From DEPARTMENT OF MEDICINE SOLNA Karolinska Institutet, Stockholm, Sweden

# **"IT'S NOT A QUICK FIX"**

# CONSEQUENCES OF WEIGHT LOSS DURING LIFE AND EXPERIENCES OF WEIGHT REGAIN AFTER BARIATRIC SURGERY

Liisa Tolvanen



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## "It's not a quick fix" Consequences of weight loss during life and experiences of weight regain after bariatric surgery

### Thesis for Doctoral Degree (Ph.D.)

By

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The thesis will be defended in public at the lecture hall Saffran at Academic Specialist Center, 4<sup>th</sup> floor, Solnavägen 1E, Stockholm, on Friday, October 20<sup>th</sup>, 2023, at 01:00 pm.

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To Jakob -my beloved son

## Popular science summary of the thesis

It is common for people to regain weight after weight loss. A general misconception is that we can easily control our body weight if we have enough willpower. Some piece of advice is often, "Eat less and move more." The fact is that weight is affected by many factors, several of which are not under our control. Some people are more likely to gain weight than others are. Since too much fat tissue in the body may increase the risk of other chronic diseases, weight loss may be necessary to improve health and well-being. Considering the growing global prevalence of overweight and obesity, gaining increased knowledge regarding the challenges surrounding weight loss and weight maintenance is crucial.

A major part of this thesis has focused on how people who have undergone surgical treatment for weight loss experience weight regain. Our results showed that participants felt lonely and lacked support from healthcare and family members. They blamed themselves for regaining weight. We found that they experienced several difficulties, such as problems with physical and mental health, and that different everyday challenges could make weight management even more complicated. We found that participants experienced challenges with food and eating behavior, changes in appetite, emotional eating, and increased alcohol consumption. They tried dieting methods that did not lead to permanent weight loss – instead, their disappointments increased.

There are uncertainties regarding whether weight loss increases the risk of early death. In a large study, we asked people living in Sweden about their previous weight loss. We followed them for more than 20 years using the national registries. Our results showed an association between weight loss and repeated weight loss with early death, especially in men with heart disease but not with cancer. These results indicate that all, especially men, may need more support to sustain their weight loss. Stable weight should be encouraged in individuals with normal weight.

We studied whether previous weight loss is associated with self-esteem and eating behaviors in young people with obesity. We found that weight loss was associated with eating behavior, where the individual controls eating to a high degree. No other associations were found. These results indicate that young people with obesity try to control their eating and weight. However, without sustained weight loss.

Weight loss maintenance is not a "quick fix." Weight loss and weight regain may increase mental, psychosocial, and physical health problems. Therefore, healthcare professionals should provide long-term, individualized, and empathetic support for weight management to promote the health and well-being of patients.

## Populärvetenskaplig sammanfattning

Det är vanligt att många ökar i vikt igen efter viktminskning. En allmän missuppfattning är att det är lätt att kontrollera kroppsvikt, bara det finns tillräckligt med viljestyrka. Det enkla rådet är ofta, "Ät mindre och rör på dig mer". Faktum är att vikten påverkas av många faktorer, flera av dem är helt utanför vår kontroll. Vissa individer ökar i vikt lättare än andra. Eftersom för mycket fettvävnad på kroppen kan öka risk för andra kroniska sjukdomar, kan viktminskning vara nödvändigt för att förbättra hälsa och välbefinnandet. Med tanke på att antalet individer med övervikt och obesitas (fetma) ökar i värden, är det viktigt att förstå mer om viktminskningens och viktåtertagandets utmaningar.

En stor del av den här avhandlingen har fokuserat på hur personer som genomgått kirurgisk behandling för viktminskning, har upplevt att vikten åter ökat. Våra resultat visade att deltagarna upplevde ensamhet och saknade stöd från sjukvården och familjemedlemmarna. De anklagade ofta sig själva för viktökningen. Vi fann att olika faktorer kunde bidra till svårigheter med vikthantering, såsom problem med fysisk och psykisk hälsa, olika vardagsutmaningar, som stress och familjekonflikter. Deltagarna beskrev förändringar i matlust, känsloätande och ökad alkoholkonsumtion som kunde bidra till svårigheter med vikthantering. Deltagarna försökte kontrollera sin vikt med olika metoder, vilket inte ledde till permanent viktminskning – i stället ökade besvikelsen.

Vi vet inte om viktminskning kan öka risken för förtidig död. I en stor studie, frågade vi personer i Sverige om deras tidigare viktminskning och följde dem i över 20 år via nationella register. Våra resultat visade på en association mellan tidigare viktminskning och förtidig död, särskilt hos män, i hjärt- och kärlsjukdomar, men inte i cancer. Dessa resultat tyder på att alla, men speciellt män, kan behöva mer stöd för att behålla en viktminskning och att viktstabilitet bör rekommenderas för dem med normalvikt.

Vi studerade om tidigare viktminskning hos unga personer med obesitas kunde ha associationer med självkänsla och ätbeteenden. Vi hittade en association mellan tidigare viktnedgång och ett återhållsamt ätbeteende. Detta kan betyda att unga personer med obesitas försöker kontrollera sitt ätande och vikt utan bestående resultat. Inga andra samband hittades.

Att bibehålla en minskad vikt, efter viktnedgång, är ingen "quick fix". Att minska i vikt och öka i vikt igen kan bidra till problem med den psykiska, psykosociala och fysiska hälsan. Därför bör personal inom hälso- och sjukvården erbjuda långsiktigt, individualiserat och empatiskt stöd för att underlätta vikthantering samt för att främja hälsa och välbefinnande hos personer med obesitas.

## Populaaritieteellinen yhteenveto

Painon uudelleen nousu on tavallista painonlaskun jälkeen. Yleinen käsitys on, että painoa voidaan helposti hallita itse, kunhan vain on tarpeeksi tahdonvoimaa. Yksinkertainen neuvo on usein, "Syö vähemmän ja liiku enemmän". Itseasiassa painoon vaikuttavat monet tekijät, joista läheskään kaikkia emme voi itse kontrolloida. Jotkut ovat muita alttiimpia painon nousemiselle. Koska liiallinen rasvakudos kehossa voi lisätä muiden pitkäaikaisten sairauksien riskiä, painonpudotus voi olla tarpeellista terveyden ja hyvinvoinnin edistämiseksi. Ajatellen että ylipaino ja lihavuus lisääntyy koko ajan maailmassa, on tärkeää ymmärtää paremmin painonpudotuksen ja painon uudelleen nousun haasteet, ja täten antaa tukea kestävässä painonhallinnassa.

Suuri osa tästä väitöskirjasta on keskittynyt siihen, kuinka lihavuusleikkauksen läpi käyneet potilaat ovat kokeneet painon uudelleen nousun. Tuloksemme osoittivat, että tutkimukseen osallistuneet kokivat yksinäisyyttä painonhallinnassa ja he toivoivat enemmän tukea terveydenhoidon ammattilaisilta ja perheenjäseniltä. He syyttivät itseään painon uudelleen noususta. Painonhallinnan vaikeuksiin vaikuttivat monet tekijät, kuten fyysisen ja henkisen terveyden ongelmat, arjen haasteet, stressi ja perheongelmat, muutokset ruokahalussa, tunnesyöminen ja lisääntynyt alkoholinkäyttö. He yrittivät laihduttaa eri keinoin, mutta ne eivät johtaneet pysyvään painonpudotukseen – sen sijaan pettymyksen tunne lisääntyi.

On epävarmaa voiko painonpudotus lisätä varhaisen kuoleman riskiä. Kysyimme monilta Ruotsissa asuvilta henkilöiltä heidän aiemmasta painonpudotuksestaan ja seurasimme heitä sitten yli 20 vuoden ajan kansallisten rekisterien kautta. Tuloksemme osoittivat yhteyden painonpudotuksen ja ennenaikaisen kuoleman välillä. Tämä yhteys oli erityisesti havaittavissa miehillä sydän- ja verisuonitauteihin, mutta ei syöpään. Nämä tulokset osoittavat, että kaikki, mutta erityisesti miehet, saattavat tarvita enemmän tukea painonpudotuksen ylläpitämiseksi. Painon vakautta tulisi suositella normaalipainoisille.

Tutkimme jos aiempi painonpudotus on voinut vaikuttaa lihavuudesta kärsivien nuorten itsetuntoon ja syömiskäyttäytymiseen. Löysimme yhteyden aiemman painonpudotuksen ja kontrolloidun syömiskäyttäytymisen välillä. Muita yhteyksiä ei löytynyt. Potilaat yrittävät hallita syömistään ja painoaan ilman kestäviä tuloksia.

Vähentyneen painon ylläpitäminen painonlaskun jälkeen ei ole mikään pikaratkaisu. Painon lasku ja painon uudelleen nouseminen voivat lisätä psyykkisiä, psykososiaalisia ja fyysisiä terveysongelmia. Siksi on tärkeää, että terveydenhuollon ammattilaiset tarjoavat potilaille pitkäaikaista, yksilöllistä ja empaattista tukea painonhallintaan sekä terveyden ja hyvinvoinnin edistämiseen.

## Abstract

Maintenance of weight loss is challenging for most people who intentionally lose weight. Complex factors interact with each other and obstruct weight management. This thesis focuses on the consequences of weight loss and experiences of regaining weight. These results could be helpful in treatment recommendations for individuals who live with obesity.

Studies I, II, and III were qualitative studies that analyzed data from semistructured interviews with participants living with obesity who had regained an average of 36% from the lowest weight point after bariatric surgery. All participants had undergone gastric bypass surgery.

Study I focused on how participants experienced support from healthcare professionals, families, and friends during weight regain following bariatric surgery. The thematic analysis showed that participants felt lonely and abandoned during post-surgical weight management. In addition, shame and self-blame could further obstruct the search for medical support. However, participants described social support from healthcare and family members as desired and helpful for a healthier lifestyle and weight management. Our findings indicate the importance of an empathetic and non-judgmental approach towards patients and access to a multi-professional healthcare team for long-term support.

In Study II, we investigated the experiences of patients who had undergone bariatric surgery and struggled with weight regain. Further, we aimed to understand the factors that might be of interest in improving post-bariatric care. Thematic analysis showed that weight regain was a complex and unexpected experience that induced a negative emotional response. In addition, post-surgery weight management became challenging due to multiple daily obstacles, alterations in appetite, and physical and mental health issues. Nevertheless, most participants experienced lasting benefits from gastric bypass surgery, despite regaining weight. To reduce the burden of weight management, participants wished to focus more on self-care and receive positive support from healthcare providers.

In Study III, we explored patients' experiences with food- and eating-related behaviors during weight regain after gastric bypass surgery. In the thematic analysis, we found that participants experienced overwhelming dietary challenges. They had not expected to need to struggle with dietary issues such as mealtimes, sizes of portions, and cravings. They also described emotional and disordered eating and drinking patterns. Participants experienced a lack of nutritional knowledge and support. They turned to restrictive eating and dieting behaviors to manage their weight.

In a prospective cohort study, Study IV, we investigated the association between weight loss earlier in life and mortality outcomes, specifically for all-causes, cardiovascular disease (CVD), and cancer mortality. We followed 34,346 individuals from the Swedish National March Cohort for over two decades to assess mortality. To calculate Hazard Ratios (HR) and 95% confidence intervals (CI), we employed Cox Proportional Hazard Models, with age serving as the timescale. We adjusted for multiple confounders and found that individuals who had lost >10 kg or  $\geq$ 5 kg on three or more occasions had higher mortality rates for all causes and cardiovascular disease than 10 kg had higher mortality rates for all causes and cardiovascular disease than men who had not lost weight. We did not observe any associations between weight loss and cancer mortality.

Study V was a cross-sectional study in which we examined whether weight loss earlier in life in adolescents and young adults with obesity before starting a medical obesity treatment program might be associated with self-esteem and eating behaviors. We used self-reported data from 224 participants to determine associations using linear regression models. Our findings showed that those who had lost 5-10 kg and  $\geq$ 5 kg two times or more often had higher cognitive restraint eating scores than adolescents and young adults with obesity who had not lost weight. However, we did not find any association between weight loss, self-esteem, and other eating behaviors such as uncontrolled eating and emotional eating.

In conclusion, existing post-surgical support was experienced as insufficient by participants who had regained weight after bariatric surgery. They may have had unrealistic expectations concerning postoperative weight management and eating behaviors. Various internal and external challenges may obstruct weight management and eating behaviors, contributing to emotional distress and feelings of personal failure. Our results show the need for an extended follow-up. Special focus should be directed toward those with difficulties in weight loss maintenance. Weight loss earlier in life may increase all-cause and cardiovascular mortality, particularly in men. Furthermore, previous weight loss attempts may affect adolescents and young adults with obesity, leading them to struggle to control their eating behavior to a high degree without sustained weight loss. Healthcare professionals should assess patients' weight loss history and eating behaviors, and encourage healthy eating for sustained weight management, regardless of sex, throughout life.

## List of scientific papers

- Tolvanen, L., Svensson, Å., Hemmingsson, E., Christenson, A., Trolle Lagerros Y. Perceived and Preferred Social Support in Patients Experiencing Weight Regain after Bariatric Surgery – A Qualitative Study. *Obesity Surgery*. 2021; 31(3):1256–1264. The final published version is available at https://link.springer.com/article/10.1007/ s11695-020-05128-5.
- II. Tolvanen, L., Christenson, A., Surkan, P.J., Trolle Lagerros, Y. Patients' Experiences of Weight Regain after Bariatric Surgery. *Obesity Surgery*. 2022; 32(5):1498–1507. The final published version is available at https://link.springer.com/article/10.1007/s11695-022-05908-1.
- III. Tolvanen, L., Christenson, A., Bonn, S.E., Surkan, P.J., Trolle Lagerros, Y. Patients' Perspectives on Dietary Patterns and Eating Behaviors during Weight Regain after Gastric Bypass Surgery. *Obesity Surgery*. 2023; 33(8):2517–2526. The final published version is available at https://link.springer.com/article/10.1007/s11695-023-06718-9.
- IV. Tolvanen, L., Ghilotti, F., Adami, H-O., Weimin, Y., Bonn, S.E., Bellocco, R., Trolle Lagerros, Y. Prospective Study of Weight Loss and Allcause-, Cardiovascular-, and Cancer Mortality. *Scientific Reports*. 2023; 13: 5669. The final published version is available at https://www.nature.com/articles/s41598-023-32977-8.
- V. Tolvanen, L., Christenson, A., Eke, H., Bonn S.E., Trolle Lagerros, Y. Weight Loss History and its Association with Self-esteem and Eating Behaviors among Adolescents and Young Adults with Obesity. *Obesity Facts.* 2023; 16(3):293-300. The final published version is available at https://www.karger.com?doi=10.1159/000529267.

The articles will be referred to in the text by their Roman numerals and are found in their published form at the end of the thesis. Papers I-IV are reproduced with permission from Springer Nature. Paper V is reproduced with permission from Karger Publishers.

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## List of abbreviations

BMI	Body Mass Index, kg/m <sup>2</sup>
CI	Confidence Interval
CVD	Cardiovascular disease
GIP	Glucose-dependent insulinotropic polypeptide
GLP-1	Glucagon like peptide-1
HR	Hazard Ratio
Kcal	Kilocalorie, 1 Kilojoule (KJ) = 0,239 kcal; 1 kcal = 4,184 KJ. A unit of measure of energy
LAGB	Laparoscopic Adjustable Gastric Banding
LISA	Longitudinal Integrated Database for Health Insurance and Labour Market Studies
Look Ahead	Action for Health in Diabetes
MNT	Medical Nutrition Therapy
ΡΥΥ	Peptide Tyrosine Tyrosine
p-value	Probability value
%EWL	Percentage of Excess Weight Loss
%TWL	Percentage of Total Weight Loss
%TWR	Percentage of Total Weight Regain
RSES	Rosenberg Self-esteem Scale
RYGB	Roux-en-Y Gastric Bypass
SD	Standard Deviation
SG	Sleeve Gastrectomy
SNMC	Swedish National March Cohort
SOReg	Scandinavian Obesity Surgery Registry
SOS-Study	Swedish Obese Subjects Study
SYO	Swedish Youth with Obesity
TFEQ-R21	Three-Factor Eating Questionnaire-Revised21
WHO	World Health Organization

## Introduction

Obesity has become a major global public health concern in the 21<sup>st</sup> century, with its prevalence rising worldwide <sup>1</sup>. To date, no country has been able to stop the increase in obesity rates. Obesity is characterized by the accumulation of body fat with harmful health consequences metabolically, mentally, and physically <sup>2</sup>. Excess adiposity is a considerable factor associated with disability and mortality. People living with obesity often experience negative attitudes and discrimination, so-called weight bias, and obesity stigma in their everyday lives <sup>3</sup>.

The food environment has changed rapidly, promoting hyper-palatable foods and beverages with high energy densities <sup>4</sup>. In obesity, appetite regulation may be disturbed with less signaling for satiety and more signaling for hunger, increasing vulnerability in the obesogenic environment <sup>5</sup>. Furthermore, challenges in body weight regulation are derived from a combination of different interacting factors, such as genetics, biology, hormones, lifestyle, living conditions, and psychosocial factors. Obesity has been recognized as a multifactorial and complex chronic disease, <sup>6-8</sup> not simply an individual responsibility or personal choice. Weight loss is strongly recommended to reduce the risk of obesity-related comorbidities <sup>9</sup>. However, sustained weight loss is a challenge, often followed by weight regain <sup>10</sup>. Setpoint theory suggests that biological mechanisms defend against weight loss and contribute to weight regain <sup>11</sup>. Bariatric surgery is an effective way to achieve sustained weight loss and reduce the risk of comorbidities and mortality in people with severe obesity <sup>12</sup>. However, weight regain is possible, even after surgical treatment <sup>13</sup>.

This thesis focuses on various aspects of weight loss and regain, which are common phenomena in people living with obesity. A major part concerns various aspects of weight regain after bariatric surgery. Increased understanding of patients' experience of support, weight management, and food and eating-related behaviors during weight regain may provide us with essential knowledge on how to improve the follow-up and support for these patients pre- and post-surgically. Furthermore, this thesis explored the possible consequences of weight loss during life. Difficulties in weight management may begin at an early age, persist for decades, and negatively impact physical and mental health. Weight loss and repeated weight loss during life may affect self-esteem and eating behaviors, and even increase mortality. This thesis may provide improved knowledge to understand the complexity of weight management.

## 1 Literature review

### 1.1 Prevalence of overweight and obesity

The prevalence of overweight and obesity has escalated to a level that elicits serious concern for public health, health policy, healthcare systems, and people in numerous countries <sup>1</sup>. According to the World Health Organization (WHO), the prevalence of obesity has tripled globally since the mid–1970s, affecting not only high–income countries but also rural and low–income regions <sup>1</sup>. The WHO's Regional Office for Europe estimates that approximately 60% of adults, and almost 30% of adolescents and children are living with overweight or obesity in the European region <sup>8</sup>. There are no signs of global decline in the prevalence of obesity <sup>14</sup>. From 1995 to 2017, the levels of moderate and severe obesity (Body mass index, a BMI greater than 35.0 kg/m<sup>2</sup>) increased by 153% in Sweden <sup>15</sup>. The World Obesity Federation has predicted that more than half of the world's population will be living with overweight or obesity by the year 2035 <sup>14</sup>. Along with the increasing numbers of overweight and obesity, the coexistence of undernutrition may contribute to the double burden of malnutrition <sup>8</sup>.

According to the latest self-reported data from the Public Health Agency of Sweden in 2022, 51.1% of the population aged between 16 and 84 years had a BMI  $\geq$ 25.0 kg/m<sup>2</sup> and, 16.3% had a BMI  $\geq$ 30.0 kg/m<sup>2</sup>. These numbers can be compared to 45.8% vs. 11.7% in 2006 <sup>16</sup>, showing an increase in obesity across all age groups. The prevalence has increased in adolescents and young adults (16–29 years), from 22.1% to 28.3% (obesity from 5.4% to 7.2%), between 2006 and 2022 <sup>16</sup>. Additionally, 23% of children between the ages of 6 and 10 years were having overweight, and 7.2% had obesity, in school year 2021/2022 <sup>17</sup>.

### 1.2 Definition of overweight and obesity

### Body mass index (BMI)

The nutritional status of adults is often assessed using BMI as a surrogate marker for excess fat tissue <sup>18</sup>. According to the WHO, BMI is calculated using the formula: "a person's weight in kilograms divided by the square of the person's height in meters  $(kg/m^2)$ " <sup>18</sup>. In adults, a BMI of 25.0–29.9 kg/m<sup>2</sup> is defined as overweight or pre-obesity and BMI  $\geq$ 30.0 kg/m<sup>2</sup> as obesity <sup>18</sup>. The nutritional status related to different BMI levels is presented in Table 1.

BMI	Nutritional status	
<18.5	Underweight	
18.5–24.9	Normal weight	
25.0–29.9	Overweight/pre-obesity	
30.0-34.9	Obesity, class I	
35.0–39.9	Obesity, class II	
<u>&gt;</u> 40	Obesity, class III	

 Table 1. The World Health Organization's classification of Body mass

 index BMI (kg/m<sup>2</sup>) and nutritional status <sup>18</sup>

At the population level, BMI is useful for predicting how excess body fat accumulation may impact health <sup>1</sup>. However, risk prediction is challenging at the individual level. Since body composition has an impact on body weight, using BMI may cause over- or underestimation of the accumulation of body fat in different individuals. For instance, athletes with a high proportion of muscle mass may be misclassified when using their BMI. Ethnicity may also have an impact on how BMI and associated health risks should be interpreted. Therefore, suggestions for lower BMI cut-off levels have, for example, been made to better predict risks among the Asian population <sup>19</sup>. The American Medical Association (AMA) has recently recognized the limitations of using BMI alone as a diagnostic criterion for obesity and suggested that BMI should be used together with other measurements, such as waist circumference or body composition for adipose tissue <sup>20</sup>.

The International Obesity Task Force (IOTF) recommends using specific cut-offs for different ages and sexes to assess the body weight status of children aged between 2 and 18 years <sup>21</sup>.

The individual risk of developing diseases associated with excess adiposity may vary even with higher BMI levels, sometimes called "metabolically healthy obesity" <sup>22</sup>. These individuals appear to have a phenotype of obesity that protects them against adverse metabolic health outcomes associated with adiposity. However, the metabolically healthy obesity phenotype seems to develop into metabolically unhealthy obesity over time <sup>22</sup>. Therefore, it has been suggested that even those with a metabolically healthy obesity phenotype have a higher risk for cardiovascular disease than those with normal weight phenotypes <sup>23</sup>.

Nonetheless, BMI is easy to calculate, provides valuable objective information on nutritional status, and is helpful for screening obesity in clinical practice. However, BMI has several limitations and should be combined with other methods to assess health. Overweight is a commonly used term for BMI levels of 25.0–29.9 kg/m<sup>2</sup>. However, the term "overweight" is sometimes used in a broader sense to

encompass individuals with a BMI above 25.0 kg/m<sup>2</sup>, including those who are considered having obesity (BMI  $\geq$ 30.0 kg/m<sup>2</sup>). Therefore, the term pre-obesity has been used by WHO Europe <sup>18</sup> and adopted by the European Commission <sup>24</sup> to clarify the specific stage before obesity.

### Waist Circumference

Waist Circumference measurement is an adequate method for assessing excess visceral fat. It can be used as a complement to BMI, especially to assess cardiometabolic risk, Table 2 <sup>25</sup>.

Waist Circumference	Risk of disease				
Women					
>80 cm	Increased metabolic risks				
>88 cm	Substantially increased metabolic risks				
Men					
>94 cm	Increased metabolic risks				
>102 cm	Substantially increased metabolic risks				

Table 2. The World Health Organization's classification of waist circumference and risk of disease  $^{\rm 25}$ 

As for BMI, lower cut-off levels for waist circumference, have been suggested for certain ethnic groups, such as those originating from Asia <sup>25</sup>. Waist circumference should be measured in a standardized manner by placing a measuring tape between the lowest rib and the iliac crest after two normal breaths <sup>25</sup>.

The recently updated clinical guidelines on obesity by the National Institute for Health and Care Excellence (NICE) in the United Kingdom <sup>26</sup> suggests that the waist-height ratio may be a useful and evidence-based <sup>27</sup> complement to BMI in assessing health risks if the BMI is below 35, independent of sex or ethnic background. The guidelines propose that if the waist measurement is more than half of the people's height, there is an increased risk of metabolic health. Therefore, a ratio >0.5 is used as an indicator of increased health risks.

Other measures for abdominal and visceral fat are waist-hip-ratio <sup>25</sup> and sagittal abdominal diameter <sup>28</sup>. However, waist circumference is most often recommended in obesity management guidelines to assess excess visceral fat <sup>6.29</sup>.

#### Body composition

The importance of muscle mass, strength, and function has been highlighted in people with obesity <sup>30,31</sup>. Low muscle mass and poor functional quality of muscle mass are risk factors for ill-health if co-existent with excess fat mass, known as sarcopenic obesity <sup>30</sup>.

The suggested underlying mechanisms include low-grade inflammation, low protein intake, lack of physical activity, high-energy intake, lipotoxicity, hormonal imbalance, and aging <sup>32,33</sup>. Acute and chronic diseases may be major pathways for the loss of muscle mass and function, and an increase in fat mass. However, weight change plays a role in the development of sarcopenic obesity.

For instance, patients who may be at risk of muscle mass loss are individuals with rapid and excessive weight loss after bariatric surgery <sup>34,35</sup>. Non-surgical interventions have demonstrated similar, but less obvious, loss of fat-free mass than surgical treatments have <sup>36,37</sup>. The loss of muscle mass seems to be proportional to the reduction in energy intake, level of physical activity, and amount of lost weight in non-surgical intervention <sup>37</sup>. The loss of muscle mass after bariatric surgery might be influenced by decreased protein intake combined with energy deficit and inactivity. Some studies have highlighted changes in the hormone panel as well as the influence of metabolic factors on the loss of muscle mass after bariatric surgery <sup>38,39</sup>.

Repeated weight loss and weight regain have been discussed concerning sarcopenic obesity, since every weight cycle may lead to accumulation of fat mass and loss of fat-free mass <sup>40</sup>. A meta-analysis of 12 prospective cohort studies reported that people with sarcopenic obesity have a 24% higher risk of death from all causes than those with normal weight or body composition <sup>41</sup>.

While BMI and waist circumference are ways to assess excess body weight, body composition can be assessed more accurately using Bioelectrical Impedance Analysis (BIA) or Dual-energy X-ray Absorptiometry (DEXA) <sup>33</sup>.

#### The obesity staging system

Different staging systems have been established for a more comprehensive approach to obesity assessment to complement anthropometric measurements at the individual level. The Edmonton Obesity Staging System and King's Obesity Staging Criteria are two examples of staging systems used to identify people with excess body weight and a heightened risk of morbidity and mortality <sup>42</sup>. The Canadian Clinical Practice Guidelines for Obesity in Adults suggest the use of the Edmonton Obesity Staging System because it might be a more accurate method for assessing the severity of obesity and the risk of all-cause mortality in individuals than anthropometric measures alone <sup>6,43</sup>. With the Edmonton Obesity Staging System, mental, medical, and functional assessments are performed and categorized into stages 0-4 (from no apparent risk factors to severe obesity-related physical and/or mental co-morbidities) according to individual health status rather than weight or BMI only <sup>44</sup>.

### 1.3 Etiology of Obesity

The WHO added obesity as a disease in the Sixth International Classification of Diseases, in 1948 <sup>45</sup>. A crucial step in classifying obesity as a chronic disease was the 1997 WHO report, "Obesity. Preventing and managing the global epidemic", which highlights the alarming prevalence of obesity worldwide and its numerous health and economic consequences for individuals across their lifespan <sup>46</sup>. The WHO specifies obesity as "abnormal or excessive fat accumulation that may impair health"<sup>1</sup>. Recently, the definition of obesity was extended in the International Classification of Diseases 11<sup>th</sup> revision (ICD-11) <sup>47</sup> to "Obesity is a chronic complex disease defined by excessive adiposity that can impair health. It is in most cases a multifactorial disease due to obesogenic environments, psycho-social factors, and genetic variants". Furthermore, the definition explains that there are subgroups of individuals in which a single factor has affected the etiology of obesity, such as diseases, physical disability, medications, and monogenetic or genetic syndromes <sup>47</sup>. However, the underlying causes of obesity are not yet fully understood and multiple complex interrelated factors are involved.

### Energy imbalance

The fundamental factor is the imbalance between the energy intake and expenditure <sup>48</sup>. This imbalance results in the storage of excess energy in subcutaneous adipose tissue when the energy intake exceeds the body's energy requirements.

### The obesogenic environment

Our environment has dramatically changed during the last decades, and these changes have promoted sedentary behavior, physical inactivity, and unhealthy

eating <sup>4</sup>. This is reflected by the increasing prevalence of obesity <sup>2</sup>. Access to energy-dense foods with high fat and sugar content has increased worldwide <sup>49</sup>. Unhealthy eating habits have been associated with increased mortality and lost healthy years of life, globally as well as in Sweden <sup>50</sup>. Hyper-palatable foods with added sugar, fats, and salt challenge the appetite system <sup>51</sup>. These foods are often called ultra-processed and found to be associated with weight gain <sup>52</sup> and have also been proposed to increase the risk of associated co-morbidities <sup>53</sup>. The marketing and advertising of unhealthy food further drive overconsumption and contribute to an obesogenic environment. It has been suggested that the global food system has a synergic impact on the economy, equity, and human wellbeing, and therefore is a driver for undernutrition, obesity, and climate-change in co-occurrence <sup>54</sup>. Obesity appears to be more common in populations with a low socioeconomic status (SES) <sup>55</sup>. The vulnerability that comes with low education, low income, and insecure social situations contributes to an additional dimension to the complexity of obesity.

#### Dietary patterns and eating behaviors

Dietary patterns can be defined as the "quantities, proportions, variety, or combination of different foods, drinks, and nutrients in diets and the frequency with which they are habitually consumed "according to the Dietary Guidelines for Americans, the United States <sup>56</sup>. Nordic Nutrition Recommendations 2023 (NNR23) <sup>57</sup> provides a scientific basis for recommendations of dietary guidelines and nutrient recommendations for the general population in the Nordic and Baltic countries. A healthy diet primarily includes vegetables, legumes, fruits, and wholegrain products <sup>57</sup>. It also includes low-fat dairy products in moderation, fish, and other seafoods. A healthy dietary pattern should include less red meat, processed meat, saturated fat, sodium, sugar-sweetened foods, and energy-dense beverages <sup>57</sup>. These recommendations are suitable even for those with overweight or obesity and for the prevention of obesity-related co-morbidities. Current evidence has not identified a superior nutritional strategy in terms of macronutrient composition or meal frequency for optimal weight loss or maintenance of lost weight <sup>58</sup>. There is no "one-size-fits-all" strategy. Instead, there are several nutritionally adequate strategies available 58,59, but they should be accompanied by a lower energy intake than the required energy levels to achieve weight loss.

Eating behaviors are complex practices that are important to consider in relation to overweight and obesity. They are defined by LaCaille to include "food choice, and motives, feeding practices, dieting, and eating-related problems such as obesity, eating disorders, and feeding disorders" <sup>60</sup>. Furthermore, how, what, and when we eat are influenced by various factors, such as genetics <sup>61</sup>, the obesogenic environment, living conditions, and social and cultural aspects that interact with each other <sup>62</sup>. Eating behaviors are also influenced by physiological circumstances, e.g., feelings of hunger and satiety <sup>63</sup> and psychological processes, e.g., beliefs, attitudes, emotions, and cognitions <sup>64</sup>. Together, these findings may contribute to the fact that eating, food choices, and feeding practices are experienced as private, sensitive, and complicated matter.

Eating behaviors such as emotional eating, cognitive restraint eating, and uncontrolled eating are associated with obesity <sup>65</sup>. Emotional eating is characterized by behaviors in which food is used to respond to negative emotions. It has been found to be associated with internalized weight bias and anxiety in women and body shape in men during adolescence <sup>66</sup>. Uncontrolled eating is defined as loss of control in eating situations. Cognitive restraint eating refers to individuals consciously restricting their eating <sup>67</sup>. This type of eating can be detrimental or beneficial for self-regulation. Understanding and managing one's own behaviors and reactions are crucial for weight management. Individuals with higher cognitive restraint scores seem to experience more favorable weight loss outcomes, such as those observed in adolescence following bariatric surgery <sup>68</sup> or in adulthood through lifestyle treatment <sup>69</sup>. However, dietary restraint has also been shown to be associated with high BMI and may promote weight gain in women <sup>70</sup>.

#### Disordered eating behaviors

Disordered eating behaviors may coexist in people with overweight and obesity <sup>71</sup>, and may affect weight management. For example, it has been estimated that 16% of those seeking bariatric surgery may have binge eating disorder (BED) and 2% have bulimia nervosa <sup>72</sup>. Eating disorders often have a negative impact on overall health and well-being and are associated with mental health problems <sup>72</sup>.

There have been concerns that obesity treatment may lead to an increase in the prevalence of eating disorders. However, a systematic review and meta-analysis found that, in most adults, behavioral obesity treatment does not pose a significant risk of developing eating disorders <sup>73</sup>. There may even be reduced symptoms of eating disorders such as binge eating after obesity treatment. However, some patients may still experience and develop eating disorders. Therefore, assessing possible problematic eating patterns is essential in the treatment of obesity <sup>73</sup>. In children and adolescents (5–19 years) with overweight

and obesity, obesity management programs in healthcare settings may reduce the prevalence –, risk –, and symptoms of eating disorders  $^{74}\!$ 

After bariatric surgery, binge eating behavior becomes less prevalent due to anatomical changes, but there are indications for increasing prevalence over time <sup>75</sup>. Pre-surgical problematic eating behaviors have not been shown to be predictors of poor postoperative weight outcomes. Instead, new onset or recurrence of disordered eating behaviors post-surgery is associated with insufficient weight loss and even weight regain <sup>76</sup>. Grazing, nibbling, picking, and loss of control eating are examples of problematic eating behaviors that may impede weight control post-surgically <sup>77</sup>.

#### The neurobiology of body weight regulation

The brain, i.e., the hypothalamus, in interaction with other organs, is important in the regulation of functions such as blood pressure, body temperature and body weight <sup>5</sup>. Energy balance is highly influenced by neural processes in the hypothalamus, with complex feedback mechanisms involving gut hormones, adipose tissue, and peripheral organs indicating e.g., nutritional status <sup>78</sup>. Neural and hormonal signals influence hunger, satiety response, and energy expenditure. The mesolimbic area in the brain, also called the hedonic area, plays a reward-driven and emotional role in appetite regulation <sup>5</sup>. The mesolimbic area is highly responsive to external stimuli and food cues such as smell, taste, vision, and texture of food, but also to cultural and social factors, emotions, and the pleasure of eating <sup>5</sup>.

Gut hormones, such as cholecystokinin (CCK), peptide tyrosine (PYY), and glucagon-like peptide-1 (GLP-1), and ghrelin produced in the gastric fundus, play a role in regulating appetite <sup>79</sup>. These hormones communicate with the brain and provide information about hunger, satiety, and energy stores <sup>78</sup>. Signaling is immediate and regulates appetite in the short term. Appetite regulation is also triggered by changes in blood glucose and free fatty acids <sup>80</sup>.

The long-term regulation of metabolism, homeostasis, and energy balance is influenced by hormones, such as leptin and insulin. Leptin, produced in adipose tissue, provides information about the amount of stored fat <sup>81</sup>. Increased levels of leptin signal the brain to reduce appetite, promote satiety, and increase energy expenditure. In turn, decreased levels of leptin signal to increase appetite and decrease energy expenditure <sup>79</sup>. Leptin levels decrease in response to weight loss, thereby promoting hunger and weight regain <sup>81</sup>. Leptin resistance in the brain has

been suggested as a factor that complicates weight management for people living with obesity <sup>79</sup>. Insulin, which is produced in the pancreas, is important in the regulation of glucose levels, weight, and adipose tissue <sup>82</sup>.

### The set point theory

The set point theory posits that the body has an inherent biological mechanism to maintain stable body weight <sup>11</sup>. This mechanism is triggered when energy intake is reduced or physical activity is increased, resulting in hormonal and metabolic adaptations that prevent weight loss and promote weight regain <sup>83</sup>. Weight loss induced by reduced energy intake starts a compensatory mechanism to maintain or defend body weight <sup>78</sup>. The hunger hormone ghrelin increases, and satiety hormone levels, GLP-1 and PYY, are reduced <sup>78</sup>. These changes led to more hunger and less satiety. In addition, total energy expenditure and non-resting energy expenditure are reduced <sup>84</sup>. These changes may persist for at least one year after weight loss and therefore contribute to difficulties in weight loss maintenance <sup>85</sup>. There are large individual differences in the compensatory effects of hormonal responses that may diminish over time.

Bariatric surgery may change the set point to a lower level due to hormonal and metabolic changes <sup>78</sup>. Bariatric surgery procedures (i.e., Roux-en-Y gastric bypass or sleeve gastrectomy) reduce ghrelin levels and increase levels of GLP-1, PYY, and bile acids, thereby promoting reduced hunger and perceived satiety <sup>78</sup>. Additionally, patients may experience changes in their food preferences <sup>78</sup>. However, there appear to be individual disparities in hormonal and metabolic adaptations that can partially explain the variation in weight loss responses and weight regain following bariatric surgery <sup>86,87</sup>.

### **Medical factors**

Obstructive sleep apnea syndrome, shift work, and sleep deprivation may contribute to weight gain <sup>88</sup>. Psychological challenges such as trauma, depression, anxiety, and stress, also seem to play key roles <sup>88</sup>. Medications e.g., corticosteroids, insulin, antidepressants, antipsychotics, and antiepileptics, may contribute to weight gain <sup>88</sup>.

Individuals with medical conditions, such as hypothyroidism, hypogonadism, and Cushing's disease, may be more likely to develop obesity <sup>88</sup>. It has also been suggested that altered gut microbiota may be involved in the difficulties in weight management <sup>89</sup>. The underlying causes of obesity are complex and people living with obesity comprise a heterogeneous group.

#### Genetics

Based on twin studies, it has been estimated that obesity has a heritability of 40%–70% <sup>90,91</sup>. Several genes are associated with the development of obesity. Genetic factors may have different impacts, but the regulation of appetite control, energy balance, and metabolism seems to be central <sup>90</sup>. Furthermore, an individual's response to an environment that promotes weight gain may vary. For example, people may have different abilities to regulate their food intake. Energy expenditure may differ from person to person. There are also different weight responses to dietary changes, energy restriction, physical activity, anti-obesity medications, and even bariatric surgery <sup>92–94</sup>. Therefore, genetic factors may predispose how an individual responds to obesity treatment.

There are rare forms of obesity caused by mutations in specific genes, such as leptin deficiency or leptin receptor deficiency <sup>95</sup>. Furthermore, rare genetic obesity syndromes, such as Prader-Willi syndrome, are also associated with severe obesity and co-morbidities in early childhood <sup>96</sup>.

Epigenetics have also been discussed in relation to obesity phenotypes. It has been proposed that epigenetics is associated with changes in gene activity in an unpredictable environment <sup>97</sup>. Environmental factors, such as food choices, physical activity, fetal period, aging, and genetic predisposition, interact with the epigenome during the development of obesity <sup>97</sup>.

### 1.4 Health consequences of excess body weight

Obesity is often associated with metabolic complications, including insulin resistance and metabolic syndrome <sup>98</sup>, and the development of certain comorbidities, such as type 2 diabetes <sup>99</sup>, non-alcoholic fatty liver disease <sup>100</sup>, cardiovascular diseases <sup>101</sup>, and several types of cancer <sup>102</sup>. The primary drivers of these complications include visceral fat accumulation, adipose tissue dysfunction, and chronic inflammation <sup>103,104</sup>. Obesity has also been associated with more severe Covid–19 outcomes <sup>105</sup>. Furthermore, musculoskeletal disorders such as arthritis <sup>106</sup>, and other functional problems such as gastroesophageal reflux disease <sup>107</sup>, are also common. Additionally, psychological consequences, impairment of quality of life, and mood disorders are prevalent among people with obesity. Studies have demonstrated a bidirectional association between obesity and mental health <sup>108,109</sup>. Mental factors also involve the impact of the societal stigma associated with obesity <sup>110</sup>.

The signs of health risks associated with obesity start appearing early during adolescence and young adulthood with changes in blood lipids, fasting insulin, and other markers for co-morbidities associated with a rising weight <sup>III</sup>. Large epidemiological studies have demonstrated evidence for an association between BMI and all-cause mortality <sup>II2,II3</sup>. According to the Global Burden of Health Study, BMI is among the five main risk factors for loss of healthy years of life in Sweden <sup>50</sup>. The economic consequences of obesity, such as loss of income and productivity, affect individuals with obesity, as well as society as a whole <sup>55</sup>. The Public Health Agency of Sweden has estimated that obesity generates a cost of 70 billion SEK for society <sup>II4</sup>.

### 1.5 Psychosocial factors in obesity

#### Weight bias and obesity stigma

In 1963, Goffman posited that stigma is "an attribute that is deeply discrediting" <sup>115</sup>. Stigma is widely perceived because of societal stereotypes and norms related to physical appearance, conduct, and lineage. When an individual deviates from what is considered socially accepted or "normal," social interactions may be negatively affected. Weight bias implies that people living with obesity meet negative attitudes and beliefs towards them <sup>3</sup> and may result in obesity stigma. Negative beliefs, stereotypes, and attitudes may lead to subtle or overt acts of discrimination and marginalization <sup>3</sup>. People living with obesity face weight bias and obesity stigma in many contexts as well as in the home environment and healthcare settings <sup>110</sup>.

Internalized weight bias means that people start to adopt and internalize negative beliefs about the weight and size that they encounter in their daily lives. This has been reported among patients with obesity, including those waiting for bariatric surgery <sup>116</sup>. Moreover, weight bias and stigma have been associated with activation of the hypothalamic-pituitary-adrenal axis (HPA) and increased levels of cortisol, which in turn negatively influences physical and mental health <sup>117</sup>. Furthermore, internalized weight bias has been associated with a negative self-image, low selfesteem, self-doubt, maladaptive eating habits, substance abuse, and impaired psycho-social functioning <sup>118,119</sup>. Stigmatization of people living with obesity is a serious public health concern, especially for adolescents and young adults. Experiences of internalized weight bias and obesity stigma may, in turn, lead to excess energy intake and weight gain in youth <sup>120</sup> and, in extension, to avoidance of healthcare and inequalities in health <sup>121</sup>. Young people may have experienced teasing, bullying, or other expressions of stigmatization among their peers and in school and family settings <sup>120</sup>. These experiences are damaging, induce feelings of shame and social exclusion, and negatively affect self-esteem and quality of life.

During adolescence and young adulthood, difficulties in weight management due to social and societal factors may negatively affect self-esteem. Individuals with obesity, particularly children and adolescents, may have lower self-esteem than those with normal weight <sup>122</sup>. Puhl and Lessard reported that low self-esteem and poor body image may lead to mental health problems, dysfunctional dieting strategies, and other maladaptive eating behaviors <sup>120</sup>.

#### Social support

Social support is an interactive process in which individuals receive encouragement and help from their social networks <sup>123</sup>. Social support and social networks are included in the larger context of social capital <sup>123</sup>. Social capital, in turn, can be seen as a resource produced by networks of relationships established through shared norms, reciprocity, and trust <sup>123,124</sup>. It is deeply ingrained in the structure of interpersonal relationships and can positively support individuals and groups when needed <sup>123,124</sup>.

Social support is described as structural (the size of a network, relationships, and activities), functional (integration, quality, and depth of a social network), and formal or informal <sup>123</sup>. According to the stress-buffering hypothesis, it is an important resource, "a social fund", in stressful situations <sup>125,126</sup> and thereby may be a lifetime health-promoting factor <sup>127</sup>. However, positive social support has been suggested to be beneficial, regardless of whether an individual is under stress or not <sup>128</sup>.

Social support has several qualitative and structural functions, including, "emotional, informational, instrumental assistance and companionship" <sup>123,129</sup>. Encouragement, appraisal, empathy, advice, information, sharing daily activities, role modeling, and support in problem–solving are examples of support that can be delivered by informal social networks such as family members, spouses, friends, and formal networks such as healthcare providers. However, professional support is somewhat different from the social support provided by the closest ones. Healthcare professionals are often perceived as trustworthy experts in the medical context <sup>129</sup>. They play an important role in delivering support in a people–

centered, empathetic manner to empower patients in self-care <sup>123</sup>. In obesity care, long-term support and follow-up are recommended in the international <sup>6,130</sup> and national guidelines <sup>7</sup>.

For example, social support seems to play an essential role in psychological wellbeing after bariatric surgery, and it has been suggested that it could reduce possible negative effects <sup>131</sup>. Additionally, participation in bariatric support groups has been positively associated with weight-loss outcomes after bariatric surgery <sup>132</sup>. Thus, a lack of support or negative support can counteract the behavioral changes necessary for weight management <sup>133</sup>.

### 1.6 Obesity Treatment

In the Swedish National Guidelines for Obesity Care, combined lifestyle treatment, pharmacological therapy, and bariatric surgery are recommended treatment options for obesity <sup>7</sup>. The updated edition of the guidelines was published in April 2023 and is directed at policymakers and managers in healthcare. These guidelines emphasize the early identification of obesity, assessment, adequate treatment, monitoring, and follow-up throughout life. The guidelines also highlight the need for coordinated care, education, and training of healthcare professionals. They also underline the importance of a respectful, non-stigmatizing attitude and demeanor toward people living with obesity.

### Combined lifestyle treatment

Combined lifestyle interventions aim to provide qualified, individualized behavioral support for changes in dietary patterns and eating behaviors as well as physical activity and sedentary behavior <sup>7</sup>. Holistic multidisciplinary strategies are needed to customize the treatment. Healthcare professionals trained in obesity care, including physicians, dietitians, nurses, psychologists, and physiotherapists, are essential for delivering person-centered combined lifestyle interventions and involving patients in self-care. Self-care can include other lifestyle-related factors besides nutrition and physical activity such as sleep and stress management. Motivational, person-centered communication is a core strategy in which shared decision-making between patients and healthcare professionals enhances patient empowerment <sup>134</sup>. Psychological interventions that include multi-component approaches are central to combined lifestyle interventions. The utilization of behavioral modification strategies, such as problem-solving, goal setting, and self-monitoring <sup>134</sup>, cognitive reframing methods from Cognitive Behavioral Therapy <sup>134</sup>, and value-based action approach from Acceptance and

Commitment Therapy <sup>134</sup> are used in supporting weight management, overall mental well-being, and quality of life <sup>6</sup>.

Physical activity strengthens the effects of nutritional treatment, contributes to the maintenance of weight loss, and is beneficial for body composition <sup>135,136</sup>. However, physical activity alone contributes to modest weight loss of 2–3 kg, irrespective of the length of the intervention <sup>136</sup>. Physical activity has multiple health benefits including cardiovascular risk reduction <sup>136</sup>.

An example of a combined lifestyle intervention is the Action for Health in Diabetes Study (Look Ahead Study). In that study, participants with type 2 diabetes and moderate obesity (an average BMI of 36.0 kg/m<sup>2</sup> at baseline) maintained an average weight loss of 4.7% (compared to controls who had a 2.1% weight loss) eight years after the intensive lifestyle intervention <sup>94,137</sup>. Additionally, 26% of the participants maintained 10% of their total weight loss 8 years after the intervention <sup>94</sup>.

#### Pharmacological treatment

For individuals with a BMI  $\geq$ 30.0 kg/m<sup>2</sup> or 27 kg/m<sup>2</sup> (or 28.0 kg/m<sup>2</sup> for Orlistat) and at least one obesity-related health condition such as pre-diabetes or high blood pressure, medication can be added to the lifestyle changes to manage patients' weight. Weight loss results are individual, and there are vast differences in outcomes. Orlistat (a lipase inhibitor) in combination with lifestyle intervention has been shown to decrease body weight by an average of 5,8 kg (placebo -3,0 kg) in a four-year study <sup>138</sup>. Orlistat is the only anti-obesity medication prioritized in the National Guidelines for Obesity Treatment in Sweden <sup>7</sup>.

Medications that target homeostatic regulation of appetite and areas in the mesolimbic reward system that control hedonic food intake may lead to even more significant weight loss. Naltrexone (32 mg) – Bupropion (360 mg), in addition to a combined lifestyle intervention, showed a weight loss of 6.1% (placebo –1.3%) after 56 weeks of use <sup>139</sup>. Injections with Liraglutide (a GLP-1 receptor agonist), together with combined lifestyle intervention, have led to a weight loss of 9,2% (placebo –3,5%) after one year of treatment and 6,1% (placebo –1,9%) within three years <sup>140</sup>. Semaglutide (another GLP-1 receptor agonist) 2,4 mg weekly injections with lifestyle intervention have been shown to lead to an average weight loss of 14.9% (placebo –2,4%) in adults <sup>141</sup> and 16.1% (placebo 0.6%) in adolescents <sup>142</sup> in 68 weeks of follow-up. Furthermore, weekly injections of Tirzapatide (a glucose-dependent insulinotropic polypeptide, (GIP)), which regulates energy balance in

combination with GLP-1 receptor agonist at doses of 5 mg, 10 mg, or 15 mg when compared to placebo, resulted in 15.0%, 19,5%, 20,9% vs. 3.1% weight loss, respectively, after 72 weeks of follow-up <sup>143</sup>.

Currently, there is a rapid development of new pharmacotherapy options showing promising weight loss results in phase-2 studies, such as oral medication, Orforglipron (a GLP-1 receptor agonist)<sup>144</sup>, and weekly injections of Retatrutide (a triple hormone receptor agonist with GIP, GLP-1, and Glucagon)<sup>145</sup>.

Therefore, all medications targeting appetite regulation may induce substantial additional weight loss compared to weight loss promoted by lifestyle changes alone. However, when the intake of anti-obesity medications is discontinued, patients may experience a return of hunger and increase their energy intake, which may lead to weight regain <sup>140</sup>.

### Bariatric surgery

Bariatric surgery, also referred to as metabolic and bariatric surgery (MBS) or obesity surgery, is an option for adults with BMI  $\geq$ 35.0 kg/m<sup>2</sup> or BMI  $\geq$ 30 kg/m<sup>2</sup> with severe obesity-related conditions such as type 2 diabetes <sup>7</sup>. Even adolescents aged 15 to 17 years with BMI  $\geq$ 35.0 kg/m<sup>2</sup> can be considered for bariatric surgery if they have not responded enough to combined lifestyle interventions or pharmacological treatment <sup>7</sup>. Treatment guidelines have also suggested that older (>60 years) patients with obesity may benefit from surgical treatment <sup>146</sup>.

Since the late 90' has Roux-en-Y gastric bypass (RYGB) has been the most frequently performed bariatric procedure in Sweden <sup>147</sup>. Sleeve gastrectomy (SG) has become more common, and during years 2018-2021 RYGB and SG were nearly equally performed <sup>147</sup>. However, in 2022 RYGB became the main surgical method again <sup>147</sup>. During laparoscopic RYGB, a small stomach pouch is created and connected to the Roux limb, bypassing a significant portion of the small intestine <sup>148</sup>. In laparoscopic SG, approximately two-thirds of the stomach is removed, leaving a narrow tube <sup>148</sup>. While biliopancreatic diversion with a duodenal switch (BDP/DS) is also performed in Sweden <sup>147</sup>, it can cause severe malabsorption of proteins, vitamins, and minerals <sup>148</sup>, and is seldom performed <sup>147</sup>.

Surgical procedures can cause restriction and/or malabsorption. However, the main effect is thought to be due to changes in metabolic and hormonal signaling within the body after surgery <sup>149</sup>. These changes include modifications in the secretion of hormones and peptides in the gut, such as GLP-1, GIP, and PYY, and in

the gastric pouch/sleeve, such as ghrelin <sup>78</sup>. Additionally, there are alterations in bile acid secretion and microbiota <sup>149</sup>. These metabolic and hormonal changes result in increased satiety, reduced hunger, and improved gut-brain communication, leading to reduced body weight <sup>149</sup>. The exact mechanisms need to be further explored.

Weight loss following bariatric surgery is superior to that following lifestyle interventions <sup>150</sup>. In a systematic review and meta-analysis, RYGB showed to lead to greater decrease of BMI compared to sleeve gastrectomy at year one (-1.25 kg/m<sup>2</sup>) and year three (-1.71 kg/m<sup>2</sup>) after surgery <sup>151</sup>. The data were insufficient with respect to a longer follow-up time and differences in the reduction in BMI <sup>151</sup>. The Swedish Obese Subject Study (SOS-Study) reported that gastric bypass patients reached their maximal weight loss (32 +8%) 1-2 years after surgery <sup>12</sup>. In addition, at the ten years follow-up, those who had undergone gastric bypass maintained a 25+11% weight loss. Optimal weight loss after bariatric surgery is sometimes measured as the percentage of excess weight loss, achieving >50% EWL and maintaining it in the long term. It has been reported that patients may maintain a 68% EWL two years post-surgically <sup>152</sup>, and 57% EWL 10 years after gastric bypass surgery. Weight loss after bariatric surgery contributes to improvements in the quality of life, reduced risk of co-morbidities, and total mortality <sup>12,151</sup>. Improved glucose control, insulin sensitivity, and reduced inflammation are examples of positive health outcomes that may occur after bariatric surgery <sup>153</sup>. Life expectancy is increased post-surgically by 3.0 years when compared to controls during more than 20 years of follow-up, as reported in the SOS-Study <sup>154</sup>. However, the life expectancy in those who underwent bariatric surgery was 5.5 year shorter than that in the general Swedish population. Furthermore, weight regain is possible even after bariatric surgery <sup>13</sup>.

Bariatric surgery is an effective method for reducing energy intake <sup>155,156</sup>. This is partly accompanied by changes in taste and smell perception <sup>157</sup>, promoting the increased intake of food items with low energy density, such as fruits and vegetables. It is expected that energy intake increases with time but remains lower even eight years after RYGB <sup>158</sup>. All bariatric procedures may lead to deficiencies in micronutrients; therefore, patients require life-long supplementation as well as nutritional monitoring to prevent deficiencies <sup>159</sup>.

#### Medical nutrition therapy

Registered dietitians are nutrition experts skilled in providing dietary interventions and medical nutrition therapy (MNT) <sup>160</sup>. Dietitians use the nutrition care process

(NCP), where MNT is an evidence-based approach for treating, e.g., obesity <sup>160-162</sup>. Combined lifestyle treatment is an intervention that dietitians gualify to provide. Dietitians follow a systematic approach to stepwise problem-solving in the nutrition care process <sup>163</sup>. This approach, originally developed by the Academy of Nutrition and Dietetics in the US, consists of four stages: "nutrition assessment and reassessment, nutrition diagnosis, nutrition intervention, and nutrition monitoring and evaluation"<sup>163</sup>. Dietitians are experts in tailoring personalized energy-reduced (or -adjusted), healthy, and nutritionally adequate meal plans that are feasible for patients to accept in the long term. Dietary education and practical, individualized advice in shared decision-making are central. The MNT addresses improved overall health and maintained good nutritional status, prevention, and treatment of complications related to obesity or other conditions, in addition to weight loss or weight loss maintenance <sup>161</sup>. Other conditions include, e.g., food allergies, kidney diseases, diabetes, and digestive disorders. Dietitians also identify possible problematic, maladaptive eating behaviors and support patients in a healthy relationship with food. Family members are involved when applicable and desired by the patient. Considering patients' taste and food preferences, in addition to the social, cultural, and religious contexts, are crucial.

For some patients, partial meal replacements (200–250 kcal per meal) substitute one or two meals per day and are therefore useful for energy reduction <sup>94,162</sup>. Very Low-Energy Diets (VLED 600–800 kcal/day) or Low-Energy Diets (LED 800–1200 kcal/day)<sup>164</sup> may be treatment options, especially if there is a need for rapid weight loss. These diets require careful monitoring and long-term follow-up for weight loss maintenance, like all dietary interventions in obesity treatment.

MNT focuses on food quality and adequate nutrient intake to prevent malnutrition <sup>162,165</sup>. Individuals with obesity are at a higher risk of developing micronutrient deficiencies, particularly vitamin D, vitamin B12, folate, and iron deficiencies <sup>166</sup>. This risk increases further after bariatric surgery <sup>159</sup>. Bariatric surgery may add additional nutritional challenges in which MNT is crucial. For example, the intake of macronutrients, such as proteins, needs to be assessed and monitored to prevent the loss of muscle mass during weight loss <sup>165</sup>. Patients may experience challenges, such as intolerance, gastrointestinal symptoms, or malabsorption after bariatric surgery, where MNT is required. Additionally, patients with frequent dumping syndrome, post-bariatric hypoglycemia, or weight regain may require qualified nutritional counselling, i.e., MNT <sup>165</sup>.

Medical nutrition therapy is recommended to be a part of all stages of obesity treatment, i.e., combined lifestyle interventions, pharmacological treatment, and

bariatric surgery to support patients with different nutritional challenges and behavior change <sup>146,160-162</sup>.

### 1.7 Weight loss and Weight regain

It is recommended that patients with obesity lose weight to improve their overall health <sup>6,7</sup>. Weight loss of 5–10 % improves several health parameters, such as blood glucose <sup>167</sup>, lipid profile <sup>168</sup>, blood pressure <sup>169</sup>, and non–alcoholic fatty liver disease <sup>170</sup>. Furthermore, weight loss greater than 15 % increases the likelihood of diabetes remission <sup>171</sup> and may even reduce cardiovascular mortality <sup>172,173</sup>. The overall quality of life improves dramatically after weight loss induced by bariatric surgery <sup>12</sup>. It has been suggested that weight maintenance, under standardized conditions, should be defined as <3% weight change in body weight, between 3–5% as small fluctuations, while weight changes of more than 5% may have a clinical impact <sup>174</sup>.

#### Repeated weight changes

Repeated weight loss and weight regain are commonly referred to as weight cycling or weight fluctuation. This phenomenon lacks a standardized definition. The simplest definition of weight cycling is a process in which body weight is repeatedly lost and gained <sup>175</sup>. However, a weight cycle may vary in magnitude, number of kilograms lost and gained, and length of the weight cycle.

Furthermore, weight cycling can be intentional or unintentional. Intentional weight cycling refers to voluntary attempts to lose weight through dieting (sometimes called yo-yo-dieting). It may also occur in some sports, such as power sports, in which a specific weight is required to compete <sup>176</sup>. Unintentional weight cycling may be due to severe illnesses <sup>177</sup>, eating disorders <sup>178</sup>, lack of food, or starvation <sup>179</sup>. Weight cycling and dieting are not only limited to persons with overweight or obesity but also to those with BMI <25.0 kg/m<sup>2</sup> <sup>180</sup>. Even young children and adolescents may try to lose weight because of social pressure on appearance <sup>181</sup>.

Weight cycling may have adverse negative health consequences on psychosocial factors and the quality of life <sup>182</sup>. People often blame themselves for regaining weight and not having enough willpower to maintain an energy-reduced diet. This may contribute to further difficulties in weight management <sup>183</sup>. Repeated weight changes have been suggested to contribute to further weight gain <sup>184</sup>, have a negative impact on body composition <sup>30</sup>, and are associated with increased morbidity and mortality <sup>185,186</sup>. However, evidence concerning adverse negative health effects is mixed, and there are disagreements regarding the negative impact of weight changes on metabolism and weight gain <sup>187</sup>, as well as morbidity

and mortality <sup>188</sup>. In middle of 90' the National Task Force on the Prevention and Treatment of Obesity stated that the benefits of moderate weight loss were greater than possible adverse effects and recommended in obesity <sup>175</sup>.

### Weight regain after bariatric surgery

Weight regain may occur regardless of the weight-loss method, not only after combined lifestyle interventions <sup>189</sup>, but also after treatment with anti-obesity medication <sup>140</sup> and bariatric surgery <sup>13</sup>. Consequently, maintaining long-term weight loss is a major challenge in obesity treatment <sup>190</sup>.

Weight regain after bariatric surgery can be due to hormonal and metabolic changes, increased energy intake, sedentary behavior, mental health, and anatomical changes related to surgical factors <sup>191</sup>. Differences in appetite-regulating gut hormones, such as GLP-1 and PYY, may contribute to differences in weight loss outcomes post-surgically <sup>86,87</sup>. In addition, weight regain is associated with post-bariatric hypoglycemia <sup>192</sup>. Furthermore, complications associated with surgical treatment, such as gastro-gastric fistula, may lead to weight regain <sup>193</sup>.

Following bariatric surgery, patients are expected to regain some weight <sup>13</sup>. In fact, within 5 years up to 20–24% of patients who undergo gastric bypass or sleeve gastrectomy may regain >15% of their weight <sup>13,194</sup>. However, the reported prevalence of weight regain varies, with some studies reporting a lower rate of regain. For example, the Longitudinal Assessment of Bariatric Surgery Study (LABS) from the United States found that patients who underwent RYGB had a weight regain of approximately 4% after seven years of follow-up <sup>195</sup>. There has been a lack of a clear definition of weight regain. Below are some examples of the definitions used in studies concerning weight regain <sup>13,196,197</sup>:

- >10% weight regain from nadir
- >15% total weight regain from nadir
- 25% weight regain of the lost weight
- <50% excess weight loss
- Regain of 5 BMI points from nadir
- Weight regain to BMI >35 kg/m<sup>2</sup>

However, in late August 2023, The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) published a consensus book in which the authors suggested reporting standards for "a late postoperative clinical deterioration" and "a suboptimal initial clinical response" to bariatric surgery. The "late postoperative clinical deterioration" was defined with a weight recurrence of >30% of the initially lost weight or with significant impairment in an obesityrelated complication <sup>198</sup>. Furthermore, "a suboptimal initial clinical response" to was defined as a total weight loss or BMI loss of less than 20%, or that an obesityrelated complication does not improve adequately after surgery <sup>198</sup>. The reporting standards were based on at least a 70% consensus in a three-round Delphi survey with 43 obesity management experts from different parts of the world.

There is limited evidence on how medical nutrition therapy or combined lifestyle interventions could be most beneficial in preventing and treating weight regain <sup>199</sup>. However, supporting healthy eating behavior is central. A systematic review and meta-analysis showed that behavioral interventions might improve suboptimal weight loss outcomes post-surgically <sup>200</sup>. A pilot study showed that an acceptance-based behavioral digital treatment program may reverse weight regain, at least in the short term <sup>201</sup>. Anti-obesity medication, along with combined lifestyle interventions, has shown promising results in patients with weight regain after bariatric surgery <sup>202,203</sup>, with results comparable to those achieved through pharmacological obesity treatment without bariatric surgery. Additional resurgery may also be an option in some patients <sup>204,205</sup>. In conclusion, the evidence for the prevention and treatment of weight regain is limited <sup>199</sup>.

# 1.8 Knowledge Gaps

There is convincing evidence that bariatric surgery is the most efficient way to achieve sustained weight loss and reduce the risk of obesity-related health issues and mortality in individuals with obesity <sup>12</sup>. However, weight regain exists even after bariatric surgery. Knowledge about the lived experience of weight regain after bariatric surgery should be expanded. Knowledge gaps exist regarding how patients have experienced weight regain and what factors they believe have made it difficult for them to maintain a lower weight. Furthermore, there is limited understanding regarding patients' experience with respect to food- and eating-related behaviors during the process of weight regain after bariatric surgery.

There are concerns that weight variation (gain, loss, and regain) may have adverse physical and psychological health consequences. Attempts to lose weight are common, especially among women <sup>206</sup>. A deeper understanding of weight loss and its frequency in relation to mortality outcomes, specifically all-cause, cardiovascular, and cancer outcomes, is needed. Adolescents and young adults with obesity have rarely been a focus of research. Little is known about their previous weight loss efforts, including the frequency and extent of such attempts and how these experiences may be associated with self-esteem and eating behaviors.

# 2 Research aims

### General aim

The overall aim of this thesis was to explore various perspectives on weight loss and regain with the objective of improving the understanding of patients' experiences with weight regain, weight management, dietary challenges, and social support after bariatric surgery. Another objective was to gain deeper insights into the consequences of previous weight loss on self-esteem, eating behavior, and mortality.

### Study specific aims

- Study I To explore the support experiences of patients who regained weight after bariatric surgery, including the support they received from family, friends, and healthcare providers, as well as the support they believed would have been helpful in maintaining a lower weight.
- **Study II** To explore the experiences of patients regarding weight regain after bariatric surgery and to identify factors that could enhance post-bariatric care.
- **Study III** To explore the perspectives of patients regarding their dietary patterns and eating behaviors during the process of weight regain after bariatric surgery.
- **Study IV** To assess and quantify the association between weight loss earlier in life with mortality from all causes, cardiovascular disease, and/or cancer.
- Study V To assess the association between previous weight loss with selfesteem and/or eating behaviors in young people aged 16-25 years, with obesity.

Research questions, study design, and expected results

Expected results	Increased knowledge	experiences of weight dietary patterns, weig management, and soc	support among patier regained weight after bariatric surgery.	Increased knowledge association between loss, self-esteem, eati behavior. and mortalit	
Study design	<ul> <li>Qualitative interview study</li> </ul>	<ul> <li>Qualitative interview study</li> </ul>	<ul> <li>Qualitative interview study</li> </ul>	<ul> <li>Prospective cohort study</li> </ul>	•Cross-sectional study
Research questions	How have patients with weight regain after bariatric surgery experienced support from family, friends, and healthcare post-surgically? What kind of support would have been helpful in maintaining a lower weight?	How have patients experienced weight regain after bariatric surgery? What factors could enhance post- bariatric care?	How have patients with weight regain after bariatric surgery experienced dietary patterns, and eating behaviors post-surgically?	ls weight loss earlier in life associated with all-cause, cardiovascular- and/or cancer mortality?	Is there an association between previous weight loss with self-esteem and/or eating behaviors in adolescents and young adults with obesity?

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Figure 1. Overview of the research questions, study designs, and expected outcomes of the included studies

# 3 Materials and methods

This chapter contains brief information about the materials and methods used in the five studies included in this thesis. More detailed information can be found in the attached articles (I-V).

### Qualitative and quantitative research

This thesis includes three qualitative and two quantitative articles. There are essential ontological (the theory of being) and epistemological (the theory of knowledge) differences in how these paradigms, quantitative and qualitative research relate to reality and knowledge <sup>207</sup>. Positivism is a basic scientific ideal of quantitative research where it is assumed than researchers can objectively observe, analyze, and report reality. The ontological assumption for qualitative research is that there are multiple ways to describe reality. The theoretical basis may rely on varied ideals such as hermeneutics, phenomenology, or constructionism <sup>208</sup>. Epistemology in quantitative research implies that the researcher can study the phenomenon objectively, free from personal interests, perspectives, values, and biases. In qualitative research, it is also essential to remain as objective and impartial as possible. However, the interaction between the researcher and the informants/data material is considered and acknowledged. Therefore, reflexivity is a central consideration in qualitative research <sup>209</sup>.

Qualitative studies are descriptive and explore phenomena, opinions, perceptions, and experiences in depth using an interpretative approach <sup>208</sup>. Data are collected through methods such as interviews or observations and can be used to form hypotheses. Non-numerical data (e.g., words or pictures) are analyzed systematically for example by coding, categorizing, thematizing, and searching for patterns <sup>208</sup>. Quantitative studies can have experimental (e.g., randomized controlled trials) or observational (e.g., cohort or cross-sectional) designs <sup>210</sup>. Using quantitative methods, the researcher can test a hypothesis, show associations, and obtain generalizable data. Statistical methods quantify and analyze the numerical data.

Concepts of validity i.e., the accuracy of a measure, and reliability i.e., the consistency of a measure, are essential in quantitative research <sup>210</sup>. In qualitative research, the concept of trustworthiness is central and can be achieved when the study design, analysis methods, and results are credible, confirmable, dependable, and transferable <sup>211</sup>.

### Overview of all studies included in this thesis

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	Study design	Analyses methods	No. of participants	Women	Age	Body mass index, kg/m <sup>2</sup>
			n	n (%)	mean (SD)	mean (SD)
Studies I, II, III	Qualitative interview studies	Thematic analyses with inductive approach	16	12 (75.0)	49.0 (11.0)	46.0 (7.8)
Study IV	Prospective cohort study	Cox Proportional Hazard models	34,346	22,475 (65.4)	49.1 (14.9)	25.4 (3.5)
Study V	Cross- sectional study	Descriptive statistics Linear Regression models	224	163 (72.8)	21.0 (3.0)	41.8 (6.6)

**Table 3.** Overview of participants, study design, and data analyses of the included studies in the thesis

# 3.1 Studies I, II and III

Studies I, II and III were qualitative interview studies.

**Research question in Study I:** How have patients with weight regain after bariatric surgery experienced support from family, friends, and healthcare post-surgically? What kind of support would have been helpful in maintaining a lower weight?

**Research question in Study II:** How have patients experienced weight regain after bariatric surgery? What factors could enhance post-bariatric care?

**Research question in Study III:** How have patients with weight regain after bariatric surgery experienced dietary patterns, and eating behaviors post-surgically?

### Participants

Studies I, II and III were based on the same data material. Study participants were recruited through purposive sampling <sup>208</sup> at the Center for Obesity in the Region Stockholm. Purposive sampling included informants with relevant experiences of a phenomenon. They were the so-called "Information-rich cases," which could

best answer research question <sup>208</sup>. We were interested in obtaining a deeper understanding of the first-person perspective and lived experience of the phenomenon of weight regain after bariatric surgery. Therefore, we aimed to recruit participants with obesity (BMI  $\geq$ 35 kg/m<sup>2</sup>) who had experienced weight regain after bariatric surgery but who also had various sociodemographic characteristics.

The Center for Obesity, Academic Specialist Center, provides medical specialty obesity treatment for adolescents aged 16 years and above, young adults aged 18–25 years, and adults over 25 years. The center collaborates with the surgical clinics in the Region Stockholm. Young adults seeking bariatric surgery are referred to the Center for Obesity for pre-operative evaluation, education, and preparation. Patients also receive extended support post-operatively in addition to what the surgical clinic offers. Patients are referred to the Center for Obesity for treatment by physicians in primary care or other specialty clinics. See Table 4 for the criteria for referrals to the Center for Obesity.

Adults <u>&gt;</u> 26 years	BMI >45			
	BMI >35 with obesity related complications			
Youth 16–25	BMI 35			
years	BMI >30 with obesity related complications			

Table 4. Criteria for referrals to the Center for Obesity

We included participants from April 2018 to December 2019. The inclusion criteria are shown in Table 5. Patients who had undergone laparoscopic adjustable gastric banding (LAGB) were excluded from the study because it is common for patients who have undergone this procedure to regain weight. Additionally, surgical clinics in Sweden no longer perform LAGB <sup>212</sup>.

Table 5. Inclusion criteria for studies I, II and III

	-
Body mass index	BMI <u>&gt;</u> 35 kg/m <sup>2</sup>
-	-
Age	≥18 years
Weight regain	≥10% total weight regain (TWR) from nadir
Bariatric surgery	Sleeve gastrectomy (SG) or gastric bypass (RYGB)

We defined weight regain as a total increase in weight of <u>></u>10%TWR from the nadir, which is the lowest weight point after surgery. Since there is no standardized definition for weight regain <sup>196</sup>, we used a definition based on the Swedish Obesity Subject Study (SOS-Study) 10-year follow-up results <sup>12</sup>. Those who had undergone

gastric bypass in the SOS-Study regained approximately 7% of their weight. The definition of  $\geq$ 10% weight regain has been used in a previous study <sup>197</sup>.

We calculated the total weight regain percentage (%TWR) = (body weight at interview – body weight at nadir) / (body weight at nadir in kg) x 100% in two steps, as presented in Table 6.

Table 6. Calculation of total weight regain percentage (%TWR) <sup>13</sup>

<b>Step 1</b> Weight regain (kg)	Total body weight in kg at the interview – self- reported total body weight in kg at nadir		
Step 2 Percentage	For example: 154 kg – 120 kg = 34 kg (Weight regain in kg / self-reported total body		
weight regain (%)	weight in kg at nadir) x 100 For example: (34kg/120kg) x 100= 28.3%		

Additional calculations of weight loss

- Percentage excess weight loss (%EWL) = (pre-op body weight post-op body weight) / (pre-op body weight – ideal body weight) x 100% (Ideal body weight = BMI 25 kg/m<sup>2</sup>) <sup>213</sup>
- Percentage total weight loss (%TWL) = (pre-op body weight in kg post op body weight in kg) / (pre-op body weight in kg) x 100% <sup>213</sup>

### Pre-conceptions and reflexivity

Reflexivity is an important practice in qualitative research, in which researchers examine their pre-conceptions and possible influences on the research. Pre-conceptions of the author of this thesis may have been influenced by her being an obesity specialist dietitian and cognitive behavioral therapist. She has worked in primary care and specialty obesity care for more than 25 years. At the Center for Obesity, she meets patients with obesity aged ≥16 years. She has experience in both pre- and post-surgical follow-up during her clinical work at the Center for Obesity. Additionally, several of her adult patients with obesity have experienced weight regain after bariatric surgery. The co-authors have vast research backgrounds, all of whom had experience in qualitative studies. Some co-authors were experts in the clinical specialty obesity medicine. Reflexivity was maintained by actively reflecting on oneself and how these subjective experiences may impact the research. Furthermore, discussions in the research group were an important part of reflexivity.

### Interview guide

We used an interview guide with open-ended questions that addressed a wide range of topics related to the experiences of weight regain after bariatric surgery and the support provided during weight regain. The interview guide ensured that all interviewed participants had the same basic questions. As our interviews were semi-structured, follow-up questions were allowed to enhance in-depth inquiry. To strengthen dependability, the same researcher (i.e., the author of this thesis), conducted all interviews.

A semi-structured interview guide was created and evaluated in a pilot interview with one patient who had experience of weight regain after bariatric surgery. However, based on that interview, no changes to the interview guide were required. The pilot interview was essential in evaluating the interview questions, assessing the interview situation, and obtaining a patient perspective early in this research. The interview guide included background questions and three different question areas. Additional follow-up questions were allowed.

# **Background questions**

To gather background information, we sought details about age, year of bariatric surgery, type of surgery, weight before surgery, lowest weight after surgery, current weight, and overall health status as well as questions about occupation, family, and personal relationships.

### Question area 1: Experiences of weight regain

- Tell me about your experiences with bariatric surgery.
- What were your expectations of bariatric surgery?
- What factors do you believe have facilitated or impeded your weight management after bariatric surgery?
- How did you experience the process of weight regain?
- In your opinion, what do you think made it hard for you to maintain a lower weight after the surgery?

### Question area 2: Support from Health care providers

- What are your experiences of support from healthcare pre- and post-surgically?
- How have healthcare professionals responded to your weight regain?
- What kind of support would you like to have from healthcare providers?

### Question area 3: Support from family and friends

- What are your experiences regarding your social life after bariatric surgery?
- What are your experiences with support from your family and friends?
- What kind of support would you like to have from your family and friends?

Of the 19 patients who were asked to participate in the study, 16 agreed to be interviewed. The author of this thesis conducted all interviews in a treatment room at the Center for Obesity. They had the possibility of choosing another location, if preferred. It was ensured that the interview situation would be uninterrupted by others. Only the person interviewed, and interviewer were present. It was allowed to ask supplementary questions to stimulate participants' narratives and deepen their answers. The interview topic was a sensitive matter for most participants and the interviewer needed to consider their emotional reactions.

Furthermore, we could offer contact with a cognitive therapist if more support were required after the interviews. However, no one needed it. All participants also had their personal healthcare provider at the clinic, so they had someone to turn to, if needed. All interviews were digitally recorded, with the approval of the participants. Notes on the researcher's immediate thoughts were made during and after the interviews.

The decision regarding the number of interview persons needed to answer the research questions was made together with the research team. After 13 interviews, the data appeared to be sufficiently rich. However, we decided to conduct three more interviews to enhance the variation in the participants' backgrounds regarding age, sex, and origin. After 16 interviews the data were diverse, and complex, and no further interviews were conducted. We assessed that we had reached the so-called informational redundancy <sup>208</sup>.

The author of this thesis transcribed all interviews verbatim. Participants were provided with the opportunity to review the interview text and add their comments. However, no alterations were required.

Studies I and II had clear question areas in the interview guide. Our first focus was on support experience. In Study II, we aimed to increase the understanding of participants' overall experiences with regaining weight. Finally, participants provided rich narratives concerning their experiences of dietary patterns and eating behaviors. These perspectives formed the basis of the analysis in Study III. Since time passed between the analyses, it enabled new insights and perspectives on the material.

# Theoretical perspective

We aimed to describe participants' lived experiences, perceptions, and meanings of the phenomena and their reality from the philosophical assumption of realism, intending to understand the deeper essence of the phenomenon for participants <sup>209,214</sup>.

# Data analysis

De-identified interview data were analyzed using thematic analysis with an inductive approach according to Braun and Clarke in Studies I <sup>214</sup>, II <sup>214</sup>, and III <sup>209,214</sup>. Thematic analysis, characterized by a systematic method in which we developed, analyzed, and unfolded deeper meaning in patterns, with reflexivity being a central concept. Braun and Clarke prefer to call this method for reflexive thematic analysis nowadays <sup>209</sup>. Figure 2. shows the terminology used in thematic analysis.

Data corpus	<ul> <li>All data collected during the interviews</li> </ul>			
Data sets	• Data used in the analyses from entire data corpus			
Data items	<ul> <li>Individual parts of data that bilds the data set/data corpus</li> </ul>			
Data Extracts	• Coded part of data			

Figure 2. Terminology used about data material in the thematic analysis <sup>214</sup>

In the Table 7. the analysis processes with data extracts, codes, sub-themes, and themes are presented from Studies I, II, and III as examples.

	Data extracts	Code	Sub-theme	Theme
Study I	l did not feel that there was much support [at surgical clinic]. They just, I met the dietitian twice.	Lack of support	Insufficient support	A lonely struggle
Study	"It might be enough if a dietitian called and asked how much you weigh. [Laugh] Only that could help. I probably wouldn't have been able to answer that at the time, but I would have had to look for a scale."	Regular contact with a dietitian	Individually tailored care	Others as source of compassion and control
Study II	"Eh, I must have been quite desperate. Eh, and with this feeling, "how will it go? How will it end?". And I felt so ashamed."	Desperate and ashamed	Negative emotional response	Loss of control and focus
Study II	"If I had not done it [surgery], I would have been even bigger. So, for me the surgery was really a lifesaver."	Surgery as a lifesaver	Lasting benefits of surgery	Reducing the burden of weight management
Study III	"After all, some people stop craving sweets. // I am one of the two who didn't [stop craving for sweets]. So, it was like hell."	Cravings for sweets remained	Cravings	Overwhelming dietary challenges
Study III	"My body is down to starvation all the time. I cannot really eat anything because I gain weight from everything."	Gaining weight from nothing	Confusing weight response	Overwhelming dietary challenges

 
 Table 7. Examples of the analysis processes with data extracts, codes, subthemes, and themes in the late stage from Studies I, II, and III

During data analysis, we followed a stepwise method to identify, analyze, and report the semantic and latent themes generated from the data. Latent content is more interpretative and deeper than semantic content. Semantic content refers to the detailed and explicit data.

Familiarization with the data started during the interview and continued while listening to and transcribing audio by taking notes. This was followed by repeated readings of the transcribed interview texts. To ensure the trustworthiness of the study, it was essential to return interview data during the process. The stepwise process depicted in Figures 3 and 4 generated premature themes when the datasets were searched for data items. Figure 3 shows the continuation of the process by sorting codes and identifying the sub-themes and themes. The co-authors were active in reviewing, renaming, defining, and refining the sub-themes

and themes until agreement was reached. In this process, we moved back and forth continuously until the final themes were created. Finally, we chose quotations to strengthen trustworthiness.

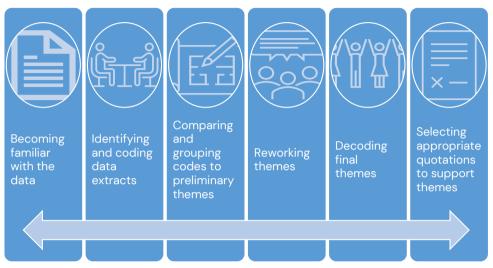


Figure 3. The stepwise analysis processes

To reduce the impact of the author of the thesis's preconceptions and to enhance the rigor of the study, we used researcher triangulation <sup>208</sup>. The first author and coauthor conducted the first initial analyses separately, and the preliminary results were compared with each other. During this process, discussions and decisions were made in collaboration with the research team.



Figure 4. An example of an early stage of a thematic map with sub-themes and theme in Study II

# 3.2 Study IV

Study design: Study IV was a prospective cohort study.

**Research question:** Is weight loss earlier in life associated with all-cause, cardiovascular-, and/or cancer mortality?

#### The Swedish National March Cohort

In September 1997, the Swedish Cancer Society organized a 4-day fundraising event in more than 3,600 locations throughout Sweden, which resulted in the establishment of the Swedish National March Cohort (SNMC)<sup>215</sup>.

#### "One hour for research"

During the Swedish National March event, participants completed a 36-page questionnaire and returned it to a local supermarket or by mail. It was estimated that it took an average of one hour for the participants to answer all questions. They provided informed consent to use their 10-digit national registration numbers for linkage with different national registries. The SNMC was comprised of 43,865 participants. Compared to the general population (16-84 years) at that time, participants had a lower educational level, overweight and obesity were more common, and the frequency of smoking was lower <sup>215</sup>.



**Figure 5**. The front page for the questionnaire used in the Swedish National March Cohort. Published here with approval from the Lukas Production

### The cohort - Study IV

The study cohort was created based on the SNMC participants. We excluded those with inaccurate national registration numbers, those who were younger than 18 years old, those who died, or those who moved from Sweden before the start of follow-up. Additionally, those with a previous cancer diagnosis or cardiovascular disease were also excluded. Moreover, participants with underweight (BMI <18.5 kg/m<sup>2</sup>) or with no information about weight loss were excluded. After these exclusions, the cohort consisted of 34,346 participants.

### Exposure assessment

Figure 6 shows the questions used to assess the weight loss. Those who answered "No" were included in the reference group. Those who answered "Yes" were divided into weight loss categories of 5–10 kg and >10 kg. In addition, participants were also categorized by the number of times of weight loss, i.e., 0, 1, 2, and  $\geq$  3 times.

Have you ever lost 5 kg or more in less than a year? Women should disregard weight changes in connection with pregnancy.							
If Yes, how much and how many times?							
	1	2	3	4	5 times or more		
More than 10 kg	1	2	3	4	5 times or more		

**Figure 6.** Questions about the amount and frequency of weight loss were obtained from the Swedish National March Cohort Questionnaire "One hour for the research."

### Follow-up and outcomes

We followed participants from October 1, 1997, until death, emigration, or the end of follow-up in April 2018, through linkage to different national registries. The median follow-up time was 20.6 years. For cause-specific mortality, we followed participants until December 2016.

- The Total Population Registry and migration registry were used to obtain death dates, relocation dates, and emigration dates <sup>216</sup>.
- The Longitudinal Integrated Database for Health Insurance and Labour Market Studies (LISA) was used to gather information regarding education and income <sup>217</sup>.

- The National Cause of Death Registry was used to provide death cause data 218.
- The National Patient Registry was used to obtain information on cardiovascular disease <sup>219</sup>.
- The National Cancer Registry was used to obtain data on cancer <sup>220</sup>.

Statistics Sweden is responsible for the Total Population Registry and for the LISA database. The last three registers are maintained by the Swedish National Board of Health and Welfare.

# **Statistical Analyses**

First, we divided the baseline characteristics into the following weight loss categories: no weight loss, 5-10 kg, and >10 kg. We then summarized the continuous variables using means and standard deviations (SD). Furthermore, we used absolute numbers and percentages (%) to outline categorical variables.

The Cox proportional Hazard model is a survival analysis in which time-to-event is of interest. We chose age as an underlying time scale to estimate the Hazard ratios (HR) and 95% confidence intervals (95% CI) for the association between the amount of weight loss and the number of times of weight loss with all-cause-, cardiovascular-, and/or cancer mortality:

- 1. First we adjusted for age and sex.
- The analyses were further adjusted for: BMI, smoking, alcohol use, education, income, physical activity, sleeping hours, and subjective health. We did not use waist circumference as a confounder because it had approximately 25% of missing values.

Additionally, we estimated Sub-distribution Hazard Ratios (SHR) to assess the presence of competing risks. We used Schoenfeld's residuals on time to check for proportionality. In our analysis, proportionality was fulfilled for all-cause mortality analysis, but not for sex in the cause-specific analysis. Therefore, we stratified the participants according to their sex. Finally, to test for reverse causality, we performed sensitivity analysis. We excluded those who died during the first two years of follow-up. They might have had a medical condition that had not been identified and had an unintentional impact on weight loss. Because missing values were present in the covariates, we also performed multiple imputation using the Multiple Imputation by Chained Equations algorithm, assuming a missing value at the random mechanism. All statistical tests were two-sided, and p-values <0.05 were considered statistically significant.

# 3.3 Study V

Study design: Study V had a cross-sectional study design.

**Research question:** Is there an association between previous weight loss with selfesteem and/or eating behaviors in young people aged 16-25 years with obesity?

### Participants

The Center for Obesity has an ongoing open clinical cohort, "the Swedish Youth with Obesity" (SYO) cohort, of adolescents and young adults (16–25 years of age) with obesity who have been accepted for treatment at the clinic <sup>221</sup>. This cohort was initiated in 2018. Participants in this study were recruited from the SYO cohort. Table 4 presents the BMI criteria for referral to the Center for Obesity for both adolescents and young adults. Patients with other severe conditions, such as eating disorders, substance/alcohol use disorders, or severe mental illness, are not admitted to treatment before they have received adequate medical or psychiatric care. We included individuals aged 16–25 years old. We used the same BMI classification criteria as those used for the adults.

Patients who fulfilled the inclusion criteria received information about the study before the enrollment visit, and completed a questionnaire on their background data, health, lifestyle, weight loss, self-esteem, and eating behavior. The questionnaire is used in the clinic. In addition, when patients provided informed consent, the data were used in the research. In April 2020, we added questions about weight loss and frequency of weight loss to the questionnaire. The data used in this study, were collected between May 5, 2020, and June 2, 2022.

### Weight loss history

In Study V, the question about weight loss and frequency of weight loss was the same as in the Swedish National Cohort Study, as shown in Figure 6. We also categorized the weight loss according to the amount, into three categories: no weight loss, 5-10 kg weight loss, and weight loss of more than 10 kg. Furthermore, we classified the number of times of weight loss into three categories: 0, 1, and  $\geq$  2.

#### Self-esteem

We assessed the participants' self-esteem using the Rosenberg Self-esteem Scale (RSES) <sup>222</sup>. Rosenberg developed the RSES in the middle of the 1960' for high school students in the United States as a measure of global self-esteem <sup>222</sup>. The RSES is a validated measure in young adults <sup>223</sup> and is frequently used <sup>224</sup>.

The RSES includes five positive and five negative statements about self-respect and personal worth, respectively. Two examples of statements: "I feel that I'm a person of worth, at least on equal plane with others" and "I feel I do not have much to be proud of" <sup>225</sup>. Participants were asked to respond to all ten statements by selecting the answer option that aligned best with their self-attitudes, using alternatives that ranged from strongly agree to strongly disagree. Negatively worded items were reverse scored. Each statement was scored between 0 and 3, with the total score ranging from 0 to 30.

There are no cut-off points defined for distinct levels of self-esteem. However, the midpoint of the scale has been suggested as an indicator of low self-esteem <sup>226</sup>. We retrieved scoring instructions from the Department of Sociology, University of Maryland, United States <sup>224</sup>.

### Eating behavior

Participants eating behaviors were evaluated using the Three-Factor Eating Questionnaire-Revised21 (TFEQ-R21) (159). The TFEQ-R21 has been previously validated in people with obesity <sup>227,228</sup>. This questionnaire evaluates three key aspects of eating behavior: uncontrolled eating (nine items), emotional eating (six items), and cognitive restraint eating (six items). The TFEQ, which consists of 51 items, was originally developed by Stunkard and Messick in 1985 <sup>229</sup>. TFEQ measures cognitive restraint eating, disinhibition, and hunger. The TFEQ-R21 comprises 21 items, where a four-point scale is utilized for questions 1-20, and an 8-point scale is utilized for item 21. We computed scores for individual eating behaviors, ranging from 0 to 100.

Uncontrolled eating implies overeating caused by physical hunger or visual cues of food <sup>230</sup>. An example of a statement: "I am always hungry enough to eat"<sup>67</sup>. The eating behaviors used for mood regulation were assessed through emotional

eating. An example of a statement: "I start to eat when I feel anxious" <sup>67</sup>. In addition, cognitive restraint eating captures continuous and intentional restrictive eating behavior <sup>230</sup>. An example of a statement: "I consciously restrict how much I eat during the meals to avoid gaining weight" <sup>67</sup>. A low score implies less of each eating behavior. TFEQ-R21 lack cut-offs. We followed the scoring instructions of the HRQL Group AB, Sweden <sup>231</sup>.

### Statistical analyses

We performed descriptive statistics and comparative analyses between the groups. Finally, we conducted linear regression analyses to investigate any associations between the amount and frequency of weight loss with self-esteem and eating behavior scores, including uncontrolled eating, emotional eating, and cognitive restraint eating. In the final models, we adjusted for the following confounders: age, sex, BMI, and smoking status. Statistical significance was defined as a p-value of <0.05.

# 3.4 Ethical considerations

### Beneficence

To tackle the growing epidemic of obesity and overweight, there is a need for advanced strategies. This thesis aimed to provide insights into enhancing interventions for weight management with a focus on the consequences of weight loss and experiences of weight regain.

Understanding of weight regain after bariatric surgery is relatively scarce. Little is known about patients' experiences, and the kind of support required for those who experience weight regain. It is an ethical and moral obligation to increase knowledge in this area as it has the potential to lead to improvements in patients and healthcare. Beneficence in our study also concerned interview situations in which participants may have found valuable. Sharing difficult experiences can be experienced as relief.

Because weight loss is recommended for those with overweight, and especially with obesity, it is important to understand the consequences of weight loss. The life situation of young people aged 16–25 with obesity has not been well-studied. Therefore, understanding how weight loss at an early age may be associated with self-esteem and eating behavior among young adults with obesity is an important step to improve treatment options targeting their needs.

### Non-maleficence

The researcher should protect the integrity of the research participants and protect them against physical and mental harm. None of the studies posed any risk of physical side effects or pain to participants. However, being interviewed or filling out a lengthy questionnaire might be uncomfortable, and questions about lifestyle and health might be highly personal.

Body weight, weight change, and weight regain are sensitive topics for most people. Sharing these experiences may pose emotional risks. In our qualitative interviews, participants were informed of the possibility of stopping the interview if they felt uncomfortable with the questions or situation. They could also skip the questions. Participants could see a cognitive therapist if needed after the interview. However, none of the participants required any additional support. They were in contact with ordinary healthcare providers during the treatment program at the Center for Obesity. Further, participant and researcher interactions and power relationships are essential to consider in qualitative research. We decided not to include any participants with an ongoing treatment relationship with the author of this thesis. We were concerned that this might have a negative impact on the participant and could negatively influence further treatment if the participant shared something they regretted later. Maintaining the anonymity of participants while staying true to their narratives was our objective when reporting qualitative data.

In the Swedish National March Cohort, Study IV, no intervention was offered to those with weight problems. In the study of adolescents and young adults with obesity, participants were included in a comprehensive program for obesity management, where any psychological issues were followed up and participants were offered long-term support.

All data collected during the qualitative interviews (Studies I, II, III) and Study V were de-identified and safely stored. Only a few people on the research team have access to the code key. In Study IV, data from the Swedish National March Cohort are stored in a de-identified database. Personal information such as the national registration number is not accessible to researchers.

In Study V, some participants were between the ages of 16 and 18. According to Swedish law, there are special rules concerning informed consent for children and adolescents. The Act (2003:460) concerning the Ethical Review of Research Involving Humans declares that persons who have turned 15 years of age but are not yet 18 can independently provide written informed consent without their guardian's approval <sup>232</sup>. However, it is crucial for them to understand the study information. During recruitment, the staff at the Center for Obesity carefully considered this account, and only individuals who understood the study information were asked to participate. For instance, we did not invite persons with intellectual disabilities or language barriers to participate. All individuals were encouraged to ask questions about the study and their participation regardless of their age.

The General Data Protection Regulation (GDPR)<sup>233</sup> was followed, and these regulations mirror good research practices to a great extent. The fundamental principles of GDPR are lawfulness, fairness, and transparency. Lawful means that personal data are handled according to regulations and laws concerning research and done for the public's good in a credible organization, such as Karolinska Institutet and Region Stockholm. Fairness refers to respecting participants' rights and ensuring that the data collected are handled correctly. Transparency means

that correct and precise information about managing personal data is provided in plain language.

### Autonomy

The Declaration of Helsinki <sup>234</sup> was followed for all studies. Participation has been entirely voluntary. We informed the participants of the research both verbally and in writing. We obtained their signed consent via an informed consent form. Participants had the opportunity to ask complementary questions in all studies. The results from the statistical analyses were presented at the group level and did not threaten the integrity of the participants. In qualitative studies, we used quotes from interview data to strengthen our results. These were presented anonymously. Participants were informed about the use of quotes and had the opportunity to read the transcribed interview text. The Swedish National March Cohort participants in Study IV obtained information about the linkages to the registers and the use of their national registration number.

### Justice

Participation or non-participation in the studies did not affect any other treatment. We only included participants who could make autonomous decisions regarding participation. Participation required participants to speak and understand the oral and written Swedish language. This may have excluded some of participants. In addition to the Declaration of Helsinki <sup>234</sup> several national and international laws and regulations control the field of research to protect human rights and values.

### **Ethical approvals**

**Studies I, II, and III**: The Regional Ethical Review Board in Stockholm, Sweden, approved the study, with registration number 2018/294-31/1 and amendment 2019-01415.

**Study IV:** The regional Ethical Review Board at the Karolinska Institutet approved the study with registration numbers 97-205, and 2017/796-31.

**Study V:** The Regional Ethical Review Board in Stockholm approved the study with registration number 2017/334-31 and amendments 2019-03755 and 2020-04597.

# 4 Results

# Participants in Studies I, II and III

Participants (n=16) underwent RYGB between 2004 and 2016. Three participants had previously undergone another surgery for obesity. As shown in Table 3, 75 % of the participants were women. The participants had various backgrounds including family relationships, national origins, and occupations. They also experienced multiple physical and mental health problems. At the time of the interview, the participants had an average age of 49 years and an average BMI of 46 kg/m<sup>2</sup>. The average total weight regain (%TWR) was 36%. Their weight regain started at an average 2.6 years after RYGB. They reported a mean percentage of excess weight loss (%EWL) of 70% at the nadir (lowest weight after RYGB) and an average of 25% EWL after weight regain. They had a 35% total weight loss (%TWL) at the nadir and the remaining 13%TWL at the time of the interview.

# 4.1 Study I

Study I aimed to explore the support experiences of patients who regained weight after bariatric surgery, including the support they received from family, friends, and healthcare providers as well as the support they believed would have been helpful in maintaining a lower weight.

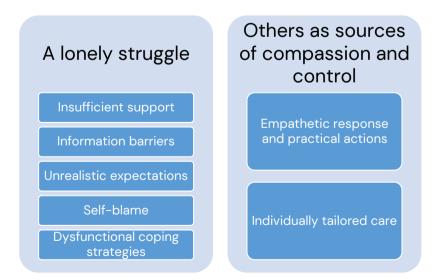


Figure 7. Main themes, and sub-themes generated during the thematic analysis in Study I.

The main themes and sub-themes are shown in Figure 7.

# A lonely struggle

The first main theme captured participants' feelings of loneliness during their post-surgical journey and weight regain.

### Insufficient support

Only one participant was satisfied with the support offered by the healthcare services. All other participants expressed that they perceived the support and follow-up to be insufficient. They experienced too little support before, in the first year, or later after the surgical procedure. There was confusion about who to contact when issues arose, causing them to bounce between the surgical clinic and their primary care provider. They expressed a lack of acknowledgment of their problems with eating behaviors and, consequently, insufficient support with long-term healthy eating and weight management.

"And no one really picked up on it [maladaptive eating behavior], /.../ and I was still losing weight during that time. So that's why no one reacted." (Interview 8)

Participants' experiences with social support from their family environment and friends varied substantially. Some mentioned that actions or statements by family members could cause harm.

"When I visit my mother, she places a picture of a painting with an extremely fat woman on the fridge. /.../ 'Look at yourself. This is what you've eaten yourself up to'." (Interview 5)

### Information barriers

One challenge for participants was to obtain information concerning self-care pre- and post-surgery. Various recommendations in online forums or other bariatric clinics were perceived as confusing. The brochures provided by the surgical clinics remained unread or were sometimes lost.

"I have a bunch like those on the fridge [points towards brochures in the room]. But I don't notice anything hanging there. What should I do? You must help people in some way. These [brochures] do not help." (Interview 3)

# Unrealistic Expectations

Participants believed that surgery would cause permanent weight loss. The effortless weight loss during the initial phase led some participants to believe that they did not have to work on their eating habits.

"I've been dieting my whole life and tried hundreds of different methods. I lost and gained weight, all the time, back and forth. So, yes, now I will lose weight. Now I will get the help I need." (Interview 11)

"It was probably this "a quick fix" [my expectations]. Okay, now they will do the surgery, and I will lose weight. I will never regain again. Everything will be good [my weight, my headaches...]. These were my expectations. That [losing weight permanently] is the only thing you think about when you have overweight." (Participant 8).

### Self-blame

Participants blamed themselves for regaining weight.

"I wasn't that mature then. I just thought, "oh, whatever." A bit careless. But now, when several years have passed, and I think about it, I wonder, "Why didn't I do differently? Why didn't I think in other way?" I should have reacted to or done something earlier. But I was so young at that time..."(Interview 6)

Participants expressed shame and guilt regarding regaining weight. They tried to hide possible unhealthy eating behaviors or weight gain for their family members.

### Dysfunctional coping strategies

Participants reported that weight regain induced the use of self-directed dieting strategies. They described the use of maladaptive eating patterns and disordered eating behaviors.

"...so it was that I immediately fell into these dieting thoughts. Which is very sad actually..." (Interview 7)

Participants avoided activities that could have supported weight management because they did not want to be judged by others. In addition, they mentioned social isolation and avoidance of healthcare.

### Others as sources of compassion and control

The second major theme encompassed participants' opinions on the type of social support they valued or desired. Although participants' stories about receiving helpful support were less prevalent than those about receiving insufficient support, their narratives provided valuable insights into their social support preferences.

#### Empathetic response and practical actions

They particularly expressed the importance of empathetic responses from healthcare professionals, family members, and others. Self-efficacy improved when participants felt that others understood them, provided supportive comments, and showed acceptance. In addition, participants appreciated practical efforts, such as healthy family meals, exercising together, and other supportive everyday activities.

"I'm honestly bad at taking my medicine. So, then he's [husband] on to me, "Have you taken your meds? Have you? Have you?" So, he genuinely supports me a lot, to be honest." (Interview 10)

### Individually tailored care and support

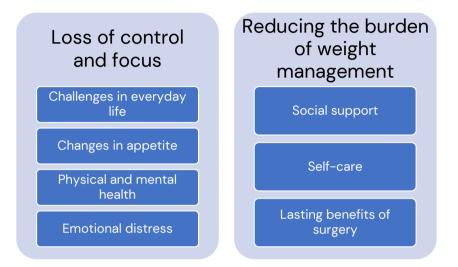
Participants suggested that pre- and post-surgical support should be more individualized and offered in the long term. They wished for more dietary and psychological support. They wanted access to peer support and regular check-ups with healthcare services. Additionally, the participants suggested that their family members should be offered the possibility of receiving more information about surgery and associated issues.

"I would absolutely like to have been followed up annually and to have been supported in it [eating habits], and it wasn't there. So that's what I missed." (Interview 2)

# 4.2 Study II

In Study II, we aimed to explore the experiences of patients regarding weight regain after bariatric surgery and identify factors that could enhance postbariatric care.

In Study II, thematic analysis generated two main themes and seven sub-themes, as shown in Figure 8.



**Figure 8.** Theme and sub-themes generated during the thematic analysis in Study II.

### Loss of control and focus

The first of the two major themes highlighted the gradual process of regaining weight, characterized by loss of control over weight management and loss of focus on self-care.

# Challenges in everyday life

A diversity of stressors, such as family conflicts, work, economy, housing, and an unhealthy food environment, were identified as factors that affected their ability to maintain a lower weight. The participants also mentioned that pregnancy was a challenge for weight management. Furthermore, some participants said that they prioritized other people's well-being and needs instead of their own. "That's what was wrong. I've just given, given, and given my whole life. Throughout my career, I have just given to all people." (Interview 12)

### Changes in appetite

Initially, surgical procedures reduced sensation of hunger and increased satiety. Participants were surprised that the "barrier" to eating vanished. This was unexpected and worrying, inducing thoughts about possible complications. Some reported that they sometimes forgot that they had undergone the surgery.

"But then I discovered after a while that the feelings of hunger returned. And now it was possible to eat more than two meatballs." (Interview 13)

### Physical and mental health

Participants reported being affected by physical and mental health problems that made weight management secondary. They described chronic diseases, as well as acute illnesses. Some medications may have contributed to weight regain. In addition, participants mentioned that they were challenged by depression, anxiety, alcohol use disorder, sleeping problems, and difficulties with body image. Maladaptive eating behaviors were mentioned as coping strategies.

"I was sensitive at the time. Things were happening at work, and issues with body image. It still didn't catch up with me and made me extremely sensitive. [Got a depression]. So, I got meds and started comforting myself by eating. I didn't eat regularly anymore. I didn't sleep, I... was craving chocolate." (Interview 14)

### Emotional distress

The participants experienced stressful weight changes and had not expected to regain their weight. Instead, they hoped to achieve an extensive and lasting weight loss. Participants described a negative emotional response to this. They expressed feelings of hopelessness and frustration. Above all, they described feelings of shame and guilt. The participants blamed themselves for their weight gain. Negative comments from others could also increase emotional distress.

"Dad was 'Oh' like he had a new daughter [after weight loss]. But then I started regaining, and he started getting negative [as before weight loss]. He has this idea that he should have two princess daughters, stick-thin barbie dolls." (Interview 4)

### Reducing the burden on weight management

Participants experienced weight management as an almost impossible burden. However, they also expressed perspectives on support that could reduce stress induced by difficulties in weight management, as captured in the second main theme.

### Social support

Participants wished for improved support from family members and healthcare providers. Empathetic and individualized support could contribute to increased well-being and engagement in self-care. In addition, some participants emphasized the need for improvements in the food environment of their families.

"I cannot decide how my adult children should live their lives. At the same time, I want them to know that I need support. They can also think a little about how and what they eat, because they need to lose weight. So, I could probably influence them with my...[habits] 'This is how we do it.'" (Interview 1)

### Self-care

During the weight change journey before and after bariatric surgery, participants experienced challenges and facilitators when trying to follow a meal plan and keep track of weight management. They wished support with behavioral strategies. Further, they expressed the importance of how healthy habits, such as physical activity, could have a positive meaning.

"I want to swim much more often. So now, I have pool rehab training, that's all. And it's perfect for my body. Because suddenly, I can bend my legs a little more than I usually do, so the mobility starts to increase anyway." (Interview 2)

### Lasting benefits of surgery

Only one participant regretted having undergone bariatric surgery.

"I bitterly regret undergoing that [surgery]. I don't know if it would have been better elsewhere [another surgical clinic]. But performing such a large surgery on a person affects their life until they die [crying]. So, it [the follow-up] must be better." (Interview 12)

All the other participants were satisfied with their decision to undergo surgery and experienced health benefits despite regaining weight.

"So, the surgery itself, absolutely. I couldn't lose weight without it. /.../ I feel that this operation, it still works, it does what it should." (Interview 7)

# 4.3 Study III

In Study III, we aimed to explore the perspectives of patients regarding their dietary patterns and eating behaviors during the process of weight regain after bariatric surgery.



Figure 9. Theme and sub-themes generated during the thematic analysis in Study III

Theme and sub-themes are presented in Figure 9. The main theme captured the difficulties participants described with their dietary patterns and eating behaviors. Challenges induced frustration, and participants lacked adequate tools and support to manage eating-related problems.

### Meal structure and portion sizes

Participants reported that meal patterns changed with time after gastric bypass surgery. They had eaten more frequently after surgery. However, at the time of the interview, the meal patterns had changed to fewer meals or grazing behavior. Stress, working conditions, and family related factors were mentioned as disturbing the meal structure.

"But it [the feeling of hunger] just appeared, "now I want to eat," like that. At that time, I stopped eating regularly and doing things I had used to do before. So, it could also be why I stopped losing more weight." (Interview 10) Portion size increased in most participants with time from surgery. However, there were large individual differences between participants in perceived portion sizes. Some participants experienced their portion sizes as extremely small, whereas others described larger, normal portions.

*"Portions got bigger and bigger. They turned out to be normal portions in the end."* (Interview 1)

# Cravings

Participants were surprised by unexpected cravings for sweet and fatty foods, and their intake increased when they noticed that they could eat these foods.

"In the beginning, I was so afraid that I would get dumping, so I only took such small pieces to taste and only occasionally. Then, it was like 'oh I can handle this. I'll take a little more, a little more'..." (Interview 14)

# Food- and meal-related unpleasant reactions

Participants highlighted problems with gastrointestinal symptoms related to food and meals. For example, they experienced nausea and variations in stool consistency. Dumping syndrome and early satiety could also induce difficulties, particularly in situations involving other people.

"So, I don't dare to eat certain things because I've had problems with chicken and meat like that, big pieces of steak. Yes, steaks, I have a very hard time with that." (Interview 4)

*"I mean, the stomach is a very sensitive place. I've had enormous diarrhea, and I've always been afraid when I've eaten. /.../ What if I can't make it to the toilet? I didn't have such problems before."* (Interview 12)

### Emotional and disordered eating/drinking

Participants highlighted difficulties with emotional and disordered eating and drinking behaviors during weight regain. Some participants used terms such as sugar or food addictive about themselves.

*"I don't know, I think it has to do with sugar, that I have a sugar addiction."* (Interview 13)

### Confusing weight response

Weight regain was unexpected. Participants tried to manage their weight using methods they knew, such as dieting and restrictive eating behaviors.

"I have been a Weight Watcher for many years, many rounds since the age of 20, but after the surgery, which was in 2006, so until 2008, I was thin. There were no problems then, but when I started to gain weight, I returned to Weight Watchers. So, that was what I knew and with what I was familiar. But it costs money, and nothing happened in terms of weight loss." (Interview 8)

### Insufficient nutritional knowledge and support

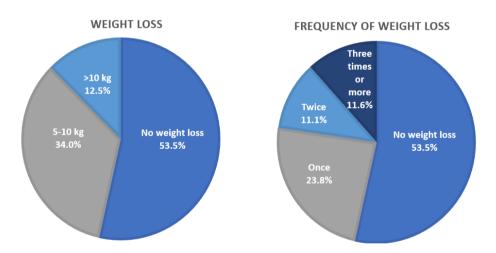
There was variability in participants' nutritional knowledge of food and eating patterns. They wanted more nutritional and psychological support before and after the surgical procedure.

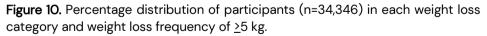
"I wished that she [the nurse] had followed me up, given me lists [of suitable foods], menus, and some tools for behavioral change, and offered a possibility to call her if I felt there were some problems." (Interview 12)

# 4.4 Study IV

In Study IV, we aimed to assess and quantify the association between weight loss (including the kilograms and frequency of lost weight) earlier in life with mortality from all cause, cardiovascular disease, and/or cancer.

Participants (n=34,346) were categorized into different weight loss groups: 53.5% had not lost weight, 34.0% had lost 5–10 kg, and 12.5% had lost more than 10 kg, as shown in Figure 10. In total, 46.5% of the participants reported weight loss of  $\geq$ 5 kg at least once. Those who had lost more than 10 kg had the highest BMI (an average of 27.3 kg/m<sup>2</sup>) compared to those who had lost between 5–10 kg (average, 25.0 kg/m<sup>2</sup>), while those who had not lost any weight had an average BMI of 23.8 kg/m<sup>2</sup>. We found that participants who had not lost weight were older, slept longer, had better subjective health, and were non-smokers more frequently than those who had lost weight. Figure 10 shows the frequency of weight loss. Almost one-fourth (23.8%) reported having lost  $\geq$ 5 kg once, 11.1% twice, 11.6% three times or more times, and 53.5% reported no weight loss.

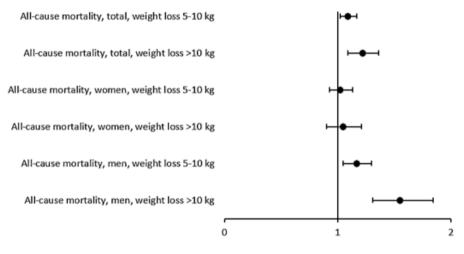




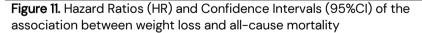
During the follow-up period, from October 1997 to April 2018, we observed 5,627 deaths. We identified 1,783 deaths caused by cancer and 1,596 deaths caused by cardiovascular diseases in the cause-specific analyses, where information was available until December 2016.

### Weight loss and all-cause mortality

We found an association between weight loss and all-cause mortality, as presented in the forest plot in Figure 11. There was a 9% (HR 1.09; 95%Cl 1.02–1.17) higher rate of all-cause mortality in those who had lost 5–10 kg and a 22% (HR 1.22; 95%Cl 1.09–1.36) higher rate of all-cause mortality in those who had lost >10 kg than in those with no weight loss. We also found sex differences, where the association between weight loss and all-cause mortality was present in men, but not in women. In men who had lost 5–10 kg, we found a 17% (HR 1.17; 95%Cl 1.05–1.30) higher rate of all-cause mortality than among those who had not lost weight. We observed a 55% (HR 1.55; 95%Cl 1.31–1.84) higher rate of all-cause mortality in men who had lost more than 10 kg than in men with no weight loss.



Hazard Ratio (HR), 95% Confidence Interval (95%CI)

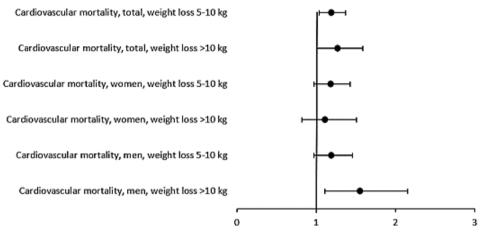


Participants who had lost  $\geq$ 5 kg three times or more had a 16% (HR 1.16; 95%Cl 1.03– 1.30) higher rate of all-cause mortality than those who had not reported any weight loss.

### Weight loss and cardiovascular mortality

We found an association between weight loss and cardiovascular mortality. These associations are presented in the forest plot in Figure 12. Those who reported

having lost 5–10 kg had a 19% (HR 1.19; 95%Cl 1.04–1.37) higher rate of cardiovascular mortality, and those who reported having lost >10 kg had a 27% (HR 1.27; 95%Cl 1.01–1.59) higher rate of cardiovascular mortality than those who did not lose weight. We did not find any association between weight loss and cardiovascular mortality in women. In men, the association was found in the weight loss category >10 kg (HR 1.55; 95%Cl 1.11–2.15). Additionally, no association was found between a weight loss of 5–10 kg and cardiovascular mortality in men.



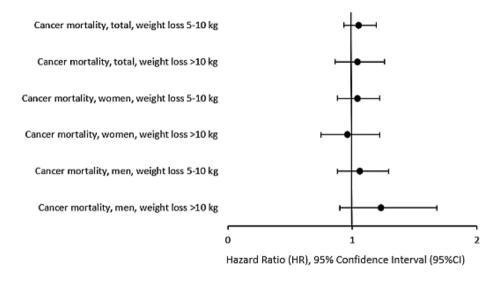
Hazard Ratio (HR), 95% Confidence Interval (95%CI)

**Figure 12.** Hazard Ratios (HR) and Confidence Intervals (95%CI) of the association between weight loss and cardiovascular mortality

Participants who had lost  $\geq$ 5 kg three times or more had a 49% (HR 1.49; 95%Cl 1.20–1.85) higher rate of cardiovascular mortality than those who had never lost weight.

#### Weight loss and cancer mortality

We observed no association between weight loss and cancer mortality. Weight loss of 5–10 kg (HR 1.05; 95%Cl 0.93–1.19) nor weight loss >10 kg (HR 1.04; 95%Cl 0.86–1.26) nor the number of times participants had lost at least 5 kg were associated with cancer mortality. Hazard Ratios and Confidence Intervals are presented in Figure 13.



**Figure 13.** Hazard Ratios (HR) and Confidence Intervals (95%CI) of the association between weight loss and cancer mortality

## 4.5 Study V

In Study V, we aimed to assess the association between past weight loss (both kilograms and frequency) with self-esteem and eating behaviors in young people aged 16-25 years with obesity.

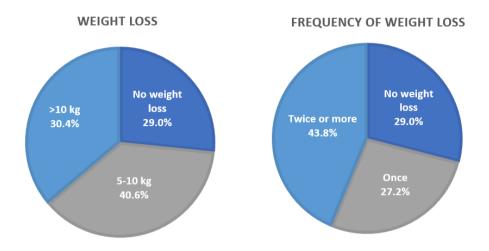
The participants (n=224) were adolescents and young adults with a mean age of 21.0 years. All of them had obesity, with an average BMI of 41.8 kg/m<sup>2</sup>. Of the participants, 72.8% were women. The Table 8. shows the differences in the participants' characteristics concerning the number and frequency of past weight loss.

	Reference category No weight loss	Number of kg weight loss			Frequency of weight loss of <u>&gt;</u> 5 kg		
		5-10 kg	>10 kg		Once	Twice or more	
	n (%)	n (%)	n (%)	p-valueª	n (%)	n (%)	p-valueª
Number of	65 (29.0)	91 (40.6)	68 (30.4)		61 (27.2)	98 (43.8)	
participants							
Sex				0.43			0.06
Women	51 (78.5)	61 (67.0)	51 (75.0)		49 (80.3)	63 (64.3)	
Men	13 (20.0)	29 (31.9)	17 (25.0)		11 (18.1)	35 (35.7)	
Other	1 (1.5)	1 (1.1)	0 (0.0)		1 (1.6)	0 (0.0)	
Country of birth				0.34			0.34
parents							
Nordic country <sup>1</sup>	39 (60)	46 (51.7)	42 (62.7)		37 (61.7)	51 (53.1)	
Other country <sup>2</sup>	26 (40)	43 (48.3)	25 (37.3)		23 (38.3)	45 (46.9)	
Civil status				0.83			0.56
No partner	46 (70.8)	62 (68.1)	42 (61.8)		39 (63.9)	65 (66.3)	
Partner/married	17 (26.1)	27 (29.7)	24 (35.3)		19 (31.2)	32 (32.7)	
Other	2 (3.1)	2 (2.2)	2 (2.9)		3 (4.9)	1 (1.0)	
Occupation				0.01			0.25
Student	43 (67.2)	65 (72.2)	32 (47.1)		40 (65.6)	57 (58.8)	
Employed	12 (18.8)	18 (20.0)	26 (38.2)		18 (29.5)	26 (26.8)	
Other <sup>3</sup>	9 (14.1)	7 (7.8)	10 (14.7)		3 (4.9)	14 (14.4)	
Smoker				0.12			0.76
No	50 (82.0)	73 (83.0)	47 (70.1)		46 (78.0)	74 (77.1)	
Yes	11 (18.0)	15 (17.0)	20 (29.9)		13 (22.0)	22 (22.9)	
	mean (SD)	mean (SD)	mean (SD)	p-value <sup>b</sup>	mean (SD)	Mean (SD)	p-value <sup>b</sup>
Age, years	20.0 (2.9)	20.8 (3.0)	22.2 (2.7)	0.0001	21.0 (3.1)	21.6 (2.8)	0.002
BMI, kg/m <sup>2</sup>	41.9 (6.8)	41.2 (6.4)	42.7 (6.6)	0.37	41.6 (6.7)	41.9 (6.5)	0.94

**Table 8.** Differences in the participants (n=224) characteristics between the number of kg past weight loss and frequency of past weight loss >5 kg

<sup>a</sup>Chi-squared test, <sup>b</sup>One-way ANOVA, <sup>l</sup>One parent from the Nordic country <sup>2</sup>Two parents outside of the Nordic country<sup>3</sup>E.g. Parental allowance, sickness benefit, financial support.

Most participants (71.0%) reported having lost weight previously, Figure 14.



**Figure 14.** Percentage distribution of participants (n=224) in each weight loss category and frequency of weight loss <u>></u>5 kg

#### Weight loss and self-esteem

The participants mean self-esteem score was 16.7, as measured using Rosenberg Self-esteem Scale. The reported self-esteem score was the lowest (15.1) among those who had lost >10 kg. Those who reported having lost 5–10 kg had a mean self-esteem score of 17.6, and those who reported no previous weight loss had a mean self-esteem score of 17.0. Participants who had lost  $\geq$ 5 kg at least once reported an average self-esteem score of 15.7, and those who had lost weight two times or more had a slightly higher score (17.0). However, we did not observe any statistically significant differences between the number of kilograms lost or the frequency of weight loss with self-esteem. Furthermore, we found no statistically significant associations in the linear regression models.

#### Weight loss and eating behavior

Participants reported the following mean scores: uncontrolled eating 46.0, emotional eating 39.4, and cognitive restraint eating 45.9, for their eating behaviors. No significant differences in eating behavior were found between the weight loss categories. Participants who reported having lost >10 kg had the highest mean scores of 49.9 for uncontrolled eating compared to those who did

not having lost weight (43.1) and lost 5–10 kg (45.2). The mean score for emotional eating was 44.2, compared to 37.4 (no weight loss) and 37.2 (5–10 kg). Participants who had lost between 5 and 10 kg reported an average score of 48.8 in cognitive restraint eating, compared to 46.1 among those who had lost more than 10 kg, and 41.7 among those who reported no weight loss.

We did not observe any significant difference in eating behaviors according to the frequency of weight loss. The average score for uncontrolled eating was nearly the same for those who had lost weight once (47.1), and twice or more (47.3). Participants who had not lost weight had a mean score of 43.1. Regarding emotional eating, participants who had not lost weight once and 38.9 for those who had lost weight two times or more often. Participants who had lost weight two or more times reported the highest score (49.1) for cognitive restraint eating compared to those who had lost weight once (45.3) or those who reported no weight loss (41.7).

Linear regression models showed that those who lost 5–10 kg had a significantly higher cognitive restraint eating score of 7.03 points (95%CI:0.004 to 14.05) than those who did not lose weight. Participants who lost >5 kg two or more times had a significantly higher score of 8.32 points (95%CI:1.20 to 15.43) for cognitive restraint eating. No association was found between weight loss and uncontrolled or emotional eating.

# 5 Discussion

## 5.1 Main findings

This thesis explored various perspectives on weight regain after bariatric surgery and investigated the consequences of weight loss during adolescence, young adulthood, and later in life. Taken together, the results show that weight loss maintenance is not "a quick fix." Instead, it requires long-term commitment from the patient, healthcare system, and society.

Our findings indicate that social support is crucial. However, it was nearly absent during weight regain after the bariatric surgery. Participants viewed weight regain as a personal failure and consequently experienced negative emotional reactions. The complexity of weight regain was captured by the experiences of multiple internal and external contributors, such as everyday challenges, increased hunger, and health problems. Participants also perceived their dietary patterns and eating behaviors as challenging and overwhelming post-surgery. These results highlight the importance of improved follow-up and care after bariatric surgery. In particular, there is a need for regular medical nutrition therapy and psychological support for patients with nutritional and psychological challenges.

Furthermore, we found that previous weight loss was associated with all-cause and cardiovascular mortality, especially in men. Previous weight loss was not found to be associated with cancer mortality. We also found that weight loss was common among adolescents and young adults who had entered specialty obesity treatment. We found an association between the amount and frequency of previous weight loss and cognitive restraint eating, indicating that patients try to control their eating and weight, yet still have obesity and seek treatment.

The studies included in this thesis emphasized the challenge of weight loss maintenance and showed the importance of providing person-centered longterm support in weight management based on individual needs.

## 5.2 Discussion of the findings

## Follow-up and social support

This thesis has shown that patients who have undergone bariatric surgery and regain weight may face a lack of support from healthcare providers in surgical clinics and primary care, families, and friends. Another Swedish qualitative study that followed patients for 10 years after undergoing RYGB or biliopancreatic diversion with a duodenal switch reported similar findings<sup>235</sup>. That study found

that patients were content with follow-up from the surgical clinic but experienced ignorance and difficulties with follow-up in primary care. These results suggest that it is especially important to provide healthcare professionals in primary care settings with improved knowledge and capacity for long-term post-surgical follow-up. However, access to the surgical clinic after significant weight regain is recommended to assess possible complications related to the bariatric procedures <sup>146</sup>. The participants in this thesis appreciated being examined by a bariatric surgeon to ensure that nothing was wrong with the anatomy.

It has previously been reported that inadequate post-surgical follow-up or missed appointments are associated with weight regain <sup>236-238</sup>. In our study, only one participant was satisfied with the follow-up received from healthcare services, whereas others experienced a lack of support and follow-up. Nordic guidelines <sup>239</sup> were published after participants underwent surgical procedures, and the absence of guidelines may have been reflected in participants' perceptions regarding insufficient follow-up and support. The need for support is individual. Other studies have reported that some patients may need more follow-up during the first year post-surgically <sup>240</sup>, others may experience a more extensive need for support later on <sup>241</sup>. These results are consistent with those reported in this thesis.

Social support plays a crucial role in determining health, and is important for overall well-being and quality of life <sup>242</sup>. Although participants described many negative experiences, they also provided examples of beneficial support. The helpful support was in line with the existing theory about functions of social support <sup>126</sup> emphasizing "Companionship, emotional, informational, and instrumental support," which could increase the coping capacity during weight regain. This thesis highlights family members and healthcare providers as important sources of social support. It has been proposed that counseling and education for families and couples could be incorporated into follow-up care, since interpersonal relationships within families and couples may undergo alterations following surgery <sup>243</sup>.

Even though some weight regain is common and expected after patients have achieved their lowest weight <sup>13</sup>, this thesis has shown that patients may not be aware of this possibility. Some participants had built up expectations to lose a lot of weight and keep that off in the long term. These results are in line with previous research reporting that patients have a strong belief in losing nearly all or all, 90-106% of their excess body weight after bariatric surgery <sup>244,245</sup>. Patients undergoing bariatric surgery may sometimes have their expectations fueled by posts in online discussion forums <sup>246</sup>. Online forums may be an essential source of information

concerning bariatric outcomes, especially if there is a lack of support from healthcare providers, as reported in this thesis. Furthermore, our findings suggest that patients may believe that their food-related challenges cease following surgery. Thus, there is a need for improved and balanced information regarding changes in weight, dietary habits, and eating behaviors after surgery. However, a study conducted in the Netherlands found that less than 25% of patients who underwent RYGB desired detailed information about weight loss <sup>247</sup>. They also found that almost 90% of the patients desired more information about the everyday consequences of surgery <sup>247</sup>. This may indicate that patients are not always ready for conversation regarding weight trajectories following surgery. In addition, they may have forgotten information about the possibility of regaining weight received during the pre-surgical period <sup>248</sup>. Health literacy, which Berkman and McCormack define as the "degree to which individuals can obtain, process, understand, and communicate about health-related information needed to make informed health decisions" <sup>249</sup>, may be essential to consider when informing patients. Patients may need different methods of education and communication because of the variations in health literacy <sup>250</sup>.

The reasons for weight regain following bariatric surgery are not well understood but are thought to be related to a combination of metabolic, hormonal, anatomic, lifestyle, and mental health factors <sup>191</sup>. This thesis encountered numerous daily obstacles, stressors, life changes, and physical and mental health issues that could result in feelings of loss of control over weight management and self-care. These perceived post-surgery barriers, especially regarding managing everyday challenges that affect the adoption of a healthier lifestyle, were similar to those in an Australian qualitative study <sup>251</sup>. Participants expressed several similar barriers during the post-surgical phase, as presented in this thesis, including lack of time, parental obligations, managing emotions, cravings, illness, and mobility issues <sup>251</sup>. These obstacles may impede patients' ability to follow nutritional guidelines and lifestyle recommendations.

Our findings highlight the importance of person-centered individualized support in the long term. Providing person-centered care may be a crucial way to encourage patient involvement and enhance healthcare, which is also recommended in the national <sup>7</sup> and international guidelines <sup>6,29</sup>. Person-centered care involves a partnership between healthcare providers and patients, with shared decision-making and patient involvement at its core <sup>252</sup>. It is important to consider patients' perspectives and narratives <sup>252</sup>, which align with participants' desires to be heard and empowered by healthcare providers. Empathetic and compassionate approaches and communication skills are powerful tools to support self-efficacy and confidence in post-surgically coping with negative weight outcomes <sup>131</sup>. Additionally, creating a health plan that includes goals and plans for follow-up <sup>252</sup> may affect positively the quality of care and health outcomes of patients. However, evidence is still limited regarding the best practice to support patients in weight loss maintenance post-surgically <sup>199</sup>.

#### Dietary and eating behavior-related challenges

Previously, it was reported that inadequate nutritional follow-up is associated with weight regain after bariatric surgery <sup>237</sup>. This thesis highlights the importance of addressing this issue. Participants reported various eating-related challenges for which they would have needed medical nutrition therapy and psychological intervention. They were confused about their level of energy intake and weight management. It is well known that energy intake decreases immediately after gastric bypass surgery. However, people are expected to successively increase their energy intake to some extent over time <sup>155</sup>. Patients with weight regain may have a less pronounced effect on appetite hormones after bariatric surgery and, therefore, have an increased risk of weight regain <sup>86</sup>. In contrast, some reports have shown no differences in appetite hormones or appetite changes among patients with different weight outcomes after RYGB <sup>253</sup>. In this thesis, participants with weight regain self-reported large variations in appetite.

The results from this thesis indicate that individuals with obesity, regardless of age and previous obesity treatment, attempt to control their energy intake. However, these efforts may only be effective for weight loss and not weight loss maintenance. It has been suggested that cognitive restraint used to regulate food intake may not necessarily lead to reduced energy intake <sup>254</sup>. Weight loss may occur in the short term. However, strategies to sustain weight loss in the long term may differ <sup>255</sup>. These difficulties may also arise from metabolic adaptation, in which weight loss may induce e.g., changes in hormones and peptides that regulate satiety and appetite, resulting in increased energy intake and weight regain <sup>80,85</sup>. Participants who experienced weight regain after gastric bypass attempted to control their eating through dieting and restrictive eating behaviors without sustained weight loss. Previous weight loss, as reported in Studies IV and V, could have been caused by self-directed dieting or professionally led weight-loss interventions. Experiences of societal pressure on appearance may lead children and adolescents to self-directed and unhealthy weight loss attempts <sup>256</sup>, as those in older age groups. Unfortunately, the reasons for previous weight loss were not be identified in Studies IV and V. Self-directed strict diets may lead to an increased risk of repeated weight changes and maladaptive eating behaviors <sup>257</sup>.

Cognitive restraint eating behavior is necessary for weight loss <sup>258</sup>. Flexible cognitive restraint eating may be more favorable than rigid cognitive restraint eating for weight loss maintenance <sup>259</sup>. Rigid cognitive restraint eating is characterized by deprivation, such as strict dietary rules, fasting, or skipping meals, which is common in self-directed weight management, as reported by participants with weight regain. In contrast, flexible cognitive restraint eating focuses on sustainable healthy eating and limiting unhealthy food without forbidding any food. Professional medical obesity treatment may facilitate flexible cognitive restraint eating in adults <sup>260</sup>. This was requested by participants in our studies. Comparable results have been reported in children and adolescents. Structured obesity treatment by healthcare professionals is associated with less and even reduced risk and symptoms of disordered eating psychopathology <sup>73,74</sup>. Flexible cognitive restraint eating may also support psychosocial health and wellbeing <sup>259</sup>. Additionally, young people with obesity may need even more support to practice flexible cognitive restraint eating strategies, since neurocognitive maturity is under development <sup>261</sup>. We also found that uncontrolled eating and emotional eating behaviors were common among adolescents and young adults. These results indicate that different eating behaviors challenge weight management. However, the current screening tools used to identify problematic and disordered eating behaviors may require improvement to better suit individuals with obesity <sup>262</sup>.

Binge eating behaviors seem to decline with bariatric surgery, but patients may instead practice behaviors with a small amount of food at a time, such as grazing behavior <sup>263</sup>, as reported by some participants in this thesis. A systematic review and meta-analysis concluded that eating psychopathology, such as grazing after bariatric surgery, may be associated with weight regain <sup>264</sup>. Eating small amounts of energy-dense food is possible, which leads to difficulties in controlling the energy intake. Grazing could also be a way to cope with post-bariatric hypoglycemia associated with weight regain <sup>192</sup>.

Participants with weight regain reported experiencing emotional and disordered eating behaviors, although this could contribute to dumping or other meal-related problems. This finding differs from that of a previous qualitative study, in which patients who underwent bariatric surgery experienced dumping syndrome as a protective factor against excessive energy intake <sup>265</sup>. By avoiding foods that could cause symptoms of the dumping syndrome, they also regulated their weight more

optimal. Individuals with poor emotional regulation skills in stressful situations may be more likely to engage in emotional eating behaviors <sup>266</sup>. Our study found that participants seemed to blame themselves for their exposure to dumping, which is consistent with previous research <sup>265</sup>. It is important that patients who experience difficulties with stress and coping strategies receive psychosocial support and training in emotion-regulation skills <sup>266</sup>. Difficulties with eating behaviors may explain, at least partly, findings from previous studies reporting dietary patterns with energy-dense (high sugar/high fat) foods being problematic in weight regain after bariatric surgery <sup>197,237,267</sup>.

In some participants, alcohol consumption became a problem after bariatric surgery. Changes in alcohol absorption and metabolism after gastric bypass <sup>268</sup> may lead to rapid intoxication and increase the risk of alcohol use disorder <sup>269</sup>. Approximately one-fifth of patients report symptoms of alcohol use disorder five years post-surgically <sup>270</sup>. Alcohol provides energy (7.1 kcal/g) and is essential to consider in relation to weight management. Alcohol consumption may increase appetite, lead to excessive energy intake, and disinhibited eating <sup>271</sup>.

Mental health problems, such as depression, have been shown to be high in patients with problematic alcohol consumption after RYGB <sup>272</sup>, which was also mentioned by the participants in our study. A nationwide healthcare registry study found that alcohol or other substance use disorders may complicate the treatment of depressive disorders owing to inadequate antidepressant treatment effects <sup>273</sup>. This may contribute to additional mental health challenges among the bariatric population experiencing weight regain.

There are also suggestions concerning "addiction transfer," that is, one addiction may be transferred to another after bariatric surgery <sup>269,274</sup>. When food is not as rewarding as before surgery, it is assumed that some people could develop a new addiction to alcohol instead.

#### The benefits and disadvantages of weight loss

Almost half of the participants in the SNMC study and >70% of adolescents and young adults with obesity had previously lost weight. Similarly, nearly half of the adults in the US had tried to lose weight during the last year according to the National Health and Nutrition Examination Survey (NHANES, 2013–2016) <sup>275</sup>. These numbers indicate that weight loss attempts are prevalent in many groups, especially among those with obesity, in Western societies.

This thesis has shown that previous weight loss was associated with all-cause and cardiovascular mortality. This association was found in men, but not in women. Our results point in the same direction as the results from previous studies such as the Erfurt Male Cohort Study (ERFORT study), showing an association between weight loss with all-cause mortality in men <sup>276</sup>. Findings from the Nurses' Health Study (NHS) support that weight changes in women are not associated with all-cause or cardiovascular mortality <sup>277</sup>. A potential explanation for this sex difference may be that women tend to develop CVD later in life than men do. It has been suggested that estrogens may protect against cardiovascular disease in women <sup>278</sup>.

Moreover, bariatric surgery contributes to a significant weight loss in most patients. It has been associated with reduced mortality from all-cause and cardiovascular diseases (heart failure, myocardial infarction, and stroke but not atrial fibrillation), as reported in a systematic review and meta-analysis <sup>279</sup>. These results support the positive health benefits associated with weight loss. Reduced chronic inflammation and oxidative stress induced by weight loss appear to be important factors in reducing the risk of cardiovascular disease <sup>101</sup>.

We did not detect any association between weight loss, repeated weight loss, and mortality due to cancer. These results are consistent with those of previous studies by Zou et al. <sup>186</sup> and Stevens et al. <sup>280</sup>. However, there is convincing evidence that bariatric surgery is associated with reduced cancer mortality <sup>281</sup>, indicating that weight loss can improve health outcomes and protect against co-morbidities associated with obesity.

Excess body fat has been associated with increased morbidity <sup>103,104</sup> and mortality <sup>112,113</sup>. Nevertheless, bariatric surgery has been associated with increased life expectancy <sup>154</sup>. If weight regain occurs after bariatric surgery, the number of comorbidities associated with body fat may return to <sup>282</sup>, negatively affecting the life expectancy. However, this thesis found that most participants who underwent bariatric surgery still experienced benefits even after regaining weight, and despite regaining weight, they had lower weight than before surgery.

For those with obesity, weight loss may be necessary to reduce several risk factors associated with cardiovascular health <sup>283</sup>. Young individuals with obesity may also be at a risk of developing multiple metabolic issues that can increase their likelihood of experiencing ill health and early death later in life. Therefore, the weight loss is promoted <sup>284</sup>. In contrast, those with BMI in the normal weight range may have the greatest benefits in terms of weight stability to maintain a low risk

of mortality <sup>113</sup>. Furthermore, it is essential to be aware that weight loss may sometimes be unintentional, caused by underlying severe illness, physical or mental health conditions, being a risk factor for malnutrition, and associated with increased mortality <sup>285</sup>. A limitation of this thesis is that we had no information on whether the weight loss was intentional or unintentional.

This thesis has shown that there are challenges with weight loss and weight regain, but the possible negative health effects of weight loss may still be lower than the benefits of weight loss on metabolic and cardiovascular health. Those with excess body fat that negatively affects their health should be encouraged to lose weight using evidence-based methods and receive long-term support. However, healthcare professionals need to detect possible unintentional weight loss and assess and treat underlying causes of that <sup>285</sup>. Ultimately, we need to find better tools to support patients with obesity in weight loss maintenance in the long-term to decrease the risk factors for cardiovascular health and reduce future mortality.

#### Weight bias and obesity stigma may impede weight management efforts

People with obesity may experience weight bias and obesity stigma in our society <sup>3</sup>. Participants experiences indicated that weight bias and obesity stigma were present in their context. Negative comments and unsupportive actions were experienced, particularly in private settings, as well as in healthcare. These comments and actions may originate from the belief that weight management is completely influenced by people's willpower and behavior.

Weight bias and obesity stigma are common in western countries. For example, they may be present in interpersonal relationships, family environments, healthcare, and employment settings <sup>110,286</sup>. Adolescents and young adults with obesity may be at an elevated risk of bullying and teasing by peers, due to weight bias and stigma <sup>120</sup>. Weight bias and obesity stigma has a negative impact on psychological and physiological well-being, social and economic disparities, and the overall quality of life <sup>286,287</sup>. These experiences may have contributed to more attempts to control the eating behavior of young people with obesity stigma may prevent patients from seeking adequate care, complicate weight management, and increase self-directed weight loss attempts and dieting <sup>120,287</sup>. The prevalent weight bias in society may even drive normal weight individuals to try to lose weight, as might have been the case in the Swedish National March population with possible long-term negative effects.

Weight bias and obesity stigma in healthcare settings are concerning issues. If healthcare professionals hold negative beliefs about individuals living with obesity <sup>10,288</sup> it may negatively affect the quality of care provided <sup>3</sup>. The potential negative effect on the quality of care provided may arise from the feeling that healthcare professionals are ignorant and uncertain about their treatment of weight regain. Bariatric surgery, as a treatment for obesity, may also be subject to weight bias from healthcare professionals, patients, and the public, who may view it as "a shortcut" <sup>289</sup> or "a last resort" <sup>290</sup>. These attitudes and beliefs may delay patients from receiving effective surgical treatment for obesity or follow-up after bariatric surgery. Ensuring that people living with obesity feel respected and heard of when seeking medical attention is critical. Healthcare professionals and society must recognize and combat the weight bias and obesity stigma. It is essential to understand that obesity is not a choice.

Patients may experience the need to undergo bariatric surgery as a "failure" in the first place. Weight regain may enhance feelings of self-blame and induce a feeling of a "double failure" <sup>291,292</sup>. Individuals may think that they gained weight in the first place and need to undergo surgery, an ultimate action, to lose weight, and still not succeed in keeping the weight off. They may think that having "spoiled" their last chance of weight loss <sup>291</sup>. Participants' self-accusations and negative statements about themselves may have originated in feelings of shame. Negative self-talk such as "I failed.," "my fault," "I must be stupid" were stated by some participants and could indicate a presence of low self-esteem and internalized weight bias. Low self-esteem is associated with weight regain after bariatric surgery <sup>293</sup>. Feelings of failure, shame, and quilt have been reported in other studies as well <sup>236,292</sup>. Individuals who perceive obesity stigma and weight bias may experience stress that may increase their food intake. Stress, in turn, is associated with maladaptive eating behavior and disordered eating <sup>294</sup>.

Although we could not identify any associations between previous weight loss and self-esteem, we found that low self-esteem was prevalent among adolescents and young adults seeking treatment for obesity. There might be several reasons for low self-esteem during adolescence or young adulthood among those with obesity. First, this period is challenging, because it is a transitional period between adolescence and young adulthood <sup>295</sup>. Second, mental health problems, such as depression and anxiety, are common among young treatment-seeking individuals with obesity <sup>296</sup> and may contribute to a negative perception of oneself and self-worth <sup>222</sup>. Experiences of weight stigma and internalized weight bias during childhood and adolescence <sup>297,298</sup> may also influence self-esteem during young adulthood. However, self-esteem tends to remain constant throughout life <sup>299</sup>.

Differences in childhood experiences, family environment  $^{\rm 274}$ , and genetic vulnerability  $^{\rm 300}$  might at least partially explain the differences in self-esteem scores.

In this thesis, men were in the minority in all the included studies. Although the prevalence of obesity is almost the same in both men and women, women seek treatment for overweight or obesity to a greater extent. Sociocultural factors, socioeconomics, biological and metabolic factors, values, and attitudes toward ideal body weight, food, and eating may be factors that may explain these differences to some extent <sup>301</sup>.

Media play a key role in how weight, the human body, and sex are portrayed, which in turn affects norms and attitudes. For example, it has been reported that overweight is generally considered as a female problem <sup>302</sup>. The media may have a more accepting attitude towards overweight and obesity among men. Thus, societal factors may contribute to gender differences in body image and weight perception. Differences in attitudes, stereotypes, and beliefs regarding obesity treatment may affect incentives to seek care. Furthermore, it has been reported that women experience weight-based discrimination to a higher degree than men <sup>303</sup>, which could also be a driver of weight loss attempts.

## 5.3 Methodological considerations

Methodological considerations are made separately for qualitative and quantitative studies because the methods differ considerably.

#### 5.3.1 Qualitative studies

Qualitative methods are excellent choices when researchers aim to gain a deeper understanding of people's experiences, perspectives, and perceptions of a phenomenon <sup>208</sup>. Additionally, qualitative methods can capture the meaning of lived experiences <sup>208</sup>. We concluded that individual in-depth interviews were the most suitable option to capture first-person narratives and allow participants to freely elaborate their perspectives. The semi-structured interview guide, with open-ended questions, provided a framework in which all the participants were asked the same basic questions <sup>208</sup>. We ensured that the interviews were performed in a calm and undisturbed room so that the participants could express their narratives in a safe and respectful environment <sup>208</sup>.

We chose to use thematic analysis, as outlined by Braun and Clarke <sup>209,214</sup>, in all our qualitative analyses. Thematic analysis is a robust, flexible, and well-described

method <sup>209,214</sup>. Considerations regarding the choice of method were made by the research group and guided by the aim of the study and the research questions. We adopted an inductive approach in our analyses, which meant that patterns, themes, and sub-themes were derived from the data without a pre-existing theory or coding protocol <sup>208,214</sup>. We aimed to generate new insights and understanding from the data, a process driven by our research questions.

We performed both semantic and latent analyses <sup>214</sup>, focusing on explicit meaning as well as the underlying, deeper essence. Our ambition was to stay close to the participants' narratives from a theoretical perspective of realism, while making sense of the meaning of their realities. Braun and Clarke described interpretation as a "so what" process where researchers are working out what is important and what that means for participants <sup>209</sup>. We produced three distinct articles from the same data set. There was some overlap in the results, which was unavoidable. However, the articles are self-contained and can be read independently, though they also complement each other.

#### Reflexivity

In qualitative research, reflexivity is a core approach in which a researcher actively examines his or her own pre-conceptions and experiences that may influence the research <sup>209</sup>. The pre-conceptions of the author of this thesis from the field of obesity may have been beneficial in understanding the patient's situation and settings. However, it was very important to be aware of and critically reflect on one's own beliefs and attitudes <sup>209</sup>. The co-authors played a key role in questioning and suggesting the interpretation of the data and contributed to interdisciplinary criticism, reflexivity, and meta-positions . When reporting the study results, we disclosed the researchers' pre-conceptions to improve reflexivity.

To enhance reflexivity, it could have been beneficial to have more of patient and public involvement (PPI) in the research process. However, we included one patient to test the interview guide, and the participants had the opportunity to comment on the transcribed interview data. It could also have been beneficial to have had a bariatric surgeon in the research team to increase understanding and pre-conceptions regarding surgical procedures and follow-up in the context of surgical clinics. However, our research team had extensive experience regarding obesity care and meeting patients before and after bariatric surgery. Braun and Clarke underline that researcher subjectivity should be seen as a resource rather than a bias in reflexive thematic analysis <sup>209</sup>. Researchers experience is an important tool when interpreting the data.

#### Informational redundancy or saturation

Another aspect to consider is whether we had sufficient data for analyses. Data saturation or informational redundancy <sup>208</sup> is often used synonymously to describe this. Lincoln and Guba <sup>211</sup> suggest that informational redundancy indicates that the sample size is sufficient for a decision when nothing new is mentioned in the interviews. Theoretical saturation is a term that originates from the Grounded theory <sup>304</sup>. This refers to when similar data repeatedly appear in the data collection and analysis, and no new data emerges from the material.

Braun and Clarke state that the term saturation may be problematic <sup>209</sup>. They suggest that the point of saturation may not always be possible to predict the number of interviews in reflexive thematic analysis <sup>305</sup>. Instead, they suggest that the adequacy, diversity, richness, and complexity of the data may be more important when determining a sample size <sup>305</sup>. Further, Braun and Clarke suggest that themes and sub-themes are actively generated through step-wise analysis and interpretation, not passively emerging from the data <sup>305</sup>. This means that interpretations are always situated and subjective, and therefore may never be completely definite, affecting the decision of sample size <sup>305</sup>.

In this thesis, we employed the concept of "informational redundancy" <sup>208,211</sup>. As the data collection process continued, we ceased recruiting new participants for the interviews once a little new information was mentioned. During the data collection process, we regularly reviewed the interview data and made joint decisions on whether the data had sufficient variation and richness. Nonetheless, additional specific questions regarding food and eating behaviors might have provided more in-depth information on this topic. However, for the third analysis, we assessed whether the narratives provided by the participants were sufficiently rich in dietary- and eating-related challenges. In future studies, the results from Study III could influence the interview guide to capture eating-related behaviors more precisely so that participants could explore them in more detail.

#### Trustworthiness

Trustworthiness is a central concept that ensures the quality of the research process, and includes four concepts: credibility, dependability, confirmability, and

transferability <sup>208,21]</sup>. Credibility refers to aspects of the truth and correctness of study findings <sup>208</sup>. Dependability, in turn, affects the quality and consistency of the research and how others can replicate the study. Confirmability relates to how the research process is documented and controlled, and the findings are verifiable and derived from interview data <sup>208</sup>. Finally, transferability refers to the aspects of generalizability to other settings and contexts <sup>208</sup>.

To increase the credibility, dependability, and confirmability of our studies, we used systematic and rigorous analysis processes and carefully documented each step <sup>208</sup>. The co-authors played a key role in interdisciplinary critiques. To increase credibility and confirmability, we used the researcher triangulation <sup>208</sup>. According to Braun and Clarke <sup>209</sup>, the purpose of what they called "collaborative coding" is to increase reflexivity.

To ensure credibility and transferability, we included participants with different ages, sexes, and backgrounds. However, our studies have some limitations. We included only Swedish-speaking participants in our study, and we may have excluded important perspectives by doing so. People with language barriers may have other perspectives in this topic. However, more than 30% of the participants had origins outside Europe, providing diversity to our population. Most participants were women, reflecting relatively well the proportions of sexes in the bariatric population in Sweden <sup>306</sup>. It would have been beneficial to include individuals who had experienced weight regain after gastric bypass surgery, but who were not seeking treatment. These participants may have had different experiences and perceptions than those who actively participated in the obesity treatment program. We also excluded individuals who had undergone LAGB because weight regain is common after this procedure. Additionally, all participants had undergone RYGB surgery. This may not be surprising, because RYBG has been the most common procedure since the late 90s' <sup>147</sup>. Therefore, future studies could explore how patients experience weight regain after sleeve gastrectomy.

We strived to describe the materials and methods used carefully to increase the dependability and replicability of our studies <sup>208</sup>. In addition, we selected quotes from the interview data to strengthen our results, so that the reader could confirm the findings. By carefully describing the participants and the context of the study, we aimed to provide readers with sufficient information to decide whether the results from our analyses were transferable to other contexts <sup>208</sup>.

#### 5.3.2 Quantitative studies

The quality aspects of quantitative research include validity (both internal and external) and reliability <sup>210</sup>. Validity refers to the relevance of the measurement. Reliability represents the consistency of the measure. In observational studies, bias, misclassification, and confounding factors may influence the association between exposure and outcome, affecting the interpretation of the results and leading to systematic errors <sup>210</sup>.

#### **Misclassification bias**

Misclassification bias and information bias are concerns when the exposure or outcome is not classified correctly <sup>210</sup>. Self-reported data concerning weight loss may have been incorrectly reported and therefore classified into the wrong weight loss category. Participants may have forgotten how much and how often they lost weight because of recall bias. As weight may often be experienced as a sensitive matter, especially among those with overweight and obesity, there may also be concern regarding social desirability <sup>307</sup>. Consequently, individuals may underreport weight and weight loss. To actually measure and monitor weight changes had strengthen our results. However, it has been shown that self-reported anthropometric measurements are valid in epidemiological studies <sup>308,309</sup>. In Study V, we had access to objectively measured baseline weight status. We used confounders from the questionnaires. This information could have been inaccurate concerning e.g., the level of physical activity, hours of sleep, amount of alcohol, and number of cigarettes.

Another concern was whether the weight loss was unintentional or intentional. It would have been preferable to determine the reasons for weight loss. Intentional weight loss refers to voluntary actions to reduce energy intake to lose weight, whereas unintentional weight loss refers to weight loss caused by diseases or starvation. To minimize the potential impact of unintentional weight loss, we excluded participants with existing diagnoses of cancer or cardiovascular disease at enrollment. We also decided to exclude those with BMI <18.5 kg/m<sup>2</sup> since low weight may indicate existing diseases. Moreover, we conducted sensitivity analyses by omitting the first two years of follow-up, and these analyses yielded the similar results as the main analysis. Adolescents and young adults with obesity could have also been affected by the disease before inclusion. However, given their younger age and the fact that the Center for Obesity has an inclusion criterion that other diseases should be assessed and treated before enrollment in the obesity management program, this was minimized.

There were also concerns regarding whether participants regained lost weight. They might have lost weight several times, but never regained it. We did not have access to information that could confirm possible weight fluctuations. However, it is common for individuals who intentionally lose weight to regain their weight. This may have occurred in some of the participants.

Follow-up with the Swedish national registries strengthened the internal validity of Study IV. These registries are highly valid and reliable in terms of emigration, cause of death, and date of death <sup>310</sup>. During data collection, participants provided informed consent to use their national registration numbers and to link them to national registries during follow-up.

In Study V, we used Rosenberg Self-esteem Scale (RSES) to evaluate self-esteem and the Three-Factor Eating Questionnaire-R21 (TFEQ-R21) to assess eating behavior. Both questionnaires have been used widely in research. The RSES was developed and validated for high school students in the US <sup>222</sup>. This onedimensional global self-esteem scale assesses people's feelings about the self. The RSES has been criticized for being sensitive to the situation and for the "feeling at the moment" <sup>311</sup>. In our study, we measured self-esteem at the baseline during the first visit to the clinic. This may have been a sensitive time for some participants, which could have affected the validity of the measure. However, it has been stated that self-esteem is quite constant within an individual throughout lifespan <sup>299</sup>.

There are other methods to assess self-esteem, such as the Self-Concept Questionnaire (SCQ), which has 30 items and is positively correlated with the RSES <sup>312</sup>. The Self-Concept Questionnaire is a multidimensional scale that captures "significance, worthiness, appearance/social acceptability, resilience and determination, competence, control over personal destiny, and value of existence" <sup>312</sup>. The Self-Concept Questionnaire was developed for the adult population <sup>312</sup>. In our study, Rosenberg self-esteem scale was a good choice since it was developed and validated in young high school students <sup>222</sup> and has also been used in young people with obesity <sup>68</sup>.

We assessed three different eating behaviors: uncontrolled, emotional, and cognitive restraint eating behavior using the TFEQ-R21. This questionnaire is frequently used and validated in people with obesity <sup>228</sup>. The TFEQ-R21 lacks cutoffs; a higher score indicates more of the respective eating behavior. An example of a questionnaire with cut-offs is the Yale Food Addiction Scale 2.0 (YFAS 2.0) <sup>313</sup>, which assesses a mild, moderate, or severe degree of problems with eating behavior. However, the TFEQ-R21 is used in clinical practice at the Center for Obesity and has previously been used in research on a similar population <sup>68</sup>. The original TFEQ <sup>229</sup>, with 51 questions, could have helped assess rigid and flexible cognitive restraint eating. However, the study participants already had comprehensive questionnaires to complete, and it was reasonable to choose the shorter TFEQ-R21, with 21 questions.

#### **Selection bias**

Selection bias may have occurred if the participants were not representative of those eligible for the study <sup>210</sup>. This may happen if some participants are more interested in participating than others are. For example, individuals with family members or friends affected by a cancer diagnosis may have been keen to participate in an event promoting fundraising for cancer research. These individuals may have a genetic vulnerability or a lifestyle similar to their close ones with a cancer diagnosis, leading to an increased risk of the disease later in life. The healthy volunteer bias (healthy worker effect) may have had an impact on the representativeness of our cohort <sup>210</sup>, meaning that participants in the cohort may have been more health conscious. For example, our participants smoked less than the Swedish population by the end of the 1990s but had a higher BMI than the general population <sup>215,314</sup>.

Study V included adolescents and young adults with obesity. Only 26.0% of the participants were men, which restricts the applicability of our findings to the male population. Furthermore, we excluded those who could not understand the study information because of language barriers, cognitive impairment/intellectual disabilities, or who had not signed an informed consent form. Patients with current or possible eating disorders, substance use, or mental health problems were excluded from the study. These exclusions may have contributed to some degree of selection bias. Despite this, there was diversity in the population. More than 40% of the participants had parents who originated outside the Nordic countries. The generalizability of our results to the general population may have some limitations, because we only included young participants with obesity starting in the obesity treatment program, affecting external validity. These groups have seldom been studied in detail. Therefore, this study provides valuable information regarding their situations.

### Confounding

A confounder is a variable that impacts both exposure and outcome, and may influence the observational effect and threaten validity <sup>210</sup>. Therefore, it is important to address the confounding factors in observational studies. In Study IV, the 36-page questionnaire provided information on several possible confounders adjusted for during the analyses. One confounder we wanted to adjust for was waist circumference, but this was impossible due to the high number of missing values. Furthermore, smoking was an important confounder adjusted for during the analysis because it is strongly associated with morbidity and mortality <sup>315</sup>. The years since quitting and number of cigarettes consumed daily among current smokers could have been valuable when adjusting for smoking. We obtained only data on the number of cigarettes smoked per day. However, we did not have many current smokers in our data (2,558/34,346, 7.4%), and among these, <10% reported being heavy smokers (>20 cigarettes per day), which limited the ability to perform sub-group analysis. Causality can never be conclusively inferred from epidemiological studies because of the possible presence of residual confounding and unknown confounders.

Socioeconomic factors are important in obesity and may also be important for weight changes. In Study V, we had no access to household income or parental educational levels. However, we asked the participants about their occupation. Young individuals may be highly affected by their parents' socioeconomic status. The high prevalence of smoking (21.3%) compared with 3.8% in the general population aged 16–29 years in Sweden in 2022 <sup>316</sup> may indicate a complex vulnerability to socioeconomic inequity in this population. Low socioeconomic status has been identified as a predictor of early onset cigarette smoking among young people (<18 years) <sup>317</sup>. We adjusted for smoking status, which may have functioned at least partially as a proxy covariate even for socioeconomic factors.

An experimental design, such as a randomized controlled trial with objective anthropometric measurements, and controlled weight loss regarding amount and frequency, could have been an alternative study design. We could have minimized the biases in a randomized controlled trial and controlled for known and unknown confounders through randomization. However, collecting data from so many individuals to a reasonable cost, effort, and during a very long follow-up period would have been impossible. We would probably have encountered a huge problem with attrition in such a study. Therefore, a prospective cohort study is likely the most appropriate approach to investigate the association between previous weight loss and mortality.

## 6 Conclusions

The overall conclusions of this thesis are as follows:

- Patients who experience weight regain after bariatric surgery may perceive existing post-surgical support as insufficient. However, feelings of personal failure, self-blame, and shame may make attending follow-up visits more challenging. Therefore, multidisciplinary healthcare professionals should have an empathetic and non-judgmental attitude and demeanor toward patients with weight regain. Additionally, patient support groups and education of family members may add value to long-term social support.
- Patients who regain weight after bariatric surgery may perceive weight recurrence as emotionally challenging. Negative emotional responses accompanying weight regain may add to those of various internal and external challenges. They struggled with increasing appetite, mental and physical health issues, and everyday problems. However, patients may need more support in focusing on self-care and behavioral strategies.
- Dietary and eating-related behaviors may be overwhelming during weight regain after bariatric surgery. Patients may not expect to struggle with weight and food to continue. Challenges such as irregular meals, portion sizes, cravings, disordered eating patterns, unpleasant meal-related experiences, insufficient nutritional knowledge, and non-functional weight loss methods may complicate weight management. The results of this thesis emphasize the importance of a multidisciplinary team that includes dietitians and psychologists in supporting patients with healthier eating behaviors after bariatric surgery.
- Weight loss earlier in life appears to be associated with all-cause and cardiovascular mortality, particularly in men. Weight loss previously in life does not appear to be associated with cancer mortality.
- In adolescents and young adults (16-25 years) with obesity, weight loss previously in life seems to be associated with cognitive restraint eating behavior. Weight loss does not appear to be associated with self-esteem, uncontrolled eating, or emotional eating.

## 7 Points of perspective

The 2030 Agenda for Sustainable Development Goals <sup>318</sup> is crucial for the wellbeing of all people and the planet. Global crises such as the Covid-19 pandemic, climate change, the ongoing war in our immediate area in Europe, and the costof-living crisis have shown that our world is vulnerable and more connected than ever. Additionally, we have ever-increasing rates of obesity, challenging the health of individuals and the healthcare system. Our food system does not work well in promoting health for everyone. Therefore, the health, environment, economic, and social dimensions are essential when discussing and researching sustainable development. When planning future perspectives in research, all these dimensions, as well as Sustainable Development Goals should be considered. However, above all, goal number three: "Ensure healthy lives and promote wellbeing for all at all ages" <sup>318</sup> is important in medical research.

## 7.1 Future research

The Swedish National Guidelines for Obesity Care <sup>7</sup> have given high priority to surgical obesity treatment because of its superior effect on health and quality of life and durable long-term weight loss results. The Swedish National Board of Health and Welfare <sup>7</sup>, predicts that approximately 220 000 individuals may need to be assessed for bariatric surgery in Sweden. In 2022, the volume of bariatric surgery was nearly 5000 performed surgeries <sup>147</sup>. Thus, politicians and healthcare authorities must provide resources to surgical clinics to perform more operations in the future. This may lead to more people needing extra support with post-surgical weight management. Thus, research and clinical practice should focus on post-surgical follow-up to optimize long-term health, quality of life, and patient weight outcomes.

There is a growing body of research on weight regain after bariatric surgery. However, there are still many gaps in our understanding. There is a need for increased knowledge on how patients can be better supported in eating habits post-surgically to prevent and reverse weight regain. For example, the associations among post-bariatric hypoglycemia, eating behaviors, and weight regain should be studied more closely. Future studies are necessary to determine which patients are at a risk of significant weight regain after surgery. Family members, spouses, and friends play an essential role in the post-surgical period. Therefore, future studies could involve interventions toward family members, spouses, or other close ones and study their experiences to increase the understanding further. It is also important to study how healthcare professionals experience the care of patients who have regained weight, and what kind of education and support they would need. The recently presented reporting standards of "a suboptimal initial clinical response" and "a late post-operative clinical deterioration" after bariatric surgery by the International Federation for the Surgery of Obesity and Metabolic Disorders, in the IFSO consensus book <sup>198</sup> should be evaluated, communicated, and implemented in research and clinical practice.

The Swedish Youth with Obesity (SYO) cohort <sup>221</sup> allows us to follow up young adults undergoing bariatric surgery and identify profiles vulnerable to insufficient weight loss and weight regain. Follow-up analyses can be performed from different perspectives, such as mental health, alcohol, or drug use, sleeping habits, and pain, in addition to eating behavior or self-esteem. Qualitative research can also be performed within this patient group to increase our understanding of their situation and the challenges they face in weight management. Increased knowledge of these challenges may impact society by changing the food environment and regulations regarding, e.g., food marketing.

Healthy eating is important to everyone. However, a healthy relationship with food is central to the long-term weight stability and overall health. Therefore, future research could focus on how to increase patients' eating competence <sup>319</sup>, where attitudes toward eating, acceptance of food, food intake regulation, and factors related to the eating context could be further explored.

Studies have also demonstrated a bidirectional relationship between obesity and mental health. Young and older adults with obesity, especially those who regain weight after bariatric surgery, may experience elevated stress and mental health problems. It is known that nature experiences have a positive effect on mental health. Individuals with obesity and poor coping strategies for stress management may have difficulty accessing the nature for relaxation. If nature can come to patients as a Virtual Reality (VR) solution, they may start seeking it more frequently for relaxation by themselves. Therefore, virtual reality may also have the potential to reduce emotional eating behaviors.

## 7.2 Clinical Implications

Traditionally, weight management has been seen as an individual's responsibility, and care offered by the healthcare system has been, and still is, limited and unequally distributed in Sweden. Therefore, higher education and training need to prepare healthcare professionals with sufficient tools and knowledge to provide evidence-based, combined, and comprehensive obesity care. As obesity has been recognized as a chronic, complex disease, people-centered care is required in the long term and across the lifespan. Healthcare professionals are crucial for building trustful relationships with patients, supporting weight loss maintenance, and positive health outcomes. They should be aware of the sensitive matter of body weight and carefully focus on alliances with patients for long-term obesity treatment regardless of age and sex.

In many patients, bariatric surgery leads to sustained weight loss and improved health. Nevertheless, pre-surgical preparations should address weight loss, and eating behavior change expectations to a larger extent. Given the chronic nature of obesity, regaining body weight may be an indicator of disease severity. Patients should never be blamed for the sub-optimal weight outcomes. Care for people with obesity should be adopted according to a chronic care model with long-term support, focusing on health, well-being, and sustained weight outcomes that are realistic for patients. To achieve equity, not just equality, in health, some patients may need more resources from the healthcare system, such as patients with low socioeconomic status or health literacy, psychological comorbidities, high BMI levels, difficulties in weight loss maintenance, and problematic eating behaviors. It is essential to detect the possible remaining positive effects of surgery to empower patients in self-care. However, when weight regain is significant, the risk of obesity-related comorbidities should be assessed regularly. Pharmacotherapy can effectively complement combined lifestyle interventions if weight regain begins. The treatment of obesity through pharmacotherapy is rapidly advancing and may be an effective option for patients living with obesity. However, reassessment at a bariatric surgery clinic may be necessary when weight regain is significant.

Complex individual factors may contribute to weight regain. By assessing physical and mental health, potential eating disorders, alcohol consumption, appetite, family situation, and coping with stress, we can identify factors affecting patients' ability to manage their weight. Interventions should be tailored according to patients' needs. Support groups and involving/educating family members can serve as alternative areas of improvement.

Individually tailored medical nutrition therapy provided by registered dietitians, along with psychological interventions, are cornerstones of pre- and post-surgery, as in all obesity treatments. All patients should have access to medical nutrition therapy provided by dietitians with expertise in obesity or in bariatric nutrition. Dietitians need to have knowledge of behavioral treatment strategies and a collaborative communication style. Primary care dietitians can play a key role in providing life-long annual support for patients after bariatric surgery. That support could also include the evaluation of vitamin and mineral supplementation and nutritional blood tests, in collaboration with general practitioners. Telehealth and digital solutions can facilitate structured care processes and follow-up.

Clinical obesity care should focus on offering treatment that is suitable and appealing to men, women, other gender identities, and all ages. Although men may not seek obesity care as frequently as women, they can experience severe health consequences from obesity. Assessing patients' weight loss history may provide valuable information regarding their previous experiences and possible challenges. It is essential for patients to receive treatment that supports weight loss maintenance after weight loss to reduce the possible adverse effects of repeated weight loss on health and life expectancy. Adults with normal weight should be encouraged to maintain a stable weight throughout their life course.

There is a need to improve treatment strategies that target eating behaviors in young people with obesity. Healthcare providers should be aware of possible rigid cognitive restraint eating behaviors that may complicate weight management and support healthy, more flexible cognitive restraint eating behaviors. The development of easy-to-use screening tools for assessment and the basis for conversations regarding problematic eating behaviors should be prioritized.

Clinicians hold a critical position in providing evidence-based support and people-centered care for their patients. However, there is also a pressing need for changes in the food system and the implementation of policies aimed at combating obesity. Additionally, as a society, we need to take actions towards ending the weight bias and obesity stigma. A broader perspective is needed to find solutions to support people with healthier lifestyles, living conditions, and weight management across their lifespan. "It is not a quick fix."

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