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REVIEW ARTICLE

Risk of Suicide and Self-harm Is Increased After Bariatric Surgery—a Systematic Review and Meta-analysis

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Abstract

Background Bariatric surgery is endorsed by multiple societies as the most effective treatment for obesity. Psychosocial functioning has also been noted to improve for most patients after bariatric surgery. However, some studies have shown an increase in post-operative suicide risk. The aim of this study was to review the published literature and evaluate the association of bariatric surgery with suicide events and suicide/self-harm attempts in patients who have undergone weight loss surgery.

Methods MEDLINE and Embase were searched from inception through January 2018 for retrospective or prospective studies reporting mortality outcomes and self-harm or suicide rates after bariatric procedures. The primary outcome was the pooled event rate with 95% confidence interval (95% CI) for suicide. Secondary outcomes were suicide/self-harm attempts after bariatric surgery compared to same population prior to surgery and to matched control subjects, with the respective calculated odds ratios (OR) and 95% CI.

Results From 227 citations, 32 studies with 148,643 subjects were eligible for inclusion. The patients were predominantly females (76.9%). Roux-en-Y gastric bypass (RYGB) was the most commonly performed procedure (58.9%). The post-bariatric suicide event rate was 2.7/1000 patients (95% CI 0.0019–0.0038), while the suicide/self-harm attempt event rate was 17/1000 patients (95% CI 0.01–0.03). The self-harm/suicide attempt risk was higher after bariatric surgery within the same population with OR of 1.9 (95% CI 1.23–2.95), and compared to matched control subjects, OR 3.8 (95% CI, 2.19–6.59).

Conclusions Post-bariatric surgery patients had higher self-harm/suicide attempt risk compared to age-, sex-, and BMI-matched controls. Various pre- and post-surgical psychosocial, pharmacokinetic, physiologic, and medical factors may be involved.

Keywords Bariatric surgery · Suicide · Self-harm · Outcomes · Laparoscopic band · Roux-en-y bypass · Gastric bypass · Sleeve gastrectomy · Obesity

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Introduction

Bariatric surgery is the most effective treatment for obesity in patients refractory to dietary and lifestyle changes. Many of the complications associated with long-standing obesity, such as myocardial infarction, hypertension, stroke [1, 2], dyslipidemia [3, 4], diabetes mellitus [3–5], obstructive sleep apnea [6], and osteoarthrosis [7], decrease after bariatric surgery. Additionally, there is a 24% decrease in overall mortality, as reported by the Swedish Obese Subjects Study [8].

Short- and long-term clinical and psychosocial outcomes have been studied after bariatric surgery. While many aspects of psychosocial function improve after bariatric surgery, a proportion of patients report the return of depressive symptoms that have initially improved after surgery or absence of any psychological benefit [9]. This is a vulnerable population even prior to surgery. Bariatric surgery candidates have been found to have a higher proportion of pre-surgical psychiatric disease and psychotropic medication use compared to the general population [10–13], as well as an increased prevalence of pre-operative mental distress and binge-eating disorder [14, 15]. Between 21 and 61% of weight loss surgery candidates suffer from a psychiatric disease. Some studies suggest that individuals who seek weight loss surgery or pharmacotherapy are more likely to have depression and anxiety than BMI-matched individuals seeking behavioral interventions [15, 16]. The frequency of depressive symptoms decreases substantially following gastric bypass surgery but then may worsen over the following 24 months [17]. The prevalence of substance and alcohol abuse is also high, affecting about one third of candidates [18].

Depressive symptoms may also be exacerbated by the presence of medical comorbidities and occurrence of post-surgical complications and persistence/recurrence of comorbidities after surgery [19]. Depression is associated with many of the obesity-related comorbidities. It is twice as common in patients with diabetes and three times as common in chronic heart disease as in the general population, and is associated with decreased quality of life and worsening disease severity [20–22]. Mood disorders are prevalent in patients before any major surgery, not just bariatric, due to associated pain, morbidity, and decreased well-being [23]. If not addressed, they may predict increased morbidity and mortality after the operation. These issues have raised concerns of the potential impact of bariatric surgery on mental health and outcomes in a population that is considered at risk at baseline.

Psychiatric evaluation before and after bariatric surgery are recommended by the International Federation for the Surgery of Obesity (IFSO) [24], the American Society for Metabolic and Bariatric Surgery (ASMBS) [25], and The Obesity Society (TOS) [26] to identify patients with high risk of self-harm or suicide. Current guidelines recommend a face-to-face interview by a qualified evaluator to determine psychosocial, developmental, cognitive, personality, lifestyle, motivational, and social support aspects pre-operatively. Post-operative follow-up is also recommended to assess the need for psychotherapy or pharmacological interventions [24–26]. However, adoption of guidelines may vary among bariatric centers.

For all of the above reasons, bariatric surgery may be associated with higher suicide/self-harm rates. The aim of this study is to assess the rate of suicide/self-harm attempts after bariatric surgery and mortality from suicide in this patient population via a systematic review and meta-analysis of the published literature.

Methods

Search Strategy

A systematic electronic search and data extraction from two bibliographic databases (MEDLINE and Embase) was performed by two researchers from inception through January 15, 2018 using the Ovid interface. Studies in English with greater than ten adult participants were included. The terms used for data search included "suicide," "mortality," "self-harm," "gastric bypass," "Roux-en-Y gastric bypass", "RYGB," "sleeve gastrectomy," "sleeve gastroplasty," "LAGB," "lap band," "laparoscopic band," "bariatric surgery," and "biliopancreatic diversion" (Suppl. Materials).

Selected articles and abstracts were independently evaluated by two of the researchers. Disagreements were resolved by discussion and consensus, with the senior authors (V.P. and C.T.) serving as the final arbiters if consensus was not achieved.

Study Selection

Study Design and Population

Studies included in the analysis met the following criteria: [1] randomized controlled trials (RCTs) or observational studies (case-control, cross-sectional or cohort studies) published or presented as original research evaluating the suicide or self-harm risk in patients following bariatric surgery, [2] provided sufficient data to calculate odds ratios (OR) and event rates with 95% confidence intervals (95% CI), [3] reported short- and long-term outcomes after bariatric procedures, [4] had a sample size of more than ten patients, [5] included bariatric procedures currently performed, and [6] reported outcomes from inpatient admissions for suicide/self-harm attempts and hospital or insurance records. Studies that used mailed questionnaires to track data and mortality cases attributed to accidents or motor-vehicle accidents were excluded from the analysis.

Data Extraction

Two investigators utilized a standardized data collection form to extract the following information: author, year of publication, country of origin, study design, type of surgery, sample size, average age, sex distribution, time to follow-up, primary outcome, inpatient admissions for suicide attempt pre-op/post-op, self-harm attempt pre-op/post-op, substance use disorders pre-op/post-op, mortality post-op, and body mass index (BMI) pre-op/post-op.

Intervention/Comparison

The study therapy was defined as any type of bariatric surgery currently in use: adjustable laparoscopic gastric banding (LAGB), Roux-en-Y gastric bypass (RYGB), vertical banded gastroplasty (VBG), and/or sleeve gastrectomy (SG).

The comparison group was defined as the same population before bariatric procedures if a mirror-image analysis was performed or a relevant control group with similar demographic characteristics followed for the duration of the research study.

Outcomes

The primary outcome was the suicide mortality rate in patients who had undergone bariatric surgery. The secondary outcomes were occurrence of self-harm attempts after bariatric surgery, suicide mortality rate by person-years after bariatric surgery, and comparison between the incidence of suicide and self-harm attempts before and after bariatric surgery within the same population or a relevant control cohort. Control groups were considered appropriate if the cohort was age-, sex-, or BMI-matched with the study group. Additionally, the suicide events in studies that reported pre-existent psychiatric diagnosis were evaluated in a subgroup analysis.

Data Analysis

For all included studies, the pooled event rates for suicide and self-harm attempt after bariatric surgery were calculated with 95% CI and p values. The calculated pooled suicide rate was compared to the World Health Organization (WHO) suicide rates from 2000 to 2015 (worldwide and per country rates). To control for the different follow-up times, a person-years variable was calculated [27]. Odds ratios for suicide and self-harm attempt were calculated for the studies including a control group or data on suicide/self-harm attempts in the same population before and after bariatric surgery.

Risk of bias assessment for randomized controlled trials was evaluated using the Cochrane Collaboration Risk-of-Bias Tool [28]. The Newcastle-Ottawa scale [29] was used to assess the quality of case-control studies. Prospective case-control studies were considered to have acceptable quality if the study received six out of eight possible points.

Results were combined using a random-effects analysis due to the initial assumption of variation among the individual studies. Heterogeneity among the individual studies was assessed by Cochrane's Q test and the I [2] statistic. Heterogeneity was defined as significant if I [2] was greater than 50%. If significant heterogeneity was detected, a sensitivity analysis was performed for outliers, subgroup analysis by surgery type, and meta-regression by baseline BMI, time to follow-up, and procedure type if there were more than nine studies to be analyzed. A funnel plot was constructed to evaluate for publication bias for the main outcomes. The funnel plot was visually inspected for asymmetry, and Eggers test was reported for analyses with greater than ten studies. All analyses were done using Comprehensive Meta-Analysis software, version 2.0 (Biostat, Inc. Englewood, NJ, USA) unless specified otherwise.

Results

Study Characteristics

A total of 227 original studies were identified after the initial query. Thirty-two studies, with a total of 148,643 subjects, met the inclusion and exclusion criteria (Fig. 1). There were 14 prospective cohort studies and nine retrospective or cross-sectional cohort studies. No randomized controlled trials were available for analysis. A total of nine case-control studies were included in the analysis. The control groups in these studies were matched from the general population or from a mirror-image analysis done in the same population prior to surgery. The control population in four studies was matched to the intervention group by weight, BMI, age, and sex; one study compared the cohort to a non-matched control group of patients with moderate to severe obesity; one study compared the cohort to the general population (non-matched).

The studies included in the analysis originated from Australia [30, 31], Belgium [32, 33], Brazil [34, 35], Canada [36, 37], Denmark [38, 39], Italy [40, 41], the Netherlands [42], Sweden [43–47], Switzerland [48, 49], and USA [50–61]. The main objectives of the studies were to evaluate post-surgical complications (12 studies), followed by the evaluation of post-operative mortality (12 studies). Other studies evaluated weight loss, mental health outcomes, and hospitalization rates. The average follow-up was 3.85 years, with a range of 0.85–35 years. Age range for the participants was between 18 and 54.3 years. Sex distribution showed 77.03% female patients, with a range of 65–90.2% (Table 1).

From the studies included in the analysis, 58.9% evaluated subjects undergoing RYGB; 27.9% evaluated RYGB, LAGB, or any restrictive procedure; 5.8% undergoing LAGB; and

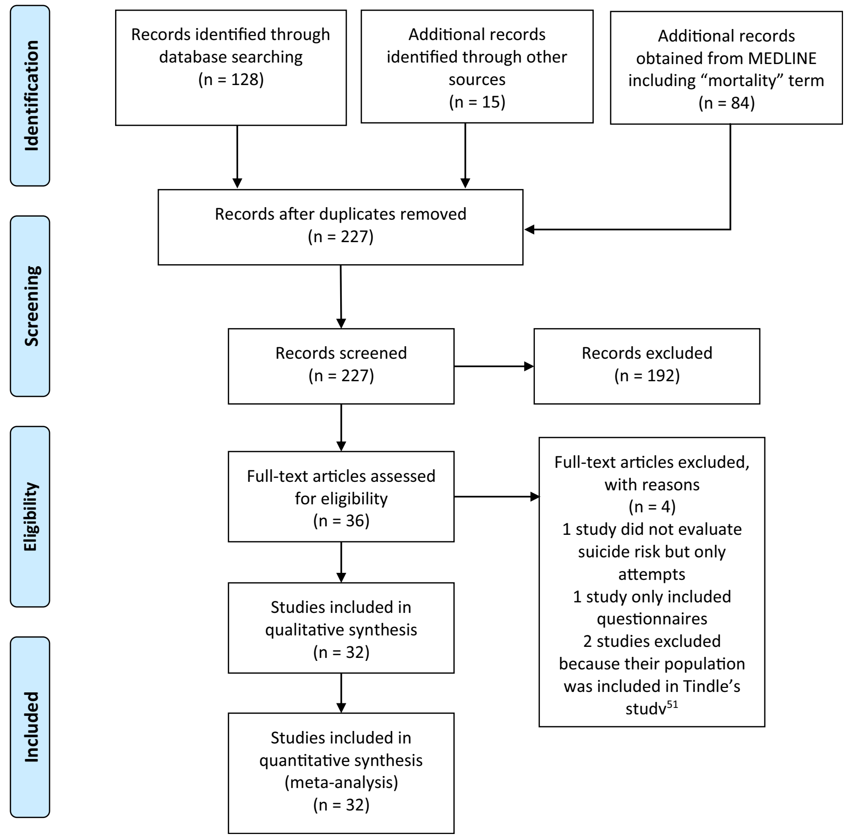

Fig. 1 PRISMA diagram of the study design

7.4% other restrictive procedures, including SG and revision procedures. The proportion of surgeries performed in each of the studies was the following: 22 included patients with RYGB, 16 had LAGB, seven had VBG, and six had SG. All nine case-control studies were of acceptable quality, with at least six out of eight points on the Newcastle-Ottawa scale (Suppl. Table 1).

Primary Outcome

Mortality from suicide after bariatric surgery was 2.7 per 1000 patients (event rate 0.0027, 95% CI 0.0019–0.0038). Twenty-nine studies with a total of 126,608 patients were included (Fig. 2). Significant heterogeneity was noted (I^2 = 76%, Tau^2 = 0.53).

Secondary Outcomes

The event rate for inpatient admissions due to self-harm or attempted suicide was 17 per 1000 patients (event rate 0.017; 95% CI 0.010–0.030). A total of 60,862 subjects from seven studies were included in this analysis (Suppl. Fig. 1). The self-harm/attempted suicide inpatient admission event rate by person-years was 3.0 per 1000 person-years of follow-up (event rate 0.003, 95% CI 0.002–0.0042) (Suppl. Fig. 2). There was increased risk for self-harm or suicide attempt after bariatric surgery compared to rates before procedure within the same population (mirror-image analysis), with an OR of 1.9 (95% CI 1.23–2.95) based on three studies with a sample of 43,406 subjects (Suppl. Fig. 3). Five case-control studies reported event rates of mortality or self-harm in a comparable cohort of non-surgical patients. Bariatric surgery patients had increased risk of suicide compared to age, gender and BMI-matched controls, with an OR of 3.8 (95% CI, 2.19–6.59), I^2 = 15%, Tau^2 = 0.02 (Fig. 3).

Mortality from suicide after bariatric surgery by person-years was 0.25 per 1000 person-years of follow-up (Event rate 0.00025; 95% CI 0.00018–0.00032, I^2 = 48%, Tau^2 = 0.0, 27 studies) (Fig. 4). Nine studies reported results from more than one bariatric surgical procedure without providing separate mortality data for each procedure. These studies were excluded from subgroup analysis. Grouping by procedure type could explain the dispersion of effects, with $p = 0.009$ for the difference. The mortality rates from suicide were significantly higher after RYGB than after LAGB (Table 2).

Pre-existent psychiatric diseases [10–12] and psychotropic medication [62] use could affect outcomes. However, among the included studies, few reported or discussed these data. Two studies assessed pre-operative anti-depressant medication use in the bariatric and control groups [47, 61]. The calculated OR for psychotropic medication use was higher in the bariatric group compared to the control [OR 1.07 (95% CI

Table 1 Data extracted from studies evaluating the risk of post-bariatric surgery suicide and self-harm

	Study and year	Type	Surgery	Number	Age (SD)	Female (%)	Follow-up	Person-years follow-up	IPA for SA pre-op (*n*)	IPA for SA post-op (*n*)	SH pre-op (*n*)	SH post-op (*n*)	Mortality post-op (*n*)	Dropout rate (%)
1	Adams et al. [55] (2007)	CCS	RYGB	7925	39.5 (10.5)	84	7.1 years	56,618	–	–	–	–	15	NR
2	Adams et al. [60] (2017)	CCS	RYGB	418	42.5	84	12 years	4656	–	–	–	–	5	1%
3	Bhatti et al. [36] (2016)	PCS	RYGB, SG	8815	42 (10)	81.4	3 years	26,445	62	96	2.33 per 1000 patients	3.63 per 1000 patients	–	0%
4	Bruschi Kelles et al. [34] (2014)	PCS	RYGB	4344	34.9 (10.5)	79.3	1 month–10 years	17,860.5	0	8	0	5	8	NR
5	Busetto et al. [40] (2007)	CCS	LGB	821	38.2 (0.7)	75.3	0.5–10 years	4311	–	–	–	–	1	2.4%
6	Busetto et al. [41] (2014)	POS	LGB	318	38.6 (10.4)	81.8	12.7 ± 1.5 years	4038.6	–	–	–	–	1	NR
7	Cadière et al. [33] (2011)	PCS	RYGB	362	40 (12)	80	35 years	1361.8	–	–	–	–	1	18.4%
8	Capella et al. [52] (1996)	CCS	RYGB, VBG	888	37 (–)	82.2	1–5 years	1790	–	–	–	–	3	NR
9	Carelli et al. [59] (2010)	ROS	LGB	2909	44.63	68.4	1–5 years	6057.25	–	–	–	–	1	NR
10	Christou et al. [37] (2006)	ROS	RYGB	228	–	82	5–11.4 years	1910	–	–	–	–	2	16.17%
11	Diniz et al. [35] (2013)	POS	RYGB	248	39.7 (10.6)	75	1–5 years	1264.8	–	–	–	–	2	0%
12	Forsell et al. [43] (1999)	ROS	LGB	311	40 (–)	79.7	0.25–2 years	737.3	–	–	–	–	1	3%
13	Gribsholt et al. [38] (2016)	CCS	RYGB	9856	40.2 (–)	78.9	4.2 years	41,395.2	–	–	–	–	10	< 1%
14	Heinberg et al. [58] (2012)	CSS	RYGB, LGB, SG, VBG	608	–	74.6	1.5 years	912	0	70	–	–	65	N/A
15	Higa et al. [54] (2000)	ROS	RYGB	1040	–	82.6	12 years	12,480	–	–	–	–	1	NR
16	Himpens et al. [32] (2011)	POS	LGB	82	50 (0.95)	90.2	13 years	1066	–	–	–	–	1	45.7%
17	Kovacs et al. [39] (2017)	CCS	RYGB, LGB, SG, VBG	12,612	41.6 (10.7)	75.2	4 years	50,826.36	–	–	–	124	5	< 1%
18	Lagerros et al. [45] (2015)	RCS	RYGB	22,539	41.3 (11)	75.3	2 years	45,078	195	24	307	47	17	NR
19	Lent et al. [61] (2017)	CCS	RYGB	2428	46 (10.7)	83	8 years	14,122	–	–	–	–	5	0.06%
20	Marsk et al. [46] (2008)	RCS	RYGB, LGB, SG, VBG	12,379	39.5 (104)	77.6	10.9 years	134,931.1	–	–	–	–	22	NR
21	Morgan et al. [30] (2016)	POS	RYGB, LGB, SG, VBG	12,062	43 (11.6)	78.4	40.6 ± 16.6 months	40,809	–	–	1.83 per 1000 patients	110	5	NR
22	Neovius et al. [47] (2018)			22,264	42.3 (9)	78.6	10 years	118,192	–	–	–	387	42	NR
a)	Swedish Obese Subjects Study	CCS	RYGB, LGB, VBG	2008	47.2 (5.2)	70.7	18 years	34,264				79	9	
b)	Scandinavian Obesity Surgery Registry	CCS	RYGB	20,256	41.3 (10.5)	79.3	3.9 years	83,928				308	33	
23	Obeid et al. [57] (2016)	POS	RYGB	237	41.4 (9·8)	83	10–13 years	–	–	–	–	–	3	43.45%
24	O'Brien et al. [31] (2013)	POS	LGB	3132	47.1 (–)	78	6 months–16 years	19,042	–	–	–	–	1	80.7% at 10 years
25	Powers et al. [51] (1997)	POS	SG	131	39.4 (9)	85	2–5.7 years	189.5	–	–	–	–	1	36%
26	Smith et al. [50] (1995)	ROS	RYGB	3855	–	88.9	1–5 years	3745.5	–	–	–	–	3	54.55%
27	Suter et al. [48] (2006)	POS	LGB	317	38 (–)	86.4	8 years	1774	–	–	–	–	1	73.3% after 7 years
28	Suter et al. [49] (2011)	POS	RYGB	379	39.4	74.4	5 years	1895	–	–	–	–	3	58.89 after 5 years
29	Svenheden et al. [44] (1997)	POS	VBG	95	–	79.1	0.5–4 years	166.5	–	–	–	–	1	NR
30	Tindle et al. [56] (2010)	CCS	RYGB, LGB, SG, VBG	16,683	45 (–)	65	–	–	–	–	–	–	31	NR
31	Waters et al. [53] (1991)	POS	RYGB	157	36.3 (–)	84	0.5–3 years	262.5	–	–	–	–	3	52.22%
32	Weijgert et al. [42] (1999)	ROS	RYGB, VBG	200	34 (–)	86.9	6–14 years	1980	–	–	–	–	3	19.5%

IPA inpatient admission, *SH* self-harm, *BMI* body mass index, *PCS* prospective cohort study, *POS* prospective observational study, *ROS* retrospective observational study, *CCS* case-control study, *RCS* retrospective cohort study, *CSS* cross-sectional study, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy, *LGB* laparoscopic gastric banding, *VBG* vertical banded gastroplasty, *NR* not reported, *N/A* not applicable, *SA* suicide attempt

Study name	Event rate	Lower limit	Upper limit	p-Value
Bruschi Kelles, 2014	0.0018	0.0009	0.0037	0.0000
Obeid, 2016	0.0091	0.0030	0.0280	0.0000
Morgan, 2016	0.0004	0.0002	0.0010	0.0000
Lagerros, 2015	0.0008	0.0005	0.0012	0.0000
Busetto, 2014	0.0031	0.0004	0.0220	0.0000
O'Brien PE, 2013	0.0010	0.0001	0.0073	0.0000
Diniz, 2013	0.0081	0.0020	0.0317	0.0000
Tindle, 2010	0.0019	0.0013	0.0026	0.0000
Marsk, 2008	0.0018	0.0012	0.0027	0.0000
Adams, 2007	0.0019	0.0011	0.0031	0.0000
Higa, 2000	0.0010	0.0001	0.0068	0.0000
Waters GS, 1991	0.0191	0.0062	0.0576	0.0000
Busetto L, 2007	0.0012	0.0002	0.0086	0.0000
Cadière GB, 2011	0.0028	0.0004	0.0193	0.0000
Gribsholt,2016	0.0010	0.0005	0.0019	0.0000
Capella, 1996	0.0034	0.0011	0.0104	0.0000
Carelli, 2010	0.0003	0.0000	0.0024	0.0000
Christou, 2006	0.0088	0.0022	0.0344	0.0000
Forsell, 1999	0.0032	0.0005	0.0225	0.0000
Himpens, 2011	0.0122	0.0017	0.0815	0.0000
Powers, 1997	0.0076	0.0011	0.0522	0.0000
Smith, 1995	0.0008	0.0003	0.0024	0.0000
Suter, 2006	0.0032	0.0004	0.0220	0.0000
Suter, 2011	0.0079	0.0026	0.0242	0.0000
Svenheden, 1997	0.0105	0.0015	0.0709	0.0000
Weijgert, 1999	0.0150	0.0048	0.0455	0.0000
Lent 2017	0.0021	0.0009	0.0049	0.0000
Adams 2017	0.0120	0.0050	0.0284	0.0000
Neovius_1 2018	0.0045	0.0023	0.0086	0.0000
Neovius_2 2018	0.0016	0.0012	0.0023	0.0000
	0.0027	0.0019	0.0038	0.0000

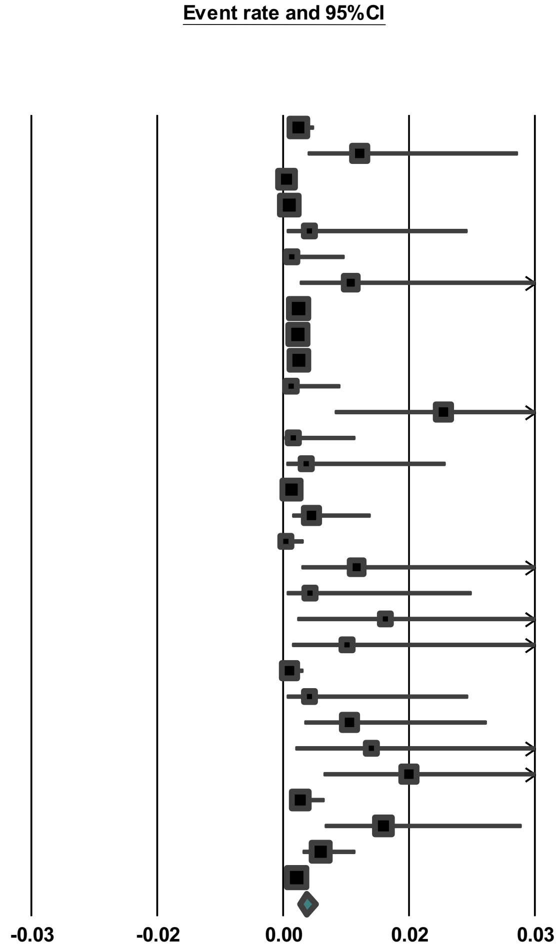

Fig. 2 Event rate for completed suicide after bariatric surgery (2.7 per 1000) ($I^2 = 76\%$, $Tau^2 = 0.53$, 29 studies, 126,608 patients)

1.02–1.11, $p < 0.01$)], with higher OR for suicide in the post-bariatric surgery group [OR 4.15 (95% CI 3.20–5.38, p = 0.02)] (Suppl. Figs. 4 and 5). Of note, one study [39] specifically excluded patients with history of pre-existing psychiatric diagnosis, with higher suicide rate in the post-bariatric group compared to controls. Another study [45] reported post-operative outcomes in patients with a diagnosis of depression, with an event rate for self-harm of 7.1 and 1.15/100 person-years in patients with a prior diagnosis of depression or on antidepressant medications, respectively, and an event rate of 0.14/100 person-years in patients without a prior diagnosis of depression.

Evaluation of Heterogeneity

A sensitivity analysis was performed to investigate the substantial heterogeneity noted for the primary outcome. Heterogeneity was reduced when event rate per person-years was used as an outcome, rather than events per person, with decrease in I^2 from 76 to 48%, thus accounting for the

Model	Study name	Rate ratio	Lower limit	Upper limit	p-Value
	Adams 2007	3.00	1.09	8.25	0.03
	Busetto 2007	3.00	0.12	73.64	0.50
	Neovius_1 2018	3.00	0.81	11.08	0.10
	Neovius_2 2018	5.16	2.02	13.22	0.00
	Adams 2017	3.09	0.60	15.91	0.18
	Lent 2017	10.42	0.58	188.42	0.11
Fixed		3.80	2.19	6.59	0.00
Random		3.80	2.19	6.59	0.00

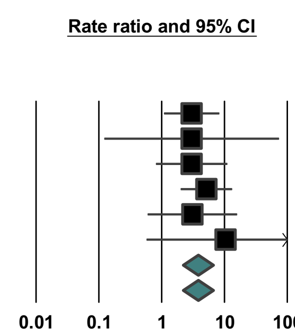

Fig. 3 Mortality from suicide is increased in bariatric surgery patients compared to BMI- and age-matched controls, OR 3.8 ($I^2 = 15\%$, $Tau^2 = 0.02$, 5 studies, 33,856 patients)

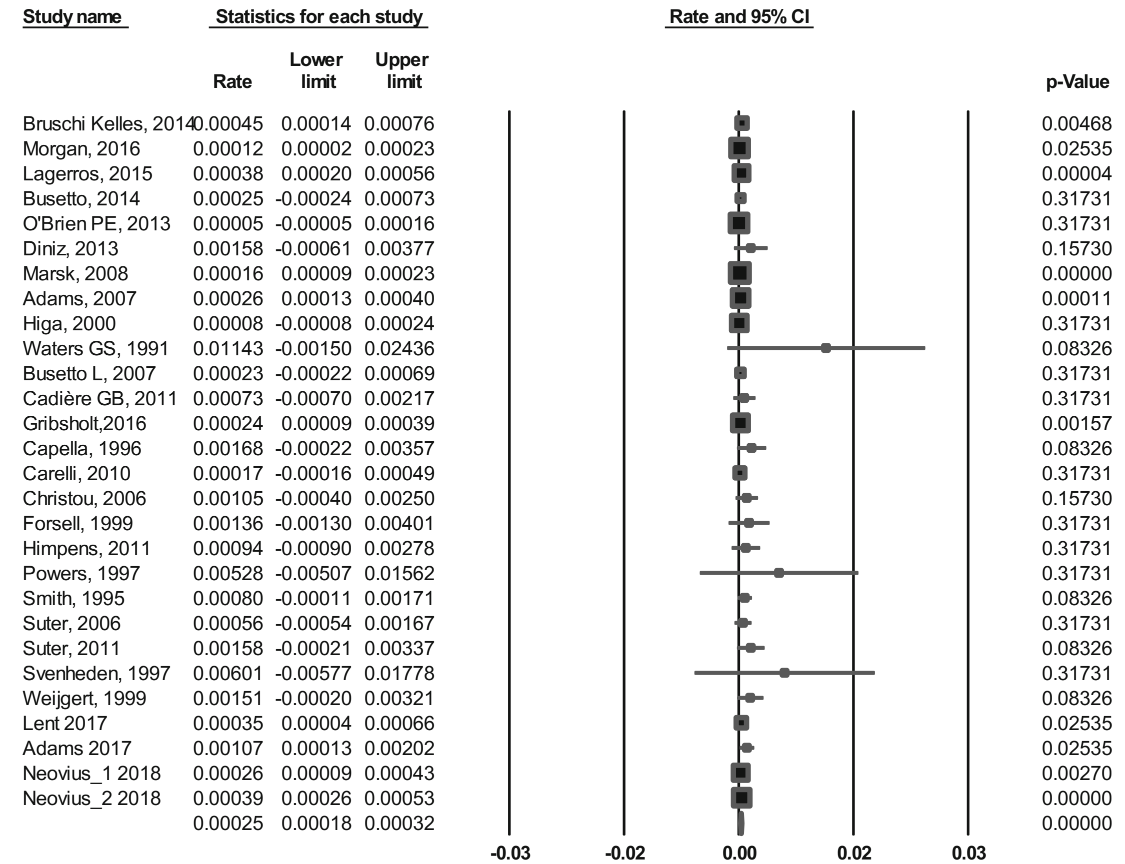

Fig. 4 Event rate per 1000 person-years for completed suicide after bariatric surgery (2.5 per 1000) ($I^2 = 39\%$, $Tau^2 = 0.0$, 27 studies, 109,688 patients)

different lengths of follow-up in the studies (Fig. 4). Subgroup analysis based on the type of surgery (RYGB versus LAGB) could explain further some of the heterogeneity in mortality from suicide. By meta-regression, the type of surgery explained 56% of the variance. Baseline BMI had no significant effect as a univariate predictor. However, a multivariate regression model with type of surgery and baseline BMI as predictors was able to explain 95% of the remaining observed variance (Suppl. Figs. 6 and 7). There was no evidence of publication bias by Eggers test (Suppl. Fig. 8) for the primary outcome.

Discussion

The analysis of the primary end point (mortality from suicide) in this meta-analysis showed higher rates in the post-bariatric patients compared to BMI- and age-matched controls and compared to the general population. In 2012, the average suicide rate worldwide reported by the WHO was 0.11 deaths per 1000 population [63], whereas the overall calculated suicide rate in the analysis was 2.7 deaths per 1000 people. This would mean an estimated 24-fold increased risk for suicide after undergoing weight loss surgery in comparison to the

Table 2 Event rates for completed suicide. Analysis performed on the overall population, by surgery type and correction by person-years

Comparison	Event rate	95% CI	No. of studies (subjects)	I^2	Tau^2	Q	P
Mortality from suicide							
Summary mean	*0.0028*	*0.0020–0.0039*	*29 studies (126,608)*	*77%*	*0.6*	*59*	*< 0.001*
Mortality from suicide by person-years							
Summary mean	*0.00023*	*0.00012–0.00034*	*27 studies (109,688)*	*39%*	*0.0*	*34*	*0.01*
Subgroup analysis for mortality from suicide by surgery type in person-years							
Lap band	0.00008	− 0.00001–0.00018	7 studies	0%	0	4	*0.009*
RYGB	0.00031	0.00019–0.00043	12 studies	42%	0	14	

Italic means statistically significant

general population. After correction with person-years calculation, the event rate remained elevated with 2.5 deaths per 1000 subjects. A previous systematic review by Peterhansel et al. [64] estimated a lower suicide mortality rate; yet, the calculated rate was higher in comparison to the general population. This analysis included studies looking at types of surgery no longer in use and had a total of 23,885 subjects. Since then, 15 new studies on the same topic have been published, bringing the total study population to 148,643 subjects.

The analysis included studies from multiple countries, with wide variability in reported suicide rates. Per the latest report from the WHO including 5-year rates since 2000 [65], Belgium was the country with the highest WHO-reported suicide rate among the diverse populations used in the meta-analysis. Remarkably, the calculated event rate of this analysis was 11 times higher than the average suicide rate reported by Belgium in 15 years (range 0.20–0.23 deaths per 1000 people), and eight times higher than the countries with the highest suicide rate in the world per WHO [65]. The suicide rates reported by the countries included in the analysis ranged from 5.2 to 20.5 deaths per 1000 people. Even though the variety of countries included in the analysis could potentially influence the suicide rates and heterogeneity, the calculated rate was consistently higher than each rate per country (Suppl. Table 2).

Furthermore, the calculated rate in the present study included only confirmed suicide cases, potentially excluding a proportion of "masked suicide events or attempts" from the total amount of accidental, substance abuse-related or unknown causes of death, from which an undetermined amount could be due to suicide. This could potentially be explained by less strict death certification regulations in specific countries and year intervals at which corrections to death registration were implemented, leading to erroneous assessment in suicide rates due to underreporting or misclassification as accidental deaths through time [66, 67]. To explore this concept, a subanalysis on 23 of the included studies listing the causes of death after bariatric surgery was performed. The pooled mortality from accidents was 0.02% (95% CI, 0.01–0.03), significantly higher than reported mortality from accidents in the 30–49 years old population. Thus, the real suicide risk after bariatric surgery may even be higher. As such, it is not possible to make a precise estimate of the effect of "masked suicide" on the calculated rate, only an acknowledgement of its contribution.

Several mechanisms may contribute to the increased suicide risk noted in the post-bariatric population, including psychiatric [11, 68, 69], medical, psychosocial causes [70–73], and physiologic changes [74–77] after bariatric surgery. As discussed, patients who have undergone bariatric surgery have significantly higher prevalence of mental health diseases such as depression and anxiety [69, 78, 79] than the general population, both before and after surgery. Some of the studies in this analysis discussed the presence of pre-existing and post-procedure mental health disease occurrence, with higher suicide rates in the post-bariatric cohorts, as well as higher pre- and post-surgical prevalence of psychiatric disease and psychotropic medication use [36, 47, 61]. Furthermore, a subgroup analysis performed by Neovius et al. [47] including post-bariatric patients without depression found higher incidence of suicide events compared to controls. Thus, underlying psychiatric diseases may have a major role on suicide incidence after bariatric surgery, with other contributors such as undiagnosed mental health issues prior to surgery. An important factor is the increased prevalence of alcohol and substance use in this population. In fact, post-operative alcohol abuse follows similar patterns to suicide events, with increased risk after gastric bypass compared to restrictive procedures, such as the LAGB [80–82].

There are other psychosocial factors that affect the outcomes. Studies have shown that candidates undergoing bariatric surgery have higher weight loss expectations than what is clinically expected. Weight loss and bariatric surgery can also impact socio-cultural relationships [70], with low tolerance thresholds for qualifying outcomes as disappointing [71–73]. Consequently, pre-determined unmet hopes may lead to frustration and have a role in psychiatric stability [51, 83]. Other potential factors that have been associated with suicide occurrence include the psychosocial maladaptation/adjustment and persistence of serious chronic non-psychiatric comorbidities, post-procedure complications [84], and underdiagnosed pre-existent psychiatric disease [68].

Possible pathophysiologic mechanisms that may be implicated in worsening psychiatric diseases after surgery include variation in the absorption of psychotropic medications and alcohol and alterations in hormone levels. Altered metabolism of alcohol [69, 80, 85] and other substances has been reported after bypass procedures due to increased and faster absorption affecting normal pharmacokinetics, along with concomitant abuse. Different pharmacodynamics after surgery affect psychotropic medications as well. For example, decreased escitalopram [86], sertraline [87], and duloxetine [88] maximal serum levels have been noted after RYGB compared to pre-procedural levels [89]. Thus, dose adjustments of medications are likely needed in post-bariatric patients.

Further, subgroup analysis evaluating the suicide rates per procedure showed a higher event rate when RYGB was performed compared to the population undergoing LAGB by a 3-fold difference. Some of these differences could be explained by the anatomical alteration performed in each procedure and changes in pharmacodynamics of various substances and medications, as well as gut hormones pathways. Specifically, chronic stress in rodents and humans can activate ghrelin signaling pathways and administration of exogenous ghrelin can mitigate symptoms of depression and anxiety in rodents [77, 90] and reduce blood pressure and blunt cardiovascular responses during acute psychological stress in humans [91]. Notably, ghrelin levels are inversely related to body weight, and subjects with obesity have lower ghrelin levels than lean controls [92]. However, levels of ghrelin are even lower after RYGB. Markedly lower plasma ghrelin levels and flattened pre- and post-prandial variations in ghrelin secretion have been reported in patients who underwent RYGB compared control with normal BMI and matched controls with obesity [75]. On the other hand, post-LAGB subjects had no change in ghrelin levels [76]. Additionally, variation in pharmacokinetics due to changes in absorption of psychiatric medications or psychotropic substances such as alcohol and recreational drugs could influence the difference in outcomes between purely restrictive and malabsorptive procedures. Further comparative clinical and experimental research on this topic is needed to draw definite conclusions.

The secondary end point (self-harm or suicide attempts) showed a positive correlation in the post-bariatric population, with almost 2-fold risk of a self-harm attempt compared to the same population prior to surgery and a 3.8 higher OR for suicide compared to BMI-, sex-, and age-matched controls. This is consistent with other studies that have shown a positive association for self-harm after comparing the post-bariatric population to controls with obesity [39, 79].

To decrease these risks, a thorough psychiatric evaluation has been recommended by experts. Application of questionnaires (like the HAM-D, BDI or MADRS) is one of the cornerstones for pre-surgical assessment [12], although superiority comparisons are scarce. Behavioral psychotherapy with positive motivational reinforcement has been proposed for pre- and post-surgical treatment of patients presenting with depression and anxiety [93], which could decrease the risk for self-harm/suicide and improve post-surgical weight loss. Although pharmacotherapy is a treatment option for mental health diseases after surgery, there is uncertainty about its role in suicide prevention and correct doses of medications. More studies investigating the role of these assessments and therapies in reducing the burden of psychiatric disease in this vulnerable population are needed. Even though, bariatric surgery is not contraindicated based on psychiatric disease or use of psychotropic medications, an adequate pre-operative treatment and post-operative follow-up should be provided to individuals in need of psychiatric support to improve outcomes and reduce the risk of complications.

Limitations

Most of the data used for analysis of the different outcomes was extracted from retrospective observational studies or case-control studies. Hence, there is a need for prospective studies and randomized controlled trials to decrease possible confounders and help determine causality. Nevertheless, there appears to be an association of suicide events and bariatric surgery, with greater risk noted after gastric bypass. Also, the data search did not include psychiatric terms, as the study aimed to compare the entire post-bariatric population to the general population and controls, with a minimal amount of the studies reporting pre-surgical psychiatric diseases.

A weakness of this study is the inability to differentiate between masked suicide events and accidental deaths; however, the calculated rate due to accidents was higher in the post-bariatric patients than the reported rates in the highest risk age group in the general population. Hence, a fraction of these deaths could potentially represent some deaths linked to suicide, initially attributed to accidental deaths (reviewers 1 and 2).

The studies included in the self-harm/suicide attempt analysis had diverse comparison groups, which could potentially explain the variability in outcomes. Most of the control groups were age-, gender-, and BMI-matched to the intervention group, but there were only a few studies to include control groups. More studies including standardized control subjects with obesity are needed to compare groups by BMI. Importantly, the majority of the studies did not report preexistent psychiatric diagnosis. The high prevalence of psychiatric diseases in the bariatric candidates and its possible under-recognition may be a major factor affecting the outcomes.

Also, two types of studies were used for risk comparison: mirror-image studies and case-control studies. Mirror-image studies compare outcomes (in this case self-harm and attempted suicide) within the same population pre- and post-intervention. These studies may be more accurate for the evaluation of risk association but carry an inherent risk of selection bias. Most of the studies analyzed did not include information regarding substance or alcohol abuse before and after surgery, which may be a contributing factor. Another limitation was the lack of available data regarding post-surgical BMI, since weight and neuro-hormonal changes have been suggested as potential explanations. Thus, further studies accounting for these variables are needed.

Conclusion

Bariatric surgery patients had higher suicide risk compared to the general population and to matched controls. The subjects undergoing bariatric procedures were found to have a 2-fold increase in risk of attempted suicide/self-harm after surgery. Furthermore, the post-RYGB subjects had a higher suicide risk than the post-LAGB subjects, an association that may be related to other medical, psychiatric, and socio-demographic factors. Evaluation of possible modifiable factors in bariatric surgery candidates and in the post-bariatric population needs to be considered in future studies, as well as investigating possible mechanistic explanations for difference in suicide rates by surgery type, such as alterations in ghrelin levels, pharmacodynamics, and alcohol metabolism.

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Compliance with Ethical Standards

Conflict of Interest Authors 1 and 3 do not have any compelling conflict of interest. Author 2 has received a grant and non-financial support from Apollo Endosurgery and research support from Spatz. Author 4 is a consultant for Boston Scientific, Medtronic, Fractyl, Olympus, USGI Medical, Apollo, and GI Dynamics; has received research support from Olympus; has received grants from USGI Medical, Apollo Endosurgery, Aspire Bariatrics, and Spatz; and has ownership interest in GI Windows and EndoTAGSS.

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References

1. Beamish AJ, Olbers T, Kelly AS, et al. Cardiovascular effects of bariatric surgery. Nat Rev Cardiol. 2016;13:730–43.
2. Kwok CS, Pradhan A, Khan MA, et al. Bariatric surgery and its impact on cardiovascular disease and mortality: a systematic review and meta-analysis. Int J Cardiol. 2014;173:20–8.
3. Sjostrom L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351:2683–93.
4. Ricci C, Gaeta M, Rausa E, et al. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25:397–405.
5. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes—3-year outcomes. N Engl J Med. 2014;370:2002–13.
6. Greenburg DL, Lettieri CJ, Eliasson AH. Effects of surgical weight loss on measures of obstructive sleep apnea: a meta-analysis. Am J Med. 2009;122:535–42.
7. Gill RS, Al-Adra DP, Shi X, et al. The benefits of bariatric surgery in obese patients with hip and knee osteoarthritis: a systematic review. Obes Rev. 2011;12:1083–9.
8. Sjostrom L, Narbro K, Sjostrom CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357:741–52.
9. Kubik JF, Gill RS, Laffin M, et al. The impact of bariatric surgery on psychological health. J Obes. 2013;2013:837989.
10. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004;292:1724–37.
11. Mitchell JE, King WC, Chen JY, et al. Course of depressive symptoms and treatment in the longitudinal assessment of bariatric surgery (LABS-2) study. Obesity (Silver Spring). 2014;22:1799–806.
12. Duarte-Guerra LS, Gorenstein C, Paiva-Medeiros PF, et al. Clinical utility of the Montgomery-Asberg Depression Rating Scale for the detection of depression among bariatric surgery candidates. BMC Psychiatry. 2016;16:119.
13. Osterhues A, von Lengerke T, Mall JW, et al. Health-related quality of life, anxiety, and depression in bariatric surgery candidates compared to patients from a psychosomatic inpatient hospital. Obes Surg. 2017;27:2378–87.
14. Abiles V, Rodriguez-Ruiz S, Abiles J, et al. Psychological characteristics of morbidly obese candidates for bariatric surgery. Obes Surg. 2010;20:161–7.
15. Higgs ML, Wade T, Cescato M, et al. Differences between treatment seekers in an obese population: medical intervention vs. dietary restriction. J Behav Med. 1997;20:391–405.
16. Fabricatore AN, Wadden TA, Sarwer DB, et al. Health-related quality of life and symptoms of depression in extremely obese persons seeking bariatric surgery. Obes Surg. 2005;15:304–9.
17. White MA, Kalarchian MA, Levine MD, et al. Prognostic significance of depressive symptoms on weight loss and psychosocial outcomes following gastric bypass surgery: a prospective 24-month follow-up study. Obes Surg. 2015;25:1909–16.
18. Sarwer DB, Wadden TA, Moore RH, et al. Changes in quality of life and body image after gastric bypass surgery. Surg Obes Relat Dis. 2010;6:608–14.
19. Sjostrom L, Peltonen M, Jacobson P, et al. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. JAMA. 2014;311:2297–304.
20. Anderson RJ, Freedland KE, Clouse RE, et al. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care. 2001;24:1069–78.
21. Thombs BD, Bass EB, Ford DE, et al. Prevalence of depression in survivors of acute myocardial infarction. J Gen Intern Med. 2006;21:30–8.
22. de Groot M, Anderson R, Freedland KE, et al. Association of depression and diabetes complications: a meta-analysis. Psychosom Med. 2001;63:619–30.
23. Liberzon I, Abelson JL, Amdur RL, et al. Increased psychiatric morbidity after abdominal aortic surgery: risk factors for stress-related disorders. J Vasc Surg. 2006;43:929–34.
24. Fried M, Yumuk V, Oppert JM, et al. Interdisciplinary European guidelines on metabolic and bariatric surgery. Obes Surg. 2014;24:42–55.
25. Sogg S, Lauretti J, West-Smith L. Recommendations for the presurgical psychosocial evaluation of bariatric surgery patients. Surg Obes Relat Dis. 2016;12:731–49.
26. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient—2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society for Metabolic & Bariatric Surgery. Obesity (Silver Spring). 2013;21(Suppl 1):S1–27.
27. Fay MP. Estimating age conditional probability of developing disease from surveillance data. Popul Health Metr. 2004;2:6.
28. Higgins JP, Thompson SG. Cochrane handbook for systematic reviews of interventions version 5.1.0 [updated March 2011], 2011.
29. Wells GA, Shea B, O'Connell D, et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Ottawa: Ottawa Hospital Research Institute, 2014.
30. Morgan DJ, Ho KM. Incidence and risk factors for deliberate self-harm, mental illness, and suicide following bariatric surgery: a state-wide population-based linked-data cohort study. Ann Surg. 2017;265:244–52.
31. O'Brien PE, MacDonald L, Anderson M, et al. Long-term outcomes after bariatric surgery: fifteen-year follow-up of adjustable gastric banding and a systematic review of the bariatric surgical literature. Ann Surg. 2013;257:87–94.

32. Himpens J, Cadiere GB, Bazi M, et al. Long-term outcomes of laparoscopic adjustable gastric banding. Arch Surg. 2011;146:802–7.
33. Cadiere GB, Himpens J, Bazi M, et al. Are laparoscopic gastric bypass after gastroplasty and primary laparoscopic gastric bypass similar in terms of results? Obes Surg. 2011;21:692–8.
34. Bruschi Kelles SM, Diniz MF, Machado CJ, et al. Mortality rate after open Roux-in-Y gastric bypass: a 10-year follow-up. Braz J Med Biol Res. 2014;47:617–25.
35. Diniz Mde F, Moura LD, Kelles SM, et al. Long-term mortality of patients submitted to Roux-en-Y gastric bypass in public health system: high prevalence of alcoholic cirrhosis and suicides. Arq Bras Cir Dig 2013;26 Suppl 1:53–6.
36. Bhatti JA, Nathens AB, Thiruchelvam D, et al. Self-harm emergencies after bariatric surgery: a population-based cohort study. JAMA Surg. 2016;151:226–32.
37. Christou NV, Look D, Maclean LD. Weight gain after short- and long-limb gastric bypass in patients followed for longer than 10 years. Ann Surg. 2006;244:734–40.
38. Gribsholt SB, Thomsen RW, Svensson E, et al. Overall and cause-specific mortality after Roux-en-Y gastric bypass surgery: a nation-wide cohort study. Surg Obes Relat Dis. 2016;13(4):581–7.
39. Kovacs Z, Valentin JB, Nielsen RE. Risk of psychiatric disorders, self-harm behaviour and service use associated with bariatric surgery. Acta Psychiatr Scand. 2017;135:149–58.
40. Busetto L, Mirabelli D, Petroni ML, et al. Comparative long-term mortality after laparoscopic adjustable gastric banding versus nonsurgical controls. Surg Obes Relat Dis. 2007;3:496–502. discussion 502
41. Busetto L, De Stefano F, Pigozzo S, et al. Long-term cardiovascular risk and coronary events in morbidly obese patients treated with laparoscopic gastric banding. Surg Obes Relat Dis. 2014;10:112–20.
42. van de Weijgert EJ, Ruseler CH, Elte JW. Long-term follow-up after gastric surgery for morbid obesity: preoperative weight loss improves the long-term control of morbid obesity after vertical banded gastroplasty. Obes Surg. 1999;9:426–32.
43. Forsell P, Hallerback B, Glise H, et al. Complications following Swedish adjustable gastric banding: a long-term follow-up. Obes Surg. 1999;9:11–6.
44. Svenheden KE, Akesson LA, Holmdahl C, et al. Staple disruption in vertical banded gastroplasty. Obes Surg. 1997;7:136–8. discussion 139-41
45. Lagerros YT, Brandt L, Hedberg J, et al. Suicide, self-harm, and depression after gastric bypass surgery: a nationwide cohort study. Ann Surg. 2017;265:235–43.
46. Marsk R, Freedman J, Tynelius P, et al. Antiobesity surgery in Sweden from 1980 to 2005: a population-based study with a focus on mortality. Ann Surg. 2008;248:777–81.
47. Neovius M, Bruze G, Jacobson P, et al. Risk of suicide and non-fatal self-harm after bariatric surgery: results from two matched cohort studies. Lancet Diabetes Endocrinol. 2018;6(3):197–207.
48. Suter M, Calmes JM, Paroz A, et al. A 10-year experience with laparoscopic gastric banding for morbid obesity: high long-term complication and failure rates. Obes Surg. 2006;16:829–35.
49. Suter M, Donadini A, Romy S, et al. Laparoscopic Roux-en-Y gastric bypass: significant long-term weight loss, improvement of obesity-related comorbidities and quality of life. Ann Surg. 2011;254:267–73.
50. Smith SC, Goodman GN, Edwards CB. Roux-en-Y gastric bypass: a 7-year retrospective review of 3,855 patients. Obes Surg. 1995;5:314–8.
51. Powers PS, Rosemurgy A, Boyd F, et al. Outcome of gastric restriction procedures: weight, psychiatric diagnoses, and satisfaction. Obes Surg. 1997;7:471–7.
52. Capella JF, Capella RF. The weight reduction operation of choice: vertical banded gastroplasty or gastric bypass? Am J Surg. 1996;171:74–9.
53. Waters GS, Pories WJ, Swanson MS, et al. Long-term studies of mental health after the Greenville gastric bypass operation for morbid obesity. Am J Surg. 1991;161:154–7. discussion 157-8
54. Higa KD, Boone KB, Ho T. Complications of the laparoscopic Roux-en-Y gastric bypass: 1,040 patients—what have we learned? Obes Surg. 2000;10:509–13.
55. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. N Engl J Med. 2007;357:753–61.
56. Tindle HA, Omalu B, Courcoulas A, et al. Risk of suicide after long-term follow-up from bariatric surgery. Am J Med. 2010;123:1036–42.
57. Obeid NR, Malick W, Concors SJ, et al. Long-term outcomes after Roux-en-Y gastric bypass: 10- to 13-year data. Surg Obes Relat Dis. 2016;12:11–20.
58. Heinberg LJ, Ashton K, Windover A, et al. Older bariatric surgery candidates: is there greater psychological risk than for young and midlife candidates? Surg Obes Relat Dis. 2012;8:616–22. discussion 622-4
59. Carelli AM, Youn HA, Kurian MS, et al. Safety of the laparoscopic adjustable gastric band: 7-year data from a U.S. center of excellence. Surg Endosc. 2010;24:1819–23.
60. Adams TD, Davidson LE, Litwin SE, et al. Weight and metabolic outcomes 12 years after gastric bypass. N Engl J Med. 2017;377:1143–55.
61. Lent MR, Benotti PN, Mirshahi T, et al. All-cause and specific-cause mortality risk after Roux-en-Y gastric bypass in patients with and without diabetes. Diabetes Care. 2017;40:1379–85.
62. Hensel J, Selvadurai M, Anvari M, et al. Mental illness and psychotropic medication use among people assessed for bariatric surgery in Ontario, Canada. Obes Surg. 2016;26:1531–6.
63. WHO. World Health Organization. World suicide rates. http://www.who.int/gho/mental_health/suicide_rates/en/, 2016.
64. Peterhansel C, Petroff D, Klinitzke G, et al. Risk of completed suicide after bariatric surgery: a systematic review. Obes Rev. 2013;14:369–82.
65. WHO. World Health Organization. Suicide rates. Data by Country. http://apps.who.int/gho/data/node.main.MHSUICIDE?lang=en, 2016.
66. Chan CH, Caine ED, Chang SS, et al. The impact of improving suicide death classification in South Korea: a comparison with Japan and Hong Kong. PLoS One. 2015;10(5):e0125730.
67. Redaniel MT, Lebanan-Dalida MA, Gunnell D. Suicide in the Philippines: time trend analysis (1974-2005) and literature review. BMC Public Health. 2011;11:536.
68. Srivatsan S, Guduguntla V, Young KZ, et al. Clinical versus patient-reported measures of depression in bariatric surgery. Surg Endosc. 2018;32(8):3683–90.
69. Mitchell JE, Crosby R, de Zwaan M, et al. Possible risk factors for increased suicide following bariatric surgery. Obesity (Silver Spring). 2013;21:665–72.
70. Bruze G, Holmin TE, Peltonen M, et al. Associations of bariatric surgery with changes in interpersonal relationship status: results from 2 Swedish cohort studies. JAMA Surg 2018.
71. Heinberg LJ, Keating K, Simonelli L. Discrepancy between ideal and realistic goal weights in three bariatric procedures: who is likely to be unrealistic? Obes Surg. 2010;20:148–53.
72. Wee CC, Hamel MB, Apovian CM, et al. Expectations for weight loss and willingness to accept risk among patients seeking weight loss surgery. JAMA Surg. 2013;148:264–71.
73. Karmali S, Kadikoy H, Brandt ML, et al. What is my goal? Expected weight loss and comorbidity outcomes among bariatric surgery patients. Obes Surg. 2011;21:595–603.

74. Bali A, Jaggi AS. An integrative review on role and mechanisms of ghrelin in stress, anxiety and depression. Curr Drug Targets. 2016;17:495–507.
75. 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.
76. Kampe J, Stefanidis A, Lockie SH, et al. Neural and humoral changes associated with the adjustable gastric band: insights from a rodent model. Int J Obes. 2012;36:1403–11.
77. Lutter M, Sakata I, Osborne-Lawrence S, et al. The orexigenic hormone ghrelin defends against depressive symptoms of chronic stress. Nat Neurosci. 2008;11:752–3.
78. Roizblatt A, Roizblatt D, Soto-Aguilar BF. Suicide risk after bariatric surgery. Rev Med Chil. 2016;144:1171–6.
79. Backman O, Stockeld D, Rasmussen F, et al. Alcohol and substance abuse, depression and suicide attempts after Roux-en-Y gastric bypass surgery. Br J Surg. 2016;103:1336–42.
80. Wander P, Castaneda D, Dognin J, et al. Risk of alcohol abuse is increased after bariatric surgery: a systematic review and meta-analysis. Am J Gastroenterol Suppl. 2017:S576–7.
81. King WC, Chen JY, Mitchell JE, et al. Prevalence of alcohol use disorders before and after bariatric surgery. JAMA. 2012;307:2516–25.
82. King WC, Chen JY, Courcoulas AP, et al. Alcohol and other substance use after bariatric surgery: prospective evidence from a U.S. multicenter cohort study. Surg Obes Relat Dis. 2017;13:1392–402.
83. Price HI, Gregory DM, Twells LK. Weight loss expectations of laparoscopic sleeve gastrectomy candidates compared to clinically expected weight loss outcomes 1-year post-surgery. Obes Surg. 2013;23:1987–93.
84. Jarvholm K, Olbers T, Marcus C, et al. Short-term psychological outcomes in severely obese adolescents after bariatric surgery. Obesity (Silver Spring). 2012;20:318–23.
85. Pepino MY, Okunade AL, Eagon JC, et al. Effect of Roux-en-Y gastric bypass surgery: converting 2 alcoholic drinks to 4. JAMA Surg. 2015;150:1096–8.
86. Marzinke MA, Petrides AK, Steele K, et al. Decreased escitalopram concentrations post-Roux-en-Y gastric bypass surgery. Ther Drug Monit. 2015;37:408–12.
87. Roerig JL, Steffen K, Zimmerman C, et al. Preliminary comparison of sertraline levels in postbariatric surgery patients versus matched nonsurgical cohort. Surg Obes Relat Dis. 2012;8:62–6.
88. Roerig JL, Steffen KJ, Zimmerman C, et al. A comparison of duloxetine plasma levels in postbariatric surgery patients versus matched nonsurgical control subjects. J Clin Psychopharmacol. 2013;33:479–84.
89. Lloret-Linares C, Bellivier F, Heron K, et al. Treating mood disorders in patients with a history of intestinal surgery: a systematic review. Int Clin Psychopharmacol. 2015;30:119–28.
90. Huang HJ, Zhu XC, Han QQ, et al. Ghrelin alleviates anxiety- and depression-like behaviors induced by chronic unpredictable mild stress in rodents. Behav Brain Res. 2017;326:33–43.
91. Lambert E, Lambert G, Ika-Sari C, et al. Ghrelin modulates sympathetic nervous system activity and stress response in lean and overweight men. Hypertension. 2011;58:43–50.
92. Tschop M, Weyer C, Tataranni PA, et al. Circulating ghrelin levels are decreased in human obesity. Diabetes. 2001;50:707–9.
93. Petasne Nijamkin M, Campa A, Samiri Nijamkin S, et al. Comprehensive behavioral-motivational nutrition education improves depressive symptoms following bariatric surgery: a randomized, controlled trial of obese Hispanic Americans. J Nutr Educ Behav. 2013;45:620–6.