

**Title: Risk factors for suicide after bariatric surgery in a population-based nationwide study in five Nordic countries**

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**Running head:** Bariatric surgery and suicide.

## **Mini-Abstract**

This population-based nationwide study in five Nordic countries including 49,977 patients undergoing bariatric surgery shows that psychiatric comorbidities, male sex and gastric bypass type surgery increase risk of suicide. Age, medical comorbidity, laparoscopic surgical approach, and calendar year of surgery were not associated with this risk.

## **Abstract**

**Objective:** To identify risk factors for suicide after bariatric surgery.

**Summary background data:** Bariatric surgery reduces obesity-related mortality. However, it is for unclear reasons is associated with an increased risk of suicide.

**Methods:** This population-based cohort study included patients having undergone bariatric surgery in 1982-2012 in any of the five Nordic countries, with follow-up through 2012.

Eleven potential risk factors of suicide (sex, age, comorbidity, surgery type, surgical approach, calendar year of surgery, history of depression or anxiety, psychosis, schizophrenia, mania, or bipolar disorder, personality disorder, substance use, and number of previously documented psychiatric diagnoses) were analyzed using Cox regression.

**Results:** Of 49,977 bariatric surgery patients, 98 (0.2%) committed suicide during follow-up. Women had a decreased risk of suicide compared to men (HR=0.48, 95%CI 0.33-0.77), while age and comorbidity did not influence this risk. Compared to gastric bypass, other types of bariatric surgery had lower risk of suicide (HR=0.44, 95%CI 0.27-0.99). There was no difference in suicide risk between laparoscopic and open surgical approach. A history of depression or anxiety (HR=6.87, 95%CI 3.97-11.90); mania, bipolar disorder, psychosis, or schizophrenia (HR=2.70, 95%CI 1.14-6.37); and substance use (HR=2.28, 95%CI 1.08-4.80), increased the risk of suicide. More of the above psychiatric diagnoses increased the risk of suicide (HR=22.59, 95%CI 12.96-39.38 for  $\geq 2$  compared to 0 diagnoses).

**Conclusions:** While the risk of suicide is low, psychiatric disorders, male sex and gastric bypass procedure seem to increase the risk of suicide after bariatric surgery, indicating a role for tailored preoperative psychiatric evaluation and postoperative surveillance.

## **Introduction**

Bariatric surgery typically results in substantial and persistent weight loss, reduction in obesity-related comorbidities, improved quality of life, and better overall survival among severely obese adults compared to severely obese individuals who do not undergo such surgery.<sup>1-6</sup> These benefits in combination with the increasing prevalence of obesity have contributed to rapidly increased use of bariatric surgery. While the health and overall survival benefits of bariatric surgery are clear, a concern after this procedure is the approximately two-fold excess relative risk of suicide, compared with non-operated obese persons as well as the background population of the corresponding age and sex.<sup>7-9</sup> The reasons for this well-documented association are unclear because studies attempting to assess risk factors for suicide after bariatric surgery have included too few cases of suicide to provide conclusive results.<sup>10-12</sup>

With the aim to identify risk factors for suicide after bariatric surgery, we used a five-nation cohort in the Nordic countries consisting of individuals who had undergone bariatric surgery. We specifically aimed to test the hypotheses that differences in sex, age, calendar period, history of psychiatric disorders, current medical comorbidities, bariatric surgical technique, and bariatric surgical approach influence the risk of suicide in these patients.

## **Methods**

### ***Study design***

This was a population-based cohort study during the 33-year study period 1980 through 2012 examining risk factors for suicide after bariatric surgery in the five Nordic countries, i.e., Denmark, Finland, Iceland, Norway, and Sweden. The source cohort, entitled the Nordic Obesity Surgery Cohort (NordOSCO), is based on merged data from well-maintained nationwide health data registers from all Nordic countries, and has been described in detail in a cohort profile publication.<sup>13</sup> The Nordic countries have similar and virtually complete recording of diagnoses and surgical procedures, and complete follow-up of death in all residents.<sup>14</sup> Reporting of this information for each individual to the national health data registries is mandatory by law, and is linked to the remuneration of the Nordic hospitals.<sup>14</sup> Upon birth or immigration, each Nordic resident receives a personal identity code, which was used for linkages of data between registers for each patient.<sup>14-16</sup> The study was approved by all relevant ethical committees, data inspectorates, and register holders in the participating countries.<sup>13</sup>

### ***Bariatric surgery cohort***

The cohort used for the present study included all individuals with an obesity diagnosis combined with a bariatric surgery code recorded in any of the Nordic patient registries.<sup>13</sup> These registries contain nationwide complete information on in-hospital care and out-patient specialist care. The concordance of diagnoses and procedures recorded in the patient registries is generally high when compared to patient records,<sup>17-19</sup> and is very high (97%) for bariatric surgery in specific.<sup>20</sup> The periods for data retrieval varied between the countries, namely from 1996 to 2011 in Denmark, 1996 to 2012 in Finland, 1999 to 2012 in Iceland, 2007 to 2011 in Norway, and 1980 to 2012 in Sweden.<sup>13</sup>

## ***Exposures***

The selected risk factors needed to be available in the dataset and be present preoperatively or during surgery and easily clinically assessed. Eleven potential etiological factors were examined (categorizations in brackets): 1) sex (male or female), 2) age (<30, 30-39, 40-49, or  $\geq 50$  years at the time of bariatric surgery), 3) comorbidity (Charlson comorbidity index 0 or  $\geq 1$ ), 4) type of bariatric surgery (gastric bypass or other bariatric surgery than gastric bypass), 5) surgical approach (open or laparoscopic), 6) calendar year of surgery (<2000, 2000-2009, or  $\geq 2010$ ), 7) history of depression or anxiety (yes or no), 8) history of psychosis, schizophrenia, mania, or bipolar disorder (yes or no), 9) history of personality disorder (yes or no), 10) history of substance use, including alcohol, stimulants, opioids and other narcotic substances (yes or no), and 11) number of previously documented psychiatric diagnoses among all those included in the etiological factors 7 to 10 (0, 1, or  $\geq 2$ ).

Information on sex and age was available from the personal identity codes available in all registries. Diagnoses recorded in the patient registries from one year prior to surgery until the date of surgery were identified to assess comorbidity, using the most recent and well-validated version of the Charlson comorbidity index.<sup>21</sup> The type of bariatric surgery and the surgical approach were defined by the specific surgical codes in the patient registries. Psychiatric disorders within 5 years before the bariatric surgery were determined using diagnosis codes in the patient registries (see Table 1, Supplemental Digital Content 1).

## ***Outcome***

The outcome was suicide after bariatric surgery. Suicide was defined from the relevant diagnosis codes in the national cause of death registries (see Table 1, Supplemental Digital

Content 1). Dates and causes of death were obtained from the cause of death registries up until December 31, 2012. The completeness for date and causes of death in these registries is over 99%.<sup>22-24</sup> Regarding the validity of death from suicide, a review of death certificates in cases of suspected suicide, or unintentional or unclear deaths did not increase the number of suicides compared to the cause of death registries in the Nordic countries.<sup>25</sup> Autopsy is mandatory for suspected suicides and deaths due to unclear reason, accidents, or injury in the Nordic countries.<sup>26</sup>

### ***Statistical analysis***

Patients entered the study at the date of bariatric surgery and were followed up until death, emigration, or end of the study period, whichever came first. The proportionality assumption was assessed using Schoenfeld residuals. The feasibility of conducting multivariable analysis was supported by the low correlations between the different psychiatric diagnoses analyzed ( $V < 0.3$  using Cramer V test). Because the number of psychiatric diagnoses was defined as the sum of the specific psychiatric diagnoses, this variable was kept separate in the analysis. For each of the eleven etiological factors, multivariable Cox regression was used to calculate hazard ratios (HR) with 95% confidence intervals (CI), adjusted for the other ten etiological factors as well as for country (Denmark, Finland, Iceland, Norway, or Sweden). To assess temporal differences, analyses were also stratified into below and above the median follow-up time after bariatric surgery into 0-3 years and >3 years. All data management and statistical analyses followed a detailed a priori study protocol and were conducted by a senior biostatistician (G.S.), using Stata/MP version 15.1 (StataCorp LLC, College Station, TX, USA).

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## Results

### *Patients*

The study included 49,977 patients who underwent bariatric surgery in any of the five Nordic countries during the study period with a total of 312,128 person-years of follow-up. The majority of patients were women (74.5%), the median age was 41.6 years, and most patients had no current comorbidity defined by the Charlson comorbidity index (93.3%). The most common type of bariatric procedure was gastric bypass (73.4%). Of those 13,249 not undergoing gastric bypass surgery, 5,487 underwent vertical banding gastroplasty, 5,450 had gastric banding, 784 underwent malabsorptive procedures such as biliopancreatic diversion or duodenal switch, and 1,578 had other or non-specified bariatric procedures. The main surgical approach was laparoscopic (72.8%). In all, 98 (0.2%) patients committed suicide during follow-up. Characteristics of patients who did and did not commit suicide are presented in Table 1. Compared to patients who did not commit suicide, those who committed suicide were more often men, underwent other types of bariatric surgery than gastric bypass, received the laparoscopic approach, and had a history of psychiatric comorbidity.

### *Patient and surgical factors in relation to suicide*

Table 2 shows the overall HRs of suicide for the eleven exposures. The HRs stratified for the follow-up periods 0-3 years and >3 years are presented in the supplement (see Table 2, Supplemental Digital Content 1). Regarding *sex*, women had a decreased risk of suicide compared to men (adjusted HR 0.48, 95% CI 0.33-0.77), and a difference was found in both follow-up categories. *Age* or *calendar period* of bariatric surgery did not statistically significantly influence the risk, although the point estimates were increased within 3 years of surgery. Among the *types of bariatric surgery*, compared to gastric bypass, other types were associated with a decreased risk (adjusted HR 0.44, 95% CI 0.27-0.99), and the point estimate

was particularly decreased within the first 3 years of surgery. Regarding *surgical approach*, laparoscopic and open surgery did not differ regarding the risk of suicide, independent of the follow-up period. *Current comorbidity* (Charlson comorbidity index) was not statistically significantly associated with the risk of suicide.

### ***Psychiatric factors in relation to suicide***

Table 2 show that a history of *depression or anxiety* prior to bariatric surgery was associated with a substantially increased risk of suicide compared to no such diagnosis (adjusted HR 6.87, 95% CI 3.97-11.90), with slightly higher point estimates within the first 3 postoperative years (see Table 2, Supplemental Digital Content 1). Previous *mania, bipolar disorder, psychosis, or schizophrenia* were associated with an increased risk (adjusted HR 2.70, 95% CI 1.14-6.37), which did not differ between the follow-up categories. *Personality disorder* increased the risk of suicide within the first 3 years of bariatric surgery (HR 6.11, 95% CI 1.98-18.88), but not later during the follow-up (see Table 2, Supplemental Digital Content 1). A pre-operative history of *substance use* was associated with a moderately increased risk of suicide (adjusted HR 2.28, 95% CI 1.08-4.80), and this association remained in both follow-up categories. Regarding *number of psychiatric diagnoses* prior to bariatric surgery, compared to patients without psychiatric diagnoses, patients with one psychiatric diagnosis (adjusted HR 5.20, 95% CI 2.91-9.28) and two or more psychiatric diagnoses (adjusted HR 22.59, 95% CI 12.96-39.38) had a strongly increased HR of suicide. The point estimates for number of psychiatric diagnoses were higher within the first 3 postoperative years compared to the later follow-up period (see Table 2, Supplemental Digital Content 1). Adjustment for covariates, particularly history of individual psychiatric diagnoses, attenuated the crude HRs (Table 2).

## Discussion

This study indicates that the excess risk of suicide after bariatric surgery occurs in patients with psychiatric conditions before the bariatric surgery in particular, and especially in patients with a history of depression and anxiety. Other risk factors were male sex and the gastric bypass surgery type. Age, calendar period, open or laparoscopic surgical approach, and medical comorbidity were not clearly associated with the risk of suicide after bariatric surgery.

Among strengths of the present study is the population-based and multi-country design, allowing for an unselected cohort of patients who had undergone bariatric surgery, which for the first time was large enough to robustly assess suicide as the outcome. The well-maintained national Nordic health data registries and personal identity code system made the follow-up complete. Any unclear causes of death were meticulously assessed, minimizing misclassification of suicide. The assessment of bariatric surgery was highly complete, which was at least partly due to the fact that the reporting of surgical procedures to the national patient registries is mandatory and the hospital reimbursement depends on this reporting. The similar sociodemographic characteristics, genetic background, cultural traditions, norms, healthcare, social and population registration systems in the Nordic countries allowed merging of homogeneous data and still facilitated generalizability.<sup>14</sup> There are also weaknesses. Despite the adjustment for several variables, confounding from socioeconomic factors and body mass index was not adjusted for. However, the healthcare costs, including bariatric procedures, are covered by the national social insurance in all Nordic countries. Thus, socioeconomic status may have less impact on access to bariatric surgery in the Nordics than in countries with different healthcare financing. The lack of data on body mass index might not be an issue because patients who committed suicide after bariatric surgery had

similar postoperative weight loss development compared to those not committing suicide.<sup>8</sup>

Finally, although the study was large, the subgroup analyses had limited statistical power.

The literature has provided strong evidence of clearly higher suicide rates after bariatric surgery than in non-operated individuals with obesity and the corresponding general population.<sup>27</sup> In our recent study based on NordOSCO, the risk of suicide after bariatric surgery was substantially increased both compared to obese individuals who had not undergone bariatric surgery (HR 1.7, 95% CI 1.3-2.1) and the corresponding general Nordic population (standardized mortality ratio 2.4, 95% CI 2.0-2.9).<sup>9</sup> The etiology of suicide in these patients has been unknown, which is mainly due to the low number of suicides (range 0-17) in the few studies that have attempted to assess this outcome.<sup>8, 10-12</sup> Cohort studies from the United States and Sweden have instead examined self-harm, which is also overrepresented after bariatric surgery, or a composite outcome of self-harm and suicide, indicating older age, lower income, living in rural areas, pre-operative mental disorders or self-harm, and gastric bypass surgery type as risk factors.<sup>8, 10-12</sup>

In the present study, including 98 suicides, pre-operative history of psychiatric conditions (depression or anxiety, mania, bipolar disorder, psychosis or schizophrenia, and substance use) indicated a strongly increased relative risk of suicide after bariatric surgery. Depression and anxiety had the strongest influence. The attenuated point estimates after adjustment for other psychiatric comorbidities and exponentially increasing hazard with increasing number of psychiatric comorbidities imply synergy between the examined psychiatric comorbidities. These conditions are associated with an increased risk of suicide in general, but the associations are far from as strong as found after bariatric surgery.<sup>28</sup> A contributing mechanism might be that the surgical trauma precipitate remaining underlying psychiatric

vulnerability in patients with a history of psychiatric conditions.<sup>29, 30</sup> Another explanation might be unrealistic expectations of the effects of bariatric surgery on the life situation, which could have led to great disappointment and exacerbation of psychiatric illness in some patients. This is supported by studies showing that better psychological health is associated with greater weight loss after bariatric surgery.<sup>31, 32</sup> On the other hand, very rapid weight loss and inability to eat as expected might also be a too major lifestyle change, resulting in depression and suicide. Additionally, the lifestyle changes that come from totally new eating behavior could introduce major issues. Research has also indicated that neuroendocrine changes and nutritional deficiencies related to malabsorption caused by bariatric surgery could contribute to suicide.<sup>33</sup>

Men had a higher risk of committing suicide than women after bariatric surgery. This could be explained by a higher incidence of completed suicide in general in men compared to women.<sup>34</sup> Gastric bypass carried a higher risk of suicide compared to other types of bariatric surgery. Because most patients underwent gastric bypass, it may seem strange that the number of suicide cases was not higher in this group. This is explained by the higher numbers of other surgeries than gastric bypass in the earlier years of the study, and Cox regression takes time-to-event into account in the calculation of hazard ratios. Gastric bypass is more invasive and associated with greater nutritional changes compared to most other procedures, e.g. gastric banding and gastroplasty.<sup>35</sup> Thus, gastric bypass can cause more neuroendocrine changes and nutritional deficiencies that might contribute to suicide.<sup>33</sup> Serious complications are also more common after gastric bypass compared to the less advanced procedures, and complications could affect the patients' quality of life, making them more prone to commit suicide.

This is the first study powered to assess risk factors of suicide in bariatric surgery patients, and more research is obviously needed. Yet, if the results are confirmed in future studies they may have clinical implications. Because the absolute risk of suicide was still limited (1.7% in those with at least two psychiatric diagnoses), clinicians should not deny even those with prior psychiatric comorbidities from having bariatric surgery only on the grounds of suicide risk. Similarly, it is important to note that the absolute risk of suicide is low in bariatric surgery patients. However, a history of psychiatric comorbidity should serve as a red flag for the clinician to assess mental health status before bariatric surgery is conducted. Postoperative psychiatric surveillance may also be considered in patients with a history of psychiatric disorders, particularly among those with a history of depression or anxiety and during the initial postoperative years when the relative risk appeared to be higher. New innovations, i.e. development of tailored web-based self-reporting tools, to identify high-risk patients may reduce the burden of psychiatric follow-up in the future.

In conclusion, this large and population-based cohort study from the five Nordic countries indicates that an excess risk of suicide among patients undergoing obesity surgery is found in particular among patients with a history of psychiatric diagnoses documented prior to obesity surgery, especially depression and anxiety. Patients undergoing the gastric bypass surgery procedure had a higher suicide rate than patients undergoing other types of bariatric surgery. Although the absolute risk of suicide is low after bariatric surgery, these findings suggest that preoperative psychiatric evaluation and intervention as well as postoperative surveillance of relative high-risk individuals may prevent suicides after bariatric surgery.

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**Table 1.** Characteristics of 49,977 patients who had undergone bariatric surgery in any of the five Nordic countries

	No suicide Number (%)	Suicide Number (%)
<b>Total</b>	49,879 (100)	98 (100)
<b>Sex</b>		
Male	12,696 (25.4)	34 (34.7)
Female	37,183 (74.6)	64 (65.3)
<b>Age at entry (in years)</b>		
<30	7,797 (15.6)	18 (18.4)
30-39	14,359 (28.8)	29 (29.6)
40-49	15,896 (31.9)	26 (26.5)
≥50	11,827 (23.7)	25 (25.5)
<b>Country</b>		
Denmark	3,267 (6.6)	2 (2.0)
Finland	4,423 (8.9)	6 (6.1)
Iceland	731 (1.5)	0 (0.0)
Norway	5,505 (11.0)	2 (2.0)
Sweden	35,953 (72.1)	88 (89.8)
<b>Calendar period at entry (years)</b>		
<2000	9,032 (18.1)	53 (54.1)
2000-2009	18,691 (37.5)	34 (34.7)
≥2010	22,156 (44.4)	11 (11.2)
<b>Charlson comorbidity index</b>		
0	46,555 (93.3)	93 (94.9)
1	3,117 (6.3)	5 (5.1)
≥2	207 (0.4)	0 (0.0)
<b>Bariatric surgery type</b>		
Gastric bypass	36,630 (73.4)	48 (49.0)
Other	13,249 (26.6)	50 (51.0)
<b>Surgical approach</b>		
Open	36,344 (72.9)	32 (32.6)
Laparoscopic	13,535 (27.1)	66 (67.4)
<b>Psychiatric diagnosis</b>		
No	44,850 (89.9)	66 (67.4)
Depression or anxiety	4,055 (8.1)	28 (28.6)
Substance use	1,029 (2.1)	10 (10.2)
Personality disorder	611 (1.2)	9 (9.2)
Mania, bipolar disorder, psychosis or schizophrenia	572 (1.2)	7 (7.1)
<b>Number of psychiatric diagnoses</b>		
0	44,850 (89.9)	66 (67.4)
1	4,029 (8.1)	15 (15.3)
≥2	1,000 (2.0)	17 (17.3)

**Table 2.** Risk of suicide after bariatric surgery, presented as hazard ratios (HRs) with 95% confidence intervals (CIs)

Variable	Number (%)	Crude HR (95% CI)	Adjusted HR <sup>a</sup> (95% CI)
<b>Sex</b>			
Male	34 (34.7)	1.00 (Reference)	1.00 (Reference)
Female	64 (63.3)	0.54 (0.36-0.82)	0.48 (0.33-0.77)
<b>Age</b>			
<30	18 (18.4)	1.00 (Reference)	1.00 (Reference)
30-39	29 (29.6)	1.06 (0.59-1.91)	0.97 (0.52-1.71)
40-49	26 (26.5)	0.97 (0.53-1.78)	0.88 (0.47-1.59)
≥50	25 (25.5)	1.53 (0.83-2.82)	1.45 (0.75-2.60)
<b>Calendar year</b>			
<2000	53 (54.1)	1.00 (Reference)	1.00 (Reference)
2000-2009	34 (34.7)	1.72 (0.99-3.01)	1.06 (0.50-2.23)
≥2010	11 (11.2)	3.04 (1.19-7.76)	1.59 (0.51-5.00)
<b>Bariatric surgery type</b>			
Gastric bypass	48 (49.0)	1.00 (Reference)	1.00 (Reference)
Other	50 (51.0)	0.42 (0.26-0.67)	0.44 (0.27-0.99)
<b>Surgical approach</b>			
Open	32 (32.7)	1.00 (Reference)	1.00 (Reference)
Laparoscopic	66 (67.3)	1.15 (0.69-1.91)	0.69 (0.36-1.29)
<b>Charlson comorbidity index</b>			
0	93 (94.9)	1.00 (Reference)	1.00 (Reference)
≥1	5 (5.1)	1.44 (0.58-3.56)	0.97 (0.41-2.55)
<b>Depression or anxiety</b>			
No	70 (71.4)	1.00 (Reference)	1.00 (Reference)
Yes	28 (28.6)	9.13 (5.81-14.36)	6.87 (3.97-11.90)
<b>Mania, bipolar disorder, psychosis, or schizophrenia</b>			
No	91 (92.9)	1.00 (Reference)	1.00 (Reference)
Yes	7 (7.1)	10.76 (4.98-23.26)	2.70 (1.14-6.37)
<b>Personality disorder</b>			
No	89 (90.8)	1.00 (Reference)	1.00 (Reference)
Yes	9 (9.2)	13.41 (6.73-26.72)	2.26 (0.98-5.20)
<b>Substance use</b>			
No	88 (89.8)	1.00 (Reference)	1.00 (Reference)
Yes	10 (10.2)	7.62 (3.96-14.68)	2.28 (1.08-4.80)
<b>Number of psychiatric diagnoses<sup>b</sup></b>			
0	66 (67.3)	1.00 (Reference)	1.00 (Reference)
1	15 (15.3)	4.75 (2.69-8.39)	5.20 (2.91-9.28)
≥2	17 (17.3)	21.10 (12.31-36.17)	22.59 (12.96-39.38)

a Adjusted for sex, age, calendar year, surgery type, surgical approach, Charlson comorbidity index, and type of psychiatric diagnosis.

b Not adjusted for type of psychiatric diagnosis

## **List of Supplemental Digital Content**

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