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Obesity and bariatric surgery in Sweden

Sociodemographic aspects and neighbourhood deprivation

ENSIEH MEMARIAN

CLINICAL SCIENCES IN MALMÖ | FACULTY OF MEDICINE | LUND UNIVERSITY 2018





The prevalence of obesity has risen both worldwide and in Sweden during the past decades due to lifestyle changes. Obesity is associated with several diseases and is a major global health problem. Obesity is more prevalent among socioeconomically disadvantaged groups. Bariatric surgery is considered to be the most effective method of weight loss for severe obesity. In this thesis, the effect of neighbourhood deprivation on childhood obesity, as well as the possible effects of sociodemographic characteristics such as income, education, employment and country

of origin on rates of bariatric surgery, in a country like Sweden, with universal healthcare insurance system were analysed.

Ensieh Memarian is a Specialist in General Medicine. She studied medicine at Lund University and graduated in 2004. She has been working in primary care since 2006. This thesis was completed during the years 2013-2018 at the Center for Primary Healthcare Research, Department of Clinical Sciences in Malmö, Lund University, Sweden.

Obesity and bariatric surgery in Sweden

Obesity and bariatric surgery in Sweden

Sociodemographic aspects and
neighbourhood deprivation

Ensieh Memarian



LUND
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DOCTORAL DISSERTATION

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Title and subtitle: Obesity and bariatric surgery in Sweden, sociodemographic aspects and neighbourhood deprivation			
<p>Abstract</p> <p>Background: During the last decades, the prevalence of obesity has risen both worldwide and in Sweden, due to lifestyle changes. Obesity is one of the major preventable causes of death in the developed world. Obesity is associated with numerous comorbidities, decreased quality of life and greater overall costs to the healthcare system. Bariatric surgery is considered to be the most effective method of weight loss for severe obesity. Multiple studies have shown that obesity is distributed along a socioeconomic gradient, with higher prevalence rates in low socioeconomic groups.</p> <p>Objectives: The aim of this thesis was to examine whether there is an association between childhood obesity and neighbourhood deprivation after accounting for sociodemographic characteristics. Another aim of this thesis was to explore whether sociodemographic characteristics, such as income, education, employment and country of origin have an effect on bariatric surgery rate in a country like Sweden, which has a universal healthcare insurance system.</p> <p>Methods: In paper I, an open cohort of all children aged 0-14 years was followed. Data were analysed by multilevel logistic regression, with familial- and individual-level characteristics at the first level and level of neighbourhood deprivation at the second level. In paper II, an open cohort of all individuals aged 20-64 years was followed. Socioeconomic differences were examined using cumulative rates. Hazard ratios (HR) of bariatric surgery were calculated using Cox regression models. In paper III, a closed cohort of all individuals aged 20-64 years was followed. Age standardised cumulative incidence rates (CR) of bariatric surgery were compared between Swedes and immigrants. Cox proportional hazards models were used in univariate and multivariate models. Paper IV was a retrospective cohort study. Data about BMI were collected from the Military Service Conscription Register for men, and from the Medical Birth Register for women. CR of bariatric surgery and Cox proportional hazard models were used to analyse the association between BMI and individual variables.</p> <p>Results: High neighbourhood deprivation remained significantly associated with higher odds of childhood obesity after adjustment for sociodemographic characteristics. The rate of bariatric surgery was almost three times higher for women than men. The number of bariatric surgeries increased substantially after 2005. The dominating bariatric surgical procedure in Sweden was gastric bypass. Immigrants as a group had a lower rate of bariatric surgery compared to Swedes. However, there were large variations in the rate of bariatric surgery between different countries of origin. Differences in rates of bariatric surgery were found between some of the socioeconomic characteristics. HRs were higher for individuals with middle educational level, those who were in relationship and had an employment. However, severe obesity seems to rule out socioeconomic differences for bariatric surgery.</p> <p>Conclusions: The results of this thesis suggest that level of neighbourhood deprivation affects the odds of childhood obesity independently of other sociodemographic characteristics. Another conclusion is: although there seem to be variations in rates of bariatric surgery considering different sociodemographic characteristics, severe obesity rules out socioeconomic differences for bariatric surgery. It seems that the Swedish healthcare system has achieved its goal of equal health care for the entire population regarding bariatric surgery.</p>			
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Obesity and bariatric surgery in Sweden

Sociodemographic aspects and
neighbourhood deprivation

Ensieh Memarian



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To Elina and Neo

Contents

Abstract	11
Abbreviations	13
Original papers	14
Introduction	15
Background	16
Quantification of adiposity	16
Pathophysiology of obesity	16
The rise of obesity	18
Obesity- a global health problem	18
Obesity- morbidity and mortality	19
Obesity paradox	19
Childhood obesity	19
Obesity and socioeconomic factors	20
Obesity and neighbourhood deprivation	21
Obesity and immigration	21
Obesity and gender perspective	22
Obesity treatment	23
Surgical treatment of obesity	23
Bariatric surgery and socioeconomic factors	25
Swedish universal healthcare insurance	25
Aims of this thesis	26
Specific aims:	26
Material and Methods	27
Material and Data Sources	27
Study Design	30
Variables Definition	31
Methodology	34

Statistical Analyses	36
Results	38
Main findings	38
Paper I:	39
Paper II:	42
Paper III:	46
Paper IV:	50
Discussion	56
Obesity a major health problem	57
Sociodemography and obesity	57
Sociodemography and bariatric surgery	59
Public health aspects	61
Strengths and limitations	62
Summary in Swedish (Populärvetenskaplig sammanfattning)	64
Delarbete I:	65
Delarbete II:	65
Delarbete III:	66
Delarbete IV:	66
Patientnytta:	67
Acknowledgements	68
References	70

Socioeconomic status is a significant dimension in that children from middle and upper classes are immersed in the academic register virtually from birth.

Encyclopedia of applied psychology, 2004

Abstract

Background: During the last decades, the prevalence of obesity has risen both worldwide and in Sweden, due to lifestyle changes. Obesity is one of the major preventable causes of death in the developed world. Obesity is associated with numerous comorbidities, decreased quality of life and greater overall costs to the healthcare system. Bariatric surgery is considered to be the most effective method of weight loss for severe obesity. Multiple studies have shown that obesity is distributed along a socioeconomic gradient, with higher prevalence rates in low socioeconomic groups.

Objectives: The aim of this thesis was to examine whether there is an association between childhood obesity and neighbourhood deprivation after accounting for sociodemographic characteristics. Another aim of this thesis was to explore whether sociodemographic characteristics, such as income, education, employment and country of origin have an effect on bariatric surgery rates in a country like Sweden, which has a universal healthcare insurance system.

Methods: In paper I, an open cohort of all children age 0-14 years was followed. Data were analysed by multilevel logistic regression, with familial- and individual-level characteristics at the first level and level of neighbourhood deprivation at the second level. In paper II, an open cohort of all individuals aged 20-64 years was followed. Socioeconomic differences were examined using cumulative rates. Hazard ratios (HR) of bariatric surgery were calculated using Cox regression models. In paper III, a closed cohort of all individuals aged 20-64 years was followed. Age standardised cumulative incidence rates (CR) of bariatric surgery were compared between Swedes and immigrants. Cox proportional hazards models were used in univariate and multivariate models. Paper IV was a retrospective cohort study. Data on body mass index (BMI) were collected from the Military Service Conscription Register for men, and from the Medical Birth Register for women. CR of bariatric surgery and Cox proportional hazard models were used to analyse the association between BMI and individual socioeconomic variables.

Results: High neighbourhood deprivation remained significantly associated with higher odds of childhood obesity after adjustment for individual sociodemographic characteristics. The rate of bariatric surgery was almost three times higher for women than men. The number of bariatric surgeries increased substantially after 2005. The dominating bariatric surgical procedure in Sweden was gastric bypass. Immigrants as a group had a lower rate of bariatric surgery compared to Swedes. However, there were large variations in the rate of bariatric surgery between different countries of origin. Differences in rate of bariatric surgery were found between some of the socioeconomic characteristics. HRs were higher for

individuals with middle educational level, those who were in relationship and had an employment. However, severe obesity seems to rule out socioeconomic differences for bariatric surgery.

Conclusions: The results of this thesis suggest that level of neighbourhood deprivation affects the odds of childhood obesity independently of other sociodemographic characteristics. Another conclusion of this thesis is that, although there seem to be variations in rates of bariatric surgery considering different sociodemographic characteristics, severe obesity rules out socioeconomic differences for bariatric surgery. It seems that the Swedish healthcare system has achieved its goal of equal health care for the entire population regarding bariatric surgery.

Abbreviations

BMI	Body mass index
CPF	Center for primary healthcare research
CI	Confidence interval
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CR	Age standardized cumulative incidence rate
DNA	Deoxyribonucleic acid
DXA	Dual-energy X-ray absorption
FTO	Fat mass and obesity-associated gene
HR	Hazard ratio
ICD-10	The International Classification of Diseases 10 th edition
IR	Incidence rate
MRI	Magnetic resonance imaging
NO.	Number
OR	Odds ratio
P	P value
PCOS	Polycystic ovary syndrome
PR	Prevalence ratio
RYGB	Roux-en-Y gastric bypass
SAMS	Small area market statistics
SCB	Statistics Sweden
SD	Standard deviation
SES	Socioeconomic status
WHO	World Health Organization

Original papers

This thesis is based on the following papers which are referred to in the text by their Roman numerals:

- I. Li X, **Memarian E**, Sundquist J, Zöller B, Sundquist K:
Neighbourhood deprivation, individual-level familial and socio-demographic factors and diagnosed childhood obesity: a nationwide multilevel study from Sweden. *Obesity Facts*. 2014;7 (4):253-63*
- II. **Memarian E**, Calling S, Sundquist K, Sundquist J, Li X:
Sociodemographic differences and time trends of bariatric surgery in Sweden 1990-2010. *Obesity Surgery*, 2014 Dec;24 (12):2109-16*
- III. **Memarian E**, Sundquist K, Calling S, Sundquist J, Li X:
Country of origin and bariatric surgery in Sweden during 2001-2010. *Surgery for Obesity and Related Diseases*. 2015, 11(6):1332-41*
- IV. **Memarian E**, Sundquist K, Calling S, Sundquist J, Li X:
Socioeconomic factors, body mass index and bariatric surgery: A Swedish nationwide cohort study. Submitted.

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Introduction

The prevalence of overweight and obesity has risen in children and adults, both globally and in Sweden, during the past decades (1). Obesity is associated with numerous comorbidities, decreased quality of life, greater overall costs to the healthcare system and is one of the leading causes of death globally (1, 2). However, public health strategies have so far demonstrated a limited effect on reducing the obesity prevalence (3), thus making obesity management and prevention a huge challenge.

Conventional weight loss interventions, such as diet and exercise, have also often been ineffective in achieving sustained weight loss especially in severely obese individuals, and as a result have little if any effect on obesity-related comorbidities (4, 5). Weight loss surgery may be an appropriate treatment for severely obese individuals who have not succeeded with weight reduction using conventional weight loss interventions (6, 7).

Multiple studies have shown that obesity is distributed along a socioeconomic gradient with higher prevalence rates among low socioeconomic individuals in both adults and children (8, 9). Neighbourhood environments have also been shown to be an important risk factor for many childhood health problems (10, 11).

Studies have also shown that in countries with private healthcare insurance systems, socioeconomic factors may play a major role in determining which individuals undergo weight loss surgery, despite medical eligibility. Disparities according to race, income, educational level and insurance type exist (12). Surprisingly several studies from countries with publicly funded insurance system (Canada and France) have also shown disparities in socioeconomic status (13, 14). There are notable differences in sociodemographic profiles and prevalence of comorbidities between surgery-eligible subjects and those who actually receive the weight loss surgery. However, in these countries with a publicly funded system, no obvious reason for these disparities are apparent (13, 14).

Thus, investigation of the association between socioeconomic status and access to bariatric surgery, as well as effect of neighbourhood environment on childhood obesity are the main aims of the present thesis.

Background

Quantification of adiposity

Measures such as waist-to-hip ratio (WHR) or skin-fold thickness are sometimes used in clinical settings, despite their relative inaccuracy in quantification of adiposity (15). Some more technically accurate quantification of body fat are underwater weighing, dual-energy X-ray absorption (DXA), computed tomography and Magnetic resonance imaging (MRI), however these techniques are too costly and time consuming for routine care or large-scale studies (16). Body Mass Index (BMI) is the most common measure for estimating obesity (16, 17). BMI is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2).

BMI classification according to the World Health Organization is as follows:

- $<18.5 \text{ kg}/\text{m}^2$, underweight
- $18.5\text{--}24.99 \text{ kg}/\text{m}^2$, normal weight
- $25\text{--}29.99 \text{ kg}/\text{m}^2$, overweight
- $\geq 30 \text{ kg}/\text{m}^2$, obese
 - I. Obese class I $30\text{--}34.99 \text{ kg}/\text{m}^2$
 - II. Obese class II $35\text{--}39.99 \text{ kg}/\text{m}^2$
 - III. Obese class III $\geq 40.00 \text{ kg}/\text{m}^2$

Pathophysiology of obesity

Obesity is a complex disorder that results from interaction between genetics, epigenetics, metagenomics, environment and behavioural factors (18).

Twin studies indicate that genetics contributes to 40-75% of obesity cases (19). Monozygotic twins have a more similar body fat gain compared to dizygotic twins

(19, 20). Adoption studies show that the BMI of adopted children is more correlated to the BMI of their biological parents rather than their adopted parents, which indicates that the energy balance is strongly influenced by genotype (21). A total of 11 genes have been identified which are associated with monogenic obesity (regulated by a single gene) and 227 genetic variants have been associated with polygenic obesity (caused by the combined action of more than one gene). These genes are involved in different biological pathways such as the central nervous system (CNS), food sensing and digesting, insulin signalling and lipid metabolism (18). The first polygenic gene to be identified was the fat mass and obesity-associated gene (FTO), a gene that increases susceptibility to obesity in children and adults. This gene predisposes to type 2 diabetes via an increase in BMI (22).

The genotype can be influenced by biological variations such as sex and age, as well as obesogenic environment and lifestyle. Some studies have shown that the effect of the genes on BMI increases from childhood to early adulthood. This indicates that when the puberty stage advances the effect of genes on BMI increases whereas the effect of environment decreases (23).

Epigenetics is an alteration in gene transcription and expression which results in long-term changes in cellular and biological functions without any changes to DNA sequence. This suggests that nutritional and other environmental exposures in early life can “reprogram” the foetus (24). A study of twins has shown that even if twins were epigenetically similar early in life, they could differ considerably later due to the effect of acquired epigenetic changes (25). It has been shown that children born after maternal weight loss by bariatric surgery have a lower risk of obesity compared to children born before maternal weight loss, thus indicating a strong epigenetic effect early in life and the development of obesity in adulthood (26).

Some studies suggest a diversity of the microbiota in obese compared with slim individuals and that weight loss changes the microbiota (27, 28).

Genes that predispose to obesity affect several organs. The CNS is the main regulator of energy usage and feeding behaviour, and mutation in this region results in impaired appetite regulation and increase in bodyweight. In the digestive tract, mutations in taste receptor genes and digestive enzymes in the mouth are associated with higher BMI. Furthermore, mutations in genes associated with lipid and glucose metabolism could result in obesity. Genes involved in fat distribution and adipogenesis can also result in obesity through changes in energy homeostasis (18).

Obesity is an increase in fat mass that can adversely affect health and reduce life expectancy (29). Adipose tissue releases adipokines, which are inflammatory and

result in diverse effects such as insulin resistance, hyperlipidaemia, hypertension, type 2 diabetes mellitus, atherosclerotic plaque and is a major risk factors for many cancers (30).

The rise of obesity

Worldwide, the prevalence of overweight and obesity combined has risen by 27.5% for adults and 47.1% for children between 1980 and 2013. This increase in obesity prevalence has become an important concern, initially only in high income countries but subsequently even in low- and middle-income countries, especially in cities (31). In a systematic analysis of the global prevalence of obesity and overweight, it was shown that the prevalence of overweight and obesity has risen significantly. However, there are some variations across countries in the levels and trends in overweight and obesity. In developed countries, there is some indication that the increase in obesity, which began in the 1980s, has slowed down over the last few years, whereas the trend continues to increase in the developing world, where almost two third of the world's obese individuals live (31).

The rise of obesity is due to several major societal and environmental changes such as excessive use of energy dense foods, sedentary lifestyles, urbanization and socioeconomic-dependent access to a healthy diet (3, 32).

Obesity- a global health problem

According to the World Health Organization (WHO), the prevalence of obesity (i.e. body mass index $BMI \geq 30 \text{ kg/m}^2$) has been nearly tripled worldwide between 1975 and 2016 (1) . In 2016, more than 1.9 billion adults (39 % of adults) were overweight (i.e. $BMI 25-29 \text{ kg/m}^2$) and 650 million of them (13 % of adults) were obese. Most of the world's population lives in countries where overweight and obesity kills more people than underweight. Obesity is one of the major causes of preventable death in developed countries (33, 34).

According to the Swedish public health authority the percentage of individuals who are obese increased from 11% in 2004 to 15% in 2016 for both men and women. However the total percentages of overweight and obesity in 2016 were higher for men compared to women (57% and 44% respectively) (35).

Obesity- morbidity and mortality

Obesity is associated with numerous co-morbidities such as type 2 diabetes mellitus, hypertension, dyslipidaemia, cardiovascular diseases, sleep apnea, respiratory difficulties, joint and mobility issues, psychological distress, polycystic ovarian syndrome (PCOS), female infertility and certain types of cancer (33, 36, 37). Obesity is correlated to premature death, decreased quality of life, and greater overall costs to the healthcare system due to co-morbidities (2, 38, 39). The majority of deaths caused by overweight and obesity are cardiovascular deaths (40).

Obesity paradox

It is well-known that obesity is associated with a higher risk of cerebrovascular disease, type 2 diabetes, certain cancers and increased mortality at population level (41, 42). Paradoxically, some antidiabetes medications such as insulin and sulfonylureas, which lead to increased weight, are associated with a decreased risk of both micro- and macrovascular complications (43). Similarly, weight gain has been observed after smoking cessation or when β -receptor blocking agents are used as secondary prevention after myocardial infarction. But at the same time the risk for complications decreases. It is also observed that among those patients who have already established coronary artery disease, heart failure and those undergoing percutaneous coronary intervention, obesity appears to be protective (44, 45). Some observational studies have shown that weight loss is associated with an increased mortality risk (46, 47). Nevertheless, higher target BMIs should not be recommended to patients with established cardiovascular disease, since it might lead to unwanted results. It appears that fitness influences the relationship between obesity and clinical prognosis in obesity paradox. Physical inactivity appears to have a greater influence on mortality than high BMI (45, 48).

Childhood obesity

In 2016, an estimated 41 million of preschool-aged children were overweight or obese worldwide, and this prevalence is estimated to rise to 9.1 % by 2020 if current trends are maintained (49). According to the WHO, more than 340 million children and adolescents aged 5-19 were obese or overweight in 2016 (1). The prevalence of overweight and obesity among children and adolescents has risen substantially from just 4% in 1975 to over 18% in 2016 (1). Obesity in childhood

is correlated with higher risk of both obesity in adulthood and other conditions including low self-esteem and obesity related comorbidity (50, 51). Childhood obesity is associated with a higher risk of premature death and disability in adulthood. In addition to future risks, obese children experience breathing difficulties, increased risk of fractures, hypertension, early signs of cardiovascular disease, insulin resistance and psychological effects (1).

Studies show that parental overweight/obesity is associated with the risk of overweight/obesity in children and is an important predictor of obesity in adulthood (52, 53).

Obesity and socioeconomic factors

Socioeconomic status (SES) is widely known as an economic and sociological combined total measure of a person's work experience, economic and social position in relation to others, based on income, education, and occupation. Socioeconomic status is typically divided into three levels: high, middle, and low. Some of the metrics of socioeconomic status are: individual's educational attainment, education of parents, current occupation, individual/household income and wealth (assets, capital) (54). Low SES has been shown to be a strong predictor of a range of physical and mental health problems (55). Demographic is individual characteristics such as age, sex, marital status, place of residence and ethnicity.

A review of 144 studies by Sobal and Stunkard (1989) demonstrated that in developed countries, obesity is inversely associated with socioeconomic status (SES) among women, whereas relationships for men and children were inconsistent. However, in developing countries, a strong direct relationship exists between SES and obesity among men, women and children (56). A recent meta-analysis (2017) of Newton et al. showed that mean BMI was higher among individuals with lower SES compared with those with higher SES (8). A systematic review of childhood obesity showed that over half of the studies indicated increasing prevalence of obesity among low SES children and adolescents (9).

Those with a low level of education have two times higher prevalence of obesity than those with a high level of education, in both men and women (57). Obesity may also adversely affect socioeconomic status and even decrease the likelihood of being employed (56).

Higher stress levels may cause weight gain due to several different reasons such as increase in food intake, particularly energy-dense, palatable foods (i.e. comfort foods) (58-60). Stress can also lead to reduced physical activity (61, 62). Stress

increases the secretion of glucocorticoids, which in turn leads to increased central adiposity (63, 64). There is evidence suggesting a stronger association between stress and comfort eating in women than men (64, 65). However, why women are more susceptible to stress-related weight gain compared with men is still unclear.

Obesity and neighbourhood deprivation

Several studies on neighbourhood effects on health have shown that individuals living in highly disadvantaged neighbourhood environments have increased mortality and other health problems, independent of individual covariates (66-68).

Although low individual SES may influence the risk of obesity in multiple ways, it does not fully explain disparities in obesity risk that exist between different population groups (69, 70). For this reason, efforts have been made to study whether the socioeconomic environment is associated with the risk of childhood obesity. Studies have shown that neighbourhood environments are an important independent risk factor for many childhood health problems (10, 11). However, no previous studies have investigated whether neighbourhood deprivation is associated with diagnosed childhood obesity after accounting for family and individual factors.

Obesity and immigration

There has been an increase in immigration to Sweden during the last decades. In 1990, 11.3% of the total population were foreign born whereas in 2016 the percentage was 17.9% (71). Immigrants in Sweden, similar to many other Western European countries, are very heterogeneous. This is due to reasons for immigration, age at immigration, the time of immigration and earlier educational level, social class and health status. During the 1950s and 1960s, the majority of immigrants came from Europe to meet the increasing need for industrial labour, whereas immigrants after the 1970s were mainly political refugees (72). In general, immigrants have more health problems compared to the majority of the population (55, 72) even though newly arrived migrants tend to be healthier than the host population- a phenomenon called *the healthy migrant effect* (73, 74) due to positive selection bias. The healthy migrant effect subsides with acculturation, some of the host culture might promote more unhealthy weight gain than some heritage culture (75). Decline of the psychosocial status (76) and changes in lifestyle might be possible explanations. Changes in lifestyle may include unhealthy dietary patterns and sedentary habits, which might explain why many

immigrants in Sweden have higher rates of obesity (77-79). Two Swedish studies have shown that individuals who migrated from developing countries to reside at developed countries appear to be more prone to overweight and obesity than their host country counterparts (80, 81). The weight gain among migrants appears to rise significantly over 10-15 years after migration (82-84). However, this weight gain is not the same across all migrant groups. Differences may appear due to actual diversity between groups such as country of origin, gender and age at the time of migration (85, 86). Thus, the relationship between migration and health-related factors such as weight appears to be affected by a wide variety of other circumstances.

The ethnic-dependent pattern of obesity prevalence could be explained by specific lifestyles or environmental factors. However, studies have shown an important influence of genes (17). Beauty and weight ideals differ in different cultures. Some ethnic groups have a positive perception of larger body size (87).

Obesity and gender perspective

According to a British study that investigated the global prevalence of obesity and gender inequality, obesity was more common in females than males (three obese women for every two obese men) in almost all the countries investigated with exception for a few countries, e.g. Scandinavian countries (88).

Despite the fact that men had a higher percentage of overweight and obesity in Sweden, women experienced more difficulties due to obesity (28% women and 22% men, 2015) (35). A British cross-sectional study has shown that overweight women were at an increased risk of depression with a dose response relationship across the overweight and that relationship between adiposity and depression was stronger in women than in men (89). An American study showed that the number of stressful life events was positively and significantly associated with increases in BMI in women but not men (90). Another American study showed that increased association with obesity and the number of all-cause hospitalizations was larger in women than men (91).

Moreover, women report a higher dissatisfaction regarding their weight and have a preference toward smaller ideal body size regardless of ethnicity (92).

Obesity treatment

Lifestyle modification such as diet, exercise and behavioural changes, are most often recommended for obese individuals, including those that are severely obese (BMI ≥ 40 kg/m²) (6, 7, 93). A systematic review of the literature showed that reducing the proportion of energy intake from total fat leads to lower body weight (by 1.6 kg) and BMI (94). However, conventional methods of weight loss have often been ineffective in achieving a sustained weight loss in morbidly obese individuals. A Swedish qualitative study showed that maintenance after weight reduction was difficult and considered to be “*a constant struggle*” (95). The best weight loss programs have only maintained a sustained excess body weight reduction of 10%. This small reduction in excess body weight has little if any effect on obesity-related comorbidities in the morbidly obese population (4, 5, 96). A large scaled intervention study, Look AHEAD, was stopped early due to ineffectiveness when the results indicated that intensive lifestyle intervention focusing on weight loss did not reduce the rate of cardiovascular events in overweight or obese adults with type 2 diabetes (97). A meta-analysis focusing on effect of weight loss interventions for individuals with type 2 diabetes who were overweight or obese found that most of the interventions did not lead to significant weight loss or improvement of metabolic outcome (98). Several studies have shown that a long period of insufficient diabetes control leads to future diabetic complications even if good control is achieved later, this phenomenon is called *metabolic memory* (99, 100), indicating the importance of early intensive metabolic controls.

Pharmacological treatment of obesity consists of several substances: Orlistat (Xenical ®), Lorcaserin, naltrexone-bupropion (Mysimba ®), phentermine-topiramate, and liraglutide (Saxenda ®), were all substances associated with achieving at least 5% weight loss after 52 weeks, compared with placebo (80). Indications for pharmacological treatment are BMI ≥ 30 kg/m² or BMI ≥ 27 kg/m² and an obesity-related comorbidity.

Weight loss surgery is an alternative treatment in patients, who are refractory to nonsurgical treatments, who have morbid obesity (BMI ≥ 40 kg/m²) or moderate obesity (BMI ≥ 35 kg/m²) plus a major obesity-related comorbidity (6, 7).

Surgical treatment of obesity

Weight loss surgery also known as bariatric surgery (obesity surgery) includes a variety of surgical procedures performed on obese individuals. Some subtypes of bariatric surgery are gastropasty, gastric bypass (Roux-en-Y gastric

bypass/RYGB) and gastric banding. Weight loss is achieved by reducing the size of the stomach as in gastric banding and/or by inducing malabsorption and calorie restriction as in gastric bypass. Currently, the most commonly performed bariatric surgical procedure in Sweden and worldwide is Roux-en-Y gastric bypass (101, 102). Remarkably, most type 2 diabetes patients who undergo RYGB, experience remission and improved glycaemia long before weight loss occurs (103). The exact mechanism for these improvements are unknown but it appears that RYGB induces powerful and immediate effects, within hours after surgery, on insulin and incretin response to food, independently of changes caused by calorie restriction(104). Incretins are hormones that are released from the gut after ingestion of food (105). Incretins functions are to inhibit gastric emptying and decrease food intakes (106). They also slow the production of endogenous glucose (107). All of these actions help to reduce the blood glucose in type 2 diabetes patients. It has also been shown that incretins stimulate β -cell proliferation (108). A Swedish study showed that gastric bypass improves β -cell function and β -cell mass (109). The primary function of β -cells of the pancreas is to store and release insulin.



Studies show that bariatric surgery reduces weight by 33% at early postoperative years (110) and 14-25% 10 years postoperative (111). Bariatric surgery results in remission of obesity comorbidities at a rate of 66-88% (112, 113). A significant

reduction in 15-years mortality is also achieved in comparison to nonsurgical-matched controls (111). Quality of life, self-esteem and employment status are also improved after bariatric surgery (114). Bariatric surgery leads to reduction of sick leave and disability pension, compared to controls (115). Surgical costs appear to be recouped within 2-4 years (116, 117).

According to Sveus (Sveus is a research collaboration where seven Swedish regions develop systems for value-based monitoring of healthcare. The overarching aim of Sveus is to stimulate value-driven, efficient and patient-centered healthcare) weight loss is not the primary goal of bariatric surgery, it is rather prevention and management of obesity related comorbidities and enhancement of quality of life (118).

Bariatric surgery and socioeconomic factors

Many studies have shown significant disparities in socioeconomic characteristics between the morbidly obese population and the subgroup that actually receives bariatric surgery (12, 119, 120). In countries with a private healthcare system, some of these variations might be explained by financial inequalities. In these countries significant disparities, which are associated with ethnicity, income, educational level and insurance type, have been shown (12). However, in countries with a publicly funded system, no obvious reasons for these disparities are apparent (13, 14). Few studies have systematically analysed the factors that cause the variation in receiving bariatric surgery. It is generally assumed that much of the variation is explained by socioeconomic barriers.

Swedish universal healthcare insurance

Sweden has a universal healthcare insurance system. According to Swedish law, the tax-financed healthcare service should be provided on equal terms for the entire population and those who are in the greatest need of healthcare should be prioritised (121). This means that patients' financial resources should not be a barrier for receiving bariatric surgery.

Aims of this thesis

The general aim of this thesis was to investigate the associations between socioeconomic factors and obesity in children and adults with particular focus on the effect of neighbourhood deprivation on childhood obesity, as well as association of socioeconomic variables and access to bariatric surgery.

Specific aims:

- To determine whether the effect of neighbourhood deprivation on risk of childhood obesity remains significant even after adjusting for family- and individual-level sociodemographic factors, and to determine whether the level of neighbourhood deprivation has a differential effect on risk of childhood obesity across subgroups of families and individuals (effect modification). (paper I)
- To investigate whether sociodemographic characteristics have an impact on the rate of bariatric surgery and to study the changes in the rate and type of surgical method of bariatric surgery over time. (paper II)
- To explore whether there is a difference in access to bariatric surgery in Sweden for Swedish born and those with another country of origin and if this hypothesised difference remains after adjustment for socioeconomic factors. (paper III)
- To study the possible differences in the access to bariatric surgery for different socioeconomic groups after accounting for BMI. (paper IV)

Material and Methods

Material and Data Sources

We used national registers that contain information on the entire population in Sweden for a period of 40 years. These registers include the total Population Register, the Multi-Generation Register, the Hospital Discharge Register and the Outpatient Register. All linkages were performed by the use of a personal identification number that is assigned to each permanent resident in Sweden for their lifetime. This number was replaced by a serial number for each person to provide anonymity. These registers were used in papers I-IV.

The Population Register

The Population Register contains data on age, gender, marital status, income, education, and country of birth and data were released to us by Statistics Sweden (SCB), the Swedish Government-owned Statistics Bureau (122). The register includes annual data on, for example, marriages, divorces, immigration to and emigration from Sweden. This register was used in papers I-IV.

The Immigration Register

The Immigration Register contains data on country of birth, dates of immigration to and/or emigration from Sweden. Data from this register were released to CPF by SCB. This register was used in papers I-IV.

The Multi-Generation Register

The Swedish Multi-Generation Register is a family register, and initially included all individuals born in Sweden since 1947, linked to their biological parents (123). Since 1961, the Multi-Generation Register is made up of persons who have been registered in Sweden at some point in time and those who were born in 1932 or later. Data from this register was made available to CPF by SCB. This register was used in paper I.

The Cause of Death Register

The Swedish Cause of Death Register includes annually updated data on all deaths and causes of death of persons that were registered in Sweden at the time of death (124). This register uses available data from 1961 onwards and is based on death certificates. The diagnoses in this register are based on the international classification of diseases (ICD). Data from this register were released to CPF by the National Board of Health and Welfare. This register was used in papers I-IV.

The Hospital Discharge Register

The Swedish National Hospital Discharge Register, also called Inpatient Register, is partly available with data from 1964 onwards and has national coverage from 1987 (125, 126). It includes individual information on date of admission and discharge and diagnoses (according to the International Classification of Diseases (ICD)). The register is based on ICD codes. Different versions of the ICD have been used in Sweden over time. For example, ICD 9 was used between 1987 and 1996 and ICD 10 from 1997 and onwards). Data from this register were released to CPF by the National Board of Health and Welfare. This register was used in papers I-IV.

The Outpatient Register

The Swedish National Outpatient Register is available with data from 2001 onwards (126). Data from private and public outpatient clinics are included but the register does not cover data from primary care. Data from this register were released to CPF by the National Board of Health and Welfare. This register was used in papers I-IV.

The Geographic Register

The home addresses of all Swedish adults have been geocoded to small geographic units that have boundaries defined by homogeneous types of buildings. The boundaries also match the municipality borders. These neighbourhood areas, called small area market statistics (SAMS), have an average of 1000–2000 people and were used as proxies for neighbourhoods, as has been done in previous research (127-130). Adults whose addresses were not able to be geocoded to a SAMS were excluded as well as SAMS with fewer than 50 people aged 25–64. SAMS were created by SCB and are available for use at CPF. This register was used in paper I.

The Military Conscription Register

The military service conscription examination involves a structured, standard medical assessment of physical and mental health and intelligence since 1969 (131, 132). During 1969-2010 military conscription was mandatory for all Swedish men, and participation was enforced by law, although individuals with severe handicaps or chronic diseases, and non-Swedish citizens would be exempt from conscription. Hence, practically the total male population went through the 2-day test protocol. However, the data completeness decreased slightly in the late 1990s after a lag period of ~10 years post-cold war. After accounting for deaths and emigration before 20 years of age, and non-Swedish origin, the overall participation of the birth cohorts from 1951 to 1987 was 88%. This register is owned by the Swedish Defence Recruitment Agency and the Swedish National Archives. This register was used in paper IV.

The Medical Birth Register

The Swedish Medical Birth Register, which is a register of all pregnancies, prenatal care and birth records for all mothers and children in Sweden since 1973 (133). On average, 110,000 pregnancies and/or new born infants are registered per year in Sweden. This register covers 99% of all births in Sweden from 1973 onwards and includes prospectively collected information about complications during pregnancy and delivery. In Sweden, prenatal care is standardised and free of charge. Registration for prenatal care generally occurs at 8-12 gestational weeks. Prenatal care includes visits every four weeks up to 24 gestational weeks, then every two weeks to 36 weeks, and weekly thereafter. At each visit, blood pressure is measured and urine is checked for protein using a dipstick. More than 95% of the pregnant population attends antenatal care before the 15th gestational week, and 90% of pregnant women make at least nine visits to antenatal care. Data from this register were released to CPF by the National Board of Health and Welfare. This register was used in paper IV.

Study Design

Table 1
Overview of Studies

Paper	I	II	III	IV
Data source	Population Register Immigration Register Multi-generation Register Hospital Discharge Register Out-Patient Register Cause of Death Register Geographic Register	Population Register Immigration Register Hospital Discharge Register Out-Patient Register Cause of Death Register	Population Register Immigration Register Hospital Discharge Register Out-Patient Register Cause of Death Register	Population Register Immigration Register Hospital Discharge Register Out-Patient Register Cause of Death Register Military Conscription Register Medical Birth Register
Sample size	Total of 948,062 children, 10,799 diagnosed with childhood obesity	Total of 6,082,206 men and 6,092,368 women, 22,198 (5,258 men and 16,940 women) with bariatric surgery	Total of 5,101,303 individuals, 12,791 Swedes, 2060 immigrants with bariatric surgery	Total of 814,703 women and 787,027 men. 7,433 women 1,961 men with bariatric surgery
Outcome variable	Diagnosed Childhood Obesity	Bariatric Surgery	Bariatric Surgery	Bariatric Surgery
Predictor variable	Neighbourhood Deprivation	Individual SES variables	Country of Origin	Individual SES variables and BMI
Study design	Open Cohort	Open Cohort	Closed Cohort	Retrospective closed Cohort
Methods	Cumulative rate, Multilevel logistic regression	Age standardised Incidence rates, age standardised cumulative incidence rate, Hazard ratio, Cox proportional Hazard models	Age standardised Cumulative incidence rate, Hazard ratio, Cox proportional Hazard models	Age standardised Cumulative incidence rate, hazard ratio, Cox proportional Hazard models Interaction tests
Follow-up	2000-2010	1990-2010 divided in two periods 1990-2005 2006-2010	2001-2010 divided in two periods 2001-2005 2006-2010	2005-2012

Variables Definition

Outcome variables

Diagnosed Childhood Obesity (paper I): The outcome variable in paper I was a hospital or out-patient diagnosis of childhood obesity (age at diagnosis 0-14) during the study period. The International Classification of Diseases 10 (ICD-10) codes E65 (localised adiposity) and E66 (adiposity and overweight) were used.

Bariatric surgery (paper II-IV): The Swedish Classification of Operations and Major Procedures from the Hospital Discharge Register were used to identify patients who underwent bariatric surgery: operation codes 4751-4753 before 1997, or codes JDF00-JDF01, JDF10-JDF11, and JDF20-JDF21 from 1997 and onwards. The subtypes of bariatric surgery were defined as gastroplasty (codes 4751 and JDF00-JDF01), gastric bypass (codes 4752 and JDF10-JDF11), and gastric banding (codes 4753 and JDF20-JDF21).

Predictor Variables:

Neighbourhood-Level Deprivation (paper I): The home addresses of all Swedish individuals have been geocoded to small geographic units with boundaries defined by homogeneous types of buildings. These neighbourhood areas, called small area market statistics or SAMS, each contain an average of 1,000 residents and were created by the Swedish Government-owned statistics bureau Statistics Sweden. SAMS were used as proxies for neighbourhoods, as they were in previous research studies. Neighbourhood of residence is determined annually using the National Land Survey of Sweden register.

A summary index was calculated to characterise neighbourhood-level deprivation. The neighbourhood index was based on information about female and male residents aged 20 to 64 because this age group represents those who are among the most socioeconomically active in the population (i.e. a population group that has a stronger impact on the socioeconomic structure in the neighbourhood than children, younger women and men, and retirees do). The neighbourhood index was based on four items: low education level (<10 years of formal education), low income (income from all sources, including interest and dividends, that is <50% of the median individual income), unemployment (excluding full-time students, those completing military service, and early retirees), and in receipt of social welfare. The index of the year 2000 was used to categorise neighbourhood deprivation as low (more than one standard deviation (SD) below the mean), moderate (within one SD of the mean), and high (more than one SD above the mean) (130).

Country of Origin (paper III): was defined as Swedish-born and foreign-born, the latter subdivided further as described below.

The dataset included people from 64 countries and regions of birth and 12 regions (Nordic countries, Southern Europe, Western Europe, Eastern Europe, Baltic countries, Central Europe, Africa, North America, Latin America, Asia, Russia and countries belonging to the southern part of the former Soviet Union, and other countries). Countries/country groups with more than 10 cases of obesity surgery were analysed separately. These countries included Denmark, Finland, Norway, Greece, Italy, other Southern European countries, Great Britain/Ireland, Germany, Bosnia, former Yugoslavia, Romania, Poland, Hungary, Chile, Turkey, Lebanon, Iran and Iraq.

BMI (paper IV): BMI was categorised as follow

1. BMI <25 kg/m² (underweight and normal weight)
2. BMI 25-29.99 kg/m² (overweight)
3. BMI 30-39.99 kg/m² (obese class I and II)
4. BMI ≥ 40 kg/m² (obese class III/morbidly obese)

Individual variables

Gender: Male or female

Age:

- In paper I: child age ranged from 0 to 14 years and was divided into three categories: 0-4, 5-9, and 10-14-years.
- Paper II and III: Age was categorized as 20-29, 30-39, 40-49, or 50-64 years.
- Paper IV: For men, 98% were included who were aged between 18 and 27 years at the time of conscription. For women, 98% were included who were aged between 18-39 years (i.e. women of childbearing ages).

Family income: Family income was calculated as annual family income divided by the number of members in the family. The final variable was calculated as empirical quartiles from the distribution (134) and classified as low, middle-low, middle-high, and high in paper I-III. Since there was an overlap between the middle-low and middle-high income groups in papers II and III, we decided to

combine these two groups in paper IV, to create one middle-income group, which consisted of 50% of the population.

Marital Status: In paper I, marital status was defined according to maternal marital status, categorized as (1) married/cohabitating or (2) never married, widowed, or divorced. In papers II-IV the same categories were used for all the individuals.

Employment (paper II-IV): was defined as yes or no.

Educational attainment (papers I, II, and IV): Educational attainment was categorised in paper I according to maternal and paternal educational level and in papers II and IV according to all individuals. In papers I and II the categories are as follow:

- Low: completion of compulsory school or less (≤ 9 years)
- Middle: practical high school or some theoretical high school (10–11 years)
- High: completion of theoretical high school and/or college (≥ 12 years).

In paper IV high educational attainment is defined as attending college and/or university (>12 years).

In paper III information about earlier educational attainment of many immigrants was missing.

Maternal and paternal country of birth (paper I): was categorised as Sweden, Western country (Western Europe, USA, Canada, Oceania), and other.

Maternal urban/rural status (paper I): this variable was included because access to preventive antenatal care may vary according to urban/rural status. Mothers were classified as living in a large city, a middle-sized town, or a small town/rural area.

Mobility (paper I): children were classified as having “not moved” or having “moved” to another neighbourhood with the same or a different level of deprivation within five years.

Maternal and paternal age at childbirth (paper I): maternal age at childbirth was categorized as <20 , 20-24, 25-29, 30-34, 35-39, 40-44, and ≥ 45 years) and paternal age at childbirth was categorized as <20 , 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, and ≥ 50 years.

Maternal/paternal and individual hospitalisations (paper I): were defined as the first diagnosis during the follow-up period of: 1) diabetes, 2) chronic obstructive pulmonary disease (COPD), and 3) alcoholism and related liver disease.

Family history of hospitalisation of obesity (paper I): Because obesity is known to cluster in families, children were classified according to whether or not they had a family history (parents or siblings) of hospitalisation of obesity.

Methodology

Paper I

The study was an open cohort of all children aged 0-14 years old. Follow-up period was January 1, 2000 until December 31, 2010. Childhood residential locations were geocoded and classified according to neighbourhood deprivation. Data were analysed by multilevel logistic regression, with family- and individual-level characteristics at the first level and level of neighbourhood deprivation at the second level. The total study population was 948,062 children.

Paper II

The study was an open cohort of individuals aged 20-64 years. Follow-up period was January 1, 1990 until December 31, 2010. Socioeconomic differences were examined, using cumulative rates, during two periods, i.e. 1990-2005 and 2006-2010 since there was a large increase in the number of surgeries during the second period. HRs of bariatric surgery were calculated in these two periods using Cox regression models. A total of 12,174,574 individuals (6,082,206 men and 6,092,368 women) were included in the study during the follow-up period.

Paper III

The follow-up period started on January 1, 2001 and proceeded until the first hospitalisation for bariatric surgery, death, emigration or the end of the study period on December 31, 2010. Further analyses were done in two periods separately, i.e., 2001-2005 and 2006-2010, as there was a large increase in the number of surgeries during the second period. Since the analyses were done as closed cohorts, the total number of operated cases for the period 2001-2010 was not the same as the sum of the number of cases for 2001-2005 and 2006-2010. The study population included 4,379,014 Swedish born and 722,289 individuals with other country of origin during the follow up period.

Paper IV

The study was a retrospective cohort. The total population was 814,703 women (Medical Birth register) and 787,027 men (Military Service Conscription Register). Individuals whose BMI was measured during 1985-2010 were included. Follow-up period was January 1, 2005 until December 31, 2012. Men who were 18-27 years old at the time of BMI measurement at conscription and women who were 18-39 years old at the time of BMI measurement at mother healthcare service were included. The birth years were 1958-1989 for men and 1950-1989 for women.

Statistical Analyses

Specific statistical analysis for paper I

The age-standardized cumulative rate (per 100) of obesity was calculated for the total study population and for each subgroup after assessment of neighbourhood of residence for children. Multilevel logistic regression models were used to estimate odds ratios (ORs). The analyses were performed using MLwiN version 2.27. To determine the crude risk of childhood obesity by level of neighbourhood deprivation, a model that included only neighbourhood-level deprivation was calculated (model 1). Next, a model that included neighbourhood-level deprivation and sex, age and the family and individual-level sociodemographic variables, added simultaneously to the model, was calculated (Aim 1). To determine whether the effects of neighbourhood-level deprivation on childhood obesity differed across the sociodemographic variables, a full model for cross-level interactions between the family- and individual-level sociodemographic variables and neighbourhood-level deprivation was tested (Aim 2).

Random effects: The between-neighbourhood variance was estimated both with and without a random intercept. It was regarded to be significant if it was more than 1.96 times the size of the standard error, in accordance with the precedent set in previous studies (135-137).

Specific statistical analysis for paper II

Age-standardized Incidence rates (IR) per 100,000 person-years for bariatric surgery were calculated for all individuals during the follow-up period.

Hazard ratios (HRs) for bariatric surgery were performed separately for the periods 1990 to 2005 and 2006 to 2010. The rationale for dividing the entire follow-up period into two unequal periods was that there was a large increase in the number of performed bariatric surgery procedures from 2006 onwards.

The associations between the individual variables and the bariatric surgery were analysed with Cox regression models. Cox proportional hazard models are used to study the association between certain variables and the time it takes for a specified event to happen, in this case the first event of bariatric surgery. First, a univariate Cox regression was performed for each variable. Next, a multivariate Cox regression model including all variables was calculated.

All analyses were performed using the SAS version 9.2 (SAS Institute, Cary, NC, USA) (138).

Specific statistical analysis for paper III

Age-standardized cumulative incidence rates (CR) of bariatric surgery were compared between Swedes and immigrants considering individual variables. Age was standardized according to the age in the study population. The associations between the individual variables and bariatric surgery were analysed with Cox proportional hazards models. Firstly, univariate Cox regression was performed for each variable. Secondly, a multivariate Cox regression model including all variables was calculated. Separate analyses were performed for the periods 2001 to 2005 and 2006 to 2010.

All analyses were performed using the SAS version 9.2 (SAS Institute, Cary, NC, USA) (138).

Specific statistical analysis for paper IV

Age-standardised cumulative incidence rates (CR) of bariatric surgery were compared between different BMI groups considering the other individual variables. Age was standardised according to the age in the study population.

The associations between the individual variables and bariatric surgery were analysed with Cox proportional hazards models. Both a univariate and a multivariate Cox regression model including all variables were calculated.

Interaction tests were performed in order to examine whether the association between BMI and surgery was affected by any of the individual characteristics.

All statistical analyses were performed using STATA version 14.1.

Ethical considerations

All the studies were approved by the Ethics Committee at Lund University

Results

Main findings

- Incidence of diagnosed childhood obesity increased with increasing levels of neighbourhood deprivation independently of familial and individual sociodemographic characteristics. The effect of high neighbourhood deprivation was strongest on odds of diagnosed childhood obesity for some subgroups of families and individuals, particularly for families with a history of obesity, children with hospitalisation for diabetes, and children whose mothers were hospitalised for diabetes. **(paper I)**
- The rate of bariatric surgery was highest for individuals with intermediate income, intermediate educational level, those married and those who had an employment. Hazard ratio of bariatric surgery was lowest for low family income during 1990-2005. There was a substantial increase in bariatric surgery after 2005. The dominating surgical method through the whole period was gastric bypass. **(paper II)**
- The lowest rate for bariatric surgery was among male immigrants. Immigrants as a group had lower CR and HR for bariatric surgery compared to Swedes, during 2006-2010. The largest difference in CR of bariatric surgery between Swedes and immigrants was among those with no employment and low-income. When considering different country of origin per se, immigrants from Chile and Lebanon had much higher HR compared to Swedes and immigrants from Bosnia had the lowest HR compared to Swedes. **(paper III)**
- HR for bariatric surgery was higher for those with high family income, middle educational level in men, and for low/middle family income, middle educational level in women. All individuals who were married and had an employment had a higher HR. For all the individuals with BMI ≥ 40 kg/m², there was no significant difference in HR for different individual characteristics except for middle education in women that showed a higher HR. **(paper IV)**
- Rate of surgery for females were almost three times higher compared to males. **(paper II-IV)**

Paper I:

Neighbourhood deprivation, individual-level familial and socio-demographic factors and diagnosed childhood obesity

The study population was 948,062 children, of which 20% lived in low-, 62% in moderate- and 18% in high-deprivation neighbourhoods. A total of 10,799 children were diagnosed with obesity. Cumulative rates (per 100) of childhood obesity increased from 0.6 in neighbourhoods with low deprivation to 1.2 with moderate deprivation and 1.6 with high deprivation. A similar pattern of higher rates of diagnosed obesity was observed with increasing neighbourhood deprivation across all family- and individual-level socio-demographic categories (data not shown in tables).

As shown in table 2, high neighbourhood-level deprivation remains significantly associated with the odds of diagnosed childhood obesity after adjustment for all family- and individual variables, compared to low-deprivation neighbourhood (OR 1.70, 95% CI 1.55-1.87; $p < 0.001$). The odds of diagnosed childhood obesity were highest in children in the following subgroups respectively: family history of obesity, the child hospitalised for diabetes, maternal hospitalisation for diabetes, low paternal and maternal educational level, paternal hospitalisation for chronic lower respiratory disease and diabetes, paternal and maternal middle educational level, maternal hospitalisation for chronic respiratory disease, maternal and paternal high age at child birth.

There were significant differences in diagnosed childhood obesity between neighbourhoods after accounting for neighbourhood deprivation and the individual-level variables. Neighbourhood deprivation explained 22% of the between-neighbourhood variances in the null model. After inclusion of the familial- and individual-level variables, the explained variance was 44%.

Table 2:
OR and 95% CI for diagnosed childhood obesity; Results of multi-level logistic regression models

	Model 1			Model 2			Model 3			Model 4			P-value
	OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		
Neighborhood-level variable (ref. Low)													
- Moderate	1.84	1.70 2.00		1.85	1.70 2.00		1.56	1.44 1.69		1.51	1.39 1.63		<0.001
- High	2.44	2.22 2.68		2.43	2.21 2.67		1.80	1.64 1.99		1.70	1.55 1.87		<0.001
Family income (ref. High income)													
- Middle-high income							1.07	1.01 1.14		1.05	0.99 1.12		0.110
- Middle-low income							1.15	1.09 1.22		1.10	1.03 1.17		0.002
- Low income							1.04	0.97 1.10		0.97	0.91 1.03		0.368
Marital status (ref. Married/co-habiting)													
- Never married, widowed, or divorced							1.16	1.11 1.21		1.15	1.11 1.20		<0.001
Maternal education attainment (ref. ≥ 12 years)													
- ≤ 9 years							1.67	1.57 1.78		1.55	1.45 1.65		<0.001
- 10–11 years							1.58	1.49 1.67		1.49	1.41 1.58		<0.001
Paternal education attainment (ref. ≥ 12 years)													
- ≤ 9 years							1.66	1.56 1.77		1.58	1.48 1.68		<0.001
- 10–11 years							1.57	1.48 1.67		1.50	1.42 1.60		<0.001
Maternal age at child birth (ref. <30 years)													
- 30-39							1.14	1.09 1.20		1.15	1.09 1.20		<0.001

-	≥ 40									1.29	1.14	1.45	1.30	1.15	1.47	<0.001
Paternal age at child birth (ref. ~30 years)																
-	30-39									1.05	1.00	1.10	1.04	1.00	1.10	0.072
-	≥ 40									1.32	1.23	1.42	1.26	1.17	1.36	<0.001
Maternal hospitalisation of diabetes (ref. No)																
Maternal hospitalisation of chronic lower respiratory disease (ref. No)																
Maternal hospitalisation of alcoholisms and related liver disease (ref. No)																
Paternal hospitalisation of diabetes (ref. No)																
Paternal hospitalisation of chronic lower respiratory disease (ref. No)																
Paternal hospitalisation of alcoholisms and related liver disease (ref. No)																
Hospitalisation of diabetes (ref. No)																
Family history of obesity (ref. Without family history)																
Variance (S.E.)		0.355 (0.018)								0.319 (0.017)			0.253 (0.015)			
Explained variance (%)		22								30			44			
Intra class correlation (ICC)*		0.097								0.088			0.071			

*ICC is, the intra-neighbourhood correlation—in order to estimate to what extent the individual propensity for childhood obesity for individuals within the same SAMS was similar compared with individuals in other SAMS areas. The ICC expresses the proportion of the total variance that is at the neighbourhood level.

Paper II:

Sociodemographic differences and time trends of bariatric surgery in Sweden 1990-2010

A total of 22,198 individuals (5,258 men 23.7% and 16,940 women, 76.3%) underwent bariatric surgery (data not shown in tables).

As shown in table 3, individuals who were married/cohabiting, had intermediate-low income or intermediate educational level had higher rates for surgery in both periods. The cumulative rates were higher for employed individuals during the first period whereas it was equal for both employed and unemployed individuals during the second period.

Table 3
Population, bariatric surgery events, and age-adjusted cumulative rates for bariatric surgery (per 1,000 individuals) by individual characteristics, closed cohort

	Period 1990-2005						Period 2006-2010					
	Population	Events	Rate	95 % CI	Population	Events	Rate	95 % CI				
Total population	5517045	8350	1.51	1.48	1.55	6061363	12533	2.07	2.03	2.10		
Gender												
- Men	2804513	1903	0.68	0.65	0.71	3090682	3125	1.01	0.98	1.05		
- Women	2712532	6447	2.38	2.32	2.43	2970681	9408	3.17	3.10	3.23		
Family income (quartiles)												
- Low	1332555	1543	1.02	0.97	1.07	1517062	2535	1.51	1.45	1.57		
- Intermediate-low	1408640	2872	1.91	1.84	1.98	1514053	4678	3.02	2.93	3.10		
- Intermediate-high	1380609	2260	1.70	1.63	1.77	1515775	3397	2.24	2.17	2.32		
- High	1395241	1675	1.31	1.25	1.37	1514473	1923	1.31	1.25	1.36		
Marital status												
- Married/cohabiting	2637039	3938	1.97	1.91	2.03	2s300169	5022	2.52	2.45	2.59		
- Never married, widowed/divorced	2880006	4412	1.42	1.38	1.46	3761194	7511	1.99	1.94	2.03		
Educational attainment												
- Low	2149491	2860	1.52	1.47	1.58	1652415	2434	1.56	1.49	1.62		
- Intermediate	1672815	3969	2.20	2.14	2.27	1422141	4729	3.56	3.46	3.66		
- High	1694739	1521	0.86	0.81	0.90	2986807	5370	1.76	1.71	1.80		
Employment status												
- Employment	4160163	6889	1.64	1.60	1.68	4108665	8698	2.08	2.03	2.12		
- Unemployment	1356882	1461	1.13	1.07	1.19	1952698	3835	2.08	2.02	2.15		

Table 4
Hazard ratios (HR) of bariatric surgery by individual characteristics, Cox regression analysis, adjusted for covariates.

	Period 1990-2005						Period 2006-2010					
	Univariate model		Multivariate model		Univariate model		Multivariate model		Univariate model		Multivariate model	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Gender												
- Men	1.00		1.00		1.00		1.00		1.00		1.00	
- Women	3.45	3.28 3.63	3.49	3.32 3.68	3.11	2.99 3.24	3.08	2.95 3.21				
Family income (quartiles)												
- Low	1.08	1.01 1.16	0.65	0.60 0.70	1.49	1.40 1.58	1.32	1.24 1.41				
- Intermediate-low	1.69	1.59 1.80	1.01	0.95 1.08	2.44	2.31 2.57	1.41	1.33 1.50				
- Intermediate-high	1.36	1.28 1.45	0.97	0.91 1.04	1.77	1.67 1.87	1.27	1.20 1.36				
- High	1.00		1.00		1.00		1.00		1.00		1.00	
Marital status												
- Married/cohabiting	1.00		1.00		1.00		1.00		1.00		1.00	
- Never married, Widowed, or divorced	1.08	1.04 1.13	0.91	0.87 0.96	0.96	0.92 0.99	1.11	1.07 1.15				
Educational attainment												
- Low	1.60	1.50 1.70	2.38	2.23 2.54	0.91	0.87 0.95	1.67	1.59 1.76				
- Intermediate	2.62	2.47 2.78	2.52	2.37 2.68	1.84	1.77 1.92	2.01	1.93 2.10				
- High	1.00		1.00		1.00		1.00		1.00		1.00	
Employment status												
- Employment	1.00		1.00		1.00		1.00		1.00		1.00	
- Unemployment	0.76	0.71 0.80	0.88	0.82 0.94	1.03	0.99 1.07	1.37	1.31 1.43				

Table 4 shows the Cox regression models that estimate the probability of undergoing bariatric surgery in relation to the individual variables in two different models (univariate and multivariate models). Female gender was associated with significantly higher covariate-adjusted hazard ratios (HRs) of surgery in both periods. Having an intermediate educational level was associated with higher probability of undergoing surgery in both periods in Cox regression models (HR 2.52, 95% CI 2.37-2.68 and 2.01, 95% CI 1.93-2.10 in first and second periods respectively). HR for intermediate-low income was significantly higher only in the second period. HR for marital status and employment did not follow the same pattern in the first and second period.

Figure 2 shows the total number of bariatric surgeries for each year between 1990 and 2010. Except for a small peak in 1994, there was a substantial increase in the number of surgeries after 2006.



Figure 2.
Number of cases of bariatric surgery in Sweden, 1990-2010

Figure 3 shows the rates of surgery, by the different surgical methods. Gastric bypass was the dominating surgical method during the whole period (69.4 %), and after 2007, it contributed to 97.5 % of all bariatric surgery procedures in Sweden (139).

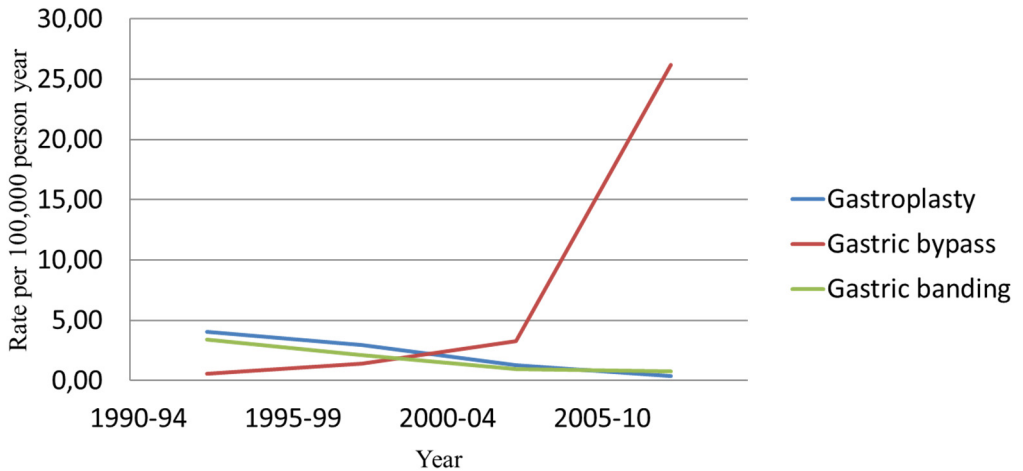


Figure 3. Age-adjusted incidence rates (per 100,000 person-years) of bariatric surgery 1990-2010

Paper III:

Country of origin and bariatric surgery in Sweden during 2001-2010

A total number of 14,851 (12,791 Swedes and 2060 immigrants) underwent bariatric surgery during the whole follow-up period. The lowest rates of bariatric surgery were among men with another country of origin (CR 1.1, 95% CI 1.0-1.3) (data not shown in the tables).

As shown in table 5, immigrants as a group had lower CR for bariatric surgery compared to Swedes, during 2006-2010 (CR 2.1, 95% CI 2.0-2.2 for immigrants and CR 2.5, 95% CI 2.4-2.5 for Swedes). The largest difference in CR of bariatric surgery between Swedes and immigrants was among those with no employment (CR 2.1 immigrants and CR 4.4 for Swedes) and low-income (CR 2.1 for immigrants and CR 3.3 for Swedes). For income, the highest CR was among Swedes with the lowest income, whereas for the immigrants, the highest CR was among those with middle-low income.

Table 5
Distribution of population, number of obesity surgery events, and age-standardized cumulative rates (per 1000) of obesity surgery, 2006-2010

	Born in Sweden						Immigrants							
	Population		Events		CR		Population		Events		CR			
	No.	%	No.	%	CR	95% CI	P-value*	No.	%	No.	%	CR	95% CI	P-value
Total population (%)	4373452		10769		2.5	2.4 2.5		835443		1776		2.1	2.0 2.2	
Gender														
- Men	2237855	51.2	2685	25.0	1.2	1.2 1.3	<0.001	409283	49.0	370	20.8	0.9	0.8 1.0	<0.001
- Women	2135597	48.8	8074	75.0	3.8	3.7 3.9	-	426160	51.0	1406	79.2	3.2	3.1 3.4	-
Family income (quartiles)**														
- Low income	913344	20.9	3402	31.6	3.3	3.2 3.4	<0.001	389845	46.7	800	45.0	2.1	1.9 2.2	<0.001
- Middle-low income	1110900	25.4	3379	31.4	3.1	3.0 3.2	<0.001	192884	23.1	529	29.8	2.7	2.5 2.9	<0.001
- Middle-high income	1158073	26.5	2487	23.1	2.1	2.1 2.2	<0.001	143114	17.1	292	16.4	2.0	1.7 2.2	<0.001
- High income	1191135	27.2	1501	13.9	1.3	1.2 1.4	-	109600	13.1	155	8.7	1.4	1.2 1.6	-
Marital status														
- Married/cohabiting	1796063	41.1	4173	38.8	3.0	2.9 3.1	-	420449	50.3	914	51.5	2.1	1.9 2.2	-
- Never married, widowed, or divorced	2577389	58.9	6596	61.2	2.6	2.5 2.6	<0.001	414994	49.7	862	48.5	2.1	2.0 2.3	0.338
Employment status														
- No	853303	19.5	3025	28.1	4.4	4.3 4.6	<0.001	380233	45.5	779	43.9	2.1	2.0 2.3	0.163
- Yes	3520149	80.5	7744	71.9	2.2	2.1 2.2	-	455210	54.5	997	56.1	2.1	2.0 2.2	-

No.=number; CR= Cumulative incidence rates; CI=confidence interval. *P-value is calculated according to reference group in each category (shown with "-"), for Swedes and immigrants separately. **Annual Family income in Swedish crowns: Low income 0-92000; Middle-low income 92001-121500; Middle-high income 121501-161000; High income more than 161000.

Table 6
 Hazard ratios of bariatric surgery in immigrants , 2001-2005 and 2006-2010

Birth country	2001-2005				2006-2010			
	Population	Cases	HR*	95 % CI	Population	Cases	HR*	95 % CI
Sweden	4379014	2695	ref.		4373452	10769	ref.	
Nordic countries	183674	135	1.21	1.02	161503	462	<u>1.18</u>	<u>1.07</u>
Denmark	22964	10	0.76	0.41	26658	52	0.81	0.61
Finland	133613	100	1.24	1.01	107693	329	<u>1.28</u>	<u>1.14</u>
Western Europe	44534	12	0.49	0.28	46711	46	0.43	0.32
Great Britain-Ireland	13326	3	0.45	0.14	14856	12	<u>0.39</u>	<u>0.22</u>
Germany	21977	4	0.32	0.12	22049	28	<u>0.51</u>	<u>0.36</u>
Eastern Europe	106202	40	<u>0.50</u>	<u>0.36</u>	122515	137	<u>0.38</u>	<u>0.32</u>
Bosnia	36602	5	<u>0.17</u>	<u>0.07</u>	42278	32	<u>0.26</u>	<u>0.18</u>
Yugoslavia	50750	29	0.77	0.54	58141	76	0.44	0.35
Baltic Countries	5553	0			7658	13	0.50	0.29
Central Europe	36346	23	0.81	0.54	45735	54	<u>0.39</u>	<u>0.30</u>
Poland	31078	20	0.80	0.52	40636	50	<u>0.40</u>	<u>0.30</u>
Africa	45191	8	<u>0.24</u>	<u>0.12</u>	61530	60	<u>0.32</u>	<u>0.25</u>
Latin America	37601	68	<u>2.39</u>	<u>1.88</u>	44432	278	<u>2.16</u>	<u>1.91</u>
Chile	21254	59	<u>3.76</u>	<u>2.90</u>	22932	209	<u>3.30</u>	<u>2.87</u>
Asia	196933	144	0.89	0.75	288748	589	0.69	0.63
Turkey	26186	17	0.82	0.51	30786	60	<u>0.64</u>	<u>0.49</u>
Lebanon	16109	26	2.00	1.35	19432	87	1.43	1.16
Iran	41563	53	<u>1.71</u>	<u>1.30</u>	48470	161	1.15	0.99
Iraq	38175	32	1.04	0.73	60667	154	<u>0.79</u>	<u>0.67</u>
Russia	11896	7	0.63	0.30	20107	33	<u>0.45</u>	<u>0.32</u>
All immigrants	722289	471	0.92	0.83	835443	1776	<u>0.74</u>	<u>0.71</u>

HR = hazard ratios; CI = confidence interval
 Bold type: 95% CI does not include 1.00. Underline: 99% CI does not include 1.00.
 *Adjusted for age, gender, marital status, family income, and employment status.

Results from the two periods 2001-2005 and 2006-2010, are shown in Table 6. In the first period, the HRs of bariatric surgery were not significantly different comparing Swedes and all immigrants whereas in the second period the HR was lower for immigrants (HR 0.74, 95% CI: 0.71-0.78). When considering different country of origin per se, immigrants from Chile (HR 3.76, 95% CI 2.90-4.87 in first period and 3.30, 95% CI 2.87-3.78 in the second period) and Lebanon (HR 2.00, 95% CI 1.35-2.96 in the first period and 1.43, 95% CI 1.16-1.77 in the second period) had much higher HR compared to Swedes and immigrants from Bosnia had the lowest HR (HR 0.17, 95% CI 0.07-0.42 in the first period and 0.26, 95% CI 0.18-0.36 in the second period) compared to Swedes. Immigrants from Nordic countries, especially Finland, had higher HRs compared with Swedes in both periods. With the exception of Nordic countries, immigrants from all other European countries had a lower HR compared with Swedes.

The differences in HRs for different country of origin did not change statistically after adjustment for socioeconomic factors, when men and women were analysed separately (data not shown in the tables).

Paper IV:

Socioeconomic factors, body mass index and bariatric surgery: A Swedish nationwide cohort study

As shown in table 7, a total of 7,433 women and 1,961 men underwent bariatric surgery during the follow-up period. The prevalence of individuals with high income, high education, with employment and in relationship was highest in the group with BMI < 25 kg/m², whereas the prevalence of individuals with low income, low education, no employment and not in a relationship were highest in the group with BMI ≥ 40 kg/m².

Table 7

Distribution and percentages of the female and male study population by BMI and individual characteristics (the highest percentages are in bold and underlined). Follow-up for bariatric surgery between 2005 and 2012.

	Female, Median age 28 years			Male, Median age 22 years				
	Study population	Average BMI	BMI <25 at baseline, n (%)	BMI ≥40 at baseline, n (%)	Study population	Average BMI	BMI <25 at baseline, n (%)	BMI ≥40 at baseline, n (%)
Age less than median	463,067		342,894	1,910	780,930		662,456	936
Age more than median	351,636		252,435	1,742	6097		4,465	11
Study population	814,703	23.50	595,329 (73.1%)	3,652 (0.5%)	787,027	22.27	666,921(84.7%)	947 (0.1%)
Operated	7,433 (0.9%)	32.31	843 (11.3%)	865 (11.6%)	1,961	30.97	258 (13.2%)	122 (6.2%)
Family Income								
• Low (25%)	204,204	23.74	142,812 (69.9%)	1,119 (0.6%)	196,474	22.48	162,476 (82.7%)	354 (0.2%)
• Middle (50%)	407,104	23.45	299,302 (73.5%)	1,783 (0.4%)	394,008	22.28	333,033 (84.5%)	473 (0.1%)
• High (25%)	203,395	23.34	153,306 (75.3%)	750 (0.4%)	196,545	22.05	171,412 (87.2%)	120 (0.1%)
Education								
• Low	63,615 (7.8%)	23.75	43,877 (69.0%)	447 (0.7%)	59,863 (7.6%)	22.62	47,784 (79.8%)	152 (0.3%)
• Middle	163,872 (20.1%)	23.47	118,773 (72.5%)	791 (0.5%)	172,898 (22.0%)	22.29	144,831 (83.8%)	215 (0.1%)
• High	587,216 (72.1%)	23.47	432,679 (73.7%)	2,414 (0.4%)	554,266 (70.4%)	22.22	474,306 (85.6%)	580 (0.1%)
Employment								
• Yes	584,962 (71.8%)	23.43	432,377 (73.9%)	2,295 (0.4%)	512,626 (65.1%)	22.18	439,063 (85.7%)	430 (0.1%)
• No	229,741 (28.2%)	23.65	162,952 (70.9%)	1,357 (0.6%)	274,401 (34.9%)	22.43	227,858 (83.0%)	517 (0.2%)
Marital status								
• Married/cohabiting	353,317 (43.4%)	23.22	266,645 (75.5%)	1,133 (0.3%)	157,229 (20.0%)	22.05	137,731 (87.6%)	53 (0.03%)
• Single	461,384 (56.6%)	23.70	328,684 (71.2%)	2,519 (0.6%)	629,798 (80.0%)	22.32	529,190 (84.0%)	894 (0.1%)

Table 8a and 8b show hazard ratios (HRs) for bariatric surgery in women and men, respectively, by the individual characteristics in three different models, where model 1 is univariate, model 2 is adjusted for BMI and model 3 is multivariate (adjusted for all the included variables, i.e. BMI, income, education, employment and marital status). In women, the HRs for bariatric surgery were higher for low and middle income (HR 1.4, 95% CI 1.3-1.5) and educational levels (HR 1.7, 95% CI 1.5-1.8 and 2.1, 95% CI 2.0-2.1 respectively), table 8a, whereas in men, HR was higher among those with high income (HR 1.0) and low/middle education (HR 2.1, 95% CI 1.9-2.4 and 2.6, 95% CI 2.4-2.9 respectively), table 8b. In both men and women, the HRs were higher for those in relationship and those with employment (HR 1.0), compared with single and non-employed.

Table 8a

Unadjusted and adjusted HR for bariatric surgery by the individual characteristics. Cox regression analysis with univariate, adjusted for BMI and multivariate models for women (the highest HRs are in bold and underlined)

	Univariate, model 1			Adjusted for BMI, model 2			Multivariate, model 3		
	Hazard ratio, 95% CI	P value	Hazard ratio, 95% CI	Hazard ratio, 95% CI	P value	Hazard ratio, 95% CI	Hazard ratio, 95% CI	P value	
Family income									
• Low	<u>1.9</u> (1.8-2.0)	0.001	<u>1.6</u> (1.5-1.7)	<u>1.4</u> (1.3-1.5)	0.001	<u>1.4</u> (1.3-1.5)	<u>1.4</u> (1.3-1.5)	0.001	
• Middle	1.7(1.6-1.8)	0.001	1.5(1.4-1.6)	<u>1.4</u> (1.3-1.5)	0.001	1.0	1.0	0.001	
• High	1.0		1.0	1.0		1.0	1.0		
Education									
• Low	<u>2.2</u> (2.0-2.3)	0.001	1.8(1.6-1.9)	1.7(1.5-1.8)	0.001	1.7(1.5-1.8)	1.7(1.5-1.8)	0.001	
• Middle	2.1(2.0-2.2)	0.001	<u>2.1</u> (2.0-2.2)	<u>2.1</u> (2.0-2.1)	0.001	2.1(2.0-2.1)	2.1(2.0-2.1)	0.001	
• High	1.0		1.0	1.0		1.0	1.0		
Employment									
• Yes	1.0		1.0	1.0		1.0	1.0		
• No	<u>1.4</u> (1.3-1.5)	0.001	<u>1.1</u> (1.0-1.2)	<u>0.9</u> (0.9-0.9)	0.001	0.9(0.9-0.9)	0.9(0.9-0.9)	0.01	
Marital Status									
• Married	1.0		<u>1.0</u>	<u>0.9</u> (0.9-0.9)	0.001	<u>1.0</u>	<u>1.0</u>	0.01	
• Single	<u>1.1</u> (1.0-1.1)	0.001	0.9(0.9-0.9)	0.9(0.9-0.9)	0.001	0.9(0.9-0.9)	0.9(0.9-0.9)	0.01	

Table 8b Unadjusted and adjusted HR for bariatric surgery by the individual characteristics. Cox regression analysis with univariate, adjusted for BMI and multivariate models for men (the highest HRs are in bold and underlined)

	Univariate, model 1			Adjusted for BMI, model 2			Multivariate, model 3		
	Hazard ratio, 95% CI	P value	Hazard ratio, 95% CI	Hazard ratio, 95% CI	P value	Hazard ratio, 95% CI	Hazard ratio, 95% CI	P value	
Family income									
• Low	1.3, (1.1–1.5)	0.001	0.9, (0.8–1.0)	0.9, (0.8–1.0)	0.05	0.8, (0.7–0.9)	0.8, (0.7–0.9)	0.02	
• Middle	1.4, (1.3–1.6)	0.001	1.1, (1.0–1.2)	1.1, (1.0–1.2)	0.11	1.0, (0.9–1.2)	1.0, (0.9–1.2)	0.74	
• High	1.00		<u>1.00</u>	<u>1.00</u>		<u>1.00</u>	<u>1.00</u>		
Education									
• Low	3.5, (3.1–4.0)	0.001	2.2, (1.9–2.5)	2.2, (1.9–2.5)	0.001	2.1, (1.9–2.4)	2.1, (1.9–2.4)	0.001	
• Middle	3.1, (2.8–3.4)	0.001	<u>2.8, (2.5–3.1)</u>	<u>2.8, (2.5–3.1)</u>	0.001	<u>2.6, (2.4–2.9)</u>	<u>2.6, (2.4–2.9)</u>	0.001	
• High	1.00		1.00	1.00		1.0	1.0		
Employment									
• Yes	1.0		1.0	1.0		1.0	1.0		
• No	1.1, (1.0–1.2)	0.02	0.8, (0.8–0.9)	0.8, (0.8–0.9)	0.001	1.0, (0.9–1.1)	1.0, (0.9–1.1)	0.32	
Marital Status									
• Married	1.0		1.0	1.0		1.0	1.0		
• Single	0.8, (0.7–0.9)	0.001	0.5, (0.5–0.6)	0.5, (0.5–0.6)	0.001	0.6, (0.5–0.7)	0.6, (0.5–0.7)	0.001	

We estimated the HRs for the different individual characteristics stratified by BMI, to further analyse the association between socioeconomic factors and bariatric surgery. The results are presented in table 9. When comparing the different socioeconomic groups in those with BMI ≥ 40 kg/m², the HRs showed no significant results, except for middle educational level in women (HR 1.3, 95% CI 1.1-1.5).

In those with BMI 30-39 kg/m², women had higher HRs for low and middle family income (HR 1.5, 95% CI 1.3-1.6 and 1.4-1.6 respectively) and education (HR 1.5, 95% CI 1.3-1.6 and 1.7, 95% CI 1.6-1.9 respectively). Those who were single had a lower HR (HR 0.8, 95% CI 0.8-0.9) compared to those in relationship. The results remained significant even in multivariate models. For men with BMI 30-39 kg/m², the HRs were only significantly higher among those with low and middle educational level (HR 1.9, 95% CI 1.6-2.3 and 2.3, 95% CI 2.0-2.7 respectively) in multivariate models (data not presented in the tables).

Table 9

HRs for bariatric surgery by the individual characteristics for women and men with BMI ≥ 40 kg/m². Cox regression analysis, univariate models (significant p value are in bold and underlined)

	Women BMI ≥ 40 kg/m ²		Men BMI ≥ 40 kg/m ²	
	Univariate*		Univariate*	
	Hazard ratio, 95% CI	P value	Hazard ratio, 95% CI	P value
Family income				
• Low	1.0, (0.9-1.3)	0.77	0.9, (0.5-1.7)	0.76
• Middle	1.0, (0.9-1.3)	0.57	1.3, (0.7-2.2)	0.43
• High	1.00		1.00	
Education				
• Low	1.1, (0.9-1.3)	0.49	1.2, (0.8-1.9)	0.42
• Middle	<u>1.3, (1.1-1.5)</u>	<u>0.001</u>	1.0, (0.6-1.5)	0.84
• High	1.00		1.00	
Employment				
• Yes	1.00		1.00	
• No	1.1, (0.9-1.2)	0.32	0.9, (0.7-1.4)	0.75
Marital Status				
• Married/cohabiting	1.00		1.00	
• Single	0.9, (0.8-1.1)	0.34	0.7, (0.4-1.4)	0.30

Discussion

The overall objective of this thesis was to assess the association between sociodemographic factors respectively, neighbourhood deprivation and obesity in children and adults and the access to bariatric surgery in adults in a country like Sweden with a comparatively strong system of universal health care insurance and social welfare.

This thesis showed that neighbourhood deprivation is independently associated with increased odds of diagnosed childhood obesity, after accounting for family- and individual-level socio-demographic factors. Living in a deprived neighbourhood increases the odds of diagnosed childhood obesity by 70%.

Another result of this thesis was that those in the lowest socioeconomic groups are less likely to undergo bariatric surgery compared to those with intermediate income, educational level and employment, although earlier studies have shown that those with low socioeconomic status have the highest rates of severe obesity.

Immigrants as a group had a lower rate of bariatric surgery compared to Swedes. However, when considering different countries of origin, there were large variations in the rate of bariatric surgery among groups. Men in general and men with another country of origin in particular, and some immigrant groups receive bariatric surgery at a lower rate. Moreover, the differences in rate of surgery between Swedes and immigrants are more pronounced in the individuals with low socioeconomic status (low income and no employment). It is unclear if the underlying barriers to receive bariatric surgery are due to patients' preferences/lack of knowledge or healthcare structures or combination of both. The differences in rate of bariatric surgery between groups with different countries of origin sometimes reflect the rate of obesity in some immigrant groups but not always.

There are some differences in rate of bariatric surgery and different individual sociodemographic characteristics, however these differences disappears when accounting for $\text{BMI} \geq 40 \text{ kg/m}^2$, which indicates that severe obesity rules out socioeconomic differences. It seems that the Swedish healthcare system has achieved its goal of equal health care for the entire population regarding bariatric surgery.

Obesity a major health problem

Prevalence of obesity has increased both worldwide (1) and in Sweden, among adults and children (1, 139, 140). The reasons for increased prevalence are almost the same globally and nationally, i.e. excessive use of energy dense foods, sedentary lifestyles, urbanization and socioeconomic-dependent access to a healthy diet.

Obesity is associated with higher mortality, decreased quality of life, and greater overall costs to the healthcare system due to its numerous co-morbidities (2, 33, 38). Obese children experience breathing difficulties, increased risk of fractures, hypertension, early signs of cardiovascular disease, insulin resistance, psychological effects and lower self-esteem (1). The lower self-esteem might be due to social discrimination that an obese child perceives.

Most of the world's population lives in countries where overweight and obesity kills more people than underweight. Obesity is one of the major causes of preventable death in developed countries (33, 34).

Due to the above reasons, obesity is a major global health problem that should be prevented and managed effectively, preferably at early ages but even later in adulthood. Factors that contribute to obesity should be eliminated and aspects that promote healthy lifestyle and normal weight should be encouraged.

The first step in prevention of obesity is to identify factors that promote obesity and contribute to its maintenance, in order to be able to eradicate those factors. The next step is to acquire effective strategies to manage and treat an already established obesity. This should be done through a cooperation of the healthcare system and decision makers, both nationally and globally.

The most essential aspects in treatment and management of obesity are behavioural modifications and lifestyle changes, such as healthy diet and regular physical activity. For those patients that are refractory to the conventional methods of weight loss, and weight loss medication, and those who have a severe obesity ($\text{BMI} \geq 40 \text{ kg/m}^2$) or a moderate obesity ($\text{BMI} 35\text{-}39.9 \text{ kg/m}^2$) plus a major obesity related comorbidity, bariatric surgery might be an appropriate treatment.

Sociodemography and obesity

Many studies have shown that health in general and weight specifically are affected by individual/familial socioeconomic status. Low SES has been shown to be a strong predictor of a range of physical and mental health problems (55). Generally, individuals with high SES tend to be in better health than people of

poorer status (141). The interaction between SES and health is very complex. Individuals with low SES may not have time, knowledge/education or/and financial resources to maintain a healthy lifestyle. Besides from education and income, the social status (often evaluated by occupation) and personal autonomy have an important impact on health, probably due to the stresses that result from low social status and low autonomy (142). SES can be evaluated at different levels i.e. individual, household, and neighbourhood. The effect of individual/household SES might be magnified/modified by other factors like the level of neighbourhood deprivation and ethnicity.

SES at the individual level, i.e. person's education, financial resources and social status, influence the lifestyle choices like diet and physical activity. Additionally, access to healthcare is also affected, especially in countries with a private health insurance system. The effect of individual SES on obesity was shown in paper IV where the prevalence of individuals with high income, education and employment was highest in the group with $BMI < 25 \text{ kg/m}^2$, whereas the opposite was among the group with $BMI \geq 40 \text{ kg/m}^2$, i.e. low income/education and no employment.

SES at a household level affects not only children's access to healthy diet and physical activity but also partner's lifestyle. In paper I, children raised in families with parents who had low/middle educational level had more than 50% increased odds of obesity. In paper II-IV all individuals who were married/cohabiting had a higher rate of bariatric surgery, probably due to encouraging role of their spouses or higher motivation to achieve a healthier lifestyle.

SES at a neighbourhood level influences a person's lifestyle through several factors. Secure neighbourhood environment and access to parks, playgrounds and green environment promote daily activity like walking, jogging and cycling for adults and playing and cycling for children. Studies have shown that the density of fast-food restaurants is associated with neighbourhood-level deprivation (143, 144). Vicinity to fast food restaurants might promote unhealthy diets. By contrast, closeness to affordable fruit-, vegetable- and grocery markets might favour healthy diet. Schools that place an emphasis on healthy eating and daily physical activity, play an important role concerning children's cultivation of a healthy lifestyle. Neighbours and friends that a person socialises with regularly are also an important influencing factor on lifestyle both positively and negatively. All the above reasons explain why neighbourhood environments have been shown to be an important independent risk factor for many health problems (69, 145). The results in paper I of this thesis adds important evidence to this field, i.e. high neighbourhood deprivation is significantly associated with higher odds of childhood obesity after adjustment for familial and individual sociodemographic characteristics. This should not be of any surprise in a country with low social

welfare, whereas it is somehow unexpected in a country like Sweden with a comparatively strong system of universal health care insurance and social welfare.

The effect of another country of birth on SES and health is explained by the fact that the process of migration involves major challenges in an individual-/family's life such as social, familial, occupational, and economical disruption, which leads to stress and unhealthy behaviours like physical inactivity and obesity (146). Many immigrants with high educational level from their country of origin cannot get a job in their fields of expertise, leading to higher rate of unemployment or employment in jobs with lower status/income. This was apparent in paper III that showed a higher percentage of unemployment and low income in immigrants compared to Swedes. Decline of psychosocial status, changes in lifestyle and dietary patterns, partly explain why some immigrants groups in Sweden have higher rates of obesity (77, 79).

Sociodemography and bariatric surgery

Previous studies have shown that, although obesity is more prevalent among socioeconomically disadvantaged and ethnic minorities, these patients undergo bariatric surgery less than expected (12, 120). In countries with a private healthcare system, some of these variations might be explained by financial inequalities. However, in countries with publicly funded insurance system, no obvious reasons for these disparities are apparent (13, 14). Few studies have systematically analysed the factors that cause variation in receiving bariatric surgery. It is generally assumed that much of the variation is explained by socioeconomic barriers. In paper II in this thesis, the rate of bariatric surgery was higher among those with middle income and educational level and lowest among those with high income and educational level, which we interpreted, was due to lower rate of obesity in high SES groups. However, in paper IV the individual socioeconomic variables were analysed in different BMI categories. In individuals with BMI ≥ 40 kg/m², no apparent differences in bariatric surgery were found between different socioeconomic groups.

An American study emphasised the patients' perspective (147). In that study, men were less likely than women and African Americans were less likely than Caucasians to have considered bariatric surgery after accounting for sociodemographic factors. In paper III, immigrants as a group underwent bariatric surgery at a lower rate; however there were large differences in rates of bariatric surgery between different countries of origin. A lower rate of bariatric surgery among individuals with low SES and some ethnic minorities might have various explanations.

One of the explanations might be the individual's/cultural perception of ideal body weight. Some cultures may have higher ideal weight and desire less weight loss than others, whereas in other cultures obesity is more stigmatised. Thus the motivation to seek a potentially risky weight loss treatment such as bariatric surgery may differ among subgroups of immigrants. These cultural differences could be more prevalent among low SES immigrants. This diversity in ideal body weight might explain the huge difference in rate of bariatric surgery among different countries of origin, aside from higher rate of obesity in some of those groups. Having a lower ideal weight and vigilance can explain the huge gender differences and much higher rate of bariatric surgery among women.

Another explanation is a person's inadequate awareness about the harmful effects of obesity. Men may consider bariatric surgery less than women, which may be due to them being less concerned about the negative impact of extreme obesity on health (13).

A Chinese study showed that patients' gluttonous behaviours were positively correlated with the acceptance level of bariatric surgery (148). According to an American study, the physicians' recommendation were also a strong independent factor for patients to consider bariatric surgery (147). This study shows that men and African Americans were less likely to be recommended bariatric surgery by their doctors.

According to Swedish national guidelines, there are some contraindications for bariatric surgery (149). The medical contraindications are serious heart- and lung diseases. Other exclusion criteria for bariatric surgery are patients who lack insight and motivation to change their lifestyle and eating habits after bariatric surgery. Patients, who have an ongoing or earlier drug/alcohol abuse without documented drug/alcohol free period of at least two years, are also excluded. Another exclusion criterion is severe mental disorder which is not medically under control. Patients who have not done serious attempts to reduce their weights are excluded as well.

Thus, differences in socioeconomic status do not solely explain the differences in the rate of bariatric surgery. The individual-, cultural- and physicians' attitude might also be important factors. Higher rate of bariatric surgery among women, despite relatively equal socioeconomic status and rate of obesity compared to men, indicates influence of other factors.

Public health aspects

Reducing morbidity and mortality related to overweight and obesity is a public health priority.

Studies have shown that factors in childhood such as place of birth and familial SES affect the risk of obesity in adulthood (150, 151). Children in lower socioeconomic groups have reduced access to healthy food and fewer opportunities to join sports clubs (152). Thus, socioeconomic factors in early life influence the health conditions in adulthood. Children should be the primary target population for all preventive actions.

It is of ultimate importance for the health care system and decision makers to implement health promoting factors and apply preventive measures early in life, especially in neighbourhoods with high deprivation and for those groups that are socioeconomically disadvantaged. This can be done, as early as during infancy, at children healthcare centres, in the form of parental education with an emphasis on healthy diet and regular physical activity. Screening of children for overweight both at children healthcare centres and at schools should be done regularly. In the case of, a child being diagnosed with overweight, necessary interventions should be used without delay. Schools should promote healthy eating and physical activity on a regular basis. Parks, green areas and bicycle paths should be provided at neighbourhoods, especially those with high deprivation, in order to facilitate daily physical activity for both adults and children. Healthy food, fruit and vegetables should be affordable and markets that provide this kind of food should be close to all neighbourhoods. Another drastic measure might be a higher tax for unhealthy food and prohibition of advertisements for junk food (rich in fat and sugar and poor in vitamins and minerals). There should be access to sports clubs that are free of charge or at least affordable and close to neighbourhoods with high deprivation.

Worksite settings is a location where adults spend substantial time. These settings can provide ample opportunities for nutrition and physical activity interventions.

Asides from healthcare prevention methods, there ought to be political/social strategies that reduce the socioeconomic disparities, i.e. targeting higher employment rates and better salaries for employments that historically have low status. Public education should be encouraged. Public awareness about the harmful effect of obesity should be raised and healthy lifestyles such as regular physical activity and healthy diet should be promoted

In those cases where prevention has failed and overweight has been already established, effective methods of weight loss should be offered. Multidisciplinary interventions that include behavioural- and dietary changes and encouragement to

physical activity should be used in order to prevent that overweight to exceed to severe obesity and its comorbidities.

Primary health care and general practitioners are usually the first health care contact that an individual will encounter. The role of primary healthcare in prevention and treatment of overweight and obesity is essential. When prevention has failed and obesity is a fact, efforts should be made to manage overweight and obesity. Lifestyle changes are, without a doubt, of utmost importance and primary actions should be taken. However, physicians should consider and suggest bariatric surgery for those patients that are refractory to conventional weight loss interventions, and have a severe obesity with a BMI ≥ 40 kg/m² with obesity related comorbidities.

Strengths and limitations

The results of this thesis must be interpreted in the context of its limitations. In paper I, socioeconomic status cannot be fully measured by family income and educational level. Thus it is possible that residual confounding exists.

In paper II and III, BMI or any other anthropometric parameters were not available, making it difficult to assess whether BMI affected the likelihood of undergoing bariatric surgery. As in paper I, socioeconomic variables cannot fully measure socioeconomic status. Thus residual confounding most likely exists.

In paper III, comparable information about incidence rates of obesity and bariatric surgery in the country of origin were missing. In the same paper individual educational level could not be included, due to missing data on educational level for many immigrants especially those that were newly arrived.

The most important limitation of paper IV was the lack of access to BMI at time of bariatric surgery. There was a time lag between BMI measurements and bariatric surgery. The time lag was shortest for those with BMI ≥ 40 kg/m², and longest for those with BMI < 25 kg/m². However, previous research has found that BMI increases in all age groups in Sweden during the study period (140). Yet, it is unclear, how many of those with BMI < 40 kg/m², actually achieved a BMI ≥ 40 kg/m², and thus became eligible for bariatric surgery. Another limitation in paper IV was that only women who had a contact with maternal healthcare service during their pregnancy were included. All other women could not be included. An additional limitation of this paper was that women and men were not completely comparable as most men completed their military service between the ages of 18-20 years, whereas the women's childbearing age was mainly between 18-39 years. Furthermore, pregnant women are likely to have a higher BMI compared to men

and those women who are not pregnant. As shown in this paper average BMI was higher for women compared to men.

The limitation of this thesis is somehow balanced by its strengths. One of the most important strengths is the ability to analyse data on a large national cohort and access to several nationwide database with information about individuals' characteristics and diagnoses and surgical procedures. The Swedish National Hospital Discharge Register is extensively validated in previous studies (125). For childhood obesity, the overall diagnostic validity of this register is close to 90%. In paper I, very few data were missing (e.g. only 1% of the data on maternal education level and family income were missing). Another strength in paper I was the ability to adjust for familial- and individual sociodemographic characteristics. Accounting for family SES is particularly important, as it is a major confounder that can affect an individual's choice of neighbourhood.

This database also includes all publicly funded surgeries and the main purpose of the paper II-IV was to examine whether the publicly funded bariatric surgery is equally distributed, regardless of socioeconomic factors. To the author's knowledge, paper III is the first nationwide study that compares differences in bariatric surgery rates between Swedes and immigrants. Likewise, paper IV is the first nationwide study that considers socioeconomic characteristics in relation to rates of bariatric surgery, considering levels of BMI. Another strength of paper II-IV was that both men and women were included and analysed separately.

Summary in Swedish (Populärvetenskaplig sammanfattning)

Förekomsten av övervikt och fetma har ökat hos vuxna och barn, både över hela världen och i Sverige, under de senaste decennierna. Förklaringen är livsstilsförändringar som minskad fysisk aktivitet och ökat intag av energirik mat. Övervikt är en av de största orsakerna till för tidig död i den utvecklade delen av världen. Övervikt ökar risken för många allvarliga sjukdomar som diabetes typ 2, högt blodtryck, hjärtkärlsjukdomar, andningsuppehåll under sömnen, vissa cancerformer, ledvärk och barnlöshet hos kvinnor. Övervikt och fetma är också förknippad med minskad livskvalitet och större totala kostnader för samhället och sjukvården. Överviktskirurgi anses vara den mest effektiva metoden för viktminskning för personer med svår fetma som inte lyckats med viktreduktion genom livsstilsförändring. Många studier har visat att överviktskirurgi minskar risken att dö tidigt och förbättrar tillståndet för sjukdomar som är kopplade till övervikt. Studier har också visat att livskvalitet, självkänsla och möjlighet till anställning förbättras efter kirurgi. Överviktskirurgi är kostnadseffektiv för samhället genom en minskning av de kostnader som är kopplade till överviktsrelaterade sjukdomar.

Flera studier har visat att fetma har högre förekomst i låga socioekonomiska grupper. I länder som har en privat hälsoförsäkring kan ekonomiska begränsningar styra tillgång till överviktskirurgi. Sverige har en allmän sjukförsäkring som innebär att alla, oavsett ekonomi få ha tillgång till överviktskirurgi om de uppfyller kriterierna.

Syftet med denna avhandling var att undersöka om det finns ett samband mellan förekomst av barnövervikt och typ av bostadsområde, även när individerna och familjerna har samma socioekonomiska status. Ett annat syfte med denna avhandling var att undersöka huruvida socioekonomiska egenskaper, såsom inkomst, utbildning, arbete och ursprungsland, påverkar graden av överviktskirurgi i ett land som Sverige, som har ett allmänt sjukförsäkringssystem. Ett ytterligare syfte var att kartlägga tidstrender för frekvens och typer av överviktskirurgi.

Delarbete I:

I delarbete I hittades ett samband mellan barnövervikt och typ av bostadsområde. Det innebär att barn som bor i socioekonomiskt utsatta bostadsområden har högre risk att bli överviktiga oberoende av familjens socioekonomiska position, jämfört med de som bor i socioekonomiskt välbärgade områden. Graden av effekten av bostadsområde på barnövervikt var större i vissa subgrupper av familjer och individer, särskilt för familjer med överviktiga medlemmar, barn med sjukhusvistelse på grund av diabetes och barn vars mödrar var inlagda på sjukhuset på grund av diabetes.

Effekt av bostadsområdet på barnövervikt kan förklaras av att otrygga bostadsområden inte tillåter daglig fysisk aktivitet. Det kan också bero på tillgång till snabbmatsrestauranger som bidrar till ohälsosamma matvanor. Grannar och kompisar som individen umgås med på daglig basis, kan också bidra till ogynnsamma livstilvanor. Skolor har också stor betydelse i utveckling av barnens livsstilsvanor.

Delarbete II:

Delarbete II visade att graden av överviktskirurgi var högst bland de individer som tillhörde gruppen med medelinkomst och medellång utbildning, de som var i ett parförhållande och de som hade ett arbete.

Graden av överviktskirurgi var nästan 3 gånger högre för kvinnor jämfört med män. Detta kan bero på skillnader i sociala normer om kroppsvikt för män och kvinnor och att kvinnor har en lägre kroppsviktideal. Kosmetiska aspekter och hälsofarliga effekter av övervikt kan ha större betydelse för kvinnor. Eftersom fetma kan leda till barnlöshet, kan en del överviktiga kvinnor söka överviktskirurgi med önskan om att kunna bli gravid efter viktnedgång.

Delarbete II visade att antal överviktsoperationer ökade kraftigt efter 2005. Detta beror inte endast på den ökade graden av fetma i hela populationen utan även ökad medvetenhet om att övervikt/fetma är en sjukdom som har skadliga effekter på hälsan och att det kräver en effektiv behandling. I takt med att nya effektiva kirurgiska metoder utvecklades, visade också många studier att överviktskirurgi har bevisat bästa metoden för viktnedgång för de som har svår fetma. Ökning av överviktskirurgi skedde framför allt efter publicering av SBU-rapporten, 2002 (Statens beredning för medicinsk och social utvärdering) som rapporterade följande: Kirurgisk behandling, som kan vara aktuell för patienter med svår fetma, reducerar vikten med, i genomsnitt, något mer än 25 procent, upp till fem år efter

operation. Efter tio år kvarstår en viktminskning om cirka 16 procent, eller i genomsnitt, drygt 20 kg. Detta innebär betydande hälso- och livskvalitetsvinster för denna patientgrupp (153).

Delarbete III:

Invandrare som grupp hade en lägre frekvens av överviktskirurgi jämfört med svenskar. Män med en annan bakgrund än svensk hade lägsta graden av överviktskirurgi jämfört med alla andra grupper. Största skillnaden i operationsgraden mellan svenskar och invandrare var mellan de grupper som hade låg inkomst. Det fanns även stora variationer i frekvensen av överviktskirurgi beroende på vilket ursprungsland individen hade. Chile och Libanon hade mycket högre operationsfrekvens jämfört med Sverige medan Bosnien hade den lägsta frekvensen. Alla europeiska länder hade lägre frekvens av överviktskirurgi jämfört med Sverige, med undantag för nordiska länder.

Skillnader i frekvensen av överviktskirurgi mellan vissa länder kunde ibland förklaras av förekomsten av övervikt i dessa länder, men inte alltid. Det finns andra faktorer som kan påverka frekvensen av överviktskirurgi i vissa grupper såsom kulturella eller individuella skillnader i idealkroppsvikt och om man uppfattar övervikten som hälsofarlig. Det är oklart om skillnader i frekvens av överviktskirurgi mellan invandrargrupper beror på individuella/kulturella skillnader eller om det föreligger strukturella fel i sjukvården så att vissa grupper inte erbjuds överviktskirurgi trots att de behöver det.

Delarbete IV:

Gruppen som hade kroppsmasseindex ($BMI < 25 \text{ kg/m}^2$) hade störst andel individer med hög inkomst, hög utbildning, hög anställningsgrad och individer i partnerskap. De individer som hade $BMI \geq 40 \text{ kg/m}^2$ hade högst andel med låg inkomst, låg utbildning, lägre anställningsgrad och fler singlar. Resultaten av det här delarbetet stämmer med tidigare studier som visade att övervikt/fetma är vanligare i lägre socioekonomiska grupper.

Det föreligger vissa socioekonomiska skillnader mellan grupper som genomgår överviktskirurgi. Frekvensen av överviktskirurgi var högre bland individer med medel inkomst, de som var i partnerskap och de som hade en anställning. Däremot hittades inga skillnader i frekvens av överviktskirurgi mellan olika socioekonomiska grupper bland individer med svår fetma ($BMI \geq 40 \text{ kg/m}^2$), med

undantag för kvinnor som hade medelinkomst. Den gruppen genomgick överviktskirurgi i större utsträckning.

En av slutsatserna av denna avhandling är att även om det verkar föreligga variationer i frekvensen av överviktskirurgi mellan olika socioekonomiska grupper, så är det framför allt svår fetma ($\text{BMI} \geq 40 \text{ kg/m}^2$) som är mest avgörande för att en individ ska genomgå överviktskirurgi. Detta tyder på att svensk sjukvård har lyckats att uppnå jämlik vård för hela populationen beträffande överviktskirurgi. Skillnader som finns i graden av överviktskirurgi mellan olika socioekonomiska grupper kan ha andra förklaringar än ekonomiska begränsningar.

Patientnytta:

I avhandlingen har vi identifierat att bostadsområde i sig har en oberoende effekt på risken för övervikt hos barn. Genom att identifiera och förebygga faktorer som bidrar till övervikt i socioekonomiskt utsatta bostadsområden kan man minska graden av övervikt hos barn i de utsatta områdena.

Individer med svår fetma som inte lyckats med viktnedgång genom livsstilsförändring, och särskilt de som har utvecklat en allvarlig sjukdom på grund av fetman, får erbjudas överviktskirurgi om man bedömer att de kan följa instruktionerna för att bibehålla en lågkalorikost efter operationen. En stor del av ansvaret för denna patientgrupp ligger på läkare som jobbar inom primärvården.

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