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General introduction and outline of the thesis

Background

Obesity is a growing global health problem and affects individuals of all ages, genders and socioeconomic backgrounds. Obesity impacts physical and psychological well-being and poses a considerable burden on individuals and societies all over the world. Metabolic and bariatric surgery (MBS) has proven to be the most effective intervention for individuals living with severe obesity who have been unable to achieve sustainable weight loss through conservative methods [1]. This type of surgery entails multiple approaches that modify the gastrointestinal anatomy by reducing the capacity of the stomach and/or length of the small bowel. These anatomical changes also affect the body's gut hormone profile, including hormones such as Glucagon-Like Peptide-1 (GLP-1) and Peptide YY (PYY), as well as the gut microbiota and bile acids [2]. These alterations influence appetite, satiety and metabolism, thereby contributing to the weight loss process. However, the full extent of their impact is still being explored in ongoing research.

The introductory chapter of this thesis aims to provide an overview of the prevalence of overweight and obesity, their associated medical conditions, and the factors that are associated with obesity and weight loss after MBS.

Prevalence of overweight and obesity

Definitions and classifications

A healthy weight is defined by a Body Mass Index (BMI) ranging from 18.5 to 24.9 kg/m^2. A BMI above 25 is categorized as overweight. A BMI above 30 is classified as obesity, which is further divided into classes: Class I (BMI 30-34.9), Class II (BMI 35-39.9), and Class III (BMI ≥40). However, BMI alone does not fully capture the severity of obesity or its associated health risks; waist circumference and obesity-associated medical conditions must also be considered to assess overall weight-related health risks. Table 1 summarizes these health risks for adults according to the Dutch Guideline for Obesity [3].

Global Perspective

Overweight and obesity have reached epidemic proportions. On World Obesity Day in 2022, the World Health Organization reported that the global count of individuals affected by obesity exceeded 1 billion [4]. This number included an estimated 650 million adults, 340 million adolescents, and 39 million children. Over the past

decades, there has been a consistent upward trend in obesity rates, and this trajectory is still ongoing.

Table 1. Levels of weight-related health risk in adults.

BMI kg/m^2	**NO increase in waist circumference and no obesity-associated medical condition(s)**	**Increased waist circumference** Male ≥ 102cm Female ≥ 88cm	**Obesity-associated medical condition(s) present**
≥25 BMI <30 Overweight	Increased	High	
≥30 BMI <35 Obesity class I		Very high	
≥35 BMI <40 Obesity class II	Very high	Extremely high	
BMI ≥40 Obesity class III	Extremely high		

For individuals aged 70 and above, or those of ethnicities other than European or Middle-Eastern Mediterranean, different cut-off values apply.

Obesity in The Netherlands

Like this global trend, The Netherlands has also experienced a substantial increase in obesity prevalence. Data from the Netherlands Health Survey showed that 50.2% of the Dutch adult population is currently overweight, with 15.1% classified as having obesity [(5)]. These increasing numbers emphasize the need to address the obesity epidemic within the global as well as Dutch context.

Physical and psychological implications

Physical problems

Obesity, acknowledged by the WHO as a chronic disease, is a complex health problem. It is characterized by excessive adipose tissue accumulation, resulting in an elevated BMI with significant implications for physical and psychological well-being. Obesity is associated with various medical conditions, including cardiovascular diseases, type 2 diabetes, many types of cancer, obstructive sleep apnea, and osteoarthritis [(6)].

Psychological problems

In addition to the physical health problems, the psychological impact of obesity cannot be overlooked. Mental health disorders, such as depressive disorders,

anxiety disorders, substance use disorders and eating disorders, particularly binge eating disorders, are frequently observed in people living with obesity [7, 8]. The association between psychological disorders and obesity is often bidirectional. For example, research shows that individuals living with obesity have a 55% higher risk of developing depression, while those with depression have a 58% higher risk of developing obesity [9]. The lifetime prevalence of binge eating disorder in individuals living with obesity is estimated at 5.49% in women and 2.87% in men [10]. Among patients referred for MBS, 30% have previously received a DSM-5 diagnosis [11]. In addition, it is known that body dissatisfaction is more prevalent in individuals with obesity, when compared to people with a lower BMI [12].

Weight stigma is another challenge faced by individuals living with obesity. It refers to the negative stereotypes and discrimination faced by people with obesity, often based on incorrect beliefs about the causes of obesity [13]. This stigma can lead to harmful assumptions about their character, resulting in significant psychological, social, and physical consequences [13].

Understanding the associations between obesity and physical and psychological problems is crucial for developing strategies to effectively address the growing obesity epidemic. By recognizing obesity as a complex disease, healthcare professionals can implement comprehensive strategies that go beyond weight loss alone. These approaches should prioritize prevention and management of obesity-associated medical conditions to improve the overall well-being of individuals living with obesity.

The significance of addressing the obesity epidemic

Loss of healthy life years

The increasing prevalence of obesity has profound implications for public health. The total disease burden, expressed in Disability Adjusted Life Years and comprising both years lost due to premature mortality and years lived with health conditions weighted by their severity (disease year equivalents), in the Netherlands is attributed to 3.7% caused by severe obesity alone [14]. Additionally, prior research shows that severe obesity can lead up to 13.7 years of life lost [15].

Economic burden

Obesity places an enormous burden on healthcare systems and societies, resulting from increased healthcare costs and reduced work productivity [16, 17]. These costs include direct expenses associated with the treatment of obesity-related diseases, as well as indirect costs stemming from disability, absenteeism and unemployment [16-18]. Fortunately, many of the previously described obesity-related health problems can be reversed by achieving sufficient and sustained weight loss, thereby reducing risk of weight-related health problems [19].

Non-surgical treatment of overweight and obesity

Identifying underlying causes of obesity

According to the Dutch guideline released in 2023, it is crucial to first determine, optimize and treat the underlying causes and factors contributing to weight gain and maintenance of obesity [3]. Possible contributing factors may include lifestyle choices, socio-economic circumstances, psychological factors, medication usage, hormonal influences, hypothalamic function, and/or genetic predispositions.

Lifestyle advice and guidance

The cornerstone of every treatment plan is a healthy, varied diet with minimal processed food products, alongside adequate physical activity. In the Netherlands, individuals with overweight or class I obesity, particularly those with increased waist circumference and/or obesity-associated medical conditions, should be referred for combined lifestyle intervention (CLI). For patients with severe obesity (a BMI ≥40 kg/m^2) or those with a BMI ≥35 kg/m^2 combined with increased waist circumference and/or obesity-associated medical conditions, a specialized CLI where cognitive behavioral therapy is included can be considered [3].

Obesity management medication

Obesity management medication should be considered as an adjunct to a CLI for individuals with obesity (BMI ≥30 kg/m2) or overweight (BMI ≥27 kg/m2) with an increased waist circumference and/or obesity-associated medical conditions [3].

Surgical treatment of obesity

Indications for metabolic and bariatric surgery

Clinical practice guidelines are developed for, among other objectives, determining the indications for MBS [11, 20]. According to the Dutch Guideline, MBS is primarily recommended for individuals with severe obesity, typically defined as a BMI of 40 kg/m² or higher [11]. People with a BMI between 35 and 39.9 kg/m² may also be considered for surgery if they have significant obesity-associated medial conditions like type 2 diabetes, hypertension, dyslipidemia or obstructive sleep apnea. Recently, the criteria for considering MBS have expanded to include patients with a BMI of 30 to 34.9 kg/m² and type 2 diabetes with inadequate glycemic control despite optimal lifestyle changes and medical therapy [11].

Metabolic and bariatric procedures

In The Netherlands, the Roux-en-Y gastric bypass (RYGB) is the most performed procedure, followed by sleeve gastrectomy (SG) [21, 22]. However, the most frequently performed procedure varies by country, as shown in the IFSO Global Registry Report [22]. Indications for RYGB and SG are influenced by various factors, including the patient's BMI, obesity-associated medical conditions, surgical risks, and individual's or surgeon's preferences [20]. Both procedures are effective for achieving weight loss and improving obesity related medical problems [23]. Perioperative counselling programs that focus on behavioral change and monitor medical aspects are considered essential for optimal outcomes, regardless of the chosen procedure [20].

Outcomes after metabolic and bariatric surgery

The weight loss following MBS is dependent on the duration after the procedure and the surgical method that is performed [1, 24]. It is frequently quantified as a percentage of total weight loss (%TWL) using the following formula:

$$\%TWL = \frac{\text{preoperative weight} - \text{postoperative weight}}{\text{preoperative weight}} * 100$$

RYGB generally results in better weight loss outcomes compared to SG [23]. A prior randomized controlled trial observed that one year post-surgery, individuals who underwent RYGB had a %TWL of 29.9%, while those who had SG exhibited a %TWL of 28.4% [25]. At five-year follow-up, RYGB patients sustained a %TWL of 26.0%, whereas SG patients had a %TWL of 22.5% [25]. Weight loss seems to be higher in

the population studied in this thesis: data from the Nederlandse Obesitas Kliniek (Dutch Obesity Clinic, NOK), revealed that after one year, average %TWL was 32.1% for RYGB and 29.9% for SG [26]. After five years, these percentages were 27.2% and 24.7% TWL respectively for RYGB and SG.

Undoubtedly, MBS has been widely acknowledged for resulting in long-term sustained weight loss. However, the significance of MBS goes beyond weight reduction alone. MBS improves or resolves various obesity-related medical conditions, such as type 2 diabetes, hypertension, and obstructive sleep apnea [1, 19]. Moreover, individuals who have undergone MBS experience improvements in health-related quality of life and enhanced body image [27, 28]. Additionally, a recent meta-analysis comparing people living with obesity who underwent MBS to those who did not undergo MBS, revealed that MBS was correlated with a decreased overall occurrence of cancer, specifically obesity-related cancers, and cancer-related mortality [29]. So, it can be concluded that MBS leads to a reduction of health risk, which is important not only for individual well-being but also for the overall welfare of society.

Complications, adverse- and side effects of metabolic and bariatric surgery

While MBS is a highly effective treatment for severe obesity, offering numerous physiological and psychological benefits, it is equally important to acknowledge and address the complications, potential long-term adverse events and side effects in both the physical and psychological domains.

Apart from the immediate surgical complications like bleeding, leakage or infection, patients who undergo MBS may develop other significant physical consequences. There is a risk of nutritional deficiencies, especially in vitamins B12, D, calcium, and iron, which can cause conditions such as anemia, osteoporosis, or peripheral neuropathy [30]. To prevent this, the lifelong supplementation of tailored multivitamins is recommended [30]. Gastrointestinal side effects may also arise, such as dumping syndrome, gastro-esophageal reflux disease and alterations in stool patterns, all of which depend on the type of MBS performed [30, 31]. Furthermore, there is a potential risk for late complications, like bowel obstruction, ulcerations and perforations that may require additional surgical interventions [30].

There are also psychological complications associated with MBS, like the increased risk of suicide and substance misuse after surgery [32]. This underscores the need for continued psychological support after surgery.

Factors associated with weight loss

Individual variations in weight loss outcomes

Despite the reduction of health risk after MBS, it is crucial to acknowledge that the outcomes of surgical interventions can vary significantly among individuals. Approximately 10-15% of patients undergoing MBS experience suboptimal weight loss outcomes, often defined as achieving a %TWL of less than 20% within the first year after surgery [21, 33, 34]. Factors that have previously found to be related to lower postoperative weight loss include higher age, higher baseline weight, ethnicity, the presence of diabetes, and gastrointestinal hormone levels [35-38].

Preoperative prerequisites

International guidelines recommend that all individuals considering MBS undergo a thorough screening process [20]. This evaluation aims to detect potential risk factors that could affect treatment outcomes and long-term adherence and to facilitate proper postoperative monitoring. This step is crucial as achieving and maintaining weight loss post-surgery necessitates lifestyle improvements [20, 39]. Previous studies have established a correlation between non-adherence to these lifestyle changes and reduced weight loss following MBS [40, 41].

Several approaches have been utilized to identify patients who are willing to commit to the necessary lifestyle changes. Historically, clinics, insurance companies and policymakers have used the "last resort criterion" as a guideline, suggesting MBS only after traditional weight loss attempts or mandatory weight loss programs (MWPs) were unsuccessful [42]. The rationale behind MWPs is based on the belief that these programs would facilitate preoperative weight loss, help patients adapt to lifestyle modifications, and consequently result in greater postoperative weight loss [43]. However, over the past decade, the practice of requiring patients to follow a MWP before MBS has not shown to increase postoperative weight loss [42, 44]. Consequently, MWPs are no longer advised in the most recent guidelines [20, 45].

Another approach to identify patients' motivation involves requiring a certain amount of weight loss before surgery. Nonetheless, studies have reported inconsistent results on the effects of preoperative weight loss on weight loss after MBS [46-49]. The conflicting evidence highlights the complexity of this issue. While some patients may benefit from preoperative weight loss programs by adopting healthier

habits and preparing for lifestyle changes, others might not experience a significant impact on their postoperative outcomes. Therefore, the effectiveness of mandating preoperative weight loss as a criterion to predict postoperative success remains uncertain and needs further investigation.

Psychological factors

As discussed earlier in this introduction, psychopathological conditions are common among individuals who undergo MBS. The most prevalent mental health disorders in this population are depression and eating disorders, particularly binge eating disorders [7, 8]. A psychological evaluation by a licensed professional should always be part of the preoperative screening process before MBS [11, 20]. The Dutch guideline for bariatric psychology recommends to use the Cleveland Clinic Behavioral Rating System during the preoperative screening [50]. This tool provides a structured psychodiagnostic assessment to identify risk factors that may impede optimal weight loss outcomes or increase the likelihood of postoperative psychological complications. Psychological contraindications for MBS include confirmed eating disorders, an insufficiently extensive social network, and other psychiatric disorders that are unstable, severe, or untreated, such as severe depression, anxiety disorders, post-traumatic stress disorder, and substance abuse [11].

Prior studies have examined the relationship between mental health and weight loss following MBS; however, findings have been inconclusive. Some studies suggest that various mental and behavioral factors, such as eating disorder pathology, loss of control over eating, depressive symptoms, impulsiveness, and body avoidance, are associated with suboptimal postoperative weight loss [51-53]. Conversely, other studies suggest that these factors do not notably affect post-surgical weight loss [54-57].

Food and health literacy

Food literacy is defined as the combination of knowledge, skills, and behaviors required for planning, managing, selecting, preparing, and consuming food to meet dietary needs and regulate food intake [58]. Health literacy is the ability to locate, comprehend, and utilize information and services to make informed decisions and take actions regarding one's own health and that of others [59]. Despite guidelines suggesting that insufficient knowledge about healthy eating may require dietary counseling and potentially delay surgery, conducting a formal evaluation of food and health literacy is not standard clinical practice [11].

Assessing food and health literacy used to be challenging; however, measurement is now possible with validated questionnaires. Still, in the context of patients undergoing MBS, there is often a lack of information about their existing nutritional knowledge, dietary skills, and health literacy, resulting in a substantial knowledge gap [60]. Further research is needed to bridge this gap and to develop effective treatment programs or interventions for individuals undergoing MBS.

Aims and outline of the thesis

The studies in this thesis primarily aim to identify and analyze factors potentially influencing weight loss outcomes following MBS. It aims to establish the associations among these factors and to determine their clinical implications. Identifying these factors is crucial to recognize patients who are vulnerable to suboptimal (long-term) weight loss, thereby enabling to provide them with appropriate support.

The thesis comprises of three parts. **Part I** focuses on understanding psychological factors associated with weight loss after MBS. In **Chapter 2,** a systematic review and meta-analysis is reported, which examines preoperative and postoperative behavioral and mental factors related to weight loss following MBS. In **Chapter 3,** it is assessed whether a psychologic screening tool (the Cleveland Clinic Behavioral Rating System) can predict weight loss or postoperative compliance.

Part II of this thesis aims to evaluate if preoperative prerequisites for MBS are correlated with postoperative weight loss. **Chapter 4** reports the usefulness of mandatory weight loss programs considered a "last resort criterion" before MBS. In **Chapter 5** it is examined whether preoperative weight changes impact postoperative and total weight loss outcomes.

Part III aims to explore the preoperative levels of food and health literacy among people who undergo MBS and compares these levels with those of the general population, as detailed in **Chapter 6**.

Part IV integrates the findings of this thesis within a comprehensive framework discussed in **Chapter 7**, including a summery, clinical implications and future research perspectives. **Chapter 8** provides a Dutch summary of the thesis.

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