


# Use of Opioid Analgesics Before and After Gastric Bypass Surgery in Sweden: a Population-Based Study

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## Abstract

**Background** Little is known regarding the use of opioid analgesics among patients who have undergone bariatric surgery.

The Roux-en-Y gastric bypass (RYGB) procedure has been shown to significantly increase the rate of absorption of and exposure to morphine, raising concerns regarding the potentially increased risk of side-effects and the development of substance-use disorder.

**Objectives** The aim of this study was to describe the pattern of opioid use over time following RYGB and to see if the pattern differs between patients with a high opioid consumption (HOC) prior to surgery and those with a low consumption (LOC).

**Setting** University Hospital of Örebro, Sweden.

**Methods** The study was a descriptive retrospective population-based cohort study where two registers with complete coverage were cross-matched.

**Results** The study population comprised 35,612 persons (1628 HOC, and 33,984 LOC). After surgery, the number of HOC patients increased to 2218.

Mean daily opioid consumption in the total population and the LOC group increased after surgery ( $p < .0005$ ). In the HOC group, there was no difference between mean daily consumption before and after surgery.

**Conclusion** In this nationwide study, we have showed that there is an increase in consumption of opioid analgesics after gastric bypass surgery in Sweden. The increase in the number of individuals with high opioid consumption in the total population was mainly due to an increase in the group of patients with a low consumption prior to surgery.

**Keywords** Bariatric surgery · Opioid analgesics · Gastric bypass surgery · Obesity · Pain · Oral morphine equivalents · Roux-en-Y gastric bypass

## Introduction

Morbid obesity is associated with various conditions causing musculoskeletal pain [1] often leading to use of prescription

analgesics [2], including opioids. Bariatric surgery has proved to be an efficient intervention in the management of obesity resulting in lasting weight-loss and reduced obesity-related co-morbidity [3], improved physical function [4], and

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health-related quality-of-life (HRQoL) [5]. As a result, the number of post-bariatric surgery patients in the population is growing. Little is known regarding the use of opioid analgesics among patients who have undergone bariatric surgery. Recent studies has shown an increase in postoperative use of opioid analgesics both regarding the total dose and number of new persistent users [6–9]. The anatomical changes after Roux-en-Y gastric bypass (RYGB) can lead to changes in the pharmacokinetic properties of opioid analgesics leading to faster and more complete absorption of morphine oral solution [10], which is similar to the changes seen with ethanol [11]. This raises concerns regarding a potentially increased risk of developing substance-use disorder (SUD) [12–14]. The increased risk of side effects of non-steroidal anti-inflammatory drugs (NSAID) [15] after RYGB limits the pharmacological options available and likely pushes patients and prescribers toward opioids. It is thus important to gain a deeper understanding of the use of opioids after bariatric surgery.

The aim of this retrospective cohort study, including all patients undergoing gastric bypass surgery in Sweden between May 2007 and November 2013, was to describe the pattern of opioid use over time following surgery, and to see if the pattern differs between patients with a high opioid consumption prior to surgery (HOC) and those with a low consumption (LOC).

## Methods

### Study Design

The study was a descriptive retrospective population-based cohort study where two registers with complete coverage were cross-matched.

### Patient Population

Patient data were obtained from the Scandinavian Obesity Surgery Register (SOREg), a Scandinavian bariatric surgery register used for research and quality improvement. The SOREg has nationwide coverage and is >98% complete in terms of patient enrolment [16]. All patients undergoing bariatric surgery in Sweden May 2007–Nov 2013 were identified in the SOREg and data cross-matched with the Swedish Prescribed Drug Register (SPDR). This register contains patient data on all prescription medications dispensed in Sweden. It is intended to be used for epidemiological studies, research, and statistics within the health-care system [17]. From the SPDR, we obtained information on all opioid analgesics prescribed and dispensed (identified by ATC-codes N02AA01, N02AA03, N02AA05, N02AA55, N02AA59, N02AB01, N02AB02, N02AB03, N02AE01, N02AF02, N02AG01, N02AG02, N02AX02, and

N02AX06). Participants were excluded if they had not been operated with gastric bypass (duodenal switch ( $n = 222$  (0.6%)), gastric banding ( $n = 266$  (0.7%)), sleeve gastrectomy ( $n = 644$  (1.7%)), if they had died ( $n = 126$  (0.3%)), and if they had had multiple bariatric surgery procedures ( $n = 22$  (0.1%)).

### Morphine Equivalents

Each participant's daily intake of opioid was calculated as milligrams of oral morphine equivalent (OMEQ) using a previously described method [8, 9]. More accurate oral morphine equivalence factors [18] were used for transdermal and transmucosal buprenorphine [19], transdermal fentanyl, and oral tapentadol. Oral and rectal administration of ketobemidone [20] was included since this had not been considered in previous studies. Total opioid consumption was calculated as number of tablets/suppositories/ml/patches multiplied by strength in milligrams (milligrams per hour for patches) multiplied by the opioid conversion factor.

### Opioid Use

In this study, dispensed opioids were considered to be the dose taken. The participants were divided between two groups according to total amount of opioid consumed prior to surgery, HOC with a mean daily intake greater than 10 mg OMEQ, and LOC with a mean daily intake of 10 mg OMEQ or less. Definition of HOC was chosen based on classification of chronic users from previous studies [8, 9]. Chronological data on use were presented as mean daily intake in mg OMEQ over a series of 3-month periods starting 24 months prior to surgery ending 24 months after surgery. This interval correlates to the 3-month period traditionally applied when renewing an opioid prescription for chronic pain in Sweden.

### Statistical Analysis

Difference in mean daily consumption (OMEQ) before and after bariatric surgery was analyzed using paired-sample *T* test, and difference between men and women was analyzed using independent-sample *T* test. Analysis was performed on the full time-line and excluding the 3-month periods immediately before and after surgery. Data were analyzed using IBM SPSS Statistics version 22.

## Results

The study population comprised 35,612 persons (Table 1) who had undergone gastric bypass surgery (1628 HOC, and 33,984 LOC). After surgery, the number of HOC patients

**Table 1** Base-line characteristics

	Total	Low opioid consumption	High opioid consumption
Gender, <i>n</i> (%)			
Women	27,012 (75.9)	25,760 (75.8)	1252 (76.9)
Men	8600 (24.1)	8224 (24.2)	376 (23.1)
Age (years) mean $\pm$ SD	40.9 ( $\pm$ 11.0)	40.7 ( $\pm$ 11.0)	46.6 ( $\pm$ 9.2)
Body mass index (kg/m <sup>2</sup> ) mean $\pm$ SD	42.5 ( $\pm$ 5.4)	42.5 ( $\pm$ 5.4)	42.0 ( $\pm$ 5.5)
Surgical access, <i>n</i> (%)			
Laparoscopic	34,269 (96.2)	32,720 (96.3)	1549 (95.1)
Open	1046 (2.9)	989 (2.9)	57 (3.5)
Converted	297 (0.8)	275 (0.8)	22 (1.4)
Year of surgery, <i>n</i> (%)			
2007	762 (2.1)	723 (2.1)	39 (2.4)
2008	2731 (7.7)	2593 (7.6)	138 (8.5)
2009	3980 (11.2)	3802 (11.2)	178 (10.9)
2010	6921 (19.4)	6577 (19.4)	344 (21.1)
2011	7798 (21.9)	7433 (21.9)	365 (22.4)
2012	7070 (19.9)	6742 (19.8)	328 (20.1)
2013	6350 (17.8)	6114 (18.0)	236 (14.5)

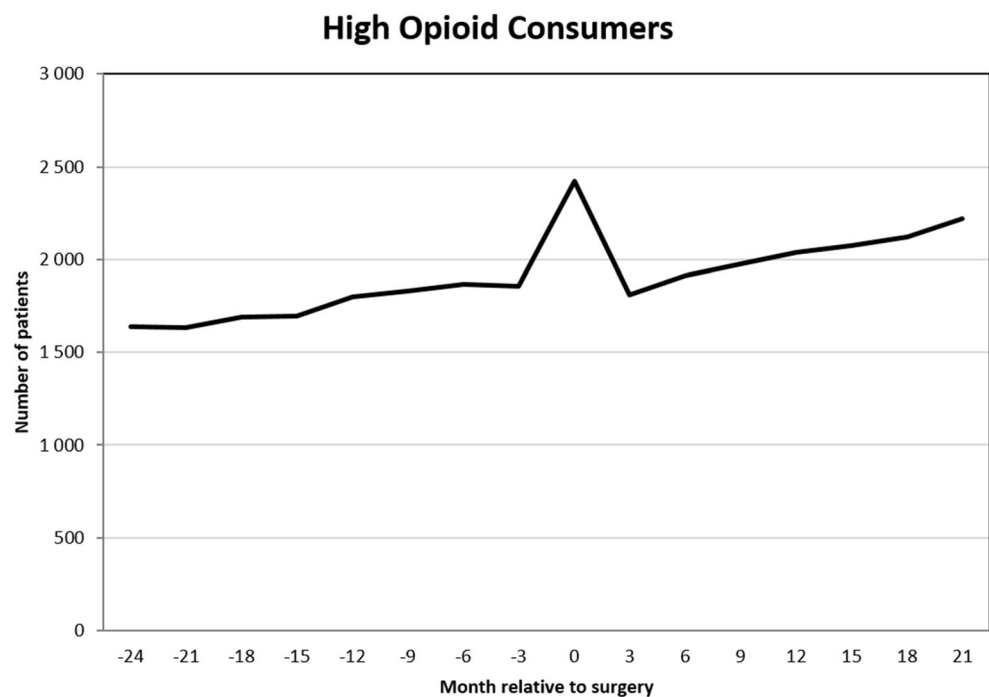
increased fairly consistently to 2218 at end of follow-up (Fig. 1).

When comparing mean daily opioid consumption in the total population prior to and after surgery, there was a statistically significant increase. In the HOC group, there was no difference between mean daily consumption before and after surgery. In the LOC group, however, there was a statistically significant increase in mean daily consumption after surgery.

Furthermore, the amount of opioid consumed daily more than doubled after surgery in this group (Table 2). This increase remained when the 3-month periods immediately before and after surgery were excluded from the analysis.

In the group classified as high opioid consumers prior to surgery, 422 participants (25.9%) used 10 mg or less opioid analgesics after surgery (from a mean daily consumption before surgery of 22.9 to 3.0 mg after surgery) and 1206

**Fig. 1** Number of patients with a mean daily consumption > 10 mg



**Table 2** Statistics on mean daily consumption of opioid analgesics (mg oral morphine equivalents (OMEQ)) during the 2-year periods before and after gastric bypass surgery

	Before surgery	After surgery	<i>p</i>
Participant classification, <i>n</i> (%)			
All participants	35,612 (100.0)	35,612 (100.0)	
HOC	1628 (4.6)	1966 (5.5)	
LOC	33,984 (95.4)	33,646 (94.5)	
Mean daily use OMEQ (mean ± SD)			
All participants	1.9 (± 10.2)	2.5 (± 14.0)	< .0005
HOC	31.9 (± 36.2)	32.3 (± 51.4)	.70
LOC	0.4 (± 1.3)	1.1 (± 6.1)	< .0005
Mean age in HOC group (mean ± SD)	46.6 (± 9.2)	45.0 (± 9.9)	< .0005
	Before surgery	After surgery	%
Change in consumption group, <i>n</i> (%)			
HOC becoming LOC	1628 (4.6)	1206 (3.4)	− 1.2
LOC becoming HOC	0 (0)	760 (2.1)	2.1
	Women, <i>n</i> = 27,012	Men, <i>n</i> = 8600	<i>p</i>
Mean daily use OMEQ (mean ± SD)			
Before surgery	1.9 (± 10.0)	2.0 (± 11.0)	.35
After surgery	2.5 (± 14.2)	2.7 (± 13.8)	.09

Participants were classed as low opioid consumer (LOC) if they had a mean daily consumption of 10 mg OMEQ or less during the 2-year period before surgery and high opioid consumer (HOC) if they had a mean daily consumption higher than 10 mg OMEQ

participants (74.1%) continued or increased their consumption after surgery (mean daily consumption before surgery 31.5 to 43.8 mg after surgery).

In the LOC group 33,224 participants (97.8%) used 10 mg/day or less after surgery (from mean daily consumption 0.4 mg before surgery to 0.6 mg after surgery), and 760 LOCs (2.2%) became high opioid consumers after surgery (mean daily consumption 2.4 mg before surgery to 40.6 mg after surgery) (Figs. 2 and 3).

There was no significant difference in mean daily use before and after surgery between women and men (Table 2).

## Discussion

This study is one of few looking at the consumption of opioid analgesics in patients undergoing bariatric surgery. Our results show that there is an increase in opioid consumption after gastric bypass surgery, both the number of HOC patients and the amount of opioids consumed.

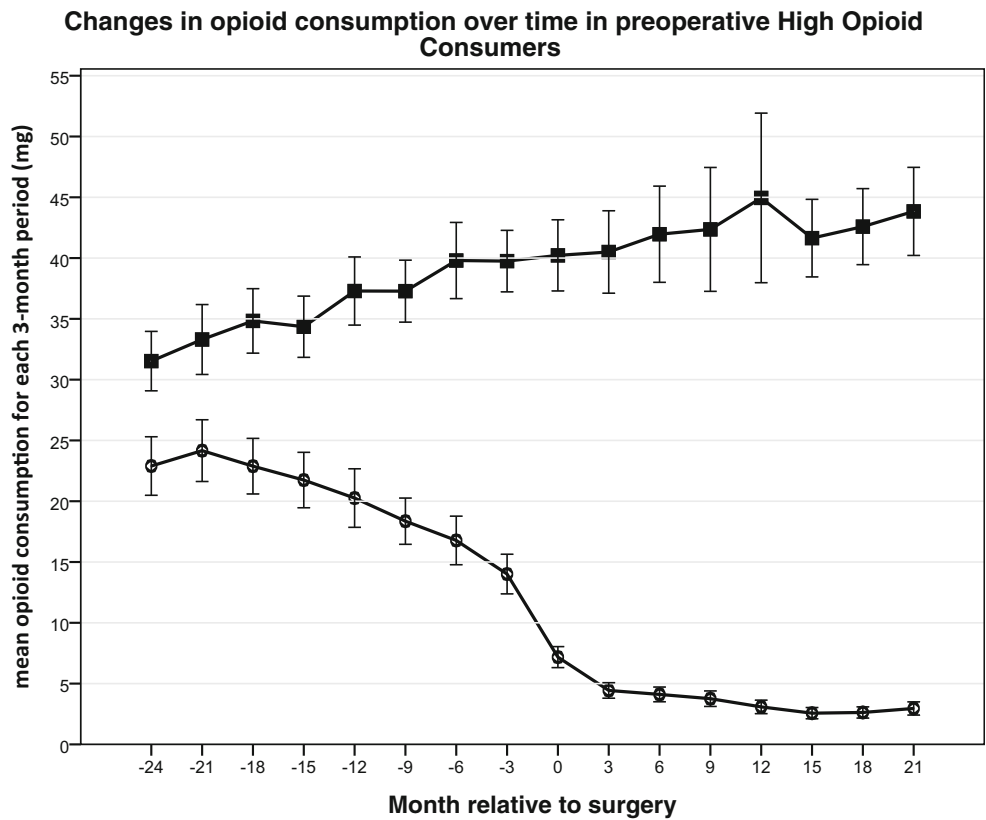
Previous studies have shown an unexpected increase in opioid analgesics consumption after bariatric surgery [6–9]. Our results with a larger population are consistent with their findings. However, in our study, the ratio of high opioid consumers before surgery and of low opioid consumers before surgery that became high consumers after surgery is slightly lower compared to previous studies. This can most likely be attributed to differences in classification of HOC. It is worrying that 760 patients in the LOC group became high opioid consumers during the 2 years following surgery, especially

since 169 had not taken opioids during the 2 years prior to surgery. The post-surgery increase in consumption of opioids in the LOC group was probably the result of painful postoperative complications but other causes such as substance-use disorder cannot be ruled out. Patients considering gastric bypass surgery in general and opioid naïve patients in particular should be informed of the possible risks regarding postoperative opioid use. Consumption of opioid analgesics in the HOC group as a whole did not change after surgery, but, as can be seen in Fig. 2 approximately 25% of these patients significantly decrease their consumption and the remainder increase it. Mean age among HOCs was significantly lower after surgery (Table 2); this potentially protective effect has been shown previously [8] but not repeatedly [7], and there are many potentially confounding factors that we in this study are unable to adjust for. The number of HOC individuals in the total population appeared to increase fairly consistently, and if the 3-month period after surgery is excluded, bariatric surgery does not seem to have had an impact on this increase (Fig. 1).

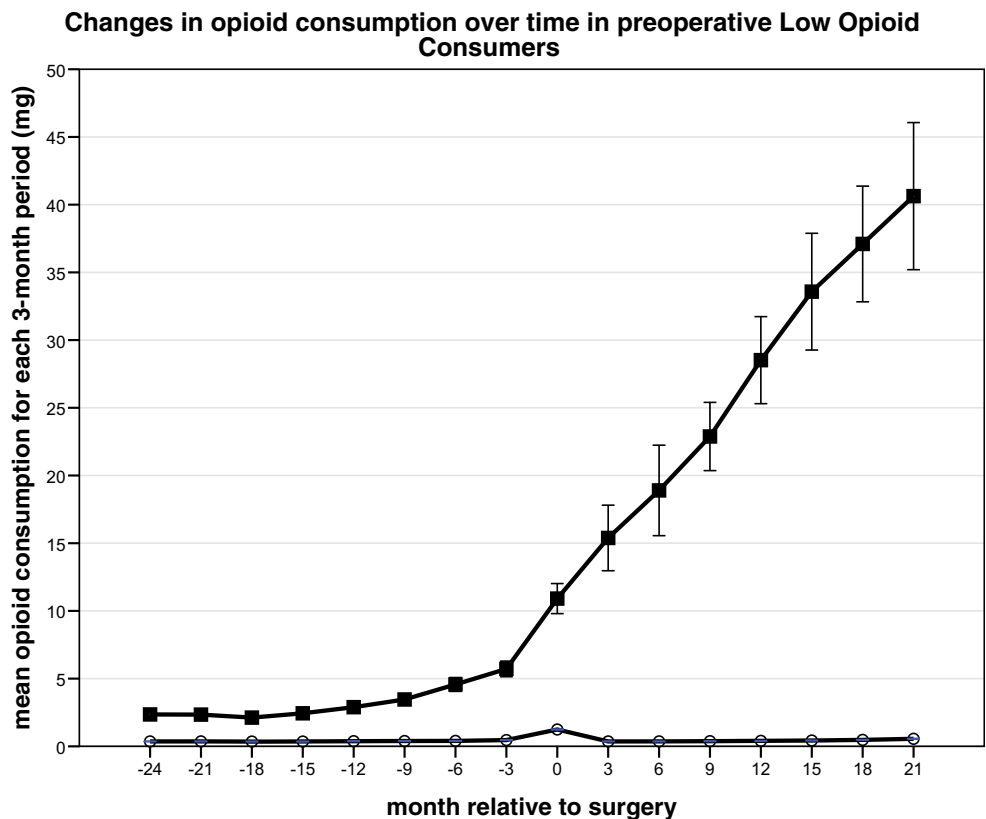
Future studies prompted by these results would be to compare opioid use in patients who have undergone gastric bypass surgery with an obese control group and an in-depth analysis of the group of opioid-naïve patients that after surgery became HOC to find out what caused this change.

The strength of this study is that it used cohort data from comprehensive nationwide registers covering all patients undergoing gastric bypass surgery in Sweden, as well as having complete information on dispensed opioid analgesics. Furthermore, we used a previously described and established method to calculate morphine equivalents. Limitation of this

**Fig. 2** Full square indicates mean daily opioid consumption for patients with high opioid consumption before operation that used > 10 mg daily after surgery (*n* = 1206). Hollow circle indicates mean daily opioid consumption for patients with high opioid consumption before operation that used ≤ 10 mg daily after surgery (*n* = 422)



**Fig. 3** Full square indicates mean daily opioid consumption for patients with low opioid consumption before operation that used > 10 mg daily after surgery (*n* = 760). Hollow circle indicates mean daily opioid consumption for patients with low opioid consumption before operation that used ≤ 10 mg daily after surgery (*n* = 33,224)



study is the lack of a control group with obesity. It should also be noted that we cannot be certain that all dispensed opioids have been used and that our data do not include opioids given during hospital admissions.

## Conclusion

In this nationwide study, we have showed that there is an increase in consumption of opioid analgesics after gastric bypass surgery in Sweden. There was no difference in use of opioid analgesics between women and men. The increase in the number of individuals with high opioid consumption in the total population was mainly due to an increase in the group of patients with a low consumption prior to surgery. Mean daily opioid consumption remained unchanged in the group with high consumption prior to surgery.

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## Compliance with Ethical Standards

**Conflict of Interest** Author 1 has no conflict of interest; author 2, no conflict of interest; author 3, no conflict of interest; author 4 has received fees for consulting and speeches from Baricol Bariatrics AB, Sweden, outside the submitted work.

**Ethical Approval** The trial design was approved by the Regional Ethics Review Board in Uppsala, Sweden; dnr2015/219.

**Informed Consent** Informed consent was obtained from all individuals participating in the study.

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