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Swedish Obese Subjects, SOS

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Swedish Obese Subjects (SOS) is an ongoing intervention study of obesity that was started in 1987. At that time it was not known if long-term intentional weight loss would decrease the elevated morbidity and mortality of obesity. Thirteen years later we still do not know, and SOS is so far the only study that has been designed to answer this question. SOS results on hard endpoints such as myocardial infarction and total mortality cannot be expected until 2004 to 2008, but several reports on changes in risk factors, cardiovascular function, health economy and quality of life induced by intentional weight loss have been published. In this review, reference is given to the number of patients in the published reports rather than to currently (February 2000) available patients (if not stated otherwise).

Some parts of this chapter overlap with a similar review in Swedish to be written for The Swedish Council on Technology Assessment in Health Care and with a review on obesity surgery printed in *Endocrine* (1).

SOS AIMS

The main goal of SOS is to examine if large and long-term intentional weight loss will reduce the elevated morbidity and mortality of obese subjects. Several secondary aims, related to the genetics of obesity, quality of life and health economics, have also been defined (2).

STUDY DESIGN

SOS originally consisted of one registry study and one intervention study (2). Later one randomized reference study and one genetic sib pair study were added.

In the registry study 6000–7000 obese men (BMI ≥ 34) and women (BMI ≥ 38) in the age range 37–60 years are examined by GPs at 480 of the 700 existing primary health care centres in Sweden. From the registry, patients are recruited into the intervention study consisting of one surgically treated group (goal $n = 2000$, February 2000, $n = 1870$) and one matched control group (same numbers) treated conventionally at the 480 primary health care centres. The surgically treated patients obtain (variable) banding, vertical banded gastroplasty (VBG) or gastric bypass (3) (Figures 35.1–35.3).

SOS is a matched and not a randomized study since, in 1987, ethical approval for randomization was not obtained due to the high operative mortality (1–5%) observed in most surgical study groups from the 1970s and 1980s. Thus, partients choose for themselves if they want surgical or conventional treatment. When a surgical patient has been accepted according to a number of inclusion and exclusion criteria, a matching programme taking 18 different matching variables into account selects the optimal control among eligible individuals in the registry study (2). The selection is based on an algorithm moving the mean values of the matching

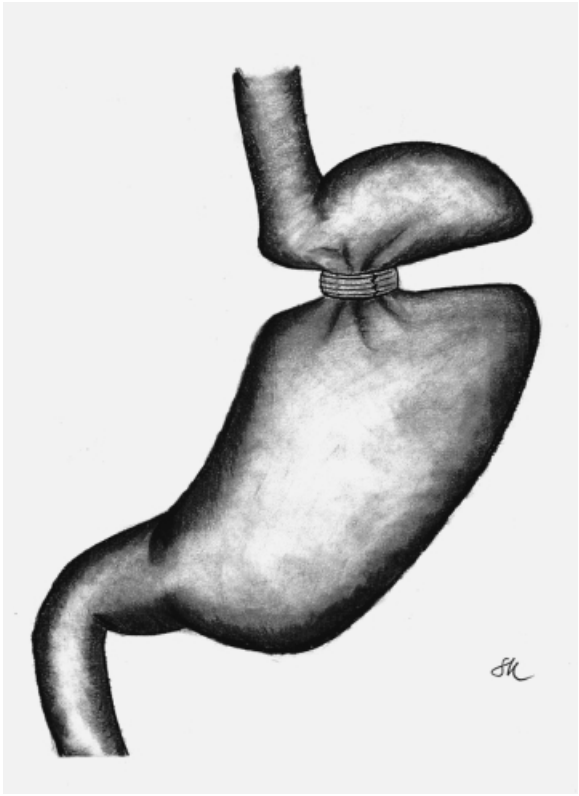

Figure 35.1 Gastric banding as originally described by Bö (59) and Solhaug (60). Later adjustable gastric banding was introduced (61–63). Copyright Sofia Karlsson and Lars Sjöström

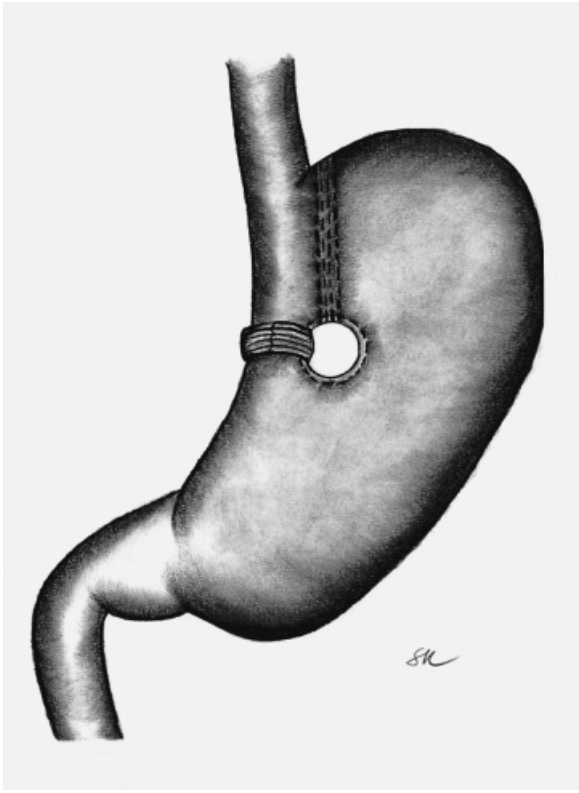

Figure 35.2 Vertical banded gastroplasty as described by Mason (64, 65). Copyright Sophia Karlsson and Lars Sjöström

variables of the control group towards the current mean values of the surgically treated patients. Thus a group match rather than an individual match is undertaken. The participating centres cannot influence the matching programme.

The surgically treated patient and the control start the intervention on the operation day of the former. Both patients are examined just before inclusion and then after 0.5, 1, 2, 3, 4, 6, 8 and 10 years. According to the original protocol the follow-up was planned to be 10 years for both groups, but recently, it was decided to add one 15- and one 20-year examination. Centralized biochemistry is obtained at 0, 2, 10, 15 and 20 years. All visits are automatically booked by a computer at the SOS secretariat and all centres obtain the necessary forms, test tubes etc. for a given visit some weeks before the booked appointment. If information is not coming back as expected from patients or centres, the programme is automatically sending out reminders or asks the staff of the secretariat to solve the problem by phone.

WEIGHT LOSS

In one 2-year report on 767 surgically treated patients and 712 obese controls, the weight loss was 28 ± 15 kg (means $\pm$ SD) and 0.5 ± 8.9 kg, respectively (4). The percentage reductions after gastric bypass, VBG and banding were 33 ± 10, 23 ± 10 and $21 \pm 12\%$, respectively. Similar 2-year changes in body weight were recently reported for 1210 surgically treated and 1099 control subjects of SOS (5).

The energy intake before and during weight loss was studied by means of a validated dietary questionnaire (6,7) in 365 patient operated with VBG or banding and in 34 patients operated with gastric

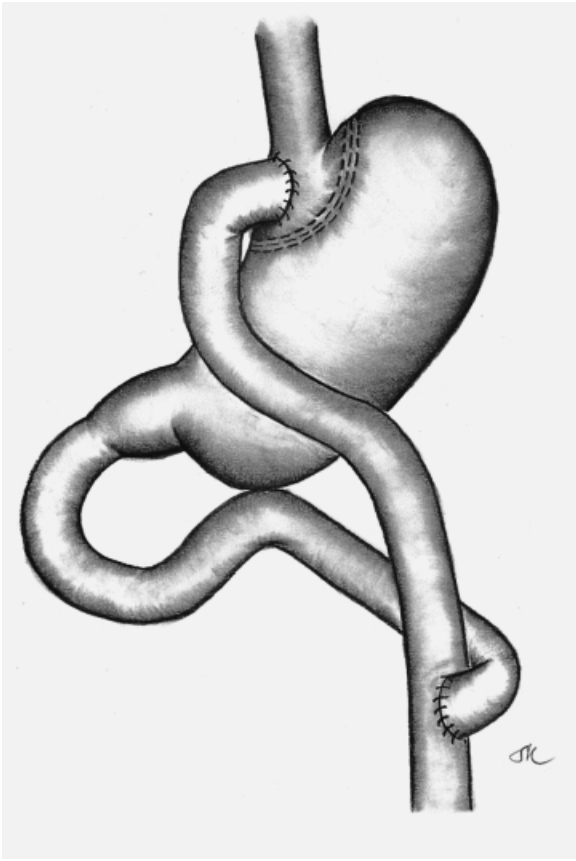

Figure 35.3 Gastric bypass as originally described by Mason (66,67) and later modified by several investigators (53,70–72). Copyright Sofia Karlsson and Lars Sjöström

bypass (8). Although the weight loss was 38.6 kg in the gastric bypass group but only 26.7 kg in the combined VBG and banding group, the energy intake before and after surgery did not differ between the groups (Figure 35.4). It has been shown that gastric bypass is associated with increased energy expenditure (9), perhaps due to an increased secretion of glucagon-like peptide 1 (GLP-1) (10,11).

In another report, 346 surgically treated patients and 346 controls were followed for 8 years (12). At 8 years, 251 surgically treated patients (73%) and 232 controls (67%) had completed the study. All dead individuals are included among non-completers since mortality figures are not yet released from the safety monitoring committee of SOS. Weight changes of completers in the four groups are shown in Figure 35.5. As in the 2-year report, there was no significant weight change in the control group while the surgically treated groups reached minimum weights after one year. As expected, gastric bypass was more efficient than VBG and banding. Between the end of year 1 and the end of year 8, a slow relapse was seen in all of the surgically treated groups. However, as compared to inclusion, the surgically induced weight loss was still 20.1 ± 15.7 kg (16.5%) after 8 years, while the controls had increased their body weight 0.7 ± 12.0 kg. The difference in the 8-year body weight change between the two groups was highly significant ($P < 0.001$).

Figure 35.5 illustrates also that conventional, non-pharmacological treatment of severe obesity is of little benefit when undertaken by non-specialized treatment units. This implies personal tragedies for millions of obese persons not having access to specialized treatment and immense consequences from a public health point of view.

SURGICAL COMPLICATIONS

Four postoperative deaths in 1870 operated patients have occurred in the SOS study (0.21%, February 2000). Three of these fatal cases were due to leakage that was detected too late. One death was caused by a technical mistake during a laparoscopic operation.

Peri- and postoperative complications have been calculated on 1164 patients followed for 4 years (13, and unpublished observations). During the primary stay at the hospital the following complications occurred: bleeding 0.5%, embolus and/or thrombosis 0.8%, wound complications 1.8%, deep infections (leakage, abscess) 2.1%, pulmonary 6.1%, other complications 4.8%. The number of complications was 193 and the number of patients with complications 151 (13%). In 26 patients (2.2%) the postoperative complications were serious enough to cause a reoperation.

Over 4 years 12% of the 1164 patients were reoperated, usually due to poor weight loss, but in some cases due to vomiting or other side effects.Usually banding and VBG were converted to gastric bypass but in some cases the original operation was repaired.

Over the 4 years a number of other operations were undertaken in both groups. In the control group 10.1 operations per 100 person-years were undertaken while the corresponding figures in the

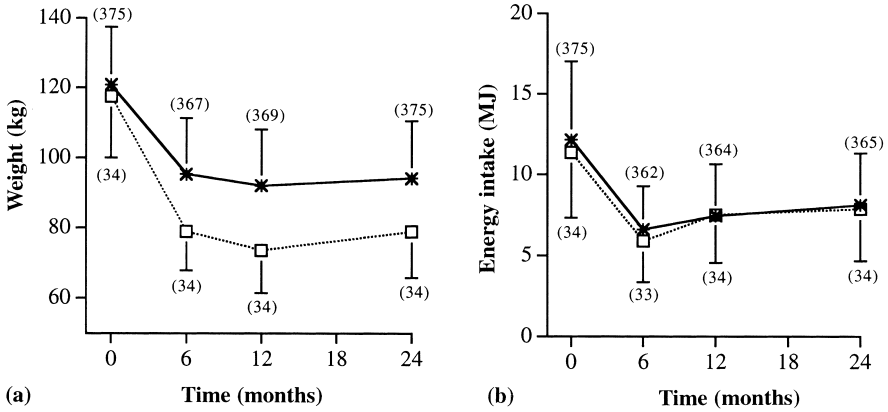

Figure 35.4 Weight loss (a) and energy intake (b) over 2 years in SOS patients who underwent gastropalsty (★) or gastric bypass (□). The gastroplasty operations were banding and VBG pooled. Mean ± SD. Values in parentheses indicate number of patients at each examination. Energy intake, estimated with validated technique (6,7), did not differ between groups at any time point. Body weights were significantly lower in gastric bypass patients at all time points after surgery $P < 0.0001$), whereas body weight before surgery did not differ significantly between groups. From Lindroos *et al.* (8) with permission

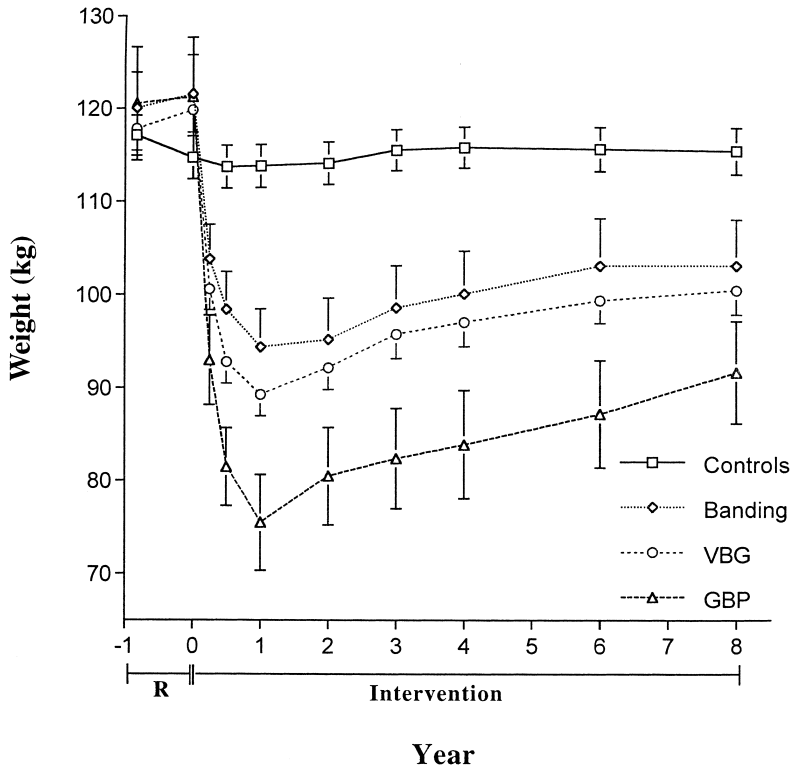

Figure 35.5 Weight change (95% CI) in 232 obese controls and 251 surgically treated patients from matching until end of year 8 in the SOS intervention study. Analysis based on completer population. R, registry study with collection of matching variables. Banding, $n = 63$. Vertical banded gastroplasty, VBG, $n = 164$, gastric bypass, GBP, $n = 24$. Each one of the surgical groups had a significantly ($P < 0.01$) larger weight reduction than the controls. From C.D. Sjöström *et al.* (12), with permission

Table 35.1 BMI and risk factors in 50-year-old men and women from SOS and in 50-year-old randomly selected reference subjects. Risk factor levels for other age groups, see Sjöström *et al.* (2)

	SOS males	Ref. males	$P <$	SOS females	Ref. females	$P <$
No.	102	220		121	398	
Age (years)	48–52	50		48–52	50	
BMI	37.3 ± 3.9	24.0		41.4 ± 4.4	24.8	
Systolic (mmHg)	146 ± 16	137 ± 22	0.001	147 ± 18	140 ± 22	0.01
Diastolic (mmHg)	94 ± 9	90 ± 14	0.01	89 ± 9	85 ± 11	0.001
Blood glucose (mmol/L)	5.9 ± 2.0	4.7 ± 1.3	0.001	5.5 ± 1.6	4.2 ± 0.9	0.001
Insulin (mU/L)	31 ± 25	9.6 ± 8.0	0.001	22 ± 12	14 ± 5	0.001
Triglycerides (mmol/L)	2.7 ± 2.0	1.3 ± 0.8	0.001	2.0 ± 1.0	1.3 ± 0.6	0.001
HDL cholesterol (mmol/L)	1.2 ± 0.4	1.6 ± 0.4	0.001	1.4 ± 0.4	—	
Total cholesterol (mmol/L)	6.2 ± 1.2	6.4 ± 1.3	NS	6.1 ± 1.1	7.2 ± 1.1	0.001

From L. Sjöström *et al.* (2), with permission.

surgical groups was 15.2. Operations due to ventral hernia, gallbladder disease, intestinal obstruction and surplus of skin were more common in the surgical group while, on average, operations due to malignancy, gynaecological disorders and all other reasons taken together were more common in the control group.

RISK FACTORS AT BASELINE

In an early cross-sectional analysis of 450 men and 556 women from the registry study of SOS it was shown that as compared to randomly selected controls most cardiovascular risk factors were elevated in the obese (Table 35.1) (2). The exception was total cholesterol, which was similar in obese and non-obese males and lower in obese women as compared to reference women.

Later, risk factors have also been analysed in relation to body composition in 1083 men and 1367 women from the SOS registry study (14). This analysis revealed one body compartment–risk factor pattern and one subcutaneous adipose tissue distribution–risk factor pattern. Within the first pattern risk factors were positively and strongly related to the visceral adipose tissue mass and, somewhat more weakly, also to the subcutaneous adipose tissue mass. Some risk factors, such as glucose and triglycerides in men and insulin in women, were negatively related to lean body mass. In addition, the subcutaneous adipose tissue distribution was related to risk factors both when and when not taking the body compartments into account statistically. A preponderance of subcutaneous adipose tissue in the upper part of the trunk, as indicated by the neck circumference, was positively related to risk factors while the thigh circumference was negatively related to risk factors. These two risk factor patterns have also been observed longitudinally, i.e. changes in risk factors and changes in body composition and adipose tissue distribution are related (15) in the same way as in the cross-sectional observations (14).

RISK FACTOR CHANGES

In a 2-year report of 282 men and 560 women, pooled from the surgically treated group and the control group, risk factor changes were examined as a function of weight change (15). Ten kilogram weight loss was enough to introduce clinically significant reductions in all traditional risk factors except total cholesterol (Figure 35.6). Although it is known that total cholesterol is reduced short term (1–6 months) by moderate weight losses (16,17), Figure 35.6 illustrates that 30 to 40 kg maintained weight loss is required to achieve a preserved reduction in total serum cholesterol after 2 years.

In another 2-year report on 767 surgically treated patients and 712 controls, the weight loss of the surgical group resulted in dramatic reductions in the incidence of hypertension, diabetes, hyperinsulinaemia, hypertriglyceridaemia and low HDL cholesterol (4) (Figure 35.7). In the case of diabetes a 32-fold risk reduction was observed while the incidence of other risk conditions was reduced 2.6- to

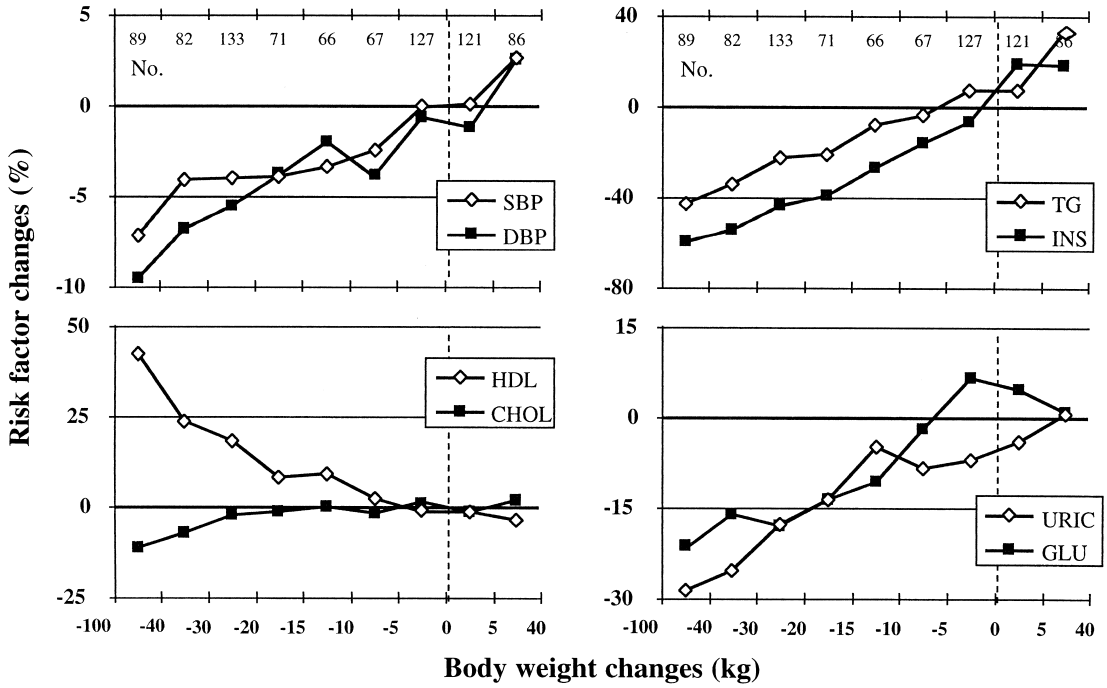

Figure 35.6 Adjusted risk factor changes (%) in relation to body weight changes (kg) over 2 years in 842 obese men and women pooled from the surgically treated group and the obese control group of the SOS Intervention study. The percentage change in each risk factor was adjusted for the basal value of that risk factor, initial body weight, sex, age and height. The number of subjects in each weight-changing class is shown at the top of the figure (as No). SBP and DBP, systolic and diastolic blood pressure; HDL, serum HDL cholesterol; CHOL, serum total cholesterol; TG, serum triglycerides; INS, serum insulin; URIC, serum uric acid; GLU, blood glucose. All serum samples collected after overnight fast. From C.D. Sjöström *et al.* (14), with permission

10-fold. In analogy with Figure 35.6, weight loss had no effect on the incidence of hypercholesterolaemia (figure 35.7). To give a visual impression of the weight loss necessary to prevent development of diabetes, the surgically treated group and the control group were pooled and the diabetes incidence plotted by decentiles of weight change (18). As can be seen in Figure 35.8, weight changes close to zero were associated with a 2-year diabetes incidence of 7–9%. A Mean weight loss of 7% was still associated with a 2-year diabetes incidence of 3% while no new cases of diabetes were seen for mean weight losses 12% or larger.

In the 8-year follow up (12) the incidence of diabetes was still five times lower in the surgical group than in the control group (figure 35.9). However, there was no difference between the two groups with respect to the 8-year incidence of hypertension (Figure 35.9). This was the case with or without multiple adjustments in the completer population as well as in the intention-to-treat population (12). In a follow-up study, the final blood pressure has been shown to be closely related to recent weight changes and the length of the follow-up but more weakly associated with initial weight and the initial weight loss (19).

Unpublished 10-year data from SOS show that insulin, glucose, triglycerides and HDL cholesterol are improved by surgical treatment while blood pressure and total cholesterol are not.

While short-term weight losses improve all cardiovascular risk factors (see Figure 35.6 and (16,17)), several observational epidemiological studies have shown an association between weight loss and increased total as well as cardiovascular mortality, even in those who were obese at baseline (20). This discrepancy has usually been explained by the inability of observational studies to separate intentional from unintentional weight loss. Williamson has provided some evidence for this in women (21) but not in men (22). The 8-year study discussed above (12) suggests another possibility: long term,

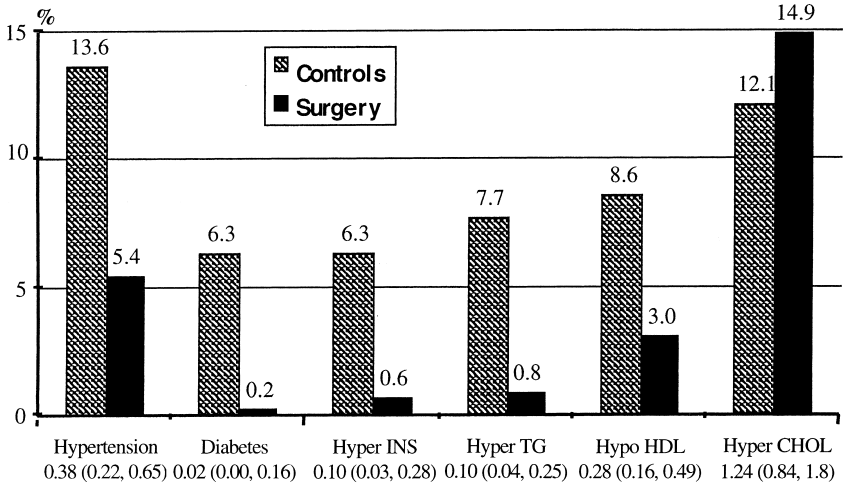

Figure 35.7 Two-year unadjusted incidence of indicated conditions in 712 obese controls (striped bars) and in 767 surgically treated completers (filled bars) from the SOS intervention study. Below bars, Odds Ratios (95% CI) adjusted for baseline values of age, sex, weight smoking and matching value of perceived health. $P < 0.001$ for all differences between groups except for hypercholesterolemia. Abbreviations as in Figure 35.6. From C.D. Sjöström *et al.* (4), with permission

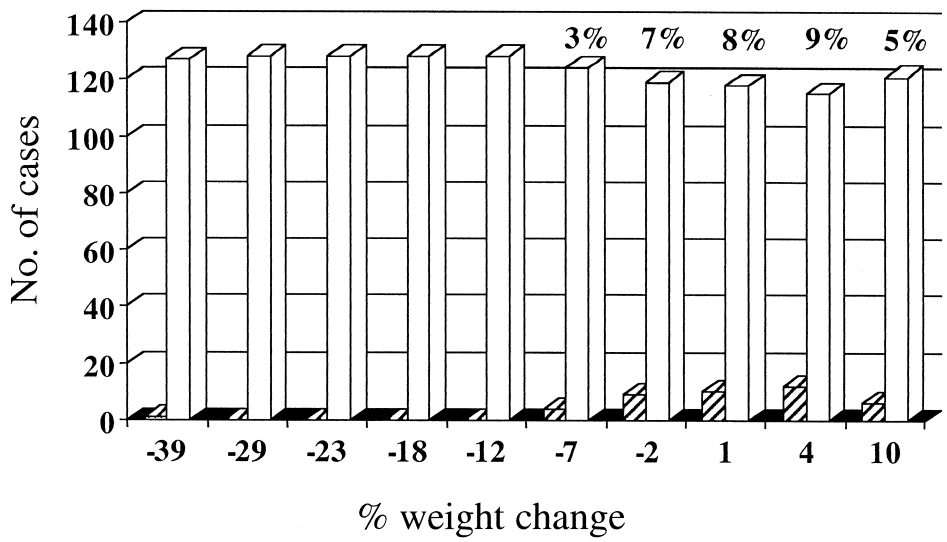

Figure 35.8. Two-year incidence of diabetes by decentile of percentage weight change in the SOS intervention study. Pooled data from 1281 obese controls and surgically treated subjects not having diabetes at baseline. Striped bars indicate new cases of diabetes. At bottom, the average percentage weight change within each decentile. At top, the 2-year incidence of diabetes within each weight change decentile. Data based on ref. (4) and figure reproduced from C.D. Sjöström (18), with permission

some risk factors, such as blood pressure, may relapse in spite of maintained weight loss.

A third explanation may be that non-traditional risk factors deteriorate during weight loss. Recently, 10-year data from SOS have demonstrated that homocysteine increases with increasing weight loss, independent of method of weight loss (surgery or conventional), also when adjusting for changes in folate and B_{12} (23). Homocysteine levels have been shown to be related to cardiovascular mortality (24). Since homocysteine and folate are negatively related and since folate intake is reduced during

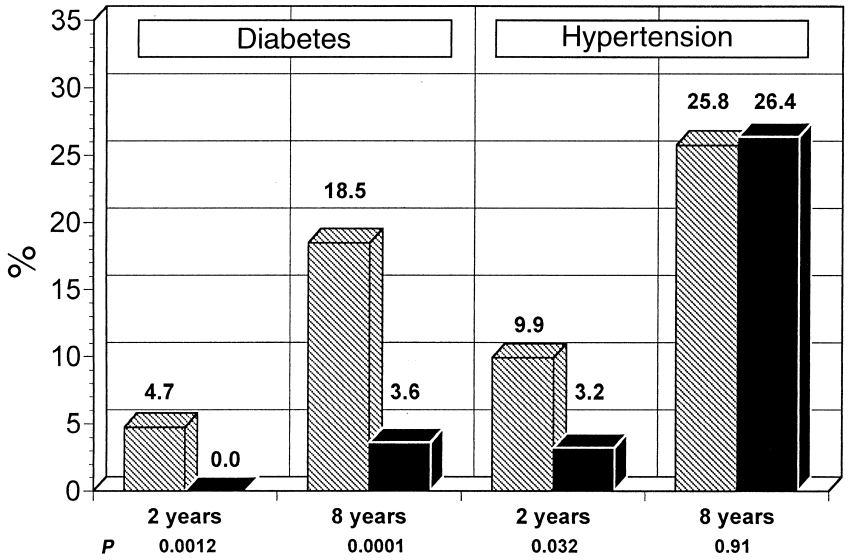

Figure 35.9 Two- and 8-year unadjusted incidence of diabetes and hypertension in 232 obese controls (striped bars) and 251 surgically treated patients (filled bars) from the SOS intervention study. Calculations based on completer population. Almost identical odds ratios were obtained with and without adjustments in completer and intention-to-treat populations (now shown). From C.D. Sjöström *et al.* (12), with permission

caloric restriction, our observations suggest that all weight-reducing treatments, whether surgical or not, should be accompanied by substitution with multivamin pills, folic acid and possibly B_{12} in order to counteract an increased incidence of cardiovascular disease due to hyperhomocysteinaemia.

EFFECTS ON THE CARDIOVASCULAR SYSTEM

In subsamples of the SOS study, cardiac function was examined at baseline and after 1 to 4 years of follow-up.

At baseline a surgically treated group ($n = 41$) and an obese control group ($n = 31$) were compared with a lean refrence group ($n = 43$) (25,26). As compared to lean subjects, the systolic and diastolic blood pressure, left ventricular mass and relative wall thickness were increased in the obese while the left ventricular ejection fraction (systolic function) and the E/A ratio (diastolic function) were decreased at baseline. After 1 year, all these variables had improved in the surgically treated group but not in the obese control group. When pooling the two obese groups and plotting left ventricular mass or E/A ratio as a function of quintiles of weight change, a 'dose' dependency was revealed, i.e. the larger the weight reduction, the larger the reduction in left ventricular mass (Figure 35.10) and the more pronounced the improvement in diastolic function (Figure 35.11). Unchanged weight was in fact associated with a measurable deterioration in diastolic function over 1 year.

In other small subgroups from SOS, heart rate variability from 24-hour Holter ECG recordings and 24-hour catecholamine secretion were examined (27). As compared to lean subjects, our examinations indicated an increased sympathetic activity and a withdrawal of vagal activity at baseline. Both these disturbances were normalized in the surgically treated group but not in the obese control group after 1 year of treatment.

Furthermore, questionnaire data from 1210 surgically treated patients and 1099 obese SOS controls examined at baseline and after 2 years were analysed with respect to various cardiovascular symptoms (5). At baseline the two groups were comparable in most respects. After 2 years, dyspnoea and chest discomfort were reduced in a much larger fraction of surgically treated as compared to controls. For instance, 87% of the surgically treated reported baseline dyspnoea when climbing two flights of stairs while only 19% experienced such

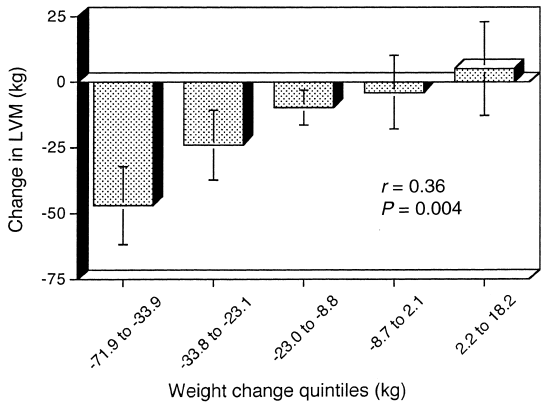

Figure 35.10 Changes in left ventricular mass (LVM) as a function of 1-year weight change quintiles (kg) in the SOS intervention study. Mean ± SEM. Pooled echocardiographic data of 38 surgically treated patients and 25 obese controls. Correlation for trend based on individual observations ($n = 63$). From Karason *et al.* (25), with permission

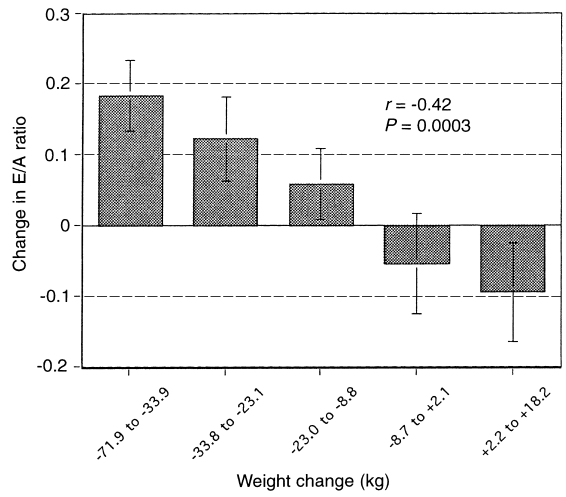

Figure 35.11 Changes in diastolic function, as indicated by the E/A ratio, in relation to 1-year weight change quintiles (kg) in the SOS intervention study. Mean ± SEM. Pooled transmitral Doppler data of 41 surgically treated patients and 30 obese controls. Correlation for trend based on individual observations ($n = 71$). From Karason *et al.* (26), with permission

dyspnoea at the 2-year follow-up. In the obese control group the corresponding figures were 69 and 57%, respectively ($P < 0.001$ for difference in change between groups).

Similarly, a high likelihood for sleep apnoea was observed in 23% of the surgically treated patients at baseline but only in 8% after 2 years of treatment. In the control group the corresponding figures were 22 and 20%, respectively ($P < 0.001$).

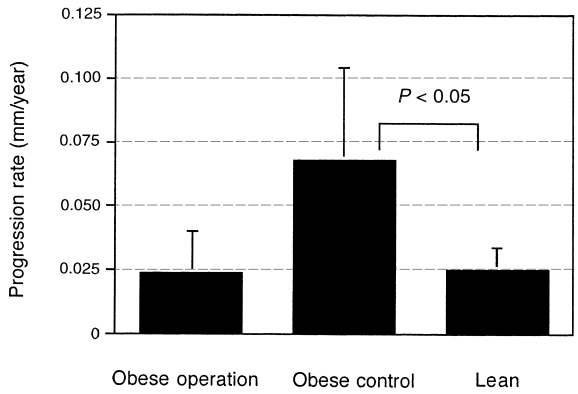

Figure 35.12 Annual progression rate of intima-media thickness in the carotid artery bulb in surgically treated obese patients ($n = 14$), obese controls ($n = 9$) and lean controls ($n = 27$) matched for gender, age and height. Mean ± SEM. Progression rate measured ultrasonographically over 4 years in the two obese groups and over 3 years in the lean reference group. The weight change was -22 ± 10 kg in the operated group and 0 ± 13 kg in the obese control group. From Karason *et al.* (28), with permission

Physical inactivity was observed in 46% of the surgically treated group before weight reduction but only in 17% after 2 years. Corresponding figures in the obese control group were 33 and 29%, respectively ($P < 0.001$) (5). Thus physical inactivity not only contributes to the development of obesity but obesity prevents physical activity. This vicious circle is broken by surgical treatment.

Finally, the intima-media thickness of the carotid bulb was examined by means of ultrasonography at baseline and after 4 years in the SOS intervention study (28). A randomly selected lean reference group matched for gender, age and height was examined at baseline and after 3 years. As shown in Figure 35.12 the annual progression rate was almost three times higher in the obese control group ($n = 9$) as compared to lean reference subjects ($P < 0.05$). In the surgically treated group, the progression rate was normalized. Although resuls from this small study group need to be confirmed in larger trials, this study nevertheless offers the first data on hard endpoints after intentional weight loss.

We have also shown that the pulse pressure increases more slowly in the surgically treated group than in the obese control group after a mean follow-up of 5.5 years (19). In gastric bypass individuals the pulse pressure is in fact decreasing. These observa-

tions are of interest since it has been shown that, at a given systolic blood pressure, a high pulse pressure is associated with increased artrial stiffness (29), increased intima-media thickness (30) and increased cardiovascular mortality (31). Thus pulse pressure changes (19) as well as ultrasonographic measurements (28) indicate that surgical treatment is slowing down the increased atherosclerotic process in the obese.

ECONOMIC CONSEQUENCES OF OBESITY AND WEIGHT LOSS IN SOS

In cross-sectional studies of SOS patients it was shown that independent of age and gender, sick leave was twice as high and disability pensions twice as frequent as in the general Swedish population (32–34). The annual extra indirect costs (sick leave plus disability pension) attributable to obesity were estimated to be 6 billion SEK, or 1 million US dollars per 10 000 inhabitants per year.

The number of lost days due to sick leave and disability pension the year before inclusion into the SOS intervention was almost identical in the surgically treated group and the obese control group (104 and 107 days, respectively, Figure 35.13) (35). The year after inclusion the number of lost days were higher in the surgically treated group but over years 2 to 4 after inclusion the lost days were lower in the surgically treated group (figure 35.13). This was particularly evident in those individuals above median age (46.7 years) (not shown) (35).

The direct costs attributable to obesity and their changes after weight loss are currently being examined in the SOS study. So far we know that weight loss is associated with decreased costs for medication for diabetes and cardiovascular disease (36).

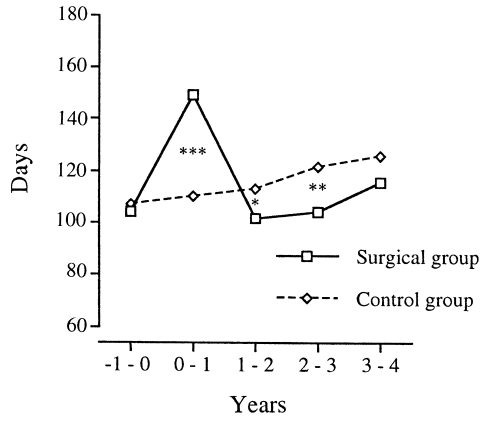

Figure 35.13 Days of sick leave plus disability pension per year in 369 surgically treated and 371 obese controls the year before inclusion and over 4 years after inclusion into the SOS intervention study. All data adjusted for age, gender, and several predictive variables. During years 1–4, the number of days are also adjusted for days of sick leave plus disability pension the year beforre inclusion. Significant differences between groups indicated as $*P < 0.05$, $**P < 0.01$, $***P < 0.001$. From Narbro *et al.* (35), with permission

QUALITY OF LIFE BEFORE AND AFTER WEIGHT LOSS

Cross-sectional information from 800 obese men and 943 women of the SOS Registry study demonstrated that obese patients have a health-related quality of life (HRQL) that is much worse than in the age-matched reference groups (37). In fact, HRQL in the obese was as bad as, or even worse than, in patients with severe rheumatoid arthritis, generalized malignant melanoma or spinal cord injuries. The measurements were performed with general scales such as General Health Rating Index, Hospital Anciety and Depression scale, Mood Adjective Check List and Sickness Impact Profile in original or short form (37,38) and with an obesity-specific psychosocial scale (37). All scales have been validated during Swedish measuring conditions.

In 2- (39) and 4-year (see Chapter 33) reports, results from all measurement instruments are improving dose dependently, i.e. the larger the weight loss, the larger the improvement in HRQL, and in particular in the obesity-specific psychosocial scale (Figure 35.14).

OTHER STUDIES COMPARING NON-SURGICAL AND SURGICAL TREATMENT

While SOS has compared surgical treatment with treatment delivered by general practitioners at 480 primary heath care centres in Sweden (2), three other studies have compared surgical treatment with dietary treatment undertaken by more or less specialized obesity clinics (40–45).

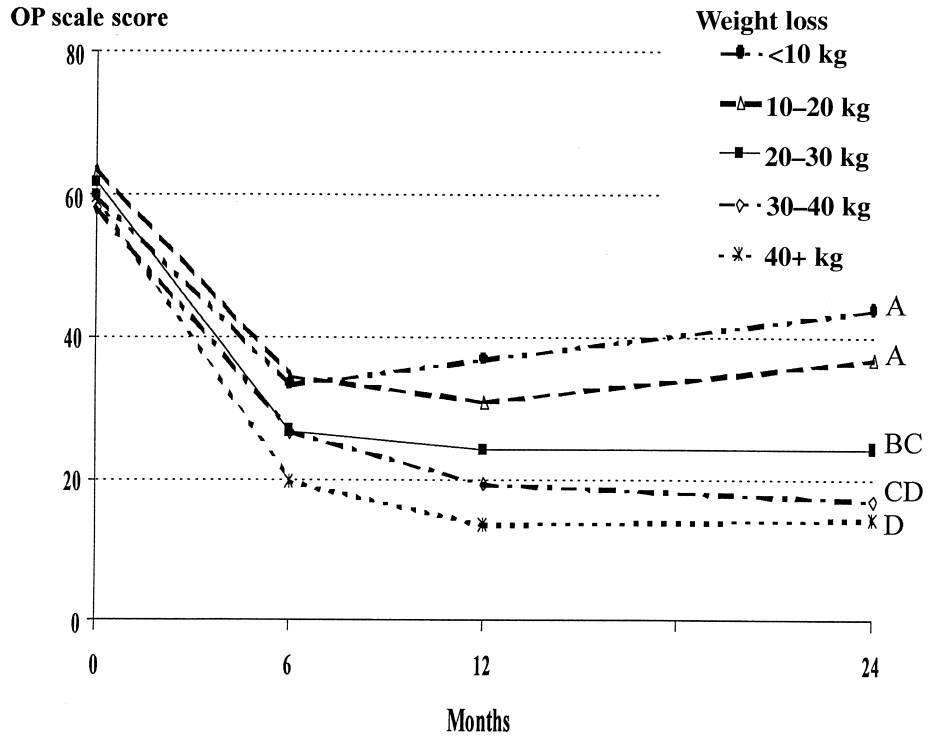

Figure 35.14 Obesity-related psychosocial problems in everyday life by weight reduction during 2 years intervention in the SOS study. Indicated weight change classes obtained after pooling of 487 surgically treated patients and 487 obese controls followed for 2 years. The psychosocial problems were estimated with the validated OP instrument. High scores represent dysfunction. Groups with different letters are significantly different at 2-year follow-up ($P < 0.05$, Turkey's range test). From Karlsson *et al.* (39), with permission

Jejuno-ileal Bypass vs. Diet

In 'The Danish Obesity Project' (40,41) 202 patients were randomized in the proportions 2 : 1 to jejuno-ileal bypass or diet treatment. Six patients never came to treatment. The remaining 130 surgically treated and 66 diet treated patients were followed for 2 to 3 years. After 2 years, the weight loss was 42.9 kg in the surgically treated group and 5.9 kg in the diet group. Quality of life as well as blood pressure were markedly improved in the surgical group. However, the surgical group had a large number of complications some of which were serious. As discussed below, jejuno-ileal bypass is no longer recommended due to serious side effects.

Horizontal Gasroplasty vs. VLCD Followed by Diet

In another early Danish study 60 patients were randomized to horizontal gastroplasty or very low calorie diet (VLCD) followed by traditional dieting. A 2-year (42) and 5-year (43) report appeared in the mid-1980s. Unfortunately, less than 50% of the patients had in fact been followed for 2 and 5 years, respectively, when the reports were written. At 2 years the weight loss was 30.6 kg in the gastroplasty group and 8.2 kg in the VLCD/diet group. Weight losses are not reported at 5 years. Instead, a 'cumulated success rate' defined as more than 10 kg maintained weight loss was given. This success rate was 16% in the patients operated with horizontal gastroplasty and 3% in the VLCD/diet group. Horizontal gastroplasties are no longer in use due to poor long-term results (1,44,45).

Gastric Bypass vs. VLCD and Diet

In a prospective, non-randomized, non-matched study Martin *et al.* compared gastric bypass (GBP)

($n = 201$) with VLCD followed by diet ($n = 161$) 46). After VLCD, the diet group was offered one counselling session per week for 18 months and then annual follow-ups. The follow-up ranged from 2 to 6 years. At 6 years the follow-up rate was 34.5% in the GBP group and 19.7% in the VLCD/diet group. In the GBP group BMI dropped from 49.3 kg/m^2 to a minimum of 31.8 after 2 years. At 6 years BMI was 33.7 kg/m^2. In the VLCD/diet group the corresponding figures were 41.2, 32.1 and 38.5. As compared to VLCD/diet treatment, GBP thus resulted in twice as large a BMI drop and in a much smaller relapse.

BMI CUT-OFFS

At the consensus conference 1991, the National Institutes of Health (NIH) recommended that obesity surgery should be restricted to individuals with BMI $\geq 40\,kg/m^2$ although a somewhat lower cut-off could be accepted in subjects with pronounced metabolic complications (47). At that time the SOS project had already used the BMI cut-off 38 kg/m^2 for women and 34 kg/m^2 for men for 4 years. Our preliminary impression in the early 1990s did not make us change our cut-off and today it is obvious that a cut-off of 40 kg/m^2 leaves a larger fraction of the obese population virtually without efficient treatment and often in very bad shape in spite of the fact that new anti-obesity drugs have been added to the therapeutic arsenal.

In a preliminary report, Näslund (13) has analysed effects and complications in surgically treated SOS patients with BMI < 40 and BMI $\geq 40\,kg/m^2$. In absolute terms, weight loss was larger in the heavier group while this was not the case in relative terms. The frequency of complications was similar in both groups and from a risk factor point of view both groups benefited similarly from surgical treatment.

SURGICAL METHODS OF CHOICE

GBP results in larger weight loss than vertical banded gastroplasty (VBG) and gastric banding. The two latter techniques give similar weight reductions. Banding is associated with more reoperations than GBP and VBG. GBP is technically more demanding than VBG and banding and it results in iron and B_{12} insufficiency that must be treated. It is not known whether GBP will cause negative calcium balance or other malabsorptive problems in a 10- to 30-year perspective. Such hypothetical problems are less likely with VBG and banding since these methods do not change the normal passage of food through the gastrointestinal tract. Finally, patients subjected to GBP cannot easily have their stomach examined endoscopically, which makes examinations of sucpect malignancy more complicated.

Taken together these circumstances suggest that GBP should be reserved for individuals with a considerable degree of obesity (BMI $\geq 40\,kg/m^2$) while VBG according to SOS experience can be used in the BMI interval 34–45 kg/m^2. Banding in its original form (SOS data) as well as all forms of horizontal gasroplasties (48) should not be used due to the increased need for revisions. Variable banding has not been evaluated in randomized studies but seems to have a place in the obesity therapy, particularly when used with laparoscopic techniques (49,50).

Several efficient techniques that have not been included in the SOS study have been developed. Jejuno-ileal bypass (JIB) is as effective as gasric bypass (51). However, JIB is associated with a large number of serious side effects and therefore not recommended any longer (52). The biliopancreatic diversion (53) is outstanding in achieving weight reduction but it is also associated with malabsorption of protein, fat-soluble vitamins and calcium (53,54). Treatment with this technique should be reserved for the heaviest (BMI > 45) and should only be undertaken by surgical departments (rather than individual surgeons) that are prepared to take a lifelong responsibility for the patients. The experience with biliopancratic diversion with duodenal switch (55) is still limited. It seems as if this technique is at least as efficient as the original biliopancreatic diversion and associated with less frequent and milder side effects (56,57).

Randomized studies comparing gastric bypass, biliopancreatic diversion and biliopancreatic diversion with duodenal switch are urgently needed. While randomized studies were fairly common in the early days of bariatric surgery no such studies seem to have been published since 1993 (1).

OVERALL CONCLUSIONS

The prevalence of obesity is high and rapidly increasing (58) and obesity is associated with a dramatically increased morbidity and mortality.

Surgery is the only obesity treatment resulting in more than 15% average weight loss over 10 years. This treatment has dramatic positive effects on most but not on all risk factors over a 10-year period. Large weight reductions achieved by surgery improve the cardiovascular system in several respects. Long-term direct and indirect costs seem to be reduced after surgical obesity treatment and quality of life is markedly improved.

Conventional treatment at specialized obesity units may achieve 5% weight loss over 2 to 5 years of follow-up. This is not enough to keep risk factors down long term. Non-pharmacological, conventional obesity treatment at primary health care centres is not associated with weight loss, short or long term (4,12), and unfortunately most obese patients worldwide have no access to specialized obesity treatment.

Treatment with currently available anti-obesity drugs results in 8–12% weight reduction over 2 years as compared to 4–6% in the placebo groups (16). This is encouraging even if more efficient drugs are needed in the future. So far no randomized drug trials with a longer duration than 2 years have been published.

Primary health care centres will constitute the worldwide basis for obesity treatment in the future. Within the next 5–10 years, treatment given by these centres will hopefully improve with better programmes and more efficient anti-obesity drugs.

There is an urgent need for one specialized obesity centre per approximately 500 000 inhabitants. At these centres, internists, nurses and dietitians need to work full-time with obese subjects referred to them from GPs. The demand for such treatment is almost unlimited. In a region with 500 000 inhabitants, obese patients overall will be in need of at least 20 000–30 000 visits annually.

While waiting for more efficient anti-obesity drugs, the surgical treatment of obesity must increase dramatically. The real need is 500–1000 operations annually per 500 000 inhabitants in most Western countries, even if the current demand for operations is smaller. All obese patients with BMI $\geq 40\,kg/m^2$ need detailed information on surgical treatment options and a very large number of individuals with BMI above as well as below $40\,kg/m^2$ will benefit from surgical treatment. Surgical treatment is particularly important in obese patients with associated cardiovascular risk factors.

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