

## Original Investigation

# Remission of Type 2 Diabetes Mellitus in Patients After Different Types of Bariatric Surgery

## A Population-Based Cohort Study in the United Kingdom

Jan Peter Yska, PharmD; Eric N. van Roon, PharmD, PhD; Anthonius de Boer, MD, PhD; Hubert G. M. Leufkens, PharmD, PhD; Bob Wilffert, PharmD, PhD; Loek J. M. de Heide, MD; Frank de Vries, PharmD, PhD; Arief Lalmohamed, PharmD, PhD

 Supplemental content at [jamasurgery.com](http://jamasurgery.com)

**IMPORTANCE** To our knowledge, an observational study on the remission of type 2 diabetes mellitus (T2DM) after different types of bariatric surgery based on data from general practice has not been carried out.

**OBJECTIVE** To assess the effect of different types of bariatric surgery in patients with T2DM on diabetes remission compared with matched control patients, and the effect of the type of bariatric surgery on improvement of glycemic control and related clinical parameters.

**DESIGN, SETTING, AND PARTICIPANTS** A retrospective cohort study conducted from May 2013 to May 2014 within the Clinical Practice Research Datalink involving 2978 patients with a record of bariatric surgery (2005-2012) and a body mass index (calculated as weight in kilograms divided by height in meters squared) of 35 or greater. We identified 569 patients with T2DM and matched them to 1881 patients with diabetes without bariatric surgery. Data on the use of medication and laboratory results were evaluated.

**EXPOSURES** Bariatric surgery, stratified by type of surgery (gastric banding, Roux-en-Y gastric bypass, sleeve gastrectomy, or other/unknown).

**MAIN OUTCOMES AND MEASURES** Remission of T2DM (complete discontinuation of glycemic therapy, accompanied with a subsequently recorded hemoglobin A<sub>1c</sub> level <6.0%).

**RESULTS** Among patients undergoing bariatric surgery, we found a prevalence of 19.1% for T2DM. Per 1000 person-years, 94.5 diabetes mellitus remissions were found in patients who underwent bariatric surgery compared with 4.9 diabetes mellitus remissions in matched control patients. Patients with diabetes who underwent bariatric surgery had an 18-fold increased chance for T2DM remission (adjusted relative rate [RR], 17.8; 95% CI, 11.2-28.4) compared with matched control patients. The greatest effect size was observed for gastric bypass (adjusted RR, 43.1; 95% CI, 19.7-94.5), followed by sleeve gastrectomy (adjusted RR, 16.6; 95% CI, 4.7-58.4) and gastric banding (adjusted RR, 6.9; 95% CI, 3.1-15.2). Body mass index and triglyceride, blood glucose, and hemoglobin A<sub>1c</sub> levels sharply decreased during the first 2 years after bariatric surgery.

**CONCLUSIONS AND RELEVANCE** Population-based data show that bariatric surgery strongly increases the chance for remission of T2DM. Gastric bypass and sleeve gastrectomy have a greater effect than gastric banding. Although the risks and possible adverse effects of surgery should be weighed against its benefits, bariatric surgery and, in particular, gastric bypass or sleeve gastrectomy may be considered as new treatment options for T2DM.

*JAMA Surg.* 2015;150(12):1126-1133. doi:10.1001/jamasurg.2015.2398  
Published online September 30, 2015.

**Author Affiliations:** Author affiliations are listed at the end of this article.

**Corresponding Author:** Frank de Vries, PharmD, PhD, Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht University, PO Box 80082, 3508 TB Utrecht, the Netherlands ([f.devries@uu.nl](mailto:f.devries@uu.nl)).

Obesity is a growing problem worldwide. Since 1980, the obesity rate has more than doubled. The World Health Organization estimated that in 2014, more than 600 million adults were obese.<sup>1</sup> Overweight status and obesity are linked with more deaths worldwide than underweight status. Raised body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) is a major risk factor for diseases such as cardiovascular diseases, diabetes mellitus (DM), musculoskeletal disorders (such as osteoarthritis), and some cancers.<sup>1</sup> For inducing weight loss, bariatric surgery is more effective than pharmacotherapy or lifestyle interventions.<sup>2,3</sup> Several bariatric procedures are available including laparoscopic adjustable gastric banding, Roux-en-Y gastric bypass, sleeve gastrectomy, and biliopancreatic diversion.<sup>2,3</sup> Bariatric surgery is not only a weight reduction therapy, but also reduces obesity-related complications such as DM, hypertension, and hyperlipidemia.<sup>3,4</sup> Improvement of comorbidities after bariatric surgery is shown by a reduction in use of medication.<sup>5-7</sup>

As much as 23% of patients with morbid obesity have had type 2 DM (T2DM).<sup>8</sup> Bariatric surgery effectively prevents and treats T2DM.<sup>4</sup> Surgical treatment for obese patients may be considered an additional treatment option for the management of T2DM.<sup>9</sup> Previously, the International Diabetes Federation developed a position statement on bariatric surgery in T2DM, intending to create awareness of other treatment options in T2DM.<sup>10</sup> In this statement, criteria were set for remission or optimal metabolic state and substantial improvement of DM. So far, 5 randomized clinical trials have shown the superiority of surgery over medical care. In all trials, different surgical techniques were used: gastric banding,<sup>11</sup> Roux-en-Y gastric bypass,<sup>12,13</sup> Roux-en-Y gastric bypass and biliopancreatic diversion,<sup>14</sup> and gastric bypass and sleeve gastrectomy.<sup>15,16</sup> In a systematic review, Meijer et al<sup>17</sup> showed that glycemic control improved in the months after laparoscopic gastric banding; however, after Roux-en-Y gastric bypass surgery, improvements were more rapid and complete. They found that both types of surgery are capable of improving or curing T2DM, but they suggested that the underlying mechanisms may differ.<sup>17</sup> Whether bariatric surgery is as successful in real-life situations as it is in well-controlled studies is as yet not known.

To our knowledge, an observational study on the remission of T2DM, defined as a combination of discontinuation of antidiabetic medication and normalization of hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) levels, after different types of bariatric surgery based on data from general practice has not been carried out yet. The objectives of this study were to assess (1) the effect of different types of bariatric surgery in patients with T2DM on the chance for DM remission in comparison with morbidly obese patients with T2DM who did not have surgery and (2) the effect of the type of bariatric surgery on improvement of HbA<sub>1c</sub> level and related clinical parameters.

## Methods

### Data Source

Information for this retrospective cohort study, conducted from May 2013 to May 2014, was obtained from the Clinical Prac-

tice Research Datalink (CPRD). The CPRD consists of the computerized medical records of 10 million patients under the care of general practitioners in the United Kingdom. These data include the patients' demographic information, prescription details, clinical events, preventive care provided, specialist referrals, hospital admissions, and major outcomes. This database contains the data of approximately 8% of the UK population and is representative for the total UK population. It has been the source for numerous epidemiologic studies in previous years and the accuracy and completeness of these data have been well documented and validated.<sup>18-23</sup> The protocol for the current study was approved by the CPRD Independent Scientific Advisory Committee (protocol 13\_015). Patient consent was waived because only anonymized data from the CPRD were used.

### Study Population

We selected all patients who underwent bariatric surgery between January 2005 and August 2012 with a BMI of at least 35 at any time before surgery. We assessed the prevalence of T2DM, defined as having at least 1 noninsulin antidiabetic drug (NIAD) prescription in the 6 months before surgery, as well as NIAD use over time. Noninsulin antidiabetic drugs were stratified by type (ie, metformin, sulfonylurea, glitazones, dipeptidyl peptidase 4 inhibitors, glucagon-like peptide 1 agonists, and other). Individuals with a record of polycystic ovary syndrome treated with metformin during the study period were excluded. The index date was defined as the date of bariatric surgery. For each patient in this cohort, we selected up to 4 control patients with T2DM without bariatric surgery, who were matched by age at date of surgery (in increments of 1 year to a maximum of 5 years), sex, and BMI (up to a difference of 10%). Control patients were only eligible if they had an NIAD prescription in the 6 months before the index date.

### Exposure

The exposure of interest was bariatric surgery, stratified by type of surgery (ie, gastric banding, Roux-en-Y gastric bypass, sleeve gastrectomy, or other/unknown). The type of surgery was assessed by reviewing CPRD medical codes.

### Study Outcomes

Our primary study outcome was remission of T2DM after the index date. Remission was defined as a complete discontinuation of all NIADs and insulin, accompanied with a subsequently recorded HbA<sub>1c</sub> value of less than 6.0% (42 mmol/mol; to convert to proportion of 1.0, multiply by 0.01). To evaluate complete discontinuation, patients had to have at least 6 months of follow-up after the last NIAD/insulin prescription, with at least 1 recording of HbA<sub>1c</sub> level less than 6.0%. If this interval was less than 6 months, the patient was not identified as having a complete discontinuation. Patients were censored if they died, moved out of the practice area before remission of T2DM, or if the study period had ended.

For our secondary outcome, we evaluated the change in diabetes-related clinical tests, including HbA<sub>1c</sub>, blood

**Table 1. Baseline Characteristics of Bariatric Patients and Matched Nonbariatric Patients With Diabetes Mellitus**

Characteristic	Patients With Diabetes, No. (%)	
	Bariatric Surgery	No Bariatric Surgery
Total No.	569	1881
Follow-up, mean (SD), y	2.4 (1.7)	2.4 (1.7)
Female	380 (66.8)	1223 (65.0)
Age, mean (SD), y	50.9 (10.4)	52.2 (10.1)
BMI, mean (SD)	45.9 (8.5)	42.8 (7.5)
35-39	123 (21.6)	637 (33.9)
40-49	274 (48.2)	942 (50.1)
≥50	172 (30.2)	302 (16.1)
Smoking status		
Never	275 (48.3)	979 (52.0)
Current	80 (14.1)	365 (19.4)
Former	214 (37.6)	535 (28.4)
Unknown	0 (0.0)	2 (0.1)
Type of bariatric surgery		
Gastric banding	200 (35.1)	NA
Gastric bypass	280 (49.2)	NA
Sleeve gastrectomy	83 (14.6)	NA
Other/unknown	6 (1.1)	NA
HbA <sub>1c</sub> level, mean (SD), %	7.8 (1.6)	7.9 (1.8)
Glucose level, mean (SD), mg/dL	171 (77.4)	171 (77.4)
Duration of diabetes mellitus, mean (SD), y	6.3 (5.0)	5.9 (5.1)
Drug use within 6 mo		
Antidepressants	225 (39.5)	537 (28.5)
Systemic glucocorticoids	28 (4.9)	77 (4.1)
β-blockers	85 (14.9)	335 (17.8)
Antipsychotics	12 (2.1)	84 (4.5)
Insulin	142 (25.0)	272 (14.5)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA<sub>1c</sub>, glycosylated hemoglobin A<sub>1c</sub>; NA, not applicable.

SI conversion factor: To convert glucose to millimoles per liter, multiply by 0.0555; and HbA<sub>1c</sub> to proportion of total hemoglobin, multiply by 0.01.

glucose, total cholesterol, low-density lipoprotein cholesterol, triglyceride, and blood pressure levels, and body mass index. The changes over time were compared with baseline levels (paired *t* test) and were expressed as absolute differences.

### Covariates

With the exception of age, confounders were assessed at baseline (not in a time-dependent manner, as this may be in the causal pathway). These confounders included age, BMI, socioeconomic status, HbA<sub>1c</sub> level, duration of T2DM prior to bariatric surgery, switch to insulin in the year before surgery, and use of antidepressants, systemic glucocorticoids, β-blockers (stratified by cardioselectivity), antipsychotics (stratified by typical/atypical classification), and insulin in the 6 months before. Duration of T2DM prior to bariatric surgery was assessed by reviewing both NIAD prescriptions and T2DM READ codes, the standardized clinical terminology

system used in UK general practice. We considered a switch to insulin in the year before surgery and the use of more than 1 NIAD in the previous 6 months as potential confounders because these may indicate progression of T2DM.

### Statistical Analysis

We compared T2DM remission rates in bariatric surgery patients vs matched nonbariatric patients with diabetes. The analyses were fully adjusted using Cox regression, and relative rates (RRs) were calculated using SAS version 9.2 (SAS Institute). Bariatric surgery patients were further stratified according to the type of surgery, time since surgery, age at index date, sex, the number of unique NIADs at baseline, and the use of insulin before surgery. The timing of T2DM remission was visualized using Kaplan-Meier plots. Changes in T2DM-related laboratory values were displayed in relation to time since bariatric surgery.

## Results

A total of 2978 bariatric surgery patients with a BMI value of at least 35 met our inclusion criteria (eTable 1 in the Supplement). Among these patients, 19.1% had been prescribed an NIAD in the 6 months before surgery and were, therefore, classified as patients with T2DM. Most of these patients were taking metformin (93.2%), and 25.0% of the patients with T2DM using an NIAD also used insulin at baseline.

eTable 2 in the Supplement displays the results of T2DM-related clinical recordings by the general practitioner in patients with T2DM who underwent bariatric surgery. At baseline (within 6 months before the index date), the rate for recording for HbA<sub>1c</sub> level was 54.5%; for blood glucose level, 31.3%; for total cholesterol level, 54.8%; for triglyceride level, 42.2%; for blood pressure, 74.9%; and for BMI, 100% (case definition). In general, the rates for recording tended to go down when the time beyond bariatric surgery increased. At baseline, similar rates for recording were found for patients with T2DM who did not undergo bariatric surgery, with higher rates for recording during follow-up (eTable 3 in the Supplement).

We identified a total of 569 bariatric surgery patients with T2DM and 1881 age-, sex-, and BMI-matched nonbariatric surgery control patients with T2DM (Table 1). The mean age was 50.9 years for bariatric surgery patients and 52.2 years for control patients. Most patients were female: 66.8% among bariatric surgery patients and 65.0% among matched control patients. Control patients tended to be less obese (BMI: 42.8) compared with bariatric surgery patients (BMI: 45.9). Hemoglobin A<sub>1c</sub> and blood glucose levels at baseline were similar between bariatric surgery patients and control patients. More patients with T2DM undergoing bariatric surgery used insulin (25.0%) compared with control patients (14.5%). Within each matched set, there were no differences in age and sex, and BMI did not differ more than 10% between the bariatric surgery and matched control patients.

Per 1000 person-years, 94.5 T2DM remissions were found in patients who underwent bariatric surgery compared with

**Table 2. Diabetes Mellitus Remission Rates in Bariatric Surgery Patients vs Nonbariatric Matched Control Patients With Diabetes Mellitus**

Variable	Events	Rate <sup>a</sup>	Rate Ratio (95% CI)	
			Crude	Adjusted <sup>b</sup>
<b>Surgery</b>				
No bariatric	22	4.9	1 [Reference]	1 [Reference]
Bariatric	107	94.5	17.6 (11.1-27.8)	17.8 (11.2-28.4)
<b>Type of surgery</b>				
Gastric banding	18	28.1	5.9 (2.7-12.7)	6.9 (3.1-15.2)
Gastric bypass	69	185.8	38.3 (17.6-83.3)	43.1 (19.7-94.5)
Sleeve gastrectomy	19	195.6	21.6 (6.4-73.2)	16.6 (4.7-58.4)
Other/unknown	1	42.5	1.2 (0.1-13.8)	... <sup>c</sup>
<b>Time since surgery, y</b>				
<1	98	236.0	24.9 (14.2-43.6)	24.8 (14.1-43.7)
1-1.9	6	20.4	3.4 (1.2-10.3)	3.7 (1.2-11.4)
≥2	3	5.5	11.7 (1.2-112.4)	15.6 (1.5-160.4)
<b>Age at index date, y</b>				
18-39	12	70.0	4.4 (1.7-11.3)	4.4 (1.6-12.2)
40-59	82	104.5	24.7 (13.5-45.3)	27.2 (14.7-50.3)
≥60	13	73.8	18.4 (5.2-64.7)	17.4 (4.9-62.4)
<b>Sex</b>				
Male	31	88.6	23.2 (9.0-59.8)	24.2 (9.2-63.3)
Female	76	97.2	15.8 (9.3-26.8)	16.1 (9.4-27.4)
<b>Use of insulin in the 6 mo before surgery</b>				
No	103	125.3	19.8 (12.5-31.3)	17.4 (10.9-27.7)
Yes	4	12.9	... <sup>c</sup>	... <sup>c</sup>
<b>No. of NIADs at baseline</b>				
1	66	102.3	12.2 (7.4-20.1)	12.9 (7.7-21.4)
2	31	88.3	56.6 (13.6-236.6)	55.1 (13.1-232.2)
≥3	10	73.7	... <sup>c</sup>	... <sup>c</sup>

Abbreviation: NIADs, noninsulin antidiabetics.

<sup>a</sup> Calculated as the number of diabetes mellitus remissions per 1000 person-years.

<sup>b</sup> Adjusted for age; body mass index; socioeconomic status; glycosylated hemoglobin A<sub>1c</sub> level; duration of diabetes mellitus; switch to insulin in the year before surgery; and the use of antidepressants, systemic glucocorticoids, β-blockers, antipsychotics, insulin, and more than 1 NIAD in the previous 6 months.

<sup>c</sup> No calculations are made because of too few sample observations.

4.9 T2DM remissions in matched control patients. Patients with T2DM who underwent bariatric surgery had an 18-fold increased chance of T2DM remission compared with patients with T2DM who did not undergo surgery (adjusted RR, 17.8; 95% CI, 11.2-28.4; **Table 2; Figure 1**).

The greatest effect size was observed for gastric bypass (adjusted RR, 43.1; 95% CI, 19.7-94.5), followed by sleeve gastrectomy (adjusted RR, 16.6; 95% CI, 4.7-58.4) and gastric banding (adjusted RR, 6.9; 95% CI, 3.1-15.2). Diabetes remission developed mostly during the first year after bariatric surgery and in patients aged 40 years or older at the time of surgery.

In **Figure 2**, for all patients, the distributions of time of follow-up and the time between bariatric surgery or index date and latest recording of HbA<sub>1c</sub> level are shown. The mean time of follow-up was the same for bariatric surgery patients and for patients who did not undergo surgery (2.4 years) (**Table 1**). **Table 3** shows the trends of T2DM-related parameters after gastric banding, gastric bypass, or sleeve gastrectomy. Body mass index and HbA<sub>1c</sub>, blood glucose, triglyceride, and blood pressure levels sharply decreased during the first year after bariatric surgery. Thereafter, decreases of most parameters tended to attenuate. In contrast, total cholesterol level did not decrease after bariatric surgery. In all bariatric surgery patients,

the use of statins decreased from 22.4% before surgery to 14.3% 5 years after surgery (**eTable 1** in the **Supplement**); the use of antihypertensive drugs decreased from 36.6% before surgery to 26.7% 5 years after surgery.

According to the British guidelines and the Quality and Outcomes Framework for Diabetes, patients should be monitored for HbA<sub>1c</sub> and glucose levels every 15 months.<sup>24</sup> In our study population, 87% of patients with T2DM indeed had at least 1 HbA<sub>1c</sub> recording in the 15 months after the index date. In the 15 months thereafter, the HbA<sub>1c</sub> recording rate dropped slightly to 78%.

## Discussion

The present study found that bariatric surgery is associated with remission of T2DM. We found an 18-fold increased chance of T2DM remission after bariatric surgery in comparison with patients not undergoing surgery, with the greatest effect size observed for gastric bypass (adjusted RR, 43.1), followed by sleeve gastrectomy (adjusted RR, 16.6) and gastric banding (adjusted RR, 6.9). The largest decreases in HbA<sub>1c</sub> and blood glucose levels were observed in the first 2 years after bariatric surgery.

Figure 1. Kaplan-Meier Plot of Diabetes Mellitus Remission in Bariatric Surgery Patients and Matched Nonbariatric Surgery Patients With Diabetes Mellitus

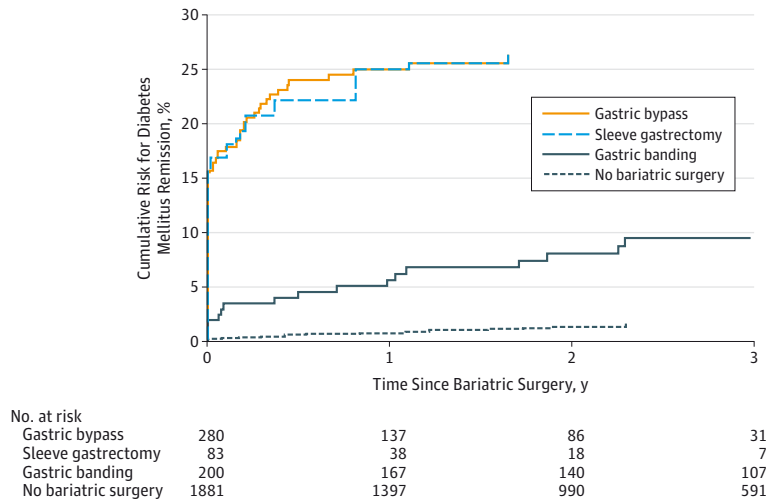
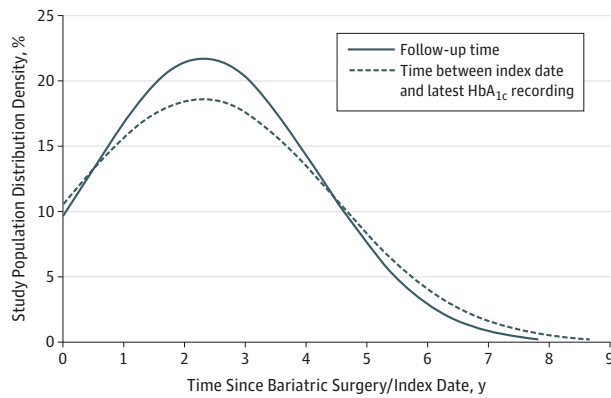


Figure 2. Distribution of Time of Follow-up and the Time Between Bariatric Surgery or Index Date and Latest Recording of Hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) Level in All Patients



To our knowledge, this is the first population-based study to investigate the remission rate of T2DM in patients who underwent bariatric surgery in comparison with matched patients with T2DM without surgery using data from medical records from general practitioners. The results of our study are comparable with those of a systematic review and meta-analysis of randomized clinical trials on bariatric surgery vs nonsurgical treatment for obesity by Gloy et al.<sup>25</sup> They found that after bariatric surgery, patients had a higher remission rate of T2DM (relative risk, 22.1 for 4 studies; complete case analysis) compared with nonsurgical treatment. However, different definitions for T2DM remission were used. We used strict criteria for the definition of remission of T2DM.

In our study, gastric banding had a smaller effect on T2DM remission than gastric bypass and sleeve gastrectomy. This is in agreement with the results of a review by Buchwald et al.<sup>26</sup> They found that T2DM resolution was

greatest for patients undergoing biliopancreatic diversion/duodenal switch, followed by gastric bypass, gastroplasty, and then laparoscopic adjustable gastric banding.<sup>26</sup> Results from a review on long-term follow-up after bariatric surgery by Puzziferri et al<sup>27</sup> also showed that gastric bypass has better outcomes for T2DM control and remission than gastric band procedures.

Although we found a relative difference in T2DM remission in patients after gastric bypass and sleeve gastrectomy, the results are comparable (adjusted RR, 43.1; 95% CI, 19.7-94.5 vs adjusted RR, 16.6; 95% CI, 4.7-58.4).

The field of bariatric surgery is continuously evolving with global and regional trends. In a study to describe national trends in bariatric surgery in England, Burns et al<sup>28</sup> found that between April 2000 and March 2008, 6953 primary bariatric procedures were carried out. Of these operations, 52.5% were gastric band procedures, 45.9% were gastric bypass procedures, and 2% were sleeve gastrectomy procedures. In the past, in Europe, gastric banding was a more commonly applied procedure in bariatric surgery.<sup>29</sup> Therefore, in our study, patients with gastric banding had a longer period of follow-up after surgery than patients with gastric bypass or sleeve gastrectomy. Although the number of sleeve gastrectomy operations in the United Kingdom is rising, this type of surgery is less prevalent than in other countries.<sup>29</sup>

Among patients undergoing bariatric surgery, we found a prevalence of 19.1% for T2DM, based on prescription of an NIAD in the 6 months before surgery. In our study, we excluded patients only using insulin because most of these patients will have type 1 DM. Thus, the real prevalence for T2DM in our study population may be slightly higher than 19.1% and comparable with the prevalence of known diabetes (23%) in morbidly obese patients reported by Hofsø et al.<sup>8</sup> Similar prevalences were found by Crémieux et al<sup>7</sup> (16.3%) in their study on the medication use of 5502 patients who underwent bariatric surgery and by Buchwald et al<sup>26</sup> (22.3%) in their review of studies on weight loss and

**Table 3. Change in Clinical and Laboratory Values After Bariatric Surgery in Bariatric Surgical Patients and Matched Nonbariatric Surgical Patients With Diabetes Mellitus**

Variable	Change in Clinical Laboratory Test Values Compared With Presurgery							
	No Bariatric Surgery	P Value	Bariatric Surgery				Sleeve Gastrectomy	P Value
			Gastric Banding	P Value	Gastric Bypass	P Value		
<b>HbA<sub>1c</sub> level, %</b>								
0-0.9 y	-0.1	.14	-1.2	<.01	-1.5	<.01	-1.4	<.01
1-1.9 y	0.1	.02	-1.3	<.01	-1.6	<.01	-0.9	<.01
≥2 y	0.3	<.01	-0.7	<.01	-1.1	<.01	-1.5	<.01
<b>Blood glucose level, mg/dL</b>								
0-0.9 y	-3.6	.21	-37.8	<.01	-54.0	<.01	-43.2	<.01
1-1.9 y	1.8	.11	-36.0	<.01	-55.8	<.01	-39.6	<.01
≥2 y	1.8	.08	-21.6	<.01	-50.4	<.01	-28.8	<.01
<b>Total cholesterol level, mg/dL</b>								
0-0.9 y	-3.9	<.01	0.0	.52	-11.6	<.01	-3.9	.23
1-1.9 y	-3.9	.05	0.0	>.99	-11.6	.32	3.9	.93
≥2 y	-7.7	<.01	3.9	.43	-11.6	.53	-15.4	.16
<b>Triglyceride level, mg/dL</b>								
0-0.9 y	0.0	.80	-35.4	<.01	-70.9	<.01	-44.3	.04
1-1.9 y	0.0	.78	-53.2	<.01	-88.6	<.01	-44.3	.08
≥2 y	-8.9	.42	-53.2	<.01	-70.9	<.01	-35.4	<.01
<b>Systolic blood pressure, mm Hg</b>								
0-0.9 y	-1	.04	-6	<.01	-8	<.01	-8	<.01
1-1.9 y	-1	.11	-6	<.01	-7	<.01	-9	<.01
≥2 y	-1	.45	-3	<.01	-5	<.01	-10	<.01
<b>Diastolic blood pressure, mm Hg</b>								
0-0.9 y	-1	.01	-3	<.01	-3	<.01	-3	.06
1-1.9 y	-2	<.01	-4	<.01	-4	<.01	-3	.14
≥2 y	-2	<.01	-2	<.01	-3	<.01	-3	.34
<b>BMI</b>								
0-0.9 y	-1.5	<.01	-6.1	<.01	-11.6	<.01	-10.4	<.01
1-1.9 y	-1.8	<.01	-7.8	<.01	-13.0	<.01	-11.5	<.01
≥2 y	-2.3	<.01	-8.0	<.01	-10.7	<.01	-8.2	<.01

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HbA<sub>1c</sub>, glycosylated hemoglobin A<sub>1c</sub>.

SI conversion factors: To convert glucose to millimoles per liter, multiply by

0.0555; HbA<sub>1c</sub> to proportion of total hemoglobin, multiply by 0.01; and triglycerides to millimoles per liter, multiply by 0.0113.

T2DM-related outcomes in patients treated with any form of bariatric surgery.

In our study, the use of NIADs decreased from 19.1% to 8.4% 2 to 3 years after bariatric surgery. Crémieux et al<sup>7</sup> reported a decrease in the use of oral antidiabetics from 16.3% to 4.0% on average 3 years after bariatric surgery. However, as several types of gastric bypass surgery were used in more than 85% of the patients included in their study, their results should not be compared with results from our study population in which gastric banding was more common.

One of the strengths of this study was the use of data from the medical records of patients under the care of general practitioners, as registered in the CPRD, representative for the total UK population. Previously, Booth et al<sup>30</sup> used the CPRD database in a population-based matched cohort study on the incidence of T2DM after bariatric surgery. They found that bariatric surgery was associated with reduced incidence of clinical diabetes after surgery in obese patients without diabetes at

baseline.<sup>30</sup> Other strengths of this study included a strict definition of remission of diabetes including cessation of all diabetic medication and HbA<sub>1c</sub> level less than 6.0% after at least 6 months of follow-up and mean follow-up of 2.4 years. In addition, this study had a nonsurgical, comparable control group. Results of our population-based study with inclusion of patients who underwent different types of bariatric surgery may better reflect daily practice than results from randomized clinical trials.

Our study had several limitations. In the CPRD, data are recorded in primary care. Data from secondary or intermediary services (eg, hospitals and private clinics) may be incompletely ascertained. There may also be a discrepancy between the patient's actual use of medication and the use as recorded in the database. Also, the recording of clinical and laboratory tests was far from complete. However, these limitations apply to both the surgical and the control patients in this study.

Although the rates for recording clinical and laboratory tests (eTable 2 and eTable 3 in the Supplement) do not suggest that patients with T2DM who underwent bariatric surgery were checked for HbA<sub>1c</sub> more frequently than patients with T2DM who did not undergo surgery, we cannot exclude, however, the possibility of different intensity of follow-up (ie, more motivational support by the general practitioner) between surgical and nonsurgical patients. Moreover, bariatric surgery patients may indeed be more compliant and motivated, for which we could not adjust.

With the present study, using a strict definition of remission of T2DM, the benefit of bariatric surgery in improving glycemic control as well as remission of T2DM was confirmed by data from primary health care records.

## Conclusions

Data from a very large UK primary health care database show that bariatric surgery increases the chance of remission of T2DM. Gastric bypass and sleeve gastrectomy show higher remission rates compared with gastric banding. The largest decreases in HbA<sub>1c</sub> and blood glucose levels were observed in the first 2 years after bariatric surgery.

Although the risks and possible adverse effects of surgery should be weighed against its benefits, bariatric surgery and, in particular, gastric bypass or sleeve gastrectomy may be considered a realistic treatment option for T2DM in patients with a BMI of 35 or greater.

### ARTICLE INFORMATION

**Accepted for Publication:** May 29, 2015.

**Published Online:** September 30, 2015.  
doi:10.1001/jamasurg.2015.2398.

**Author Affiliations:** Department of Clinical Pharmacy and Clinical Pharmacology, Medical Centre Leeuwarden, Leeuwarden, the Netherlands (Yska, van Roon); Unit of Pharmacotherapy and Pharmaceutical Care, Department of Pharmacy, University of Groningen, Groningen, the Netherlands (van Roon, Wilffert); Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht University, Utrecht, the Netherlands (de Boer, Leufkens, de Vries, Lalmohamed); Department of Clinical Pharmacy and Pharmacology, University Medical Centre Groningen, Groningen, the Netherlands (Wilffert); Department of Internal Medicine, Medical Centre Leeuwarden, Leeuwarden, the Netherlands (de Heide); Care and Public Health Research Institute (CAPHRI), Maastricht, the Netherlands (de Vries); MRC Lifecourse Epidemiology Unit, Southampton General Hospital, Southampton, England (de Vries); Department of Clinical Pharmacy and Toxicology, Maastricht University Medical Centre, Maastricht, the Netherlands (de Vries); Department of Clinical Pharmacy, University Medical Center Utrecht, Utrecht, the Netherlands (Lalmohamed).

**Author Contributions:** Drs De Vries and Lalmohamed had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.  
**Study concept and design:** Yska, van Roon, Wilffert, de Vries, Lalmohamed.

**Acquisition, analysis, or interpretation of data:** Yska, van Roon, de Boer, Leufkens, de Heide, de Vries, Lalmohamed.

**Drafting of the manuscript:** Yska, van Roon, de Heide, de Vries, Lalmohamed.

**Critical revision of the manuscript for important intellectual content:** Yska, van Roon, de Boer, Leufkens, Wilffert, de Vries, Lalmohamed.

**Statistical analysis:** van Roon, de Boer, Lalmohamed.

**Administrative, technical, or material support:** Lalmohamed.

**Study supervision:** Yska, van Roon, Leufkens, Wilffert, de Vries.

**Conflict of Interest Disclosures:** Dr Leufkens is a researcher at the World Health Organization Collaborating Centre for Pharmaceutical Policy and

Regulation, which receives no direct funding or donations from private parties, including the pharmaceutical industry. No other disclosures were reported.

**Funding/Support:** The Division of Pharmacoepidemiology and Clinical Pharmacology, which employs Drs Lalmohamed, Leufkens, de Vries, and de Boer, has received unrestricted funding from the Netherlands Organisation for Health Research and Development, the Dutch Health Care Insurance Board, the Royal Dutch Pharmacists Association, the private-public-funded Top Institute Pharma (<http://www.tipharna.nl>, which includes cofunding from universities, government, and industry), the EU Innovative Medicines Initiative, the EU 7th Framework Program, and the Dutch Ministry of Health and Industry (including GlaxoSmithKline, Pfizer, and others). Research funding from public-private partnerships (eg, EU Innovative Medicines Initiative and Top Institute Pharma) is accepted under the condition that no company-specific product or company-related study is conducted. The World Health Organization Collaborating Centre for Pharmaceutical Policy and Regulation has received unrestricted research funding from public sources (eg, Netherlands Organisation for Health Research and Development, the Dutch Health Care Insurance Board, EU 7th Framework Program, Dutch Medicines Evaluation Board, and Dutch Ministry of Health).

**Role of the Funder/Sponsor:** The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Additional Contributions:** We thank Marloes Emous, MD (bariatric surgeon, Department of Surgery, Medical Centre Leeuwarden), for her review of the manuscript. She did not receive compensation for her contribution.

### REFERENCES

- World Health Organization. Obesity and overweight: fact sheet No. 311. <http://www.who.int/mediacentre/factsheets/fs311/en/>. Updated January 2015. Accessed March 21, 2015.
- Leff DR, Heath D. Surgery for obesity in adulthood. *BMJ*. 2009;339:b3402.

- Arterburn DE, Courcoulas AP. Bariatric surgery for obesity and metabolic conditions in adults. *BMJ*. 2014;349:g3961.
- Sjöström L, Lindroos AK, Peltonen M, et al; Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med*. 2004;351(26):2683-2693.
- Hodo DM, Waller JL, Martindale RG, Fick DM. Medication use after bariatric surgery in a managed care cohort. *Surg Obes Relat Dis*. 2008;4(5):601-607.
- Segal JB, Clark JM, Shore AD, et al. Prompt reduction in use of medications for comorbid conditions after bariatric surgery. *Obes Surg*. 2009;19(12):1646-1656.
- Crémieux PY, Ledoux S, Clerici C, Cremieux F, Buessing M. The impact of bariatric surgery on comorbidities and medication use among obese patients. *Obes Surg*. 2010;20(7):861-870.
- Hofsø D, Jenssen T, Hager H, Røislien J, Hjelmessaeth J. Fasting plasma glucose in the screening for type 2 diabetes in morbidly obese subjects. *Obes Surg*. 2010;20(3):302-307.
- Dixon JB, le Roux CW, Rubino F, Zimmet P. Bariatric surgery for type 2 diabetes. *Lancet*. 2012;379(9833):2300-2311.
- Dixon JB, Zimmet P, Alberti KG, Rubino F; International Diabetes Federation Taskforce on Epidemiology and Prevention. Bariatric surgery: an IDF statement for obese type 2 diabetes. *Diabet Med*. 2011;28(6):628-642.
- Dixon JB, O'Brien PE, Playfair J, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA*. 2008;299(3):316-323.
- Ikramuddin S, Korner J, Lee WJ, et al. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial. *JAMA*. 2013;309(21):2240-2249.
- Liang Z, Wu Q, Chen B, Yu P, Zhao H, Ouyang X. Effect of laparoscopic Roux-en-Y gastric bypass surgery on type 2 diabetes mellitus with hypertension: a randomized controlled trial. *Diabetes Res Clin Pract*. 2013;101(1):50-56.
- Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med*. 2012;366(17):1577-1585.

15. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med*. 2012;366(17):1567-1576.
16. Schauer PR, Bhatt DL, Kirwan JP, et al; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes: 3-year outcomes. *N Engl J Med*. 2014;370(21):2002-2013.
17. Meijer RI, van Wagenveld BA, Siegert CE, Eringa EC, Serné EH, Smulders YM. Bariatric surgery as a novel treatment for type 2 diabetes mellitus: a systematic review. *Arch Surg*. 2011;146(6):744-750.
18. Jick SS, Kaye JA, Vasilakis-Scaramozza C, et al. Validity of the general practice research database. *Pharmacotherapy*. 2003;23(5):686-689.
19. Azoulay L, Schneider-Lindner V, Dell'aniello S, Filion KB, Suissa S. Thiazolidinediones and the risk of incident strokes in patients with type 2 diabetes: a nested case-control study. *Pharmacoepidemiol Drug Saf*. 2010;19(4):343-350.
20. Eppenga WL, Lalmohamed A, Geerts AF, et al. Risk of lactic acidosis or elevated lactate concentrations in metformin users with renal impairment: a population-based cohort study. *Diabetes Care*. 2014;37(8):2218-2224.
21. Bazelier MT, de Vries F, Vestergaard P, et al. Risk of fracture with thiazolidinediones: an individual patient data meta-analysis. *Front Endocrinol (Lausanne)*. 2013;4:11.
22. Lalmohamed A, de Vries F, Bazelier MT, et al. Risk of fracture after bariatric surgery in the United Kingdom: population based, retrospective cohort study. *BMJ*. 2012;345:e5085.
23. Driessen JH, van Onzenoort HA, Henry RM, et al. Use of dipeptidyl peptidase-4 inhibitors for type 2 diabetes mellitus and risk of fracture. *Bone*. 2014;68:124-130.
24. Diabetes UK. Quality and outcomes framework (QOF) update. <https://www.diabetes.org.uk/Documents/About%20Us/Consultations/Quality%20and%20Outcomes%20Framework%20public%20update%202011.pdf>. Published 2011. Accessed March 28, 2015.
25. Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2013;347:f5934.
26. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *Am J Med*. 2009;122(3):248-256.e5.
27. Puzziferri N, Roshek TB III, Mayo HG, Gallagher R, Belle SH, Livingston EH. Long-term follow-up after bariatric surgery: a systematic review. *JAMA*. 2014;312(9):934-942.
28. Burns EM, Naseem H, Bottle A, et al. Introduction of laparoscopic bariatric surgery in England: observational population cohort study. *BMJ*. 2010;341:c4296.
29. Buchwald H, Oien DM. Metabolic/bariatric surgery worldwide 2011. *Obes Surg*. 2013;23(4):427-436.
30. Booth H, Khan O, Prevost T, et al. Incidence of type 2 diabetes after bariatric surgery: population-based matched cohort study. *Lancet Diabetes Endocrinol*. 2014;2(12):963-968.