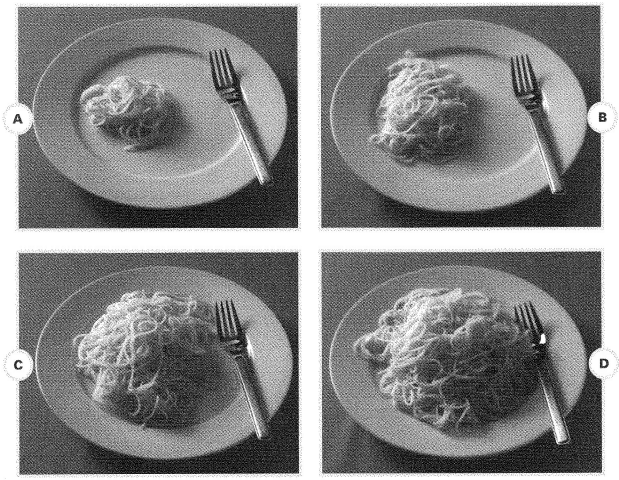
4. CORNFLAKES (FROKOSTBLANDING)



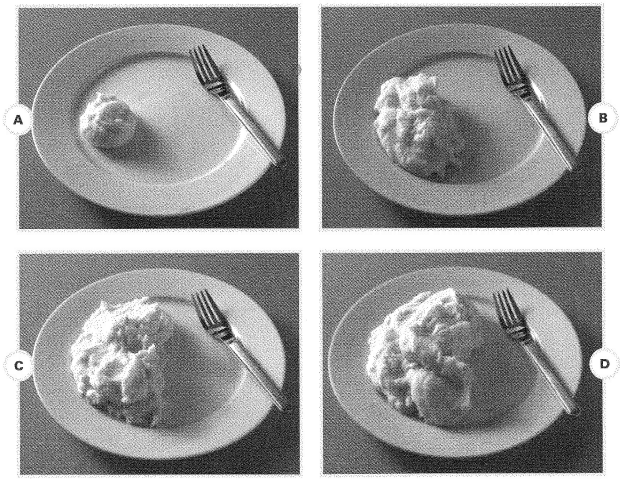
5. GRØT



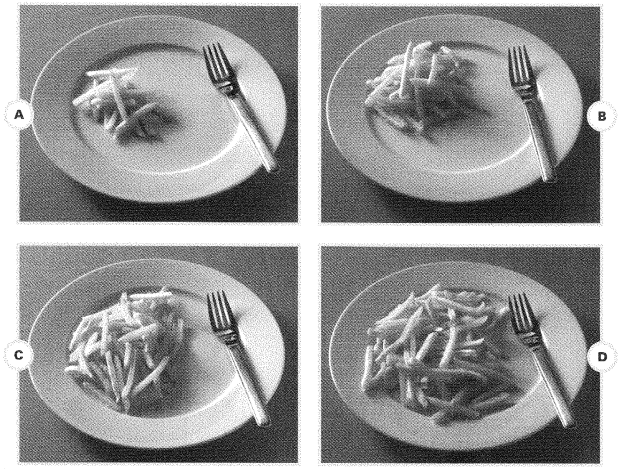
6. SPAGHETTI / PASTA (RIS)



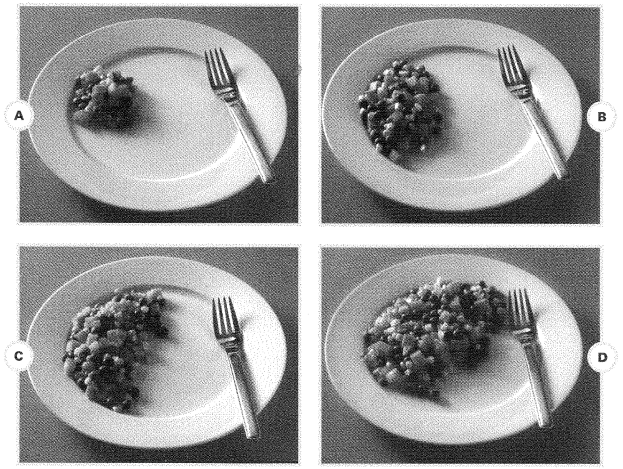
7. POTETMOS



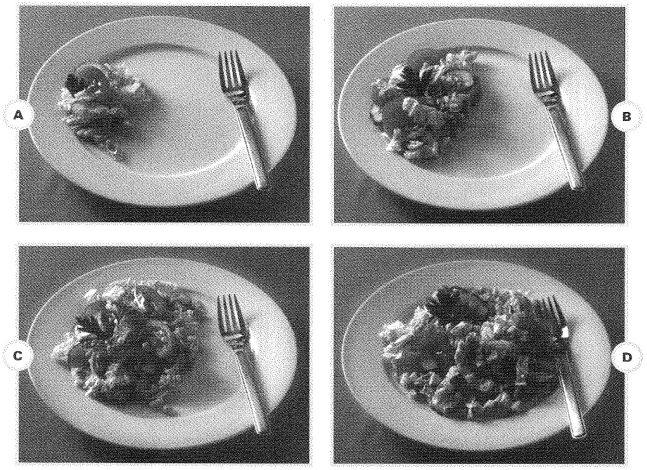
8. POMMES FRITES (STEKT POTET)



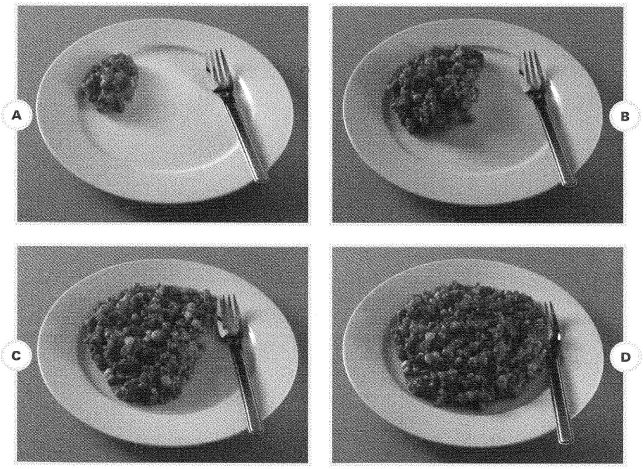
9. GRØNNSAKSBLANDING (RÅKOST)



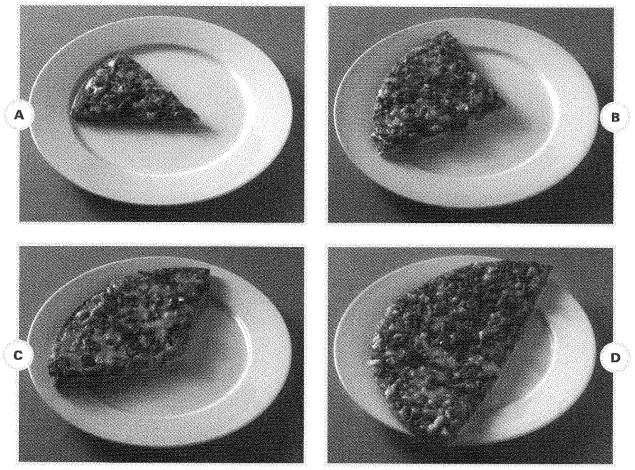
10. SALAT



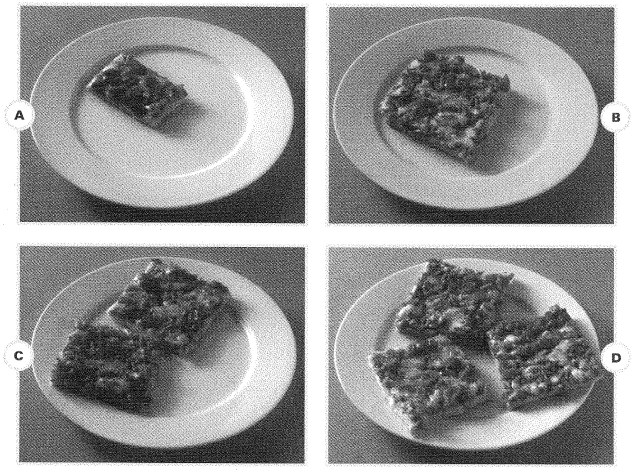
11. KJØTTSAUS (LAPSKAUS)



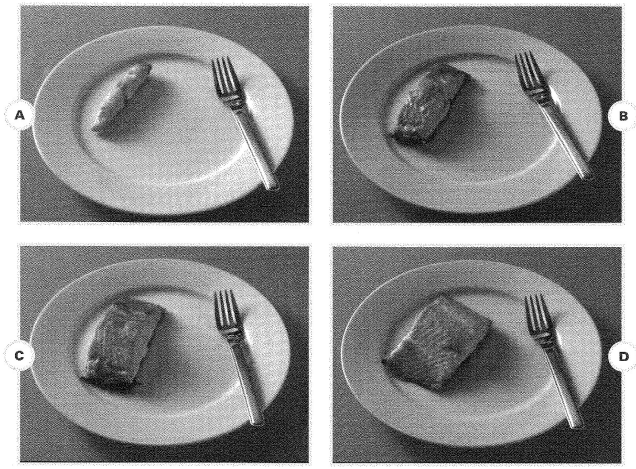
12. PIZZA, TREKANTSTYKKER



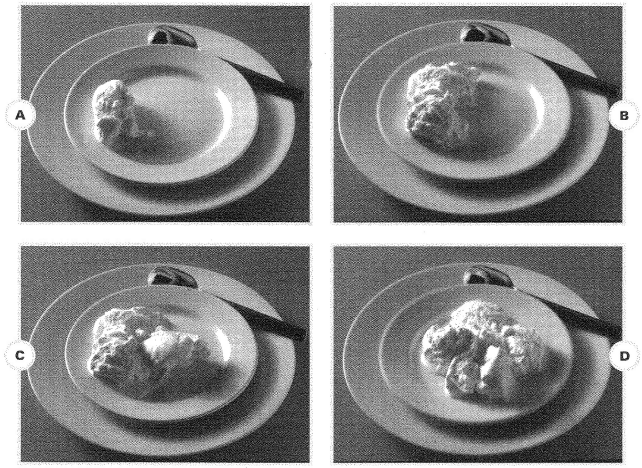
13. PIZZA, FIRKANTSTYKKER



14. FISK



15. IS (PUDDING)



Appendix F Binge eating scale (BES) questionnaire

BES

VEILEDNING:
På de følgende sider er det grupper av nummererte uttalelser. Les alle uttalelser i hver gruppe og sett et kryss ved den uttalelse i hver gruppe som best beskriver dine følelser i forhold til de problemer du har med å kontrollere dine spisevaner.

1

1.	☐	Jeg er ikke flau over vekten min eller størrelsen på kroppen min når jeg er sammen med andre.
2.	☐	Jeg tenker på hvordan andre ser meg, men det gjør meg normalt ikke skuffet over meg selv.
3.	☐	Jeg blir flau over mitt utseende og vekten min, og det gjør meg skuffet over meg selv.
4.	☐	Jeg er veldig flau over vekten min og jeg føler ofte dyp skam og avsky for meg selv. Jeg prøver å unngå kontakt med mennesker, fordi jeg er så flau.

2

1.	☐	Jeg har ingen vanskeligheter med å spise behersket og sakte.
2.	☐	Selv om jeg later til å "sluke" maten, føler jeg meg ikke overmett fordi jeg har spist for mye.
3.	☐	Noen ganger har jeg en tendens til å spise fort, og da føler jeg meg ubehagelig mett etterpå.
4.	☐	Jeg har for vane å sluke maten, uten å tygge den ordentlig. Når jeg gjør det, føler jeg meg som regel ubehagelig overmett, fordi jeg har spist for mye.

3

1.	☐	Jeg føler at jeg kan beherske min spisetrang, når jeg vil.
2.	☐	Jeg har en følelse av at jeg er dårligere til å beherske spisingen min enn gjennomsnittsmenneske.
3.	☐	Jeg føler meg helt hjelpeløs når det gjelder å beherske min spisetrang.
4.	☐	Fordi jeg føler meg så hjelpeløs når det gjelder å beherske spisingen min, er jeg blitt helt desperat for å prøve å få kontroll.

4

1.	☐	Jeg har ikke for vane å spise, når jeg kjeder meg.
2.	☐	Iblant spiser jeg, når jeg kjeder meg, men ofte klarer jeg å "finne på " noe for å få tankene bort fra mat.
3.	☐	Jeg har for vane å " kjedespise " men det hender at jeg kan foreta meg noe for å få tankene vekk fra å spise.
4.	☐	Jeg har en innbitt vane med å "kjedespise". Ingenting synes å hjelpe meg til å bli kvitt denne vanen.

5

1.	☐	Som regel er jeg fysisk sulten når jeg spiser noe.
2.	☐	Noen ganger spiser jeg noe helt impulsivt, selv om jeg egentlig ikke er sulten.
3.	☐	Jeg har den uvane å stadig spise mat som egentlig ikke smaker meg for å tilfredsstille en sultfølelse, enda jeg ikke trenger maten rent fysisk.
4.	☐	Selv om jeg ikke er fysisk sulten, får jeg en følelse av sult i munnen, som bare ser ut til å kunne tilfredsstilles hvis jeg spiser noe mat, f.eks. et stykke smørbrød som fyller munnen min. Noen ganger, når jeg spiser mat for å tilfredsstille munnsulten, spytter jeg ut maten for ikke å legge på meg.

6

1.	☐	Jeg føler ikke skyld eller selvforakt etter at jeg har spist for mye.
2.	☐	Når jeg har spist for mye føler jeg iblant skyld eller selvforakt.
3.	☐	Nesten hele tiden føler jeg skyld eller selvforakt når jeg har spist for mye.

7

1.	☐	Jeg mister ikke helt kontrollen med spisingen min under en slankekur, selv etter perioder hvor jeg har spist for mye.
2.	☐	Noen ganger når jeg spiser mye " forbudt " mens jeg er på slankekur, føler jeg at nå har jeg ødelagt alt og så spiser jeg enda mer.
3.	☐	Jeg sier ofte til meg selv, når jeg har spist for mye under en slankekur: " nå har jeg ødelagt det, så nå kan jeg like gjerne fortsette. " Når det hender, spiser jeg enda mer.
4.	☐	Jeg starter regelmessig på en streng slankekur, men jeg bryter kuren ved å begynne et "etegilde". Mitt liv ser ut til å være enten et "etegilde" eller en sultekur.

8

1.	☐	Jeg spiser sjelden så mye at jeg føler meg ubehagelig mett etterpå.
2.	☐	Noen ganger (kanskje en gang i måneden) spiser jeg så mye mat, at jeg ender opp med å føle meg ubehagelig overmett.
3.	☐	Jeg har regelmessige perioder hver måned, jeg konsumerer store mengder mat, enten til måltidene eller som mellommåltider.
4.	☐	Jeg spiser så mye mat at jeg stadig føler meg meget uvel etter å ha spist, og noen gang litt kvalm.

9

1.	☐	Mitt kalori-inntak hverken stiger eller synker meget på en regelmessig basis.
2.	☐	Noen ganger etter at jeg har spist for mye, prøver jeg å redusere kalori-inntaket mitt til nesten ingenting for å kompensere for de ekstra kaloriene, jeg har spist.
3.	☐	Jeg spiser for mye om kvelden. Det virker som om det er naturlig for meg å ikke være sulten om morgenen, men å spise for mye om kvelden.
4.	☐	I mitt voksne liv har jeg hatt ukelange perioder hvor jeg nesten har sultet meg. Disse har etterfulgt perioder, hvor jeg har "overspist". Jeg synes å leve et liv enten i matorgier eller i sult.

10

1.	☐	Jeg er normalt i stand til å slutte å spise, når jeg vil det. Jeg vet når "nok er nok".
2.	☐	En gang i mellom får jeg en tvingende trang til å spise som jeg ikke synes å beherske.
3.	☐	Jeg får ofte en voldsom trang til å spise som jeg ikke synes å kunne beherske, men andre ganger har jeg min spisetrang under kontroll.
4.	☐	Jeg føler meg ute av stand til å beherske trangen til å spise. Jeg er redd for ikke å kunne stanse å spise frivillig.

11

1.	☐	Jeg har ingen problemer med å slutte å spise, når jeg føler meg mett.
2.	☐	Jeg kan som regel slutte å spise, når jeg er mett, men iblant spiser jeg for mye, så jeg blir ubehagelig mett.
3.	☐	Jeg har vanskelig for å slutte å spise når jeg først har begynt. Vanligvis føler jeg meg ubehagelig overmett etter et måltid.
4.	☐	Fordi jeg ikke klarer å slutte å spise når jeg vil, må jeg noen ganger tvinge meg til å kaste opp for å lette på følelsen av å ha spist for mye.

12

1.	☐	Det synes som om jeg spiser akkurat like mye når jeg er sammen med andre (familie, i selskaper) som når jeg er alene.
2.	☐	Noen ganger, når jeg er sammen med andre, spiser jeg ikke så mye som jeg har lyst til, fordi jeg er flau over spisingen min.
3.	☐	Ofte spiser jeg bare litt, når det er andre tilstede, fordi jeg er så veldig flau over spisingen min.
4.	☐	Jeg skammer meg sånn over den overdrevne spisingen min at jeg velger å "ete" på tider, da jeg vet at ingen ser meg. Jeg føler meg som en "skap-eter".

13

1.	☐	Jeg spiser tre måltider om dagen og tar bare iblant et mellommåltid.
2.	☐	Jeg spiser tre måltider om dagen, men jeg spiser normalt også litt mellom måltidene.
3.	☐	Når jeg småspiser for mye vender jeg meg til å hoppe over ordentlige måltider.
4.	☐	Det er hele perioder, hvor jeg later til å spise uavbrutt, uten noen planlagte måltider.

14

1.	☐	Jeg tenker ikke mye på å prøve å beherske min uønskede spisetrang.
2.	☐	Jeg føler i det minste noe av tiden, at tankene kretser om å prøve å beherske min spisetrang.
3.	☐	Jeg føler at jeg ofte bruker mye tid på å tenke på hvor mye jeg spiste eller på å prøve å ikke spise mer.
4.	☐	Jeg synes at jeg mesteparten av mitt våkne liv er opptatt med tanke om å spise eller ikke spise. Jeg føler det som om jeg stadig kjemper for ikke å spise.

15

1.	☐	Jeg tenker ikke særlig på mat.
2.	☐	Jeg har sterke anfall av trang til mat, men de er kortvarige.
3.	☐	Det er dager, hvor det virker som om jeg ikke kan tenke på annet enn mat.
4.	☐	Det meste av min tid synes å være opptatt med tanker på mat. Jeg føler at jeg lever for å spise.

16

1.	☐	Jeg vet normalt om jeg er fysisk sulten eller ikke. Jeg spiser en passende porsjon for å bli mett.
2.	☐	Det hender at jeg er usikker på om jeg er fysisk sulten eller ikke. Da er det vanskelig å vite hvor mye mat jeg skal spise for å bli mett.
3.	☐	Selv om jeg vet hvor mange kalorier jeg bør spise, har jeg ikke noen ide om hva som er "normal" mengde mat for meg.

Appendix G Three-factor eating questionnaire (TEFQ)

Avsnittene nedenfor handler om matvaner og sultfølelse. Les hver påstand eller spørsmål og angi hvilket svar som passer best til deg.
Sett ett kryss i avkrysningsboksen til venstre for det svaret som passer best.

1. **Jeg tar med hensikt små porsjoner for å holde kroppsvekten nede.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

2. **Når jeg føler meg urolig, oppdager jeg ofte at jeg spiser.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

3. **Av og til når jeg begynner å spise, er det akkurat som om jeg ikke klarer å slutte.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

4. **Når jeg føler meg nedstemt, spiser jeg ofte for mye.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

5. **Jeg unngår visse typer mat fordi de er fetende for meg.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

6. **Når jeg er sammen med andre som spiser, får jeg selv ofte lyst på mat og begynner å spise.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

7. **Når jeg er anspent eller "oppgiret", føler jeg ofte trang til å spise.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

8. **Jeg får ofte så lyst på mat at magen føles som et stort hull som ikke kan fylles.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

9. **Jeg har alltid lyst på mat, så det er vanskelig for meg å slutte å spise før jeg har spist opp alt på tallerkenen.**
   - ☐ *Stemmer helt*
   - ☐ *Stemmer ganske bra*
   - ☐ *Stemmer ikke særlig bra*
   - ☐ *Stemmer ikke i det hele tatt*

10. **Når jeg føler meg ensom, trøster jeg meg selv med å spise.**
    - ☐ *Stemmer helt*
    - ☐ *Stemmer ganske bra*
    - ☐ *Stemmer ikke særlig bra*
    - ☐ *Stemmer ikke i det hele tatt*

11. **Jeg holder bevisst igjen ved måltidene for å ikke gå opp i vekt.**
    - ☐ *Stemmer helt*
    - ☐ *Stemmer ganske bra*
    - ☐ *Stemmer ikke særlig bra*
    - ☐ *Stemmer ikke i det hele tatt*

12. **Når jeg kjenner lukten av en biff som stekes eller ser en saftig kjøttbit, er det veldig vanskelig å la være å spise selv om jeg akkurat har avsluttet måltidet.**
    - ☐ *Stemmer helt*
    - ☐ *Stemmer ganske bra*
    - ☐ *Stemmer ikke særlig bra*
    - ☐ *Stemmer ikke i det hele tatt*

Avsnittene nedenfor handler om matvaner og sultfølelse. Les hver påstand eller spørsmål og angi hvilket svar som passer best til deg.
Sett ett kryss i avkrysningsboksen til venstre for det svaret som passer best.

13. Jeg har alltid lyst på noe å spise, så jeg kan spise når som helst.

- ☐ *Stemmer helt*
- ☐ *Stemmer ganske bra*
- ☐ *Stemmer ikke særlig bra*
- ☐ *Stemmer ikke i det hele tatt*

14. Hvis jeg kjenner meg ille til mote, forsøker jeg å dempe ubehaget med å spise.

- ☐ *Stemmer helt*
- ☐ *Stemmer ganske bra*
- ☐ *Stemmer ikke særlig bra*
- ☐ *Stemmer ikke i det hele tatt*

15. Når jeg ser noe som ser veldig godt ut, får jeg ofte så lyst på det at jeg må det spise med en gang.

- ☐ *Stemmer helt*
- ☐ *Stemmer ganske bra*
- ☐ *Stemmer ikke særlig bra*
- ☐ *Stemmer ikke i det hele tatt*

16. Når jeg føler meg dyster til sinns eller lei meg, vil jeg ha noe å spise.

- ☐ *Stemmer helt*
- ☐ *Stemmer ganske bra*
- ☐ *Stemmer ikke særlig bra*
- ☐ *Stemmer ikke i det hele tatt*

17. Hvor ofte unngår du å ha fristende mat tilgjengelig?

- ☐ *Nesten aldri*
- ☐ *Sjelden*
- ☐ *Ofte*
- ☐ *Nesten alltid*

18. Hvor sannsynlig er det at du bevisst spiser mindre enn det du vil ha?

- ☐ *Usannsynlig*
- ☐ *Ikke særlig sannsynlig*
- ☐ *Ganske sannsynlig*
- ☐ *Veldig sannsynlig*

19. Fortsetter du å spise selv om du ikke er sulten lenger?

- ☐ *Aldri*
- ☐ *Sjelden*
- ☐ *Iblant*
- ☐ *Minst en gang i uken*

20. Hvor ofte har du lyst på mat?

- ☐ *Bare til måltidene*
- ☐ *Iblant mellom måltidene*
- ☐ *Ofte mellom måltidene*
- ☐ *Nesten alltid*

21. På en skala fra 1 til 8, der 1 står for ingen begrensning (spiser hva jeg vil, når jeg vil) og 8 står for streng begrensning (begrenser alltid matinntaket, gir aldri etter), hvor på skalaen befinner du deg?
Sett en ring rundt det tallet som passer best for deg.

1	2	3	4	5	6	7	8
Spiser hva jeg vil, når jeg vil							*Begrenser alltid matinntaket, gir aldri etter*