Individuals with morbid obesity in Reykjalundur: Dropout and success in treatment

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Thesis for the degree of Master of Science in Human Nutrition Faculty of Food Science and Nutrition, School of Health Sciences University of Iceland

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Einstaklingar með alvarlega offitu á Reykjalundi: Brottfall og árangur meðferðar

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ÁGRIP

Bakgrunnur og markmið: Fáar rannsóknir hafa verið gerðar á því hversu mismunandi niðurstöður mælinga á líkamssamsetningu, blóði og sálfræðilegum þáttum eru hjá einstaklingum með alvarlega offitu, sem taka þátt í mismunandi meðferðarleiðum, og hvað það er sem einkennir þá einstaklinga sem hætta í meðferð. Markmið þessarar rannsóknar var að skoða brottfall og meðferðarleið, þ.e. magahjáveituaðgerð og offitumeðferð, hjá einstaklingum með alvarlega offitu á Reykjalundi, endurhæfingarmiðstöð sem og að skoða þyngdartap í meðferðinni.

Aðferðir: Gögn frá konum með alvarlega offitu, sem komu í forskoðun á Offitu- og næringarsvið Reykjalundar milli 2007 og 2009, voru notuð. Tiltæk gögn voru líkamsmælingar, niðurstöður blóðmælinga, niðurstöður úr sálfræðimati og lyfjanotkun. Gögnum um brottfall og hvort einstaklingar fóru í magahjáveituaðgerð eftir offitumeðferðina, var einnig safnað, sem og upplýsingum um þyngdartap í meðferðinni. Inntökuskilyrði voru að þátttakendur væru á aldrinum 18-65 ára, með líkamsþyngdarstuðul (LÞS) > 35 kg/m^2 og að áfengis- og fíkniefnasjúklingar væru óvirkir.

Niðurstöður: Af þeim 292 konum sem komu í forskoðun á Reykjalundi hættu 113 (39%) í meðferðinni, 100 (34%) kláruðu dagdeildarmeðferð og 79 (27%) kláruðu dagdeildarmeðferð og fóru í kjölfarið í magahjáveituaðgerð. Samkvæmt fjölþáttalíkani voru einstaklingar með alvarlegt þunglyndi 2,4 sinnum líklegri (P=0,01) til að hætta í meðferð en einstaklingar með miðlungsalvarlegt eða ekkert þunglyndi. Einstaklingar með LÞS milli 40-50 kg/m^2 voru þrisvar sinnum líklegri (P=0,02) til að gangast undir magahjáveituaðgerð en þeir sem voru með LÞS <40 kg/m^2 og þeir sem voru með LÞS ≥50 kg/m^2 voru um tíu sinnum líklegri til að gangast undir aðgerð (P<0,001). Einstaklingar sem gengust undir aðgerð voru einnig með fleiri áhættuþætti hjarta- og æðasjúkdóma. Meðal þyngdartap á mánuði meðan á meðferð stóð var svipað hjá öllum hópum, óháð meðferðarleið eða fylgikvillum en einstaklingar með þunglyndi léttust minna en aðrir.

Ályktun: Mjög stór hluti einstaklinga með alvarlega offitu hætti í meðferð á Reykjalundi sem fyrst og fremst mátti rekja til einkenna þunglyndis. Einstaklingar með alvarlega offitu, sem voru í hæsta flokki LÞS (≥50,0 kg/m^2), voru tíu sinnum líklegri til að gangast undir magahjáveituaðgerð miðað við þá sem voru í lægsta flokki LÞS (<40,0 kg/m^2). Þyngdartap var svipað í öllum hópum.

ABSTRACT

Background and aims: A limited amount of studies have examined how morbidly obese individuals who participate in different treatments differ in relation to anthropometrical measurements, blood measurements and psychological characteristics and what characterizes those who drop out of weight loss treatments. The main aim of the study was to investigate attrition and treatment choice, i.e., bariatric surgery and conservative treatment, of morbidly obese subjects at Reykjalundur Rehabilitation Center (RRC) as well as examine the weight loss in the treatment.

Methods: Data was collected during screening from 292 morbidly obese women who participated in an obesity treatment at Reykjalundur between 2007 and 2009. Information on body composition, fasting blood samples, psychological characteristics and medication use were available. Data also included information on dropouts and whether patients underwent bariatric surgery after the obesity treatment at Reykjalundur, as well as the weight loss in the treatment. Inclusion criteria were age between 18 and 65 years and BMI > 35 kg/m^2, exclusion criteria were alcohol- or drug addiction.

Results: Of the 292 women who finished screening, 113 (39%) dropped out, 100 (34%) finished the obesity treatment and 79 (27%) finished the treatment and consecutively underwent surgery. According to multivariate models individuals with severe depression were 2.4 times more likely (P=0.01) to drop out than individuals with mild or no depression. Individuals with BMI between 40-50 kg/m^2 were three times more likely (P=0.02) to undergo bariatric surgery than individuals with BMI <40 kg/m^2 and those with BMI ≥50 kg/m^2 were about ten times more likely (P<0.001). Individuals who underwent surgery also displayed a poorer cardiovascular risk factor profile. The mean weight loss per month during the treatment was similar for all groups, independent of their treatment option or comorbidity status but individuals with depression lost less weight than others.

Conclusion: This study shows that a very large proportion of morbidly obese individuals dropped out of an obesity treatment at Reykjalundur and that was mostly related to symptoms of depression. We also found that morbidly obese individuals in the highest BMI category (≥50.0 kg/m^2) had ten times higher odds of bariatric surgery compared to those in the lowest category (<40.0 kg/m^2). Weight loss was similar in all groups.

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ABBREVATIONS

AP	Active patients
APS	Active patients and surgery
BAI	Beck anxiety inventory
BDI-II	Beck depression inventory
BMI	Body mass index (kg/m^2)
CI	Confidence interval
CVD	Cardiovascular disease
ESR	Erythrocyte sedimentation rate
DO	Dropout
GI	Gastrointestinal
IQR	Interquartile range
MCV	Mean corpuscular volume
NIH	National Institutes of Health
OR	Odds ratio
QoL	Quality of life
RCT	Randomized controlled trial
RRC	Reykjalundur Rehabilitation Center
SD	Standard Deviation

1 INTRODUCTION

Obesity is increasing worldwide (1) and morbid obesity has also become more prevalent (2). Morbid obesity is associated with high all-cause mortality (3) and physical (4, 5) and psychological (6-8) comorbidities are common for these individuals. The long term efficacy of conservative treatment, including diet, exercise and behavior modification are relatively small for these individuals (9, 10). Therefore most studies on morbidly obese individuals focus on bariatric surgery and the changes after surgery (11-13). Bariatric surgery has been proven to be the most successful treatment today regarding weight loss and control of comorbidities (10-13). Studies are inconsistent regarding the different characteristics, especially regarding BMI and the presence of comorbidities, of surgery candidates and participants in conservative treatment (14, 15). Until now there have been no consistent predictors of bariatric surgery.

A limited amount of studies have examined the reason for attrition from weight management treatments (16) and there are no consistent predictors of dropout of obesity treatments. In general, research on overweight or obese individuals has shown that psychological and behavioral factors are the most predictive factors of attrition, including poorer body image and mental health (17).

Predictors of weight loss are relatively few at this time (18). Most studies examining weight loss have focused on psychological predictors of weight loss (19) and suggest that e.g. body image and self-esteem might predict weight loss. Other studies have shown that weight loss depends on initial weight (18, 20, 21).

It is important to identify predictors of success in weight loss treatments in order to optimize treatment and to prevent attrition from weight loss programs.

This thesis is based on data from morbidly obese women who entered the obesity treatment at Reykjalundur between March 2007 and May 2009. The main aim was to examine whether body composition, the presence of physical or psychological comorbidities, blood chemical parameters and medication use, recorded during screening in the beginning of the obesity treatment at Reykjalundur, predicts who drops out of the treatment and who goes to bariatric surgery. Additional aims were to examine if weight loss differs between individuals of different treatment choice and if comorbidity status influences weight loss. Scientific background is presented in the review of literature in this thesis.

2 REVIEW OF THE LITERATURE

2.1 Obesity

Obesity is defined as abnormal or excessive fat accumulation in adipose tissue, to the extent that it may impair health (22). The body mass index (BMI) is a commonly used measure of overweight and obesity in adults. Classification of overweight and obesity using BMI was originally defined by the World Health Organization (23) and later adopted by the National Institutes of Health (24). The classification of obesity using BMI is shown in table 1.

Table 1 Classification of overweight and obesity by BMI (24)

	BMI (kg/m^2)	Obesity class
Underweight	<18.5	
Normal	18.5-24.9	
Overweight	25.0-29.9	
Obesity	≥ 30.0	
	30.0-34.9	class I
	35.0-39.9	class II
Extreme Obesity	≥ 40	class III

Obesity increases the risk of several diseases, including hypertension, type 2 diabetes, dyslipidemia, coronary heart disease, stroke, osteoarthritis, gallbladder disease, obstructive sleep apnea and various types of cancers including breast, colon and prostate (24, 25). Higher BMI is also associated with increased all-cause mortality (24). A recent systematic review indicated that class II and III obesity is associated with significantly higher all-cause mortality, compared to normal weight, but class I obesity was not associated with higher mortality (3).

Over the last three decades the worldwide prevalence of obesity has been steadily increasing, although it has remained unchanged in the last few years. In 2009 - 2010 the prevalence of obesity in the United States was 35.5% among men and 35.8% among women, with no significant change compared with 2003 - 2008 (1). In Iceland the prevalence of obesity has also been increasing. Between 1990 and 2010 it increased from 7.2% to 22.7% for men and from 9.5% to 19.3% for women, but the prevalence has decreased for women from 2007 when it peaked at 21.3% (26, 27). These numbers are based on self-reported weight and height values and can therefore be underestimated as heavier people tend to underreport their weight (28) and most people tend to overreport their height (29).

2.1.1 Morbid obesity

A more severe form of obesity is referred to as morbid obesity or extreme obesity, and is defined as BMI ≥ 40 kg/m^2 or, if there is a serious comorbid condition present, ≥ 35 kg/m^2 (24). This form of obesity has become more prevalent in recent years. In the US the prevalence of morbid obesity (≥ 40 kg/m^2) increased until 2005 (the most recent data), when it reached 3.1%, 52% higher than in 2000 (2, 30). Morbid obesity also increased from 2.5% in 1993 - 1997 to 4.2% in 2004 - 2008 among Australian women (31).

2.1.1.1 Physical comorbidities

Morbid obesity is associated with significantly higher all-cause mortality, compared to normal weight (3) and is also associated with an increase in years of life lost (32). Comorbidities are common for morbidly obese individuals (4, 5). Prevalence of at least one metabolic complication is about 57% to 76% (5, 33) in this group of individuals. Diabetes has been reported to range from 18% to 43%, hypertension from 30% to 68% (5, 14, 15, 25, 34) and dyslipidemia from 32% to 72% (5, 14, 15).

Other physical factors that influence the daily life of morbidly obese individuals are difficulties walking, bathing and dressing (35). A recent study on walking capacity of bariatric surgery patients indicated that walking limitations are common for these individuals, with four out of five participants reporting inability to walk more than a mile (1.6 km) due to poor health (36). Furthermore greater pain was independently associated with higher odds of using walking aid (for example a cane or a wheel chair), physical discomfort during the walking test and inability to complete it. Several comorbidities and symptoms of depression were independently related to at least one measure of reduced walking capacity (36). Work-restricting pain in the neck and back area, knee, hip and ankle is more common in the morbidly obese than in the general population (37).

2.1.1.2 Psychiatric comorbidities

Psychiatric comorbidities are common in the morbidly obese. Research has reported that 40% to 56% of morbidly obese patients have a psychiatric disorder (6-8). The prevalence of psychiatric disorders for morbidly obese individuals has been reported to be higher than for both the general population (6) and normal-weight controls (38-40).

Many studies have found depression to be common among morbidly obese individuals (6, 7, 35, 38-43), especially women, and increasing severity of obesity is associated with increasing risk of depression (40). Lifetime prevalence of major depression for morbidly

obese individuals has been reported to range from 29% to 56% (6, 7, 41) and current major depression from 25% to 30% (6, 35, 41).

A study by Onyike et al. (40) reported that the prevalence of past month major depression in individuals with BMI ≥40 kg/m^2 was 12.5% compared to 2.8% for their normal-weight counterparts and a BMI ≥40 kg/m^2 was associated with about 4 times higher odds of past-month major depression. Current depressive symptoms according to a study by Amann et al. (39) in individuals with obesity, of whom most were morbidly obese, were higher than for normal-weight controls. 40.8% of the obese compared to 14.4% of the normal-weight individuals were considered to have a depressive episode. Another study by Scott et al. (44) showed that individuals with obesity (BMI ≥30 kg/m^2) had 27% higher odds of past 12-months major depression than normal weight individuals.

Other psychological impairments for the morbidly obese, that are also more common in women, include anxiety, eating disorders (for example binge eating and night eating syndrome) (6-8, 38-41), low self-esteem (7, 38, 41) and poor body image (35, 45).

2.1.1.3 Social consequences and quality of life

The morbidly obese also suffer social consequences of obesity. Problems such as social isolation (7, 38), dissatisfying relationships (7, 38), especially sexual relationships (7, 35) and occupational problems (7, 38, 45) have been reported. A few individuals in a recent qualitative study indicated that they were unable to perform their job the way they should because of their weight (45). A systematic review on the psychological profile of the morbidly obese stated that these individuals earn less than normal-weight colleagues and they have less educational, vocational and advancement opportunities (7). The same review reported that these individuals feel social stigmatization and discrimination where people often assume that they are responsible for their state because of lack of self-control and willpower (7).

Due to physical and psychological complications, the health-related quality of life (QoL) is often poor among morbidly obese individuals and studies have associated increasing BMI with decreased health-related QoL (7, 35, 37, 46). Number of comorbidities has been associated with impairment in health-related QoL, in particular depression and pain (47).

2.2 Weight loss in obesity treatments

2.2.1 Weight loss treatments

Weight loss in overweight and obese individuals has been shown to reduce risk factors for cardiovascular disease (CVD) such as total cholesterol, serum triglyceride levels and blood pressure, and it also reduces risk factors for diabetes, i.e. reduces blood glucose levels (24). Even a modest weight loss (about 5% of initial weight) can have these effects (48). Treatment of obesity usually involves long-term lifestyle changes, including dietary therapy and increased physical activity with the addition of behavior therapy (24, 48, 49). The goal of dietary therapy is to reduce calorie intake which can be achieved with many different types of diets, including low-calorie diet, very-low-calorie diet, vegetarian diets or other diets (48, 49).

Physical activity is important for weight loss as it increases energy expenditure, it can help reduce body fat and protect against the loss of muscle mass and it also reduces the risk of CVD (24, 48, 49). Diet and physical activity also play an important role in maintaining the weight loss (48-50). Consumption or avoidance of certain food groups (49, 50) has been associated with body weight changes over time or weight loss maintenance. Behavior therapy should be included in any weight management program as it involves strategies for overcoming barriers to compliance with dietary therapy and/or increased physical activity (48, 49). When lifestyle changes are insufficient, pharmacotherapy can be added. Antiobesity medications should always be used as part of comprehensive weight-management program but never alone (48, 49).

Research on weight loss usually involves individuals who are overweight and obese (51) but not necessarily morbidly obese. The long term efficacy of conservative treatment, including diet, exercise and behavior modification are relatively small for morbidly obese individuals (9, 10) and bariatric surgery has been proven to be the most successful treatment today regarding weight loss and control of comorbidities (10-12). Therefore most studies on morbidly obese individuals focus on this treatment factor.

2.2.2 Successful weight loss

The pre-treatment predictors of weight loss are relatively few at the present time (18). Studies have shown that weight loss for overweight or obese individuals depends on their initial weight and BMI (18, 20, 21). Research has demonstrated that higher baseline BMI is associated with greater weight loss (21, 52), e.g. individuals with obese class I (BMI 30-34.9

kg/m^2) are more likely to have successful weight loss (>5% of initial body weight) compared to overweight individuals (BMI 25-29.9 kg/m^2). However in higher BMI regions this relation seems to turn around and individuals in obese class I are more likely to have successful weight loss than individuals in obese class II and III (20, 53, 54).

Metabolism and endocrine function also influence body weight and weight loss although those factors are not fully understood and studies have found few metabolic and hormonal biomarkers that predict weight loss (18). Research has shown that e.g. baseline leptin in blood predicts successful weight loss (55, 56).

Additionally, comorbidities have been associated with both decreased and increased weight loss, e.g. diabetes and arthritis have been associated with decreased weight loss (21) and hypertension with more weight loss (52). One study found that triglyceride levels were a positive predictor, while cholesterol was a negative predictor (54). However, results from these studies were not always congruent (21, 54). Most of these studies included individuals who are both overweight and obese (21, 52, 54, 56) and some of them were morbidly obese. Since none of these studies exclusively included morbidly obese individuals it is difficult to conclude if the same association can be expected in our study population.

Most studies examining weight loss focus on psychological predictors of weight loss. A review of psychological pre-treatment predictors of weight control (19) states that evidence suggests that factors such as body image and self-esteem might predict weight loss but other variables, such as depression, do not predict weight loss in treatment.

2.3 Bariatric surgery

2.3.1 In general

Bariatric surgery can be a valid option for morbidly obese individuals who have failed to lose weight using conservative methods and are well informed and motivated (24). This procedure should be one of the last options considered for morbidly obese patients when all other treatments have failed (57). The aim of the surgery is to decrease energy intake by modifying the gastrointestinal (GI) tract (13). There are two types of operations: malabsorptive, which limits the absorption of food by bypassing parts of the GI tract, and restrictive in which the stomach is decreased in size so that the patient gets satiation with less food (57). Biliopancreatic Diversion (BPD) is an example of malabsorptive operation and Vertical Banded Gastroplasty (VBG) and Adjustable Gastric Banding (AGB) are examples of restrictive operations. Roux-en-Y Gastric Bypass (RYGB) has both restrictive and

malabsorptive aspects. All of these operations may be performed as an open surgery or laparoscopically (57).

Potential candidates for bariatric surgery, according to the National Institutes of Health (NIH) guidelines, fit the category of morbid obesity, that is they have a BMI exceeding 40 kg/m^2 or 35 kg/m^2 and an obesity-related comorbidity (58). Candidates should be evaluated by multidisciplinary team, which includes people with medical, psychological, surgical, and nutritional expertise (58). Each patient should be assessed individually, they should be physically and psychologically qualified to proceed to surgery and the team must decide on the individual's ability to comply with post-operative care (59). The same guidelines have also been used in Iceland (60).

2.3.2 Weight loss and remission of comorbidities and complications after surgery

Bariatric surgery provides clinically significant sustained weight loss for more than 5 years in most patients (24). The excess weight loss after bariatric surgery reported by systematic reviews and meta-analyses differs depending on the surgical type and the follow-up time. Studies have reported excess weight loss from 45% to 87% six months after surgery (11, 61), from 33% to 78% 12 months after surgery, from 39% to 84% two years after surgery (13, 61), and from 18% to 69% three years after bariatric surgery (11, 13, 61).

Accompanying this weight loss are improvements in obesity-related comorbidities. Physical comorbidities, including diabetes, hypertension and dyslipidemia are known to improve or resolve completely after bariatric surgery. Studies have shown that 29% to 100% of patients show improvement or resolution of diabetes, 25% to 100% show improvement or resolution of hypertension and 14% to 99% show improvement or resolution of dyslipidemia (12, 57).

Psychological condition, such as depression and anxiety, is also known to improve after bariatric surgery (13, 35, 42) as well the QoL (11, 42). Individuals experience physical, professional and social improvements and improvements in sexual health and function (42) which influence the QoL. Wellbeing, self-confidence, body image, ability to interact with others (11) and physical activity (9, 35) are factors that are known to improve after bariatric surgery. Work-related activities, including performance and satisfaction, improve as well (35). Weight-related pain (35), and the long-term risk of developing work-restricting musculoskeletal pain is reduced after bariatric surgery and the likelihood of recovering from such pain increases (37).

Although bariatric surgery is an effective way for morbidly obese individuals to lose weight and gain control of comorbidities there are also potential risks following surgery, which differ according to the type of surgery. They include wound infection, bleeding, leakage, acute gastric dilatation, pulmonary embolism, vomiting and diarrhea (10, 13). Additionally, nutritional deficiencies are also a known complication of bariatric surgery (62, 63).

2.3.3 Nutritional status after bariatric surgery

Micronutrient deficiencies are well known complications following bariatric surgery due to malabsorption of nutrients and altered eating patterns (62, 63). Protein malnutrition is common after surgery and is mostly related to excessive malabsorption from bypassing parts of the small intestine where protein is absorbed (62). The most common vitamin and mineral deficiencies involve vitamins B_{12}, B_1, A, D, K and folic acid, and the trace minerals iron, selenium and zinc (62, 63).

Deficiencies of vitamin B_{12}, folic acid and iron may result in various types of anemia (64) and vitamin B_1 deficiency, often caused by persistent vomiting, may lead to Wernicke encephalopathy (62, 63). Vitamin D deficiency leads to secondary hyperparathyroidism causing elevated bone resorption which increases the risk of pathologic fractures (63) and deficiency of vitamin A causes a rare occurrence of night blindness and ocular xerosis. Even though vitamin K deficiencies have been reported after bariatric surgery, evidence of clotting abnormalities and increased bleeding tendency is absent (62, 63). Symptoms of selenium deficiency include cardiomyopathy, weakness and muscle cramps and symptoms of zinc deficiency include hair loss, diarrhea and emotional disorders (63). These deficiencies are more common after the malabsorptive procedures such as Biliopancreatic Diversion (62).

2.3.4 Nutritional status before bariatric surgery

Micronutrient deficiencies have not only been identified following bariatric surgery but also prior to surgery in morbidly obese patients (34, 65-73). This might partly be explained by intake of high energy foods that are low in nutritional value. Research has shown that morbidly obese individuals have poor dietary habits (72, 74-76). In particular their diet often lacks in wholegrain cereal products, dairy products (72, 74), nuts, beans (72), vegetables and fruits (74), which are a valuable source of vitamins and minerals and their diet is high in fat (72, 74), and low in fiber (74). Most prevalent are deficiencies of vitamins D, B_{12}, B_1, folic

acid, iron, zinc and selenium in addition to the presence of anemia (34, 65-72). Deficiencies have been reported up to 18% for vitamin B_{12} (72), 29% for vitamin B_1 (66), 68% for vitamin D (66, 72), 44% for iron (66), 24% for folic acid (34), 32% for zinc (72), 58% for selenium (69) and 22% for anemia (66, 72).

2.3.5 Characteristics of individuals who undergo surgery

Studies are inconsistent regarding characteristic differences between surgery candidates and those who participate in conservative treatment and do not undergo surgery, especially regarding the presence of comorbidities and influence of BMI on treatment choice. In general there is a lack of research in this area and it may relate to the fact that treatment strategies and policies for these individuals differ widely between countries and as a result common predictors are few. It has been mentioned that the disadvantage of previous research is that they focus on individuals who are actually undergoing surgery and therefore lack the comparison group of people who do not have surgery (15).

Recently, one study concluded that bariatric surgery patients had lower self-reported rates of smoking and depression and fewer cardiovascular risk indicators (e.g. dyslipidemia) than non-surgery candidates and there was no difference between the BMI of the patients (15). Additionally, depression was a negative predictor of bariatric surgery. Another recent study concluded that the prevalence of hypertension and dyslipidemia, but not diabetes, was lower for surgical recipients than for those who were eligible for surgery but did not necessarily have surgery (77). Moreover the comparison between these two groups is difficult as the data is based on two different data sources (survey data and registry based data).

Interestingly a study by Jakobsen et al. showed different results (14). The study concluded that surgery candidates and non-surgery candidates were comparable in relation to prevalence of comorbidities (for example hypertension, hyperlipidemia, diabetes, anxiety and depression), current smoking and drug use but the individuals in the surgery group were younger and had higher BMI (14). Moreover increasing BMI and younger age were associated with increased odds of a patient opting for surgery but obesity-related comorbidities were not associated with increased or decreased odds of surgery.

Increased BMI and the presence of comorbidities (diabetes and hypertension) have been associated with increased likelihood of a surgeon’s decision to operate on morbidly obese patients (78). Along with BMI, social support and age were the main factors that influenced selection for surgery where younger age decreased the odds of selection.

2.4 Dropout of obesity treatment

Up to this time, only few studies have investigated the reason for attrition from weight management treatments for obese individuals (16). Attrition rates have been reported from 10% to 80% depending on the weight loss treatment and follow-up time (16, 17, 79). No systematic review on predictors of dropout in morbidly obese subjects is available but a recent systematic review for overweight and obese individuals by Moroshko et al. states that the limitation of past studies is that many authors neither report attrition rates nor the characteristics of the individuals who drop out (17). This systematic review did not find consistent predictors of treatment attrition but indicated that older age and higher level of education may be protective against attrition. It also indicated that psychological and behavioral factors rather than patient background characteristics, may contribute to attrition. These factors include poor body image and mental health, numerous dieting attempts and low social support, as well as high weight loss expectation and/or low initial weight loss (17).

This review was not without its limitations, as indicated by the small number of studies exploring each variable, many different methodologies used, inconsistent findings across studies and inconsistent reporting of results (17).

Despite the lack of studies investigating solely attrition in morbidly obese individuals, one such study found that individuals with the highest BMI (BMI >50 kg/m^2) had significantly higher dropout rates than individuals with BMI 40-50 kg/m^2 (80). Moreover, individuals who were more likely to drop out of a weight loss program were of any age, had little initial successful weight loss and had poor impulse management.

Few studies have been published since the systematic review by Moroshko et al. and they indicate that younger age (81, 82), lower BMI (81) and certain psychological and socio-demographic factors, such as unemployment and pessimism, were predictors of dropout (82). Furthermore individuals, who dropped out, were more depressed than those who did not and there were no significant differences between individuals who dropped out or not regarding somatic and metabolic variables, including body composition, blood pressure, cholesterol and glucose levels (82).

2.5 Obesity treatment at Reykjalundur

Few other theses have addressed different aspects of the obesity treatment at Reykjalundur in Iceland. This chapter will review the previous theses as well as the personnel's experience of the individuals' success in treatment, based on discussion with the personnel.

2.5.1 Results of obesity treatment in Reykjalundur with or without gastric bypass surgeries, 2-year follow-up

This Cand. Psych. thesis from 2011 focused on the effectiveness of the obesity treatment from baseline to the end of two years of follow-up (83). The research did not cover those who dropped out of treatment but only those who attended the 2-year follow-up. The aim was to examine changes in body composition, depressive and anxiety symptoms (BDI-II and BAI) and quality of life associated with obesity, both for individuals who underwent bariatric surgery and those who did not. Participants were women, who attended 2-year follow up from November 2010 to April 2011. Out of 42 women, 29 (71%) underwent surgery before the end of the 2-year follow up and 13 (19%) did not. The results as a whole showed significant changes in body weight, BMI, percentage of body fat, waist circumference, depression symptoms and quality of life associated with obesity, from baseline to end of two years of follow-up. Both groups experienced significant improvements, the surgery group in weight, BMI, percentage body fat, waist circumference, and quality of life and the non-surgery treatment group in waist circumference and quality of life. The results of this study show that the obesity treatment at Reykjalundur is effective regarding health progress and is more successful for those who undergo bariatric surgery.

2.5.2 Patients health changes in the obesity treatment in Reykjalundur

This master's thesis from 2010 emphasized on the exercise component in the obesity treatment (84). The study examined the results from beginning of the treatment (screening) to the end of five week stationary treatment, with respect to measurements of body composition, physical fitness, heart rate, blood pressure and results from an endurance test. Additionally, the patients' own evaluation of their physical and mental condition and health-related quality of life was also examined. 47 women participated in the study and the measurements used in this study were from October 2007 to July 2009. No participant underwent surgery during the study period and dropouts were not included in the study**.** The results showed significant average weight loss of 11 kg, significant changes in BMI of 4 kg/m^2, and significant increase in fitness (watts/kg) of 21% measured with a cycle ergometer test. Blood pressure and heart rate reduced significantly, except maximum heart rate. Both depression and anxiety symptoms improved significantly as well as obesity related quality of life.

2.5.3 The Socially Accepted Size

This bachelor's thesis from 2010, focused on the change in psychosocial functioning from screening until one year after the end of the stationary treatment (85). It also compared psychosocial functioning after weight loss between surgery patients and non-surgery patients. 15 individuals, men and women, participated in the study; eight of them had gone through bariatric surgery while seven had not and the timeframe of the study was from January 2008 to September 2009. The psychosocial functioning was evaluated with the OP scale which is an obesity-specific measurement that evaluates the impact of obesity on psychosocial functioning. Only individuals who had both baseline and end-point data were included in the study. The results showed significant relationship between psychosocial functioning and weight loss, with greater weight loss resulting in greater improvements in psychosocial functioning of the patients. Patients who underwent bariatric surgery had significantly higher psychosocial improvements than non-surgery patients. The sample size in this study was small and, consequently, the results should be interpreted cautiously.

All these abovementioned theses, although focusing on different time frame in the treatment, show the success of the obesity treatment at Reykjalundur, regarding factors such as weight loss and depression symptoms (83-85). The shortcoming of these studies is that they did not include individuals who dropped out of the treatment. Furthermore they did not examine predictive factors of success in the treatment or try to find predictors of bariatric surgery as the main focus of these theses was the effectiveness of the treatment.

2.5.4 Personnel's experience of success and failure in treatment

The personnel in the obesity treatment at Reykjalundur include a physician and a dietician. In their experience, the individuals' success in the treatment depends on his or her motivation when they begin the treatment. As expected the personnel conclude that those individuals, who are not health-conscious and have a negative attitude towards a healthy lifestyle, do often not succeed and frequently drop out of the treatment. Individuals, who are not motivated, often lack social support and have difficult family circumstances. It is the personnel's experience that the mental health of many participants is rather poor at the beginning of treatment which affects their performance during the treatment. On the other hand individuals who succeed in the treatment are perceived to be those who are well motivated when they begin the treatment. As the program and its personnel can sometimes motivate those who are

not already motivated, it is often difficult to predict in the beginning of the treatment if the treatment will be successful for individuals.

The personnel's experience is that many participants suffer from iron, vitamin D and B_{12} deficiencies. These deficiencies can hinder the treatment progress since these individuals are tired and lack energy. It is not standard protocol to measure iron, vitamin D and B_{12} in blood during screening before the obesity treatment starts and, therefore, not all participants are identified with those deficiencies prior to treatment. Moreover it is the personnel's experience that the diet of the individuals, who seek treatment, is poor and lacks certain vitamins and minerals, including iron, and that their diet is high in fat which can often be seen in the triglycerides blood sample. The individual's tiredness and lack of energy is sometimes reversed when they start the treatment and begin to eat healthier food and exercise.

2.6 Summary and research questions

Obesity is increasing worldwide and morbid obesity has also become more prevalent. Morbid obesity is associated with both physical and psychological comorbidities, including hypertension, diabetes and depression. Bariatric surgery has been proven to be the most successful treatment today for morbid obesity regarding weight loss and control of comorbidities but no consistent predictors of bariatric surgery exist up to this time.

Although past literature provides information about dropout, weight loss and bariatric surgery for obese individuals, there are several factors that need to be considered. This includes inconsistent reporting of the characteristics between surgery candidates and those who do not undergo surgery, exclusion of individuals who do not undergo surgery, lack of reporting attrition rates and characteristics of individuals who drop out of obesity treatments. This results in difficulty in identifying predictors of bariatric surgery and dropout of obesity treatments. Additionally, previous studies have mostly focused on psychological and behavioral factors rather than physical or metabolic factors. Some studies indicate that e.g. poor mental health and depression are associated with dropout.

Studies investigating dropout and weight loss mostly focus on individuals who are overweight or obese, but not necessarily morbidly obese. It is therefore not known whether results from overweight/obese individuals can be extrapolated and whether they apply also for morbidly obese individuals. These above-mentioned observations have prompted the need to further define the impact of important parameters in the beginning of the obesity treatment

and whether these parameters predict dropout or bariatric surgery in morbidly obese individuals.

Major research questions to be answered in this thesis are:

1. Does body composition, biomarkers of metabolic disorder and psychological scores recorded at the beginning of the obesity treatment at Reykjalundur predict dropout of the treatment?

2. Does body composition, biomarkers of metabolic disorder and psychological scores recorded at the beginning of the obesity treatment at Reykjalundur predict who goes to bariatric surgery?

Additional research questions:

1. Is the weight loss during the obesity treatment at Reykjalundur different between patients who later proceed to bariatric surgery and those who do not go to surgery?

2. Is the weight loss during the obesity treatment at Reykjalundur different between patients with physical, psychological or no comorbidities at the beginning of the treatment?

3 METHODS

Methods related to the analysis of screening values for different groups of patients and the association between screening values and odds of dropout and bariatric surgery are described in detail in the manuscript (see chapter 4). The obesity treatment at Reykjalundur is described as well in the manuscript (in materials and methods).

In chapter 5 additional results regarding weight loss for different groups of patients is presented, and the methods relating to the results are described here. Results are presented as mean and standard deviation (SD) for normally distributed variables and median with interquartile range (IQR) for nonparametric distributions. T test was used to test the difference between the groups of Active patients (AP) and Active patients and surgery (APS) when distributions were normal and Mann-Whitney test for nonparametric distributions.

For statistical analysis of weight loss for patients with different comorbidities, the subjects were divided into four categories according to what comorbidity they suffered from; hypertension, diabetes, severe depression or none of those comorbidities (reference group). Subjects with two or more of these comorbidities are in all relevant groups. Differences between groups were analyzed using one-way ANOVA when distributions were normal and Kruskal Wallis test for nonparametric distributions. P-values <0.05 were considered statistically significant.

3.1 Authors‘ contribution

The preparation for the study started in September 2011. I applied along with my supervisors for permission from the National Bioethics Committee and The Data Protection Authority which was received early in 2012. In the autumn of 2011 I also applied for two funds, The University of Iceland Research Fund and The Science Fund of Reykjalundur, along with my supervisors. In March 2012 I also applied for the Icelandic Research Fund (RANNIS).

The data collection began in February 2012 and it finished in May the same year. The data was entered into excel files. All data was then prepared to be imported into SAS. I made the statistical analysis presented in this thesis under the supervision of Dr. Þórhallur Ingi Halldórsson and wrote the draft of the manuscript “Predictors of dropout and bariatric surgery in Icelandic morbidly obese patients” which is ready for submission.

In April 2013 I took part in poster session at “Science in the spring” at Landspítali National University Hospital: Benediktsdottir A, Halldorsson TI, Bragadottir GJ, Gudmundsson L, Ramel A. *Predictors of dropout and bariatric surgery in Icelandic morbidly obese patients*.

4 MANUSCRIPT

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Predictors of dropout and bariatric surgery in Icelandic morbidly obese patients

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Abstract

Background: Little is known on how morbidly obese individuals who participate in different treatments differ in relation to anthropometrical measurements and psychological characteristics. In the present study we investigated attrition and treatment choice, i.e., bariatric surgery and conservative treatment, of morbidly obese subjects at an Icelandic rehabilitation center.

Methods: Data was collected during screening from 292 morbidly obese women who participated in a weight loss program at an Icelandic rehabilitation center between 2007 and 2009. Information on body composition, fasting blood samples, psychological characteristics, medication use and socio-demographic details were available. Data also included information on dropouts and whether patients underwent bariatric surgery after the weight loss program at the rehabilitation center. Inclusion criteria were age between 18 and 65 years and BMI > 35 kg/m^2, exclusion criteria were alcohol- or drug addiction.

Results: Of the 292 women who finished screening, 113 (39%) dropped out, 100 (34%) finished the weight loss program and 79 (27%) finished the weight loss program and consecutively underwent surgery. According to multivariate models individuals with BMI between 40-50 kg/m^2 were three times more likely (P=0.02) to undergo bariatric surgery than individuals with BMI <40 kg/m^2 and those with BMI ≥50 kg/m^2 were about ten times more likely (P = 0.001). Individuals with severe depression were 2.4 times more likely (P = 0.01) to drop out than individuals with mild or no depression.

Conclusion: Our study shows that a very large proportion of morbidly obese individuals dropped out of a weight loss program at an Icelandic rehabilitation center and that having severe depression symptoms more than doubles this risk. We also found that morbidly obese

individuals in the highest BMI category (≥50.0 kg/m^2) had ten times higher odds of bariatric surgery compared to those in the lowest category (<40.0 kg/m^2).

Keywords: morbid obesity, attrition, treatment choice

Introduction

Morbid obesity is associated with increased morbidity and mortality and represents a major healthcare problem with increasing incidence worldwide.[1,2,3,4,5] Treatment, e.g., diet, physical activity and behavior modification, is often challenging for morbidly obese individuals due to their physical state and relatively high prevalence of psychiatric disorders.[6,7,8] Most studies on morbidly obese individuals focus therefore on bariatric surgery and the changes after surgery.[9,10,11] Bariatric surgery for morbidly obese individuals has been proven to be the most successful treatment today with regard to weight loss and control of comorbidities.[9,10,11] Hypertension, hyperlipidemia, type 2 diabetes and obstructive sleep apnea are comorbidities that are known to improve or resolve after bariatric surgery, although complications following surgery are well known, e.g., micronutrient deficiencies due to malabsorption of nutrients and altered eating patterns.[12,13] Studies are inconsistent regarding the different characteristics, e.g., depression or cardiovascular risk factors, of surgery candidates and those who participate in conservative treatment.[14,15]

Attrition is an important yet understudied issue in the failure of weight management treatment.[16] In general, research on overweight or obese individuals has shown that psychological and behavioral factors are the most predictive factors of attrition from weight loss programs. Studies have associated depression,[17] poorer quality of life, more previous weight loss attempts and more stringent weight outcome evaluations[18] with higher attrition rates. The only few studies available in morbidly obese patients have associated younger age,[19,20,21,22] lower BMI[19] and symptoms of depression[20] with attrition.

In order to prevent attrition from a weight loss program and to be able to give the best possible treatment for morbidly obese individuals it is important to get a better understanding of how the individuals who participate in different treatments differ in relation to

anthropometrical measurements and psychological characteristics. Thus, in the present study we investigate attrition and treatment choice, i.e., bariatric surgery and conservative treatment, of morbidly obese subjects. The aim of this study was to examine whether body composition, psychological characteristics, particularly anxiety and depression, blood chemical parameters, comorbidities and/or medication use as recorded during screening are associated to attrition or treatment choice in morbidly obese subjects participating in weight loss program at a rehabilitation center in Iceland.

Materials and methods

Subjects and data

Data was collected during screening from 292 morbidly obese women who aimed to participate in the weight loss program at the Reykjalundur Rehabilitation Center (RRC), Iceland, between March 2007 and May 2009. The data from the RRC database included information on body composition, fasting blood samples, psychological characteristics, blood pressure, medication use and socio-demographic details. Data also included information on dropouts and if the patients underwent surgery or not (the results from surgery are not discussed in the present paper). Inclusion criteria were age between 18 and 65 years and BMI > 35 kg/m^2, exclusion criteria were alcohol- or drug addiction. A recommendation from a general practitioner was required to enter the program. Permission for this study was granted from the Icelandic Bioethics Committee (VSNb2011120004/03.7) and The Icelandic Data Protection Authority (2011121359HGK).

Weight loss program at the RRC

In general, the aim of the program at the RRC is to assist morbidly obese individuals to lose weight using behavioral intervention as treatment. Several patients use this program as

preparation for bariatric surgery. The treatment plan is identical for subjects, whether they will undergo surgery later or not. After screening, the program starts with ambulatory treatment, where individuals visit the RRC regularly, i.e., every other week, and where they get information and education on a healthy diet and physical activity. They also receive a treatment plan (diet and exercise) and support, e.g., by a psychologist, if problems during the program arise. During this period (usually 3-9 months) patients have to achieve predefined goals (e.g., 7% weight loss) before they are allowed to enter the stationary treatment, which takes five weeks in which individuals participate in intensive behavior therapy at RRC that includes education about nutrition, physical activity and other obesity related issues (see Figure 1).

Measurements

Body weight (BW) was measured in light underwear on a calibrated scale (model no. 708, Seca, Hamburg, Germany) and height was measured with a calibrated stadiometer (model no. 206; Seca, Hamburg, Germany). Body mass index (BMI) was calculated from the recorded height and weight (kg/m^2). Waist circumference was measured halfway between the top of the lateral iliac crest and the lowest rib. All measures were performed twice using a tape measure and recorded to the nearest centimeter. Body composition was estimated using bioelectrical impedance analysis (BIA; Bodystat 1500, Bodystat Ltd, Douglas, Isle of Man, British Isles).

Depression and anxiety were measured using the Beck depression inventory (BDI-II)[23] and the Beck anxiety inventory (BAI)[24]. Cut off values for moderate and severe depression/anxiety are shown in Table 2. Smoking and medication use were also assessed. Blood samples were analyzed at the laboratory of the Landspitali-University Hospital in Reykjavik (see Table 2).

Statistical Analysis

Results are expressed as means (SD), median, or percentages (%). For statistical analysis, the subjects were divided into three groups: "Dropouts" (DO) quit before the end of the treatment. "Active patients" (AP) completed both the ambulatory and stationary treatment. The group "Active patients and surgery" (APS) completed also both treatments and underwent bariatric surgery thereafter. Differences between groups were analyzed using one-way ANOVA when distributions were normal and Mann-Whitney test for nonparametric distributions. Those variables that were found to be (borderline) different were then entered into the logistic regression models to find predictors for surgery and for dropout. In the multiple logistic regression models we adjusted for age, smoking (yes/no) and BMI. P-values <0.05 were considered statistically significant. SAS version 9.2 was used to perform statistical analysis.

Results

General characteristics and body composition

Of the 292 women who finished screening, 113 (39%) were DO, 100 (34%) were AP and 79 (27%) were APS (Fig. 1). General characteristics and body composition of the participants are shown in Table 1. Compared to AP, both APS and DO showed higher levels of body fatness.

Comorbidities, depression, anxiety and medication use

There was a high (>50%) prevalence of dyslipidemia in all groups and it was highest in the APS group (Table 2). The prevalence of hypertension ranged between 35.7% and 46.2%, the prevalence of diabetes and pre-diabetes combined was between 24.7% and 37.1%. Between 19.2% and 37.3% and 15.4% and 25.2% of the patients suffered from severe depression and severe anxiety, respectively. Patients in the DO group used more pain killers and blood lipid drugs compared to AP group, differences for other drugs were not significant (Table 3).

Logistic regression – odds of having surgery

In both unadjusted and adjusted models higher BMI was associated with higher odds of having surgery. Individuals with BMI between 40-50 kg/m^2 were about three times more likely to undergo bariatric surgery than individuals with BMI <40 kg/m^2 and those with BMI ≥50 kg/m^2 were about ten times more likely. Dyslipidemia and hypertension were also associated with significantly higher odds for having surgery (Table 4).

Logistic regression – odds of dropout

Individuals with severe depression were 2.4 times more likely to drop out than individuals with mild or no depression. Higher serum glucose was also associated with higher odds of dropout. Both use of blood lipid drugs and psychotropic drugs were also associated to drop out of treatment (Table 5).

Discussion

In the present study we investigated anthropometrical variables, psychological characteristics and blood chemical parameters of morbidly obese individuals who subsequently aimed to participate in a weight loss program and how these variables related to treatment choice or dropout. We found that the large proportion of 39% of the participants dropped out of the program and that severe depression appeared to be the primary underlying cause. Increasing BMI was associated with increasing likelihood of patients undergoing bariatric surgery.

Concerning studies on morbidly obese subjects, the overwhelming focus has to date been on those who undergo bariatric surgery and the status of the individuals before and/or after the surgery. As also observed in this study, medication use is very common,[11] comorbidities, e.g.,

type II diabetes, dyslipidemia and hypertension are common[25,26] and their psychological health is often poor.[6,8]

Predictors for dropout

In the present study severe depression, higher serum glucose level as well as the use of blood lipid- and psychotropic drugs were predictors of dropout. No systematic review on predictors of dropout in morbidly obese subjects is available. However, a recently published systematic review for overweight and obese individuals did not find consistent predictors of treatment attrition although the results indicate that older age and higher education may be protective factors against attrition.[17] The review also indicates that the limitation of past studies is that many do report neither attrition rates nor the characteristics of the individuals who dropped out. Out of ten studies examining depression and attrition included in the review, five studies associated higher depression levels with higher attrition rates, four found no association and one associated lower levels of depression with higher attrition rates.[17]

Increased serum glucose level was associated with higher odds of dropout in our study. A potential explanation for this is that higher levels of fasting glucose in individuals without diabetes have been associated with lower muscle mass[27] and it is possible that these subjects find it difficult to engage in physical activity as part of the treatment due to poor physical function. We also found an association between blood lipid medication use and very high odds of attrition. Reported side effects of the commonly used blood lipid drugs *statins* include muscle pain and muscle damage[28,29] and in that case it might be difficult for subjects to engage in physical activity as part of the treatment. Similarly, antidepressant use was also associated to drop out in our study, which has been reported earlier in overweight and obese individuals.[30] However, in the current study we could not answer the question whether

antidepressant use was causally related to dropout or whether antidepressant use was solely a marker of depression or poor mental health in general.

Predictors for bariatric surgery

In our study higher BMI was a predictor of surgery which has been previously shown.[15,31] We also found an association between dyslipidemia and hypertension and odds of having surgery. The presence of comorbidities has been previously associated with increased likelihood of the surgeon's decision to operate on morbidly obese patients,[32] although not all studies have seen such association.[14,31]

In a previously mentioned study[14] individuals with depression had lower odds of undergoing surgery and the prevalence of depression for non-surgery patients was significantly higher than for surgery candidates. Although severe depression was not a significant predictor for surgery in our study ($P > 0.1$) the low odds ratio around 0.5 indicates the same tendency in our study participants.

Strengths and Limitation

The strength of this research is that we have extensive screening information for nearly 300 patients prior to participation in the treatment. We also have complete information on everyone that dropped out during treatment and also on everyone who underwent bariatric surgery thereafter. However, the data is derived from a clinical rather from a pure research environment and is therefore not standardized for all participants and some information are lacking for some individuals. Because of this reason we did not have all the information we wanted, e.g., education or marital status. Finally, the study participants consisted of only females and therefore the results may not be valid for males.

Conclusion

Our study shows that a very large proportion of morbidly obese individuals dropped out of a weight loss program at an Icelandic rehabilitation center and that having severe depression symptoms more than doubles this risk. We also found that morbidly obese individuals in the highest BMI category (≥50.0 kg/m^2) had ten times higher odds of bariatric surgery compared to those in the lowest category (<40.0 kg/m^2).

Acknowledgements

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Conflict of Interest

The authors declare no competing financial interests in relation to the work described.

Table 1 General characteristics of the patients

	Active patients (n =100)	Active patients and surgery (n =79)	Dropout (n =113)	p_1 value	p_2 value
Age (years)	41.6 (12.3)	38.4 (10.7)	41.9 (13.9)	0.09	0.89
Smoking (yes)	19 (24%)	15 (23%)	24 (28%)	0.97	0.51
Weight (kg)	118.6 (18.1)	131.4 (16.6)	122.5 (23.0)	<0.001	0.15
Height (cm)	167.1 (6.3)	167.7 (6.2)	166.5 (5.9)	0.54	0.44
BMI (kg/m^2)	42.4 (6.0)	46.7 (5.3)	44.0 (7.0)	<0.001	0.06
Waist (cm)	115.0 (11.7)	122.3 (10.8)	120.1 (13.6)	<0.001	0.004
Fatpercent (%)	46.0 (3.8)	48.0 (2.9)	47.1 (3.9)	<0.001	0.02
Fatfree mass (kg)*	64 (8.8)	67.2 (11.4)	62.5 (9.2)	<0.001	0.68

*Data shown as median (IQR). Other data is mean (SD)

p1 value refer to difference between group of active patients and active patients who undergo surgery

p2 value refer to difference between group of active patients and dropout group

BMI: Body mass index

Table 2 Prevalence of abnormal blood values

	Abnormal level	Active patients (*n* =100)	Active patients and surgery (*n* =79)	Dropout (*n* =113)	*p1* value	*p2* value
Hemoglobin	<120 g/L	6 (6.7%)	3 (4.0%)	5 (5.2%)	0.44	0.65
Hematocrit	<0.35 L/L	2 (2.3%)	2 (2.7%)	1 (1.1%)	0.84	0.59
MCV	<80 fL	6 (6.7%)	1 (1.3%)	6 (6.7%)	0.12	1
ESR	>20 mm/h	31 (39.7%)	37 (56.1%)	38 (46.3%)	0.05	0.40
Creatinine	<60 µmol/L	20 (25%)	25 (34.3%)	27 (31.4%)	0.22	0.37
Creatinine	>120 µmol/L	2 (2.5%)	1 (1.4%)	0 (0%)	0.53	0.15
Hypertension	140/90 mmHg	35 (35.7%)	36 (46.2%)	40 (36.7%)	0.16	0.89
B-Hba1c	>7 %	2 (3.0%)	3 (4.8%)	5 (6.3%)	0.65	0.37
Pre-diabetes & diabetes	Diabetes: S-glucose >6.7 mmol/L or diabetes/blood sugar drugs Prediabetes: S-glucose 5.5-6.7 mmol/L	22 (24.7%)	21 (28.4%)	36 (37.1%)	0.61	0.07
Dyslipidemia	tg ≥1.7 mmol/L and/or HDL <1.3 mmol/L	47 (52.8%)	57 (77.0%)	65 (66.3%)	0.001	0.05
Moderate depression	20-28	15 (15.8%)	19 (24.4%)	20 (19.6%)	0.16	0.50
Severe depression	> 29	29 (30.5%)	15 (19.2%)	38 (37.3%)	0.10	0.30
Moderate anxiety	16-25	25 (26.3%)	13 (16.7%)	22 (21.4%)	0.13	0.40
Severe anxiety	> 26	16 (16.8%)	12 (15.4%)	26 (25.2%)	0.81	0.14

*Data shown as median (IQR). Other data is mean (SD)

p1 value refer to difference between group of active patients and active patients who undergo surgery

p2 value refer to difference between group of active patients and dropout group.

MCV: Mean corpuscular volume. ESR: Erythrocyte sedimentation rate

Table 3 Medication use

	Active patients (*n* =100)	Active patients and surgery (*n* =79)	Dropout (*n* =113)	*p1* value	*p2* value
Total medication use	84%	79%	86%	0.45	0.78
Antihypertensive drugs	36%	32%	40%	0.68	0.70
Psychotropic drug	32%	33%	44%	0.73	0.12
Pain killers	14%	16%	28%	0.53	0.03
Blood sugar drugs	10%	15%	19%	0.30	0.13
Respiratory drugs	9%	12%	12%	0.44	0.51
Blood lipid drugs	6%	4%	19%	0.70	0.01
Inflammation drugs	24%	18%	27%	0.44	0.72
Thyroid hormones	15%	15%	19%	0.86	0.55

Data shown as percentage

p1 value refer to difference between group of active patients and active patients who undergo surgery

p2 value refer to difference between group of active patients and dropout group

Table 4 Odds for having surgery

Explanatory variables	Unadjusted				Adjusted*			
	OR	95% CI		*p* value	OR	95% CI		*p* value
BMI								
<40.0 kg/m^2	1				1			
40.0-49.9 kg/m^2	3.67	1.6	8.4	0.002	3.07	1.29	7.33	0.01
≥50.0 kg/m^2	11.11	3.59	34.4	<0.0001	10.25	2.92	35.98	0.0003
Dyslipidemia	2.84	1.43	5.67	0.003	2.97	1.31	6.77	0.009
Hypertension	1.66	0.9	3.08	0.11	2.5	1.08	5.77	0.03
Diabetes	1.45	0.59	3.59	0.42	1.84	0.62	5.45	0.27
BDI-II								
<20	1				1			
20-28.5 (moderate)	1.38	0.63	3.05	0.42	1.05	0.41	2.69	0.92
≥29 (severe)	0.58	0.28	1.24	0.16	0.46	0.17	1.2	0.11

*BMI adjusted for age and smoking. Other variables are adjusted for BMI, age and smoking

OR: Odds ratio. CI: Confidence interval. BMI: Body mass index. BDI-II: Beck Depression Inventory

Table 5 Odds for dropout

Explanatory variables	Unadjusted				Adjusted*			
	OR	95% CI		*p* value	OR	95% CI		*p* value
BMI								
<40.0 kg/m^2	1				1			
40.0-49.9 kg/m^2	0.96	0.55	1.68	0.88	0.98	0.52	1.84	0.94
≥50.0 kg/m^2	1.18	0.56	2.47	0.67	1.55	0.67	3.57	0.3
S-glucose (mmol/L)	1.31	1.06	1.63	0.01	1.35	1.02	1.81	0.04
BDI-II								
<20	1				1			
20-28.5 (moderate)	1.27	0.66	2.45	0.48	1.33	0.63	2.83	0.46
≥29 (severe)	1.87	1.06	3.27	0.03	2.39	1.23	4.64	0.01
Psychotropic drugs	1.50	0.91	2.47	0.11	1.73	0.99	3.04	0.05
Blood lipid drugs	4.05	1.7	9.66	0.002	4	1.36	11.75	0.01

*BMI adjusted for age and smoking. Other variables are adjusted for BMI, age and smoking

OR: Odds ratio. CI: Confidence interval. BMI: Body mass index. BDI-II: Beck Depression Inventory

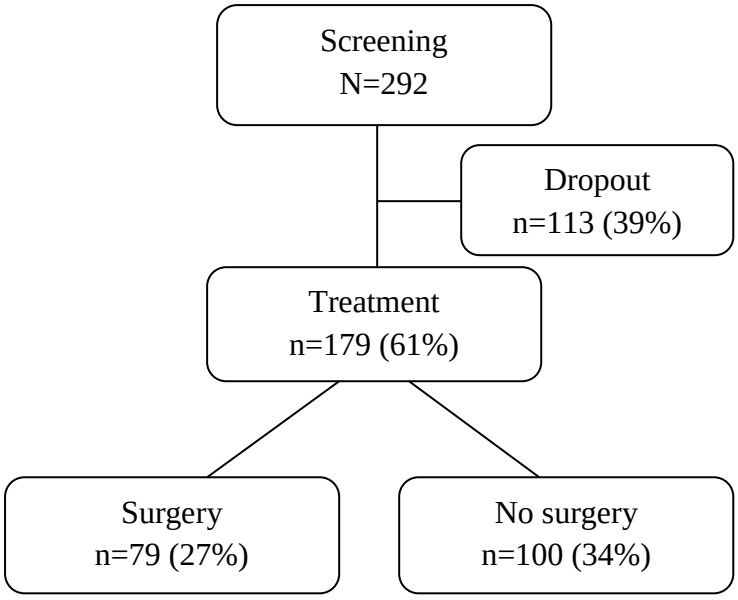

Figure 1 Flowchart of patients and their treatment

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5 RESULTS – SECONDARY ANALYSIS

The main results are presented in chapter 4 in the manuscript. In this chapter results from secondary analysis will be presented and then discussed in chapter 6.

5.1 Weight loss in ambulatory and stationary treatment

The weight loss of the participants in the obesity treatment is shown in tables 6 and 7. Both weight loss in the ambulatory treatment (from screening to start of stationary treatment) is presented as well as the weight loss during the stationary treatment.

5.1.1 Active patients and active patients and surgery

Weight loss of AP and APS groups is shown in table 6. The mean weight loss in the ambulatory treatment was 5.4 kg for AP and 6.1 kg for APS group, not significantly different between groups. When weight loss was divided by months needed to achieve the weight loss, both groups showed similar weight loss, 1.3 kg and 1.4 kg per month, also not significant.

The weight loss during the stationary treatment was 3.4 kg and 4.1 kg for AP and APS respectively (P=0.02) but when adjusted for baseline weight it was not significant (P=0.13).

Table 6 Weight loss for AP and APS groups during ambulatory and stationary treatment

		Active patients (n =100)	Active patients and surgery (n =79)	p value
	Baseline weight (kg)	118.6 (18.1)	131.4 (16.6)	<0.001
Ambulatory treatment	Weight loss (kg)	-5.4 (5.7)	-6.1 (5.3)	0.36
	Duration of treatment (days)*	154 (141)	118 (164)	0.22
	Weight loss per month (30 days)	-1.3 (1.3)	-1.4 (1.2)	0.43
Stationary treatment	Weight loss (kg)	-3.4 (2.1)	-4.1 (1.6)	0.02†
	Duration of treatment (days)*	31 (2)	30 (2)	0.09

* Data shown as median (IQR). Other data is mean (SD)

† When adjusted for baseline weight, it becomes non-significant (p=0.13)

5.1.2 Patients with different comorbidities

Weight loss of patients with different comorbidities is shown in table 7. All p-values are based on unadjusted values. The weight loss in the ambulatory treatment was more in the

hypertension (7.2 kg vs. 4.5 kg, P=0.003) and diabetes (8.3 kg vs. 4.5 kg, P=0.007) groups compared to the reference group (individuals who do not have hypertension, diabetes nor depression). But when weight loss was divided by months needed to achieve the weight loss in the ambulatory treatment, it was not statistically significant between groups. The weight loss during the stationary treatment was also not significant except between the reference group and the depression group (4.1 kg vs. 3.0 kg respectively, P=0.01). When adjusting for baseline weight the difference becomes borderline significant (P=0.06).

Table 7 Weight loss for different groups of comorbidities during ambulatory and stationary treatment

		Hypertension (n=71)	Diabetes (n= 23)	Depression (n=44)	Reference (n=61)	*p1* value	*p2* value	*p3* value
	Baseline weight (kg)	128.5 (20.7)	126.6 (17.2)	123.1 (19.9)	120.1 (19.4)	<0.01	0.07	0.32
Ambulatory treatment	Weight loss (kg)	-7.2 (5.6)	-8.3 (7.7)	-5.1 (5.9)	-4.5 (4.7)	<0.01[1]	<0.01[1]	0.55
	Duration of treatment (days)*	158 (123)	239 (217)	167 (205)	116 (113)	0.29	0.03	0.03
	Weight loss per month (30 days)	-1.5 (1.3)	-1.3 (0.9)	-1.2 (1.2)	-1.2 (1.3)	0.18	0.76	0.98
Stationary treatment	Weight loss (kg)	-3.7 (1.6)	-3.6 (1.6)	-3.0 (1.9)	-4.1 (2.1)	0.26	0.33	0.01[2]
	Duration of treatment (days)*	30 (2)	30 (2)	30 (2)	30 (2)	0.85	0.79	0.53

* Data shown as median (IQR). Other data is mean (SD)

p1 value refers to difference between reference group and hypertension group

p2 value refers to difference between reference group and diabetes group

p3 value refers to difference between reference group and depression group

[1] Still significant when adjusted for baseline weight

[2] When adjusted for baseline weight it becomes borderline significant (*p*=0.06)

6 DISCUSSIONS

The main results are discussed in the manuscript in chapter 4. In this chapter additional discussions will be provided as well as discussions regarding the results from the secondary analysis in chapter 5.

6.1 Predictors of dropout and bariatric surgery

In this study we found that individuals with severe depression had higher odds of dropping out of the treatment and individuals with higher BMI had increasing odds of undergoing bariatric surgery. Comorbidity status also influenced if patients underwent surgery or not as individuals with dyslipidemia and hypertension had increased odds of undergoing surgery.

6.1.1 Comorbidities

In general, we expected a higher prevalence of biomarkers of metabolic disorders (see table 2 in chapter 4) as the individuals in this study were morbidly obese and the prevalence of micronutrient deficiencies (65-68) and comorbidities (4, 5) have previously been reported to be very common among these individuals. E.g. taken together for all participants the prevalence of abnormal hemoglobin, hematocrit, MCV or Hba1c was lower than 7%. The prevalence of hypertension was also lower than expected, 36% to 42%, as most studies have shown higher prevalence numbers, e.g. up to 63% in morbidly obese women (4). However, as expected, these numbers were higher than for normal weight individual, where prevalence has been reported to be 16% (25) and 23% (4).

The prevalence of both pre-diabetes and diabetes was 25% to 37% in our study. Studies have reported diabetes to range from 23% to 28% among Caucasian morbidly obese population which consist mostly of women (5, 14) and even higher, 43%, in a morbidly obese population consisting mostly of men (15). Dyslipidemia was the most prevalent comorbidity in our study, 53% to 77%, and it was highest in the APS group. Other studies have found similar prevalence numbers (14) but others lower, 32% to 54% (15) and 49% (5).

The prevalence of severe depression in our study was quite high, or 19% to 37%. It is difficult to compare these prevalence numbers to other studies as studies use various diagnostic tools for depression. The Beck Depression Inventory (BDI-II), used in this study, measures current depression symptoms (for the past two weeks) (86). Other studies assessing current depression, using other measurements than the BDI-II, have found the prevalence to be 13% (40) and 32% (6) among morbidly obese women. One study using the BDI reported 40.8% of morbidly obese individuals, who were mostly women, scoring more than 18 on the

BDI (39) which is considered a depressive state. In our study 46.3%, 43.6% and 56.9% of AP, APS and DO groups respectively scored more than 19 on the BDI. There are no official prevalence numbers for current depression symptoms in Iceland but in a report about state of health of Icelanders from 2007 15% of men and 20% of women reported having experienced symptoms of long-term major depression some time in their life (87). This is not comparable to current depression as measured by the BDI but it gives an idea about the mental state of the Icelandic people and according to this the individuals in our study have worse mental health than the general population in Iceland.

Erythrocyte sedimentation rate (ESR) was high in all groups (40% to 56%) but highest in the APS group. ESR is an inflammatory marker which increases with obesity (88) since obesity is a state of inflammation (89). High ESR has been reported in morbidly obese individuals in previous literature (33) and it is known to decrease after bariatric surgery (33, 88).

6.1.2 Predictors of dropout

Individuals with severe depression had more than twice the odds of dropping out than those with mild or no depression. Depression (82) and poor mental health (17) has previously been associated with dropout in overweight and obese individuals. Our results are consistent with, for example, the results of a randomized controlled trial on obese individuals that concluded that each additional point on the BDI-II scale increased the odds of attrition by 7% (90).

Given that depression increased the odds of dropout it is possible that previous studies on morbidly obese individuals did not include those who have poor mental health as they could have had previously dropped out of the weight loss treatment or before pre-surgery evaluation. These studies should therefore be interpreted cautiously. Many studies do not report attrition rates and therefore we often do not know what characterizes those individuals who drop out. The high dropout rate in our study highlights the importance of taking better care of this group of individuals and interfering before they drop out of treatment.

Psychotropic drug usage was also associated with dropout in our study, which can further strengthen the assumption that individuals who dropped out had poorer mental health than those who did not drop out.

Increased serum glucose and the use of blood lipid medication were also associated with increased odds of dropping out in our study but we found no research with the same association. The prevalence of dyslipidemia was statistically higher in the dropout group

compared to the AP group. That could be a possible explanation to the association of blood lipid medication and dropout even though one might think that the medication would lower the blood lipids. A possible explanation for the association between serum glucose levels and blood lipid medication with dropout is that the individuals who dropped out had worse health in general and were less prepared to deal with the necessary lifestyle changes in the obesity treatment.

6.1.3 Predictors of bariatric surgery

Increasing BMI increased the odds of undergoing bariatric surgery. The candidates for surgery, according to the National Institutes of Health (NIH) guidelines (58), are those who have a BMI exceeding 40 kg/m^2 or 35 kg/m^2 and an obesity-related comorbidity. It was therefore expected that individuals in the lowest BMI category (BMI <40 kg/m^2) were less likely to have surgery; however the big difference between the categories was surprising. In the adjusted model individuals with a BMI 40-49.9 kg/m^2 had three times the odds and individuals with a BMI ≥50 kg/m^2 had ten times the odds of undergoing surgery compared to those with a BMI <40 kg/m^2. It should be noted that even though the individuals were categorized as having BMI <40 kg/m^2 they were all morbidly obese (>35 kg/m^2). In a study by Jakobsen et al. (14) a similar association was also found, yet individuals with a BMI ≥50 kg/m^2 had about six times the odds of undergoing surgery compared to those with a BMI <40 kg/m^2.

The presence of hypertension and dyslipidemia was associated with higher odds of undergoing surgery in this study. The presence of hypertension and diabetes has been previously associated with increased likelihood of the surgeon's decision to operate on morbidly obese patients (78) but most other studies have not found this association (14, 15, 77).

It seems as the individuals who undergo bariatric surgery have poorer physical health in general; they have higher BMI and are more likely to have obesity-related comorbidities. Nevertheless our results indicate that severe depression decreases the odds of surgery, even though this finding was not significant (P=0.11) in this study. This could possibly be because individuals with depression are not allowed for surgery as their mental health condition may complicate recovery after surgery. Pre-surgery psychological assessment is recommended in order to address any early factors that might jeopardize compliance after surgery and compromise weight loss (91).

6.2 Weight loss

6.2.1 Active patients and Active patients and surgery

In our study we found that the mean weight loss in the groups of AP and APS did not differ in the ambulatory treatment, neither the total weight loss nor weight loss per month.

The weight loss in the stationary treatment was greater in the group of APS. Individuals in the APS group had higher baseline weight and when adjusted for that the difference between the groups ceased to be significant. Higher initial body weight often predicts greater weight loss (18) as heavier people have a greater excess body mass they can to lose. Therefore it seems that weight loss is independent regarding treatment option, whether individuals go to bariatric surgery or not.

The mean weight loss from screening to the end of five week stationary treatment was similar as in a previous thesis that was conducted at Reykjalundur. Our results show 8.8 kg to 10.2 kg mean weight loss compared to average weight loss of 11 kg in the other thesis (84).

6.2.2 Patients with different comorbidities

We wanted to find out if comorbidity status influences or possibly prevents weight loss in the obesity treatment. When categorizing individuals according to comorbidity status we found that the total mean weight loss in the ambulatory treatment was significantly greater for individuals with hypertension and diabetes than for the reference group. These groups had also higher weight at baseline. However the mean weight loss per month was not significantly different between the groups. Individuals with diabetes spent more days in the ambulatory treatment than the reference group and had therefore more time to achieve the predefined goals of ambulatory treatment (e.g. weight loss) before going to the stationary treatment.

Interestingly individuals with depression spent more time in the ambulatory treatment than the reference group, but they did not lose significantly more weight during that time. Yet the mean weight loss per month was similar for both groups.

The mean weight loss in the stationary treatment was similar for all groups except for individuals with depression compared to the reference group. The mean weight loss in the reference group was significantly 1.1 kg greater than in the depression group and after adjusting for baseline weight the difference becomes borderline significant. Depression has not been found to be a predictor for weight loss and the reason is that improvements in depression symptoms occur during weight loss treatment and tend to covary with weight changes (19). As the Beck Depression Inventory (BDI-II), used in this study, only measures

current depressive symptoms (86) we cannot exclude that the depressive symptoms changed during the course of the treatment. We do not have information on the psychological status of the individuals after the screening and can therefore not conclude on that matter. However it seems that individuals with depression do not succeed as well as the reference group in losing weight.

It should be mentioned that even though individuals in the reference group had none of the comorbidities the other groups had, it cannot be excluded that they had other comorbidities, such as dyslipidemia or sleep apnea, which we did not take into account in the weight loss analysis.

The obesity treatment at Reykjalundur is similar for all individuals as it is based on group treatment but each individual gets the support he needs during the treatment. It seems that the weight loss in the ambulatory and stationary treatments is similar for all individuals and that their comorbidity status does not prevent weight loss. However individuals with depression seem to lose a little less weight than others.

7 CONCLUSION

Our study on Icelandic morbidly obese individuals adds to the current knowledge on predictors of bariatric surgery and dropout from weight loss programs. The participants displayed a high prevalence of comorbidities and abnormal blood values, in particular pre-diabetes, diabetes, dyslipidemia and depression.

Our findings show that a very large proportion of individuals dropped out of the obesity treatment and that having severe depression symptoms more than doubles this risk. We also found that individuals in the highest BMI category ($\geq$50.0 kg/m^2) had ten times greater odds of going to bariatric surgery compared to those in the lowest category (<40.0 kg/m^2).

Interestingly, weight loss was similar in all groups, independent of their treatment option and their comorbidity status did not substantially affect weight loss.

8 FUTURE PERSPECTIVES

It is important to focus more on the individuals who drop out of the obesity treatment at Reykjalundur and to intervene before they do so. A possible solution is to refer individuals to a psychologist as soon as they are diagnosed with depression, where the psychological complications would be addressed. Furthermore the obesity treatment might not be suitable for all individuals and therefore it might be more efficient if it would be divided into sections in order for each individual to find a treatment option that is suitable for him or her. Assessing the individuals' readiness for behavioral change with the Transtheoretical Model of Behavior Change might be useful to assess if individuals are ready to make necessary lifestyle changes when they start the obesity treatment and thereafter give them the support they need in changing their lifestyle.

Further research is needed on both those who drop out and those who go to bariatric surgery. It is interesting to examine in more detail what happens to those who drop out and if they enter obesity treatment again later, and whether their health, e.g. psychological health, and their body weight has changed from when they first entered the obesity treatment.

It is also interesting to research what happens to those who undergo bariatric surgery and how they succeed in maintaining weight loss in a few, e.g. 10, years. Another interesting question is whether some individuals regain weight and what differentiates those who maintain weight loss and those who regain weight. Are there any factors in screening before the individuals begin the obesity treatment that can predict how the individuals will do some years after bariatric surgery?

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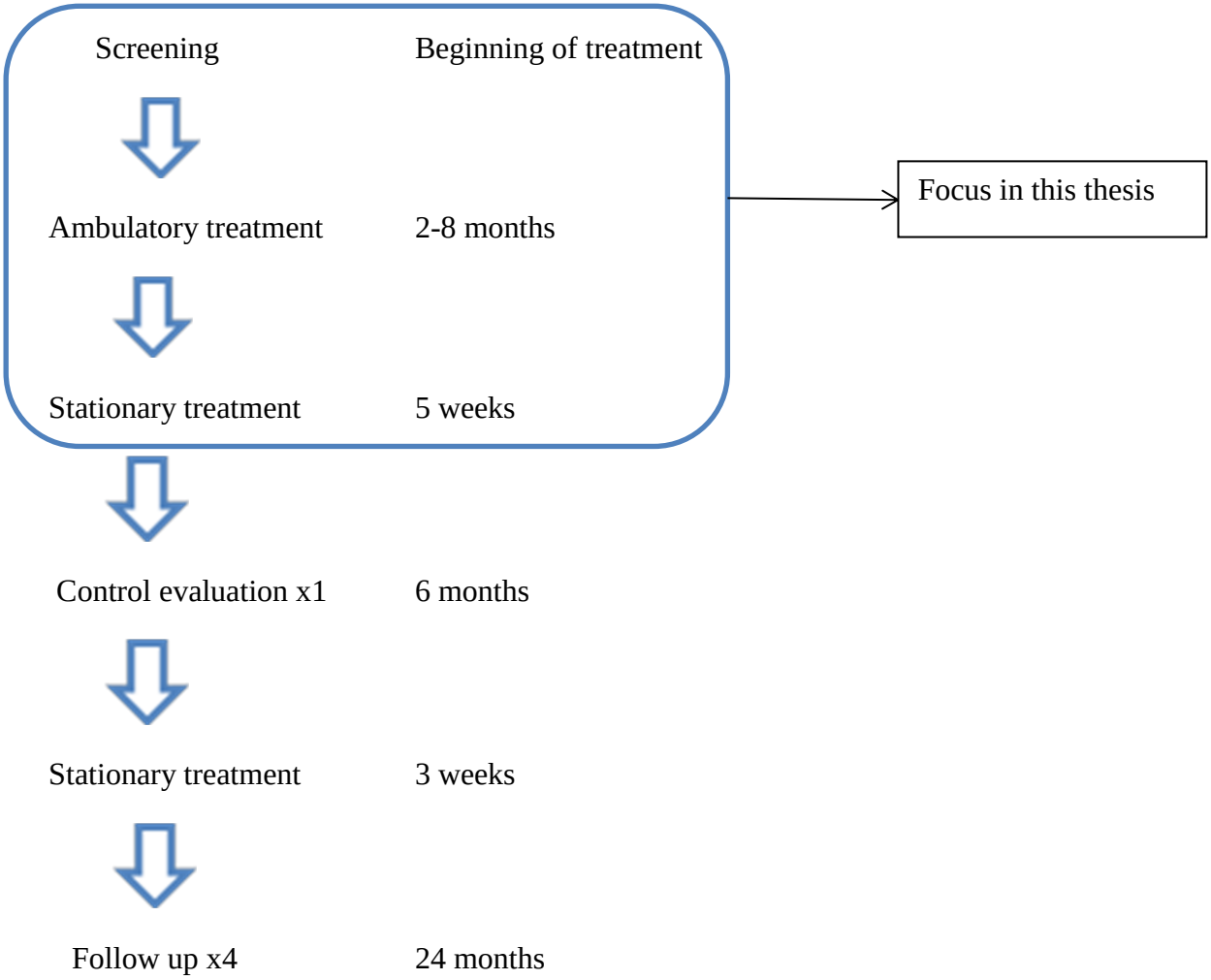
APPENDIX I

Overview of the obesity treatment at Reykjalundur



APPENDIX II

Permission from the National Bioethics Committee

VÍSINDASIÐANEFND

Hafnarhúsið, Tryggvagata 17
101 Reykjavík,

Sími: 551 7100, Bréfsími: 551 1444

netfang: visindasidanefnd@vsn.stjr.is

Reykjalundur, Næringar- og offitusvið
Ludvig Guðmundsson, yfirlæknir
Reykjalundur, Mosfellsbær
270 Mosfellsbær

Reykjavík 13. desember 2011
Tilv.: VSNb2011120004/03.7

Efni: Varðar: 11-175-afg Árangur í offitumeðferð Reykjalundar.

Á fundi sínum 13.12.2011 fjallaði Vísindasiðanefnd um umsókn þína, vegna ofangreindrar rannsóknaráætlunar. Meðrannsakendur þínir eru Auður Benediktsdóttir, Alfons Ramel, Þórhallur Ingi Halldórsson og Guðrún Jóna Bragadóttir.

Eftir að hafa farið vandlega yfir umsókn þína og innsend gögn gerir Vísindasiðanefnd ekki athugasemdir við framkvæmd rannsóknarinnar en áréttar meginreglu sína um að rannsóknargögnum öðrum en sjúkraskrárgögnum verði eytt innan fimm ára frá rannsóknarlokum. Rannsóknaráætlunin er endanlega samþykkt með framangreindri áréttingu.

Vísindasiðanefnd bendir rannsakendum vinsamlegast á að birta VSN tilvísunarnúmer rannsóknarinnar þar sem vitnað er í leyfi nefndarinnar í birtum greinum um rannsóknina. Jafnframt fer Vísindasiðanefnd fram á að fá send afrit af, eða tilvísun í, birtar greinar um rannsóknina. Rannsakendur eru minntir á að tilkynna rannsóknarlok til nefndarinnar.

Með kveðju,
f.h. Vísindasiðanefndar,

dr. med., Björn Rúnar Lúðvíksson, læknir, formaður

APPENDIX III

Permission from the Data Protection Authority

Ludvig Guðmundsson
Dalaþingi 14
203 Kópavogur

Persónuvernd

Rauðarárstíg 10 105 Reykjavík
sími: 510 9600 bréfasími: 510 9606
netfang: postur@personuvernd.is
veffang: personuvernd.is

Reykjavík, 20. janúar 2012
Tilvísun: 2011121359HGK/--

Heimild skv. 3. mgr. 15. gr. laga nr. 74/1997 til aðgangs að sjúkraskrám

I.
Umsókn

Persónuvernd hefur borist umsókn frá Ludvig Guðmundssyni, yfirlækni næringar- og offitusviðs á Reykjalundi, Alfons Ramel, fræðimanni á rannsóknarstofu í næringarfræði í Háskóla Íslands og Þórhalli Inga Halldórssyni, lektor við rannsóknarstofu í næringarfræði í Háskóla Íslands, dags. 6. desember 2011, um leyfi til aðgangs að sjúkraskrám vegna rannsóknar sem ber yfirskriftina „Árangur í offitumeðferð Reykjalundar".

Í umsókninni er tilgangi vinnslunnar lýst á eftirfarandi hátt:

> „Að rannsaka hvort og að hve miklu leyti kyn, aldur, búseta (höfuðborgarsvæði/utan höfuðborgarsvæðis), niðurstöður mælinga á líkamssamsetningu, blóði, sálfræðilegum þáttum og kvíða, sem framkvæmdar eru við forskoðun í upphafi offitumeðferðar á Reykjalundi, hafi forspárgildi um árangur eintaklinga í sjálfri meðferðinni. Þættir sem hafa forspárgildi um þyngdarbreytingar hjá eintaklingum í yfirþyngd hafa verið rannsakaðir ítarlega en lítið er vitað hvort hægt sé að heimfæra þá þekkingu á einstaklinga sem eru með alvarlegri stig sjúkdómsins, þ.e.a.s. morbid-offitu. Með þessari rannsókn er ætlunin að varpa betur ljósi á hvaða þættir hafi forspárgildi um þyngdarbreytingar og árangur í offitumeðferð hjá eintaklingum með morbid-offitu."

Samkvæmt umsókninni verður úrtakið valið með eftirfarandi hætti:

> „Einstaklingar sem mættu í forskoðun á næringar- og offitusvið Reykjalundar á árunum 2007-2011, ca. 1000 talsins. Einstaklingarnir eru allir með mikla offitu (þ.e. líkamsþyngdarstuðul (LÞS) > 35

kg/m2), og eru flestir með morbid offitu (LÞS>40 kg/m2).“

Samkvæmt umsókninni er fyrirhugað að afla upplýsinga frá næringar- og offitusviði Reykjalundar. Eftirfarandi upplýsingum verður safnað í þágu rannsóknarinnar:

> „Við óskum eftir að fá aðgang að og safna heilsufarsupplýsingum sem skráðar eru við forskoðun á Reykjalundi til að meta ástand sjúklings áður en offitumeðferð hefst; og upplýsingum sem eru skráðar meðan á meðferð stendur. Nánar tiltekið: Upplýsingar um kyn, aldur, búseta innan eða utan höfuðborgarsvæðis, líkamssamsetningu (hæð, þyngd, fituprósentu og mittismál) og niðurstöður úr blóðmælingum (m.a. hemóglóbín, MVC, kólestról, þríglýseríð og blóðsykur), blóðþrýsting, niðurstöður úr sálfræðiprófum (þunglyndis- og kvíðapróf), lyfjanotkun og þyngdarbreytingar sjúklinga á meðan meðferð stendur.“

Varðandi skráningu persónuauðkenna og varðveislu rannsóknargagna í tengslum við rannsóknina segir eftirfarandi:

> „Persónueinkenni (nafn, heimilisfang, kennitölur og aðrar sambærilegar persónurekjanlegar upplýsingar) verða skilin frá og þátttakendur fá númer með slembivali. Eingöngu verður unnið með gögn undir númerum. Persónugreinanlegur númeralisti verður varðveittur hjá verkefnastjóra á Reykjalundi og mun hann einn hafa aðgang að þeim lista. Vert er að taka það fram að þeir sem koma til með að greina gögnin munu ekki hafa aðgang að persónurekjanlegum upplýsingum og hafa ekki komið nálægt meðferð eða umgengist sjúklinga á Reykjalundi.“

Af framangreindu er ljóst að í rannsókninni felst öflun upplýsinga um einstaklinga úr sjúkraskrám þeirra. Samkvæmt 3. mgr. 15. gr. laga nr. 74/1997, um réttindi sjúklinga, þarf leyfi Persónuverndar til aðgangs að sjúkraskrám í þágu vísindarannsókna. Getur stofnunin bundið slíkt leyfi þeim skilyrðum sem hún telur nauðsynleg hverju sinni.

II.
Leyfi og leyfisskilmálar

Persónuvernd hefur nú ákveðið, m.a. að virtum ákvæðum 29., 33. og 34. gr. í formálsorðum persónuverndartilskipunarinnar nr. 95/46/EB, 9. tölul. 1. mgr. 9. gr. laga nr. 77/2000 um persónuvernd og meðferð persónuupplýsinga og að veita yður umbeðið leyfi til aðgangs að sjúkraskrám vegna rannsóknarinnar: „Árangur í offitumeðferð Reykjalundar“ samkvæmt 3. mgr. 15. gr. laga nr. 74/1997.

Leyfi þetta gildir til **31. desember 2012** og er bundið eftirfarandi skilyrðum:

1. *Ábyrgðaraðilar að vinnslu persónuupplýsinga*
   Ludvig Guðmundsson, Alfons Ramel og Þórhallur Ingi Halldórsson (sem hér eftir kallast leyfishafar), teljast vera ábyrgðaraðilar vinnslunnar í skilningi 4. tölul. 2. gr. laga nr. 77/2000. Fer Ludvig Guðmundsson með allt fyrirsvar gagnvart Persónuvernd um alla þætti er varða þetta leyfi, þ.á m. álitaefni, er upp kunna að rísa, um það hvort vinnsla persónuupplýsinga hafi verið í samræmi við lög, reglur og ákvæði þessa leyfis.

2. *Lögbundnir leyfisskilmálar*
   a. Þegar leyfishafar fara þess á leit við ábyrgðarmenn sjúkraskráa, sbr. 12. tölul. 3. gr. laga nr. 55/2009 um sjúkraskrár, að fá aðgang að viðkomandi sjúkraskrám, ber þeim að framvísa leyfi þessu.
   b. Leyfi þetta er bundið því skilyrði að ábyrgðarmenn umræddra sjúkraskráa hafi lýst því yfir að þeir séu því samþykkir fyrir sitt leyti að leyfishafar fái aðgang að þeim.
   c. Leyfi þetta er bundið því skilyrði að siðanefnd, eða eftir atvikum vísindasiðanefnd, hafi

lagt mat á rannsóknina og látið í té skriflegt álit sitt þess efnis að hvorki vísindaleg né siðfræðileg sjónarmið mæli gegn framkvæmd hennar, sbr. 3. mgr. 15. gr. laga nr. 74/1997, sbr. 4. mgr. 2. gr. sömu laga.

d. Þegar leyfishafar skoða sjúkraskrá á grundvelli leyfis þessa ber þeim að skrá það í sjúkraskrána, sbr. 4. mgr. 15. gr. laga nr. 74/1997.

3. Ótvírætt og yfirlýst samþykki

Öll notkun persónuupplýsinga um lifandi og sjálfráða einstaklinga er óheimil án skriflegs, upplýsts samþykkis hlutaðeigandi, enda séu þeir nægilega heilir heilsu til þess að gera sér grein fyrir þýðingu og afleiðingum slíks samþykkis nema annað sé tekið fram í leyfi þessu. Sé um að ræða sjálfræðissviptan einstakling eða einstakling sem er ósjálfráða fyrir ásku sakir skal lögráðamaður hans ákveða hvort samþykki verði veitt til að vinna með persónuupplýsingar um hann. Fylgt skal reglum Persónuverndar nr. 170/2001 um það hvernig afla skal upplýsts samþykkis fyrir vinnslu persónuupplýsinga í vísindarannsókn á heilbrigðissviði.

4. Lögmæt vinnsla persónuupplýsinga og þagnarskylda

a. Leyfishafar bera ábyrgð á því að vinnsla persónuupplýsinga vegna rannsóknarinnar fullnægi ávallt kröfum 1. mgr. 7. gr. laga nr. 77/2000.

b. Farið skal með upplýsingar úr sjúkraskrám, sem skráðar eru vegna rannsóknarinnar, í samræmi við lög nr. 77/2000, lög nr. 74/1997 um réttindi sjúklinga, læknalög nr. 53/1988 og lög nr. 55/2009 um sjúkraskrár. Hvílir þagnarskylda á leyfishöfum og öðrum þeim sem koma að rannsókninni um heilsufarsupplýsingar sem unnið er með, sbr. 15. gr. laga nr. 53/1988. Þagnarskylda helst þótt látið sé af störfum við rannsóknina.

c. Taki háskólanemar eða aðrir, sem ekki teljast til löggiltra heilbrigðisstétta, þátt í framkvæmd rannsóknarinnar skulu þeir undirrita sérstaka þagnarskylduyfirlýsingu, þar sem þeir m.a. ábyrgjast að tilkynna leyfishöfum ef í rannsóknargögnum eru viðkvæmar persónuupplýsingar um þá sem eru eða hafa verið maki viðkomandi, skyldir eða mægðir honum í beinan legg eða að öðrum lið til hliðar eða tengdir honum með sama hætti vegna ættleiðingar. Er viðkomandi þá óheimilt að kynna sér gögn um þá einstaklinga. Leyfishöfum eða fulltrúa þeirra ber að votta rétta undirskrift hlutaðeigandi og dagsetningu slíkrar yfirlýsingar og koma henni til Persónuverndar innan tveggja vikna frá útgáfu leyfis þessa eða frá því viðkomandi hefur störf við rannsóknina. Persónuvernd hefur borist slík yfirlýsing frá Auði Benediktsdóttur. Þagnarskyldan er byggð á 3. mgr. 35. gr. laga nr. 77/2000. Á heimasíðu Persónuverndar er að finna staðlað eyðublað fyrir þagnarskylduyfirlýsingu. Ef þagnarskylduyfirlýsingum er ekki skilað innan tilskilins frests getur Persónuvernd afturkallað leyfi þetta.

d. Leyfi þetta heimilar einvörðungu að safnað verði úr sjúkraskrám þeim heilsufarsupplýsingum sem gildi hafa fyrir rannsókn leyfishafa og samrýmast markmiðum hennar. Hafi sjúkraskráruppl ýsingar í sjúkraskrá verið merktar sérstaklega viðkvæmar í samræmi við 2. mgr. 13. gr. laga nr. 55/2009 heimilar leyfi þetta eingöngu að slíkum upplýsingum verði safnað hafi þær augljóst vægi fyrir gæði rannsóknar og niðurstöður.

e. Leyfi þetta heimilar ekki rannsakendum aðgang að sjúkraskráruppl ýsingum hafi viðkomandi sjúklingur eða umboðsmaður hans lagt bann við því að rannsakandi, eða annars tiltekinn aðili sem starfar á hans vegum, hafi slíkan aðgang að sjúkraskrá viðkomandi skv. 4. mgr. 13. gr. sjúkraskrárlaga nr. 55/2009.

5. Auðkenning rannsóknargagna

a. Í rannsóknargögn má skrá upplýsingar um fæðingarmánuð, fæðingarár og kyn hvers sjúklings.

b. Óheimilt er að skrá í rannsóknargögn upplýsingar um nöfn sjúklinga, nafnnúmer, heimilisföng, símanúmer, fax-núm er, tölvupóstföng eða annað sambærilegt.

c. Persónueinkenni verða tekin út og þátttakendur fá númer með slembivali. Þau gögn verða svo greind með tilliti til rannsóknarspurninga. Vert er að taka fram að saga hvers sjúklings verður ekki skoðuð sérstaklega heldur verða niðurstöður fyrir hópinn sem heild dregnar saman með tölfræði. Í ljósi þessa er heimilt við framkvæmd rannsóknar þessarar að skrá og varðveita *tímabundið* sérstaka skrá, greiningarlykil, sem tengir saman upplýsingar um kennitölur einstaklinga og rannsóknarnúmer á meðan verið er að undirbúa rannsóknargögn. Slíka skrá/greiningarlykil skal ávallt varðveita aðskilda frá öðrum rannsóknargögnum. Þegar rannsókn er lokið, og eigi síðar en við lok gildistíma leyfis þessa, skal greiningarlykli eytt.

6. Öryggi við vinnslu persónuupplýsinga

Leyfishöfum ber að gera viðeigandi tæknilegar og skipulagslegar öryggisráðstafanir til að vernda persónuupplýsingar gegn óleyfilegum aðgangi í samræmi við 11. og 12. gr. laga nr. 77/2000. Þar er meðal annars áskilið að:

a. beita skuli ráðstöfunum sem tryggja nægilegt öryggi miðað við áhættu af vinnslunni og eðli þeirra gagna sem verja á, með hliðsjón af nýjustu tækni og kostnaði við framkvæmd þeirra, og
b. tryggja skuli að áhættumat og öryggisráðstafanir við vinnslu persónuupplýsinga séu í samræmi við lög, reglur og fyrirmæli Persónuverndar um hvernig tryggja skal öryggi upplýsinga, þ.m.t. þá staðla sem hún ákveður að skuli fylgt.

Leyfishafar bera ábyrgð á því að hver sá er starfar í umboði þeirra og hefur aðgang að persónuupplýsingum vinni aðeins með þær í samræmi við skýr fyrirmæli sem þeir gefa og að því marki að falli innan skilyrða leyfis þessa, nema lög mæli fyrir á annan veg, sbr. 3. mgr. 13. gr. laga nr. 77/2000.

7. Almennir skilmálar

a. Ávallt skal tryggt að rannsóknargögn séu varðveitt á tryggum stað og aðeins þar sem lögum samkvæmt er heimilt að varðveita þau.
b. Leyfishafar bera ábyrgð á að farið sé með öll persónuauðkennd gögn sem sjúkragögn í samræmi við lög, reglur og ákvæði þessa leyfis.
c. Leyfishafar skulu ábyrgjast að engir aðrir en þeir fái í hendur persónugreinanleg gögn sem sérstaklega verður aflað í þágu þessarar rannsóknar.
d. Óski leyfishafar þess að hætta rannsókn ber þeim að leggja þetta leyfi inn til Persónuverndar á skriflegan og sannanlegan hátt. Skal þá tilgreina hvort þeim persónuupplýsingum, sem unnar voru á grundvelli þessa leyfis, hafi verið eytt. Að öðrum kosti úrskurðar Persónuvernd um hvort persónuupplýsingunum skuli eytt eða þær varðveittar með ákveðnum skilyrðum.
e. Leyfishöfum ber að veita Persónuvernd, starfsmönnum og tilsjónarmönnum hennar allar umbeðnar upplýsingar um vinnslu persónuupplýsinga sé eftir því leitað í þágu eftirlits. Brot á ákvæði þessu getur varðað afturköllun á leyfinu.
f. Persónuvernd getur látið gera úttekt á því hvort leyfishafar fullnægi skilyrðum laga nr. 77/2000 og reglna sem settar eru samkvæmt þeim eða einstökum fyrirmælum. Getur Persónuvernd ákveðið að þeir skuli greiða þann kostnað sem af því hlýst. Persónuvernd getur einnig ákveðið að leyfishafar greiði kostnað við úttekt á starfsemi, við undirbúning útgáfu vinnsluleyfis og annarrar afgreiðslu. Persónuvernd skal þá gæta þess að sá sérfræðingur, sem framkvæmir umrædda úttekt, undirriti yfirlýsingu um að hann lofi að gæta þagmælsku um það sem hann fær vitneskju um í starfsemi sinni og leynt ber að fara eftir lögum eða eðli máls. Brot á slíkri þagnarskyldu varðar refsingu samkvæmt 136. gr. almennra hegningarlaga. Þagnarskyldan helst þótt látið sé af starfi.
g. Leyfi þetta er háð því skilyrði að einungis verði safnað þeim upplýsingum sem *nauðsynlegar* eru vegna rannsóknarinnar.

Virðingarfyllst

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