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Bariatric Surgery for People with Diabetes and Morbid Obesity

An Evidence-Based Analysis

Presented to the Ontario Health Technology Advisory Committee in July, 2009

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Contact Information

The Medical Advisory Secretariat
Ministry of Health and Long-Term Care
20 Dundas Street West, 10th floor
Toronto, Ontario
CANADA
M5G 2C2
Email: MASinfo.moh@ontario.ca
Telephone: 416-314-1092

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About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The Medical Advisory Secretariat conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series*.

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practising medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact the Medical Advisory Secretariat: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Table of Contents

List of Abbreviations

AGB	Adjustable gastric banding
AUC	Area under the curve
BPD	Biliopancreatic diversion
BMI	Body Mass Index
CI	Confidence interval(s)
EWI	Excess weight loss
LAGB	Laparoscopic adjustable gastric banding
MAS	Medical Advisory Secretariat
OR	Odds ratio
OHTAC	Ontario Health Technology Advisory Committee
QALY	Quality adjusted life year
QoL	Quality of life
RCT	Randomized controlled trial
RR	Relative risk
RYGB	Roux-en-Y gastric bypass
SD	Standard deviation
SOS	Swedish obese subjects (study)
SROC	Summary receiver operating characteristic
VBG	Vertical banded gastroplasty

Executive Summary

In June 2008, the Medical Advisory Secretariat began work on the Diabetes Strategy Evidence Project, an evidence-based review of the literature surrounding strategies for successful management and treatment of diabetes. This project came about when the Health System Strategy Division at the Ministry of Health and Long-Term Care subsequently asked the secretariat to provide an evidentiary platform for the Ministry's newly released Diabetes Strategy.

After an initial review of the strategy and consultation with experts, the secretariat identified five key areas in which evidence was needed. Evidence-based analyses have been prepared for each of these five areas: insulin pumps, behavioural interventions, bariatric surgery, home telemonitoring, and community based care. For each area, an economic analysis was completed where appropriate and is described in a separate report.

To review these titles within the Diabetes Strategy Evidence series, please visit the Medical Advisory Secretariat Web site, http://www.health.gov.on.ca/english/providers/program/mas/mas_about.html,

1. Diabetes Strategy Evidence Platform: Summary of Evidence-Based Analyses
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6. Home Telemonitoring for Type 2 Diabetes: An Evidence-Based Analysis
7. Application of the Ontario Diabetes Economic Model (ODEM) to Determine the Cost-effectiveness and Budget Impact of Selected Type 2 Diabetes Interventions in Ontario

Objective

The purpose of this evidence-based analysis was to examine the effectiveness and cost-effectiveness of bariatric surgery for the management of diabetes in morbidly obese people.

This report summarized evidence specific to bariatric surgery and the improvement of diabetes from the full evidence-based analysis of bariatric surgery for the treatment of morbid obesity completed by the Medical Advisory Secretariat (MAS) in January 2005. To view the full report, please visit the MAS website at: http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html.

Clinical Need: Condition and Target Population

Obesity is defined as an excessive accumulation of body fat as measured by the body mass index (BMI) and calculated as body weight in kilograms (kg) divided by height in metres squared (m^2). People with a BMI over 30 kg/m^2 are considered obese in most countries. The condition is associated with the development of several diseases, including hypertension, diabetes mellitus (type 2 diabetes), hyperlipidemia, coronary artery disease, obstructive sleep apnea, depression, and cancers of the breast, uterus, prostate, and colon. Clinically severe, or morbid obesity, is commonly defined by a BMI of at least 40 kg/m^2, or a BMI of at least 35 kg/m^2 if there are comorbid conditions such as diabetes, cardiovascular disease, or arthritis.

The prevalence of morbid obesity among people with type 2 diabetes has been examined and of 2,460 patients with type 2 diabetes, 52% (n = 1,279) were obese (BMI ≥ 30 kg/m^2) and 23% (n = 561) had a BMI ≥ 35 kg/m^2.

Bariatric Surgery

Men and women with morbid obesity may be eligible for surgical intervention. There are numerous surgical options available, all of which can be divided into two general types, both of which can be performed either as open surgery or laparoscopically:

1. malabsorptive - bypassing parts of the gastrointestinal tract to limit the absorption of food, and
2. restrictive - decreasing the size of the stomach in order for the patient to feel satiated with a smaller amount food

Surgery for morbid obesity is usually considered a last resort for people who have attempted first-line medical management (e.g. diet, behaviour modification, increased physical activity, and drugs) but who have not lost weight permanently. Surgery is restricted to people with morbid obesity (BMI ≥ 40 kg/m^2) or those with a BMI of at least 35 kg/m^2 and serious comorbid conditions.

Evidence-Based Analysis Methods

Details of the full literature search can be found in the 2005 evidence-based analysis of bariatric surgery (http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html). Briefly, a literature search was conducted examining published works from January 1996 to December 2004, including OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cumulative Index to Nursing & Allied Health Literature (CINAHL), The Cochrane Library, and the International Agency for Health Technology Assessment/Centre for Review and Dissemination.

Inclusion Criteria

- Data on the effectiveness or cost-effectiveness of bariatric surgery for the improvement of diabetes
- Systematic reviews, randomized controlled trials (RCTs), and observational controlled prospective studies that had >100 patients
- Randomized controlled trials (RCTs), systematic reviews and meta-analyses

Exclusion Criteria

- Duplicate publications (superseded by another publication by the same investigator group, with the same objective and data)
- Non-English-language articles
- Non-systematic reviews, letters, and editorials
- Animal and in-vitro studies
- Case reports, case series
- Studies that did not examine the outcomes of interest

Outcomes of Interest

- Improvement or resolution of diabetes

The quality of the studies was examined according to the GRADE Working Group criteria for grading quality of evidence.

Summary of Findings

There is evidence that bariatric surgery is effective for improvement and resolution of diabetes in patients who are morbidly obese (BMI $\geq$35 kg/m^2). The quality of evidence for the use of bariatric surgery for the resolution or improvement of diabetes in morbidly obese people, according to the GRADE quality-of-evidence criteria, was found to be moderate (see ES Table 1).

Comparison of various bariatric techniques:

- No prospective, long-term direct comparison is available between malabsorptive and restrictive techniques.
- Retrospective subgroup analyses from a large observational study showed greater improvement and resolution of diabetes using malabsorptive techniques rather than purely restrictive methods.
- There is evidence from a meta-analysis that malabsorptive techniques are better than other banding techniques in terms of improvement and resolution of diabetes.

Keywords

Bariatric surgery, morbid obesity, comorbidity, diabetes

ES Table 1: GRADE Quality of Evidence for Bariatric Surgery for the Resolution or Improvement of Diabetes

Outcome	Quality Assessment					Summary of Findings		
	Design	Quality	Consistency	Directness	Other	No. of Patients	Effect	Quality
Improvement in HbA1c in diabetic and glucose intolerant patients	Meta-analysis	Moderate*	Consistent	Direct	None	n=171	-2.70% (-5.0% to -0.70%) weighted mean change (range)	Moderate
Resolution or improvement of diabetes *(Studies reporting combination as well as studies that only used the term "improved", but not the studies reporting only resolution)*	Meta-analysis	Moderate*	Consistent	Direct	None	414/485 (n resolved or improved/n evaluated)	86.0% (78.4% to 93.7%) mean% (95% C])	Moderate
Resolution of diabetes *(diabetes disappeared or no longer required therapy)*	Meta-analysis	Moderate*	Consistent	Direct	None	1417/1846 (n resolved/n evaluated)	76.8% (70.7% to 82.9%) mean% (95% CI)	Moderate
Recovery of diabetes *(fasting plasma glucose level of less than 126 mg per decilitre [7.0 mmol per litre])*	Observational prospective controlled study	Moderate*	Consistent	Some uncertainty†	Some uncertainty‡	control n=84 intervention n=118	3.45 (1.64 to 7.28) OR (95% CI) at 10 yrs	Moderate

* Downgraded due to study design (not randomized controlled trial)

† Unlikely to be an important uncertainty. Inclusion criteria for the SOS study not specific to conventional definition of "morbidly obese" patients (BMI $\geq$ 40 or $\geq$ 35 kg/m^2 with comorbid conditions)

‡ Unlikely to be an important uncertainty. Control group not standardized, however, this lends to the pragmatic nature of the study.

Background

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After an initial review of the strategy and consultation with experts, the secretariat identified five key areas in which evidence was needed. Evidence-based analyses have been prepared for each of these five areas: insulin pumps, behavioural interventions, bariatric surgery, home telemonitoring, and community based care. For each area, an economic analysis was completed where appropriate and is described in a separate report.

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Clinical Need and Target Population

Obesity is defined as an excessive accumulation of body fat as measured by the body mass index (BMI). BMI is calculated as body weight in kilograms (kg) divided by height in metres squared (m^2): weight (kg)/[height (m)]^2. People with a BMI over 30 kg/m^2 are considered obese in most countries. (1) The condition is associated with the development of several diseases, including hypertension, diabetes mellitus (type 2 diabetes), hyperlipidemia, coronary artery disease, obstructive sleep apnea, depression, and cancers of the breast, uterus, prostate, and colon. (2)

Clinically severe or morbid obesity is commonly defined by a BMI of at least 40 kg/m^2, or a BMI of at least 35 kg/m^2 if there are comorbid conditions such as diabetes, cardiovascular disease, arthritis, shortness of breath, gallbladder disease, back or disc disease, fatigue, or disability. (3;4) In the United States, the age-adjusted prevalence of morbid obesity for adults aged 20 years and older has increased significantly in the population, from 2.9% (1988–1994) to 4.7% (1999–2000). (5)

The incidence of morbid obesity (BMI > 40 kg/m^2) has not been reported in the literature. The prevalence of morbid obesity among people with type 2 diabetes was determined by Daousi et al. (6) In that study, it was found that of 2,460 patients with type 2 diabetes, 52% (n = 1,279) were obese (BMI $\geq$ 30 kg/m^2) and 23% (n = 561) had a BMI $\geq$ 35 kg/m^2.

Bariatric Surgery

Men and women with morbid obesity may be eligible for surgical intervention. There are numerous surgical options available, all of which can be divided into two general types, both of which can be performed either as open surgery or laparoscopically: (3)

1. malabsorptive - bypassing parts of the gastrointestinal tract to limit the absorption of food, and
2. restrictive - decreasing the size of the stomach in order for the patient to feel satiated with a smaller amount food

Surgery for morbid obesity is usually considered as a last resort for people who have attempted first-line medical management (e.g., diet, behaviour modification, increased physical activity, and drugs) but who have not lost weight permanently. Surgery is restricted to people with morbid obesity (BMI $\geq$ 40 kg/m^2), or those with a BMI of at least 35 kg/m^2 and serious comorbid conditions. (3;4)

Malabsorptive Interventions

Biliopancreatic Dversion

Biliopancreatic diversion (BPD) involves removing a large part of the stomach to control oral intake, followed by reconstructing the small intestine to divert the bile and pancreatic juices so they meet the ingested food closer to the middle or end of the small intestine. (4)

Roux-en-Y Gastric Bypass

Roux-en-Y gastric bypass (RYGB), or simply gastric bypass, combines restriction and malabsorption techniques to create a small gastric pouch and an intestinal bypass. (4) A common complication resulting from malabsorptive procedures is dumping syndrome, which occcurs when food or liquid enter the small intestine too quickly. Symptoms may include weakness, nausea, cramps, and diarrhea. (4) These may made worse by eating highly refined, high-calorie foods. Some researchers have hypothesized that dumping syndrome aids weight loss by conditioning people to avoid eating sweets. (4)

Restrictive Procedures

Vertical Banded Gastroplasty

Vertical banded gastroplasty (VBG) involves the use of both bands and staples to partition the stomach into two sections, a small vertical pouch in the upper stomach and the adjoining remainder of the stomach. The aim is to cause the patient to feel satiated from a limited intake of food, owing to the reduced capacity of the small upper section of the stomach and the slow emptying of the upper pouch through a small gap into the rest of the digestive system. (4)

Adjustable Gastric Banding

Adjustable gastric banding (AGB) limits food intake by placing a constricting ring completely around the stomach below the junction of the stomach and esophagus. Early bands were nonadjustable, but contemporary designs have an inflatable balloon in their lining to allow the size of the ring to be adjusted to regulate food intake. The bands can be inserted laparoscopically and can be adjusted without surgery by adding or removing an appropriate amount of filler material (saline).

Regulatory Status

Laparoscopic gastric banding devices are licensed by Health Canada. For a full listing of licensed devices see the full evidence-based analysis of bariatric surgery at http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html.

Methods of Analysis

Research Question

What is the effectiveness and cost-effectiveness of bariatric surgery for the management of diabetes in morbidly obese people?

Literature Search

Details of the full literature search can be found in the 2005 evidence-based analysis of bariatric surgery (http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html). Briefly, a literature search was conducted examining published works from January 1996 to December 2004, including OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cumulative Index to Nursing & Allied Health Literature (CINAHL), The Cochrane Library, and the International Agency for Health Technology Assessment/Centre for Review and Dissemination.

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- Case reports, case series
- Studies that did not examine the outcomes of interest

Outcomes of Interest

- Improvement or resolution of diabetes

Assessment of Quality of Evidence

The quality of the studies was examined according to the GRADE Working Group criteria for interventions. (7)

Results of Evidence-Based Analysis

The search identified 15 systematic reviews and 1 large, observational, controlled study. The quality of the included studies is presented below in Table 1.

Table 1: Quality of Evidence of Included Studies

Study Design*	Level of Evidence	Number of Eligible Studies
Large RCT, systematic review of RCTs	1	15 Systematic reviews
Large RCT unpublished but reported to an international scientific meeting	1(g)†	0
Small RCT	2	0
Small RCT unpublished but reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls	3a	1
Non-RCT with historical controls	3b	0
Non-RCT presented at international conference	3(g)	0
Surveillance (database or register)	4a	0
Case series (multisite)	4b	0
Case series (single site)	4c	0
Retrospective review, modeling	4d	0
Case series presented at international conference	4(g)	0

g refers to grey literature; RCT, randomized controlled trial.

*For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (8) The designation "g" was added for preliminary reports of studies presented at international scientific meetings.

Systematic Reviews

A summary of the results of all the health technology assessments is shown in Table 2.

Table 2: Summary of Findings on Diabetes Resolution in Previous Health Technology Assessments

Procedure	Resolution* of Comorbid Conditions, Range (%)
Malabsorptive	
Roux-en-Y gastric bypass	Diabetes: 74–99
Restrictive	
Adjustable gastric banding	Diabetes: 29–92
Vertical banded gastroplasty	Diabetes: 100

* Defined as the stopping of medication taken for comorbid condition.

The most recent of the 15 systematic reviews was by Buchwald et al. (9) and is summarized below.

Systematic Review by Buchwald et al.

Buchwald et al. (9) systematically reviewed and conducted a meta-analysis of studies on bariatric surgery. Their aims were:

- To analyze the impact of bariatric surgery on diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea, as well as on health care economics and disease impact;
- To analyze weight reduction efficacy in the studies selected for the comorbid conditions; and
- To summarize mortality outcomes.

Surgical procedures were grouped into the following categories:

- Gastric banding (including adjustable and nonadjustable bands)
- Gastric bypass (mainly Roux-en-Y variations)
- Gastroplasty (mainly VBG)
- BPD or duodenal switch (including a variety of modifications)
- Mixed and other (biliary intestinal bypass, ileogastrostomy, jejunoileal bypass, and unspecified bariatric)

Results were reported individually for AGB, gastric bypass, gastroplasty, and BPD or duodenal switch procedure groups. Results were also reported for the "total population," which included gastric banding, gastric bypass, gastroplasty and BPD or duodenal switch plus mixed groups and other less common bariatric surgery procedures (biliary intestinal bypass, ileogastrostomy, jejunoileal bypass, and unspecified bariatric surgery). Outcomes of diabetes were grouped into categories of "resolved" and "resolved or improved."

The initial literature review by Buchwald et al. yielded 2738 citations. In the end, 134 fully extracted primary studies were available for meta-analysis, consisting of: 5 RCTs, 28 observational studies, and 101 uncontrolled case series. Most of the studies were done at single centres (n = 126). A few were multicentre studies (n = 5). At least one categorical outcome of interest (proportion of patients with resolution or improvement in diabetes), or one continuous outcome of interest (change in a laboratory or physiological measure e.g., glycosylated hemoglobin[HbA1c]) was reported in each.

Diabetes: Resolution or Improvement

- When defined as being able to discontinue all diabetes-related medications and maintain blood glucose levels within the normal range, evidence for improvement in type 2 diabetes and impaired glucose tolerance was found for all of the surgery types.
- Within the studies reporting resolution of diabetes, 1,417 of 1,846 patients achieved complete resolution (meta-analytic mean [95% CI], 76.8% [70.7%–82.9%]). Within studies reporting both resolution and improvement, or only improvement, 414 of 485 patients achieved resolution or improvement (meta-analytic mean, 86.0% [95% CI, 78.4%–93.7%].
- Diabetes outcomes differed when analyzed according to the type of procedures. For each of the four primary procdure types the level of effect of diabetes resolution was:
  - BPD or duodenal switch: 98.9% [95% CI, 96.8%–100%]
  - Gastric bypass: 83.7% [95% CI, 77.3%–90.1%]
  - Gastroplasty: 71.6% [95& CI, 55.1%–88.2%]
  - Gastric banding: 47.9% [95% CI, 29.1%–66.7%]

The outcomes for diabetes reported by Buchwald et al. are shown in Table 3.

Table 3: Outcomes for Diabetes After Bariatric Surgery

Type of Surgery	Resolution* of Diabetes, mean% (95% CI) [n resolved/n evaluated]	Resolution or Improvement of Diabetes†, mean% (95% CI) [n resolved or improved/n evaluated]
All types of bariatric surgery	76.8% (70.7% to 82.9%) [1417/1846]	86.0% (78.4% to 93.7%) [414/485]
Roux-en-Y gastric bypass	83.7% (77.3% to 90.1%) [829/989]	93.2% (79.3% to 100.0%) [115/127]
Vertical banded gastroplasty	71.6% (55.1% to 88.2%) [45/66]	90.8% (76.2% to 100%) [34/38]
Other banding (fixed and variable)	47.9% (29.1% to 66.7%) [98/205]	80.8% (72.2% to 89.4%) [174/217]

* Studies reporting the number of patients in which diabetes disappeared or no longer required therapy.

† Studies reporting number of patients in both of these 2 categories (in which case the 2 were summed), as well as studies that only used the term "improved", but not the studies reporting only resolution.

(From Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K et al. Bariatric surgery: a systematic review and meta-analysis. JAMA 2004; 292:1724-1737).

Changes in Glycoslylated Hemoglobin (HbA1c)

- The weighted mean change of HbA1c in patients with diabetes and glucose intolerance (for both gastric bypass and gastric banding combined) was -2.70% (range -5.0% to -0.70%).
- The weighted mean change of HbA1c in patients receiving gastric bypass or gastric banding was -3.99% (range -5.0% to -0.70%) and -1.34% (range -1.60% to -0.94%), respectively.
- Weighted mean changes of HbA1c were not reported for BPD or duodenal switch or gastroplasty.

Operative Mortality

By surgery type, the rate of operative mortality was:

- 0.1% for the purely restrictive procedures (2,297 patients receiving banding and 749 patients receiving gastroplasty)
- 0.5% among 5,644 patients receiving gastric bypass procedures,
- 1.1% among 3,030 patients undergoing BPD or duodenal switch procedures.

Buchwald et al.'s Conclusions:

- Resolution of diabetes appeared to be more prevalent following treatment with the predominantly malabsorptive procedures (BPD or duodenal switch) and the mixed malabsorptive/restrictive gastric bypass, in contrast to the purely restrictive gastroplasty and gastric banding procedures.
- There appeared to be a gradation of diabetes resolution as a function of the operative procedure itself:
  - 98.9% for BPD or duodenal switch
  - 83.7% for gastric bypass
  - 71.6% for gastroplasty
  - 47.9% for gastric banding
- Diabetes resolution/improvement after surgery may be related to changes in gut-related hormones.

- The operative 30-day mortality rates of 0.1% for the restrictive procedures, 0.5% for gastric bypass, and 1.1% for BPD or duodenal switch, compare favourably with the accepted operative mortality rates for other major surgical procedures.

Limitations of the Meta-Analysis by Buchwald et al.

- As the authors commented: "The heterogeneity of the immediate postoperative and long-term morbidity data did not allow for meta-analysis."
- The postsurgical follow-up time when the outcomes of interest data were extracted varied across studies. The authors stated: "Given the emphasis on comorbidities, weight loss efficacy outcomes were preferentially extracted at time points for which comorbidity changes were reported." Therefore, time points may have varied substantially. For example, the RCTs included by Buchwald et al. had follow-ups that ranged from 6 to 36 months.
- The inclusion criteria (studies of any design, surgical outcome, guideline, health care economics, or disease impact) were very broadly defined.

Swedish Obese Subjects Registry and Intervention Study: 10-Year Outcomes

The SOS study started in 1991 as a registry and an intervention study of obese patients in Sweden. (10) Sjostrom et al. reported follow-up data for patients who had been enrolled for at least 2 years (4,047 patients) or 10 years (1,703 patients). The primary aim of the intervention study was to determine if the 10-year mortality and morbidity rates among a surgically treated group of obese patients differed from those of a conventionally treated group that was not expected to have sustained weight loss. The surgical techniques examined were gastric banding, VBG, and gastric bypass. The surgical group was recruited from the registry study and from pre-existing waiting lists at participating surgical departments

For each surgical patient, a computerized matching procedure selected an optimal control patient from the registry based on a consideration of 18 variables. All surgical and nonsurgical patients enrolled in the SOS study returned for complete medical examinations at 3 and 6 months, and at 1, 2, 3, 4, 6, 8, and 10 years post-surgery or inclusion.

The inclusion criteria for the intervention study were as follows:

- Age 37 to 60 years
- BMI > 34 kg/m^2 for men, and > 38 kg/m^2 for women

The exclusion criteria were as follows:

- Previous weight reduction surgery
- Previous gastric operations, or a gastric or duodenal ulcer in the last 6 months
- Active malignancy in the last 5 years
- Myocardial infarction in the last 6 months
- Bulimic eating pattern
- Abuse of alcohol or drugs
- Psychological problems suspected to result in poor cooperation
- Regular use of cortisone or nonsteroidal anti-inflammatory drugs
- "Other severe illnesses"

At least 10 years before the analysis, 851 surgically treated patients had been enrolled in the SOS study. These patients were contemporaneously matched with 852 obese control patients. At the time of matching, compared with control patients, the surgically treated patients:

- Were younger (46.1 years versus 47.4 years; P = .005)
- Were heavier (119.2 kg, versus 116.1 kg; P < .001)
- Had a higher mean plasma insulin level (22.8 mU per litre, versus 20.9 mU per litre; P = .009)

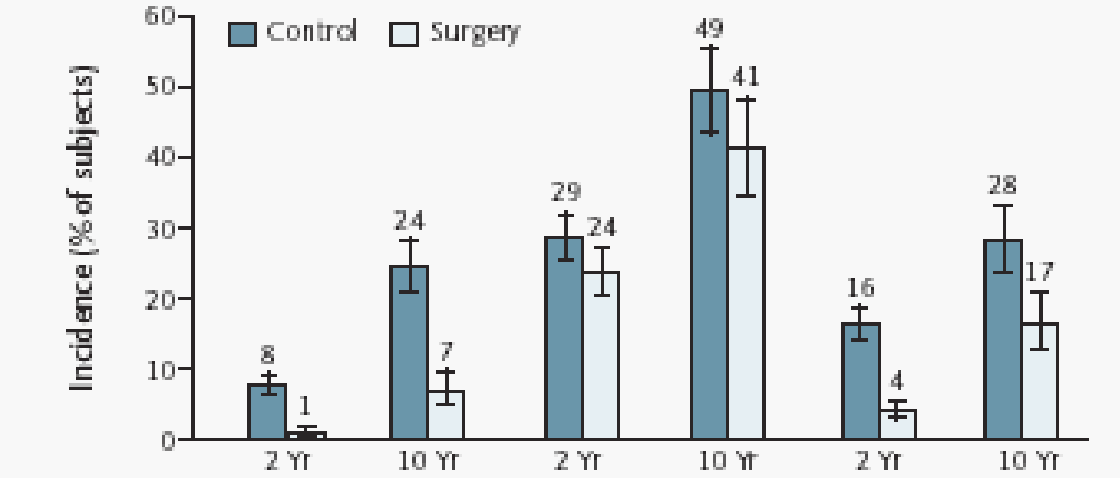
Risk Factors

Table 4 (page 19) shows the changes in weight and risk factors for the patients in the surgery and control groups. Glucose and insulin levels increased in the control group but significantly decreased in the surgically treated group, 2 and 10 years after surgery. Insulin levels improved more for patients who had gastric bypass than for those who underwent banding.

Incidence of Diabetes

The criterion for diagnosing diabetes was a fasting blood glucose level of ≥110 mg per decilitre corresponding to a fasting plasma glucose level of ≥126 mg per decilitre (7.0 mmol per litre). The incidence of diabetes was significantly lower ($P < .03$) in the surgically treated group compared to the control group at 2 and 10 years (Figure 1).

Figure 1: Incidence of Diabetes, Hypertension, and Hyperuricemia Among Subjects in the SOS Study at 2 and 10 Years



No. of subjects						
Control	1402	539	770	279	1017	382
Surgery	1489	517	623	215	1044	342
Odds ratio	0.14	0.25	0.78	0.75	0.22	0.49
95% CI	0.08–0.24	0.17–0.38	0.60–1.01	0.52–1.08	0.15–0.31	0.34–0.71
P value	<0.001	<0.001	0.06	0.13	<0.001	<0.001

Data are for patients completing 2 and 10 years of the study. The bars and values above them indicate unadjusted incidence rates; vertical bars show the corresponding 95% CI. The odds ratios, CIs, and *P* values have been adjusted for sex, age, and BMI.

Table 4: Percentage Changes in Weight, Anthropometric Variables, Risk Factors, and Energy Intake at 2 and 10 Years

Variable	Changes at 2 Yr*			Changes at 10 Yr*			Changes at 10 Yr in Surgery Subgroups		
	Control Group (N=1660)	Surgery Group (N=1845)	Difference (95% CI)	Control Group (N=627)	Surgery Group (N=641)	Difference (95% CI)	Banding (N=156)	Vertical Banded Gastroplasty† (N=451)	Gastric Bypass† (N=34)
	percent			*percent*				*percent*	
Weight	0.1	−23.4	22.2 (21.6 to 22.8)§	1.6	−16.1	16.3 (14.9 to 17.6)§	−13.2	−16.5¶	−25.0§
Height	−0.01	−0.06	0.06 (0.02 to 0.10)¶	−0.3	−0.3	−0.01 (−0.12 to 0.10)	−0.2	−0.3	−0.8§
BMI	0.1	−23.3	22.1 (21.5 to 22.7)§	2.3	−15.7	16.5 (15.1 to 17.8)§	−12.8	−16.0¶	−23.8§
Waist	0.2	−16.9	16.0 (15.4 to 16.5)§	2.8	−10.1	11.3 (10.3 to 12.4)§	−7.6	−10.2¶	−19.3§
Systolic blood pressure	0.5	−4.4	2.8 (2.1 to 3.6)§	4.4	0.5	1.1 (−0.3 to 2.6)	2.1	0.4	−4.7
Diastolic blood pressure	0.3	−5.2	3.2 (2.4 to 3.9)§	−2.0	−2.6	−2.3 (−3.5 to −1.0)§	−1.4	−2.5	−10.4‖
Pulse pressure	3.2	0.6	−0.5 (−2.3 to 1.3)	18.0	10.8	3.5 (0.1 to 6.9)¶	13.8	10.1	6.3
Glucose	5.1	−13.6	16.6 (15.0 to 18.3)§	18.7	−2.5	18.4 (14.7 to 22.1)§	−0.8	−2.5	−10.0
Insulin	10.3	−46.2	51.4 (48.0 to 54.8)§	12.3	−28.2	30.3 (23.9 to 36.6)§	−25.3	−27.2	−54.0§
Uric acid	−0.4	−14.9	13.5 (12.5 to 14.6)§	3.9	−6.2	8.8 (6.4 to 11.1)§	−5.2	−6.1	−12.3
Triglycerides	6.3	−27.2	29.9 (27.4 to 32.5)§	2.2	−16.3	14.8 (10.4 to 19.1)§	−18.0	−14.9	−28.0¶
HDL cholesterol	3.5	22.0	−18.7 (−20.1 to −17.3)§	10.8	24.0	−13.6 (−16.5 to −10.6)§	20.4	23.5	47.5¶
Total cholesterol	0.1	−2.9	1.0 (0.1 to 1.9)¶	−6.0	−5.4	−2.0 (−0.2 to −3.8)¶	−5.0	−5.0	−12.6§
Energy intake	−2.8	−28.6	19.1 (16.0 to 22.2)§	−1.0	−20.7	11.6 (8.1 to 15.0)§	−19.7	−21.6	−12.6

* Data are for all subjects who completed 2 and 10 years of the study and are independent of diagnosis and medications at or after baseline. The changes within each treatment group are unadjusted, whereas the differences between the groups in the changes have been adjusted for sex, age, body-mass index (BMI), and the baseline level of the respective variable. CI denotes confidence interval, and HDL high-density lipoprotein.

† For values within each group, minus signs denote decreases; for differences between the groups, minus signs denote smaller reductions or (in the case of HDL cholesterol) larger increases in the surgical group than in the control group.

‡ P values are for the comparison with the banding subgroup.

§ P<0.001.

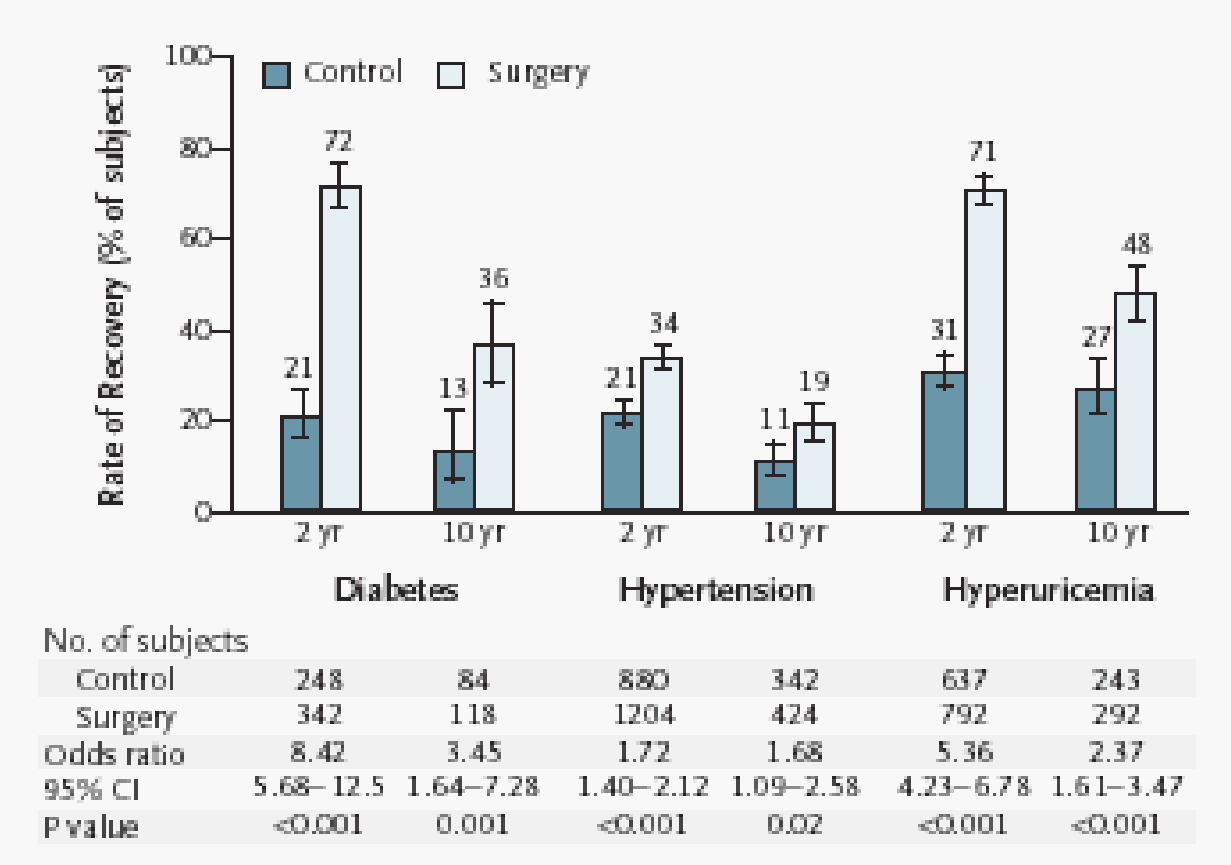
¶ P<0.05.

‖ P<0.10.

Recovery of Diabetes

Recovery from diabetes was significantly improved in the surgical group after 2 and 10 years (Figure 2).

Figure 2: Recovery from Diabetes, Lipid Disturbances, Hypertension, and Hyperuricemia at 2 and 10 Years in Surgically Treated Patients and Obese Controls



No. of subjects						
Control	248	84	880	342	637	243
Surgery	342	118	1204	424	792	292
Odds ratio	8.42	3.45	1.72	1.68	5.36	2.37
95% CI	5.68–12.5	1.64–7.28	1.40–2.12	1.09–2.58	4.23–6.78	1.61–3.47
P value	<0.001	0.001	<0.001	0.02	<0.001	<0.001

Data are for patients who completed 2 and 10 years of the study. The bars and the values above them indicate unadjusted rates of recovery; vertical bars represent the corresponding 95% CIs. The odds ratios, CIs, and *P* values have been adjusted for sex, age, and body-mass index at the time of inclusion in the intervention study.

Death and Adverse Effects

Five (0.25%) of 2010 patients who had surgery died postoperatively. Postoperative complications occurred in 151/1164 patients (13.0%), including:

- 0.5% bleeding
- 0.8% embolism or thrombosis
- 1.8% wound complications
- 2.1% deep infections (leakage or abscess)
- 6.1% pulmonary complications
- 4.8% other complications

In 26 (2.2%) patients, complications were serious enough to require reoperation.

Limitations of the SOS study:

- By definition, the inclusion criteria were not specific to "morbidly obese" patients (BMI > 40 kg/m^2 or > 35 kg/m^2 with comorbid illnesses). However, the baseline BMI was 41 kg/m^2.
- Patients were not randomized to groups. The research ethics boards of the participating centres considered the high mortality rate initially observed in the 1980s (1%–5%) as cause to preclude randomization.
- The nonsurgical treatment was not standardized and ranged from sophisticated lifestyle intervention, to behaviour modification, to no treatment. Nonetheless, this study can be considered pragmatic and reflective of 'real life.'
- It is unknown if risk factors return to baseline in the long term (10–20 years).

Quality of the Evidence

Table 5 shows the quality of evidence for the use of bariatric surgery for the resolution or improvement of diabetes in morbidly obese people according to GRADE quality-of-evidence criteria. Overall, the quality of evidence for bariatric surgery for the resolution or improvement of diabetes in morbidly obese people is moderate.

Conclusions

There is evidence that bariatric surgery is effective for the improvement and resolution of diabetes in patients who are morbidly obese (BMI $\geq$35 kg/m^2).

Comparison of various bariatric techniques:

- Retrospective subgroup analyses from a large observational study showed greater improvement and resolution of diabetes in malabsorptive than purely restrictive techniques.
- There is evidence from a meta-analysis that malabsorptive techniques are better than other banding techniques in terms of improvement and resolution of diabetes.
- No prospective, long-term direct comparison is available between malabsorptive and restrictive techniques.

Table 5: GRADE Quality of Evidence for Bariatric Surgery for the Resolution or Improvement of Diabetes

Outcome	Quality Assessment					Summary of Findings		
	Design	Quality	Consistency	Directness	Other	No. of Patients	Effect	Quality
Improvement in HbA1c in diabetic and glucose intolerant patients	Meta-analysis	Moderate*	Consistent	Direct	None	n=171	-2.70% (-5.0% to -0.70%) weighted mean change (range)	Moderate
Resolution or improvement of diabetes *(Studies reporting combination as well as studies that only used the term "improved", but not the studies reporting only resolution)*	Meta-analysis	Moderate*	Consistent	Direct	None	414/485 (n resolved or improved/n evaluated)	86.0% (78.4% to 93.7%) mean% (95% C])	Moderate
Resolution of diabetes *(diabetes disappeared or no longer required therapy)*	Meta-analysis	Moderate*	Consistent	Direct	None	1417/1846 (n resolved/n evaluated)	76.8% (70.7% to 82.9%) mean% (95% CI)	Moderate
Recovery of diabetes *(fasting plasma glucose level of less than 126 mg per decilitre [7.0 mmol per litre])*	Observational prospective controlled study	Moderate*	Consistent	Some uncertainty†	Some uncertainty‡	control n=84 intervention n=118	3.45 (1.64 to 7.28) OR (95% CI) at 10 yrs	Moderate

* Downgraded due to study design (not randomized controlled trial)

† Unlikely to be an important uncertainty. Inclusion criteria for the SOS study not specific to conventional definition of "morbidly obese" patients (BMI $\geq$ 40 or $\geq$ 35 kg/m^2 with comorbid conditions)

‡ Unlikely to be an important uncertainty. Control group not standardized, however, this lends to the pragmatic nature of the study.

Glossary

Body Mass Index (BMI)	Body weight expressed in kilograms (kg) divided by height expressed in square metres (m^2).
Excess weight loss	Percentage of excess weight loss = (weight loss/excess weight) x 100 Where excess weight = total preoperative weight – ideal weight
Morbid obesity	Body mass index greater than 40 kg/m^2 or 35 kg/m^2 with serious comorbid conditions.
Obesity	Body mass index greater than 30 kg/m^2.

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