Lifestyle, Diabetes, and Cardiovascular Risk Factors 10 Years after Bariatric Surgery

Lars Sjöström, M.D., Ph.D., Anna-Karin Lindroos, Ph.D., Markku Peltonen, Ph.D., Jarl Torgerson, M.D., Ph.D.,
Claude Bouchard, Ph.D., Björn Carlsson, M.D., Ph.D., Sven Dahlgren, M.D., Ph.D., Bo Larsson, M.D., Ph.D.,
Kristina Narbro, Ph.D., Carl David Sjöström, M.D., Ph.D., Marianne Sullivan, Ph.D., and Hans Wedel, Ph.D.,
for the Swedish Obese Subjects Study Scientific Group*

ABSTRACT

BACKGROUND

Weight loss is associated with short-term amelioration and prevention of metabolic and cardiovascular risk, but whether these benefits persist over time is unknown.

METHODS

The prospective, controlled Swedish Obese Subjects Study involved obese subjects who underwent gastric surgery and contemporaneously matched, conventionally treated obese control subjects. We now report follow-up data for subjects (mean age, 48 years; mean body-mass index, 41) who had been enrolled for at least 2 years (4047 subjects) or 10 years (1703 subjects) before the analysis (January 1, 2004). The follow-up rate for laboratory examinations was 86.6 percent at 2 years and 74.5 percent at 10 years.

RESULTS

After two years, the weight had increased by 0.1 percent in the control group and had decreased by 23.4 percent in the surgery group (P<0.001). After 10 years, the weight had increased by 1.6 percent and decreased by 16.1 percent, respectively (P<0.001). Energy intake was lower and the proportion of physically active subjects higher in the surgery group than in the control group throughout the observation period. Two- and 10-year rates of recovery from diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, hypertension, and hyperuricemia were more favorable in the surgery group than in the control group, whereas recovery from hypercholesterolemia did not differ between the groups. The surgery group had lower 2- and 10-year incidence rates of diabetes, hypertriglyceridemia, and hyperuricemia than the control group; differences between the groups in the incidence of hypercholesterolemia and hypertension were undetectable.

CONCLUSIONS

As compared with conventional therapy, bariatric surgery appears to be a viable option for the treatment of severe obesity, resulting in long-term weight loss, improved lifestyle, and, except for hypercholesterolemia, amelioration in risk factors that were elevated at baseline.

From the Departments of Body Composition and Metabolism (L.S., A.-K.L., B.C., K.N., M.S.) and Anesthesiology (B.L., C.D.S.), Sahlgrenska University Hospital, Göteborg, Nordic University of Public Health (H.W.), Göteborg; the Medical Department, Norra Älvsborgs Läns Hospital, Trollhättan (J.T.); and Börjegatan 10B, Uppsala (S.D.) — all in Sweden; the Department of Epidemiology and Health Promotion, National Public Health Institute, Helsinki, Finland (M.P.); and Pennington Biomedical Research Center, Louisiana State University, Baton Rouge (C.B.). Address reprint requests to Dr. Lars Sjöström at SOS Secretariat, Sahlgrenska University Hospital, S-413 45 Göteborg, Sweden.

OBESITY IS ASSOCIATED WITH IN-creased morbidity and mortality.[1] The increased morbidity is assumed to be mediated mainly by insulin resistance, diabetes, hypertension, and lipid disturbances — conditions that affect one quarter of the North American population.[2,3] Over the short term (one to three years), lifestyle changes resulting in weight loss result in improvements in insulin resistance,[4] diabetes,[5-7] hypertension,[8] and lipid disturbances[9-11] or in the prevention of these conditions. In contrast, several (but not all[12]) observational epidemiologic studies have suggested that weight loss is associated with increased overall mortality and mortality from cardiovascular causes, not only among thin[13] and normal-weight[14] subjects, but also among obese subjects.[15-17]

One overall aim of the Swedish Obese Subjects (SOS) Study was to address this apparent discrepancy between the effects of weight loss on risk factors and hard end points. In the current study, we assessed changes in cardiovascular risk factors over follow-up periods of 2 and 10 years in surgically treated subjects and contemporaneously matched, conventionally treated control subjects. Changes in energy intake and physical activity over the 10-year period were also evaluated.

METHODS

STUDY DESIGN

The SOS Study was a prospective, nonrandomized, intervention trial involving 4047 obese subjects. The outcomes in a surgically treated group were compared with those in a contemporaneously matched, conventionally treated control group.[18] For the purposes of this report, all subjects who had been enrolled at least 2 years (4047 subjects) or 10 years (1703 subjects) before the date of the analysis (January 1, 2004) were included. The 4047 subjects were all those who were finally enrolled in the SOS intervention study.

The seven ethics review boards involved in the SOS Study approved the protocol. Informed consent was obtained both from the subjects in the registry study and from those in the intervention study.

Registry Examination

As a result of recruitment campaigns through the mass media and at 480 primary health care centers in Sweden, 11,453 subjects living in participating counties (18 of the 24 counties in Sweden) sent standardized application forms to the SOS secretariat between September 1987 and November 2000. All 8966 applicants who fulfilled age and weight-for-height criteria were provided written information about the surgical and nonsurgical treatments offered by the SOS Study. They also completed questionnaires and were asked whether they wanted to participate as surgically treated or medically treated subjects. All 7593 subjects who returned their questionnaires were offered participation in the registry examination, and 6905 completed that examination. According to individual treatment preferences and data obtained from the registry examination, eligible subjects were assigned either to the surgery group of the intervention study or to a pool of potential control subjects.

Surgical Visit

The eligibility of candidates for surgery was determined by computer, and the result was manually checked by the examining surgeon. If a candidate was eligible, an operation was scheduled. On average, the surgical visit occurred eight months after the registry examination and five months before the operation itself, which marked the start of the intervention study. Eight weeks before a subject underwent surgery, an optimal matched control was selected, on the basis of variables described below, from among the subjects in the pool of potential controls. Thus, matching was contemporaneous and was based on registry data, both for the surgically treated subjects and for the control subjects.

Inclusion Examination

The inclusion examination for subjects for whom surgery was planned and for their matched controls was undertaken 4 weeks before surgery (i.e., 4 weeks before the start of the intervention study), on average 13 months after the registry examination. This delay was a consequence of the waiting time for surgery at the 25 participating surgical departments. The controls underwent their manual eligibility check at the time of the inclusion examination.

Intervention Study

The intervention study for a surgically treated subject and his or her matched control began on the day of the surgically treated subject's operation. The dates of all subsequent examinations (at 0.5, 1.0, 2.0, 3.0, 4.0, 6.0, 8.0, and 10.0 years) for both sub-

jects were calculated in relation to the date of surgery. Inclusion criteria for the intervention study were a body-mass index (calculated as the weight in kilograms divided by the square of the height in meters) of 34 or more (for men) or 38 or more (for women) and an age of 37 to 60 years. Exclusion criteria, described elsewhere,[18] were minimal and were aimed at ensuring that the subjects in the surgery group could tolerate the operation. Identical inclusion and exclusion criteria were used in the two study groups. Subjects with diabetes, hypertension, or lipid disturbances were not excluded, nor were subjects who had had a myocardial infarction or a stroke more than six months before inclusion.

Matching

The SOS Study was not randomized; rather, subjects were matched according to the method of sequential treatment assignment,[19] with balancing of confounding factors measured at baseline in prospective, nonrandomized intervention trials. The following 18 matching variables were considered[18]: sex, age, weight, height, waist and hip circumferences, systolic blood pressure, serum cholesterol and triglyceride levels, smoking status, diabetes, menopausal status, four psychosocial variables with documented associations with the risk of death, and two personality traits related to treatment preferences. The investigators had no influence on the computerized matching process.

Clinical and Biochemical Assessments

At each visit, measurements of weight, height, waist circumference, and blood pressure were obtained. In addition, energy intake (in kilocalories per day) was estimated with use of the validated SOS Dietary Questionnaire.[20,21] Subjects were also asked to rate their physical activity during leisure and work time on a scale from 1 to 4, in which 1 denotes sedentary activity and 4 regular strenuous exercise.[20,22] In the current report, ratings were dichotomized; a rating of 1 corresponded to physically inactive and ratings of 2, 3, or 4 to physically active.

Biochemical variables were measured at the registry examination, at the inclusion examination (year 0 of the intervention study), and at years 2 and 10 of the intervention study (Table 1). All blood samples, which were obtained in the morning after a 10-to-12-hour fast, were analyzed at the Central Laboratory of Sahlgrenska University Hospital (accredited according to European Norm EN45001).

The schedule, questionnaires, blood pressure and anthropometric measurements, and laboratory examinations were identical for surgically treated subjects and their matched controls.

TREATMENTS

The surgically treated subjects underwent fixed or variable banding, vertical banded gastroplasty, or gastric bypass.[23] The contemporaneously matched controls received the nonsurgical treatment for obesity that was customary for the center at which they were registered. No attempt was made to standardize the nonsurgical treatment, which ranged from sophisticated lifestyle intervention and behavior modification to, in some practices, no treatment whatsoever. No antiobesity drugs were approved in Sweden until 1998.

CRITERIA FOR HEALTH AND DISEASE

Criteria for health and disease were based on cutoff values or the use of medication for the condition in question, according to principles specified elsewhere.[11] However, in the course of the study, the criterion for diagnosing diabetes decreased to a fasting blood glucose level of 110 mg per deciliter (6.1 mmol per liter) or greater, corresponding to a fasting plasma glucose level of 126 mg per deciliter (7.0 mmol per liter) or greater, in accordance with the new criteria of the American Diabetes Association.[24] Similarly, the criterion for diagnosing hypertension decreased to a systolic pressure of 140 mm Hg or greater or a diastolic pressure of 90 mm Hg or greater.[25] Other criteria included the following: hypercholesterolemia (cholesterol level, 201 mg per deciliter [5.2 mmol per liter] or greater[26]); hypertriglyceridemia (triglyceride level, 150 mg per deciliter [1.7 mmol per liter] or greater[26]); a low level of high-density-lipoprotein (HDL) cholesterol (less than 39 mg per deciliter [1.0 mmol per liter][26]); and hyperuricemia (uric acid level, 7.6 mg per deciliter [450 μmol per liter] or greater in men and 5.7 mg per deciliter [340 μmol per liter] or greater in women).

OUTCOME VARIABLES

The primary outcome variable in the SOS Study as a whole was overall mortality. Three secondary outcome variables are described in this report. The first was the difference between the surgery group and the control group with respect to changes in body weight, risk factors, energy intake, and the propor-

Table 1. Characteristics of the Subjects at the Time of Matching and at the Time of the Inclusion Examination of the Intervention Study.*

Characteristic	Matching Data, Subjects Who Completed 10 Yr		Matching Data, Subjects Who Did Not Complete 10 Yr†		Inclusion Data, Subjects Who Completed 2 Yr		Inclusion Data, Subjects Who Completed 10 Yr	
	Control Group (N=627)	Surgery Group (N=641)‡	Control Group (N=225)§	Surgery Group (N=210)¶	Control Group (N=1660)	Surgery Group (N=1845)‡	Control Group (N=627)	Surgery Group (N=641)‡
Age (yr)	47.3±6.1	46.1±5.6‖	47.7±6.2**	46.3±6.0**	48.8±6.2	47.4±5.9‖	48.4±6.3	47.0±5.6‖
Male sex (%)	31.4	30.6**	32.0**	34.8**	29.7	29.3**	31.4	30.6**
Smoker (%)	19.5	25.4††	31.6‖	39.5‖	19.5	24.4‖	21.1	24.7**
Weight (kg)	115.7±15.7	118.4±15.7††	117.1±17.1**	121.4±16.7††	114.6±16.4	120.6±16.4‖	113.9±16.7	120.0±16.4‖
Height (m)	1.69±0.09	1.69±0.09**	1.69±0.09**	1.69±0.09**	1.69±0.09	1.69±0.09**	1.69±0.09	1.69±0.09**
Body-mass index	40.5±4.2	41.3±4.0‖	40.8±4.8**	42.3±4.9††	40.0±4.6	42.3±4.4‖	39.9±4.6	41.9±4.2‖
Waist (cm)	120.9±10.0	123.2±10.5‖	123.5±11.8††	126.5±10.6‖	120.0±11.0	125.5±10.8‖	119.3±11.2	124.0±10.9‖
Blood pressure (mm Hg)								
Systolic	140.1±18.8	140.6±19.1**	144.0±20.5††	139.9±17.1**	137.5±17.9	143.5±18.8‖	138.4±17.6	143.8±19.3‖
Diastolic	87.3±10.6	88.4±11.4**	89.3±11.4††	87.8±11.1**	84.7±10.5	88.7±11.2‖	85.8±10.6	89.6±11.3‖
Glucose (mmol/liter)	5.3±1.8	5.4±2.0**	5.7±2.3††	5.6±2.1**	5.2±1.9	5.4±2.1‖	5.1±1.7	5.5±2.1‖
Insulin (mU/liter)	20.7±12.6	22.1±12.7**	21.5±12.7**	24.9±23.3**	18.0±11.5	21.2±12.6‖	18.3±11.2	21.2±11.4‖
Uric acid (μmol/liter)	354.7±84.1	358.1±84.0**	360.1±83.1**	357.5±83.3**	353.3±79.3	359.4±80.1††	357.7±78.9	366.2±84.2**
Triglycerides (mmol/liter)	2.18±1.47	2.27±1.76**	2.58±2.45††	2.32±1.23**	2.01±1.35	2.23±1.52‖	2.12±1.49	2.30±1.56††
Serum cholesterol (mmol/liter)								
HDL	1.23±0.34	1.22±0.30**	1.22±0.30**	1.19±0.28**	1.19±0.29	1.20±0.28‖	1.18±0.29	1.19±0.28**
Total	5.84±1.12	5.97±1.13††	6.07±1.22††	6.05±1.13**	5.60±1.06	5.85±1.12‖	5.76±1.10	6.02±1.13‖

* Plus–minus values are means ±SD. To convert the values for glucose to milligrams per deciliter, divide by 0.05551. To convert the values for insulin to picomoles per liter, multiply by 7.175. To convert the values for uric acid to milligrams per deciliter, divide by 59.48. To convert the values for triglycerides to milligrams per deciliter, divide by 0.01129. To convert the values for cholesterol to milligrams per deciliter, divide by 0.02586. HDL denotes high-density lipoprotein.

† Among the subjects who did not complete 10 years of the study, the controls were older and had higher systolic blood pressure than the surgically treated subjects, whereas the surgically treated subjects were heavier and had a larger waist circumference (P values not shown).

‡ P values are for the comparison with data for subjects in the control group under the indicated conditions.

§ P values are for the comparison with matching data for subjects in the control group who completed the 10-year examination.

¶ P values are for the comparison with matching data for subjects in the surgically treated group who completed the 10-year examination.

‖ P<0.001.

** P values indicate that the difference is not significant.

†† P<0.05.

tion of subjects who were physically active. These calculations included all the subjects and did not take medication use or baseline disease into account. The next secondary outcome was the difference between the two groups in the incidence of risk conditions over 2- and 10-year periods among the subjects unaffected by those risk conditions at baseline (i.e., the primary preventive effect of weight loss). The final secondary outcome was the difference between the two groups in the rate of recovery from risk conditions over 2- and 10-year periods among those who had been affected by those conditions at baseline.

STATISTICAL ANALYSIS

The intervention study had 80 percent power (at an alpha level of 0.05) to detect a difference in total mortality between a group of 2000 surgically treat-

ed subjects and a group of 2000 controls followed for 10 years.[18] To evaluate the originally chosen treatment strategy according to pragmatic clinical-treatment principles,[27] subjects in the surgery group who completed 10 years of the study and who underwent reoperation (band removal in 15 subjects and conversion to another type of surgical treatment in 62) or who had a spontaneous band disruption (in 2 subjects) were considered surgically treated and remained in their original treatment subgroup. Similarly, control subjects who later underwent bariatric surgery (34 subjects) were considered controls throughout the study. All analyses presented here are based on data from subjects who completed 2 or 10 years of the study. However, for confirmatory reasons, additional calculations were performed by replacing all missing data with baseline data, according to the "baseline observation carried forward" method.[28]

Mean values and standard deviations are used to describe the baseline characteristics of the two treatment groups. Analysis of covariance was used to test for differences in changes in risk factors between the two treatment groups. Treatment group was included as a covariate, as were sex, age, body-mass index, and the baseline level of each studied variable. Adjusted differences, with 95 percent confidence intervals, are reported. Logistic regression was used to compare the incidence of disease and rates of recovery. The data were adjusted for sex, age, and body-mass index at baseline, and the resulting differences in risk are reported as odds ratios with 95 percent confidence intervals. All reported P values are two-sided. Statistical analyses were carried out with use of the Stata statistical package (version 7.0).[29]

RESULTS

SUBJECTS

At least 10 years before the date of the current analysis, 851 surgically treated subjects had been enrolled in the SOS Study. The surgically treated subjects had been contemporaneously matched with 852 obese control subjects. The matching resulted in two groups that were not significantly different with respect to sex distribution, height, blood pressure, blood glucose level, serum lipid levels, or serum uric acid level (data not shown). At the time of matching, the surgically treated subjects were slightly younger than the control subjects (46.1 vs. 47.4 years of
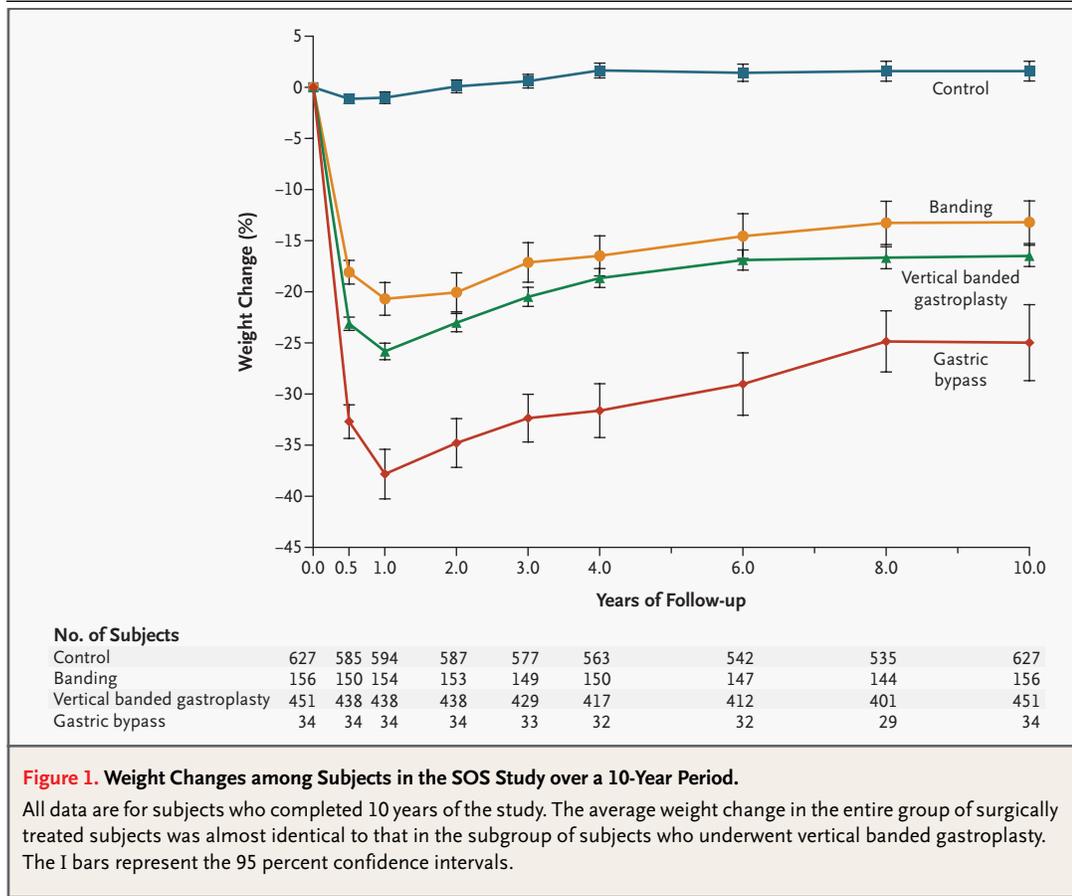
age, P=0.005), were heavier (119.2 vs. 116.1 kg, P<0.001), and had a slightly higher plasma insulin level (22.8 vs. 20.9 mU per liter, P=0.009).

Of the 851 surgically treated subjects, 210 (24.7 percent) had been lost to follow-up by the time of the 10-year laboratory examination; of the 852 controls, 225 (26.4 percent) had been lost to follow-up by that time (this difference was not significant). Thus, 641 surgically treated subjects and 627 controls completed the 10-year examination. Of the 2010 surgically treated subjects and the 2037 controls who participated in the SOS Study, 165 (8.2 percent) and 377 (18.5 percent), respectively, did not participate in the two-year examination (P<0.001). Thus, 1845 surgically treated subjects and 1660 controls completed the two-year examination.

Table 1 shows matching data from the registry examination for surgically treated and control subjects, according to whether they completed or did not complete 10 years of the study. In general, those who completed 10 years and those who dropped out before 10 years had similar matching values, although some differences between them reached statistical significance, both among the surgically treated subjects and among the controls. Table 1 also shows data obtained at the inclusion examination of the intervention study for subjects who completed 2 and 10 years of the study.

CHANGES IN WEIGHT

The changes in weight among the subjects followed for 10 years are shown in Figure 1. Weight change was maximal after six months in the control group (mean [±SD] change, −1±6 percent [where the minus sign denotes a decrease]) and maximal after one year in the three surgical subgroups (gastric bypass, −38±7 percent; vertical banded gastroplasty, −26±9 percent; and banding, −21±10 percent). After two years, weight had increased by 0.1 percent in the control group and had decreased by 23.4 percent in the surgical group (P<0.001) (Table 2). After 10 years, the controls had increased by 1.6±12 percent over the inclusion weight, whereas the maintained weight change was −25±11 percent in the gastric-bypass subgroup, −16.5±11 percent in the subgroup that underwent vertical banded gastroplasty, and −13.2±13 percent in the banding subgroup. The average weight changes in the entire group of surgically treated subjects are listed in Table 2 and were almost identical to those shown in the curve for the subgroup that underwent vertical banded

No. of Subjects									
Control	627	585	594	587	577	563	542	535	627
Banding	156	150	154	153	149	150	147	144	156
Vertical banded gastroplasty	451	438	438	438	429	417	412	401	451
Gastric bypass	34	34	34	34	33	32	32	29	34

Figure 1. Weight Changes among Subjects in the SOS Study over a 10-Year Period.
All data are for subjects who completed 10 years of the study. The average weight change in the entire group of surgically treated subjects was almost identical to that in the subgroup of subjects who underwent vertical banded gastroplasty. The I bars represent the 95 percent confidence intervals.

gastroplasty (Fig. 1). The fractions of subjects who, after completing 10 years of the study, had a loss of less than 5 percent of their initial weight were 72.7 percent (control group), 8.8 percent (gastric-bypass subgroup), 13.8 percent (vertical-banded-gastroplasty subgroup), and 25.0 percent (banding subgroup). The fractions of subjects achieving 20 percent weight loss or more over the 10-year period were 3.8 percent (control group), 73.5 percent (gastric-bypass subgroup), 35.2 percent (vertical-banded-gastroplasty subgroup), and 27.6 percent (banding subgroup).

LIFESTYLE CHANGES

Mean energy intake at the time of inclusion in the intervention study was 2882 kcal per day among the surgically treated subjects, as compared with 2526 kcal per day among the controls. As Figure 2 and Table 2 indicate, the baseline adjusted energy intake was significantly lower in the surgery group than in the control group over the 10-year period. Similarly, the fraction of subjects physically active during leisure time was higher in the surgery group over the 10-year period, and the fraction of those physically active during work time was higher in the surgery group for the first 6 years of the intervention.

EFFECTS ON ANTHROPOMETRIC VARIABLES AND MEAN RISK-FACTOR VALUES

Table 2 shows the changes in risk factors for all available subjects, independent of baseline status and medication use. The waist circumference was reduced more in the surgery group than in the control group after 2 and 10 years. Glucose and insulin levels increased in the control group, whereas substantial decreases were seen in the surgically treated group after both 2 and 10 years of observation. Similarly, changes in uric acid, triglyceride, and HDL cholesterol levels were more favorable in the surgically treated group than in the control group after 2 and 10 years. Systolic blood pressure was reduced by more in the surgery group at two years only. Diastolic blood pressure and total cholesterol were reduced by more in the surgery group than in

Table 2. 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.
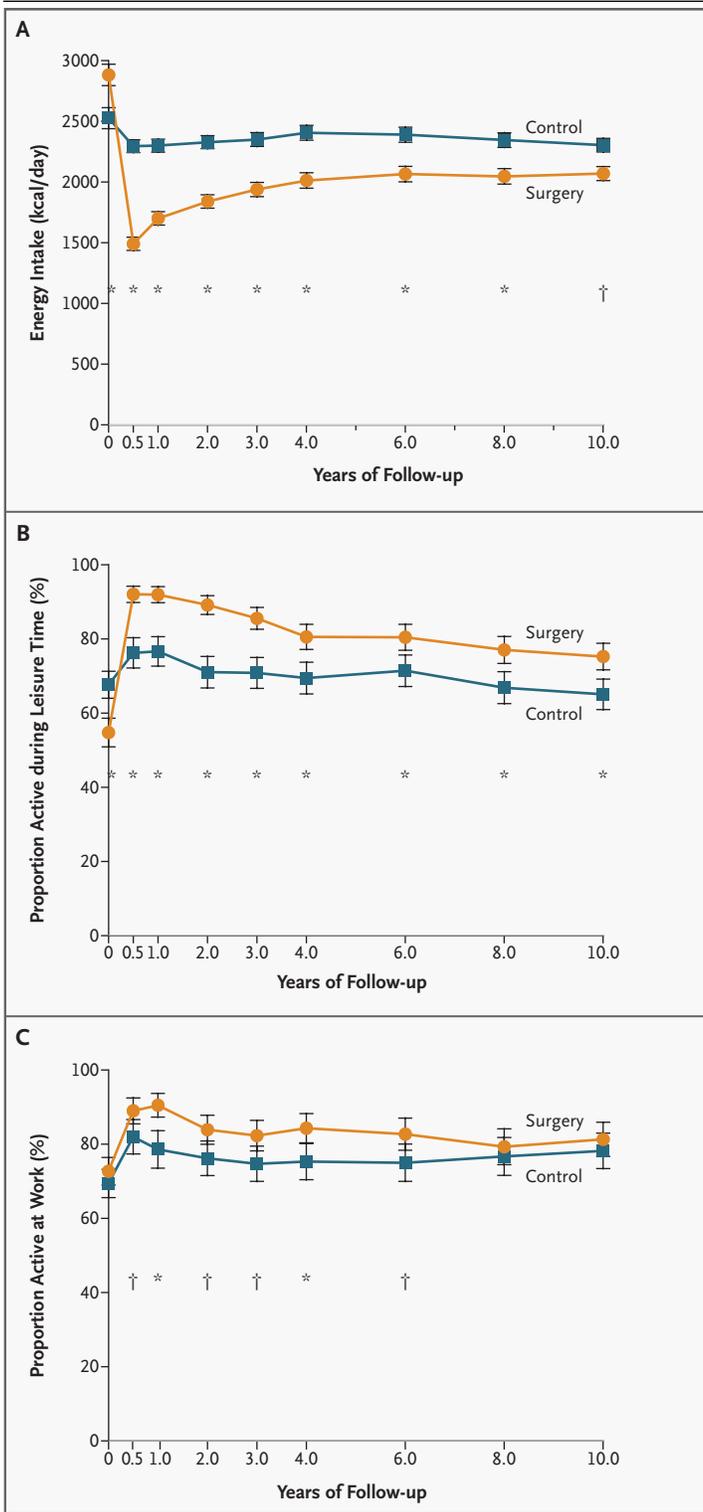
§ P<0.001.

¶ P<0.05.

‖ P<0.10.

A

B

C

the control group after 2 years but less reduced after 10 years. The pulse-pressure increase was less pronounced in the surgery group than in the control group after 10 years (Table 2).

The 10-year changes in weight, body-mass index, and waist circumference were larger for subjects who underwent vertical banded gastroplasty and gastric bypass than for those who underwent banding. Insulin, triglyceride, HDL cholesterol, and total cholesterol levels were more improved among the subjects who underwent gastric bypass than among those who underwent banding (Table 2).

EFFECTS ON INCIDENCE OF AND RECOVERY FROM RISK CONDITIONS

As Figure 3 shows, the incidence rates of hypertriglyceridemia, diabetes, and hyperuricemia were markedly lower in the surgically treated group than in the control group after 2 and 10 years. The incidence of low HDL cholesterol was significantly lower in the surgical group after 2 years but not after 10 years. The incidence of hypertension and hypercholesterolemia did not differ between the groups over the 2- and 10-year periods (Fig. 3).

Recovery from hypertension, diabetes, hypertriglyceridemia, a low HDL cholesterol level, and hyperuricemia was more frequent in the surgical group than in the control group, both at 2 and 10 years (Fig. 4). The rates of recovery from hypercholesterolemia did not differ between the two groups after either 2 or 10 years.

BASELINE OBSERVATIONS CARRIED FORWARD

In additional calculations, all missing observations were replaced by baseline observations. The conclusions with respect to mean risk-factor values, incidence rates, and rates of recovery for subjects who completed the study remained the same in the analysis in which baseline observations were carried forward (data not shown).
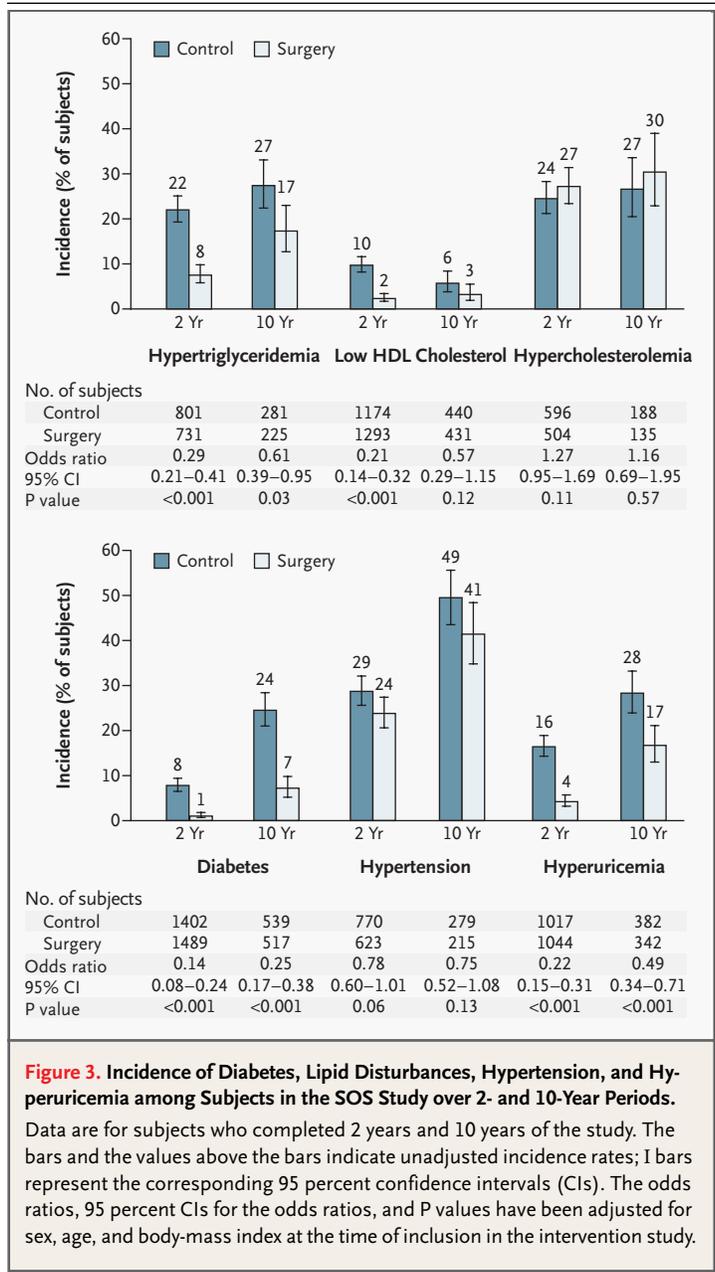
DEATH AND OTHER ADVERSE EVENTS

Five of the 2010 subjects who underwent surgery (0.25 percent) died postoperatively. As reported elsewhere for 1164 patients,[23] 151 (13.0 percent) had 193 postoperative complications (bleeding in 0.5 percent, embolism or thrombosis in 0.8 percent, wound complications in 1.8 percent, deep infections [leakage or abscess] in 2.1 percent, pulmonary complications in 6.1 percent, and other complications in 4.8 percent). In 26 patients (2.2 percent), the postoperative complications were serious enough to require reoperation. The study is ongoing with respect to analyses of mortality and the incidence of myocardial infarction, stroke, and cancer. The safety monitoring committee found no reason to interrupt the study prematurely because of positive effects or harm.

DISCUSSION

The surgically treated subjects in this study had greater weight loss, more physical activity, and lower energy intake than the control subjects over a 10-year period. Furthermore, the 2- and 10-year rates of recovery from all the studied risk factors, except hypercholesterolemia, were more favorable in the surgery group than in the control group, as were the 2- and 10-year incidence rates of hypertriglyceridemia, diabetes, and hyperuricemia. All reported results are based on subjects who completed 2 or 10 years of the study. However, the conclusions remained the same when data from all included subjects were used and missing follow-up data were replaced by baseline data, according to the conservative "baseline observation carried forward" procedure.[28]

The mean changes in weight and risk factors were more favorable among the subjects treated by gastric bypass than among those treated by banding or vertical banded gastroplasty. The low number of subjects who were followed for 10 years after gastric bypass prohibited incidence and recovery calculations, but the technique appears to be a current method of choice. The large weight loss after gastric bypass, as compared with that after the other types of surgery, may be related to altered gut-to-brain signaling.[30,31]

Most intervention studies with one to three years of follow-up are in agreement with our two-year ob-

Figure 3. Incidence of Diabetes, Lipid Disturbances, Hypertension, and Hyperuricemia among Subjects in the SOS Study over 2- and 10-Year Periods.

Data are for subjects who completed 2 years and 10 years of the study. The bars and the values above the bars indicate unadjusted incidence rates; I bars represent the corresponding 95 percent confidence intervals (CIs). The odds ratios, 95 percent CIs for the odds ratios, and P values have been adjusted for sex, age, and body-mass index at the time of inclusion in the intervention study.

(Upper panel) — Hypertriglyceridemia, Low HDL Cholesterol, Hypercholesterolemia

No. of subjects	Hypertriglyceridemia 2 Yr	Hypertriglyceridemia 10 Yr	Low HDL Cholesterol 2 Yr	Low HDL Cholesterol 10 Yr	Hypercholesterolemia 2 Yr	Hypercholesterolemia 10 Yr
Control	801	281	1174	440	596	188
Surgery	731	225	1293	431	504	135
Odds ratio	0.29	0.61	0.21	0.57	1.27	1.16
95% CI	0.21–0.41	0.39–0.95	0.14–0.32	0.29–1.15	0.95–1.69	0.69–1.95
P value	<0.001	0.03	<0.001	0.12	0.11	0.57

(Lower panel) — Diabetes, Hypertension, Hyperuricemia

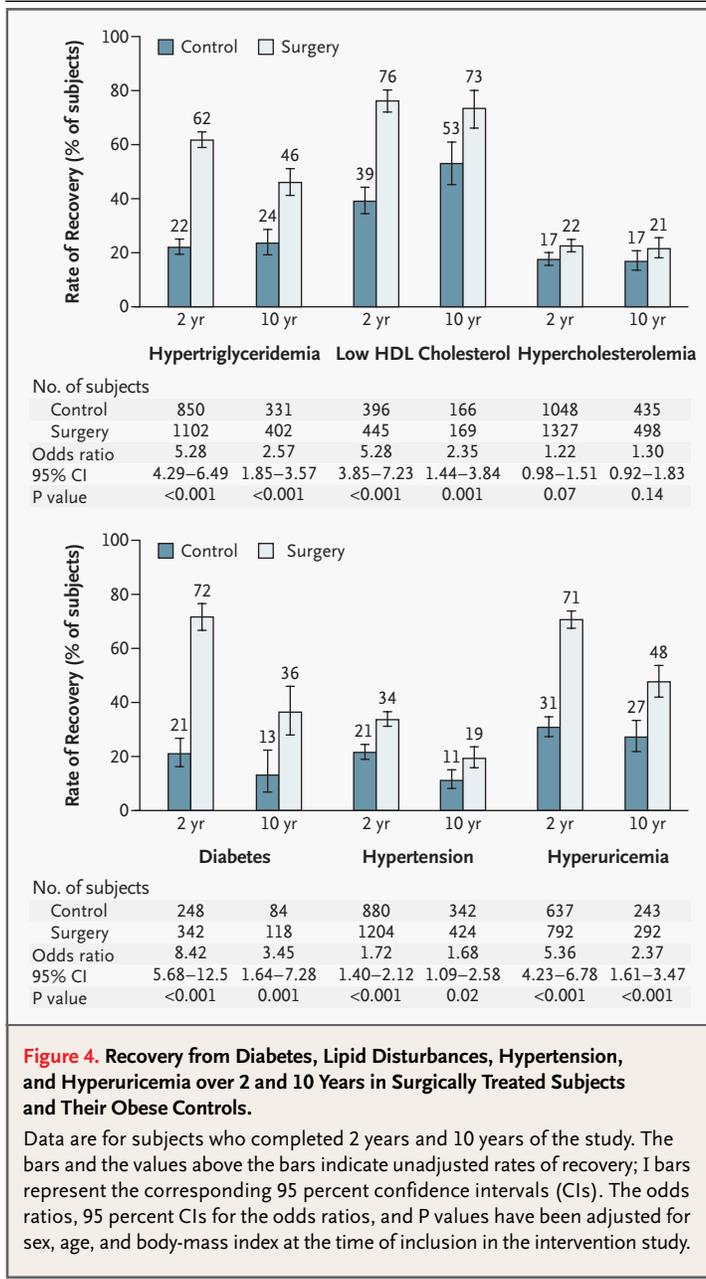| No. of subjects	Diabetes 2 Yr	Diabetes 10 Yr	Hypertension 2 Yr	Hypertension 10 Yr	Hyperuricemia 2 Yr	Hyperuricemia 10 Yr
Control	1402	539	770	279	1017	382
Surgery	1489	517	623	215	1044	342
Odds ratio	0.14	0.25	0.78	0.75	0.22	0.49
95% CI	0.08–0.24	0.17–0.38	0.60–1.01	0.52–1.08	0.15–0.31	0.34–0.71
P value	<0.001	<0.001	0.06	0.13	<0.001	<0.001

Figure 4. Recovery from Diabetes, Lipid Disturbances, Hypertension, and Hyperuricemia over 2 and 10 Years in Surgically Treated Subjects and Their Obese Controls.

Data are for subjects who completed 2 years and 10 years of the study. The bars and the values above the bars indicate unadjusted rates of recovery; I bars represent the corresponding 95 percent confidence intervals (CIs). The odds ratios, 95 percent CIs for the odds ratios, and P values have been adjusted for sex, age, and body-mass index at the time of inclusion in the intervention study.

servations concerning the effects of weight loss on blood pressure,[8,32,33] lipids,[9,34,35] uric acid,[36] and diabetes.[5-7] In contrast, to our knowledge there have been no controlled, prospective intervention trials against which our long-term results can be compared. In a retrospective, nine-year analysis, gastric bypass surgery was found to have a dramatic effect on the incidence of type 2 diabetes and overall mortality.[37] Sixteen-year observational data on weight loss from the Framingham Study[38] are in agreement with the primary preventive effect on diabetes that we found over a 10-year period. In contrast, observational, epidemiologic 12-to-15-year data on weight loss indicated a primary preventive effect on hypertension in the Nurses' Health Study,[39] but this finding could not be confirmed in our controlled 10-year intervention. Our results indicate that the long-term effects (effects at 10 years) of maintained weight loss on risk factors cannot always be estimated from short-term observations (up to 2 years).

The main limitation of the SOS Study is that it was not randomized. When it was approved as a matched, prospective intervention study in 1987, six of the seven involved ethics review boards in Sweden considered the high mortality rate after gastric surgery for obesity (1 to 5 percent in the 1970s and 1980s[40]) unacceptable for randomization.

In summary, this study indicates that bariatric surgery is a favorable option in the treatment of severe obesity. That not all obesity-associated risk factors were improved by sustained weight loss underscores the importance of obtaining long-term data concerning the effect of weight loss on overall mortality and on the incidence rates of myocardial infarction, stroke, and cancer.

APPENDIX

The SOS Study Scientific Group consists of L. Sjöström (chair), L. Backman, C. Bengtsson, C. Bouchard, B. Carlsson, L. Carlsson, S. Dahlgren, P. Jacobsson, E. Jonsson, K. Karason, J. Karlsson, B. Larsson, A.-K. Lindroos, L. Lönn, H. Lönnroth, K. Narbro, I. Näslund, M. Peltonen, A. Rydén, C.D. Sjöström, K. Stenlöf, M. Sullivan, C. Taft, J. Torgerson, and H. Wedel.

REFERENCES

1. Sjöström LV. Mortality of severely obese subjects. Am J Clin Nutr 1992;55:Suppl: 516S-523S.
2. Mokdad AH, Ford ES, Bowman BA, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. JAMA 2003;289:76-9.
3. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. JAMA 2002;287:356-9.
4. Björntorp P, De Jounge K, Sjöström L, Sullivan L. The effect of physical training on insulin production in obesity. Metabolism 1970;19:631-8.
5. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403.
6. Tuomilehto J, Lindström J, Eriksson JG,

et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344:1343-50.

7. Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care 2004;27:155-61. [Erratum, Diabetes Care 2004;27:856.]

8. Stevens VJ, Obarzanek E, Cook NR, et al. Long-term weight loss and changes in blood pressure: results of the Trials of Hypertension Prevention, phase II. Ann Intern Med 2001;134:1-11.

9. Wood PD, Stefanick ML, Dreon DM, et al. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. N Engl J Med 1988;319:1173-9.

10. Sjöström CD, Lissner L, Sjöström L. Relationships between changes in body composition and changes in cardiovascular risk factors: the SOS Intervention Study. Obes Res 1997;5:519-30.

11. Sjöström CD, Lissner L, Wedel H, Sjöström L. Reduction in incidence of diabetes, hypertension and lipid disturbances after intentional weight loss induced by bariatric surgery: the SOS Intervention Study. Obes Res 1999;7:477-84.

12. Saudicani P, Hein HO, Gyntelberg F. Weight changes and risk of ischemic heart disease for middle aged and elderly men: an 8-year follow-up in the Copenhagen Male Study. J Cardiovasc Risk 1997;4:25-32.

13. Sidney S, Friedman GD, Siegelaub AB. Thinness and mortality. Am J Public Health 1987;77:317-22.

14. Higgins M, D'Agostino R, Kannel W, Cobb J, Pinsky J. Benefits and adverse effects of weight loss: observations from the Framingham Study. Ann Intern Med 1993;119:758-63. [Erratum, Ann Intern Med 1993;119:1055.]

15. Cornoni-Huntley JC, Harris TB, Everett DF, et al. An overview of body weight of older persons, including the impact on mortality: the National Health and Nutrition Examination Survey I — Epidemiologic Follow-up Study. J Clin Epidemiol 1991;44:743-53.

16. Pamuk ER, Williamson DF, Madans J, Serdula MK, Kleinman JC, Byers T. Weight loss and mortality in a national cohort of adults, 1971-1987. Am J Epidemiol 1992;136:686-97.

17. Pamuk ER, Williamson DF, Serdula MK, Madans J, Byers TE. Weight loss and subsequent death in a cohort of U.S. adults. Ann Intern Med 1993;119:744-8.

18. Sjöström L, Larsson B, Backman L, et al. Swedish Obese Subjects (SOS): recruitment for an intervention study and a selected description of the obese state. Int J Obes Relat Metab Disord 1992;16:465-79.

19. Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biometrics 1975;31:103-15.

20. Lindroos AK, Lissner L, Sjöström L. Validity and reproducibility of a self-administered dietary questionnaire in obese and non-obese subjects. Eur J Clin Nutr 1993;47:461-81.

21. Lindroos AK, Lissner L, Sjöström L. Does degree of obesity influence the validity of reported energy and protein intake? Results from the SOS Dietary Questionnaire. Eur J Clin Nutr 1999;53:375-8.

22. Larsson I, Lissner L, Näslund I, Lindroos AK. Leisure and occupational physical activity in relation to body mass index in men and women. Scand J Nutr 2004;48:165-72.

23. Sjöström L. Surgical intervention as a strategy for treatment of obesity. Endocrine 2000;13:213-30.

24. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 2003;26:Suppl 1:S5-S24.

25. 1999 World Health Organization–International Society of Hypertension Guidelines for the Management of Hypertension: Guidelines Subcommittee. J Hypertens 1999;19:151-83.

26. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA 2001;285:2486-97.

27. Tunis SR, Stryer DB, Clancy CM. Increasing the value of clinical research for decision making in clinical and health policy. JAMA 2003;290:1624-32.

28. Ware JH. Interpreting incomplete data in studies of diet and weight loss. N Engl J Med 2003;348:2136-7.

29. Stata statistical software: release 7.0. College Station, Tex.: Stata, 2001.

30. Cummings DE, Weigle DS, Frayo RS, et al. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. N Engl J Med 2002;346:1623-30.

31. Fruhbeck G, Diez Caballero A, Gil MJ. Fundus functionality and ghrelin concentrations after bariatric surgery. N Engl J Med 2004;350:308-9.

32. Foley EF, Benotti PN, Borlase BC, Hollingshead J, Blackburn GL. Impact of gastric restrictive surgery on hypertension in the morbidly obese. Am J Surg 1992;163:294-7.

33. Carson JL, Ruddy ME, Duff AE, Holmes NJ, Cody RP, Brolin RE. The effect of gastric bypass surgery on hypertension in morbidly obese patients. Arch Intern Med 1994;154:193-200. [Erratum, Arch Intern Med 1994;154:1770.]

34. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. Am J Clin Nutr 1992;56:320-8.

35. Wadden TA, Anderson DA, Foster GD. Two-year changes in lipids and lipoproteins associated with the maintenance of a 5% to 10% reduction in initial weight: some findings and some questions. Obes Res 1999;7:170-8.

36. Nakanishi N, Nakamura K, Suzuki K, Matsuo Y, Tatara K. Relation of body weight change to changes in atherogenic traits: a study of middle-aged Japanese obese male office workers. Ind Health 2000;38:233-8.

37. MacDonald KG Jr, Long SD, Swanson MS, et al. The gastric bypass operation reduces the progression and mortality of non-insulin-dependent diabetes mellitus. J Gastrointest Surg 1997;1:213-20.

38. Moore LL, Visioni AJ, Wilson PW, D'Agostino RB, Finkle WD, Ellison RC. Can sustained weight loss in overweight individuals reduce the risk of diabetes mellitus? Epidemiology 2000;11:269-73.

39. Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. Ann Intern Med 1998;128:81-8.

40. Brolin RE. Results of obesity surgery. Gastroenterol Clin North Am 1987;16:317-38.

Copyright © 2004 Massachusetts Medical Society.