Dietary intake and vitamin status in severely obese Norwegian patients seeking weight loss treatment

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PREFACE

Every single cell in the human body is built by nutrients. Nutrients are also the sole source of the energy needed to ensure life and movement. All the nutrients we need, both - micro- and macronutrients, are present in the food we consume. It is therefore logical that malnutrition will affect health in one way or another. The importance of an understanding of the relationship between food and health is by no means new. The famous ancient Greek physician Hippocrates (460-377 BC) argued that disease was a result of environmental factors such as *diet and living habits*, rather than punishment from the gods as was a common belief at the time. Today, the efficient marketing and overwhelming distribution and availability of energy dense food, combined with a built environment which does not encourage physical activity, has resulted in an obesogenic environment. At present, obesity (body mass index (BMI) ≥30 kg/m^2) affects more than 500 million people globally and has thereby become one of the major medical concerns of our century.

At the turn of the millennium, and probably for the first time in history, the number of overweight people equalled the number of undernourished worldwide. Usually malnutrition has been associated with hunger and underfeeding. However, malnutrition is not only caused by energy deficiency, but by poor dietary quality. Diets containing excess saturated fat, added sugar and red meat, or lacking healthy foods and nutrients such as fruit and vegetables, whole grains and fibre may cause severe morbidity. Even though the causation is complex, obesity is a result of excess of energy intake compared to energy expenditure over a long period of time. One would think that excess energy would ensure enough essential nutrients, but this is not always the case. Obesity caused by the combination of excess energy and poor dietary quality may be considered a relatively new form of malnutrition.

One of the best known examples of malnutrition in obesity is vitamin D deficiency. Vitamin D deficiency is associated with a variety of the same diseases also known to be prevalent among obese subjects; coronary heart disease (CHD), type 2-diabetes and different cancer forms. In addition, obesity negatively affects the social life and psychological well-being of obese subjects and is associated with impaired quality of life. Both severe obesity and poor quality diet represent significant health risks, and the combination of the two risk factors is especially unfavourable.

As the burden of obesity includes several diseases, which in themselves impose substantial medical costs and productivity losses, obesity treatment has been prioritised by several

governments and health authorities in high, middle, and low-income countries. Even though lifestyle intervention (diet and physical activity) is fundamental to the treatment of severe obesity, bariatric surgery has become widely used during the last few decades and has proven to be the most efficient method in terms of both weight reduction and sustained weight loss. Although total weight reduction is greater after bariatric surgery, due mainly to a more pronounced reduction in energy intake, little is known about how this treatment method affects the intake of nutrients, subsequent food group intake and therewith dietary quality.

The aims of this thesis were to assess and compare changes in intake of specified food groups, energy yielding nutrients and vitamin concentrations in severely obese individuals undergoing either gastric bypass surgery or intensive lifestyle intervention during a 1-year non-randomised clinical intervention trial. Additionally the prevalence of vitamin D deficiency in a large cohort of morbidly obese Norwegian patients, as well as seasonal and gender based differences were explored.

As such, the thesis hopes to expand the current understanding of how the most recognized treatment methods; lifestyle intervention and gastric bypass surgery; affect the intake of nutrients and certain food groups. It is also hoped that the results presented here contribute to highlighting the importance of dietary counselling in the treatment of morbid obesity in clinical practice.

ACKNOWLEDGEMENTS

This thesis is the result of studies carried out at the Morbid Obesity Centre, Vestfold Hospital Trust, Tønsberg, in the period 2005-2010. This work was supported by an unrestricted educational grant from the Norwegian Resource Centre for Women's Health, Oslo University Hospital Rikshospitalet, which funded my position as a PhD-student.

As a PhD-candidate I have learned that research is a puzzle with infinite pieces, and that if you are lucky, you may contribute to the finding of one of these tiny pieces in your particular discipline of interest. Mine is clinical nutrition. More than 25 year ago, as a student at the Sahlgrenska University Hospital, Gothenburg (Sweden), I witnessed a woman undergo a vertical-banded gastroplasty operation. This was indeed an open operation, many years before laparoscopic techniques were standard procedure. I was responsible for pre- and post-operation follow-up of this woman, which included my giving her dietary advice during her hospital stay. I met her a few months later, many kilograms lighter, but with substantial gastrointestinal discomfort and hair-loss. As a young and inexperienced student this made an indelible impression. I was convinced that bariatric surgery was a “dead end” in the treatment of severe obesity and that non-surgical interventions were far better alternatives. Little did I know back then about the forthcoming prevalence of morbid obesity, about new treatment options or, for that matter, that this was going to be my field of research. Now, many years later, I can look back at a challenging and interesting period of my professional life where I have been fortunate to be surrounded by an inspiring and skilled team of co-workers at the Morbid Obesity Centre. Their contribution has made this work possible.

First of all, my sincere gratitude goes to my main supervisor, Professor Jøran Hjelmesæth. With his extensive medical and scientific knowledge he has tirelessly guided, supported and encouraged me throughout this work.

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The contribution of both former and current colleagues at the Morbid Obesity Centre has been essential to the fruition of this work. My sincere thanks go to: Dag Hofsø and Rune Sandbu as invaluable research fellows and co-authors, Linda Mathisen and Astrid Hillestad for organising patient logistics with impressive accuracy, Berit Mossing Bjørkås for help with

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To all my good friends, but first of all: Gry with whom I have shared all academic and real-life challenges in our special “think tank” since high school, and Kari who has patiently listened to my thoughts during countless walks at Nøtterøy and Norwegian mountain hikes: Thank you!

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And finally, my everlasting gratitude goes to my daughter Ingrid and my son Jon. Thank you for lighting up my life by being just the way you are!

Line Kristin Johnson, February 2013

ABBREVIATIONS

ALAT	Alaninaminotransferase
BEE	Basal energy expenditure
BMI	Body mass index
BMR	Basal metabolic rate
CCK	Cholecystokinin
CHD	Coronary heart disease
CHO	Carbohydrates
CRP	C-reactive protein
CT	Computed tomography
CVD	Cardiovascular disease
DEXA	Dual-energy X-ray absorptiometry
DIT	Diet induced thermogenesis
DLW	Doubly labelled water
E	Energy
EE	Energy expenditure
EI	Energy intake
FBDG	Food based dietary guidelines
FFQ	Food frequency questionnaire
GLP-1	Glucagon-like peptide-1
HPLC	High pressure liquid chromatography
HUNT	Helseundersøkelsen i Nord-Trøndelag
LDL	Low density lipoprotein
LED	Low-energy diet
MC4R	Melanocortin-4 receptor
MET	Metabolic equivalent
MOBIL	Morbid Obesity treatment, Bariatric surgery versus Intensive Lifestyle intervention
MRI	Magnetic resonance imaging
MUFA	Monounsaturated fatty acids
NAFLD	Non-alcoholic fatty liver disease
NHANES	National Health and Nutrition Examination Survey
NEAT	Non-exercise activity thermogenesis
NNR	Nordic Nutrition Recommendations
NWCR	National Weight Control Registry
OXM	Oxyntomodulin
PAEE	Physical activity energy expenditure

PAL	Physical activity level
PCOS	Polycystic ovary syndrome
PP	Pancreatic polypeptide
PTH	Parathyroid hormone
PUFA	Polyunsaturated fatty acids
PYY	Peptide YY
RDI	Recommended daily intake
REE	Resting energy expenditure
RIA	Radioimmunoassay
RMR	Resting metabolic rate
RYGB	Roux-en-Y gastric bypass
SCFA	Short chain fatty acids
SFA	Saturated fatty acids
SOS	Swedish Obese Subjects
TEE	Total energy expenditure
VLCD	Very-low-calorie diet
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio
$1,25(OH)_2D$	1α, 25-dihydroxycholecalsiferol
25(OH)D	25-hydroxycholecalsiferol

LIST OF PAPERS

I. Johnson LK, Andersen LF, Hofsø D, Aasheim ET, Holven KB, Sandbu R, Røislien J, Hjelmesæth J. Dietary changes in obese patients undergoing gastric bypass or lifestyle intervention: a clinical trial. Br J Nutr. 2012 Oct 30:1-8 [Epub ahead of print]

II. Aasheim ET, Johnson LK, Hofsø D, Bøhmer T, Hjelmesæth J. Vitamin status after gastric bypass and lifestyle intervention: a comparative prospective study. Surg Obes Relat Dis. 2012 Mar-Apr; 8(2):169-75.

III. Johnson LK, Hofsø D, Aasheim ET, Tanbo T, Holven KB, Andersen LF, Røislien J, Hjelmesæth J. Impact of gender on vitamin D deficiency in morbidly obese patients: a cross-sectional study. Eur J Clin Nutr. 2012 Jan; 66(1):83-90.

1 INTRODUCTION

1.1 Definition of obesity

The World Health Organization (WHO) defines overweight and obesity as abnormal or excessive fat accumulation that presents a risk to health (1). Total body fat includes essential body fat necessary for maintaining life, hormone production and reproductive function and storage fat accumulation ensuring protection of internal organs, isolation and energy reserve. Although there is no consensus as to the percentage of body fat needed to define obesity or excess percentage of body fat (2), 25% and 35% of body fat have been suggested as cut off levels for men and women, respectively (3). The percentage of body fat can be determined by a number of methods; the *air displacement plethysmography* method has been shown to be accurate and strongly correlate with the "gold standard" body fat measurement *hydrodensiometry* (underwater weighing) (4). *Dual-energy X-ray absorptiometry* (DEXA) is also considered a valid method for measuring total fat mass and fat distribution (5). However, this method exposes patients to radiation and the equipment is not always suitable (not spacious enough) for usage with severely obese individuals. Although *bioelectric impedance analysis* provides 2-6% lower values for fat mass than DEXA (6), the method is widely used given that it is inexpensive and easy to administer. Furthermore, body fat distribution can be determined by imaging techniques such as *computed tomography (CT)* and *magnetic resonance imaging (MRI)* (7;8). Accurate *anthropometric measurements* of height and weight are, however, the most common measurements used to determine the degree of obesity. Obesity defined as excess bodyweight is measured by body mass index [BMI=weight in kg/(height in m)^2] and classified as shown in Table 1 (9). There is a strong correlation between BMI and fat mass, and cutoffs of percentage of body fat that correspond to BMI cutoffs have recently been suggested (10). The BMI classification of obesity does not, however, take body fat distribution into consideration. The accumulation of intra-abdominal fat increases the risk of developing metabolic obesity-related co-morbidities (coronary heart disease and diabetes type 2) (11;12). Waist circumference (WC) is an easily performed measurement which has been shown to correlate strongly with the degree of intra-abdominal fat accumulation (5). Independent of BMI, WC predicts the prevalence of coronary heart disease in both men and women (13;14). WC is considered an even more reliable measure than waist-to-hip ratio (WHR) (5) for determining the degree of central fat mass. As fat-distribution differs between men, women, and population-groups, cut-off levels for WC are sex- and ethnicity-specific (12). WC cut off-levels for indicating an increased risk of developing metabolic obesity-related co-morbidity are currently being debated within the field. A WC threshold for abdominal obesity in Caucasian women/men of ≥80 cm/ ≥94 cm

(moderately increased risk of type 2 diabetes and cardiovascular disease (CVD) or ≥88 cm / ≥102 cm (highly increased risk of type 2 diabetes and CVD) are both being used today (12).

Table 1. Classification of obesity according to the WHO's definition (9).

Classification	BMI (kg/m^2)	Risk of morbidity
Underweight	<18,5	Low
Normal weight	18.5-24.9	Average
Overweight	≥ 25	
Pre-obese	25.0-29.9	Increased
Obese, class I	30.0-34.9	Moderate
Obese, class II[1]	35.0-39.9	Severe
Obese, class III[2]	≥ 40	Very severe

[1]Morbid obesity when combined with at least one obesity-related co-morbidity

[2]Morbid obesity

1.2 Body weight regulation and energy balance

Obesity develops as a result of the energy intake provided by food exceeding the energy expended to maintain metabolic, muscular and digestive activities (15). Although both daily energy intake and expenditure vary widely for most humans, body weight remains rather stable. Evidence indicates that both over- and underfeeding produce compensatory changes in energy expenditure in humans (16;17). However, human biology provides more effective mechanisms for protecting against underfeeding than overfeeding; humans are thus afforded better protection from weight loss than weight gain (15). Research in the last few decades has improved our understanding of the complex biological regulation of energy balance, and moreover how behavioural and environmental factors affect body weight regulation. This understanding is crucial if we are to develop strategies to halt the current obesity epidemic and treat those already affected.

1.2.1 The energy homeostasis

Complex hormonal and neural interplays regulate the energy homeostasis of humans, with the brain as the key regulator of appetite. Energy homeostasis is controlled by peripheral signals from adipose tissue, endocrine glands and enteroendocrine cells (18). Peripheral signals from the gastrointestinal tract include peptide YY (PYY), oxyntomodulin (OXM), ghrelin, pancreatic polypeptide (PP), glucagon-like peptide 1 (GLP-1) and cholecystokinin (CCK), whereas adiponectin and leptin are hormones produced in adipose tissue and insulin and PP in the pancreas. Hormones secreted from these tissues converge at the vagus

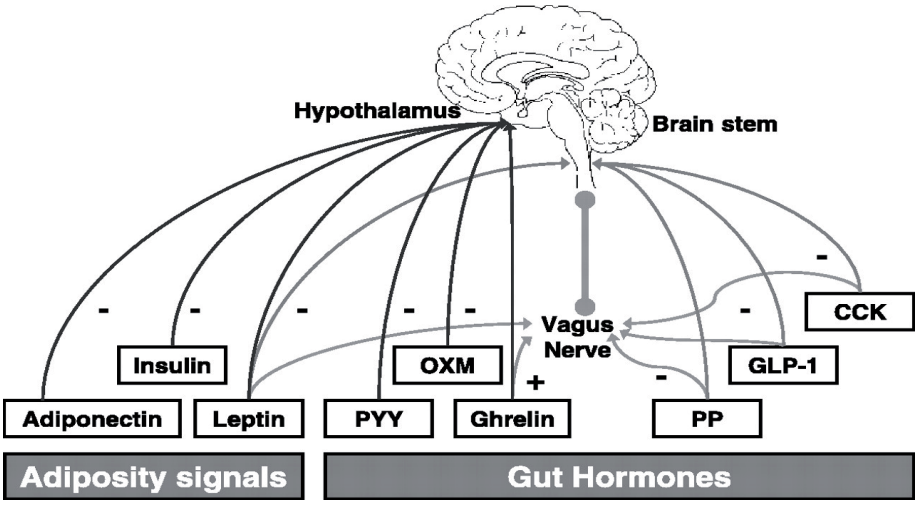
nerve, the brainstem and the hypothalamus to form complex interactions of neurotransmitters and central appetite-regulating peptides (18;19). The hypothalamus arcuate nucleus contains opposing sets of neuronal circuitry, both appetite-stimulating (+) and appetite-inhibiting (-) (Figure 1) (19;20). Two of them are the orexigenic neuropeptide Y/agouti-related peptide neurons and anorexigenic pro-opiomelanocortin/cocaine- and amphetamine-regulated transcript containing neurons (21).

Moreover, the homeostatic control of food intake is strongly influenced by hedonism and the impact of taste and appearance, emotions, environment and social cues. These non-homeostatic factors are processed in the cortico-limbic structures of the brain and seem to overpower the hypothalamus into an ingestive mode even in the presence of satiety (22). Although palatability and pleasantness are recognised as powerful determinants of food intake, the understanding of how the predicted reward value of pleasurable taste guides ingestive behaviour is currently inadequate (22).

Obesogenic environments are characterised by an abundance of palatable and energy dense food (sugar- and fat-rich) easily available with low physical effort and cost. It has become evident that in competition with this milieu, the gut satiety signals are unable to limit excess energy intake (21). In fact, increasing evidence indicates that the gastrointestinal hormone secretion can adapt to a chronic increase in dietary fat, resulting in an attenuation of the natural suppression of appetite induced by fat-ingestion (23).

Although the complex regulation of energy homeostasis is not the main theme of this thesis, it is important that one is aware of the major challenges associated with obesity treatment, in that biological and behavioural factors interact to oppose energy deficits.

Figure 1. Hormonal regulation of food intake (19). *(Permission for use of the figure is not required).*



1.2.2 Components of energy balance

The first law of thermodynamics states that the energy (E) of an isolated system is constant. This means that energy cannot be created from nothing nor can it disappear; it can only be transformed to other forms. Human physiology also follows this law. Eating and drinking provide all the energy needed for energy expenditure (EE) in humans.

Total daily energy expenditure (TEE) can be divided into three main components and includes resting energy expenditure (REE) (synonymous with resting metabolic rate (RMR)), thermogenesis induced by food intake (diet-induced thermogenesis (DIT)) and the energy expenditure of physical activity (PAEE) (24). Basal energy expenditure (BEE) is synonymous with basal metabolic rate (BMR), and is defined as the energy expended by an individual lying at complete rest, about 12 hours after their previous meal (24;25). REE is measured in less rigorous conditions than BEE; in subjects at complete rest and in a post-absorptive state. REE is considered to be 5-10% higher than BEE. REE and BEE are, however, very strongly inter-correlated and are often used interchangeably (24).

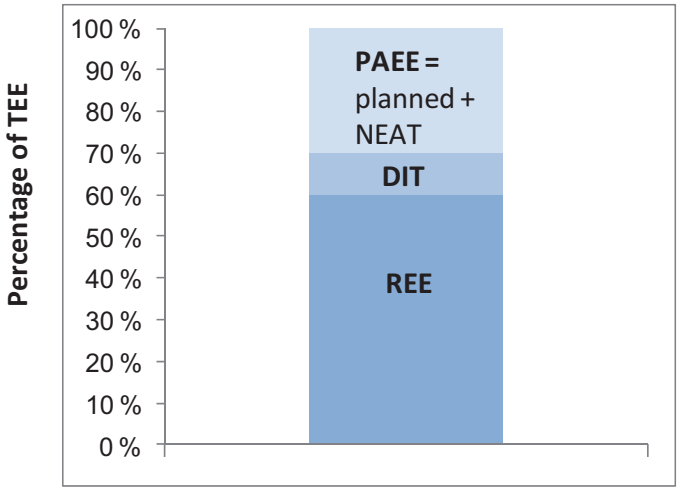
REE accounts for 50-70% of TEE. For persons in energy balance, DIT is assumed to be approximately 10% of TEE, whereas physical activity energy expenditure is estimated to be 20-40% of TEE, and even higher for athletes (Figure 2) (26). TEE is strongly related to body

mass, and particularly fat free body mass (the weight of metabolically active tissue such as muscles, internal organs and bone), which explains approximately 80 % of the variance (27).

Physical activity consists of a series of movements performed by the skeletal musculature, which in turn leads to an increase in energy expenditure. Exercise itself can be defined as planned, structured and repetitive physical activity which aims to either maintain or improve one's physical fitness or health. All other physical activity, whether performed at work or during leisure time, can be defined as non-exercise activity or everyday activity (28). Physical activity can thus be divided into two main subcategories; planned exercise and non-exercise activity. Non-exercise activity thermogenesis (NEAT) is the energy expended for all activities except sleeping, eating or planned exercise. NEAT includes energy expended on daily activities such as sitting, standing, walking, talking, gardening and all non-volitional muscle activities such as fidgeting, muscle tone and maintenance of posture (26). This non-exercise activity has been suggested to be related to weight control given that obese individuals spend on average 2 hours more per day seated than their lean counterparts, who rather spend this time standing or ambulating (29). This difference in NEAT-behaviour accounts for the expenditure of approximately 350 kcal /day (29). Metabolic equivalent of task (MET) is the unit used to estimate the metabolic cost (i.e. oxygen consumption) of all physical activity. The MET depends on the intensity of the activity performed. One MET equals the resting metabolic rate of ≈3.5 ml O_2 /kg/minute, or 1 kcal/kg/hour. MET values of different activities range from 1 MET at rest to 23 (running very fast at 23 km/hour). Light physical activity corresponds to an energy expenditure <3 METs, while moderate and vigorous physical activity correspond to an energy expenditure of 3-6 and >6 METs respectively. To calculate physical activity level (PAL), the sum of MET multiplied by time (hours) is divided by 24. Daily energy expenditure may be calculated by multiplying PAL by REE (24).

Energy expenditure can be measured using *indirect calorimetry* (measuring oxygen consumption and/or carbon dioxide production and converted to EE using appropriate formulae), *direct calorimetry* (measuring the rate of heat loss from a subject) or by a number of *non-calorimetric techniques* (predicting EE by extrapolating from physiological measurements, e.g. doubly labelled water (DLW)) (25).

Figure 2. Energy expenditure distribution.
TEE (100%) = REE (50-70%) + DIT (10%) + PAEE (20-40%)



Energy intake comes from three main categories of macronutrients: carbohydrates, protein and fat, where energy densities are 4 kcal/g or 17 kJ/g for carbohydrates and protein and 9 kcal/g or 38 kJ/g for fat. Digestibility and absorptive efficiency depends on many factors (fibre content, diet composition, preparation and gut flora). Such factors may cause variability in absorptive efficiency and therewith the net energy available for cell fuel (30).

1.2.3 Genes interacting with environments

Twin and family studies have shown that body weight is under genetic control. The role of genetics in the development of obesity has been extensively studied during the last few decades, with the results from twin studies estimating that 50-90% of the variance in BMI can be explained by genetic factors (31;32).

Only a few monogenic disorders which affect the central regulation of appetite and lead to early, severe obesity have been identified. Such conditions are rare, except for mutations in the melanocortin-4 receptor (MC4R), which affects about 5% of morbidly obese patients (BMI ≥40 kg/m) (33).

Inherited disorders of the central regulation of food intake result in an increased feeling of hunger, increased snacking, decreased satiety and thereby obesity (34). However, obesity develops as a result of the interaction between genes and environments. While genes

themselves have not changed in the last few decades, environmental changes have been extensive. Interestingly, recent studies show that genetic susceptibility to obesity can be accentuated through low physical activity and high fat diets (35;36).

We all have different heritable predispositions towards food intake and BMI. Genetic factors are, however, immutable, so to counter the effect of the obesogenic environment the controlling of energy balance (eating and exercise) is crucial. It is possible that progress in genetic research will contribute to the improvement of both the diagnosis of obesity and future efforts to tailor-make the treatment of obesity.

1.3 Trends in obesity prevalence

As of 2008 some 1.46 billion people worldwide were estimated to be overweight (BMI≥25 kg/m^2) and more than 500 million obese (BMI≥30 kg/m^2). The high prevalence of overweight and obesity has become one of the major medical concerns of the century given that this condition is associated with increased morbidity and mortality (37).

Reports from the latest National Health and Nutrition Examination Survey (NHANES) show that the prevalence of obesity among US adults (≥20 years) underwent a constant increase in the 1970s, rising from 15% to 35.5% among men and 35.8% among women in the period 2009-2010 (38). Adjusted for self-reported biases, 15.5 million adult Americans, some 6.6% of the population, were morbidly obese (BMI≥40 kg/m^2) in 2010 (39). The prevalence of morbid obesity was higher in women (8.2%) than in men (4.4%) (38). Globally, about 70% of morbidly obese subjects are women (40).

Compared with NHANES data for the period 2003-2008 there was no significant change in the prevalence of obesity in 2009-2010 (41). This trend of a slowing in the prevalence of obesity in the US has also been observed in other countries (42-45). However, this trend shift has primarily been noted among highly educated subjects living in urban environments, which could indicate that the widening of the socioeconomic gap may have a detrimental effect upon the prevalence of obesity (42;45).

In Norway the prevalence of obesity in the adult population doubled from 10% in 1984 to 20% in 2003 (46;47). Data from the HUNT 3 study (Helseundersøkelsen i Nord-Trøndelag) for the period 2006-2008 show an increase in the prevalence of obesity in both men and women (22% and 23% respectively in HUNT 3) compared to HUNT 1 (1984-1986) and HUNT 2 (1995-1997). This is shown in figure 3 and 4 (48). Especially worrying is the marked

increase of obesity among young men and women of childbearing age (48). Women account for about 70% of the morbidly obese population in Norway (49).

Figure 3. The prevalence (%) of obesity (BMI≥30) in HUNT 1, 2 and 3 in men.

(Figures 3 and 4 reproduced from (48) with permission from HUNT Research Centre).

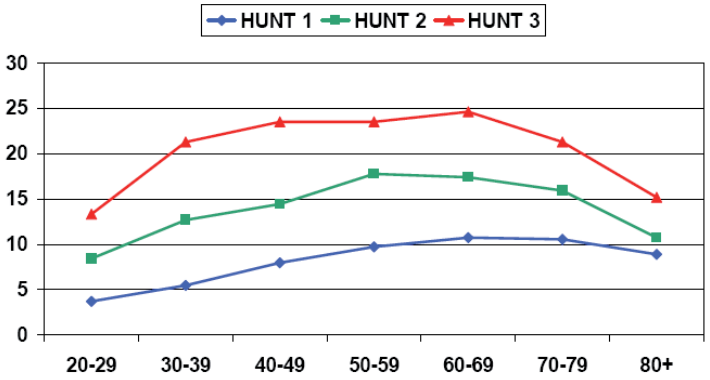


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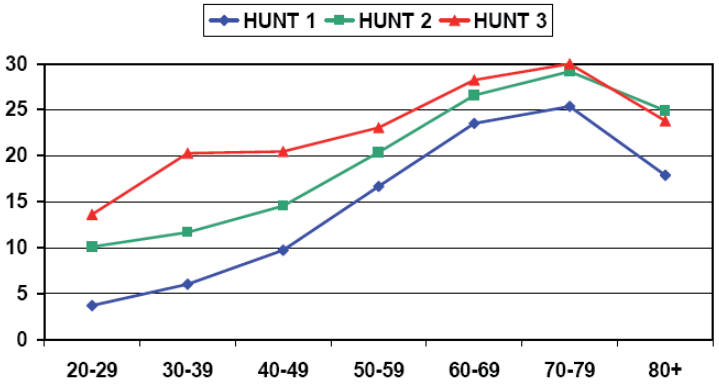
Figure 4. The prevalence (%) of obesity (BMI≥30) in HUNT 1, 2 and 3 in women.



1.4 The harmful effects of obesity

More than 2000 years ago Hippocrates observed that “sudden death is more common in those who are naturally fat than in the lean” [quoted in (50)]. Today there is an overwhelming scientific basis for stating that obesity has several serious health effects, including impaired quality of life (51), increased morbidity and premature mortality (52;53). Morbid obesity is

currently defined as a severe chronic disease, causing psychological, social and somatic disadvantages, a disease where the need for prolonged treatment is of great importance (54;55).

Raised BMI increases the risk of developing, coronary heart disease (CHD), hypertension, type 2-diabetes and many cancer forms (53;56-58). Furthermore, the incidence of non-fatal disorders such as osteoarthritis, chronic back pain, gallbladder disease and asthma is significantly increased in obese individuals (59).

The relationship between obesity and obstructive sleep apnoea is also well established (60). Moreover, several endocrine changes are associated with obesity, where irregularities in the reproductive system are among the most severe (50). Obese men are characterised by decreased testosterone levels, whereas obese women can develop functional hyperandrogenism (61). The majority of women with polycystic ovary syndrome (PCOS) are obese and characterised by abdominal fat distribution (62). The clinical manifestations of PCOS may be menstrual irregularities (oligo- or amenorrhoea), hirsutism and infertility (63).

In addition to the numerous severe health disadvantages obese individuals suffer from, the economic burden of obesity includes substantial medical costs and productive losses due to absenteeism, disability and premature deaths (64). In a recent systematic review of the direct costs of obesity, Withrow et al. concluded that on average obesity accounts for 0.7-2.8% of a country's total healthcare expenditure, and that obese individuals have approximately 30% higher medical costs than normal weight individuals (65). Advanced calculations of the total health-care costs attributable to obesity suggest that obesity will account for 16-18% of the total health-care expenditure of the US by 2030 (66). Strategies for the prevention and effective treatment of obesity are therefore of great importance, not only as a means to facilitating good health but also as a means to promoting the economical well-being of both the individual and society.

1.5 Diet and health

In view of the considerations above, the French lawyer and politician Jean Anthelme Brillat-Savarin (1755-1826) was remarkably prescient when in "The Physiology of Taste" (1825) he wrote: *"The destiny of nations depends on the manner in which they are fed".*

The associations between diet and health are very complex. Extensive international research during the last few decades has, however, provided the scientific evidence needed to

establish dietary recommendations and guidelines which promote public health and prevent chronic diseases (67;68).

Obese individuals who lose weight may reduce their risk of non-communicable diseases (CHD, hypertension, type 2-diabetes and several cancer forms) (53;58). However, health-promoting dietary changes will also enhance the preventative effect of weight reduction. The dietary treatment of obesity should thus have a double-pronged aim 1) to reduce weight through a negative energy balance and 2) prevent future disease.

Diet and disease

A diet rich in fruit, berries, vegetables, low fat dairy products, whole grains (equivalent to >25 g fiber/day), fish twice a week (preferably fatty fish) and limited total- and saturated fat content is associated with reduced risk of developing stroke and coronary heart disease (69;70). A generally consistent body of evidence documents that increased fruit and vegetable consumption is associated with a dose-response reduced risk of having a stroke. For example, in analyses of the Nurses' Health study and the Health Professionals' Follow-Up Study, persons in the highest quintile of fruit and vegetable intake (median 9.2 servings/day in men and 10.2 servings/day in women) (1 serving ≈ 100 g) had a relative risk (RR) of 0.69 (95% confidence interval [CI] 0.52-0.92) compared to those in the lowest quintile (median 2.6 servings/day in men and 2.9 servings/day in women). An increment of 1 serving per day of fruits or vegetables was associated with a 6% lower risk of ischemic stroke (RR 0.94; 95% CI, 0.90-0.99) (71). Intake of fruit, berries, vegetables and whole grain foods is associated with reduced risk of several cancer forms, while the intake of alcohol and both red and processed meat increases cancer risk and mortality (57;72;73). Data from the Health Professionals Follow-up Study (1986-2008) show a hazard ratio (HR) (95% CI) of total mortality for a 1-serving-per-day increase to be 1.13 (1.07-1.20) for unprocessed red meat and 1.20 (1.15-1.24) for processed red meat (73). The corresponding HRs (95% CIs) were 1.18 (1.13-1.23) and 1.21 (1.13-1.31) for CVD mortality and 1.10 (1.06-1.14) and 1.16 (1.09-1.23) for cancer mortality (73). Further, a diet with <30% of total energy from fat, <10 E% from saturated fat and rich in fibre and whole grain foods is associated with reduced risk of developing type 2- diabetes (74;75).

High fibre intake, especially from whole grains and vegetables, is associated with lower mortality from CVD and cancer, circulatory, digestive and non-CVD non-cancer inflammatory diseases (HR per 10 g/day increased fiber intake: 0.90; 95% CI: 0.88-0.92) (76). Total dietary fibre intake has been found to be inversely associated with inflammatory markers in blood (interleukin-6, C-reactive protein and tumor necrosis factor-α) (77;78). A possible mechanism that may explain this association is the production of short chain fatty acids (SCFA) from the

fermentation of dietary fiber in the colon (79). SCFA may affect gut microbiota and through this, although the mechanisms are not entirely clear, reduce systemic inflammation (79;80). Additionally, new findings suggest that gut microbiota might be involved in the development and maintenance of obesity (80).

Nutritional guidelines

In addition to ensuring the satisfactory development and functioning of the human body, the Nordic Nutrition Recommendations (NNR) for the intake of individual nutrients also aim to contribute to the risk-reduction of diet-associated diseases (Table 2) (24).

Table 2. Recommended daily intake (RDI)[1] of macro- and selected micronutrients (24).

Nutrient	RDI	Nutrient	RDI
Energy (MJ)	9.2-11.8	Vitamin A (RE)	700-900
Energy (kcal)	2200-2800	Vitamin D (µg)	7.5
Protein E%	10-20	Vitamin E (mg)	8-10
Total fat E%	<30	Thiamin (mg)	1.1-1.4
SFA E%	<10	Riboflavin (mg)	1.3-1.7
MUFA E%	10-15	Vitamin B_6 (mg)	1.2-1.6
PUFA E%	5-10	Folate (µg)	300
CHO, E%	50-60	Vitamin B_{12} (µg)	2
Sugar E%	<10	Vitamin C (mg)	75
Fibre (g)	≥25	Calcium (mg)	800
		Iron (mg)	15/9[2]-9

RE, retinol equivalents; E%, percentage of energy; SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; CHO, carbohydrates.

[1]RDI values from NNR shown for women and men aged 31-60 years.

[2]Pre-/postmenopausal women.

Food-based dietary guidelines (FBDG) have been characterised as a “translation” of energy and nutrient recommendations, and include advice on food choice, food quantities, eating frequencies and eating patterns. The Norwegian FBDG aims to promote public health and prevent chronic diseases and is based on convincing scientific evidence which and can be summarised in the following key points (67):

1. A largely plant-based diet rich in vegetables, fruit, berries, whole grains and fish, and with limited amounts of red meat, salt, added sugar and energy-dense food is recommended.

2. Maintenance of the balance between energy intake and energy expenditure is recommended.
3. Eat at least 5 portions (á 100-150g) of vegetables, fruit and berries every day.
4. Eat at least 4 portions of whole grains (70-90 g whole grain) every day.
5. Eat fish equivalent to 2-3 dinner portions per week (in total 300-450 g).
6. Daily consumption of low fat dairy products is recommended.
7. Lean meat, low fat meat products and limited intake of red meat and processed meat are recommended (≤500g/week).
8. Plant oil, liquid margarine and soft margarine are recommended.
9. Drinking water is recommended.
10. Limit one's intake of added sugar.
11. Limit one's intake of salt (<6 g/day for women and <7 g/day for men).
12. In some population groups supplements may be needed to ensure sufficient nutrient intake.
13. Everyone should be physically active for at least 30 minutes daily.

These national recommendations are in line with international reports on the prevention of non-communicable diseases, including obesity (57;68).

1.6 Nutritional status in obese adults

1.6.1 Macronutrients

Obesity is often the result of a relatively small prolonged excess energy intake independent of macronutrient composition. However, recently it has been questioned whether macronutrient composition may affect weight changes (loss and gain) and weight maintenance. Recent reports demonstrate a positive association between fat intake and weight gain (81;82). Notably, increases in monounsaturated fat (MUFA) and polyunsaturated fatty acids (PUFA) were not associated with weight gain, but increases in intake of animal fat, saturated fat (SFA) and trans fatty acids were positively associated with weight change (82). Additionally, higher proportions of energy from protein and animal protein have been shown to be associated with higher risk of obesity (83). By contrast, Larsen et al. found that a modest increase in protein intake and a modest reduction in glycemic index improved weight loss maintenance (84). Data from both American and European cohorts show that a low-fibre, high-fat diet is associated with the greatest increase in risk of overweight and obesity compared to a high-fibre, low-fat diet (85;86). The most energy-dense macronutrient, fat, therefore seems to contribute towards the development of obesity.

Although obese individuals have excess stores of adipose tissue due to a positive energy balance, they may have nutritional deficiencies due to poor dietary intake and/or altered nutrient absorption, distribution or metabolism of micronutrients (87;88).

1.6.2 Micronutrients with special focus on vitamin D

Compared to normal weight individuals, low levels of various micronutrients among overweight and obese adults have been demonstrated in a large cross-sectional study of adult Americans (NHANES III) (89). The data from this study demonstrates lower levels of beta-carotene, vitamin E, vitamin C, selenium and folate among obese persons compared to normal weight persons. Vitamin E, vitamin C and beta-carotene have been shown to protect low density lipoprotein cholesterol (LDL-cholesterol) against oxidation and thereby might play a role in inhibiting atherosclerosis (90;91). It has been hypothesised that the low micronutrient levels may reflect an increase in systemic and adipose tissue-specific oxidative stress in obese persons (89).

In addition to insufficient levels of the aforementioned micronutrients, low levels of vitamin B-6, B-12, ferritin, hemoglobin, copper, zinc, magnesium, albumin and phosphate have been reported in morbidly obese persons (92-95).

Vitamin D

Vitamin D is essential for calcium metabolism and bone mineralisation, though recent studies have shown that vitamin D may also play a central role in preventing some illnesses, including autoimmune disorders, some cancer forms, coronary heart disease and diabetes type 1 and 2 (96-102). There are two main forms of vitamin D, vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalsiferol). Vitamin D_3 is the only form that is found naturally in human subjects. Exposure to sunlight is the main source of vitamin D, as vitamin D_3 is synthesised in the skin from the precursor 7-dehydroksycholesterol through exposure to UVB radiation (103). There are relatively few good dietary sources of vitamin D_3, but the best is oily fish, butter, margarine (fortified) and egg yolks (104). Cod liver oil and supplements account for a significant proportion of vitamin D intake in Norway (104). While vitamin D_2 is the pharmaceutical form of vitamin D used in the USA (101), vitamin D_3 is available as both a pharmaceutical and a supplement in Europe, Canada, Japan and India (103). Vitamin D_3, (derived from UVB radiation or diet) enters the circulation and is hydroxylated in the liver to form 25-hydroxycholecalciferol (25(OH)D), which is the major circulating metabolite and a widely used marker of vitamin D status in humans. Further, 25(OH)D is hydroxylated in the kidneys to 1α,25-dihydroxycholecalsiferol ($1,25(OH)_2D$) which is the biologically active form of vitamin D. The action of vitamin $1,25(OH)_2D$ is mediated through vitamin D receptor. Vitamin D receptor is present in most human tissues, including macrophages, smooth

muscle cells, pancreatic β-cells, epithelial cells and osteoblasts (105). The vitamin D receptor may underlie the diverse effects of vitamin D and provide a mechanistic basis for the link between vitamin D deficiency and a number of the disorders mentioned above (105).

Measures of vitamin D status

Although $1,25(OH)_2D$ is the biologically active form of vitamin D, it is not an ideal measure of vitamin D status. One reason for this is the rapid circulating half-life of $1,25(OH)_2D$ of 4-6 hours, another the fact that circulating levels of $1,25(OH)_2D$ are a thousand folds lower than 25(OH)D (106). Additionally, vitamin D deficiency causes reduced intestinal calcium absorption which in turn transiently lowers ionised calcium. This is recognised by calcium sensors in the parathyroid glands, which then increase the secretion of parathyroid hormone (PTH) (107). PTH regulates calcium metabolism by increasing calcium re-absorption in the kidneys, increasing calcium release from the skeleton and by increasing renal production of $1,25(OH)_2D$ (108). The increased PTH-levels in a vitamin D deficient patient will thus result in normal or elevated levels of $1,25(OH)_2D$ which make this metabolite unsuitable as a measure of vitamin D status.

The only vitamin D metabolite used to measure vitamin D status is 25(OH)D. Circulating 25(OH)D has a half-life of 2-3 weeks (106). Although the definition of vitamin D deficiency is widely debated, most agree that a concentration of 25(OH)D <50 nmol/l is an indication of vitamin D deficiency (101;103;109).

Obesity and vitamin D levels

It is well established that obesity is associated with low serum levels of 25(OH)D (110-114). The circulating 25(OH)D-levels are inversely correlated with diverse measures of obesity (BMI, fat mass and waist circumference) (115;116). This is probably due to both decreased bioavailability from cutaneous and dietary sources, sequestration of vitamin D in adipose tissue and low exposure to sunlight (88;117). Obese persons respond less effectively to vitamin D-supplementation and ultraviolet radiation than normal weight individuals (115;117). Secondary hyperparathyroidism, which may result in bone weakening and joint pain, has been reported in conjunction with vitamin D deficiency in obese subjects (95;118).

Although there is growing evidence that obesity causes vitamin D deficiency, other possible cause-effect relationships have been explored. Whether vitamin D deficiency contributes to obesity is also a current discussion (119).

1.7 Weight loss treatment

1.7.1 Non-surgical interventions

Expected long-term (≥1 year) weight reduction as a result of lifestyle intervention (calorie restricted diets, physical activity and behavioural counselling) in severely obese subjects is lower than that resulting from surgical treatment, 5-20% vs. 30% respectively (49;120;121). A significant, meaningful weight loss (i.e. ≥5%) can be achieved non-surgically in institutions, primary care settings and clinical centres (122;123). However, a weight loss of at least 10% is a desirable and achievable goal in non-surgical treatment of severe obesity (120). There have been calls for greater effort and research such as to improve weight loss maintenance strategies (120).

Non-surgical treatment options include dieting, physical activity, drugs and behavioural interventions. To assess which type of intervention contributes most to successful weight-loss followed by long term maintenance of achieved weight-loss is complex, but adherence to any program seems to be an essential component of success.

Dietary intervention

Reducing energy intake is one of the most widespread strategies for achieving weight loss. This can be done by reducing total intake of calories from one or more macronutrients (protein, carbohydrate and/or fat).

Low fat diets are widely used in order to help patients lose weight by reducing energy and fat intake and increasing intake of whole grain, fruit and vegetables. These diets are often in accordance with the nutritional recommendations made by authorities to prevent obesity and several diseases (24;68). Diets with *low glycaemic index* contain carbohydrates digested and absorbed more slowly and are therefore supposed to increase satiety. A systematic review comparing diets of low glycaemic index or low glycaemic load with conventional restricted energy low-fat diets has shown a small but significant better effect (weighted mean difference, -1.09 kg, CI-1.99 to -0.18 kg) of the former on weight loss after 6 months follow up after intervention (124). *Low carbohydrate diet* is a term used to describe diets with a wide range of carbohydrate content. A very low carbohydrate diet, of which the Atkins diet probably is the best known, provides <30 g carbohydrate per day. Debates about which diet gives best results in terms of weight loss and maintenance are ongoing. Several randomised controlled trials have compared weight-loss diets with different macronutrient composition (125-128). Although low-carbohydrate diets seem to give a greater short-term weight-loss than more traditional low-fat diets, the long-term results (≥2 years) are comparable (125;128).

Very-low-calorie diets (VLCD), providing < 800 kcal/day produce rapid weight loss and may be recommended for people with severe obesity. Importantly, several studies indicate that greater initial weight loss improves long-term weight maintenance (122;129;130). It has been suggested that weight reduction achieved by initial use of VLCD followed by a management programme including dietary counselling, as well as a low-fat energy restricted diet and a appropriate physical activity programme, may both improve sustained weight maintenance (130).

In a large-scale pan-European controlled dietary intervention study (the Diet Obesity and Genes study – DIOGenes) diets varying in protein and glycaemic index were assessed after an 8-week VLCD-initiated weight-loss period for their effects on long-term weight loss maintenance and cardiovascular risk factors (84;131). Mean participant weight loss after these 8 weeks was 11.0 kg. Thereafter participants were randomised to 1 of 5 ad libitum diets for 26 weeks. The diets were either high or low protein or high or low glycaemic index in 4 combinations or control. Although the differences in weight maintenance were small, 0.93 kg less (95% CI, 0.31-1.55) in the groups assigned to a high-protein diet compared to those assigned to a low-protein diet and 0.95 kg less (95% CI, 0.33-1.57) in the groups assigned to a high-glycaemic-index diet compared to those assigned to a low-glycaemic index diet, the authors concluded that a modest increase in protein content (from ≈ 17% of total energy intake to ≈ 22 %) and a modest reduction in the glycaemic index (from ≈ 61 to ≈ 56), resulted in better weight loss maintenance (84). This effect may be ascribed to the satiating effect of a higher protein and fibre content in the diet (132;133).

Elements of lifestyle intervention programs and drug treatment

Currently a wide range of lifestyle intervention programmes affecting health behaviours are available. Such programs generally combine restriction of calorie intake, increased physical activity and/or drugs. The behavioural approaches followed in such programmes usually include keeping records of food intake and physical activity, nutrition education, meal planning, controlling the stimuli which activate the desire to eat, individual social support and psycho-education in groups. Although the use of the drugs orlistat, sibutramine and rimonabandt has been shown to increase weight reduction in obese subjects (134), only orlistat is currently available in Europe after both sibutramine and rimonabandt were withdrawn from the market due to their adverse side-effects.

A systematic review and meta-analysis of weight-loss clinical trials with a minimum of one year follow-up showed a relatively moderate mean weight loss of 5 to 8.5 kg (5 to 9%) after the first 6 months as a result of different interventions involving energy-reduced diets and/or exercise, and/or weight-loss medications (sibutramine or orlistat) (135). A mean weight-loss

of 3 to 6 kg (3-6%) was maintained in studies extending to 2 years. Although some weight was regained, the authors concluded that weight loss can be maintained through weight-loss interventions combining energy-reduced diets and exercise, and that the addition of weight-loss medication enhances weight-loss maintenance somewhat (135).

It has been demonstrated that intensive behavioural intervention in specialised weight loss centres can be a safe and effective treatment option for severely obese individuals (136). In one study, 1531 patients with severe obesity (BMI≥40 kg/m^2) were treated in three clinics. Of these 1100 completed a 12-week "Core"-intervention class followed by "Ongoing"-classes until participants reached their weight goal and finally entered the "Maintenance Program" (or exited the program). The weight loss options in the "Core"- and "Ongoing"-classes included defined treatment components: weekly attendance, phone calls, record keeping, intake of either a VLCD (≈ 520 kcal/day) or a low-energy-diet (LED) (≈1000 kcal/day) and regular physical activity. The "Maintenance Program" included weekly attendance and phone calls, record keeping, restricted energy intake and physical activity. The average weight loss of female completers was 31 kg (24% of initial weight) and 43 kg for male completers (27% of initial weight) over 39 weeks. Follow-up weight loss after 72 weeks was on average 23 kg (59% maintained weight loss) (136).

In a recent review of the overall efficacy of lifestyle interventions (including diet, exercise and psychological interventions) there was little evidence to indicate that any one intervention is more effective than any other (137). However, there is evidence of an additive effect of a combination of diet, exercise and behavioural interventions in the treatment of obesity. Furthermore, there was no evidence that any dietary strategy is more effective than any other, making it essential to encourage individuals to adopt a diet they can accept in the long-term (137).

Weight loss maintenance

Losing weight may be difficult and maintaining weight loss even more complex. Successful weight loss maintenance has been defined as "individuals who have intentionally lost at least 10% of their body weight and kept it off at least one year" (138). It is of great importance to identify the strategies used by successful weight loss maintainers. The National Weight Control Registry (NWCR), a database of more than 4000 adult individuals who have lost ≥ 13.6 kg and maintained this at 1 year follow-up, provides unique information in this respect (139). The members in NWCR have used different strategies to achieve weight loss, but almost without exception they have combined dieting with physical activity. Early publications document the behaviours used by members to maintain their weight loss. Four strategies have been clearly identified: consuming a low-calorie (1381 kcal/d), low-fat diet (24% of total

energy intake), consuming breakfast daily, partaking in high levels of physical activity (≈1h/d of moderate-intensity activity such as brisk walking) and weighing oneself frequently (140;141). Consuming a diet with limited variation in all food groups may contribute to the low-energy diet characteristic for successful long-term weight loss (142).

Another strategy to maintain weight loss has more recently been reported by Wing et al. (143). They found that face-to face intervention in a self-regulation program for maintenance of weight loss (mean 19.3 kg of body weight lost in the previous 2 years) combined with daily self-weighing improved the maintenance of weight loss (weight gain <2.3 kg over 18 months) compared with receiving the programme over the Internet or by receiving quarterly newsletters (control group) (143). Participants in the two intervention groups in this study were asked to report their weight weekly through an automated telephone system (face-to-face group), or a web-based form (the Internet group). Those who reported a weight gain of less than 1.4 kg (from starting weight) were in the "green zone" and provided positive reinforcement, those gaining 1.4-2.2 kg were in the "yellow zone" and were instructed to use problem-solving skills to bring their weight back into the "green zone", whilst those gaining ≥2.3 kg were in the "red zone" and encouraged to restart active weight-loss efforts (low-calorie, low-fat diet and increased physical activity) (143).

Anderson et al. assessed long-term weight-maintenance in a group of patients (n=118) who initially achieved a weight-loss of ≥45 kg (≥100 pounds) by undergoing intensive behavioural intervention in specialised weight loss centres (136;144). At an average of 5 y of follow-up 68 patients had maintained a weight loss of 30 kg of initial body weight (49.3% of initial weight loss). This shows that intensive behavioural intervention can be an effective option in the treatment of severe obesity (144).

Behavioural interventions include dietary, exercise and behavioural approaches utilised to reduce and maintain weight loss. Behavioural techniques utilised to reduce reinforcement of unhealthy eating behaviours and reinforce healthy eating behaviours include cue avoidance, practicing eating restraint, resisting social pressure to eat and relapse prevention training. High-intensity (weekly) counselling (by phone, internet and/or in groups) allied with dietary changes and physical activity may improve weight loss and maintenance in severely obese subjects (136).

1.7.2 Bariatric surgery

According to national and international guidelines, bariatric surgery may be an appropriate alternative for morbidly obese individuals who have failed to lose weight or maintain long-term weight loss despite appropriate lifestyle interventions or other medical care (55;145).

Bariatric surgery may be offered to treatment seeking subjects with morbid obesity; BMI≥40 kg/m^2 or BMI 35-39.9 kg/m^2 with at least one obesity related co-morbidity, (e.g. type 2 diabetes, hypertension, obstructive sleep apnoea, cardio-respiratory disease, arthrosis, psychological problems). Contraindications to bariatric surgery include severe respiratory failure, heart or kidney failure, failure to comply with prolonged medical follow-up, non-stabilised psychotic disorders, severe depression or personality disorders, alcohol- and/or drug-abuse (145;146). In Europe, different bariatric surgical techniques are practiced, preferably in tandem with laparoscopic procedures. The Roux-en-Y gastric bypass (RYGB) (Figure 4), adjustable gastric banding, sleeve gastrectomy (Figure 4) and biliopancreatic diversion with duodenal switch are examples of current bariatric surgical techniques (145). Of these, adjustable gastric banding and sleeve gastrectomy operations are restrictive surgical procedures which limit food intake, whereas RYGB and biliopancreatic diversion with duodenal switch are surgical methods which combine the effects of limiting food intake and the nutrients absorbed (145).

Today, laparoscopic RYGB is the most common bariatric procedure both worldwide and in Norway (147;148). As much as 90% of surgical procedures in Norway today are the RYGB operation (Figure 4) (146). Although the RYGB is mainly a restrictive procedure and the weight-reducing effect is principally caused by reduced calorie-intake, the operation additionally causes moderate malabsorption and changes in the gut hormonal and neuronal responses which affect satiety, hunger, metabolism and insulin sensitivity (145;148). In the Nordic countries the standard RYGB procedure includes a small gastric pouch (20-30 ml), a biliopanceratic limb of approximately 75 cm, an alimentary limb of 150 cm and a common channel of 2 to 5 metres (148;149). If the patient has a BMI>50 kg/m^2, then a very long limb gastric bypass procedure with an alimentary limb >150 cm and a shorter common channel may be recommended (148).

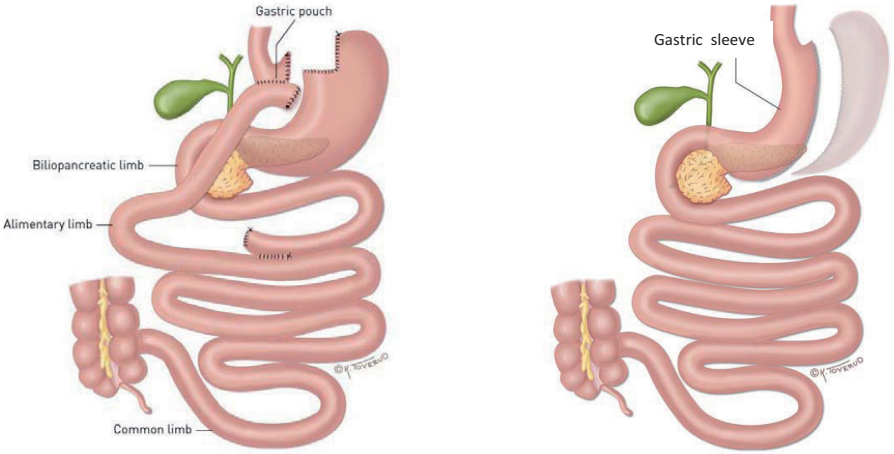


Figure 4. Roux-en-Y gastric bypass (left), gastric sleeve (right).

(Figure by K.Toverud) (146).

Surgical outcomes are often measured by improvement or resolution of co-morbidity and lost excess weight, where excess weight is defined as preoperative weight minus ideal weight (BMI=25 kg/m^2). Several studies confirm that in both the above respects, bariatric surgery achieves better results than dietary intervention, physical activity, behaviour modification and pharmacotherapy (150). In a systematic review including more than 22.000 patients, Buchwald et al. reported mean percentage excess weight loss [= (weight loss/excess weight) x 100) approximately 2 years after bariatric surgery to be 62% for RYGB, 70% for biliopancreatic diversion with duodenal switch and 48% for gastric banding (151). These are significantly greater weight losses compared to severely obese patients undergoing lifestyle intervention. In a recent report from the Look AHEAD trial, individuals participating in a lifestyle intervention program lost 9% of their initial body weight after 1 year (152), which is comparable to the findings in our group (49). In their meta-analysis of surgical treatment of obesity Maggard et al. found surgery to be more effective than non-surgical treatments for weight loss and improvement of co-morbidity in patients with BMI≥ 40 kg/m^2, however, they concluded that the efficacy of the two treatment options for less obese people need further investigation (153).

Several findings on morbidity and mortality have been reported in the non-randomised, prospective, controlled Swedish Obese Subjects (SOS) study. In this ongoing study, 2010 obese patients underwent bariatric surgery (13% gastric bypass, 19% banding and 68%

vertical banded gastroplasty) and 2037 matched controls received usual care in the Swedish primary health care system (121). The majority of patients in this study were operated upon with techniques which are rarely used in the Nordic countries today. The average weight loss at 10-year follow up was 16% in the surgical group while weight increased by an average of 1.5% during this time in the conventional group receiving usual care in the Swedish primary health care system (154). Although large weight loss is more often achieved by bariatric surgery than conventional treatment, there was great variation in weight reduction among surgical patients after 10 years. About 12% lost ≥30% of their baseline body weight, almost 25% lost 20-29.9%, 30% lost 10-19.9%, about 25% lost <10% and 9% gained weight. In the surgical subgroups there were significant differences in 10-year weight loss, with about 13% weight loss for banding, 17% for vertical banded gastroplasty and 25% for gastric bypass. In the "usual care" group 15% lost ≥10% and 54% gained weight during the 10-year follow-up period (154). After an average of 11 years follow-up, mortality in the surgical group significantly decreased compared to usual care (121).

After 10 years follow-up the recovery rates of type 2 diabetes, hypertriglyceridemia, low levels of HDL-cholesterol, (although not for hypercholesterolemia), hypertension and hyperuricemia were significantly higher in surgically treated patients than in conventionally treated ones (155). A recent SOS report showed bariatric surgery to be associated with reduced incidences of long-term cardiovascular events (median follow-up 15 years, range 0-20 years) compared with usual care (156).

Other weight related co-morbidities and conditions such as cancer, sleep apnoea, depression and sexual dysfunction in both men and women have been shown to improve after bariatric surgery (151;157-159). Additionally, when close supervision is conducted before, during and after pregnancy following bariatric surgery pregnancy outcome, maternal and fetal health improve (160).

Nutritional consequences of RYGB

The RYGB is considered mainly a restrictive procedure, but also has a malabsorptive component as the small bowel is reconfigured (Figure 4). In addition, the neuronal and gut hormonal changes will reinforce the weight loss process. These changes will individually and collectively affect the patients food choice, and thereby the intake and absorption of macro- and micronutrients.

During the first 12 months after the operation around 50% of patients experience gastrointestinal discomfort which gradually subsides (49;161). During the first months many patients experience vomiting or "spitting up stuck food" due to overeating or inadequate

chewing (162). This type of occasional vomiting is normally tolerable. If vomiting becomes frequent, low potassium, magnesium and/or vitamin B1 levels may occur, requiring replacement. And if vomiting occurs when consuming solid foods, particularly if this intolerance develops 6 months or more after surgery, it could be a symptom of stricture and stomal stenosis requiring treatment (162). Varying degrees of food aversion may be caused by the dumping syndrome, which is usually precipitated by ingestion of food with a high sugar and/or fat content (161). The multi-factorial mechanisms involved in the dumping syndrome are not fully understood, but symptoms typically occur 10-30 minutes postprandially and may be explained by accelerated gastric emptying of hyperosmolar content into the duodenum, which leads to fluid shifts from the intravascular compartment into the intestinal lumen. The clinical manifestations are often divided into gastrointestinal and vasomotor symptoms (163). The gastrointestinal symptoms include early satiety, nausea, cramps and acute diarrhoea, while sweating, palpitations, dizziness and a strong desire to lie down are typical examples of vasomotor symptoms. Most patients with dumping have a combination of gastrointestinal and vasomotor symptoms (163).

Dietary modifications will prevent most cases of dumping symptoms. These modifications include: dividing daily food intake into 6-8 small meals, restricting fluid intake during meals (avoiding liquids for at least half an hour after meals), reducing intake of simple sugars (e.g. sweets, cakes, sodas) and preference for complex carbohydrates (e.g. unsweetened cereals, fresh fruit and vegetables, potatoes and pasta). Milkshakes, sweetened yoghurt, ice cream and chocolate milk are usually poorly tolerated and should be avoided. The supine position for 30 minutes after meals may reduce postprandial hypotension by delaying gastric emptying and improving venous return (163).

Postprandial hypoglycaemia, also called “late dumping”, occurs 1-3 hours after a meal and is characterised by hypoglycaemic symptoms (shakiness, hunger, perspiration, concentration-difficulties and/or decreased consciousness) and/or symptoms similar to dumping syndrome. Severe hypoglycaemia is considered a rare consequence of RYGB and is estimated to occur in up to 7% of patients (49;164;165). Treatment should begin with dietary modifications, including low carbohydrate -and high protein meal content (166).

Supplementation with dietary fibres (bran, methylcellulose, pectin and guar gum) have been tested and shown to alleviate hypoglycaemia by forming gels with carbohydrates; they thus delay glucose absorption and prolong transit time (167;168). Treatment of postgastric bypass hyperinsulinemic hypoglycaemia may additionally require medical and/or surgical treatment (164).

Patients who have undergone bariatric surgery can develop diverse nutritional deficiencies which can cause severe morbidity if not treated.

Due to reduced protein intake or absorption postoperatively, protein malnutrition may occur. After malabsorptive procedures with alimentary limb >150 cm the risk of protein malnutrition increase and hypoalbumiemia has been reported in about 6% of patients (169).

The data available on vitamin and mineral status after bariatric surgery is scarce, but the most frequent deficiencies reported after gastric bypass surgery are insufficient levels of vitamin B 12, iron, folic acid, vitamin D and calcium (92;170;171). It has been shown that a standard multivitamin supplement cannot prevent these micronutrient deficiencies 2 years after RYGB. Gasteyger et al. reported the following proportions of patients with insufficient vitamin-/mineral levels 2 years postoperatively: 80% had insufficient levels of vitamin B12, 60% of iron, 60% of vitamin D and calcium, and 45% of folic acid. Furthermore, 13% had insufficient levels of vitamin B6, 13% of magnesium, 12% of zinc and 4% had inadequate vitamin B1 levels (170). As a consequence, almost all patients needed at least one additional nutritional supplement 1 and 2 years postoperatively (86 and 98% respectively) (170). Vitamin A deficiency has also been reported in 17% of patients 2 years after RYGB surgery (172). Another example of serious illness after bariatric surgery is Wernicke encephalopathy caused by severe thiamine (vitamin B1) deficiency. This condition may lead to death or lasting disability if not treated immediately (173). A common risk factor for developing this quite rare condition (1 out of 500 patients) is frequent vomiting the first weeks after surgery (173).

Both clinicians and patients should be aware of the risks of nutritional deficiencies following rapid weight loss after bariatric surgery. To prevent this, thorough dietary instructions should be included in patient information programmes both prior to bariatric surgery and in the follow-up period post-surgery (171).

1.8 Assessment of dietary intake

All the traditional measurement methods of habitual food intake; weighed food records, dietary history, 24-hour dietary recalls and food frequency questionnaires (FFQ) include varying levels of dietary reporting errors. One major challenge is the tendency human beings have to underreport their energy intake (EI), with this especially pronounced among obese individuals (174).

The FFQ method is extensively used to measure a person's habitual dietary intake over a predefined period of time and to investigate relationships between diet and health in nutritional epidemiologic studies. Although the FFQ, as a retrospective method, has inherent measurement errors including incorrect memory of past food choice and amount consumed, it is a relatively inexpensive and easy tool to administer. The FFQ method is well established and validated for assessing habitual diet among adults in Norway (175-178).

Validation of reported dietary intake

EI should meet the body's total energy requirements. When EI equals total energy expenditure weight maintains stable. Reported EI is a way of measuring total food intake. A valid (or accurate) report of EI measure is the true intake during a given period of time. The habitual intake is a person's intake over a prolonged period of time (weeks, months or years). Even if food intake can vary widely with season and time, the methods used for validation of reported EI rest on the assumption that EI equals total energy expenditure in a weight-stable situation (179).

The doubly labelled water (DLW) technique is considered the "gold standard" for measuring TEE. The method involves measuring the urinary excretion of stable isotopes of deuterium and oxygen-18 after administration of a predefined dose of the DLW. However, since the DLW measurement period is usually 14 days in adults, the method cannot account for monthly or seasonal fluctuations, and is not necessarily a measure of habitual TEE (179). TEE obtained by using the DLW method is frequently used to validate EI calculated from food records, dietary histories and FFQs (180;181). If the TEE measured by DLW is higher than reported EI then the reported EI has been underestimated. Even if DLW is the preferred validation method, it is too costly and technically complicated for routine validation of reported EI.

The Goldberg method is a technique whereby reported EI is evaluated against estimated energy requirements, and is now widely used (182). This technique involves using an equation to predict TEE. TEE is calculated from the product of BMR (estimated) and physical activity level (PAL). Values for variation in reported EI, BMR and PAL may be applied to classify misreporters, as suggested by Black (183). This method is currently being used to assess reported EI in dietary surveys in a simpler, cheaper and more feasible manner than the DLW method (183;184). In comparison with the DLW method, the Goldberg method is considered a reasonable approach to identifying underreporting in both 24-hour recalls and FFQs (185).

Introduction summary

Obesity is one of the main medical challenges of our time. Traditionally malnutrition has been linked to energy deficit. However, malnutrition can also result from poor dietary quality and/or increased requirements. Both obesity and a diet of poor quality pose a significant health risk. With this in mind it is important to be aware of the high prevalence of various micronutrient deficiencies morbidly obese subjects may suffer from prior to treatment. One of the best known examples is vitamin D deficiency.

Although lifestyle intervention in the form of reduced energy intake and physical activity is the cornerstone of treatment of morbid obesity, the number of patients undergoing bariatric surgery is rapidly increasing. The current understanding of how food and nutrient intake change after bariatric surgery and lifestyle intervention is inadequate. The main aims of this thesis were to investigate the changes in nutrient and food group intake and to examine changes in blood levels of selected vitamins 1 year after lifestyle intervention and gastric bypass surgery. Additionally, we sought to explore the prevalence of vitamin D deficiency in a large cohort of treatment seeking morbidly obese men and women in Norway. We expected that a better understanding of these issues might help health care professionals to improve the dietary counselling of morbidly obese patients seeking weight loss treatment.

2 AIMS OF THE THESIS

The specific aims of the studies in this thesis are:

1. To assess and compare changes in the intake of specified food groups and energy yielding nutrients in the context of recent food based dietary guidelines and nutrition recommendations in patients undergoing either gastric bypass surgery or intensive lifestyle intervention during a 1-year non-randomised clinical intervention trial.

2. To assess the 1-year changes in vitamin A, $B_{1,}$ $B_{6,}$ folic acid, $B_{12,}$ C, D and E concentrations in gastric bypass patients taking predefined supplementation, and to compare these vitamin changes with those of patients undergoing an intensive camp-based lifestyle intervention.

3. To investigate the effect of gender on vitamin D status in a large cohort of morbidly obese Norwegian patients, and to explore whether a possible gender based difference in vitamin D status might be explained by variations in overall and/or abdominal obesity.

3 MATERIALS AND METHODS

3.1 Study designs

The results in this thesis are based on longitudinal data from the one-year non-randomised controlled clinical MOBIL study (Morbid Obesity treatment, Bariatric surgery versus Intensive Lifestyle intervention) (Paper I and II) and cross-sectional data from The Morbid Obesity Biobank Registry (Paper III). Participants in all three studies were morbidly obese (Table 3).

Table 3. Study design and sample size.

Paper	N	Population	Study design
I	72 gastric bypass 54 lifestyle intervention	Men and women in the MOBIL study	Non-randomised controlled study
II	27 gastric bypass 23 lifestyle intervention	Men and women in the MOBIL study	Non-randomised controlled study
III	2026	Men and women in the Morbid Obesity Biobank Registry	Cross-sectional study

3.2 Participants

All participants were referred from local hospitals to the Morbid Obesity Centre (Vestfold Hospital Trust) for weight reducing treatment. The Morbid Obesity Centre is located in Tønsberg and is a public tertiary care centre serving approximately one million inhabitants in Southern Norway. The centre was established in September 2004 and is one of two tertiary care centres in South-East Norway Regional Health Authority which treats morbidly obese patients. The main tasks of the centres are to evaluate, assess and treat morbidly obese persons, as well as to plan and carry out obesity-related research projects and educate and support other health care personnel responsible for obesity treatment (link: www.sykehuset-vestfold.no/sso).

3.2.1 One year non-randomised clinical trial (Paper I and II)

Papers I and II include patients from the MOBIL study. The flow of the study participants is shown in Figure 5. Between December 2005 and May 2006, 228 consecutive patients were pre-screened for inclusion in the trial. One hundred and eighty-one patients who met the criteria for inclusion in the study were referred to an extensive screening examination

including oral glucose tolerance test, 24-hour ambulatory blood pressure monitoring, somnography, pulmonary function test, quality of life questionnaires and structured dietary interviews. Of the 181 patients who completed the screening, 146 were enrolled in the study. Of these, 80 were accepted for gastric bypass surgery and 66 for a camp-based intensive lifestyle intervention program.

Allocation to treatment was the result of a joint decision made between patient and physician. The decision was based on thorough assessments by a multidisciplinary team; internist, dietitian, nurse, physiotherapist and surgeon (in cases of surgery). The health-team informed patients about possible risks and benefits of the two treatments.

One year follow up was completed for both groups by June 2009. Of the 146 patients enrolled in the MOBIL study, 139 (95%) completed the one-year follow-up period (n=63 in the lifestyle intervention group and n=76 in the surgery group) (49).

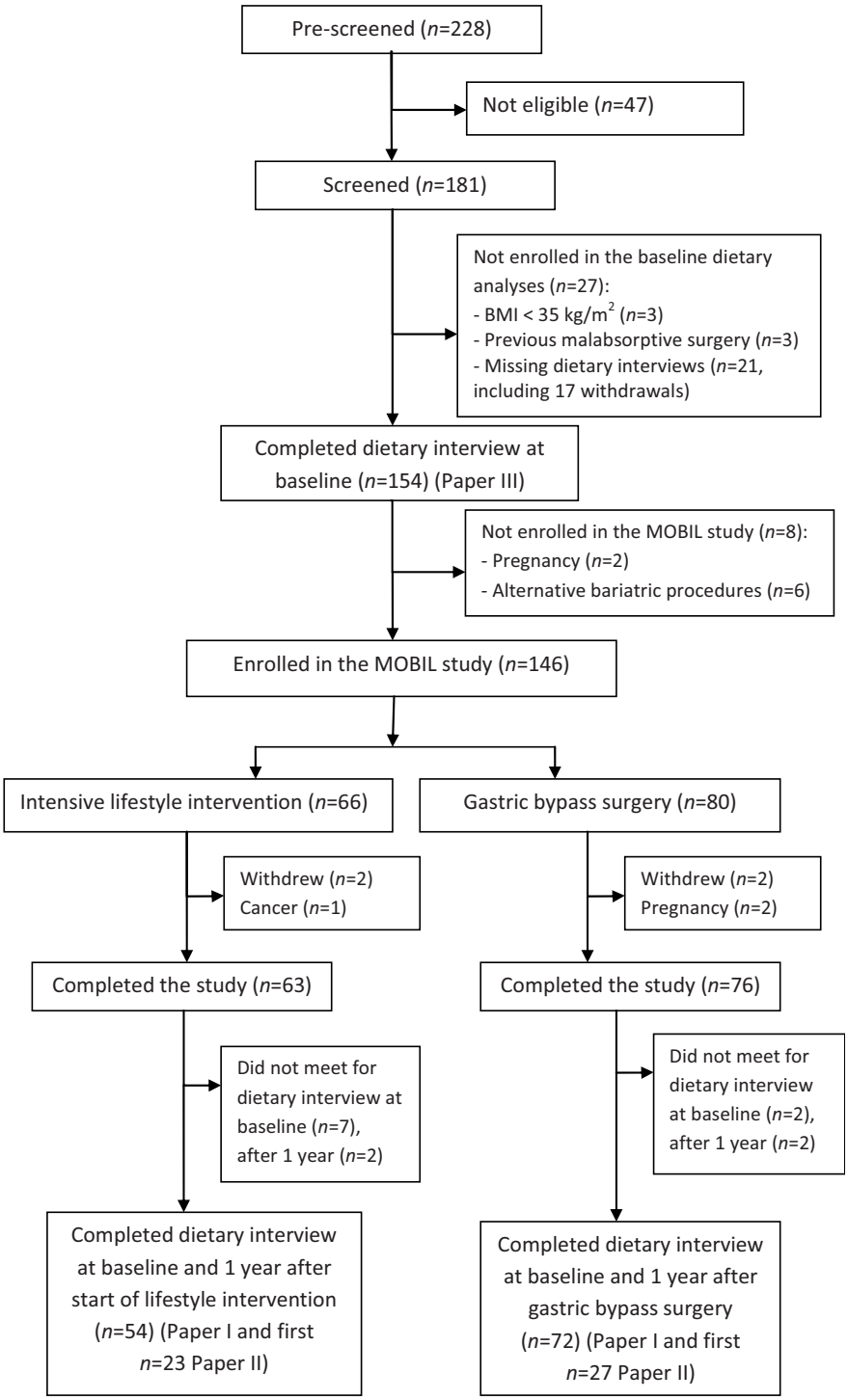
Paper I

After the exclusion of 13 patients who declined to undergo dietary interviews (9 at baseline and 4 after intervention), 126 patients (54 in the lifestyle group and 72 in the surgery group) had completed the dietary interviews both at baseline and after one year follow up and were subsequently included in the dietary analysis. Patients in the surgical group were significantly younger and heavier than those in the lifestyle group [mean (SD) age: 43 (11) versus 47 (11)] years (P=0.034) and BMI: 46 (6) versus 43 (5) kg/m^2 (P<0.001)].

Paper II

The first 64 potential participants in the MOBIL study had their vitamin concentrations measured in a separate vitamin status study (93). Of the 64 patients screened for enrolment into the trial, 53 were included and 50 (27 in the surgery group and 23 in the lifestyle group) completed the one year follow up. The groups did not differ significantly in age at baseline [median (25^{th}-75^{th} percentiles)]: surgery group 44 (36-50) versus lifestyle group 45 (35-59) years, P=0.38. Patients in the surgery group had, however, significantly higher BMI than those in the lifestyle group: 46 (42-59) versus 40 (39-44) kg/m^2, (P<0.001).

Figure 5. Flow of patients completing dietary interviews in the MOBIL study.



3.2.2 Cross sectional study (Paper III)

The study in Paper III had a cross-sectional design and included patients from The Morbid Obesity Biobank Registry. All patients who have attended the Morbid Obesity Centre since November 2005 have, after giving informed consent, been included consecutively in the Registry. The Registry comprises of clinical data and laboratory results from the first visit at the Centre.

Paper III included all the morbidly obese patients registered at the Morbid Obesity Biobank Registry in the period November 2005 – June 2010. Of the 2140 patients considered for inclusion, 39 non-morbidly obese patients with BMI<35 kg/m^2 and 75 patients with missing measurements for either 25(OH)D (n=48), BMI (n=11) or both (n=16) were excluded. The remaining 2026 were included in the analysis. In addition, a subgroup of 154 patients participating in the MOBIL study and examined between December 2005 and May 2006 were evaluated in order to assess total vitamin D intake and macronutrient composition.

3.3 Clinical characteristics

Patient demographic data, medical history, smoking habits and intake of vitamin supplements were recorded using standardised forms (Paper I-III). Anthropometric measures were made with patients in an upright position wearing light clothing and no shoes. Waist circumference was measured at the midpoint between the lowest rib margin and the iliac crest, whilst hip circumference was measured at the level of the major trochanter. Neck circumference was measured below the larynx and perpendicular to the long axis of the neck. Waist, hip and neck circumference were measured with a tape measure to the nearest cm. Height was measured with a wall mounted stadiometer to the nearest 0.5 cm, whilst weight was measured to the nearest 0.1 kg.

Patients with at history of type 2 diabetes or a fasting serum glucose concentration ≥7 mmol/l were classified as having type 2 diabetes (Paper II and III) (186). Ischemic heart disease was defined as either a history of percutaneous coronary artery bypass graft surgery or myocardial infarction and elevated C-reactive protein concentration as a level ≥7 mg/l (Paper III).

In paper III, vitamin D deficiency was defined as serum 25(OH)D<50 nmol/l and secondary hyperparathyroidism as serum parathyroid hormone concentration >6.9 pmol/l and concomitant serum calcium <2.54 mmol/l. Season of blood sampling was defined as either winter (1 November through 28 February) or summer (1 March through 31 October).

3.4 Dietary intake

Dietary intake was assessed by using a validated FFQ including 180 food items, beverages and courses grouped together according to the traditional Norwegian meal pattern (175-177;187). The FFQ was used as a structured interview lasting for 1 to 2 hours. The optically readable FFQ used is designed to measure the daily habitual food intake of the adult population in Norway and is suitable for estimating various macro- and micronutrients, including dietary supplements (175).

The interviews were conducted by registered dieticians. In all three studies patients were asked to describe their habitual dietary intake during the year previous to their intervention (baseline registration). Patients were asked to report their intake (frequency and amount) of the various food items and beverages (per day, per week or month) as fully as possible. Units (e.g. slices and pieces) and household measures were used to estimate portion sizes. In paper I and II the dietary assessments were repeated 1 year after either surgery or the start of the camp-based lifestyle intervention. The FFQ data was scanned using Teleform 10.0 (Cambridge, UK). The daily intake of food, energy and nutrients were calculated using the Kostberegningssystem computer software (version 6.0, University of Oslo), and were based on data from the Norwegian food composition table (Norwegian Nutrition Council, 1995).

Underreporting

In Paper III individuals underreporting total EI were identified by calculating cutoff levels for acceptable reported EI using Black's equations and practical guidelines (183;184). Basal metabolic rate was estimated by using Mifflin-St Jeor's equations (188). A physical activity level indicating low activity level for each gender was used (1.56 for women and 1.55 for men). Male patients were classified as under-reporters if EI:basal metabolic rate was < 1.10, whilst for female patients the threshold was <1.11.

3.5 Laboratory analyses

Blood sampling was performed by vein puncture after an overnight fast. Vitamin assay samples clotted for 30 minutes at room temperature. Thereafter, serum was separated by centrifugation. Samples were stored at either -20˚C or -80˚C (for vitamin B-2 and C) and were analysed within 28 days. Samples collected and prepared at Vestfold Hospital Trust were kept on dry ice (-57˚C) for up to 24 hours, including during their transport to Oslo University Hospital Aker. Folate and B_{12} measurements were performed at Vestfold Hospital

Trust, vitamin B_1, B_2, B_6, C, A and E were analysed at the Nutrition Laboratory at Oslo University Hospital Aker, whilst 25(OH)D was analysed at The Hormone Laboratory at Oslo University Hospital Aker (Paper II and III). An overview over the vitamin assays used is shown in Table 4.

Serum glucose and C-reactive protein were analysed at the Department of Clinical Chemistry at Vestfold Hospital Trust using dry reagent slide technology on the Vitros 950 Analyser (until November 2006) and Vitros FS 5.1 (post November 2006) (Ortho-clinical Diagnostics, New York, NY; USA). Intact parathyroid hormone was essayed using an electro-chemiluminescence immunoassay on Elecsys 2010 (Roche Diagnostics GmbH, Mannheim; Germany). Serum levels of insulin were measured by radio immunoassay (Insulin Coat-A-Count, DPC, Los Angeles, CA; USA) at the Endocrine Laboratory at Oslo University Hospital Rikshospitalet.

Table 4. Vitamin analyses.

Vitamin	Analyte	Method	Supplier
A	Retinol	HPLC	Bio-Rad Laboratories
B_1	Tiamine pyrophosphate	HPLC	In-house method
B_2	Flavin mononucleotide	HPLC	Chromsystems
B_6	Pyridoxal-5'-phosphate	HPLC	Chromsystems
B_9	Folate	Multianalyser	Siemens Medical Solutions
B_{12}	Cobalamine	Multianalyser	Abbot Diagnostics
C	Ascorbic acid	Micromethod	Noncommercial method
D	25-hydroxyvitamin-D	RIA	DiaSorin
E	A-tochopherol	HPLC	Bio-Rad Laboratories

HPLC: high pressure liquid chromatography

RIA: radioimmunoassay

3.6 Weight loss interventions

3.6.1 Non-surgical intervention in the MOBIL study

The non-surgical treatment consisted of a one year camp-based intensive lifestyle intervention programme which took place at Evjeklinikken, Evje, Norway. The clinic has developed a lifestyle programme to help morbidly obese individuals lose weight through dietary changes and physical activity. The lifestyle intervention programme was based on a cognitive approach and aimed at inducing a weight loss of 10% or more. Patients who

completed the one-year programme had four stays at Evjeklinikken, the first, third and fourth lasting for one week and the second stay lasting for four weeks (Figure 6).

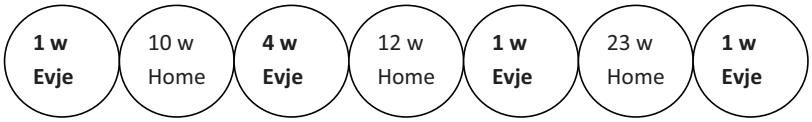


Figure 6: Overview of the stays at Evjeklinikken.

Lifestyle intervention at Evjeklinikken included individual patient consultation with a medical team consisting of a doctor, dietician, physiotherapist and a nurse. In addition, all patients attended group sessions where the health personnel team discussed nutrition, physical activity and health issues related to severe obesity, including behavioural and emotional aspects. Three to 4 hours of organised physical activity was also included in the daily programme.

No special diet, vitamin supplements or weight loss drugs were prescribed. The food served at the clinic followed guidelines from the Norwegian National Council of Nutrition with the following macronutrient composition: protein 10-20 E%, fat <30 E% (saturated fat <10 E%) and carbohydrate 50-60 E%. Meals were served as a buffet, with patients deciding the composition of their meals as well as their portions sizes.

Patients were encouraged to practice the lifestyle interventions initiated at the clinic when they returned home. All patients were contacted by phone fortnightly and encouraged to self-monitor their eating habits and physical activity by keeping a diary. Additional monthly consultations with a general practitioner were also recommended.

3.6.2 Surgical intervention

Patients opting for surgical treatment were offered individual consultations with a dietician in order to improve their eating habits prior to surgery. All patients attended a one day “operation-school” in groups of 25, where personal care, diet, supplements and the physical activity necessary to obtain and maintain successful long term weight-reduction were discussed. Relatives were welcome to attend both individual consultations and the “operation-school”.

To reduce fat-mass volume in the abdominal region and liver size, the patients undergoing bariatric surgery completed a low calorie diet (800-900 kcal/day) for 3-6 weeks pre-operation. Patients chose either a low calorie diet based on crisp-bread, low-fat protein sources and vegetables or meal replacement shakes. Roux-en-Y gastric bypasses were performed

laparoscopically with a gastric pouch of ≈25 ml, an alimentary limb measured to median 120 cm (range 80-200 cm) and a median biliopancreatic limb of 100 cm (range 50-170 cm) (Figure 4). The common channel had variable lengths.

Patients were recommended the following supplements post-operatively: 1 daily multivitamin/mineral pill and vitamin-D with calcium (10 µg D_3 and 500 mg Ca carbonate), both to be taken 2 times daily, ferrous sulphate (65 mg for men end 130 mg for women) and fish oil supplements (150 µg A, 10 µg D_3 and 10 µg E). Additionally B_{12} (1 mg cyanocobalamin) was given intra-muscularly every 3 months. (Supplement details are described in Paper II).

3.7 Statistics

In all papers data are presented as mean (SD), mean (95 % CI), median (25th to 75th percentiles) or number (%). Within-group changes were tested with paired samples t-test or Wilcoxon signed rank test as appropriate. Between-group differences were analysed using either independent samples t-test or Mann-Whitney U-test for continuous variables or chi-square or Fisher's exact test for categorical variables. Between-group differences in within-groups changes were evaluated using analysis of covariance (ANCOVA). Linear regression models with predefined dependent and independent covariates were used to assess the effect of treatment (paper I and II), while logistic regression models were used to assess odds ratio (OR) for vitamin D deficiency (25(OH)D <50 nmol/l). Statistical tests were considered significant at $P<0.05$. All statistical analyses were performed using SPSS 16.0 (SPSS, Chicago, IL).

In Paper I, the between-group differences of within-group changes in intake of food groups and nutrients were assessed using ANCOVA with adjustment for sex, age, baseline BMI and baseline values of the dependent variable.

In Paper II, multiple linear regression was used to compare changes in vitamin concentrations after the two interventions (gastric bypass or lifestyle). In the regression models, change in vitamin concentrations was the dependent variable, whilst intervention groups, baseline BMI, age, gender and smoking were the independent variables.

In paper III, one unadjusted (gender) and three adjusted logistic regression analyses with predefined explanatory variables (season, age, current smoking status, vitamin D supplements, BMI and waist circumference) were used to assess the likelihood of vitamin D deficiency (dependent yes/no).

3.8 Ethics

3.8.1 Approvals

Written informed consent was obtained from all participants. The Morbid Obesity Biobank Registry has been approved by the Regional Ethics Committee for Medical Research, [formerly the Southern Norway Regional Health Authority (reference number S-05175), the Norwegian Social Science Data Service (reference number 14029) and the Directorate for Health and Social Affairs (reference number 06/530)]. The Regional Ethics Committee for Medical Research also approved the MOBIL study. The MOBIL study is registered in the ClinicalTrials.gov-registry (identifier NCT00273104) and was conducted according to the guidelines laid down in the declaration of Helsinki.

3.8.2 Funding

The studies in this thesis have been supported by a research fellowship grant from the Norwegian Resource Centre for Women's Health, Oslo University Hospital Rikshospitalet to Line Kristin Johnson. Co-author Dag Hofsø has received unrestricted grants from Novo Nordisk A/S, Vestfold Hospital Trust and the South-Eastern Norway Regional Health Authority. None of the authors report a personal or financial conflict of interest.

4 SUMMARY OF RESULTS

4.1 Paper I

Dietary changes in obese patients undergoing gastric bypass or lifestyle intervention: a non-randomised controlled trial.

This paper presents the changes in intake of various food groups and macronutrients in morbidly obese patients who underwent either laparoscopic gastric bypass (n=72) or an intensive lifestyle camp-based intervention program (n=54). Changes in intake of fruit, vegetables, whole grains and fish were assessed. Changes in the intake of total energy, fibre and percentage distribution of the energy yielding nutrients were also explored. Patients in the two intervention groups had similar dietary patterns at baseline. Percentage intake of total and saturated fat was higher than the recommended levels, while percentage intake of total carbohydrates was lower than is recommended (24). At baseline, intake of fruit and vegetables was in accordance with current food based dietary guidelines, while intake of whole grains was lower than recommended levels and intake of red meat was higher than is recommended. At 1-year follow up, patients in the lifestyle group had a significantly higher daily intake of fruit and vegetables and fibre than patients in the surgery group, whilst they had a lower percentage energy intake of total and saturated fat (P<0.002 for all).

The intake of vegetables and fish reduced significantly in the surgery group, while intake of sugar reduced significantly in the lifestyle group. Red meat intake declined significantly within both intervention groups.

After adjustment for sex, age, baseline BMI and baseline value of the dependent variable, we found that the patients in the lifestyle group significantly improved their dietary patterns compared to the surgery group by increasing their intake of vegetables, whole grains and fibre, and by reducing their percentage intake of saturated fat (P<0.001 for all).

4.2 Paper II

Vitamin status after gastric bypass and lifestyle intervention: a non-randomised controlled trial.

In this paper we compared the changes in blood vitamin concentrations and vitamin intake in morbidly obese patients 1 year after laparoscopic gastric bypass surgery (n=27) and the start of an intensive lifestyle camp-based intervention program (n=23). The 50 patients included in this paper are the first of those who participated in the study described in Paper I. Baseline vitamin concentrations and dietary intakes were similar in the two intervention groups. Intake

of all measured vitamins was in accordance with recommended dietary intakes before intervention. Despite this, 37% of patients in the surgical group and 30% in the lifestyle group had low vitamin serum concentrations of vitamin D (25(OH)D), while 15% and 17% respectively had low vitamin C levels before treatment. The patients in the surgical group were recommended to take vitamin and mineral supplements (multivitamin, iron, calcium, vitamin D and vitamin B_{12}) after surgery, whereas no supplements were prescribed to the patients in the lifestyle group.

Compared to patients in the lifestyle group, gastric bypass patients significantly increased their concentrations of vitamin B_6, folate, vitamin B_{12} and lipid-adjusted vitamin E concentrations (P <0.02 for all using multivariate linear regression analysis), while vitamin A concentrations decreased (P<0.01) during follow-up. There were no significant differences in concentration of vitamin B1, C and 25(OH)D between the intervention groups.

A comparison of dietary intake within each treatment group showed that the gastric bypass patients had a significant reduction in intake of energy, vitamin A, B_1, B_2, C, D, E and folic acid (P<0.008 for all), while patients in the lifestyle group experienced no significant change in vitamin intake.

The surgically treated patients used significantly more multivitamins, vitamin D/calcium, vitamin B12 and fish oil supplements than the lifestyle patients at 1-year follow up (P<0.001 for all).

4.3 Paper III

Impact of gender on vitamin D deficiency in morbidly obese patients: a cross-sectional study.

In this paper we analysed the relationship between gender and vitamin D (25(OH)D) deficiency in 2026 (1336 women) morbidly obese patients seeking weight loss treatment. In addition we explored whether gender differences in vitamin D status could be explained by variations in overall and/or abdominal obesity (BMI and/or waist circumference respectively).

Mean (SD) 25(OH)D concentrations were 50.0 (22.0) nmol/l in men and 53.6 (22.4) nmol/l in women (P=0.001). Additionally, the prevalence of vitamin D deficiency (25(OH)D <50 nmol/l) was significantly higher in male patients than in female patients 56% versus 47% (P<0.001).

Dietary intake of vitamin D was assessed in a subgroup of 154 (112 women) patients by using the same FFQ as in Paper I and II. In men, the median (25-75th percentile) vitamin D intake tended to be higher during winter (10.7 (7.0-16.9) µg) than during summer 6.8 (4.5-15.4) µg (P=0.08). We observed no significant seasonal differences in female patient vitamin

D intake (9.3 (5.5-12.5) μg) during winter versus (7.0 (4.4-10.3) μg) during summer (*P*=0.45). Both men and women had adequate median vitamin D intakes during the winter, whereas both genders had lower than recommended daily intakes of vitamin D than during summer (24).

The unadjusted logistic regression analysis showed that obese men had significantly higher odds of vitamin D deficiency than women [odds ratio=1.41; (95% CI:1.17-1.70)]. When adjusting for possible confounders; season of blood sampling, age, current smoking and intake of vitamin D supplements; the association between male gender and vitamin D deficiency was slightly strengthened [odds ratio=1.52; (95% CI: 1.26-1.84)]. Adding BMI to the adjustments did not affect the odds of vitamin D deficiency, whereas further adjustment for waist circumference somewhat attenuated the relationship between male gender and vitamin D deficiency [odds ratio=1.39 (95% CI: 1.10-1.76)]. This finding suggests that abdominal adiposity may partly explain the observed higher frequency of vitamin D deficiency among men.

5 DISCUSSION

The main findings of the papers included in this thesis are:

- Morbidly obese patients who participated in a comprehensive lifestyle intervention program at a rehabilitation centre reported more favourable dietary changes compared to patients who underwent gastric bypass surgery. Patients in the lifestyle group had greater intakes (g/day) of fruit and vegetables, whole grains and fibre than patients treated with gastric bypass surgery, as well as lower intakes (E %) of total fat and saturated fat at 1-year follow up.
- Morbidly obese patients who underwent gastric bypass surgery and took predefined vitamin and mineral supplementation had stable or increased concentrations of most vitamins 1 year after surgery compared with patients attending a lifestyle intervention programme who had no significant changes in the vitamin concentrations at 1-year follow up.
- Fifty per cent of 2026 morbidly obese treatment-seeking Norwegian men and women suffered from vitamin D deficiency. Men had 40% higher adjusted odds of vitamin D deficiency than women.

5.1 Methodological considerations

5.1.1 Study designs and statistics

Paper I

Although randomised controlled trials provide high-quality evidence about the efficacy of medical interventions, the design of pragmatic (or practical) trials makes it possible to compare and assess the effectiveness of two interventions relevant to real-life clinical care (189;190). The MOBIL-study can be characterised as a non-randomised pragmatic clinical trial designed to compare the effectiveness of gastric bypass surgery and intensive lifestyle intervention including intermittent stays at a rehabilitation centre. Non-randomised designs reduce the internal validity of a study and introduce elements of selection bias. Selection bias in this trial could include risk of treatment allocation bias given that one could hypothesise that those patients referred to intensive lifestyle treatment may have had greater motivation to change their dietary habits and/or physical activity than those referred to surgery (190).

In our study, the participants in the lifestyle intervention group were older and less heavy than the surgery patients at baseline. Although differences in baseline weight and age in the

two intervention groups were adjusted for in the multivariate analyses used (ANCOVA), they might have affected our findings. One could hypothesise that the older and less heavy patients in the lifestyle group had both greater knowledge of and interest in behavioural and lifestyle changes than their younger and heavier counterparts in the surgery group, which again affected the outcome (dietary changes). Furthermore, we cannot exclude the possibility that unknown confounders (behavioural characteristics and genetic factors) or socioeconomic factors not included in our multivariate statistical analyses might have affected the results. One could, for example, speculate that individuals with less anxiety, less depression and greater intrinsic motivation for lifestyle change were referred to the lifestyle intervention group and achieved greater health promoting dietary changes.

However, as all patients participating in this study underwent ordinary assessments before treatment and routine follow-up practiced in the public Norwegian health-care system, the results of this trial are of direct relevance to clinicians and reflect the real-life effect of two common treatment-options for morbidly obese individuals. There was no crossover and few drop-outs in both treatment-groups. The results therefore provide a valid comparison of the treatment options, and may be regarded generalisable and useful when developing future guidelines for care.

Paper II

The non-randomised design in this study may be a limitation as the confounding factors in the two intervention groups may differ somewhat. Few participants were included in this study, which may increase the influence of extreme values on the results. The use of non-parametric statistical tests may, however, reduce this disadvantage. To assess between-group differences in the change of vitamin concentrations (dependent/effect variable) we used multivariate regression models with intervention group, baseline BMI, age, gender and smoking (yes/no) as 5 independent variables. Regression models including the baseline vitamin concentrations were also performed, with similar results as presented in the paper.

The strengths of this study include the prospective design, the assessment of both vitamin status and dietary intake at baseline and 1-year follow-up, a control group consisting of obese patients seeking weight loss treatment through non-surgical methods and the high participant completion rate. The results of this study provide information about the supplement-recommendations being used in clinical practice after gastric bypass surgery.

Paper III

This study had a cross-sectional design, meaning that the results cannot indicate causation, which can be considered a limitation. However, the large number of consecutive morbidly

obese men (n=690) and women (n=1336) included over during a near 5 year cross-seasonal study ensures a representative sample of participants, and moreover an adequate power with which to answer our research question. Furthermore, the adjustments for confounding variables strongly associated with vitamin D status (gender, season of blood sampling, age, current smoking, use of vitamin D supplement, BMI and waist circumference) in the multiple logistic regressions can be considered significant strengths. As the study-population was mainly of Europoid origin, the results cannot be generalised to include other ethnic groups.

5.1.2 Dietary assessment methods

Measurements of habitual food intake often include reporting bias depending on the method used and the population studied. The most commonly used methods in assessing dietary intake are 24-hour dietary recalls, dietary history, weighed food records of varying durance and FFQs. The 24-hour recall method is a brief nutritional assessment tool giving information of the dietary intake the previous day. The method does not, however, necessarily give a representative picture of habitual intake and is often combined with other dietary assessment methods, for example FFQs. Dietary history is a detailed retrospective assessment method assessing habitual intake. As this method normally requires individual food coding for analysis purposes it is regarded time consuming and expensive. The weighed food record method is a prospective dietary assessment method, giving detailed information of a participant's intake during 3-7 days. The method does, however, impose a significant respondent burden and is expensive to implement due to working and equipment costs. The FFQ method is designed to assess habitual diet over a reference period (3-12 months). The method is relatively easy to administer and imposes low respondent burden. Although respondent bias may be less if self-administered, more complete data is often achieved when the FFQ is administered by an interviewer.

Underreporting is, unfortunately, a well known bias in studies of dietary intake, and it has been shown that independent of dietary assessment obese individuals are more likely to underestimate or underreport their food intake than their lean counterparts (191-193). Recall-based methods are susceptible to reporting-bias due to the inaccuracy of the memory (194). Social self-perception (desire of respondents to avoid embarrassment and project a favourable image to others) may affect the accuracy of both the type of food eaten and the amount (195). It has been reported that food rich in fat and/or simple carbohydrates are more commonly underreported than protein rich foods (191;192). This is consistent with the observation that obese under-reporters have a lower intake of sweets, desserts and snacks than obese non-under-reporters (196).

However, despite the generalised under-estimation of total intake in all methods, the FFQ method is not associated with significant obesity-related underreporting in women (193).

In Norway, a 180 food items FFQ has been developed and validated to cover the whole diet and assess dietary habits among men and women (177;197). This method has been used in studies to evaluate possible relations between diet and disease, as well as in the surveillance of dietary development at the population level (NORKOST 1, 2 and 3) (104;197;198).

As we aimed at assessing the habitual food intake of the participants in our studies, and as foods and diet are culture-dependent, we chose to use the FFQ validated for use among Norwegian adults in the studies included in this thesis (177). Additionally, the use of this FFQ made it possible to compare our data with those from NORKOST and thereby assess dietary intake in the general Norwegian population with the severely obese individuals participating in our studies.

Patients under-reporting their intake at baseline were identified using Black's equations and guidelines to calculate cutoff levels for acceptable reported EI (183;184). Men and women with reported EI:estimated BMR <1.10 and <1.11, respectively, were classified as under-reporters. Of the 154 morbidly obese participants (Paper III) we found that 30% of the women and 38% of the men had lower EI than was plausible, with no significant difference between genders (*P*=0.41). In contrast, a former nationwide dietary survey among Norwegian adults showed that more women than men underreported EI from a self-administered FFQ (45% compared with 38%) (199). However, in the recent NORKOST 3, the proportion of men and women underreporting their EI was similar but lower than in the former survey, 15% and 17% respectively (104). The difference between the prevalence of under-reporters in these two Norwegian studies may be explained by the fact that the cut-off levels for underreporting based on reported EI:estimated BMR were defined differently, <1.35 in the former trial (199) and <0.96 in the most recent one (104). Results in a study among Canadian adults showed that 54% of men under-reported EI compared to 35% of women, and moreover that under-reporting was more prevalent among individuals who were heavier, had a higher BMI and a lower education level (200). Under-reporting is a complex matter. It has been reported that individuals who are concerned with their body image, who diet regularly and/or aim to lose weight are likely to under-report their food intake (199). With the different definitions of cut-off levels to identify under-reporters in mind, the prevalence of under-reporting in our dietary survey may be considered to be in line with results from the first Norwegian trial (199). It should be noted that in the Norwegian nationwide survey the FFQs were self-administered, while in our study the questionnaires were performed as structured interviews, which may have provided a more accurate and complete filling of the

forms, which could explain the lower proportion of under-reporters. One could, however, argue that interviewing the participants could be considered a disadvantage given the potential for interviewer bias. The presence of the interviewer could result in an under-reporting of foods considered unhealthy and an over-reporting of foods considered healthy. Both type of food consumed and amount of food consumed may potentially be misreported. However, we assume that this potential misreporting would not differ substantially between intervention groups, as both groups were aware of the importance of eating healthily. One may also hypothesise that the recent stay at the rehabilitation centre before the dietary interview at 1 year-follow up may have led participants in the lifestyle intervention group to report a healthier diet than that normally practiced in daily life.

5.2 Intake of macro- and micronutrients

5.2.1 Dietary intake before intervention

Macronutrients

Baseline energy intake and percentage distribution of energy yielding nutrients in our morbidly obese patients are presented in Table 5, column 5. Despite use of similar dietary assessment methods, mean total energy intake in our participants was approximately 200 kcal/ day lower compared to baseline data from a recent Swedish study, in which mean (95% CI) reported daily energy intake was 2986 (2619-3354) kcal/day prior to gastric bypass surgery (201). Although a validated FFQ were used in both the Swedish study and our trial, they are developed to measure habitual intake in different countries and thereby not completely comparable. Reported energy intake from other comparable studies ranges from 2100-2600 kcal/day (202-205). In these studies, other methods assessing dietary intake has been used (food diaries and dietary recall methods). Due to the diversities in dietary assessment methods used and differences in alimentary pattern among countries, one should be cautious when comparing total energy intake in these studies. Energy percentage distribution is, however, less susceptible to these concerns. The mean (95% CI) percentage energy from total fat in the recent Swedish study was 37.0 (34.2-38.8) E% and is comparable to the result in our trial. Similar energy percentage from fat was found in the SOS study, where obese women reported 37 E% from fat (206). A relatively high E% from total fat ranging from 36 to 43 E% has also been reported in similar studies (202;204;205). These results indicate that morbidly obese subjects have a higher than recommended total fat intake prior to intervention (<30 E%) (24). In other reports, data on intake of other energy-yielding nutrients, carbohydrates and protein ranges from 39-46 E% for carbohydrates and 14-19 E% for protein (202-206). These findings are in accordance with ours, with mean (SD)

E% from carbohydrates and protein being 45 (7) and 17 (3) respectively. In all these trials E% of carbohydrates was lower, while E% of protein was in accordance with current Nordic recommendations (24).

Table 5. Weight, BMI and intake of energy-yielding macronutrients in morbidly obese patients and normal weight controls compared to participants in Norkost 3.

	RDI[1]	Norkost 3 (2010-2011) (n=1787)[2]	Non-obese controls (n=30)	Obese patients (n=154)	*P*-value[3]
Weight (kg)		78	68 (8)[4]	131 (22)	<0.001
BMI (kg/m^2)		25.5	22.7 (1.5)	44.4 (5.9)	<0.001
Energy intake (MJ)	9.2-11.8	9.4 (3.3)	9.8 (2.4)	11.6 (4.5)	0.001
Energy intake (kcal)		2247 (789)	2329 (574)	2782 (1069)	0.001
Protein E%	10-20	18 (4)	17 (2)	17 (3)	0.240
Fat E%	<30	34 (7)	35 (6)	38 (6)	0.053
SFA E%	<10	13 (3)	14 (2)	15 (3)	0.088
MUFA E%	10-15	12 (3)	12 (2)	13 (2)	0.135
PUFA E%	5-10	6 (2)	7 (2)	8 (2)	0.179
Carbohydrate E%	55 (50-60)	44 (8)	46 (5)	45 (7)	0.557
Sugar E%	<10	7 (5)	6 (3)	7 (6)	0.247
Alcohol E%	<5	2 (5)	2 (1)	1 (1)	0.002
Fiber (g)	25-35	24 (10)	28 (9)	29 (10)	0.483

[1] Recommended daily intake (RDI). Nordic Nutrition Recommendations: NNR 2004 and Norwegian Recommendations for Nutrition and Physical activity (24;207).

[2] Norkost 3. A nationwide dietary survey among Norwegian men and women aged 18-70 years (104).

[3] Independent samples *t*-test used to compare values for obese patients and non-obese controls.

[4] Mean (SD), all such values.

The current understanding of the dietary intake of morbidly obese Norwegians is limited when compared to our understanding of the dietary intake of normal weight persons. We therefore had 30 non-obese controls (20 women) take the FFQ at baseline. The controls were all health-care personnel working at Vestfold Hospital Trust. (Post hoc analyses). In Table 5, body weight and the intake of energy and percentage composition of macronutrients in participants of Norkost 3 (which represents the general population in Norway), obese patients and non-obese controls in our baseline dietary survey (Paper I and III) are presented.

Except for a significant difference in energy- and alcohol intake, there were no significant differences in macronutrient composition between obese patients and the non-obese controls.

The morbidly obese men and women had similar intake of macronutrients, except for energy intake and percentage energy consumed from alcohol (significantly higher in men).

Although we have no statistical basis by which to compare the intake of patients and the controls in our survey with that of Norkost 3, it seems that the obese patients in our study differed in terms of energy intake and energy percentage distribution compared to both the participants in Norkost 3 and our non-obese controls (Table 5).

In our survey both obese and non-obese participants had a higher energy percentage consumed from saturated fat than is recommended. And, although not significant, the obese participants had an even higher intake of total- and saturated fat than the normal weight individuals. This is in line with the findings of a Belgian report which found that total energy and fat intake (kcal/day) were significantly higher in obese subjects compared to their lean counterparts (208). In contrast to our findings, protein intake was significantly higher in the obese individuals.

Alcohol is a source of energy (29 kJ or 7.1 kcal/g) that may contribute to the development of obesity. However, data from a prospective cohort study where 19220 healthy, normal weight US women were followed for 12.9 years, shows that compared with non-drinkers, women who consumed a light (0.1-4.9 g alcohol/day) to moderate (5-14.9 g alcohol/day) amount of alcohol gained less weight and had a lower risk of becoming overweight and/or obese (209). Despite contradictory findings, this corresponds with a recent review which concluded that light-to moderate alcohol intake, especially wine intake, protects against weight gain, whereas consumption of spirits and higher levels of drinking is positively associated with weight gain (210). The normal weight controls in our study had a significantly higher alcohol intake than the obese patients. It should, however, be noted that the normal weight controls were well educated (health personnel) and that wine drinking is generally associated with a higher education background (college/university) in Norway (104).

Micronutrients

Although the data concerning nutritional deficiencies in morbidly obese individuals is limited, it has been shown that vitamin and mineral deficiencies are common (93;211). A high deficiency prevalence has been reported in the following nutrients: 25(OH)D (68%), iron (44%) and vitamin B1 (29%) (211). Another recent report shows a relatively high prevalence of deficiency of folic acid (24%) and vitamin B12 (4%) in bariatric surgery candidates (212).

However, in these studies they did not compare vitamin status to normal weight controls and reported no nutrient intake data.

In Norway, it has been shown that low concentrations of several vitamins (B-6, C, 25(OH)D and lipid-adjusted vitamin E) is prevalent among morbidly obese patients seeking weight-loss treatment compared to normal weight controls (93). This has recently been confirmed in a Spanish report (205). Despite different dietary patterns and climatic conditions in southern Europe, similar differences between obese and normal weight individuals were observed as nutritional deficiencies were commonly found among obese Spaniards and were significantly more prevalent than in normal weight controls (205).

However, little data on the intake of vitamins and minerals in obese subjects has been reported. In the Spanish trial, intakes of calcium and magnesium were below RDI (205), while intake of all vitamins and minerals except vitamin D was sufficient in a Swedish study (203). In our trial, we found that the intake of micronutrients in the morbidly obese patients (both men and women) was in accordance with recommendations (Table 6, column 5). As the prevalence of nutritional deficiencies has been found to be higher among morbidly obese than normal weight individuals (93;205), we found it interesting to investigate dietary intakes in these two groups. We therefore compared the vitamin and mineral intake of both non-obese controls and the general Norwegian population participating in Norkost 3 with that of the baseline intakes of the morbidly obese individuals in our trials (Table 6).

The morbidly obese patients had a significantly higher intake of vitamin B1, C, A, D and E than the non-obese controls (supplements included). The fact that the obese had a significantly higher energy intake than the non-obese may explain the higher intake of micronutrients. Despite the significantly higher energy intake in the obese, under-reporting of energy intake is expected. One could thus speculate that under-reporting is not associated with nutritious foods, but rather with energy-dense foods with low nutrient density (sweets, desserts and snacks) (196).

Table 6. Daily intake of selected vitamins in morbidly obese patients and normal weight controls compared to participants in Norkost 3.

	RDI[1]	Norkost 3 (2010-2011) (n=1787)[2]	Non-obese controls (n=30)	Obese patients (n=154)	*P*-value
Vitamin B1 (mg)	1.1-1.4	1.6 (0.6)[3]	1.7 (0.7)[4]	2.0 (07)[4]	0.041
Vitamin B2 (mg)	1.3-1.7	1.8 (0.8)	2.1 (0.9)	2.3 (0.9)	0.226
Folic acid (µg)	300	254 (86)	278 (105)	313 (115)	0.110
Vitamin C (mg)	75	108 (74)	170 (41)	208 (160)	0.010
Vitamin A (µg)	700-900	886 (758)	1104 (351)	1562 (777)	<0.001
Vitamin D (µg)	7.5	5.8 (5.1)	7.7 (3.6)	9.5 (5.9)	0.040
Vitamin E (mg)	8-10	11 (5)	12 (4)	16 (12)	<0.001
Calcium (mg)	800	920 (457)	1026 (285)	1134 (493)	0.106
Iron (mg)	9-15[5]	11 (4)	13 (5)	14 (5)	0.253

[1] RDI from Nordic Nutrition Recommendations for women-men and Norwegian Recommendations for Nutrition and Physical activity (24;207).

[2] Norkost 3. A nationwide dietary survey among Norwegian men and women aged 18-70 years. Dietary supplements not included (104).

[3] Mean (SD), all such values.

[4] Supplements included all such values.

[5] The highest level for premenopausal women.

It is important to note that the obese individuals in our study had an adequate and, in some cases, even higher intake of vitamins and minerals compared to the normal weight controls. Despite this, we found that a significant proportion of the obese patients had low levels of vitamin B6, vitamin C, vitamin D (25(OH)D) and lipid-adjusted vitamin E before intervention (Table 3, Paper II).

Obesity is associated with elevated C-reactive protein (CRP) concentrations (93;213), and it has been proposed that systemic inflammation related to obesity may contribute to the low vitamin levels observed (93;214). Possible mechanisms explaining the association between inflammation and low vitamin levels may be reduced levels of transport proteins (albumin), alterations in vitamin distribution (lower plasma-/serum-concentrations despite stable intracellular levels) and/or increased antioxidant vitamin turnover (215). Systemic inflammation may thus contribute to the low serum vitamin concentrations frequently observed in severely obese individuals.

5.2.2 Weight loss and energy intake

Weight-loss requires a negative energy-balance. Reduced energy intake may affect dietary composition and quality. In Paper I we compared changes in energy and energy percentage distribution of macronutrients and food groups in 126 morbidly obese patients undergoing either gastric bypass surgery (n=72) or intensive lifestyle intervention (n=54). Mean (SD) weight loss was 9.3 (13.3) kg (8%) in the lifestyle group and 39.6 (12.9) kg (29%) in the surgery group after 12 months of follow-up (*P*<0.001) (Figure 6).

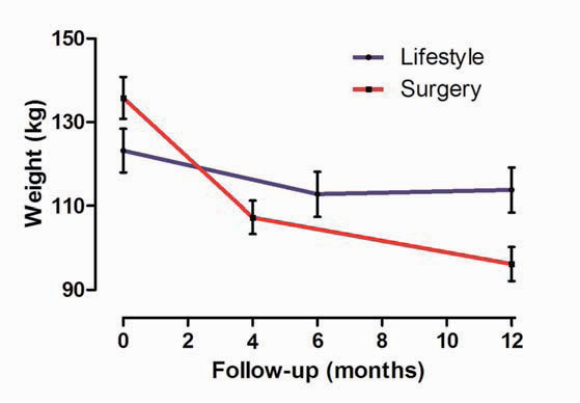


Figure 6. Mean (SD) weight from baseline to 12 months follow-up.

A weight loss of ≥ 5% is commonly regarded as clinically meaningful (123;216). However, in severely obese individuals it has been suggested that a weight loss of 15-20% (at least 10 kg) is required in order to obtain a sustained improvement in co-morbidity (217). In line with this, the 10-year data from the SOS study indicates a weight loss of 10 kg or more to be related to significant improvements in several cardiovascular risk factors (218).

The energy deficit appearing during weight loss is covered by the energy preserved as fat, protein and glycogen in the body. The metabolisable energy densities in body fat, protein and glycogen are approximately 9400, 4700 and 4200 kcal/kg respectively (219). The energy deficit required per unit weight loss is thus higher for fat than for protein and glycogen. This explains why the higher the initial body fat mass, the higher the required cumulative energy deficit to produce the same amount of weight loss. Since women typically have more body fat than men of a similar BMI, this may explain why men tend to lose more weight than women given the same energy deficit (219). The commonly used rule of thumb that a cumulative energy deficit of 3500 kcal is required to lose 1 pound (=0.454 kg) (≈ 7700 kcal to lose 1 kg) of body weight is too simplistic given that it does not take into account the dynamic physiological adaptations which follow from reduced body weight (changes in body

composition, resting metabolic rate and altered energy cost of physical activity) (220). Advanced web-based dynamic simulation models have been developed to predict the time course of weight change in response to altered energy balance. Such model simulations can be useful in setting realistic weight-loss goals and tracking adherence to an intervention (220). However, although the "rule of thumb" mentioned above is too simplistic to predict weight-loss in general, it is deemed to match the predicted weight-loss in individuals with initial body fat above 30 kg (219). This rule may therefore be useful when predicting expected weight-loss for a given energy deficit in severely obese individuals.

We collected no specific measures of body fat and have only a limited sense of physical activity levels from our data. However, a number of physical activity questions were incorporated into the FFQ. Time spent performing light (e.g. casual walking), moderate (e.g. brisk walking) and vigorous (e.g. jogging) intensity aerobic physical activities in periods ≥10 minutes were recorded (49). Patients who performed ≥150 minutes of moderate intensity and/or ≥60 minutes per week of vigorous aerobic physical activities were considered to be physically active (221). Physical activity level was generally low at baseline in both intervention groups. Although there was a greater overall increase in the physical activity level of the lifestyle group, there was no significant difference between the intervention groups in terms of median time spent performing physical activities with moderate or vigorous intensity after 1 year (49).

With these limitations in mind, the difference of 382 kcal per day in reported mean energy intake at 1 year between the two groups could account for a difference in weight reduction of approximately 18 kg (382 kcal/day x 365 days=139430 kcal : 7700 kcal/kg≈18.1 kg). The difference in mean weight loss between the groups was, however, 30.3 kg. The estimate of 18 kg assumes a constant difference in energy-intake over a year, which is not the case. Although energy intake was measured only at baseline and 12 months in our study, one would assume that both intervention groups had a lower EI in the first few months after the start of the intervention, and that patients in the surgery group probably reduced EI substantially more than those in the lifestyle group initially after the start of the intervention. An energy intake of 566 kcal has been reported 3 months after gastric bypass surgery (222). The initial assumed very low calorie intake in the surgery group may explain the steep fall in the weight-loss curve in the first 4 months, as is illustrated in Figure 6.

The 2 year data from the Louisiana Obese Subjects Study, a randomised controlled trial comparing intensive medical intervention and usual care in primary care practice, showed that a weight loss of nearly 10% was achievable in morbidly obese patients with BMI 40-60 kg/m^2 completing the intensive medical intervention (120). Intensive lifestyle intervention at

weight loss camps in Norway and Denmark show comparable results after 1 and 4 years respectively (223;224). In the Norwegian non-randomised controlled study, 1-year weight loss after bariatric surgery was compared to three conservative treatment options: a) a residential intermittent program, b) a commercial weight loss camp and c) a hospital outpatient programme. After 1 year, patients attending the conservative treatment options reduced their weight by 13.0% (a), 14.8% (b) and 5.3% (c) respectively. In the Danish study, the mean long-term weight loss maintenance after 2 to 4 years was only 5.3%. However, a total of 28% of the participants maintained a weight loss above 10% after 4 years. In accordance with findings in other studies, subjects with the highest initial weight loss had the highest weight loss maintenance (225-228). The Danish researchers found a positive association between initial body weight and weight loss. Subjects with the highest initial BMI also had the highest weight loss. They concluded that a low calorie diet and intensive physical activity at a weight loss camp seem to be of benefit for severely obese subjects (224).

Only few studies have compared bariatric surgery and lifestyle intervention in terms of their effect on weight loss and obesity related co-morbidity. In addition to the non-randomised Norwegian study already mentioned (223), two randomised controlled trials assessing the effect of laparoscopic adjustable gastric banding and lifestyle intervention in adults and adolescents have shown that gastric banding is significantly more effective at reducing weight, giving health benefits and improving quality of life than non-surgical therapy (229;230). The dietary interventions were described in these trials, but no assessment of energy intake or dietary patterns before and/or after the intervention was given.

5.2.3 Dietary intake after intervention

Changes in macronutrients, micronutrients and food groups

Our data shows that morbidly obese patients who participated in a comprehensive lifestyle program adopted greater favourable dietary changes than patients who underwent gastric bypass surgery. Patients in the lifestyle group had lower intakes (E%) of total and saturated fat and greater intakes (g/day) of fruit and vegetables, whole grains and fibre than patients in the surgery group at 1 year follow-up. It should be noted that except for the fact that women in or study (Paper I) had a significantly lower intake of energy compared to men 1 year after surgery, (1550 versus 1878 kcal/day P=0.003), there were no significant differences in the mean percentage energy from total- or saturated fat, protein or carbohydrates between genders (data not shown).

To the best of our knowledge, no previous studies have compared dietary changes in morbidly obese individuals undergoing either conventional lifestyle intervention or gastric bypass surgery, but some have assessed the intake of selected nutrients after bariatric surgery, including gastric bypass (202;203;231-233). In Table 7a and b the dietary data from some of these studies are compared to those reported in Paper I and II in this thesis.

Table 7a. Dietary data (macronutrients) 1-8 years after gastric bypass surgery (selected studies).

Study author	Näslund et al.	Olbers et al.	Kruseman et al.	Le Roux et al.	Jeffreys et al.	Paper	Paper
Year published (Reference)	1988 (203)	2006 (231)	2010 (202)	2011 (232)	2012 (233)	I	II
Follow-up (year)	1	1	8	6	1	1	1
Participants	26 Female adults	37 Adults	80 Female adults	9 Adults	9 Adolescents	72 Adults	27 Adults
Study design	RCT[1]	RCT	Non-RCT	RCT	Non-RCT	Non-RCT	Non-RCT
Dietary assessment method	Diet. hist. + 4 day WR[2]	FFQ	4 day food record	FFQ	3 day food record	FFQ	FFQ
Suppl. included	[3]				*Yes*	*Yes*	*No*
Macronutrients	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Median (25^{th}-75^{th}p)
Energy (kcal)	1063 (399)	1225	1680 (506)	2325 (184)	1015 (182)	1650 (435)	1530 (1147-1793)
Protein E%	15 (4)		18	≈ 17	24	19 (3)	
Total fat E%	41 (7)	30.5 (5.5)	40 (8)	35 (1.9)	33	35 (6)	
SFA						14 (3)	
MUFA						12 (2)	
PUFA						7 (2)	
CHO E%	42 (7)	52.0 (6.9)	42 (9)	≈ 48	44	44 (6)	
Sugar E%						5 (4)	
Fiber (g)	7 (3)				8 (5-12)	22 (6)	
Alcohol E%		1-2				1 (2)	

[1]RCT = randomised controlled trial

[2] WR= Weighed food record

[3] Open cells denote data not addressed

Table 7b. Dietary data (micronutrients and food groups) 1-8 years after gastric bypass surgery (selected studies).

Study author	Näslund et al.	Olbers et al.	Kruseman et al.	Le Roux et al.	Jeffreys et al.	Paper	Paper
Year published (Reference)	1988 (203)	2006 (231)	2010 (202)	2011 (232)	2012 (233)	I	II
Micronutrients	Mean (SD)				Mean (95%CI)	Mean[1] (SD)	Median (25^{th}-75^{th}p)
Vit B1 (mg)	[2]					2.0 (0.9)	1.0 (0.9-1.2)
Vit B2 (mg)						2.5 (1.1)	1.2 (1.0-1.8)
Folic acid (µg)					581 (116-1045)	320 (137)	170 (150-200)
Vitamin C (mg)	32 (27)					173 (95)	100 (70-140)
Vitamin A (µg)	1100 (1100)					1381 (602)	930 (630-1250)
Vit D (µg)	3.1 (1.5)				10.2 (2.5-17.8)	9.7 (5.4)	4.4 (2.8-6.5)
Vit E (mg)					11.9 (5.3-18.6)	16.4 (7.4)	6.9 (5.4-8.4)
Vit B12 (µg)	4.1 (3.7)				168 (0.32-335)		
Ca (mg)	479 (245)				814 (491-1138)	1032 (370)	
Iron (mg)	8.5 (3.1)				25.4 (13.5-37.0)	9.6 (7-25)	
Magnesium (mg)	175 (61)					329 (86)	
Zink (mg)	4.5 (1.8)						
Food group							
Fruit /vegetables						441 (213)	
Whole grains						49 (16)	
Red meat						53 (31)	
Fish						56 (40)	
Dairy products						266 (228)	

[1] Data on micronutrients are presented in this table but not included in Paper I

[2] Open cells denotes data not addressed

Table 7a and b show that data on dietary intake after gastric bypass surgery in many studies is sparse and mainly limited to intake of energy and macronutrients. As gastric bypass surgery has become the most common surgical procedure in the Nordic countries, widening our understanding of how this treatment method may affect the intake of food groups, micronutrients and macronutrient composition is of great interest both for patients, clinicians and scientists. If the novel findings in paper I and II are verified by others then they may well have significant clinical implications. Our findings indicate that dietary quality is not optimal 1 year after gastric bypass surgery, and identifies some of the dietary improvements necessary to both prevent morbidity and optimise maintenance of weight loss more efficiently.

The dietary assessment methods used in the studies presented in table 7a are described with varying accuracy. The validated FFQ used in this thesis and by others (231;232) has the advantage of providing information on typical food intake over a long period of time, and includes information on a wide range of foods. In contrast, the dietary information based on a 3-4 day food records (202;203;233) is only valid for the days recorded. As obese individuals are frequent dieters, a dietary assessment method limited to a few days may be incapable of giving an accurate picture of habitual food intake. Food recording is a time consuming activity, and one which some patients experience as a burden, which in turn may result in drop outs. However, keeping a food records may help a patient increase their self-awareness of their eating habits, and may be regarded as an intervention in itself.

Few reports include data on the intake of micronutrients after bariatric surgery. However, in a Swedish report the intake of several micronutrients was below recommended levels (203). These findings correspond with our results in Paper II, and confirm that supplements are necessary to ensure the adequate intake of micronutrients 1 year after gastric bypass surgery.

In accordance with our findings, a number of reports indicate that macronutrient composition remains largely unchanged ≥1 year after gastric bypass surgery (202-204;231-233). It should be noted that no data on intake of saturated fat (or other fatty acids) is given in any of the studies presented in Table 7a, and comparison of fatty acid patterns with our data is therefore impossible.

An increasing number of studies suggest that although gastric bypass surgery leads to a drastic reduction in the amount of food consumed initially, the caloric intake increases during the second postoperative year, whilst surgery does not alter the patient's food choice or meal

pattern significantly, which suggests that broad dietary changes are difficult to achieve and/or sustain after gastric bypass surgery (155;204;234).

Although a randomised controlled trial comparing gastric bypass and vertical-banded gastroplasty (235) showed avoidance of fatty food and a significantly reduction in fat percentage from 34.4 to 30.5% 1 year after gastric bypass (231), the percentage energy from fat had increased to 35% 6 years after gastric bypass in a subgroup (n=9) of these patients (232). The effect of gastric bypass on fat-intake has recently been investigated in an experimental rat study where it was found that gastric bypass operated rats decreased their intake of high-fat chow while intake of low-fat chow consumption increased 10 and 200 days after surgery compared to sham control rats (P<0.001) (232). The authors hypothesised that this effect was in part due to post-ingestive effects leading to the formation of conditioned taste aversions after ingestions of larger amounts of fat mediated by increased GLP-1. However, since several studies in human beings, including ours, indicate an unaltered and unfavourable macronutrient distribution 1 year or longer after gastric bypass surgery, one could question if the reduced preference for high-fat foods identified shortly after surgery slowly attenuates, and moreover whether the fat aversion and/or intolerance gradually decreases due to a probable physical (dilatation of the gastric poach and intestine) and biochemical (gut peptide) adaptation.

It has been demonstrated that gastric bypass surgery results in better weight reduction than gastroplasty 1 and 2 years after surgery (235). After 1 year, gastric bypass patients reduced their daily energy intake by 378 kcal more than gastroplasty patients (231), while no significant difference in reported energy intake was noted 6 years after surgery (2325 versus 2857 kcal/day respectively (P=0.11)) (232). This may indicate a possible transient fat aversion result in a more pronounced energy-deficit and thereby a greater weight reduction after gastric bypass compared to gastroplasty shortly after surgery. As previously noted, a greater initial weight loss is associated with improved long-term weight loss maintenance (122;129;130). The mechanisms leading to a lower energy intake in the first year after gastric bypass surgery could be a possible explanation for the greater long-term weight loss provided by gastric bypass than conventional treatment, gastroplasty and banding (155).

Laurenius et al. recently demonstrated that gastric bypass resulted in reduced meal sizes, slower eating rates and increased habitual meal frequency (236). Eating fast is positively correlated with BMI (237). A reduced eating rate may potentially be caused by the risk of dumping syndrome and altered appetite-regulatory hormones (238). Eating slowly has been associated with a more pronounced response of the anorexigenic gut peptides PYY and

GLP-1 than eating fast, and may contribute to the initially significant weight loss (6 months) after gastric bypass surgery (239).

Previous research concerning nutritional status and surgical treatment of morbid obesity has mainly focused on micronutrient status (vitamin- and minerals) during the period of rapid weight loss, while research in the context of changes in food choice and dietary pattern after bariatric surgery is limited. Moreover, of the few studies available the design is mainly cross-sectional and the results are limited to comparing gastric bypass with gastroplasty or banding techniques. It has been reported that a decreased consumption of sweets and high-calorie beverages (which may cause dumping syndrome) may partially explain the lower energy intake and greater weight loss 2 years after gastric bypass when compared to gastroplasty (240). This is in line with findings from a cross-sectional study comparing gastric bypass with banding more than 1 year after surgery (241). As there is no data on absolute intakes (grams) in these reports, comparison to our data or food based dietary guidelines is not possible.

Based on the available literature, the dietary data presented in Paper I and Paper II give additional information about dietary intake and changes following gastric bypass surgery compared to lifestyle intervention in the treatment of the morbidly obese. In summary, intake of *micronutrients* was adequate in both the lifestyle and the surgery groups at baseline. One year after intervention start the lifestyle patients had an adequate intake of micronutrients despite reduced energy intake. The bypass patients had mostly stable or increased micronutrient intake and vitamin concentrations due to dietary supplements (Table 8).
In our work, we found that the *macronutrient* composition and food group intake in the lifestyle group improved in accordance with the Norwegian and Nordic recommendations 1 year after start of intervention, while the gastric bypass patients had a less favourable macronutrient composition compared to the lifestyle patients (Figure 3, Paper I). Moreover, the change in intake of food groups moved in a less health-promoting direction in the surgery group compared to the lifestyle group (Figure 2, Paper I). There were no significant differences in macronutrient composition or food group intake between genders after intervention in any of the intervention groups (data not shown).

In line with our own findings, data from several studies (202;203;231;233) indicate that favourable changes in macronutrient composition after bariatric surgery are difficult to achieve and/or sustain. Interestingly, data from the National Weight Control Registry (NWCR) point in the same direction. In this registry, individuals who have succeeded in losing large amounts of weight (approximately 56 kg) through either bariatric surgery or non-

surgical methods and thereafter maintained their weight loss (≥13.6 kg) for 5.5 ±7.1 years have been compared (242). Both surgical and non-surgical participants report consuming a low-calorie diet (1460 vs. 1407 kcal/d). However, compared to the non-surgical participants, the surgical ones report a less healthy lifestyle marked by greater consumption of fast food and fat, less dietary restraint and less physical activity (242).

Table 8. Intake of vitamins and minerals (including supplements), data one year after intervention start.

Nutrient	RDI[1]	Total at baseline (n=126)	Intensive Lifestyle Intervention (n=54)	Gastric Bypass Surgery (n=72)	*P*-value[2]
Vitamin A (RE)	**700** ♀ **900** ♂	1371 (975, 1889)	1386 (975, 1653)	1282 (986, 1598)	0.034
Vitamin D (µg)	**7.5**	8.2 (5.1, 12.1)	8.2 (5.1-12.3)	8.8 (6.0, 119)	0.110
Vitamin E (mg)	**8** ♀ **10** ♂	13.1 (10.0, 18.9)	13.5 (10.2, 18.9)	16.2 (12.0,19.4)	<0.001
Vitamin B1 (mg)	**1.1**♀ **1.4** ♂	1.9 (1.5, 2.5)	1.8 (1.6, 2.6)	2.1 (1.4, 2.1)	0.027
Vitamin B 2 (mg)	**1.3** ♀ **1.7** ♂	2.2 (1.7, 2.9)	2.2 (1.7, 3.0)	2.4 (1.9, 3.0)	0.004
Folate (mg)[3]	**400** ♀ **300** ♂	287 (231, 371)	287 (228, 362)	312 (231, 366)	0.049
Vitamin C (mg)	**75**	170 (122, 239)	169 (116, 239)	150 (117, 205)	0.693
Calcium (mg)	**800**	1140 (725, 1441)	1140 (796, 1468)	991 (766, 1273)	0.945
Iron (mg)[4]	**9-15** ♀ **9** ♂	13.4 (10.3, 16.8)	13.5 (10.5, 16.8)	9.6 (7.2, 24.6)	0.381
Magnesium (mg)	**280** ♀ **350** ♂	402 (329,503)	410 (336, 532)	335 (270,372)	0.021

[1] Nordic Nutrition Recommendations, 2004 (24).

[2] Mann-Whitney U-test [Data given as median (25 and 75-percentile)]

[3] Women of reproductive age are recommended an intake of at least 400 µg/day.

[4] Recommended intake for postmenopausal women is 9 mg/day.

5.3 Vitamin D deficiency in morbid obesity

Although there is growing evidence that vitamin D deficiency and obesity are related, the cause-effect relationship remains unclear (103).

Both in the comparative prospective study of 53 morbidly obese patients (Paper II) and the cross-sectional study of 2026 morbidly obese patients (Paper III), we found a high prevalence of vitamin D deficiency, despite adequate dietary intake according to the current RDI (24). The definitions of vitamin D deficiency differ in the two papers and reflect the debate over this definition. At present, there is no consensus on the optimal 25(OH)D serum concentration. Some have suggested that a serum concentration of 25(OH)D ≥75 nmol/l indicate vitamin D sufficiency and <75 nmol/l insufficiency (109), while others define vitamin D deficiency to be <50 nmol/l (106). Although the considerations concerning adequate levels vary widely from 25-100 nmol/l (109;243), most agree that 25(OH)D concentrations <50 nmol/l indicate vitamin D deficiency. This is partly based on findings that individuals who have 25(OH)D concentrations ≥50 nmol/l have no significant changes in their PTH-levels (106).

In Paper II the definition of 25(OH)D deficiency was <37 nmol/l, which is the low reference value used in Norwegian laboratories, the healthcare system and in clinical practice. In Paper III the more accepted international definition of vitamin D deficiency of 25(OH)D <50 nmol/l was used. The use of these different reference levels is the main explanation for the difference in prevalence of vitamin D deficiency in the two papers. In Paper II, 37% of the surgery group and 30% of the lifestyle group was vitamin D deficient at baseline, while in the cross-sectional study (Paper III) 50% of patients were vitamin D deficient. In the latter report, the prevalence of vitamin D deficiency was significantly higher in men (56%) than in women (47%) (P<0.001). By using the same definition of vitamin D deficiency as in Paper II (<37 nmol/l), the prevalence of deficiency was 24% for all patients, and was still significantly higher in men (28%) than women (21%) (P=0.001). As expected, we also found a high prevalence of secondary hyperparathyroidism in both men (37%) and women (33%) (P=0.054), which is in accordance with the findings of others (111).

In general, our findings support previous reports showing a high prevalence of vitamin D deficiency in morbidly obese individuals (93;110-112;117;244-246). The somewhat lower 25(OH)D levels at baseline (not significant) in the heavier surgical patients (Paper II) and the higher prevalence of inadequate vitamin D levels in men compared to women (Paper III) correspond with other findings as insufficient levels of 25(OH)D is associated with higher BMI and male gender (247). In Paper II, we reported that elevated PTH at baseline was more prevalent among patients referred to surgery (41%) compared to lifestyle intervention (17%),

which partly may be explained by the difference in BMI as the surgery patients had significantly higher BMI (46 kg/m2) than the lifestyle patients (40 kg/m^2) (*P*=0.003). The pathogenesis of hyperparathyroidism in obesity is not fully understood, and it is not completely explained by vitamin D insufficiency (248). However, it has been demonstrated that weight is a determinant of increased PTH (248), and that hyperparathyroidism in morbid obesity regresses with weight loss (249). A possible mechanism may be a direct effect of adipokines on PTH secretion, as a positive relationship between PTH and serum leptin has been shown in obesity (250). It has been suggested that leptin is a PTH secretagogue as injections of leptin in leptin-deficient ob/ob mice greatly increase PTH levels (251). Interestingly, the level of PTH, but not vitamin D, has been identified as an independent predictor of the metabolic syndrome in morbid obesity (252). One possible hypothesis is that PTH may be involved in the pathogenesis of hypertension (253). Whether the lowering of PTH has beneficial effects on metabolic syndrome or its components is, however, unclear.

Possible cause-effect relationships between obesity and vitamin D deficiency

Some of the most recent information about vitamin D status and obesity comes from studies in bariatric surgery patients (93;110;111). Both body mass index and body fat mass are shown to be inversely related to serum levels of 25(OH)D (115;116). Although the literature describing vitamin D content of fat tissue is limited, it has been suggested that low levels of circulating 25(OH)D in obese persons could be the result of an extensive sequestration in adipose tissue which reduces circulating levels (117). This notion was confirmed in a recent pilot study where Blum et al. measured the concentrations of vitamin D_3 in the fat tissue and serum of obese adults. The subjects included in this study were morbidly obese men and women (mean BMI=50.6) who were scheduled to undergo bariatric surgery. Serum vitamin D_3 and 25(OH)D was measured and abdominal subcutaneous fat tissue was collected at the time of surgery. The mean 25(OH)D concentration was 43.3 nmol/l, while mean concentration of vitamin D_3 in serum and subcutaneous fat tissue was 7.8 nmol/l and 102.8 nmol/kg respectively. Blum et al. concluded that the vitamin D_3 concentrations of serum and fat tissue were positively correlated (*r*=0.68, *P*=0.003) and consistent with fat tissue as a storage reservoir (254). However, little is known about the quantity and location of vitamin D_3 in the human body, mainly because of the absence of total carcass data. Although results from pig trials have limited generalisability for humans, they permit tentative hypotheses. Through review and reanalysis of pig trials, Heaney et al. have summarised these as follows (255):

- There is not much vitamin D (vitamin D + 25(OH)D) in the body. A total storage of 15000-27000 IU (≈375-675 µg or 970-1750 nmol), accounts for a 7-12 days reserve supply.
- 65% of total vitamin D in the body is present as vitamin D_3 and 35% as 25(OH)D.
- Nearly ¾ of vitamin D is stored in fat tissue(s), while 25(OH)D is distributed more evenly in the body, (20% in muscle, 30% in serum, 35% in fat and 15% in all other tissues).
- Weight loss does not perceptibly elevate serum 25(OH)D as the amount of vitamin D in fat is simply too small.

The mechanisms explaining the increase in serum levels of 25(OH)D after weight loss is unclear, and may include reasons other than vitamin-D release from fat tissue, although several studies report an increase in serum 25(OH)D after weight reduction. In a study of changes in 25(OH)D levels 4 and 20 weeks after a low-calorie diet-induced weight loss of 10% in obese women, Tzotzas et al. concluded that 25(OH)D levels increased significantly by 34%, and that this increase was mainly associated with improvement of insulin resistance (256). In a German study, obese children who participated in a 1-year obesity intervention program including physical exercise, behaviour therapy and nutrition education, experienced normalised PTH and 25(OH)D levels after weight loss. The authors concluded that since the elevated PTH and decreased 25(OH)D observed in obese children was normalised after weight loss, these alterations were consequences rather than causes of overweight (257). However, in contrast to the findings of Tzotzas et al. in adults, the German group saw no relationship between vitamin D and insulin sensitivity in children (257).

In our studies we have explored vitamin D deficiency and PTH levels after bariatric surgery compared to lifestyle intervention. In Paper II 30% of patients in the lifestyle group and 37% in the surgery group had levels of serum 25(OH)D under reference value (<37 nmol/L) at baseline, which was reduced to 10% and 4% at 1 year follow-up. Although one must take into consideration that more patients in the lifestyle group used vitamin supplements after 1 year than at baseline, the total intake of vitamin D did not significantly change (data not shown). It is therefore possible that the increase in serum 25(OH)D 1 year after lifestyle intervention in our patients may have been caused by weight reduction. This observation corresponds with those of Tzotza et al. (256). There is greater data on vitamin D status in morbid obesity in the context of bariatric surgery than there is in the context of lifestyle intervention. In a Scandinavian randomised controlled trial, vitamin status after two bariatric surgery procedures (gastric bypass and duodenal switch) was assessed (258). In

accordance with the results in Paper II, the gastric bypass patients increased their serum 25(OH)D-levels after 1 year. The proportion of patients using of vitamin D/calcium supplements in our study (78%) were comparable with the figures reported by Aasheim et al. (74%) (258). In our study the intake of vitamin D_3 from the diet was 4.4 µg per day while supplements additionally contributed with 35 µg (5 µg from the multivitamin/mineral pill, 20 µg from Calcigran Forte and 10 µg from fish oil capsules). In the work of Aasheim et al. no dietary data was given, but the dosage of supplements was 25 µg vitamin D_3 daily. In both trials the gastric bypass patients increased serum 25(OH)D-levels 1 year after surgery, which is probably explained by supplements and a substantial weight loss. However, in a recent report vitamin D status and secondary hyperparathyroidism were assessed 5 years after gastric bypass and duodenal switch, with the prevalence of secondary hyperparathyroidism high after both gastric bypass (40%) and duodenal switch (100%) (259). The prevalence of secondary hyperparathyroidism was high in all vitamin D categories studied (25(OH)D <50, 50-74 and ≥75 nmol/l) 5 years after surgery (both groups). Secondary hyperparathyroidism was inversely associated with serum ionised calcium, but not with vitamin D. Hewitt et al. concluded that the supplementation used (comparable to those recommended in Paper I and II) was insufficient to compensate for the impaired calcium absorption after surgery (259). They also question whether current supplementation regimens may require improvement in order to counteract the risk of bone disease in the long- term after surgery. In this assessment, it should be emphasised that studies have shown that BMI is inversely associated with increase in serum 25(OH)D in response to vitamin D supplementation, indicating a decreased response to supplementation in obese individuals (117;260). In Paper III we found no association between supplementation and vitamin D deficiency, possibly because supplements in Norway commonly only provide small amounts of vitamin D_3 (5-10 µg).

Another hypothesis explaining how obesity contributes to vitamin D deficiency suggests that the synthesis of 25(OH)D in the liver is impaired in obese individuals compared to normal weight persons. Obesity, larger waist circumference and male gender are associated with non-alcoholic fatty liver disease (NAFLD) (261;262). Targher et al. have reported that serum 25(OH)D levels were inversely associated with the severity of the liver dysfunction in biopsy-proven NAFLD patients (263). This may indicate that liver disease leads to a reduced hydroxylation of vitamin D, and thereby a decrease in circulating 25(OH)D levels. NAFLD-patients additionally had significantly higher waist circumferences than healthy controls matched for age, sex and BMI (263). Although we have no measures of liver fat or NAFLD in our patients, one may speculate that the 40% higher odds of vitamin D deficiency in men (Paper III) might partially be explained by the larger prevalence of visceral obesity and

possibly an impaired liver function among men. Alaninaminotransferase (ALAT) is considered an indirect measure of liver function. In our data, men (n=690) had significantly higher mean (SD) ALAT-levels than women (n=1335); 43 (27) vs. 30 (22) U/L (P<0.001), and there was a significant positive correlation between waist circumference and ALAT (n=2025), r=0.112, (P<0.001) (Data not presented in Paper III).

It has been proposed that obese individuals are less exposed to sunlight due to their both partaking in fewer outdoor activities and their clothing habits, which therefore leaves them more prone to vitamin D deficiency (264). In some reports, outdoor physical activity is associated with vitamin D sufficiency (265;266), while others do not find that sun exposure explains low 25(OH) levels in obese individuals (267;268). In Paper III we found no association between vitamin D deficiency and physical activity.

Whether vitamin D deficiency in obese individuals is a result of increased body clearance due to obesity-related inflammation mediated by visceral adiposity's association with inflammation has been discussed in the recent literature (269).

Despite extensive research in the vitamin D field, there remains a lack of understanding as to both the direction and the strength of any possible cause/effect relationship between low vitamin D status and obesity.

5.4 Implications for treatment

An increasing number of people undergo gastric bypass surgery. Between 2002 and 2010 approximately 10000 people have had some form of bariatric surgery in Norway, with approximately 2500 Norwegians having undergone bariatric surgery in 2012 (Jøran Hjelmesæth, personal communication).

Although gastric bypass surgery is more effective than lifestyle intervention in terms of weight reduction and alleviating obesity-related morbidities, our finding of a persistent unfavourable dietary pattern potentially counteracts other positive health effects. Improvement of dietary quality by reducing intake of total and saturated fat, increasing intake of fruit and vegetables, whole grain and fibre in accordance with current food based dietary guidelines may prevent cardiovascular disease, type-2 diabetes, several cancer forms and weight regain.

Accordingly, a stronger focus on using counselling to promote a healthy diet in the post-surgery phase and long-term follow-up might further improve the beneficial effects of bariatric surgery. Several therapeutics methods may be implemented to help patients achieve long-term healthy dietary habits, including psycho-educational intervention programmes and

motivational guidance techniques which will encourage the motivation change needed to change lifestyle behaviour.

Clinicians should be aware of the high prevalence of vitamin D deficiency in morbidly obese patients. Monitoring of vitamin D status should be undertaken routinely in the treatment of morbid obesity, with special attention paid to men. As the summer season in the Nordic countries is short and dietary sources for vitamin D are few, supplements should be prescribed when a deficiency is revealed.

5.5 Topics for further research

Bariatric surgery research has traditionally focused on maintaining a satisfactory micronutrient status during the subsequent rapid weight loss period, while trials focusing on long-term food choice and dietary pattern are rare. Further studies are needed in order to explore the effects of combined lifestyle interventions (including dietary advice), physical activity and behavioural modifications on dietary patterns in the follow up period after bariatric surgery. Randomised clinical trials in gastric bypass surgery patients comparing the effects of usual care treatment, intensive lifestyle and behavioural modification-programmes on risk factors for cardiovascular disease, type-2 diabetes (blood pressure, cholesterol, triglycerides, blood glucose, arterial stiffness) and weight regain are also needed.

We evaluated the 1-year effect of a predefined supplementation regimen after gastric-bypass surgery. However, further prospective investigations exploring the long-term effects on vitamin status using current supplement regimen after bariatric surgery should be undertaken. In addition, it might be hypothesised that a normalisation of vitamin status before surgery may improve long-term vitamin status. This hypothesis may be tested in randomised controlled trials comparing the effect of various combinations of pre- and post-surgery supplementation regimens on long-term vitamin status.

Research is also needed in order to investigate the complex factors underlying the association between obesity and low circulating 25(OH)D levels. Due to extensive differences in UV-radiation and dietary habits in different parts of the world, treatment advices should be site-adapted. In view of our findings, randomised controlled trials of obese men and women exploring the dose-response effect of vitamin D supplementation during different seasons in the Nordic countries might be of particular interest.

6 CONCLUSIONS

Compared with lifestyle intervention, gastric bypass surgery was associated with less favourable dietary changes among morbidly obese patients as measured by macronutrient composition and food group choices at 1 year after start of intervention. Controlled clinical trials are needed to test the hypothesis that counselling with the aim of promoting a healthy diet after gastric bypass surgery is associated with long-term healthy eating habits and lower incidence of obesity related co-morbidities.

One year after surgery, gastric bypass patients taking a standardised set of post-operative supplements had mostly stable or increased vitamin concentrations compared to baseline values and the corresponding changes in a control group undergoing lifestyle intervention. As dietary intake of several vitamins was inadequate 1 year after gastric bypass surgery, the supplements prescribed probably ensured satisfactory vitamin concentrations 1 year post surgery.

Morbidly obese Norwegian men seeking weight loss treatment had significantly higher odds of vitamin D deficiency than women (adjusted odds ratio=1.39, 95% CI:1.10-1.76). Monitoring of 25(OH)D levels should take into account not only obesity and seasonal variations, but also gender.

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8 APPENDIX

1. Hvor mye brød pleier du å spise?

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

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

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

2. Hva pleier du å smøre på brødet?

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

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

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

En porsjonspakning på 12 g rekker til antall skiver

1 ☐
2 ☐
3 ☐
4 ☐
5 ☐
6 eller flere ☐

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

(1 glass = 1,5 dl)

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

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

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5. Påleggssorter

Bruk sum skiver pr. uke fra spørsmål 1.

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

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

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

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

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

6. Egg

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

7. Frokostgryn, grøt og yoghurt

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

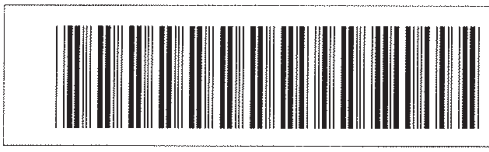
	Gang pr. måned					eller	Gang pr. uke					Mengde pr. gang			
	0	<1	1	2	3	1	2-3	4-5	6-7	8+		1	1 1/2	2	3+
Havregryn	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
4-korn	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Müsli, søtet (müsli, Solfrokost o.l.)	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	(dl)	☐	☐	☐	☐
Müsli, usøtet (Go´Dag, Fruktmüsli)	☐	☐	☐	☐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

8. Kaffe og te

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

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

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



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9. Andre drikker

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

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

10. Middagsretter

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

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

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

11. Poteter, ris, spagetti, grønnsaker

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

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

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

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5+ ☐

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

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

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

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

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

14. Desserter, kaker, godteri

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

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

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

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

Multipreparater	Hele året	Bare vinter-halvåret	Gang pr. uke 0	<1	1	2-3	4-5	6-7		Mengde pr. gang 1	2	3	4+
Sanasol	☐	☐	☐	☐	☐	☐	☐	☐	bs	☐	☐	☐	☐
Biovit	☐	☐	☐	☐	☐	☐	☐	☐	bs	☐	☐	☐	☐
Vitaplex	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Kostpluss	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Vitamineral	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

Hvis annet, hvilket?.....

Jernpreparater			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Ferro C	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Hemofer	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Duroferon, Duretter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

Hvis annet, hvilket?.....

Annet			0	<1	1	2-3	4-5	6-7		1	2	3	4+
B-vitaminer	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
C-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
D-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
E-vitamin	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Folat (folsyre)	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
			0	<1	1	2-3	4-5	6-7		1	2	3	4+
Kalktabletter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Fluortabletter	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐
Annet	☐	☐	☐	☐	☐	☐	☐	☐	tablett	☐	☐	☐	☐

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

16. Medisiner

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

☐ Ja ☐ Nei

HVIS JA, fyll ut:

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

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

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

HVIS JA: Hvor ofte bruker du avføringsmidler?

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

Hvor ofte har du avføring?

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

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

17. Fysisk aktivitet

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

☐ Nei ☐ Ja, angi grunn

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

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

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

18. Eventuelle andre matvarer

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

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

Tusen takk for innsatsen!

I

II

III

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ORIGINAL ARTICLE

Impact of gender on vitamin D deficiency in morbidly obese patients: a cross-sectional study

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Background/Objective: Obesity is associated with vitamin D deficiency (25-hydroxyvitamin D (25(OH)D) <50 nmol/l). We aimed to examine the effect of gender on vitamin D status in severe obesity.
Subjects/Methods: Cross-sectional study of 2026 morbidly obese patients examined consecutively at a tertiary care centre between November 2005 and June 2010. Serum 25(OH)D concentration and use of vitamin D supplements were registered in all patients. Total vitamin D intake (μg/day) was assessed in a subgroup of 154 patients using a validated food frequency questionnaire.
Results: The male ($n=690$) and female ($n=1336$) patients had a mean (s.d.) age of 45.0 (12.1) years and 42.2 (12.2) years ($P<0.001$), body mass index (BMI) of 44.6 (6.0) kg/m^2 and 44.3 (5.9) kg/m^2 ($P=0.30$) and waist circumference (WC) of 140 (13) cm and 127 (13) cm ($P<0.001$), respectively. Male patients had significantly lower mean 25(OH)D concentrations than female patients 50.0 (22.0) nmol/l versus 53.6 (22.4) nmol/l ($P=0.001$) and a higher rate of vitamin D deficiency (56% versus 47%; $P<0.001$). Obese men had significantly higher odds of vitamin D deficiency than women (odds ratio $=1.41$; 95% confidence interval: 1.17–1.70, $P<0.001$), also after adjustment for season, age, current smoking, intake of vitamin D supplements, BMI and WC (odds ratio $=1.39$; 95% confidence interval: 1.10–1.76).
Conclusions: Morbidly obese Norwegian men seeking weight loss treatment have significantly higher odds of vitamin D deficiency than women. Monitoring of 25(OH)D concentrations in obese patients should therefore take gender into account.
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Keywords: vitamin D (25(OH)D) deficiency; morbid obesity; gender

Introduction

Vitamin D is not only essential for calcium metabolism and bone mineralization but may also have a role in the maintenance of neuromuscular function and prevention of coronary heart disease (Zittermann and Koerfer, 2008; Giovannucci, 2009), some forms of cancer (Bertone-Johnson, 2009; Chiang and Chen, 2009) and other chronic diseases (Holick, 2007; Peterlik and Cross, 2009). Obesity is associated with increased risk of vitamin D deficiency. The inverse relationship between obesity and serum vitamin D concentrations may have several explanations, including deposition of vitamin D in body fat compartments, reduced release of vitamin D into systemic circulation and low exposure to sun light (Wortsman *et al.*, 2000). Both subcutaneous and visceral adiposity are associated with low vitamin D concentrations (Cheng *et al.*, 2010).

Morbid obesity (body mass index (BMI) $\geqslant 40$ kg/m^2 or BMI $\geqslant 35$ kg/m^2 with at least one obesity related comorbidity) is associated with a two- to threefold increased morbidity and mortality (Must *et al.*, 1999; Flegal *et al.*, 2005; Berrington de Gonzalez *et al.*, 2010). In all, 5% of the United States population and 2% of the Norwegian

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population can be classified as either morbidly or extremely obese (BMI $\geqslant$ 40 kg/m^2; Ogden *et al*., 2006; Graff-Iversen *et al*., 2007). Globally, extreme obesity is more prevalent among women than men, with up to 70% of extremely obese persons being women (Ogden *et al*., 2006). Women have relatively more body fat than men and store more fat in the gluteal–femoral region, while men typically store more fat in the visceral (abdominal) depot (Blaak, 2001; Hofso *et al*., 2009a). Some studies have found a higher prevalence of vitamin D deficiency among men than women (Aasheim *et al*., 2008; Lagunova *et al*., 2009). As vitamin D is a fat soluble vitamin that may potentially be sequestrated in adipose tissue (Wortsman *et al*., 2000), one could hypothesize that a gender difference in the prevalence of vitamin D deficiency is related to differences in the amount of body fat and/or its distribution. To address this hypothesis, we analyzed the effect of gender on vitamin D status in a large cohort of morbidly obese Norwegian patients. In addition, we explored whether a possible gender based difference in vitamin D status might be explained by variations in overall (BMI) and/or abdominal (waist circumference (WC)) obesity.

Subjects and methods

Study population, design and setting

The Morbid Obesity Centre in Vestfold is a public tertiary care centre, which serves approximately one million inhabitants in southern Norway. A total of 2140 consecutive morbidly obese patients who attended the Morbid Obesity Centre between November 2005 and June 2010 were considered for inclusion in this cross-sectional study. We excluded 39 patients with BMI $<$ 35 kg/m^2 and 75 patients because of missing measurements for either 25-hydroxyvitamin D (25(OH)D) ($n = 48$), BMI ($n = 11$) or both ($n = 16$). The remaining 2026 patients were included in the analysis. In addition, a subgroup of 154 patients (Hofso *et al*., 2009b) examined between December 2005 and May 2006 was evaluated in order to assess total vitamin D intake and macronutrient composition. All patients gave written consent before enrollment and the study was approved by the Regional Committee for Medical Research Ethics and conducted in accordance with the Declaration of Helsinki (World Medical Association, 1997).

Variables

The main outcome variables were the prevalence of vitamin D deficiency (serum concentration of 25(OH)D $<$ 50 nmol/l) and serum 25(OH)D concentration. Explanatory variables were gender, age, season of blood sampling (winter (1 November through till 28 February) or summer (1 March through till 31 October)), intake of vitamin D supplements, total vitamin D intake (in a subgroup analysis, see below), current smoking, central obesity (WC) and overall obesity (BMI).

Physical examination

All patients were examined by a physician at their first visit to the centre. Demographic data, medical history, smoking habit, physical activity level and intake of vitamin D containing supplements were recorded using standardized forms. Weight and height were measured with patients wearing light clothing and no shoes. Waist, hip and neck circumferences were measured with a tape measure to the nearest cm. Waist and hip circumference were measured with the patient standing; at the midpoint between the lowest rib margin and the iliac crest, and at the level of the major trochanter, respectively.

Definitions

Patients who had a history of type 2 diabetes or a fasting serum glucose concentration $\geqslant$ 7 mmol/l were classified as having type 2 diabetes (American Diabetes Association, 2009).

Ischemic heart disease was defined as a history of percutaneous coronary intervention, coronary artery bypass graft surgery or myocardial infarction.

Vitamin D deficiency was defined as serum 25(OH)D $<$ 50 nmol/l ($<$ 20 ng/ml; Bischoff-Ferrari *et al*., 2006, Holick, 2007). Elevated C-reactive protein concentration was defined as fasting C-reactive protein $\geqslant$ 7 mg/l, which was the lowest detection limit for the essay used.

Secondary hyperparathyroidism was diagnosed in patients with a serum parathyroid hormone concentration $>$ 6.9 pmol/l and concomitant serum calcium $<$ 2.54 mmol/l (upper limits of reference ranges).

Intake of vitamin D supplements was defined as daily intake of supplements containing $\geqslant$ 5 μg vitamin D (cod liver oil, fish oil capsules, multivitamin supplements or pure vitamin D supplements).

Data on physical activity was available in 1451 consecutive patients examined from May 2007 until June 2010. Patients were classified as physically active if they conducted $\geqslant$ 60 min of vigorous intensity aerobic physical activity per week (Kurtze *et al*., 2007).

In Northern latitudes, ultraviolet B radiation varies with season. During the winter season ultraviolet B radiation is insufficient for vitamin D to be synthesized in the skin. Patients were recruited from Southern Norway (58–60°N), where solar exposure and ultraviolet B radiation is low during winter.

Laboratory analyses

Blood samples were obtained after an overnight fast. Serum 25(OH)D was measured at the Hormone Laboratory, Oslo University Hospital by radioimmunoassay (DiaSorin, Stillwater, MN, USA). The interassay coefficient of variation for 25(OH)D was 14%. C-reactive protein was analyzed using dry reagent slide technology on the Vitros 950 Analyzer until November 2006 and thereafter using Vitros

FS 5.1 (Ortho-Clinical Diagnostics, New York, NY, USA). Intact parathyroid hormone was essayed using an electro-chemiluminescence immunoassay on the Elecsys 2010 (Roche Diagnostics GmbH, Mannheim, Germany; Hjelmesaeth *et al*., 2009).

Dietary data
Vitamin D intake was estimated in a subgroup of 154 patients who participated in a clinical intervention study (ClinicalTrials.gov:. NCT00273104; Hofso *et al*., 2009b) using a validated food frequency questionnaire (Nes *et al*., 1992; Solvoll *et al*., 1993; Andersen *et al*., 1996; Andersen *et al*., 1999). The food frequency questionnaire is designed to measure the habitual food intake of the adult population in Norway and is suitable for estimating the intake of a variety of macro- and micronutrients, including intake from dietary supplements (Nes *et al*., 1992). The food frequency questionnaire was completed in structured dietary interviews conducted by registered dieticians, with patients asked to describe their dietary habits during the last year. Questionnaires were scanned (Teleform 10.0; Cambridge, UK) and the daily intake of foods, energy and nutrients were calculated using computer software (KBS 6.0; University of Oslo) based on data from the Norwegian food composition table (National Nutrition Council Norwegian Food Safety Authority, 1995).

Calculations and equations
To identify individuals underreporting their energy intake (EI), we calculated cutoff levels for acceptable reported EI according to Blacks equations and practical guidelines (Black, 2000a, b). Basal metabolic rate was estimated with the Mifflin–St Jeor equations (Mifflin *et al*., 1990), which is deemed to be the most reliable method for estimating basal metabolic rate in both non-obese and obese individuals (Frankenfield *et al*., 2005). We assumed a physical activity level 1.56 for women and 1.55 for men, in accordance with the Food and Agriculture Organization of the United Nations (FAO)/World Health Organization/United Nations University (UNU) 1985 values of low activity level for each gender. Men and women with EI:basal metabolic rate <1.10 and <1.11, respectively, were classified as underreporters.

Statistical analysis
Data are given as either mean (s.d.; normally distributed data), median (25th–75th percentile; non-normally distributed continuous data) or proportion (%) unless otherwise stated. Differences between groups were analyzed using independent samples *t*-test, Mann–Whitney *U*-test (continuous data) or Fisher's exact test (categorical data). Multiple logistic regression with predefined explanatory variables was used to assess the likelihood of insufficient vitamin D concentration (yes/no). Hosmer–Lemeshow test was used to assess the adequacy of the fit of the logistic regression models.

We fitted four separate logistic regression models. In model 1, gender was entered (women = reference) as the sole explanatory variable in a univariate (unadjusted) logistic regression analysis with insufficient vitamin D concentration (yes/no) as the dependent variable. In model 2, we adjusted for well-known confounding factors, such as season of blood sampling, age, current smoking (Brot *et al*., 1999) and vitamin D supplement. To address the possible modifying effects of overall obesity, in model 3, we further adjusted for BMI. In model 4, a final adjustment was made for WC. Interaction terms between gender and the other explanatory variables were included and tested. A 5% statistical significance level was chosen. The analyses were implemented in SPSS 16.0 (SPSS, Chicago, IL, USA).

Results

Characteristics
The characteristics of the 2026 morbidly obese patients (66% women) are shown in Table 1. Men were on average 2.8 years older, 21 kg heavier and had 13 cm wider WC than women ($P<0.001$ for all). The prevalence of type 2 diabetes and coronary artery disease was higher among men than women, whereas ethnicity, season of blood sampling, BMI and physical activity did not differ significantly between genders. Mean 25(OH)D concentrations were approximately 4 nmol/l lower in men than in women ($P=0.001$).

Vitamin D deficiency—gender differences
Overall, about half of the patients had vitamin D deficiency. In addition, vitamin D deficiency was more prevalent in men than in women, 56% versus 47% ($P<0.001$). This gender difference seemed to be most pronounced in the winter season, but the difference was also statistically significant in the summer season (Figure 1).

Gender differences in 25(OH)D concentrations according to season
Men had significantly lower 25(OH)D concentrations than women during the winter season, mean (s.d.) 45.3 (17.8) nmol/l versus 51.6 (22.4) nmol/l ($P<0.001$), whereas there was no difference in the summer season, mean 53.0 (23.9) nmol/l versus 54.8 (22.3) nmol/l, respectively ($P=0.21$). Both men ($P<0.001$) and women ($P=0.009$) had higher 25(OH)D concentrations during the summer season than the winter season. Figure 2 shows the mean vitamin D concentrations in men and women month by month.

Characteristics of participants in the dietary survey
A subgroup of 154 subjects (112 women) was included in the dietary survey. Compared with the remaining 1872 patients in the full study population, fewer women in the dietary survey group had serum 25(OH)D measurements performed during the summer season: 49% versus 64% ($P=0.001$). There were no significant differences between

Table 1 Characteristics of morbidly obese men and women

	Total (n = *2026*)	*Men* (n = *690*)	*Women* (n = *1336*)	P[a]
Age (years)	43.1 (12.2)[b]	45.0 (12.1)	42.2 (12.2)	<0.001
Caucasian	1960 (97%)[c]	672 (98%)	1288 (97%)	0.660
Current smoker	535 (26%)	140 (20%)	395 (30%)	<0.001
Vitamin D supplement	231 (11%)	65 (9%)	166 (12%)	0.046
Winter season (November through till February)	762 (38%)	267 (39%)	495 (37%)	0.468
Anthropometric measures				
Weight (kg)	131 (22)	145 (22)	124 (18)	<0.001
Height (cm)	172 (9)	180 (7)	167 (7)	<0.001
BMI (kg/m^2)	44.4 (5.9)	44.6 (6.0)	44.3 (5.9)	0.302
Waist (cm)	131 (14)	140 (13)	127 (13)	<0.001
Hip (cm)	133 (12)	130 (12)	135 (12)	<0.001
Waist-to-hip ratio	0.99 (0.1)	1.08 (0.08)	0.94 (0.08)	<0.001
Physically active[d]	458 (32%)	165 (32%)	293 (31%)	0.723
Co-morbidity				
Type 2 diabetes	499 (25%)	233 (34%)	266 (20%)	<0.001
Coronary artery disease	91 (5%)	69 (10%)	22 (2%)	<0.001
Biomarkers				
25-hydroxyvitamin D (nmol/l)	52.4 (22.3)	50.0 (22.0)	53.6 (22.4)	0.001
Vitamin D deficiency	1019 (50%)	386 (56%)	633 (47%)	<0.001
PTH (pmol/l)	6.7 (3.8)	7.1 (4.8)	6.5 (3.2)	0.003
Secondary hyperparathyroidism	691 (34%)	255 (37%)	436 (33%)	0.054
Insulin, fasting (pmol/l)	127.1 (112.6)	144.0 (99.6)	118.4 (117.9)	<0.001
CRP (pg/ml)	10.7 (11)	9.3 (12.9)	11.5 (9.8)	<0.001
CRP⩾7 (pg/ml)	1308 (65%)	378 (55%)	930 (70%)	<0.001

Abbreviations: BMI, body mass index; CRP, C-reactive protein; PTH, parathyroid hormone.
[a]Independent samples *t*-test or Fisher's exact test where appropriate.
[b]Data given as mean (s.d.; all such values).
[c]Number (%; all such values).
[d]⩾60 min of vigorous intensity aerobic physical activity/week ($n = 1451$).

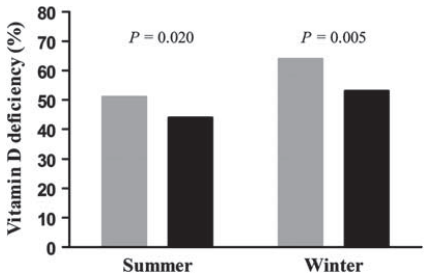

Figure 1 Gender differences in the prevalence of vitamin D deficiency (25(OH)D <50 nmol/l) according to season. Gray columns, men; black columns, women.

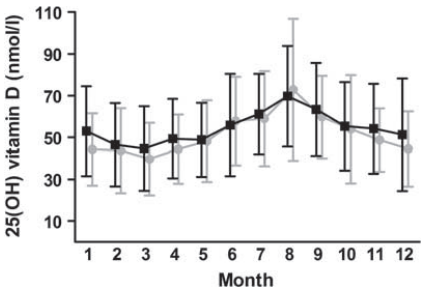

Figure 2 Mean (s.d.) vitamin D concentrations in morbidly obese men and women (*y*-axis) according to month of sampling (*x*-axis; 1 denotes January; 2, February; 3, March; 4, April and so on) Grey filled circles, men; black filled squares, women.

the two study populations with respect to age, BMI, WC, smoking habit or intake of vitamin D-containing supplements (data not shown).

Macronutrient composition and gender differences

Men tended to report higher EI than women ($P = 0.056$), but the percentage energy distribution of macronutrients did not differ significantly between genders (Table 2). Except for protein and alcohol, where men had a significantly higher absolute intake than women, 17 g higher protein ($P = 0.003$) and 1 g higher ($P = 0.018$) alcohol intake, there were no significant gender differences in terms of the absolute intake of macronutrients.

Both men and women had a higher median percentage EI from total and saturated fat, and lower median percentage

Table 2 Macronutrient and vitamin D intake in morbidly obese men and women

Nutrient	*RDI*[a]	*Total* (n = *154*)	*Men* (n = *42*)	*Women* (n = *112*)	P[b]
Energy (MJ)	9.2–11.8[c]	11.1 (8.5–13.9)[d]	11.9 (9–16.7)	10.9 (8.4–13.6)	0.056
Energy (kcal)		2647 (2043–3316)	2854 (2158–3982)	2603 (2011–3258)	0.056
Protein E%	10–20	16 (15–18)	16 (14–20)	16 (15–18)	0.897
Fat E%	<30	37 (34–41)	37 (32–42)	37 (35–41)	0.609
SFA E%	<10	15 (13–16)	14 (12–16)	15 (3–16)	0.370
MUFA E%	10–15	12 (11–14)	13 (11–14)	12 (11–14)	0.942
PUFA E%	5–10	7 (6–9)	7 (6–9)	7 (6–9)	0.727
Carbohydrate E%	50–60	45 (41–49)	45 (41–49)	45 (42–48)	0.897
Fibre (g)	25–35	27.3 (22–35)	30 (24–37)	26 (22–34)	0.207
Sugar E%	<10	6 (3–10)	5 (2–10)	6 (3–10)	0.670
Alcohol E%	<5[e]	0.3 (0–1)	0.4 (0.1–1)	0.2 (0–1)	0.062
Vitamin D (μg)	7.5	8.4 (5–12)	9.7 (5.3–15.8)	8.2 (4.7–11.3)	0.073

Abbreviations: E%, energy percentage; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; RDI, recommended dietary intake; SFA, saturated fatty acids.
[a]Nordic Nutrition Recommendations: NNR 2004 (Nordic Council of Ministers, 2004).
[b]Difference between men and women, Mann–Whitney *U*-test.
[c]Individual mean energy intake depends on several variables, such as gender, age and physical activity level. For normal weight individuals (body mass index 18.5–25) and sedentary men and women aged 31–60 years, energy intake reference is 11.8 MJ/day and 9.2 MJ/day, respectively. Exact reference value for energy intake is not possible to determine.
[d]Median; 25 and 75th percentile in parantheses (all such values).
[e]<10 g alcohol/day for women and <20 g/day for men.

Table 3 Odds of morbidly obese patients having 25-hydoxyvitamin D deficiency

Explanatory variables	*Model 1*		*Model 2*		*Model 3*		*Model 4*	
	OR (95% CI)	P	*OR (95% CI)*	P	*OR (95% CI)*	P	*OR (95% CI)*	P
Gender	1.41 (1.17–1.70)	<0.001	1.52 (1.26–1.84)	<0.001	1.52 (1.25–1.84)	<0.001	1.39 (1.10–1.76)	0.006
Season			1.52 (1.27–1.83)	<0.001	1.54 (1.27–1.85)	<0.001	1.50 (1.24–1.81)	<0.001
Age			0.98 (0.98–0.99)	<0.001	0.99 (0.98–0.99)	<0.001	0.99 (0.98–0.99)	<0.001
Current smoking			1.34 (1.09–1.64)	0.005	1.45 (1.17–1.78)	0.001	1.42 (1.15–1.75)	0.001
Vitamin D supplement			0.79 (0.60–1.05)	0.110	0.82 (0.61–1.10)	0.164	0.80 (0.60–1.08)	0.142
BMI					1.07 (1.06–1.09)	<0.001	1.06 (1.04–1.09)	<0.001
Waist							1.01 (1.00–1.02)	0.186

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratios.

intake of carbohydrates, than recommended in the Nordic Nutrition Recommendations: NNR 2004 (Nordic Council of Ministers, 2004). According to the lower cutoff level for plausible EI, 33 (30%) women and 16 (38%) men under-reported their EIs, with no significant difference between genders ($P=0.41$). Mean (s.d.) physical activity level values for women and men were 1.39 (0.51) and 1.35 (0.53), respectively ($P=0.64$).

Vitamin D intake

Men tended to have a higher total intake of vitamin D than women ($P=0.073$; Table 2). Median (25–75th percentile) vitamin D intake tended to be higher during the winter in men 10.7 (7.0–16.9) μg versus 6.8 (4.5–15.4) μg ($P=0.08$), but not in women: 9.3 (5.5–12.5) μg versus 7.0 (4.4–10.3) μg ($P=0.45$). According to the Nordic Nutrition Recommendations: NNR 2004 (Nordic Council of Ministers, 2004), both genders had low median intakes of vitamin D during the summer, whereas their vitamin D intakes were adequate during the winter.

Odds of having vitamin D deficiency

In unadjusted logistic regression (model 1), obese men had significantly higher odds of vitamin D deficiency than women (odds ratio = 1.41; (95% confidence interval: 1.17–1.70; Table 3). The association between male gender and vitamin D deficiency was somewhat strengthened when adjusting for season, age, current smoking and vitamin D supplements (model 2). Further adjustment for BMI (model 3) did not influence the odds of vitamin D deficiency, whereas the addition of WC to the model slightly attenuated the relationship between male gender and vitamin D deficiency (odds ratio = 1.39; 95% confidence interval: 1.10–1.76). Although the difference between genders in prevalence of vitamin D deficiency seemed more pronounced during the winter than summer season, the interaction term between gender and season was not significant ($P=0.45$). In addition, no significant interactions were found between gender and other explanatory variables: age ($P=0.18$), current smoking ($P=0.36$), vitamin D supplementation ($P=0.24$), waist circumference ($P=0.95$) and BMI ($P=0.33$).

Discussion

The main finding in this cross-sectional study of 2026 morbidly obese patients is that obese men had approximately 40% higher adjusted odds of vitamin D deficiency than obese women.

It is well established that obesity is associated with vitamin D insufficiency. Our data confirm previous reports showing a high prevalence of vitamin D insufficiency in morbidly obese subjects (Carlin *et al*., 2006; Aasheim *et al*., 2008; Goldner *et al*., 2008; Lagunova *et al*., 2009). Our study has demonstrated that men had higher odds of vitamin D deficiency even after adjustment for the confounders season, age, current smoking and vitamin D supplements (model 2). The fact that further adjustment for BMI (model 3) did not change this relationship suggests that the association between male gender and vitamin D deficiency could not explained by the degree of overall obesity. Conversely, further adjustment for WC (model 4) slightly attenuated the relationship, indicating that gender differences in abdominal adiposity could potentially influence the association between male gender and vitamin D deficiency. Consistent with this, previous studies have indicated that vitamin D insufficiency in obese individuals is caused by decreased bioavailability secondary to deposition of vitamin D in body fat compartments (Wortsman *et al*., 2000), especially in visceral fat stores (Cheng *et al*., 2010).

Seasonal variation, vitamin D intake and gender

Our results confirm those from previous Nordic studies showing a significant drop in serum concentrations of 25(OH)D during the winter season in both genders (Vik *et al*., 1980; Jorde *et al*., 2010). Interestingly, men had significantly lower vitamin D concentrations than women in the winter season, but not in the summer. A recent Norwegian study of both lean and morbidly obese persons also found that men had larger seasonal variation of vitamin D concentration than women, in particular young non-obese men (Lagunova *et al*., 2009). Similar findings have been reported from New Zealand and Brazil, where middle aged and older men had a larger reduction in 25(OH)D during the winter season than women (Bolland *et al*., 2007; Maeda *et al*., 2010).

In the Nordic Nutrition Recommendations: NNR 2004 (Nordic Council of Ministers, 2004), a vitamin D intake of $\geqslant 7.5\,\mu g$/day is recommended. Little is known about the dietary vitamin D intake of morbidly obese men and women. The median vitamin D intake in our sub-population of 8.4 μg/day was normal according to current Nordic recommendations. A recent Spanish study also reported adequate vitamin D intake according to regional recommendations in overweight and moderately obese (BMI 24–35) women (Rodriguez-Rodriguez *et al*., 2009). Previous studies have shown that obese subjects tend to underreport EIs (Heitmann and Lissner, 1995; Johansson *et al*., 1998), especially women (Johansson *et al*., 1998). We estimated that 30% of women and 38% of men underreported their EIs. One British study found that women were more likely than men to report avoiding high-fat foods (Wardle *et al*., 2004). Despite an expected underreporting of fat, especially in women, the total percentage fat intake was higher than recommended (37% versus $<30\%$) for both genders. Probably as a consequence of the high fat intake, the dietary intake of the fat soluble vitamin D was adequate for both genders in our study according to Nordic recommended daily intake (Nordic Council of Ministers, 2004).

Somewhat surprisingly, no association was observed between vitamin D deficiency and supplement intake. This might have several explanations, including sequestration of vitamin D in body fat compartments. The latter notion is supported by a study showing that BMI was inversely correlated with peak serum vitamin D_2 concentrations after a high dose of oral intake of vitamin D_2 (50 000 IU, 1.25 mg; $r=-0.56$, $P=0.007$; Wortsman *et al*., 2000). Our results are therefore consistent with the hypothesis that vitamin D supplementation in obese persons yield smaller increases in vitamin D concentrations (Wortsman *et al*., 2000).

Sun exposure and physical activity

It has been speculated that the inadequate vitamin D status associated with obesity is mediated in part by less ultraviolet radiation from sun exposure (Harris and Dawson-Hughes, 2007). Solarium usage could be one possible explanation of the higher 25(OH)D concentrations in women during winter. However, morbidly obese women may find the usage of solarium difficult because of the narrow space often provided. Solarium usage was not registered in our study.

Physical activity has been identified as a contributor to adequate vitamin D concentration in some (Scragg and Camargo, 2008; Brock *et al*., 2010a; Brock *et al*., 2010b), but not all (Barake *et al*., 2010; Cheng *et al*., 2010), reports. The conflicting results may be explained by varying study conditions, including differences in latitudes, age and physical activity measurements. In our study, men and women reported similar physical activity levels and we found no association between low vitamin D status and physical activity.

Study limitations

Strengths of our study include the prospective collection of data in a large, homogenous population of morbidly obese individuals and adjustment for possible confounders including season of blood sampling, age, current smoking, use of vitamin D supplements, BMI and waist circumference. Cross-sectional studies are inherently limited in that they cannot establish cause and effect relationships, and our results may not necessarily be valid in non-white populations. Performing the biochemical analyses on a routine basis throughout the study period may have limited the internal validity of the study, as this increases the risk of drift of laboratory assays.

Conclusions

Morbidly obese Norwegian men had significantly higher odds of vitamin D deficiency than obese Norwegian women. Therefore, future guidelines for monitoring 25(OH)D concentrations should take into account not only obesity and seasonal variations, but also gender. Clinicians should be especially aware of the high prevalence of vitamin D deficiency in morbidly obese men.

Vitamin D intake was comparable between men and women and could therefore not explain the difference in prevalence of vitamin D deficiency between genders. Randomized controlled trials of obese men and women exploring the dose–response effect of vitamin D supplementation during different seasons are highly warranted.

Conflict of interest

The authors declare no conflict of interest.

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