



# Asthma medication usage is significantly reduced following bariatric surgery

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## Abstract

**Introduction** Asthma is an important healthcare problem affecting millions in the United States. Additionally, a large proportion of patients with asthma suffer from obesity. These patients exhibit poor asthma control and reduced therapy response, increasing utilization of healthcare resources. Pulmonary symptoms improve after bariatric surgery (BS), and we hypothesized that asthma medication usage would decrease following BS.

**Methods** A retrospective data analysis was performed in adult patients from a single institution's database. Patients with obesity using at least one asthma medication pre-operatively who underwent BS were studied for up to 3-years post-operation. Poisson generalized linear mixed models for repeated measures were used to evaluate the effects of time and procedure type on the number of asthma medication.

**Results** Bariatric patients with at least one prescribed asthma medication (mean  $1.4 \pm 0.6$ ) were included ( $n = 751$ ). The mean age at time of operation was  $46.8 \pm 11.6$  years, mean weight was  $295.9 \pm 57$  lbs, and mean body mass index (BMI) was  $49 \pm 8.2$  kg/m<sup>2</sup>; 87.7% were female, 33.4% had diabetes, 44.2% used gastroesophageal reflux disease (GERD) medication, and 64.4% used hypertension medication. The most common procedure was Roux-en-Y gastric bypass (79%), followed by sleeve gastrectomy (10.7%), adjustable gastric banding (8.1%), and duodenal switch (2.3%). The mean number of prescribed asthma medications among all procedures decreased by 27% at 30 days post-operation ( $p < 0.0001$ ), 37% at 6 months ( $p < 0.0001$ ), 44% at 1 year ( $p < 0.0001$ ), and 46% at 3 years ( $p < 0.0001$ ) after adjusting for risk factors. No significant differences in medication use over time between procedure types were observed. In the adjusted analysis, the mean number of asthma medications was 12% higher in patients using at least one GERD medication ( $p = 0.015$ ) and 8% higher with 10-unit increase in pre-operative BMI ( $p = 0.006$ ).

**Conclusion** BS significantly decreases asthma medication use starting 30 days post-operation with a sustained reduction for up to 3 years.

**Keywords** Obesity · Asthma · Medications · Bariatric surgery

Obesity is a growing worldwide epidemic and an emerging healthcare problem affecting millions of people in the United States [1]. Obesity has significant implications for patient

care, having a wide impact on morbidity and mortality [2–7]. The prevalence of obesity has increased significantly over the past several decades, with more than one-third of adults in the United States now considered obese (body mass index; BMI > 30) according to a recent report from the US Centers for Disease Control and Prevention [1].

Asthma is another important health care problem affecting 10% of the bariatric population [8]. Over the past decades, prospective studies have demonstrated that obesity increases the risk of developing asthma by 1.4–2.6 times [9, 10], and obesity is also significantly associated with increased asthma severity [11, 12]. Furthermore, patients with obesity exhibit poor asthma control and reduced response to therapy mandating disproportionately high

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amounts of healthcare resources [7, 8, 12, 13]. Several studies have proposed a potential causal association between both conditions [2, 12, 14, 15] therefore targeting weight loss in individuals with both obesity and asthma is likely to improve asthma control.

Currently, bariatric surgery is the most effective treatment for morbid obesity, resulting in sustained weight loss and improvement of co-morbidities [16] with maximal weight loss typically occurring 1–2 years after surgery [7, 17]. Additionally, studies have demonstrated that bariatric surgery is capable of producing significant improvements in pulmonary symptoms such as those caused by obstructive sleep apnea [7, 18–20]. In particular, patients with asthma exhibited improved small airway function and decreased numbers of mast cells in the airway following bariatric surgery [21]. The present study evaluated the hypothesis that the need for asthma medications would decrease over time after bariatric surgery.

## Materials and methods

After Institutional Review Board approval, a retrospective analysis of a prospectively maintained single institution database was performed. Patients aged 18 or above, with at least one asthma medication prescribed pre-operatively who underwent bariatric surgery in Duke University Medical Center between January, 2000 and October, 2015 were identified. A list of the asthma, gastroesophageal reflux disease (GERD), and hypertension medications used in our analysis is shown in Table 1. Patient reported medications count was gathered from our institution medical records. These asthma medications were included after pulmonologist review and based on recommended medications in the National guidelines for asthma management [22]. Baseline and post-operative data including demographics, weight and BMI, co-morbidities, number of prescribed asthma, GERD and hypertension medications, type of procedure, and complications were reviewed. Patients were followed up at 30 days, 90 days, 6 months, 1 year, years, and 3 years post-operation. Continuous variables were summarized using appropriate measures of location and variability and compared using Kruskal–Wallis test, whereas categorical variables were presented as frequencies and percentages and compared using Fisher’s exact test. Over 85% of the patients had missing weight/asthma medication information after 4 years post-operation, therefore we only included records up to 3 years post-operation for the analysis. Approximately 69% of patients had complete data up to 1 year post-operation. Since missing data were present in the dataset, we investigated the missing data pattern before we determined the model of longitudinal data analysis. We found that younger patients were more likely

**Table 1** List of medications used in the analyses

Asthma
Albuterol (ventolin, proventil, proair, volmax, vospire)
Salbutamol (ventodisk)
Arformoterol
Fenoterol
Formoterol (foradil, perforomist)
Levalbuterol (xopenex)
Metaproterenol (alupent)
Pirbuterol (maxair)
Salmeterol (serevent)
Terbutaline (brethine)
Fluticasone
Ipratropium/albuterol (conbivent, duoneb)
Ipratropium/fenoterol (duovent)
Budesonide/formoterol (symbicort)
Gastroesophageal reflux
Omeprazole (prilosec)
Esomeprazole magnesium (nexium)
Lanzoprazole (prevacid)
Pantoprazole (protonix)
Rabeprazole (aciphex)
Omeprazole/sodium bicarbonate (zegerid)
Dexlansoprazole (dexilant, kapidex)
Metoclopramide (maxolon, metozolov, reglan)
Clomipramine (clopra)
Famotidine (pepcid)
Hypertension
Aripiprazole (abilify)
Acetabulol (sectral)
Atenolol (tenormin)
Amlodipine (norvasc)
Aldactone
Benazepril (lotensin)
Bisoprolol
Candesartan
Carvedilol (coreg)
Chlorthalidone
Clonidine
Diltiazem hydrochloride (cardizem, cartia, dilacor, diltzac, taztia, tiamate, tiazac)
Enalapril (vasotec)
Felodipine (plendil)
Furosemide (lasix)
Hydralazine
Hydrochlorothiazide (hydrodiuril, microzide)
Irbesartan (avapro)
Labetalol (normodyne, trandate)
Lisinopril (privilinil, zestril)
Lopressidone

**Table 1** (continued)

Losartan (cozaar)
Metolazone
Metoprolol (lopressor, toprol)
Nevibolol (bystolic)
Nifedipine (adalat, afeditab, nifedical, nifeditab, procardia)
Olemsartan (benicar)
Pindolol (visken)
Propranolol (inalder, innoproan)
Quinapril (accupril)
Ramipril (altace)
Spironolactone
Telmisartan (micardis)
Torseamide
Valsartan (diovan)
Verapamil (calan, covera, isoptin, verelan)
Hydrochlorothiazide/triamterene (dyazide, maxzide)
Amlodipine/olmesartan (azor)
Clonidine hydrochloride/chlorthalidone (clorpress)
Ramipril (altace)
Amlodipine/valsartan (exforge)
Chlorthalidone/reserpine (regroton)
Atenolol/chlorthalidone (tenoretic)
Lisinopril/hydrochlorothiazide (prinizide, zestoretic)
Losartan/hydrochlorothiazide (hyzaar, normozide)
Propranolol/hydrochlorothiazide (inderide)
Enalapril/felodipine (lexxel)
Amlodipine/benazepril (lotrel)
Telmisartan/amlodipine (twynsta)
Bisoprolol/hydrochlorothiazide (ziac)

to become loss to follow-up regardless of their weights or severity of asthma, and thus we assumed a Missing At Random (MAR) mechanism and a Generalized Linear Mixed Model (GLMM) was considered. Our primary outcome was the longitudinal number of prescribed asthma medications assessed pre-operatively and post-operatively. A Poisson GLMM with a log link for repeated measures was fit to evaluate the effect of time and procedure type, on number of asthma medications, while adjusting for risk factors including age, gender, race, pre-operative diabetes, pre-operative BMI, pre-operative use of hypertension medications (at least one medication vs. none), and pre-operative use of GERD medications (at least one medication vs. none). The GERD and hypertension medications used in our analyses (Table 1) were chosen based on national guidelines for management [23, 24]. Additionally, we performed a separate analysis to evaluate the trend of number of prescribed asthma medications for each procedure type by including interaction terms of procedure types and time. BMI was also assessed longitudinally as a secondary outcome using linear mixed effect model. All

analyses were performed using R 3.3.1 (R Core Team, Vienna, Austria) and SAS 9.4 (SAS Institute Inc., Cary, NC).

## Results

The study population consisted of 751 bariatric patients with at least one asthma medication prescribed pre-operatively (mean  $1.4 \pm 0.6$ ). Mean age at operation was  $46.8 \pm 11.6$  years, mean weight was  $295.9 \pm$  lbs, BMI was  $49 \pm 8.2$  kg/m<sup>2</sup>; 87.7% were females, 33.4% had diabetes, 44.2% used GERD medication, and 64.4% used hypertension medication. The most common type of procedure performed was Roux-en-Y Gastric Bypass (79%), followed by Sleeve Gastrectomy (10.7%), Adjustable Gastric Band (8.1%), and Duodenal Switch (2.3%). Demographic data are summarized in Table 2.

The unadjusted number of prescribed asthma medications were assessed pre-operatively and post-operatively and summarized in Table 3. The pre-operative average count of asthma medications was  $1.4 \pm 0.6$ , and it became  $1 \pm 0.8$  at 30-day post-operation and  $0.8 \pm 0.8$  at 1-year post-operation.

Table 4 displays the results of Poisson GLMM of the mean counts of prescribed asthma medications over time. Overall, there was a significant time effect on the number of asthma medications used ( $p < 0.0001$ ) while adjusting for all other risk factors. In particular, we saw a significant decrease in the number of asthma medications used after bariatric surgery in our cohort. The subject-specific rate ratios (RRs) at 30 days post-operation compared to pre-operation was 0.73 (95% confidence interval (CI) 0.66–0.80). Similarly, the average number of asthma medications used among all procedures was 31% lower at 90 days (RR 0.69, 95% CI 0.63–0.77), 37% lower at 6 months (RR 0.63, 95% CI 0.56–0.70), 44% lower at 1 year (RR 0.56, 95% CI 0.50–0.63), 48% lower at 2 years (RR 0.52, 95% CI 0.44–0.60), and 46% lower at 3 years (RR 0.54, 95% CI 0.45–0.65). We did not find a significant effect of procedure (Type III *F* tests of procedure effect  $p = 0.687$ ). However, we detected significant effects of pre-operative GERD medication use ( $p = 0.0145$ ) and pre-operative BMI ( $p = 0.0055$ ) on the number of asthma medication. Specifically, patients reporting use of at least one pre-operative GERD medication were associated with 12% higher asthma medication use compared to those not reporting use of pre-operative GERD medications (RR 1.12, 95% CI 1.02–1.23,  $p = 0.015$ ). With a 10-unit increase in pre-operative BMI, the average number of prescribed asthma medications was 8% higher (RR 1.08, 95% CI 1.02–1.14,  $p = 0.0065$ ). All other risk factors (age, race, gender, pre-operative diabetes, and pre-operative hypertension medication) were not significant in explaining the variation in the number of asthma medication. The effect

**Table 2** Baseline demographic characteristics between different bariatric surgery procedures patients

	Adjustable gastric banding <i>N</i> = 61	Duodenal switch <i>N</i> = 17	Roux-en-Y gastric bypass <i>N</i> = 593	Sleeve gastrectomy <i>N</i> = 80	Total <i>N</i> = 751	<i>p</i> value
Age at operation						0.091
Mean (SD)	49.7 (13.7)	50.8 (8.7)	46.3 (11.4)	47.1 (11.9)	46.8 (11.6)	
Range	(21, 76)	(28, 62)	(19, 72)	(18, 70)	(18, 76)	
Gender						0.0003
Female	50 (82.0%)	10 (58.8%)	534 (90.1%)	65 (81.2%)	659 (87.7%)	
Male	11 (18.0%)	7 (41.2%)	59 (9.9%)	15 (18.8%)	92 (12.3%)	
Race						0.092
Caucasian	35 (57.4%)	11 (64.7%)	372 (62.7%)	47 (58.8%)	465 (61.9%)	
African American	19 (31.1%)	5 (29.4%)	145 (24.5%)	29 (36.2%)	198 (26.4%)	
Other	5 (8.2%)	1 (5.9%)	15 (2.5%)	4 (5.0%)	25 (3.3%)	
Missing	2 (3.3%)	0 (0.0%)	61 (10.3%)	0 (0.0%)	63 (8.4%)	
Pre-operative weight (lb)						<0.0001
Mean (SD)	279.7 (50.1)	354.6 (65.2)	294.8 (55.7)	303.9 (61.9)	295.9 (57)	
Range	(200, 416)	(190, 469)	(171, 540)	(198, 480)	(171, 540)	
Pre-operative BMI						<0.0001
Mean (SD)	45.2 (7.2)	54.6 (7.9)	49 (7.9)	50.5 (9.8)	49 (8.2)	
Range	(36.5, 76.1)	(38.4, 69.6)	(33.4, 92.7)	(35.3, 82.4)	(33.4, 92.7)	
Pre-operative excess body weight (lb)						<0.0001
Mean (SD)	124.7 (43.7)	192.5 (54.2)	144.2 (49.5)	153.1 (58.4)	144.7 (51)	
Range	(63.3, 279.3)	(66.2, 284.6)	(43, 394.3)	(64.1, 334.3)	(43, 394.3)	
Count of hypertension medications before operation						0.26
Mean (SD)	1.5 (1.6)	1.8 (1.5)	1.3 (1.3)	1.4 (1.4)	1.3 (1.4)	
Range	(0, 6)	(0, 4)	(0, 7)	(0, 6)	(0, 7)	
Count of GERD medications before operation						0.31
Mean (SD)	0.6 (0.6)	0.4 (0.5)	0.5 (0.6)	0.6 (0.7)	0.5 (0.6)	
Range	(0, 2)	(0, 1)	(0, 3)	(0, 3)	(0, 3)	
Pre-operative diabetes						0.66
Insulin	10 (16.4%)	2 (11.8%)	72 (12.1%)	9 (11.2%)	93 (12.4%)	
Noninsulin	13 (21.3%)	2 (11.8%)	121 (20.4%)	22 (27.5%)	158 (21.0%)	
No diabetes	38 (62.3%)	13 (76.5%)	400 (67.5%)	49 (61.3%)	500 (66.6%)	
Pre-operative sleep apnea						0.1
No	42 (68.9%)	11 (64.7%)	460 (77.6%)	55 (68.8%)	568 (75.6%)	
Yes	19 (31.1%)	6 (35.3%)	133 (22.4%)	25 (31.2%)	183 (24.4%)	
Count of asthma medications before operation						0.78
Mean (SD)	1.3 (0.5)	1.5 (0.7)	1.4 (0.6)	1.4 (0.6)	1.4 (0.6)	
Range	(1, 2)	(1, 3)	(1, 4)	(1, 3)	(1, 4)	

*SD* standard deviation

of time on number of prescribed asthma medications within each procedure was significant for all procedures except for DS ( $p = 0.1153$ ). The subject-specific RRs at 1-year post-operation compared to pre-operation for each procedure type can be found in Table 5.

Pre-operative and post-operative BMIs by procedure types are summarized in Table 6. Mean BMI was decreased from pre-operative  $49 \pm 8.2$  kg/m<sup>2</sup> to  $45.2 \pm 8$  kg/

m<sup>2</sup> at 30-day post-operation, and it was further reduced to  $34.6 \pm 7.7$  kg/m<sup>2</sup> at 1-year post-operation. Using a linear mixed effect model that adjusted for confounders, we detected significant interaction between procedure types and time ( $p < 0.0001$ ), and the results are shown in Table 7. DS patients had the largest post-operative BMI loss (mean change at 1-year:  $-19.87$  kg/m<sup>2</sup>, 95% CI  $-21.93$  to  $-17.81$ ) whereas AGB patients had the smallest post-operative BMI

**Table 3** Asthma medication use pre- and post-operation

	Adjustable gastric banding <i>N</i> = 61	Duodenal switch <i>N</i> = 17	Roux-en-Y gastric bypass <i>N</i> = 593	Sleeve gastrectomy <i>N</i> = 80	Total <i>N</i> = 751
Count of asthma medications before operation					
Mean (SD)	1.3 (0.5)	1.5 (0.7)	1.4 (0.6)	1.4 (0.6)	1.4 (0.6)
Median (IQR)	1 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1, 2)
Range	(1, 2)	(1, 3)	(1, 4)	(1, 3)	(1, 4)
Count of asthma medications 30 days post-operation					
Mean (SD)	1 (0.7)	0.7 (0.8)	1 (0.8)	0.7 (0.8)	1 (0.8)
Median (IQR)	1 (1, 1.2)	1 (0, 1)	1 (0, 2)	1 (0, 1)	1 (0, 1)
Range	(0, 2)	(0, 2)	(0, 4)	(0, 3)	(0, 4)
Missing	1 (1.64%)	0	17 (2.87%)	3 (3.75%)	21 (2.8%)
Count of asthma medications 90 days post-operation					
Mean (SD)	1.1 (0.7)	1 (0.9)	0.9 (0.8)	1.1 (0.7)	1 (0.8)
Median (IQR)	1 (1, 2)	1 (0, 1)	1 (0, 1)	1 (1, 2)	1 (0, 1)
Range	(0, 2)	(0, 3)	(0, 4)	(0, 3)	(0, 4)
Missing	10 (16.39%)	4 (23.53%)	67 (11.3%)	22 (27.5%)	103 (13.72%)
Count of asthma medications 6 months post-operation					
Mean (SD)	1 (0.7)	0.8 (1)	0.9 (0.8)	0.8 (0.8)	0.9 (0.8)
Median (IQR)	1 (1, 1)	0.5 (0, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)
Range	(0, 2)	(0, 3)	(0, 4)	(0, 2)	(0, 4)
Missing	18 (29.51%)	5 (29.41%)	169 (28.5%)	39 (48.75%)	231 (30.76%)
Count of asthma medications 1 year post-operation					
Mean (SD)	0.7 (0.7)	0.8 (0.8)	0.8 (0.8)	0.9 (0.9)	0.8 (0.8)
Median (IQR)	1 (0, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)
Range	(0, 2)	(0, 2)	(0, 4)	(0, 3)	(0, 4)
Missing	13 (21.31%)	7 (41.18%)	175 (29.51%)	37 (46.25%)	232 (30.89%)
Count of asthma medications 2 year post-operation					
Mean (SD)	0.8 (0.8)	0.5 (0.5)	0.7 (0.8)	0.8 (1)	0.7 (0.8)
Median (IQR)	1 (0, 1)	0.5 (0, 1)	0.5 (0, 1)	1 (0, 1)	1 (0, 1)
Range	(0, 2)	(0, 1)	(0, 3)	(0, 3)	(0, 3)
Missing	28 (45.9%)	11 (64.71%)	373 (62.9%)	63 (78.75%)	475 (63.25%)
Count of asthma medications 3 year post-operation					
Mean (SD)	0.7 (0.8)	0.5 (1)	0.8 (0.9)	1.2 (1)	0.8 (0.9)
Median (IQR)	0.5 (0, 1)	0 (0, 0.5)	1 (0, 1)	1.5 (0.8, 2)	1 (0, 1)
Range	(0, 2)	(0, 2)	(0, 4)	(0, 2)	(0, 4)
Missing	35 (57.38%)	13 (76.47%)	463 (78.08%)	76 (95%)	587 (78.16%)

*SD* standard deviation, *IQR* interquartile range

loss (mean change at 1-year:  $-5.75 \text{ kg/m}^2$ , 95% CI  $-6.72$  to  $-4.78$ ).

## Discussion

During the last decades the prevalence of asthma has increased steadily along with the prevalence of obesity, suggesting a potential relationship between these conditions [25]. Many studies [26–28] and the American Thoracic Society have concluded that obesity is a risk factor

for: (1) development of de novo asthma, and (2) for complicating management in previously-diagnosed asthmatic patients [29]. The physio-pathological mechanism of this relationship is not entirely understood [30, 31] and may differ by asthma phenotypes. Nevertheless, proinflammatory effects of leptin and other obesity-related hormones may contribute to airway hyperreactivity, and, along with the restricted lung mechanics observed in obesity, these combined effects play an important role supporting the association between obesity and asthma [25].

**Table 4** Poisson generalized linear mixed effect model adjusted subject-specific rate ratios (RRs) of count of asthma medications

Model predictor covariate	RR (95% CI)	<i>p</i> value
30-day post-operative	0.73 (0.66, 0.80)	<.0001
90-day post-operative	0.69 (0.63, 0.77)	<.0001
6-month post-operative	0.63 (0.56, 0.70)	<.0001
1-year post-operative	0.56 (0.50, 0.63)	<.0001
2-year post-operative	0.52 (0.44, 0.60)	<.0001
3-year post-operative	0.54 (0.45, 0.65)	<.0001
Pre-operative	Reference	N/A
Sleeve gastrectomy	0.95 (0.81, 1.11)	0.5159
Adjustable gastric band	1.07 (0.91, 1.26)	0.4286
Duodenal switch	0.91 (0.66, 1.25)	0.5677
Roux-en-Y gastric bypass	Reference	N/A
Male	0.88 (0.76, 1.02)	0.0839
Female	Reference	N/A
African American	0.94 (0.84, 1.04)	0.2350
Other or unknown race	0.96 (0.83, 1.10)	0.5513
Caucasian	Reference	N/A
Insulin-treated diabetes	0.97 (0.84, 1.13)	0.6992
Noninsulin-treated diabetes	0.98 (0.87, 1.10)	0.6948
No diabetes	Reference	N/A
Age	1.00 (1.00, 1.01)	0.4104
Has pre-operative hypertension medication	0.99 (0.88, 1.10)	0.7887
No pre-operative hypertension medication	Reference	N/A
Has pre-operative GERD medication	1.12 (1.02, 1.23)	0.0145
No pre-operative GERD medication	Reference	N/A
Pre-operative BMI (10-kg/m <sup>2</sup> )	1.08 (1.02, 1.14)	0.0055

Model excludes follow-ups without asthma medication information. There were 3608 observations

RR rate ratio, CI confidence interval

**Table 5** Procedure type specific adjusted subject-specific rate ratios (RRs) at 1-year post-operation compared to pre-operation for count of asthma medications

Procedure type	1-year RR (95% CI)	<i>p</i> value
Sleeve gastrectomy	0.65 (0.44, 0.94)	0.0232
Adjustable gastric band	0.54 (0.36, 0.80)	0.0023
Duodenal switch	0.52 (0.23, 1.17)	0.1153
Roux-en-Y gastric bypass	0.56 (0.49, 0.63)	<0.0001

Poisson generalized linear mixed effect model was fit and adjusted for time, procedure types, time × procedure types interaction, age, gender, race, pre-operative BMI, pre-operative diabetes types, pre-operative hypertension medication, and pre-operative GERD medication

Camargo et al. [10] studied the incidence of asthma in a large prospective cohort of adult subjects and found that increased BMI is an independent factor, significantly associated with the risk of developing adult-onset asthma requiring

treatment with at least 1 medication ( $p < 0.001$ ). Likewise, Gibeon et al. [32] studied 600 patients with asthma and classified them into three groups according to their BMI: normal-weight, overweight, and obese. They found that increased BMI was significantly associated with increased use of asthma maintenance and rescue medication, concluding that asthma symptoms may be difficult to control in overweight and obese populations. Similarly, we found that pre-operative BMI has a significant effect on number of asthma medication after adjusting for other risk factors ( $p = 0.006$ ). Specifically, we found that patients with lower BMI utilize less asthma medications compared to patients with higher BMI.

Additionally, we found a strong relationship between the pre-operative numbers of asthma medications and the presence of GERD ( $p = 0.0145$ ), as the use of asthma medication was 12% higher in this population after adjusting for other risk factors. This finding is comparable with other studies that classify GERD as part of the inflammatory conditions contributing to the intensification of respiratory symptoms among patients with obesity [10, 33].

Bariatric surgery improves obesity-related co-morbidities as well as respiratory conditions such as obstructive sleep apnea [34, 35]. Furthermore, evidence suggests that bariatric surgery results in reduced medication requirements to control pulmonary symptoms [36]. In our cohort, we observed that patients significantly reduced asthma medication use over time after bariatric surgery ( $p < 0.001$ ). As early as 30 days post-operation, the number of prescribed asthma medications was 27% lower than the pre-operative average number. This reduction was found to be progressive, as at 90 days, 6 months, 1 year, and 2 years after surgery the use of asthma medications was 31%, 37%, 44%, and 48% lower than the pre-operative average, respectively. These results are consistent with other studies where a significant reduction in the use of asthma medication was also reported. Reddy et al. [36] studied over thirteen thousand patients who underwent bariatric surgery and found that 18.6% of the population was diagnosed with asthma and used medication before surgery. One year after bariatric surgery, 40% of the patients significantly reduced the number of asthma medications required for asthma control. Similarly, Sikka et al. [15] studied 320 patients with at least one respiratory medication used before bariatric surgery and found a significant reduction of medication usage 1 year post-bariatric surgery. Our study extends these findings in that we report that patients with asthma and obesity who undergo bariatric surgery experience asthma symptom control benefits immediately after surgery, and this effect is sustained up to 3 years following their surgery.

The technique and practice patterns for all procedures have remained fairly constant in our department over the extended study timeframe. We did not find a significant

**Table 6** BMI (kg/m<sup>2</sup>) by procedure types pre- and post-operation

	Adjustable gastric banding	Duodenal switch	Roux-en-Y gastric bypass	Sleeve gastrectomy	Total
Pre-operative					
<i>N</i>	61	17	593	80	751
Mean (SD)	45.2 (7.2)	54.6 (7.9)	49 (7.9)	50.5 (9.8)	49 (8.2)
Range	(36.5, 76.1)	(38.4, 69.6)	(33.4, 92.7)	(35.3, 82.4)	(33.4, 92.7)
30 days post-operative					
<i>N</i>	60	17	575	76	723
Mean (SD)	42.4 (6.8)	49.8 (7.9)	45.2 (7.8)	46.8 (9.4)	45.2 (8)
Range	(33.7, 67.5)	(35.1, 62.3)	(30.1, 101.9)	(32.6, 79.5)	(30.1, 101.9)
90 days post-operative					
<i>N</i>	51	13	526	58	648
Mean (SD)	40.6 (6.7)	42.2 (15)	40.1 (7.3)	43.6 (9.5)	40.5 (7.7)
Range	(30.9, 65.8)	(0, 58.7)	(26.9, 78.4)	(30.3, 74.1)	(0, 78.4)
6 months post-operative					
<i>N</i>	43	12	424	41	520
Mean (SD)	40 (7.1)	40.7 (6.3)	36.1 (7)	41.7 (10.5)	37 (7.6)
Range	(28.6, 65.8)	(27.5, 49.5)	(23.6, 77.1)	(28.2, 72.4)	(23.6, 77.1)
1 year post-operative					
<i>N</i>	48	10	417	43	518
Mean (SD)	39.7 (7.6)	35.2 (6.8)	33.4 (6.8)	40.5 (10.8)	34.6 (7.7)
Range	(26.5, 67.1)	(24.6, 44.3)	(20.8, 73.8)	(26.9, 76.2)	(20.8, 76.2)
2 year post-operative					
<i>N</i>	33	6	220	17	276
Mean (SD)	39.6 (7.1)	32.4 (5.9)	32.7 (7)	42.4 (11.1)	34.1 (7.9)
Range	(26, 56.7)	(26.1, 41.8)	(19.7, 54)	(29.7, 66.2)	(19.7, 66.2)
3 year post-operative					
<i>N</i>	26	4	129	4	163
Mean (SD)	37.8 (7.8)	32.8 (8.6)	33.6 (7.3)	40.5 (4.9)	34.5 (7.5)
Range	(25.8, 57.1)	(25.4, 42.8)	(20.8, 56.4)	(34.8, 45)	(20.8, 57.1)

difference in the reduction of asthma medication use between bariatric procedures, suggesting that patients of all procedure types changed the number of asthma medications used over time in the same pattern. In addition, we found that among those patients taking at least one asthma medication, significant reduction in BMI was achieved at 30 days and 1 year post-operatively, and this reduction in BMI was sustained for 3 years, regardless of the procedure type. Therefore, pre-operative asthma medication use does not inhibit weight loss following bariatric surgery in all procedures. These findings can be related to the fact that most patients in our cohort underwent RYGB, making the sample size of other procedures too small to detect a difference, which represents the greater limitation of this study. Furthermore, our study cannot show a causal relationship between post-operative asthma medication use reduction and BMI reduction using our data set. Although we demonstrate a significant association of bariatric surgery with (1) a decrease in asthma medication use and (2) reduced BMI over three years, we cannot yet disentangle whether it is a reduction in

BMI that causes the observed surgery-associated reduction in asthma medication use over time, or if the post-operative reduction in asthma medication use occurs independently of weight loss. Further analyses of data in ongoing studies in both human asthma patients and animal models of allergic and non-allergic airways disease that isolate the effects of weight loss and bariatric surgery will establish the individual impact of each of these interventions. By including time and procedure type interaction, we also tested the effect of time on number of prescribed asthma medications within each procedure. We found that the effect of time was significant for all procedures except for DS. However, as noted previously, DS group is comprised of a relatively low number of patients which makes it difficult to reach statistical significance in this analysis.

In summary, our results showed that the pre-operative number of medications required for the treatment of asthma is strongly influenced by BMI and GERD. Additionally, our results indicate that bariatric surgery reduces the usage of asthma medications starting 30 days post-operation and

**Table 7** BMI changes by procedure types

Procedure type	Time	Estimate change in BMI compared to baseline (95% CI)	p value
Roux-en-Y gastric bypass	30-day	-3.77 (-4.06, -3.48)	<.0001
Duodenal switch	30-day	-4.88 (-6.58, -3.18)	<.0001
Adjustable gastric band	30-day	-2.86 (-3.76, -1.95)	<.0001
Sleeve gastrectomy	30-day	-3.75 (-4.55, -2.95)	<.0001
Roux-en-Y gastric bypass	1-year	-15.98 (-16.30, -15.65)	<.0001
Duodenal switch	1-year	-19.87 (-21.93, -17.81)	<.0001
Adjustable gastric band	1-year	-5.75 (-6.72, -4.78)	<.0001
Sleeve gastrectomy	1-year	-11.15 (-12.13, -10.16)	<.0001
Roux-en-Y gastric bypass	3-year	-16.31 (-16.82, -15.80)	<.0001
Duodenal switch	3-year	-19.88 (-22.81, -16.95)	<.0001
Adjustable gastric band	3-year	-6.10 (-7.31, -4.89)	<.0001
Sleeve gastrectomy	3-year	-10.96 (-13.72, -8.20)	<.0001

There were 751 patients and 3604 observations for a maximum 3-year follow-up. Linear mixed effect model was fit with compound symmetry covariance structure for subject and adjusted for time, procedure types, time x procedure types interaction, age, gender, race, pre-operative diabetes types, pre-operative hypertension medication, and pre-operative GERD medication

that this reduction is sustained up to 3 years after surgery. Therefore, bariatric surgery, regardless of procedure type, is a beneficial intervention specifically for patients with asthma and obesity to improve asthma symptoms and control. Our ongoing investigations of the physiological and metabolic changes that occur with bariatric surgery will evaluate specific cellular and molecular mechanisms of improved airway inflammation, resistance and remodeling that impact asthma control and medication use. Further studies with larger cohorts would be necessary to establish the impact of each type of bariatric procedure on the required number of asthma medications over time, in order to better address the management of obesity in asthmatic patients.

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### Compliance with ethical standards

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### References

- Ogden CL, Carroll MD, Fryar CD, Flegal KM (2015) Prevalence of obesity among adults and youth: United States, 2011–2014. *National Health and Nutrition Examination Survey*. *CDC* 219:1–8
- Peters-Golden M, Swern A, Bird SS, Hustard CM, Grant E, Edelman JM (2006) Influence of body mass index on the response to asthma controller agents. *Eur Respir J* 27(3):495–503
- Beuther DA, Sutherland ER (2007) Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 175(7):661–666
- Varraso R, Siroux V, Maccario J, Pin I, Kauffmann F, Epidemiological Study on the Genetics and Environment of Asthma (2005) Asthma severity is associated with body mass index and early menarche in women. *Am J Respir Crit Care Med* 171(4):334–339
- Boulet LP (2008) Influence of obesity on the prevalence and clinical features of asthma. *Clin Invest Med* 31(6):386–390
- Engeland A, Bjørge T, Selmer RM, Tverdal A (2003) Height and body mass index in relation to total mortality. *Epidemiology* 14(3):293–299
- Heacock T, Lugogo N (2014) Role of weight management in asthma symptoms and control. *Immunol Allergy Clin North Am* 34(4):797–808
- Haslam DW, James WP (2005) Obesity. *Lancet* 366(9492):1197–1209
- Schatz M, Zeiger RS, Yang SJ, Chen W, Sajjan S, Allen-Ramey F, Camargo CA Jr (2015) Prospective study on the relationship of obesity to asthma impairment and risk. *J Allergy Clin Immunol Pract* 3(4):560–565
- Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE (1999) Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. *Arch Intern Med* 159(21):2582–2588
- Haldar F, Pavord ID, Shaw DE, Berry MA, Thomas M, Brightling CE, Wardlaw AJ, Green RH (2008) Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med* 178(3):218–224
- Moore WC, Meyers DA, Wenzel SE, Teague WG, Li H, Li X, D'Agostino R Jr, Castro M, Curran-Everett D, Fitzpatrick AM, Gaston B, Jarjour NN, Sorkness R, Calhoun WJ, Chung KF, Comhair SA, Dweik RA, Israel E, Peters SP, Busse WW, Erzurum SC, Bleeker ER (2010) National heart lung and blood institute's severe asthma research program. *Am J Respir Crit Care Med* 181(4):315–323
- Sturm R, An R (2014) Obesity and economic environments. *CA Cancer J Clin* 64(5):337–350
- Pakhale S, Baron J, Dent R, Vandemheen K, Aaron SD (2015) Effects of weight loss on airway responsiveness in obese adults with asthma: does weight loss lead to reversibility of asthma? *Chest* 147(6):1582–1590
- Sikka N, Wegienka G, Havstad S, Genaw J, Carlin AM, Zoratti E (2010) Respiratory medication prescriptions before and after bariatric surgery. *Ann Allergy Asthma Immunol* 104(4):326–330
- Angrisani L, Santonicola A, Iovino P, Vitello A, Zundel N, Buchwald H, Scopinaro N (2017) Bariatric surgery and endoluminal procedures: IFSO Worldwide survey 2014. *Obes Surg* 27(9):2290–2292

17. Sjoström L (2008) Bariatric surgery and reduction in morbidity and mortality: experiences from the SOS study. *Int J Obes* 32(7):93–97
18. Scott HA, Wood LG, Gibson PG (2017) Role of obesity in asthma: mechanisms and management strategies. *Curr Allergy Asthma Rep* 17(8):53
19. Hewitt S, Humerfelt S, Sjøvik TT, Aasheim ET, Risstad H, Kristinsson J, Mala T (2014) Long-term improvements in pulmonary function 5 years after bariatric surgery. *Obes Surg* 24(5):705–711
20. Nguyen NT, Hinojosa MW, Smith BR, Gray J, Varela E (2009) Improvement of restrictive and obstructive pulmonary mechanics following laparoscopic bariatric surgery. *Surg Endosc* 23(4):808–812
21. van Huisstede A, Rudolphus A, Castro Cabezas M, Biter LU, van de Geijn GJ, Taube C, Hiemstra PS, Braunstahl GJ (2015) Effect of bariatric surgery on asthma control, lung function and bronchial and systemic inflammation in morbidly obese subjects with asthma. *Thorax* 70(7):659–667
22. National Asthma in Education and Prevention Program (2007) Expert panel report 3 (EPR-3): guidelines for the diagnosis and management of asthma—summary report 2007. *J Allergy Clin Immunol* 120(5):94–138
23. Katz PO, Gerson LB, Vela MF (2013) Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 108:308–328
24. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, Smith SC, Svetkey LP, Taler SJ, Townsend RR, Wright JT, Narva AS, Ortiz E (2014) 2014 evidence-based guideline for the management of high blood pressure in adults. *JAMA* 311(5):507–520
25. Hampton T (2014) Studies probe links between childhood asthma and obesity. *JAMA* 311:1718–1719
26. Al-Alwan A, Bates JH, Chapman DG, Kaminsky DA, DeSarno MJ, Irvin CG, Dixon AE (2014) The nonallergic asthma of obesity a matter of distal lung compliance. *Am J Respir Crit Care Med* 189(12):1494–1502
27. Umetsu DT (2017) Mechanism by which obesity impacts upon asthma. *Thorax* 72(2):174–177
28. Bildstrup L, Backer V, Thomsen SF (2015) Increased body mass index predicts severity of asthma symptoms but not objective asthma traits in a large sample of asthmatics. *J Asthma* 52(7):687–692
29. Dixon AE, Holquin F, Sood A, Salome CM, Pratley RE, Beuther DA, Celedon JC, Shore SA, American Thoracic Society Ad Hoc Subcommittee on Obesity and Lung Disease (2010) An official american thoracic society workshop report: obesity and asthma. *Proc Am Thorac Soc* 7(5):325–335
30. Mohanan S, Tapp H, McWilliams A, Dulin M (2014) Obesity and asthma: pathophysiology and implications for diagnosis and management in primary care. *Exp Biol Med* 239(11):1531–1540
31. Mukadam S, Zacharias J, Henao MP, Kraschnewski J, Ishmael F (2017) Differential effects of obesity on eosinophilic vs. non-eosinophilic asthma subtypes. *J Asthma* 28:1–6
32. Gibeon D, Batuwita K, Osmond M, Heany LG, Brightling CE, Niven R, Mansur A, Chaudhuri R, Bucknall CE, Rowe A, Guo Y, Bhavsar PK, Chung KF, Menzies-Gow A (2013) Obesity-associated severe asthma represents a distinct clinical phenotype: analysis of the british thoracic society difficult asthma registry patient cohort according to BMI. *Chest* 143(2):406–414
33. Gupta S, Lodha R, Kabra SK (2017) Asthma, GERD and obesity: triangle of inflammation. *Indian J Pediatr*. <https://doi.org/10.1007/s12098-017-2484-0>
34. Priyadarshini P, Singh VP, Aggarwal S, Garg H, Sinha S, Guleria R (2017) Impact of bariatric surgery on obstructive sleep apnoea-hypopnea syndrome in morbidly obese patients. *J Minim Access Surg* 13(4):291–295
35. Hariri K, Kini SU, Herron DM, Fernandez-Ranvier G (2017) Resolution of symptomatic obstructive sleep apnea not impacted by preoperative body mass index, choice of operation between sleeve gastrectomy and Roux-en-Y gastric bypass surgery, or severity. *Obes Surg*. <https://doi.org/10.1007/s11695-017-3042-6>
36. Reddy RC, Baptist AP, Fan Z, Carlin AM, Birkmeyer NJ (2011) The effects of bariatric surgery on asthma severity. *Obes Surg* 21(2):200–206