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Substantial Decrease in Comorbidity Five Years after Gastric Bypass –A Population-Based Study from the Scandinavian Obesity Surgery Registry

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Key words: gastric bypass, long-term results, comorbid disease, diabetes, hypertension, dyslipidemia, depression, sleep apnea, bariatric surgery, obesity

Running title: Comorbidity and weight 5y after bypass (38 characters)

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Abstract

Objective: To evaluate effect on comorbid disease and weight loss five years after Roux-en-Y gastric bypass (RYGB) surgery for morbid obesity in a large nationwide cohort.

Summary Background Data: The number patients having surgical procedures to treat obesity and obesity-related disease are increasing. Yet, population-based, long-term outcome studies are few.

Methods: Data on 26 119 individuals (75.8 % women, 41.0 years and BMI 42.9 kg/m^2) undergoing primary RYGB between May 1, 2007 and June 30, 2012, were collected from two Swedish quality registries, Scandinavian Obesity Surgery Registry (SOReg) and the Prescribed Drug Registry (PDR). Weight, remission of diabetes mellitus (T2DM), hypertension, dyslipidemia, depression, and sleep apnea, and changes in corresponding laboratory data was studied. Five-year follow-up was 100% (9774 eligible individuals) for comorbid diseases.

Results: BMI decreased from 42.8 ±5.5 to 31.2 ±5.5 kg/m^2 at five years, corresponding to 27.7%-reduction in total body weight. Prevalence of T2DM was reduced (15.5% to 5.9%), hypertension (29.7% to 19.5%), dyslipidemia (14.0% to 6.8%) and sleep apnea (9.6% to 2.6%). Greater weight loss was a positive, while increasing age or BMI at baseline, were negative prognostic factors for remission. The use of anti-depressants increased (24.1% to 27.5%). Laboratory status was improved, e.g. fasting glucose and glycated hemoglobin decreased from 6.1 to 5.4 mmol/mol and 41.8 to 37.7%, respectively.

Conclusions: In this nationwide study, gastric bypass resulted in large improvements in obesity-related comorbid disease and sustained weight loss over a five-year period. The increased use of anti-depressants warrants further investigation.

INTRODUCTION

Studies with long-term results after bariatric surgery are surprisingly rare[1-5], especially in the light of the large number of procedures performed worldwide. In most studies there is a one to two-year follow-up[6], and at such an early point in time, it is impossible to evaluate the true effect of gastric bypass, as patients have just reached their nadir in weight. Moreover, for this group of patients the longstanding remission of obesity-related comorbidities, e.g. diabetes mellitus, hypertension, dyslipidemia, and sleep apnea are of most importance.

The Scandinavian Obesity Surgery Registry (SOReg) was launched in 2007 as a quality registry for the expanding number of bariatric surgeries in Sweden[7]. In 2015, SOReg contained more than 50 000 bariatric procedures (>98% national coverage) with all 43 operating centers reporting to the registry. There has been an expansion of bariatric surgery with 3300 bariatric procedures performed in 2008, 4800 in 2009, 7800 in 2010 and 8600 in 2011. There has been a slight decrease in procedures and currently approximately 7000 performed annually, and approximately 95% of the reported procedures have been primary laparoscopic gastric bypass[8]. Perioperative complication rates (e.g. 1.2% leaks) and mortality are low (0.04%), the latter validated with the Swedish Population Register. Regular audits are performed by randomly comparing data in SOReg with patient charts at the surgical centers, demonstrating a high validity with less than 2% incorrect values[7]. Furthermore, by cross-linkage with the national Prescribed Drug Registry (PDR) a 100% follow-up of the occurrence of comorbid disease (defined as medical treatment) can be achieved.

The present study reports outcome in weight and obesity-related comorbid disease in a nationwide cohort of 26 119 individuals over five years after primary Roux-en-Y gastric

bypass (RYGB) in Sweden, using the prospective SOReg database with cross-linkage with the PDR.

METHODS

Data sources

Data extraction from the SOReg database was performed on the 19th of November 2014. Of 26 933 primary bariatric procedures, 26 119 individuals who had undergone a primary RYGB between May 1, 2007 and June 30, 2012 were included in the present study. The study population (75.8 % women) had a mean age of 41.0 ±10.9 years, mean weight and BMI of 123.3 ±20.9 kg and 42.8 ±5.5 kg/m^2, respectively (Table 1). In SOReg, data are prospectively collected at baseline before surgery, at surgery, after 6 weeks (for days 0-30), and at 1, 2 and 5 years of follow-up. All participants and follow-up rate of eligible patients is demonstrated in the STROBE diagram, however, as bariatric surgery has been continuously increasing during the last years in Sweden, only the 9774 patients operated in 2010 or earlier, were eligible at five years. The nationwide PDR was established in 2005 and includes all dispensed prescription drugs, classified according to the World Health Organization Anatomical Therapeutic Chemical (ATC) classification system. Since prescription medications are subsidized by the Swedish public health system, very few patients obtain drugs from other sources than those who report to the PDR. Due to the 45.2% 5-year follow-up in SOReg, SOReg was cross-matched with PDR allowing a 100% 1, 2 and 5 year follow-up of comorbid disease (see definition below). Data were extracted from PDR April 30, 2015.

Studied obesity-related comorbid diseases

Comorbid disease, T2DM (ATC code: A10A, A10B), hypertension (C02, C03, C08, C09), dyslipidemia (C10), or depression (N06A) was defined as an obesity-related condition if the

patient was in need of active pharmacological treatment according to both PDR and SOReg. Obstructive sleep apnea (OSAS) was defined as on-going treatment with continuous positive airway pressure (CPAP) registered in SOReg. As a waist circumference >102 cm in men and >88 cm in women have been associated with increased risks of cardiovascular disease[9], these specific cut-off points were studied. We studied the following biochemical markers (normal values in parenthesis): glycated hemoglobin (HbA1c) (≤48 mmol/mol), fasting glucose (≤7 mmol/L (multiply by 18 for mg/dL)), triglycerides (TG) (<1.7 mol/L (multiply by 88.5 for mg/dL)), low density lipoprotein cholesterol (LDL) (<4.1 mol/L (multiply by 38.6 for mg/dL)) and high density lipoprotein cholesterol (HDL) (>1.3 mol/L (multiply by 38.6 for mg/dL)).

Outcomes

Weight was analyzed at one, two and five years postoperatively according to the SOReg study protocol, as was HbA1c, serum glucose, lipids (TG, LDL and HDL), and blood pressure. Remission of comorbid disease was strictly defined as having discontinued pharmacological treatment (both PDR and SOReg and CPAP in the case of sleep apnea). Recurrent disease was present when participants, having the specific disease at baseline, were found to have relapsed after being free of disease at some time point. New-onset of a disease was present when individuals, free of disease at baseline, were found to be pharmacologically treated during follow-up.

Covariates

Analysis of weight change was performed for men and women. All analyses concerning remission of comorbidities were adjusted for gender, age at surgery, preoperative BMI and

present total weight loss (at one, two and five years). For T2DM, HbA1c at baseline was also included in the multivariate analysis.

Statistical analysis

Normally distributed data are presented as mean ± standard deviation (SD) and comparisons made with students t-test. Differences in proportions were evaluated with chi square test. In analysis of remission of comorbid disease, a logistic regression analysis was made with remission of each comorbid disease as dependent variable and the covariates described above. $P<0.05$ was considered significant. In the statistical analyses, no imputation of data was **performed**.

Sensitivity analysis

For comorbid disease follow-up was 100% of all eligible patients (n=9774) in the PDR at 5-year follow-up, **thus these are the studied patients**. **In addition, clinical data at** five-years **was available for** 2 539 of 5 623 eligible individuals (45.2%) in SOReg. No significant difference in baseline BMI was seen between these two groups. In a multivariate logistic regression, patients having five-year data registered in SOReg were 2.2 years older ($p<0.001$) than those without, corresponding to an odds ratio (OR) of 1.02 [95% CI 1.01-1.02]. Other factors increasing the probability of having five-year data were female gender OR 1.12 [95% CI 1.01-1.23], T2DM 1.26 [95% CI 1.08-1.46], hypertension 1.16 [95% CI 1.02-1.32], and dyslipidemia 1.34 [95% CI 1.10-1.63] at baseline. The increased number of patients having three of the five studied comorbidities and being at an older age should reduce the risk for exaggeration of the results.

Ethics

This study was approved by the regional ethical committee of Stockholm, Sweden (2013/535-31/5).

RESULTS

Weight change and waist circumference

At five years, the mean weight loss was 34.5 kg, corresponding to a total body weight loss of 27.7% (men 26.2%, women 28.1%), in spite of a weight regain (4.8 kg) between two and five years. Despite this, 3 out of 4 individuals had lost more than 25 kg at five years and 10.2% of the participants had reached a normal BMI (25 or **less). Table 2**.

At baseline, the waist circumference was 137.8 ±12.8 cm for men and 124.2 ±12.4 cm for women, thus well above both normal range and the high-risk levels set by NIH (>102 cm for men and >88 cm for women)[9]. At five-year follow-up, there was a significant reduction in waist circumference (26 cm), increasing of the percentage of men without a high-risk waist circumference (<102 cm) from 0.1% to 23.7%. Corresponding figures for women (<88 cm) were 1.5% to 25.5%. Absolute values are presented in Table 2.

Changes in comorbid disease

At baseline, 50.3% of all patients reported to be on medication (or CPAP for sleep apnea) for one or more of the above specified comorbid diseases. Hypertension was most common (29.7%), followed by depression (24.1%), T2DM (15.5%), dyslipidemia (14.0%), and sleep apnea (9.6%). More men than women had at least one comorbid condition (57.5 vs. 48.3%, $p<0.001$), with sleep apnea, T2DM, and dyslipidemia more frequent in men ($p<0.001$ for all), while pharmacologically treated depression was more common in women ($p<0.001$) (Table 3).

Type 2 diabetes mellitus

Five years after surgery, the proportion of patients taking medication for T2DM was significantly lower compared to baseline, 5.9% and 15.5%, respectively ($p<0.001$). Throughout the study period, the prevalence was almost twice as high in men as in women (24.8 to 12.5% at baseline and 9.0 to 4.9% at 5-year follow-up, respectively). Patients with greater weight loss had a greater chance of diabetes remission, while high age or high HbA1c at baseline were negative prognostic factors (Table 4). In addition, a lower HbA1c at baseline characterized patients experiencing remission of their former T2DM. In terms of new cases of T2DM, 56 (0.2%), 104 (0.4%), 52 (0.5%) were noted at 1, 2 and 5-year follow-up, respectively.

Hypertension

The number of patients with medication for hypertension was significantly reduced at five years from 29.7% at baseline to 19.5% ($p<0.001$). The prevalence was almost twice as high in men as in women, 26.7% and 17.3%, respectively, at five years (Table 3). In the multivariate analysis, older individuals and those with high BMI at baseline had a decreased chance of remission. In contrast, large weight loss was a positive factor (Table 4).

Dyslipidemia

The use of medication for dyslipidemia was significantly lower at five-year follow-up, 6.8%, compared to 14.0% at baseline ($p<0.002$). Again, more men than women were affected (23.8 vs. 10.8%) (Table 3). Increased age and high BMI at baseline were negative prognostic factors, while large weight loss improved the chance of remission, at least up to two-year follow-up (Table 4).

Anti-depressant drug use

Over the study period the prevalence of pharmacologic treated depression increased (24.1% to 27.5%, $p<0.001$). This was true for both men and women. Women were nearly twice as likely to be treated for depression as men (Table 3). Male gender and high weight loss were positive prognostic factors (Table 4).

Sleep apnea

There was a **large reduction of CPAP-treated** sleep apnea with a continued improvement at five-year follow-up (9.6% to 2.6%). The prevalence of sleep apnea at baseline was greater in men than in women (21.3 vs. 5.9%), but improvement was seen in both genders (Table 3). Large weight loss increased the chance of discontinuing CPAP treatment, while high age and high BMI at baseline were negative predictive factors (Table 4).

Biochemical biomarkers and blood pressure

Glucose homeostasis

Improved fasting glucose was seen at one-year follow-up (6.1 to 5.2 mmol/L) and was sustained over time (5.4 mmol/L at 5y). The percentage of patients with fasting glucose >7.0 mmol/L was reduced from 15.6% to 6.3% at five years. In line with this, a significant improvement was seen in HbA1c at five years (from 41.8 to 37.7 mmol/mol), and the number of individuals with an HbA1c >48 mmol/mol was significantly reduced (15.9 to 7.6%). In general, men had poorer glucose control compared to women throughout the study period, with a doubled risk of having pathological values (Table 5). There was a significant reduction in fasting glucose and HbA1c both in subjects with and without diabetes.

Blood pressure

Systolic blood pressure was reduced at five-year follow-up, and the number of individuals having >140 mm Hg was reduced from 57.9% to 39.3%. A similar reduction was seen in number of individuals with a diastolic blood pressure >90 mm Hg, 31.3% to 22.6%. Throughout the study period, more men than women had on-going pharmacological treatment for hypertension, and in spite of this, more men had a blood pressure above the normal reference range (Table 5). There was a significant reduction in systolic and diastolic blood pressure in both subjects with and without hypertension.

Lipids

An improvement in lipids was seen already at one-year follow-up. At five years, triglycerides (TG) were reduced from 2.1 to 1.2 mol/L, resulting in a decrease from 34.8% to 13.2% of patients having pathological values. LDL levels were reduced (3.1 to 2.6 mol/L), and a corresponding increase in HDL levels (1.2 to 1.6 mol/L) was seen. The number of individuals with pathological LDL and HDL were significantly reduced (12.2% to 2.9% and 70.9% to 20.8%, respectively), however, a larger proportion of men than women had pathological values (Table 5). There was a significant improvement in TG, HDL, and LDL in both subjects with and without dyslipidemia.

CONCLUSIONS

In this large nationwide cohort, primary gastric bypass surgery resulted in substantial weight loss, 34.5 kg, corresponding to a total body weight loss of 27.7% at five-year follow-up. Major improvements in obesity-related comorbid diseases were seen, although relapses did occur between years two and five, parallel to partial weight regain. The most profound changes were seen in sleep apnea and T2DM, where 3 out of 4 individuals had discontinued CPAP-treatment and 2 out of 3 of former diabetics were free of any anti-diabetic medication

at five-year follow-up. In contrast, 3.4% more patients were on anti-depressant treatment during the five-year follow-up period. In general, high weight loss facilitated remission of comorbid diseases, while high age and high BMI at baseline were negative factors. Furthermore, we were able to demonstrate that the overall positive effect upon risk factors, such as HbA1c, lipids and blood pressure, was applicable to not only patients with disease, but also those without comorbid disease at baseline.

Our data are similar to those previously reported with regard to initial weight loss and reduced waist circumference. We report a five-year 27.7% loss of the initial weight, which is comparable to the 31.5% weight loss at three years in The Longitudinal Assessment of Bariatric Surgery Consortium (LABS)[10] and identical to the 27.7% weight loss reported after six years in the Utah study[3]. The Swedish obese subjects (SOS) study reported a 19%-reduction in waist circumference[1], which is similar to the 20.8% reduction seen in the present study, placing a fourth of our patients below the threshold for high-risk of metabolic disease

A meta-analysis by Buchwald et al reported a complete remission of T2DM in 74.6% of patients with more than two years of follow-up (remission defined as no diabetes medications, a fasting glucose of 5.5 mmol/L and a HbA1c <52 mmol/mol) after bariatric surgery[6], which is similar to a remission rate of 67% seen at five years in earlier studies [11,12] as well as the present 62% (defined as no diabetes medication at all). Furthermore, after up to 15 years of follow-up in the SOS-study there were 392 new cases in the control group and 110 in the bariatric surgery group, representing 28.4 and 6.8 new cases per 1000 person-years, respectively[13]. Our data with 1.1 new cases per 1000 person-years (52 new cases during the five-year period) are significantly better, perhaps reflecting choice of surgical method, gastric bypass instead of restrictive surgery[14]. In a recent systematic review on bariatric surgery with

mean follow-up of 57.8 months, hypertension came into remission in 63% of patients and dyslipidemia in 65% [15]. This is a higher remission rate than seen in the present study, however, our data are in line with those published from the LABS study[10] and somewhat better than those of the SOS study[1]. Notably, high age significantly reduced the chance for remission of hypertension in the present study.

Our results on pharmacological treatment of depression are in contrast to the few previously published studies. In the LABS study, a decrease was seen in pharmacological treatment of depression from 35.3 % of the patients at baseline to 27.5 % at three-year follow-up[10]. Moreover, in a retrospective study where 48.6 % of RYGBP-patients were on antidepressants at baseline, 16% had a decrease or discontinuation of antidepressants after surgery[16]. Although, we demonstrate an increase in medication for depression, our five-year incidence (27.5%) is similar to the postoperative findings in the previous study[10]. Also, we demonstrate an increase in pharmacological treatment which might not reflect actual depressive symptoms. Our results with regard to sleep apnea are in line with a meta-analysis reporting 80.4%-remission of sleep apnea after RYGB[17]. Although recurrent disease was seen in 1.1% of patients in the present study, the discontinuation of CPAP-treatment continued over the whole study period.

One observation warrants further discussion. Despite the **large** improvements **in comorbid diseases**, 42.3% of the studied individuals **still** required treatment for at least one comorbid disease five years after surgery. As new-onset cases (although few) in all studied comorbidities were found, continuous follow-up with assessment of treatment-demanding diseases is necessary.

Strengths of the present study include a large number of participants, all having undergone a standardized and modern surgical intervention for obesity, and the high nationwide coverage (98.5% of all procedures in Sweden). Moreover, SOReg-data has been found to be reliable with a very low risk for incorrect values, when systematically validated, or continuously searched for non-logic or unlikely values[7]. To counter the 45% follow-up rate in SOReg a cross-reference was done with the PDR allowing 100% follow-up of medically treated comorbid diseases. Finally, as older patients and those with some of the specific comorbidities were more likely to have five-year follow-up data than patients not attending a five-year visit in the sensitivity analysis, the risk for exaggeration of the positive results is reduced.

In summary, this large prospective nationwide study on outcome after primary gastric bypass has demonstrated substantial weight loss and significant improvements in sleep apnea, diabetes, hypertension and dyslipidemia in both men and women up to five-year follow-up. However, 42.3% of the included individuals still required treatment for at least one comorbid disease five years after surgery, making life-long follow-up with assessment of treatment-demanding diseases necessary. The lack of improvement in depression warrants further study.

STROBE diagram of the study population.

26,639 primary bariatric surgeries
Included in the SOReg-database until 2012-06-30 and alive at data extraction

Excluded:
191 Duodenal switch
180 Gastric band
113 Gastric sleeve
36 Other procedures

Baseline
26,119 primary gastric bypass

Comorbid **disease (PDR,** n=26,119; 100%)
Weight (**SOReg,** n=26,119; 100%)
Laboratory values (**SOReg,** n=21,006; 80.4%)

Year 1
26,119 eligible for follow-up **in both registries**

Comorbid **disease (PDR,** n=26,119; 100%)
Weight **(SOReg,** n=22,967; 87.9%)
Laboratory values (**SOReg,** n=17,689; 67.7%)

Year 2
26,119 eligible for follow-up **in both registries**

Comorbid **disease (PDR,** n=26,119; 100%)
Weight (**SOReg,** n=16,119; 61.7%)
Laboratory values (**SOReg,** n=10,873; 41.6%)

Year 5
9774 and 5623 eligible for follow-up in **PDR and SOReg**, respectively

Comorbid **disease (PDR,** n=9774; 100%)
Weight (**SOReg,** n=2539; 45.2%)
Laboratory values (**SOReg,** n=1559; 27.7%)

Prescribed Drug Registry (PDR), Scandinavian Obesity Surgery Registry (SOReg).

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Table 1. Demographics of 26,119 morbidly obese individuals undergoing primary gastric bypass surgery.

Total N	26,119	
Age ±SD	41.0 ±10.9	Men 42.8 ±11.1 Women 40.4 ±10.8
Gender, women	19796	75.8%
Height (cm)	169.2 ±9.0	
Weight (kg)	123.3 ±20.9	118 ±19.7 at surgery
BMI (kg/m^2)	42.8 ±5.5	
Waist circumference (cm)	127.4 ±13.8	
Procedure, laparoscopic Open Converted to open	24840 1004 275	95.1% 3.8% 1.0%

Mean ±SD

Table 2. Effect on weight-related parameters at 1, 2, and 5 years after primary gastric bypass.

	Baseline n=26,119	1 year n=22,967	2 years n=16,119	5 years n=2539
Height (cm)	**169.2 ±9.0**	**169.1 ±9.0**	**169.0 ±9.0**	**168.9 ±9.0**
Men	180.0 ±7.2	180.0 ±7.1	180.0±7.2	180.0 ±7.5
Women	165.8 ±6.4	165.8 ±6.5	165.7 ±6.5	165.7 ±6.5
Weight (kg)	**123.3 ±20.9**	**84.1 ±16.8**	**83.0 ±17.2**	**89.3 ±18.5**
Men	141.6 ±21.0	99.4 ±16.5	98.8 ±16.2	104.9 ±18.8
Women	117.1±17.0	79.4 ±13.9	78.3 ±14.4	84.9 ±15.8
Weight loss (kg)		**38.7 ±11.9**	**39.3 ±13.7**	**34.5 ±14.7**
Men		42.1 ±14.2	42.3 ±16.1	38.0 ±17.1
Women		37.6±10.9	38.4 ±12.7	33.5 ±13.8
BMI (kg/m^2)	**42.8 ±5.5**	**29.3 ±4.7**	**29.0 ±4.9**	**31.2 ±5.5**
Men	43.7 ±5.9	30.7 ±4.7	30.5 ±4.7	32.4 ±5.6
Women	42.5 ±5.4	28.8 ±4.6	28.5 ±4.9	30.9 ±5.4
Total body weight loss (%)		**31.5 ±7.7**	**32.0 ±9.0**	**27.7 ±10.0**
Men		29.5 ±7.8	29.6 ±8.9	26.2 ±9.7
Women		32.1 ±7.5	32.7 ±8.9	28.1 ±10.0
Waist (cm)	**127.4 ±13.8** (n=21,119)	**96.4 ±13.5** (n=17,570)	**96.0 ±14.0** (n=10,285)	**100.5 ±15.6** (n=1333)
Men	137.8 ±12.8	106.0 ±12.9	106.0 ±13.3	111.7 ±14.6
Women	124.2 ±12.4	93.4 ±12.2	92.9 ±12.8	97.5 ±14.4

Mean ±SD. * >50%EWL (%) equals the number of individuals who lost more than half of their former overweight.

Table 3. Prevalence of comorbid diseases at baseline and at 1, 2, and 5 years after primary gastric bypass with data from the Prescribed Drug Register.

Comorbid disease	Baseline (%) n=26,119	1 year (%) n=26,119	2 years (%) n=26,119	5 years (%) n=9774
Any comorbidity **	**13,178 (50.3)**	**10,803 (41.4)**	**11,118 (42.6)**	**4139 (42.3)**
Men	3650 (57.5)	2721 (42.6)	2779 (43.6)	973 (41.1)
Women	9528 (48.3)	8082 (40.9)	8339 (42.2)	3166 (42.7)
T2DM	**4056 (15.5)**	**1428 (5.5%)**	**1460 (5.6)**	**574 (5.9)**
Men	1585 (24.8)	528 (8.3)	539 (8.4)	214 (9.0)
Women	2471 (12.5)	900 (4.6)	921 (4.7)	360 (4.9)
Hypertension	**7749 (29.7)**	**5065 (19.4)**	**5079 (19.4)**	**1910 (19.5)**
Men	2275 (35.7)	1812 (28.4)	1830 (28.7)	631 (26.7)
Women	4974 (25.2)	3253 (16.5)	3249 (16.5)	1279 (17.3)
Dyslipidemia	**3655 (14.0)**	**2026 (7.8)**	**1911 (7.3)**	**668 (6.8)**
Men	1518 (23.8)	822 (12.9)	778 (12.2)	238 (10.1)
Women	2137 (10.8)	1204 (6.1)	1133 (5.7)	430 (5.8)
Depression	**6295 (24.1)**	**6562 (25.1)**	**7001 (26.8)**	**2683 (27.5)**
Men	954 (15.0)	1056 (16.5)	1155 (18.1)	413 (17.5)
Women	5341 (27.1)	5506 (27.9)	5846 (29.6)	2270 (30.6)
OSAS*	**2508 (9.6)**	**666 (2.9)**	**410 (2.6)**	**67 (2.6)**
Men	1345 (21.3)	374 (6.9)	220 (6.0)	39 (6.9)
Women	1163 (5.9)	292 (1.7)	190 (1.5)	28 (1.4)

Type 2 diabetes mellitus (T2DM) and obstructive sleep apnea syndrome (OSAS). A statistical difference ($p<0.001$) was seen in prevalence between men and women for all comorbid diseases at baseline, and between prevalence at baseline and five years after surgery ($p=0.002$ for hypertension, baseline to 5y). Data from the Prescribed Drug Register (PDR) with 100% 5-year follow-up (T2DM (ATC code: A10A, A10B), hypertension (C02, C03, C08, C09), dyslipidemia (C10), or depression (N06A). * Data from SOReg with 45.2 % 5-year follow-up rate at 5 years. ** Data only from the PDR.

Table 4. Multivariate logistic regression for remission of comorbid diseases at 1, 2 and 5 years, respectively after primary gastric bypass.

	1 year			2 years			5 years		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
T2DM									
Gender (male)	1.248	1.050-1.482	0.012	1.176	0.954-1.450	0.129	1.021	0.597-1.745	0.936
Age	0.963	0.954-0.971	0.000	0.966	0.956-0.976	0.000	0.971	0.945-0.998	0.038
BMI at baseline	0.996	0.982-1.011	0.638	1.009	0.990-1.028	0.361	1.019	0.974-1.066	0.414
HbA1c at baseline	0.965	0.960-0.970	0.000	0.965	0.959-0.971	0.000	0.955	0.941-0.970	0.000
Percent total weight loss	1.035	1.023-1.047	0.000	1.026	1.014-1.038	0.000	1.035	1.006-1.064	0.016
Hypertension									
Gender (male)	0.984	0.880-1.101	0.777	0.947	0.827-1.084	0.433	0.760	0.510-1.131	0.176
Age	0.961	0.955-0.967	0.000	0.954	0.947-0.961	0.000	0.963	0.942-0.984	0.001
BMI at baseline	0.968	0.959-0.978	0.000	0.967	0.955-0.978	0.000	0.976	0.943-1.011	0.174
Percent total weight loss	1.031	1.023-1.038	0.000	1.033	1.025-1.041	0.000	1.030	1.010-1.051	0.003
Dyslipidemia									
Gender (male)	0.986	0.831-1.171	0.875	1.034	0.836-1.278	0.760	1.148	0.654-2.014	0.630
Age	0.965	0.955-0.974	0.000	0.957	0.945-0.969	0.000	0.965	0.936-0.995	0.022
BMI at baseline	0.968	0.953-0.984	0.000	0.960	0.940-0.981	0.000	0.953	0.902-1.006	0.083
Percent total weight loss	1.031	1.019-1.043	0.000	1.037	1.024-1.050	0.000	1.208	0.999-1.058	0.054
Depression									
Gender (male)	1.499	1.225-1.836	0.000	1.397	1.074-1.817	0.013	1.423	0.721-2.813	0.309
Age	0.995	0.988-1.002	0.168	0.998	0.989-1.007	0.678	0.979	0.957-1.003	0.084
BMI at baseline	0.989	0.975-1.002	0.094	0.983	0.967-1.000	0.055	0.992	0.954-1.032	0.685
Percent total weight loss	1.016	1.007-1.026	0.000	1.021	1.011-1.031	0.000	1.013	0.992-1.035	0.219
Sleep apnea									
Gender (male)	0.780	0.637-0.955	0.016	0.871	0.670-1.136	0.308	0.582	0.278-1.219	0.151
Age	0.970	0.959-0.981	0.000	0.979	0.965-0.993	0.004	0.938	0.897-0.980	0.005
BMI at baseline	0.929	0.914-0.945	0.000	0.915	0.896-0.936	0.000	0.937	0.884-0.993	0.028
Percent total weight loss	1.059	1.045-1.074	0.000	1.091	1.074-1.109	0.000	1.096	1.052-1.141	0.000

Odds ratio (OR), 95% confidence interval (CI), and p-value (p). Data from SOReg.

Table 5. Change in laboratory values from baseline to 1, 2, and 5 years follow-up after primary gastric bypass surgery.

	Absolute values				Per cent of individuals with pathological values			
	Baseline	1 year	2 years	5 years	Pre	1 y	2 y	5 y
HbA1c	**41.8 ±12.7** (n=21,006)	**35.9 ±7.4** (n=17,689)	**36.5 ±9.0** (n=10,873)	**37.7 ±9.3** (n=1559)	**15.9**	**4.1**	**5.4**	**7.6**
Men	45.1 ±15.3	36.6 ±8.6	37.5 ±10.4	39.7 ±12.9	25.2	6.5	8.8	12.8
Women	40.7 ±11.5	35.6 ±7.0	36.2 ±8.5	37.1 ±8.0	12.9	3.3	4.4	6.2
Fasting glucose	**6.1 ±2.1** (n=9920)	**5.2 ±1.2** (n=11,124)	**5.3 ±1.3** (n=8333)	**5.4 ±1.2** (n=1336)	**15.6**	**4.5**	**5.4**	**6.3**
Men	6.6 ±2.6	5.5 ±1.4	5.7 ±1.6	5.7 ±1.5	24.6	8.6	9.7	10.2
Women	5.9 ±1.8	5.1 ±1.1	5.2 ±1.1	5.3 ±1.1	12.7	3.2	4.1	5.2
TG	**2.1 ±5.5** (n=20,760)	**1.1 ±1.1** (n=17,336)	**1.1 ±0.6** (n=10,538)	**1.2 ±1.5** (n=1470)	**34.8**	**8.3**	**8.9**	**13.2**
Men	2.1 ±2.0	1.2 ±1.2	1.2 ±0.7	1.3 ±0.7	47.4	11.9	12.7	19.9
Women	1,6 ±1.5	1.0 ±1.0	1.0 ±0.5	1.1 ±1.7	30.7	7.2	7.8	11.4
LDL	**3.1 ±1.0** (n=19,820)	**2.5 ±0.8** (n=17,215)	**2.5 ±0.9** (n=10,524)	**2.6 ±1.0** (n=1469)	**12.2**	**1.9**	**2.5**	**2.9**
Men	3.1 ±1.0	2.4 ±0.7	2.5 ±0.8	2.6 ±0.8	12.6	1.6	2.0	2.9
Women	3.1 ±1.0	2.5 ±0.8	2.5 ±0.9	2.6 ±1.1	12.1	1.9	2.6	2.8
HDL	**1.2 ±0.4** (n=20,315)	**1.5 ±0.6** (n=17,426)	**1.6 ±0.5** (n=10,587)	**1.6 ±0.6** (n=1472)	**70.9**	**28.2**	**20.8**	**20.8**
Men	1.0 ±0.4	1.4 ±0.7	1.4 ±0.6	1.4 ±0.4	86.2	43.7	37.3	36.4
Women	1.2 ±0.4	1.5 ±0.5	1.6 ±0.5	1.7 ±0.7	66.1	23.6	15.9	16.7
BP, systolic	**135 ±17** (n=14,304)	**127 ±16** (n=8447)	**127 ±17** (n=6153)	**130 ±18** (n=900)	**44.4**	**23.6**	**24.7**	**30.0**
Men	141 ±16	133 ±16	133 ±17	136 ±18	57.9	35.5	38.0	39.3
Women	133 ±16	124 ±16	125 ±16	128 ±18	39.9	19.6	20.5	27.4
BP, diastolic	**83 ±10** (n=14,296)	**78± 10** (n=8443)	**78 ±11** (n=6147)	**80 ±11** (n=897)	**31.3**	**15.6**	**16.1**	**22.6**
Men	85 ±10	81 ±10	81 ±11	84 ±12	42.4	23.0	25.2	30.2
Women	82 ±10	77 ±10	77 ±10	79 ±11	27.6	13.1	13.3	20.6

Mean ±SD, and per cent of individuals with values outside the reference range, for HbA1c ≥48, glucose ≥7.0, triglycerides (TG) >1.7, low density lipoprotein (LDL) >4.1, high density lipoprotein (HDL) <1.3, blood pressure (BP) systolic ≥140 and diastolic ≥ 90. Data from SOReg.