Risk of suicide and non-fatal self-harm after bariatric surgery: results from two matched cohort studies

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Summary

Background Bariatric surgery reduces mortality, but might have adverse effects on mental health. We assessed the risk of suicide and self-harm after bariatric surgery compared with non-surgical obesity treatment.

Methods Suicide and non-fatal self-harm events retrieved from nationwide Swedish registers were examined in two cohorts. The non-randomised, prospective Swedish Obese Subjects (SOS) study compared bariatric surgery (n=2010; 1369 vertical-banded gastroplasty, 376 gastric banding, and 265 gastric bypass) with usual care (n=2037; recruitment 1987–2001). The second cohort consisted of individuals from the Scandinavian Obesity Surgery Registry (SOReg; n=20 256 patients who had gastric bypass) matched to individuals treated with intensive lifestyle modification (n=16 162; intervention 2006–13) on baseline BMI, age, sex, education level, diabetes, cardiovascular disease, history of self-harm, substance misuse, antidepressant use, anxiolytics use, and psychiatric health-care contacts.

Findings During 68 528 person-years (median 18; IQR 14–21) in the SOS study, suicides or non-fatal self-harm events were higher in the surgery group (n=87) than in the control group (n=49; adjusted hazard ratio [aHR] 1·78, 95% CI 1·23–2·57; p=0·0021); of these events, nine and three were suicides, respectively (3·06, 0·79–11·88; p=0·11). In analyses by primary procedure type, increased risk of suicide or non-fatal self-harm was identified for gastric bypass (3·48, 1·65–7·31; p=0·0010), gastric banding (2·43, 1·23–4·82; p=0·011), and vertical-banded gastroplasty (2·25, 1·37–3·71; p=0·0015) compared with controls. Out of nine deaths by suicide in the SOS surgery group, five occurred after gastric bypass (two primary and three converted procedures). During 149 582 person-years (median 3·9; IQR 2·8–5·2), more suicides or non-fatal self-harm events were reported in the SOReg gastric bypass group (n=341) than in the intensive lifestyle group (n=84; aHR 3·16, 2·46–4·06; p<0·0001); of these events, 33 and five were suicides, respectively (5·17, 1·86–14·37; p=0·0017). In SOS, substance misuse during follow-up was recorded in 48% (39/81) of patients treated with surgery and 28% (13/47) of controls with non-fatal self-harm events (p=0·023). Correspondingly, substance misuse during follow-up was recorded in 51% (162/316) of participants in the SOReg gastric bypass group and 29% (23/80) of participants in the intensive lifestyle group with non-fatal self-harm events (p=0·0003). The risk of suicide and self-harm was not associated with poor weight loss outcome.

Interpretation Bariatric surgery was associated with suicide and non-fatal self-harm. However, the absolute risks were low and do not justify a general discouragement of bariatric surgery. The findings indicate a need for thorough preoperative psychiatric history assessment along with provision of information about increased risk of self-harm following surgery. Moreover, the findings call for postoperative surveillance with particular attention to mental health.

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Introduction

In 2014, an estimated 125 million women (5·0%) and 50 million men (2·3%) worldwide had a BMI of 35kg/m² or higher,[1] making them potentially eligible for bariatric surgery. Bariatric surgery reduces the risk of premature death,[2–4] cardiovascular events,[5,6] and microvascular and macrovascular complication of diabetes.[7,8] However, concern is growing about adverse effects on mental health, with increased alcohol and substance misuse reported after some procedures, as well as signals of an increased suicide risk compared with individuals with severe obesity not treated with surgery.[9,10] Compared with the general population, patients who have had bariatric surgery have been reported to have higher risk of both suicide[11,12] and non-fatal self-harm.[13] Non-fatal self-harm events are also more common after than before surgery.[12–15]

Because suicide is rare, a randomised trial of sufficient size and duration to assess suicide risk after bariatric surgery is unlikely to be done. Furthermore, no observational studies have been reported on suicide that compare patients treated with bariatric surgery with controls with obesity treated non-surgically. The investigators of the Utah Mortality Study[2] reported an increased risk of death not caused by disease in patients treated with bariatric surgery compared with controls who applied for a driver's licence, matched for age, sex, and BMI. The increased risk of suicide was not significant, but the point estimate was more than twice as high in patients treated with surgery compared with matched controls. In the Utah Obesity Study,[16] no difference in suicide risk over a follow-up time of up to 6 years could be detected in the bariatric surgery group

Research in context

Evidence before this study

A systematic review for the US National Institutes of Health concluded that emerging data indicate an increased risk of suicide, or deaths not caused by disease, after bariatric surgery. The cited observational studies used comparators with obesity who had applied for a driver's licence or were seeking but did not receive bariatric surgery. To our knowledge, no reports have been published on the risk of suicide after bariatric surgery versus non-surgical weight loss therapy. Furthermore, previous studies have not accounted for baseline differences in psychiatric status, such as history of self-harm, substance misuse, and depression.

Added value of this study

On the basis of two large, long-term, matched, controlled studies of individuals with obesity intending to lose weight, we identified a substantially increased relative risk of suicide or non-fatal self-harm in the surgery group, after accounting for baseline psychiatric status. The excess risk after surgery was not explained by insufficient weight loss or weight regain, as individuals dying by suicide or who had hospital treatment for non-fatal self-harm had similar or greater weight loss during follow-up than other patients. Despite our attempts to match and stratify the analyses by baseline history of self-harm, substance misuse, depression, and anxiety, we cannot rule out the possibility that the increased risk of suicide or non-fatal self-harm after bariatric surgery in these non-randomised studies is due to different patient characteristics among individuals who chose surgery instead of non-surgical weight loss methods.

Implications of all the available evidence

A randomised trial of sufficient size and duration to assess the risk of suicide between bariatric surgery and a non-surgical intervention is unlikely to be achievable, in view of the rarity of suicide as an outcome. The findings from our matched cohort studies and evidence from previous observational studies suggest that bariatric surgery is associated with an increased risk of suicide. Importantly, the absolute suicide risk is small and the association might be affected by selection bias and residual confounding. However, the relative risk of suicide and non-fatal self-harm is considerable even when accounting for multiple known suicide risk factors. The reported association of bariatric surgery (especially gastric bypass) with an increased risk of alcohol and substance misuse provides a plausible mechanism for an increased risk of suicide. For the general postbariatric population, the benefits of bariatric surgery, including lower mortality, outweigh our finding of an increased risk of suicide and self-harm. However, our findings could help to improve guidelines regarding how surgery candidates are selected and followed up over time.

(four suicides) versus a control group with severe obesity who sought but did not receive bariatric surgery (no suicides). Neither study[2,16] accounted for baseline psychiatric status (which is likely to be associated with both bariatric surgery exposure and the suicide outcome) in the surgery and control groups, nor had they included a non-surgically treated obese control group. A Danish cohort study[15] excluded patients with a history of contact with hospital-based psychiatric services and showed no difference in suicide frequency between patients treated with bariatric surgery and those admitted to hospital with a diagnosis of obesity but who had not undergone bariatric surgery.

We aimed to compare the risk of suicide and non-fatal self-harm in patients with obesity attempting to lose weight with bariatric surgery versus those treated without bariatric surgery, accounting for baseline psychiatric status, in two matched cohort studies in Sweden linked to outcome data from nationwide health-care registers.

Methods

Study design

Matched cohort designs were used to analyse the association between bariatric surgery and the outcomes suicide and non-fatal self-harm. The cohorts used for our analysis were the Swedish Obese Subjects (SOS) study[3] and a nationwide register linkage study combining the Scandinavian Obesity Surgery Registry (SOReg)[17] and the Itrim Health Database, a register including individuals treated with intensive lifestyle modifications.[6] Our rationale for using two studies was that SOS and SOReg plus Itrim have complementary strengths. SOS provides longer follow-up than any other existing controlled study, but used older surgical techniques. SOReg plus Itrim included the currently used surgical technique and an intensively treated control group, but had shorter follow-up.

Participants in SOS and SOReg plus Itrim were linked to nationwide health registers with the Swedish personal identity number, which is unique for each resident. The linkage was done by officials at the National Board of Health and Welfare and at Statistics Sweden. Seven regional ethical review boards approved the study protocol for the SOS study and written or oral informed consent was obtained from all patients. The register linkage of SOReg plus Itrim was approved by the regional ethics committee in Stockholm, Sweden, and all analyses were done on deidentified data.

Setting

The Swedish health-care system is tax funded and offers universal access to physicians, psychologists, dietitians, and other health-care specialists. In 2014, the adult prevalence of a BMI of 35 kg/m² or higher in Sweden was estimated to be 5–6%.[1] Globally, Sweden had one of the highest percentages of bariatric procedures for the total population in 2013 (0·08%, compared with 0·04% in the USA and Canada).[18] In individuals undergoing bariatric surgery, the prevalence of depression, self-harm,

and substance misuse at baseline was about twice as high as in the general population in Sweden.[13] The age-standardised death by suicide rates per 100 000 population was 12·3 in Sweden, which is similar to the Organisation for Economic Co-operation and Development average of 12·0 and that in the USA (12·5).[19]

SOS study

SOS is a prospective, non-randomised, controlled, intervention study, with patients recruited between Sept 1, 1987, and Jan 31, 2001,[3] via recruitment campaigns in the mass media and at 480 primary health-care centres. Patients choosing surgery constituted the surgery group. A contemporaneously matched control group of individuals not choosing to undergo surgery was created, with 18 matching variables: sex, age, bodyweight, height, waist circumference, hip circumference, systolic blood pressure, serum cholesterol and triglyceride concentrations, smoking status, diabetes, menopausal status, four psychosocial variables with documented associations with death, and two personality traits related to treatment preference (appendix p 3). Matching was not done at an individual level, but an algorithm selected controls so that the mean values of the matching variables in the control group became as similar as possible to those values in the surgery group, using the method of sequential treatment assignment.

Study groups had identical inclusion (aged 37–60 years and BMI ≥34 kg/m² in men and ≥38 kg/m² in women) and exclusion criteria (earlier surgery for gastric or duodenal ulcer, earlier bariatric surgery, gastric ulcer or myocardial infarction during the past 6 months, ongoing or active malignancy during the past 5 years, bulimic eating pattern, drug or alcohol misuse, psychiatric or cooperative problems contraindicating bariatric surgery, and other contraindicating conditions such as chronic glucocorticoid or anti-inflammatory treatment).

The choice of procedure in the bariatric surgery group (n=2010) was made by the operating surgeon (265 [13%] gastric bypass, 376 [19%] gastric banding, and 1369 [68%] vertical-banded gastroplasty). Open surgery was used in 1793 (89%) of 2010 patients. Laparoscopic surgery was gradually introduced from 1993, and during the final 2 recruitment years most procedures (82 [62%] of 133) were done with this technique. Control patients received the customary non-surgical obesity treatment at their registration centre. No attempt was made to standardise the non-surgical treatment, which ranged from sophisticated lifestyle intervention to no treatment.

SOReg plus Itrim study

SOReg is a nationwide, prospective register for bariatric surgery started in 2007. It has been estimated to cover 98·5% of all bariatric procedures in Sweden.[17] Data are stored electronically and recorded as part of clinical practice. For this study, data were used from Jan 1, 2007, to Dec 31, 2012.

The Itrim Health Database prospectively collects data on individuals who enrolled in the commercial weight loss programme at 38 Itrim centres across Sweden. Itrim centres use a common information technology platform for quarterly follow-up—eg, measured bodyweight, waist circumference, and blood pressure. For this study, data were available from individuals starting the programme from Jan 1, 2006, to Dec 31, 2013.

In our analysis, we included individuals aged 18 years or older with a BMI of 30–49·9 kg/m² and baseline bodyweight recorded from SOReg and Itrim. There were no mandatory national eligibility criteria for bariatric surgery during the study period, but most county councils recommended an indication of a BMI of 35 kg/m² or higher with obesity-related comorbidity or a BMI of 40 kg/m² or higher without obesity-related comorbidity. In the sample used for this study, 888 (4%) of 20 256 patients treated with surgery had a BMI less than 35 kg/m² (median BMI 34·1 kg/m² [IQR 33·3–34·6]).

Participants who had surgery underwent primary gastric bypass (96% of procedures done laparoscopically; open surgery was primarily used when a patient had had a previous open abdominal surgery or when complications arose during an initial laparoscopic procedure). Intensive lifestyle participants received the Itrim programme including a 3 month weight-loss phase with either low-calorie or very-low-calorie diets (appendix p 2) on the basis of baseline BMI, personal preference, and contraindication status. After the weight-loss phase, patients entered a 9 month weight-maintenance programme including exercise (circuit training at the centre 2–3 times per week for 30–45 min, and pedometer use to encourage walking) and dietary advice. Behavioural changes were facilitated by a structured programme, including 20 group sessions lasting 1 h. Face-to-face counselling sessions also took place throughout the programme.

See Online for appendix

Covariates in SOS and SOReg plus Itrim

Demographic data were available on age, sex, and educational level for both cohorts. For SOReg plus Itrim, data were retrieved from Statistics Sweden on marital status, disposable income, disability pension (also available for SOS), and unemployment. Measured BMI was available from baseline examinations. We retrieved data on health-care visits for self-harm, substance misuse, and other psychiatric causes, as well as for cardiovascular disease, from the National Patient Register (inpatient data from before Jan 1, 2001, for SOS, and inpatient and outpatient data from before Dec 31, 2012, for SOReg, and from before Dec 31, 2013, for Itrim). We retrieved data on psychiatric and antidiabetes drug use before inclusion via self-report in SOS and from the Prescribed Drug Register in SOReg plus Itrim (register start date July 1, 2005). Self-reported drug use in SOS is reasonably consistent with data from the Prescribed Drug Register.[20]

The International Classification of Diseases (ICD) and Anatomical Therapeutic Chemical classification system codes used are provided in the appendix (p 3). As missing data on BMI (<1% [12/61 495]) and education (<1% [254/61 495]) were rare in SOReg plus Itrim, and data were complete for the other variables, we excluded patients with missing data.

Outcome and follow-up in SOS and SOReg plus Itrim

The primary outcome in SOS was all-cause mortality, for which the study was powered.[3] The outcomes of our analysis were death by suicide, and death by suicide or non-fatal self-harm, retrieved from the Causes of Death Register and the National Patient Register until Dec 31, 2013, for SOS and Dec 31, 2014, for SOReg plus Itrim. In the main analysis, we used ICD codes to identify suicide and non-fatal self-harm (ICD9 E950–959 and E980–989; ICD10 X60–84, Y10–34, and Y870), including both confirmed suicides and deaths from undetermined intent.

Participants were followed up from the treatment start date until first event, death, emigration, or end of register-based follow-up, whichever came first. SOS controls and Itrim participants who crossed over to bariatric surgery were censored at the crossover date (SOS n=289; Itrim n=335), as were patients treated with surgery in SOS who had their procedure reversed to normal anatomy (n=100).

During follow-up, two patients treated with surgery in SOS requested to be deleted from the database, and one obtained an unlisted identity number, making linkage impossible. In SOS, both groups had identical follow-up with physical examinations and questionnaires at baseline and at years 0·5, 1, 2, 3, 4, 6, 8, 10, 15, and 20. In addition to the follow-up for the research study, patients in SOS also had routine follow-up in the public health-care system (appendix p 2).

Statistical analysis

We analysed outcomes using survival analysis and estimated hazard ratios (HRs) using Cox regression. We evaluated the proportional-hazard assumption by assessing the interaction of time and treatment. In SOS, the interaction term was not significant for suicide (p=0·11) or for self-harm and suicide (p=0·12). This term was significant for suicide in SOReg plus Itrim (p=0·0497) but not for self-harm and suicide (p=0·25). Because of the small number of events, we did not stratify the model by follow-up time.

In the sequentially matched SOS study, adjustment was made for age, sex, history of self-harm (yes or no), and

	SOS study (recruitment 1987–2001)			SOReg plus Itrim (intervention 2006–13)		
	Bariatric surgery group (n=2008)*	Control group (n=2037)	p value	Gastric bypass group (n=20 256)	Intensive lifestyle modification group (n=16 162)	p value
Sex	..	..	0·824	..	..	1·00
Female	1420 (71%)	1447 (71%)	..	16 071 (79%)	12 823 (79%)	..
Male	588 (29%)	590 (29%)	..	4185 (21%)	3339 (21%)	..
Age (years)	47·2 (5·9)	48·7 (6·3)	<0·0001	41·3 (10·5)	41·5 (10·8)	0·125
BMI (kg/m²)	42·4 (4·5)	40·1 (4·7)	<0·0001	41·1 (3·9)	40·6 (4·1)	<0·0001
University education	256 (13%)	431 (21%)	<0·0001	4660 (23%)	3718 (23%)	1·00
Married	NA	NA	..	9034 (45%)	6837 (42%)	<0·0001
Annual income (1000 €)	NA	NA	..	23·7 (14·5)	28·2 (19·4)	<0·0001
Disability pension	357 (18%)	316 (16%)	0·053	2366 (12%)	997 (6%)	<0·0001
Unemployment	NA	NA	..	2016 (10%)	883 (5%)	<0·0001
History of psychiatric illness						
Self-harm	69 (3%)	38 (2%)	0·0019	403 (2%)	322 (2%)	1·00
Substance abuse	58 (3%)	49 (2%)	0·339	294 (1%)	235 (1%)	1·00
Psychiatric health-care visits†	200 (10%)	175 (9%)	0·133	3083 (15%)	2460 (15%)	1·00
Use of antidepressants	133 (7%)	114 (6%)	0·173	6108 (30%)	4873 (30%)	1·00
Use of anxiolytics	98 (5%)	88 (4%)	0·395	3446 (17%)	2750 (17%)	1·00
Use of hypnotics and sedatives	74 (4%)	59 (3%)	0·160	4426 (22%)	2888 (18%)	<0·0001
Physical health status						
Diabetes	346 (17%)	263 (13%)	0·0001	1954 (10%)	1559 (10%)	1·00
Cardiovascular disease	383 (19%)	260 (13%)	<0·0001	4203 (21%)	3354 (21%)	1·00

Data are n (%) or mean (SD). SOS=Swedish Obese Subjects. SOReg=Scandinavian Obesity Surgery Registry. Itrim=Itrim Health Database. NA=not available. *Primary operations were 1367 (68%) vertical-banded gastroplasty, 376 (19%) gastric banding, 265 (13%) gastric bypass. †Only from inpatient care for the SOS study and SOReg plus Itrim was from both inpatient (1358 [7%] surgery *vs* 1051 [7%] intensive lifestyle; p=0·439) and hospital-based outpatient care (2506 [12%] surgery *vs* 1981 [12%] intensive lifestyle; p=0·745).

Table: **Baseline characteristics**

continuous BMI. In the SOReg plus Itrim analysis, we used coarsened exact matching[21] to match participants by BMI (<35 kg/m², 35 to <40 kg/m², 40 to <45 kg/m², and 45 to <50 kg/m²), age (18–29 years, 30–39 years, 40–49 years, 50–59 years, and ≥60 years), sex, education level, diabetes, cardiovascular disease, history of self-harm, substance misuse, antidepressant use, anxiolytic use, and history of psychiatric care (yes or no). To minimise loss of information, we allowed matching strata to include different numbers of participants who were treated with surgery or intensive lifestyle intervention. To compensate for the differential strata sizes, we weighted analyses by the strata size. For example, if one stratum had two participants treated with surgery and four participants treated with lifestyle modification, then we gave each participant treated with surgery a weight of 1 and each participant treated with lifestyle modification a weight of 0·5. We did additional adjustment for age, BMI, and income as continuous variables, and for marital status (married or unmarried), disability pension (yes or no), and unemployment benefits (yes or no).

We did subgroup analyses by procedure type (SOS only; analysis by intention to treat), psychiatric history, and education level. In SOS, we examined the 10 year bodyweight trajectory in patients treated with surgery with an event versus those patients without an event.

We did statistical analyses using SAS (version 9.4) and Stata (version 14). The SOS study is registered with ClinicalTrials.gov, number NCT01479452.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. MN, GB, and LMSC had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit for publication.

Results

After recruitment campaigns in the mass media and at primary health-care centres between Sept 1, 1987, and Jan 31, 2001, 6905 individuals completed an eligibility examination for the SOS study, of whom 5335 (77%) were found eligible. 2010 participants chose surgical treatment while the contemporaneously matched control group consisted of 2037 individuals not choosing surgery (appendix p 10).

Of the 30 081 patients in SOReg who had bariatric surgery during the study period (between Jan 1, 2007, and Dec 31, 2012), 26 388 (88%) had gastric bypass and were eligible for matching, and 18 365 (58%) of 31 414 patients were treated with intensive lifestyle modifications (initiated from Jan 1, 2006, to Dec 31, 2013) were eligible (appendix p 11). After matching, 20 256 (77%) participants treated with gastric bypass and 16 162 (88%) participants treated with intensive lifestyle modification were available for analysis (appendix p 11).

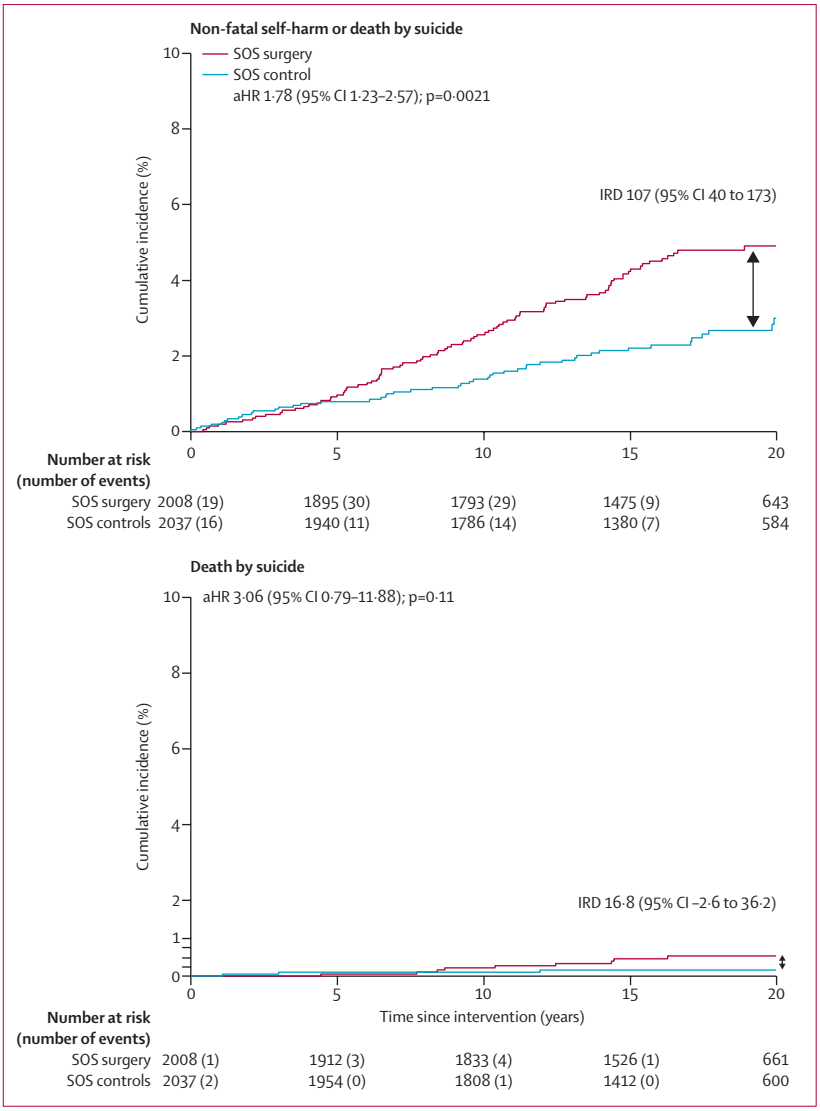
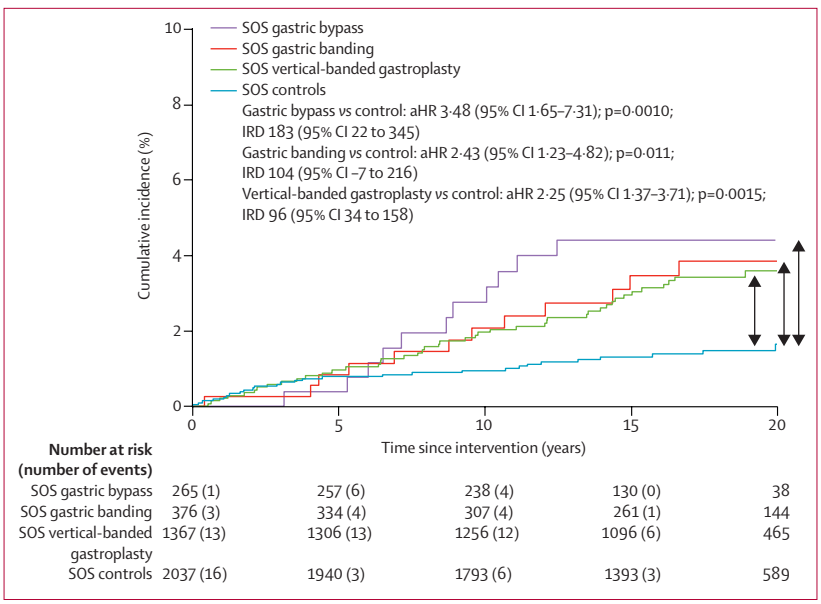


Figure 1: **Kaplan-Meier analysis of suicide and non-fatal self-harm in the SOS study**
y-axes have been truncated. aHRs were adjusted for age, sex, BMI, and history of self-harm. SOS=Swedish Obese Subjects. aHR=adjusted hazard ratio. IRD=incidence rate difference per 100 000 person-years.

When we compared baseline characteristics in the two cohort studies, patients in the SOS surgery group had lower education, more history of hospital admission for self-harm, more diabetes, and cardiovascular disease, and were younger and had a higher BMI compared with controls (table). Mean bodyweight changes in the surgery and control groups were –23% (SD 11; –28 kg [SD 14]) and 0 (8; 0 kg [9]) at 2 years, –17% (12; –21 kg [15]) and 1% (13; 1 kg [14]) at 10 years, and –16% (13; –21 kg [17]) and –1% (14; –2 kg [16]) at 15 years, respectively.

In the SOReg plus Itrim cohort, the prevalence of class I, II, and III obesity was identical after matching (appendix p 9), but patients in the gastric bypass group had a higher mean BMI than participants in the intensive lifestyle group (table). Patients in the gastric



Number at risk (number of events)					
SOS gastric bypass	265 (1)	257 (6)	238 (4)	130 (0)	38
SOS gastric banding	376 (3)	334 (4)	307 (4)	261 (1)	144
SOS vertical-banded gastroplasty	1367 (13)	1306 (13)	1256 (12)	1096 (6)	465
SOS controls	2037 (16)	1940 (3)	1793 (6)	1393 (3)	589

Figure 2: **Kaplan-Meier analysis of suicide and non-fatal self-harm in the SOS study, by primary procedure type**
y-axis has been truncated. Case ascertainment from inpatient care and Causes of Death Register only because the outpatient care component was added on Jan 1, 2001, and gastric bypass was used more in the later part of the SOS recruitment period. SOS=Swedish Obese Subjects. aHR=adjusted hazard ratio. IRD=incidence rate difference per 100 000 person-years.

bypass group also had lower income, were more often married, on disability pension, unemployed, and using hypnotics or sedatives. The mean 1 year bodyweight change was –32% (SD 7; –37 kg [SD 10]) in the gastric bypass and –15% (9; –18 kg [11]) in the intensive lifestyle modification group.

During 68 528 person-years in SOS (median 18 years, IQR 14–21), suicides or non-fatal self-harm events were higher in the surgery group (n=87) than the control group (n=49; adjusted HR [aHR] 1·78, 95% CI 1·23–2·57; p=0·0021); of these events, nine and three were suicides, respectively (3·06, 0·79–11·88; p=0·11; figure 1). Additional adjustment for baseline diabetes and cardiovascular disease resulted in similar estimates for suicide or non-fatal self-harm (1·74, 1·20–2·52; p=0·0033) and for suicide (3·33, 0·86–12·97; p=0·083). In analyses by primary procedure type, increased risk of suicide or non-fatal self-harm was seen for gastric bypass, gastric banding, and vertical-banded gastroplasty versus controls (figure 2, figure 3A). Patients in the overall surgery group in SOS who died by suicide or had a non-fatal self-harm event had similar or lower bodyweight during follow-up than patients who did not, and bodyweight did not differ at baseline (figure 4).

Poisoning was the most common method for dying by suicide (78% [7/9] for surgery *vs* 100% [3/3] for controls; appendix p 4) and of non-fatal self-harm (70% [57/81] *vs* 53% [25/47]; appendix p 5) in SOS. Of the nine suicides in the surgery group, five occurred in patients treated with gastric bypass (two who had primary gastric bypass, two who were converted from vertical-banded gastroplasty, and one who converted from gastric banding; appendix p 4). Substance misuse was recorded in 48% [39/81] of patients in the surgery group and 28% [13/47] of participants in the control group with non-fatal self-harm events (p=0·023; appendix p 5).

During 149 582 person-years (median 3·9; IQR 2·8–5·2), suicides or non-fatal self-harm events were higher in the SOReg gastric bypass group (n=341) than in the Itrim intensive lifestyle modification group (n=84; aHR 3·16, 2·46–4·06; p<0·0001); of these events, 33 and five were suicides, respectively (5·17, 1·86–14·37; p=0·0017; figure 5). As in SOS, poisoning was the most common method for dying by suicide (79% [26/33] for surgery *vs* 80% [4/5] for intensive lifestyle modification; appendix p 4) and non-fatal self-harm (68% [214/316] *vs* 59% [47/80]; appendix p 5). Among participants with non-fatal self-harm events, substance misuse diagnoses were more common after gastric bypass than after intensive lifestyle modification (51% [162/316] *vs* 29% [23/80], p=0·0003; appendix p 5).

In subgroup analyses, the risk of suicide or non-fatal self-harm was increased in both SOS and SOReg plus Itrim in participants in the surgery group versus the control group in the subgroup free of registered psychiatric disorders and without a history of self-harm at baseline (figure 3). The risk was also increased in both studies in the surgery group versus control group in those participants with university education as well as those participants without university education.

Discussion

We compared the risk of suicide and non-fatal self-harm after bariatric surgery and non-surgical obesity treatment in two large matched cohorts, and in both, patients treated with surgery were at an increased risk. However, despite certain psychiatric disorders being part of the exclusion criteria in the SOS study, patients treated with surgery had almost twice the prevalence of self-harm history at baseline compared with controls, and such a history is strongly related to future events.[12] Nevertheless, the increased risk was also seen in the subgroup of patients free of known psychiatric disorders and without self-harm history at baseline, in both the SOS and SOReg plus Itrim cohorts.

Strengths of our study include access to long-term information on self-harm, substance misuse, and other psychiatric disorders in two large, matched cohort studies of people treated with bariatric surgery and non-surgically treated controls. Nationwide health registers enabled near complete outcome ascertainment for both suicide and non-fatal self-harm resulting in hospital care for up to 8 years in SOReg plus Itrim and up to 27 years in SOS. Furthermore, the two cohorts complemented each other: SOS had very long follow-up, which by necessity means that older surgical techniques were used than in SOReg. SOS also had no standardised control treatment comparable to that for SOReg plus Itrim. Trials of bariatric

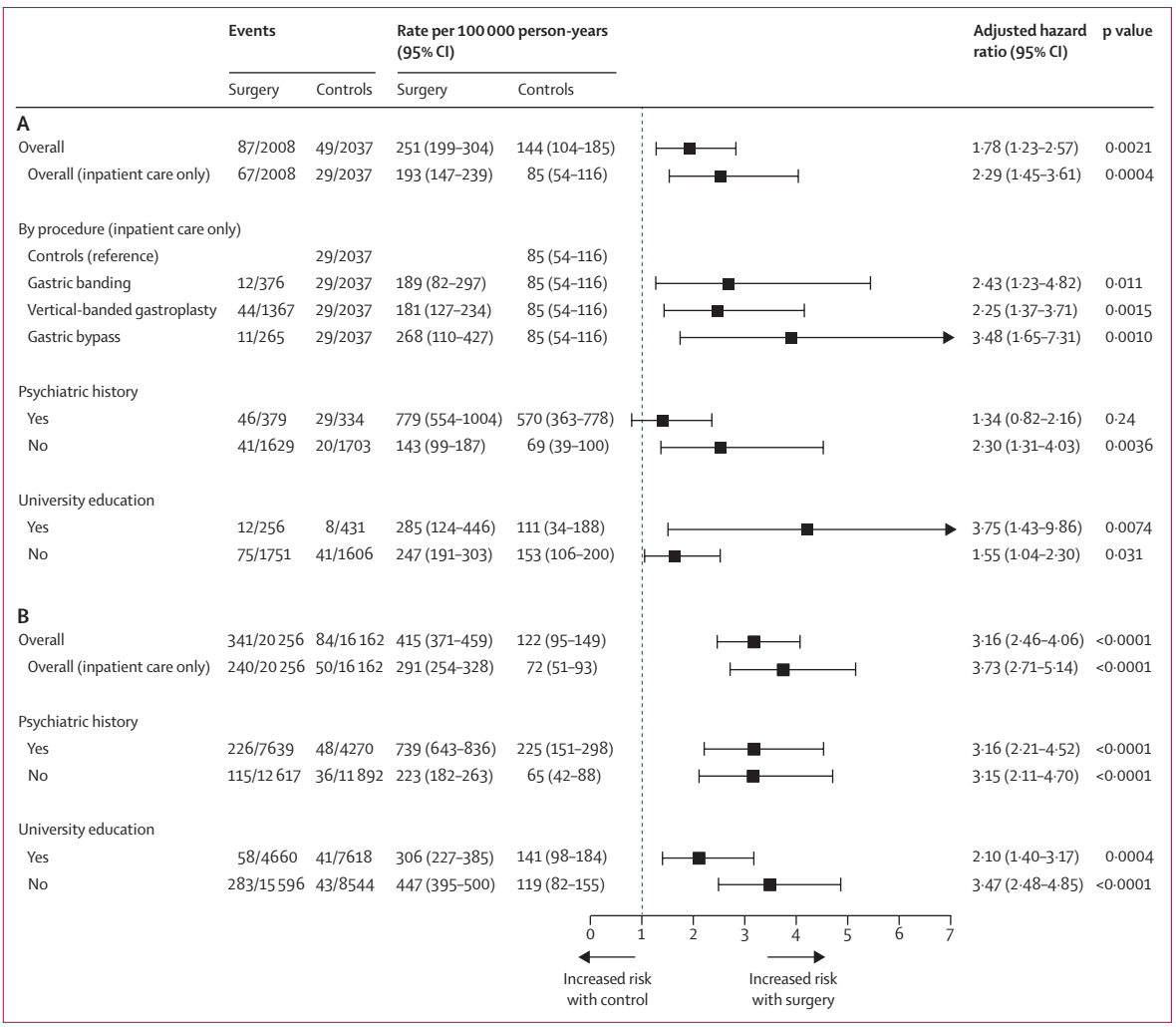


Figure 3: **Forest plots for suicide and non-fatal self-harm in the SOS (A) and SOReg plus Itrim (B) cohorts, overall and by subgroups**
(A) Adjusted for age, sex, BMI, and history of self-harm. Inpatient care only refers to case ascertainment excluding data from the outpatient component from the National Patient Register. Outpatient data were available from Jan 1, 2001, onwards. Baseline characteristics for the subgroup with psychiatric history are provided in the appendix (p 6). (B) Matched on age, sex, BMI, education level, cardiovascular disease, diabetes, history of self-harm, substance misuse, visits in psychiatric care, use of antidepressants, and use of anxiolytics. Additional adjustment was made for age, BMI, and income as continuous variables, as well as for marital status, disability pension, and unemployment status as binary variables. Incidence and aHRs are weighted by strata size to account for matching procedure. Inpatient care only refers to case ascertainment excluding data from the outpatient component from the National Patient Register. Baseline characteristics for the subgroup with psychiatric history are provided in the appendix (p 6). SOS=Swedish Obese Subjects. SOReg=Scandinavian Obesity Surgery Registry. Itrim=Itrim Health Database. aHR=adjusted hazard ratio.

surgery have been criticised for use of comparators of insufficient intensity, and very-low-calorie diets have been discussed as a component of higher-intensity regimens.[22] In a meta-analysis[23] of bariatric surgery trials, weight change during the first 2 years in controls ranged from +1 kg to –8 kg, whereas patients treated with surgery lost a mean 20–43 kg. At 1 year in our analysis of SOReg and Itrim, the intensive lifestyle modification resulted in a weight loss of 15% (18 kg) compared with 32% (37 kg) for gastric bypass.

A limitation of this study is that neither SOS nor SOReg plus Itrim were randomised studies. However, randomised trials of bariatric surgery are unlikely to have sufficient power to investigate rare events such as suicide, necessitating use of observational study designs. Both SOS and SOReg plus Itrim studies included matched controls with obesity who were attempting to lose weight and accounted for multiple suicide risk factors; however, selection bias and residual confounding might still have affected our results. The Itrim participants, by contrast with the SOS controls, paid for weight loss treatment, whereas patients in the surgery group of SOReg were more likely to be referred and not pay out of pocket, which could be important because suicidal behaviour displays a strong socioeconomic gradient. However, in subgroup analysis by education level, we noted increased risk of suicide or non-fatal self-harm after surgery in both the SOS and SOReg plus Itrim studies for all

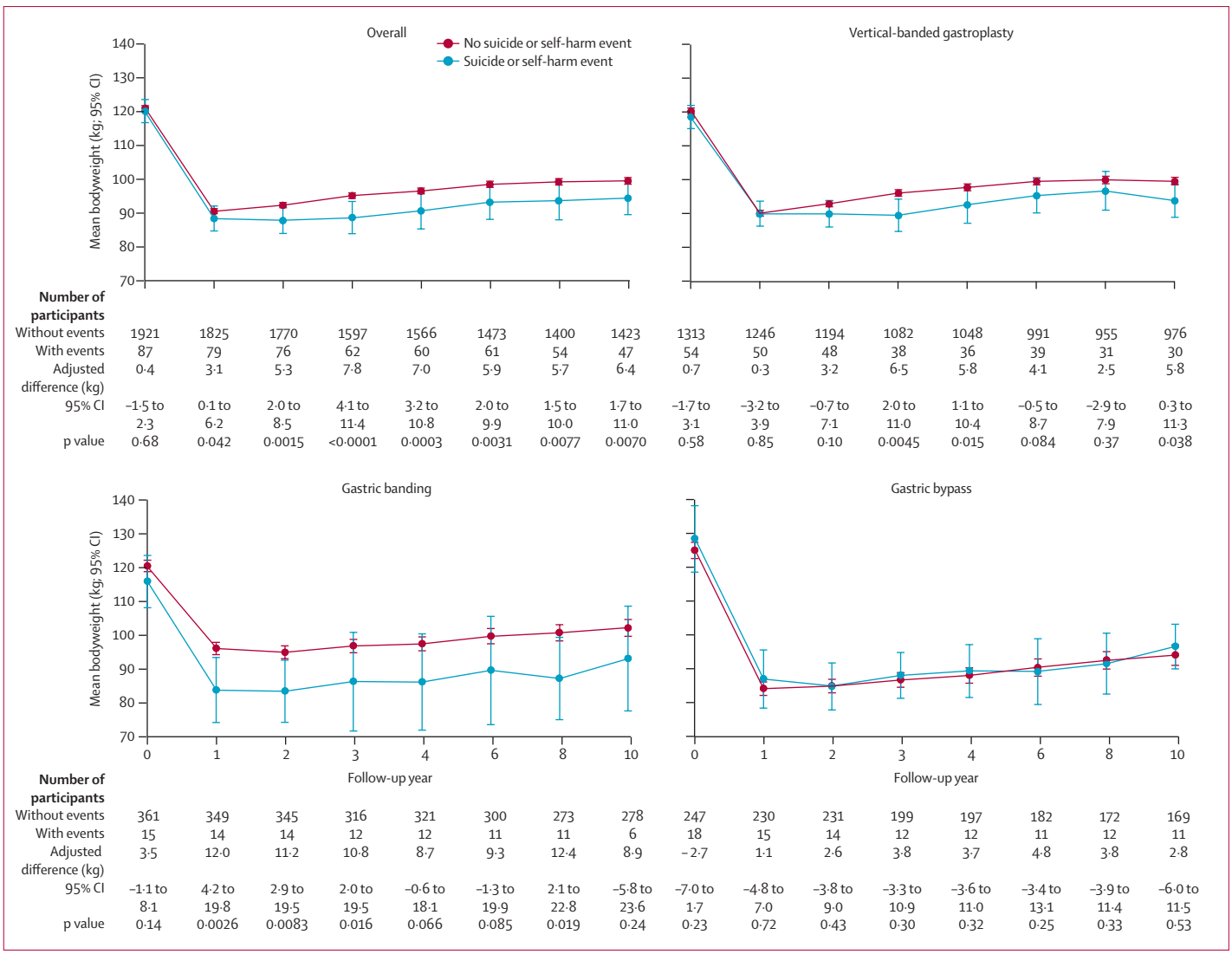


Figure 4: **Mean bodyweight over 10 years in patients treated with surgery in the SOS study, by suicide and self-harm status (overall and by primary procedure type)**
Adjustment variables were the same as in the main analysis (age, sex, baseline BMI, and history of self-harm). SOS=Swedish Obese Subjects.

education-level strata. For SOReg plus Itrim, we also adjusted for income, disability pension, and unemployment to reduce bias from differences in socioeconomic position.

Another limitation of our study is that no patients in our cohorts had sleeve gastrectomy, a method which is increasingly used. Also, Swedish people are predominantly white. Thus, we do not know if our results can be generalised to patients having sleeve gastrectomy or to other ethnic groups. Regarding procedure type in SOS, the analyses were done according to primary procedure. This analysis might overestimate the risks for vertical-banded gastroplasty and gastric banding, because conversion to gastric bypass was common. Regarding follow-up, due to the long recruitment in SOS and nationwide scope of SOReg plus Itrim, it was not possible to provide detailed information on contacts with psychologists and primary care after treatment.

Finally, by contrast with SOReg plus Itrim, suicide or non-fatal self-harm did not differ between groups during the first 5 years in SOS. A potential explanation for this difference is that SOS is a prospective study with at least annual follow-up visits during the first 4 years, in addition to routine follow-up in the health-care system. Patients in SOReg had less intensive follow-up. Furthermore, only 13% (265/2008) of surgery participants in SOS had gastric bypass, compared with 100% (20 256/20 256) in SOReg. In our analyses by procedure type and risk of self-harm or suicide in SOS, an increased risk of 3·5 times was associated with gastric bypass, 2·4 times with gastric banding, and 2·3 times with vertical-banded gastroplasty versus controls.

Several mechanisms have been suggested for an increased risk of suicide after bariatric surgery,[11,24] including disappointment among patients treated with surgery due to insufficient weight loss, subsequent weight regain, recurrence of obesity-related comorbidities after initial remission, or that weight loss did not have the expected life-changing effects.[11] However, rather than insufficient weight loss, our results show that patients treated with surgery in SOS who later died by suicide or had a non-fatal self-harm event had either similar or greater weight loss than those patients who did not, irrespective of primary procedure type.

Previous studies, including reports from SOS, have shown an increased incidence of alcohol and substance misuse after gastric bypass,[9] and such behaviours could result in impulsive acts. Also, alcohol intake has been reported to result in higher blood alcohol concentrations after gastric bypass than before.[25] The effect on uptake of other substances is largely unknown, but it is possible that gastric bypass patients get intoxicated more easily than people who have not had surgery. The higher incidence of alcohol misuse after gastric bypass compared with restrictive procedures[26–28] might partly explain why the aHRs for suicide and non-fatal self-harm are higher in SOReg plus Itrim than in SOS. In SOS, the risk of alcohol misuse diagnosis was five times higher after gastric bypass and twice as high after vertical-banded gastroplasty compared with controls, whereas no difference was detected after gastric banding.[27]

Mental health problems are much more prevalent in patients undergoing bariatric surgery than in general population comparators matched for age and sex.[13] The 4 year trajectory of antidepressant use after surgery has been reported to be similar to that in the general population, but steeper for use of benzodiazepines, hypnotics, and sedatives.[13] The association between bariatric surgery, different procedure types, and mental health is not yet well described on the basis of randomised trials or carefully matched cohort studies with controls with obesity who are attempting to lose weight.[10] In SOS, no difference between surgery and control groups in overall psychiatric drug use has been found.[29] For SOReg plus Itrim, a higher incidence of hypnotic or sedative use and higher dose increases in prevalent users have been reported after gastric bypass versus intensive lifestyle modification.[30]

Other proposed mechanisms behind an association between bariatric surgery and suicide include neuroendocrine alterations, exacerbations of depression and anxiety due to micronutrient or macronutrient deficiencies caused by malabsorption, and psychological mechanisms such as maladaptive eating behaviours.[31] In SOS, health-related quality of life has been shown to be improved up to 10 years after surgery compared with baseline, and compared with the control group.[32] However, average improvements might mask deteriorating quality of life in a subset of patients due to, for example, surgical complications or alcohol misuse. For a rare event such as suicide, this type of subset does not need to be large to produce statistically significant risk increases.

Our observational findings suggest a need for provision of information about self-harm to patients before surgery and postoperative psychiatric surveillance.[33] However, it could be difficult to design such a surveillance system, in view of the rarity of suicides: we observed 42 suicides in SOS and SOReg over 117 000 person-years after

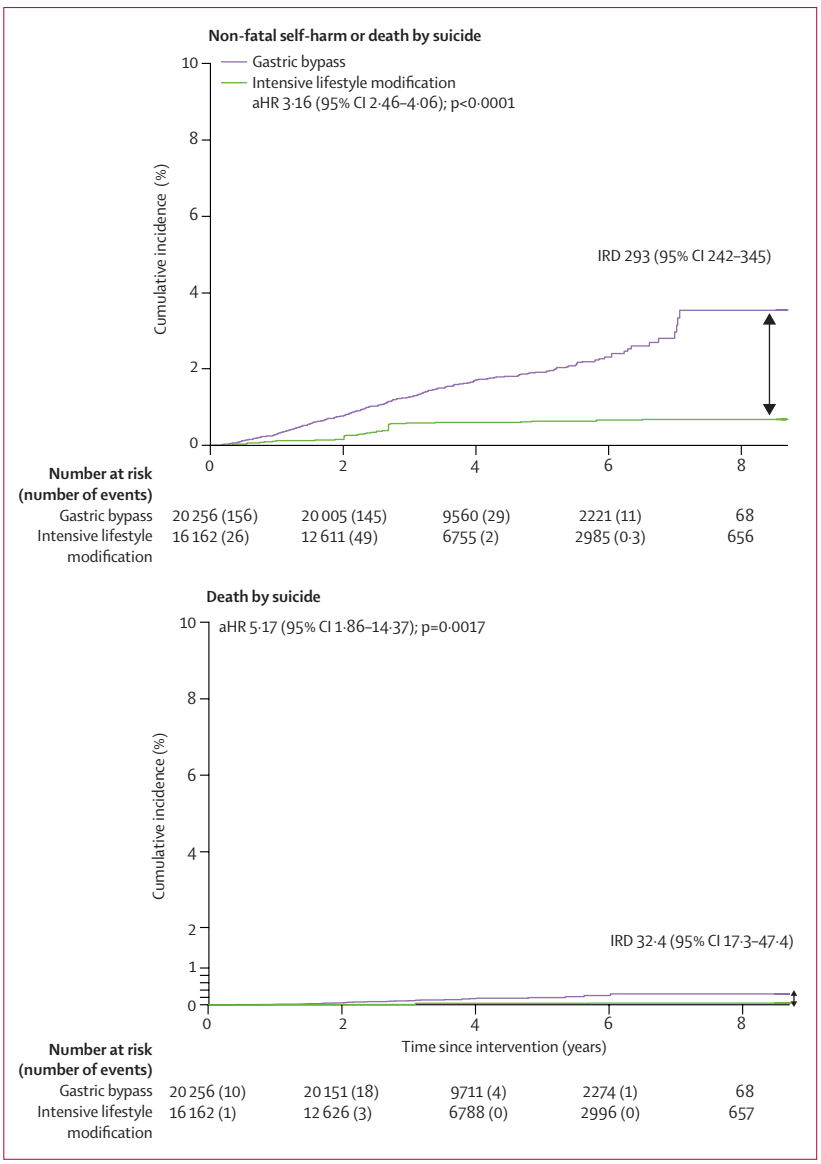


***Figure 5*: Kaplan-Meier analysis of suicide and non-fatal self-harm in the SOReg plus Itrim study comparing gastric bypass with intensive lifestyle modification**

y-axes have been truncated. Matched on age, sex, BMI, education level, cardiovascular disease, diabetes, history of self-harm, substance misuse, visits in psychiatric care, use of antidepressants, and use of anxiolytics. aHRs were adjusted for age, BMI, income, marital status, disability pension, and unemployment. Total number for intensive lifestyle modification group are weighted by strata size to account for matching procedure. SOReg=Scandinavian Obesity Surgery Registry. Itrim=Itrim Health Database. aHR=adjusted hazard ratio. IRD=incidence rate difference per 100 000 person-years.

surgery. Hence annual psychiatric surveillance is likely to be inefficient. Restricting surveillance to high-risk patients—eg, those with baseline psychiatric disorders—would be more efficient, but on the basis of our data this strategy would miss almost 50% of deaths by suicide.

International guidelines list active or recent substance misuse as a contraindication for surgery.[34] Psychiatric hospital admission and self-harm history are considered risk factors for poor outcomes, but not contraindications when appropriate mental health treatment is provided. Furthermore, the European guidelines recommend pre-operative psychological assessment by a psychiatrist or psychologist not just for diagnostic purposes, but also to identify areas of vulnerability, and higher-risk patients should be selected for postoperative monitoring.[35]

Despite our finding of an increased risk of suicide, we do not believe that these results should discourage use of bariatric surgery, at least not from a survival perspective. Several well designed observational studies[2–4] have shown a survival benefit versus controls with obesity despite the potential increased suicide risk. Importantly, although the relative risk of suicide is high, the absolute risk is low. For example, in the Utah Mortality Study,[2] the incidence of all-cause mortality was 37·6 per 10 000 person-years in participants treated with surgery and 57·1 per 10 000 person-years in matched controls, compared with incidences of suicide of 2·6 per 10 000 person-years and 0·9 per 10 000 person-years, respectively. Beyond mortality, the many documented and common benefits of bariatric surgery[9,10] are likely to outweigh our finding of an increased risk of suicide and self-harm. However, our findings could help to inform and refine guidelines regarding how surgery candidates are selected and followed up over time.

Contributors

LMSC is the principal investigator of the Swedish Obese Subjects study and MN is the principal investigator of the Scandinavian Obesity Surgery Registry with Itrim study. LMSC and MN conceived and coordinated the investigation. MN wrote the first draft of the report. MP and GB were responsible for the preparation of data. GB and MN did the statistical analyses for the initial submission and JS did the statistical analyses for the revisions. All authors undertook revisions and contributed intellectually to the development of the report. MN and LMSC are the study guarantors.

Declaration of interests

CM, MN, and JS have received consulting fees from Itrim. LMSC has received lecture fees from Johnson & Johnson, AstraZeneca, and Merck Sharp & Dohme. IN reports personal fees from Baricol Bariatrics AB, Sweden, outside the submitted work, and is the previous director of the Scandinavian Obesity Surgery Registry; JO is its current director. All other authors declare no competing interests.

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