Received: 6 October 2023 | Revised: 17 January 2024 | Accepted: 22 January 2024

DOI: 10.1002/osp4.742

ORIGINAL ARTICLE

Obesity Science and Practice Open Access WILEY

Evaluation of prescription medication changes following sleeve gastrectomy surgery

Gina Arena[1] | Alex Kitsos[2] | Jeffrey M. Hamdorf[3,4] | Mike D'Arcy-Evans[4] | Michelle Kilpatrick[2] | Alison Venn[2] | David B. Preen[1]

[1]School of Population and Global Health, The University of Western Australia, Nedlands, Western Australia, Australia

[2]Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia

[3]Medical School, The University of Western Australia, Nedlands, Western Australia, Australia

[4]Western Surgical Health, Nedlands, Western Australia, Australia

Correspondence
Gina Arena, School of Population and Global Health M431, The University of Western Australia, 35 Stirling Highway, Nedlands, WA 6009, Australia.
Email: Gina.arena@uwa.edu.au

Abstract

Objective: The increasing global prevalence of obesity, coupled with its association with chronic health conditions and rising healthcare costs, highlights the need for effective interventions; however, despite the availability of treatment options, the ongoing success of primary interventions in maintaining long-term weight loss remains limited. This study examined the prescription medication dispensing changes following sleeve gastrectomy in Australians aged 45 years and over.

Methods: In a retrospective analysis of 847 bariatric surgery patients from the New South Wales 45 and Up Study, the assessment of medication patterns categorizing into three groups: gastrointestinal, metabolic, cardiorespiratory, musculoskeletal, and nervous systems was conducted. Each drug class was analyzed, focusing on patients with dispensing records within the 12 months before surgery. This study employed interrupted time-series analysis to compare pre- and post-surgery medication usage.

Results: With a predominantly female population (76.9%) and an average age of 57.2 (standard deviation 5.71), there were statistically significant reductions in both unique medications (12.5% decrease, $p = 0.004$) and total medications dispensed (15.9% decrease, $p = 0.003$) from 12 months before surgery to 13–24 months after bariatric surgery. All medication categories, except opioids, showed reductions. Notably, the most significant reductions were observed in diabetes (38.6%), agents acting on the renin-angiotensin system (40.4%), lipid modifying agents (26.5%), anti-inflammatory products (46.3%), and obstructive airway diseases (53.3%) medications during this time frame.

Conclusion: These findings suggest that sleeve gastrectomy provides an effective therapeutic intervention for patients with comorbidities requiring multiple medications, especially for obesity-related diseases such as diabetes, cardiovascular, respiratory and musculoskeletal disorders.

KEYWORDS
bariatric surgery, obesity, prescription utilisation

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2024 The Authors. Obesity Science & Practice published by World Obesity and The Obesity Society and John Wiley & Sons Ltd.

1 | INTRODUCTION

In Australia, the prevalence of obesity is increasing, with similar trends reported in other Organization for Economic Cooperation and Development countries.[1] Obesity has been linked to an increased prevalence of several chronic health conditions such as cardiovascular disease, diabetes, and certain cancers.[2] Obesity-driven increases in these conditions have further increased the number of direct and indirect healthcare costs to the healthcare system, including greater usage of prescription medications.[3] Despite the availability of multiple treatment options, including lifestyle modification and anti-obesity medications, the long-term success of these "first line" interventions in maintaining weight loss is limited.[4,5]

Bariatric surgery has gained significant popularity over the past 2 decades as an effective treatment option for severe obesity.[4] A growing body of evidence indicates that bariatric surgery is more effective than first-line therapies in achieving and maintaining a significant weight loss over the long-term.[5,6] Surgical intervention for obesity has been associated with improved long-term physical health outcomes, including significant improvements to glycemic control, type 2 diabetes and reductions in cardiovascular risk factors, as well as improved quality of life and increased life expectancy.[5,7–9]

While the specific type of bariatric surgery has evolved over time, with advances in surgical techniques, sleeve gastrectomy is currently the most common and effective bariatric surgery option used in Australia and most high-income countries.[10,11] Little research has been undertaken in an Australian setting examining the long-term effectiveness of modern bariatric surgical techniques on the impact of prescription medication changes.

To better inform treatment decisions for severe obesity, it is essential to understand how surgical interventions, such as sleeve gastrectomy, impact pharmacotherapy in the short and longer-term. This will help to improve an understanding of the potential benefits and risks associated with these interventions and aid in the development of optimal treatment strategies following surgery.

This study aimed to examine the association between sleeve gastrectomy and changes in medication usage (overall and by specific drug classes), using linked routinely collected administrative health and medicine dispensing data for patients who underwent sleeve gastrectomy in Australia from 2006 to 2015. We hypothesize that sleeve gastrectomy will be associated with significant changes in medication usage, both overall and within specific drug classes.

2 | METHODS

2.1 | Study design

This study was a retrospective analysis of all participants from the 45 and Up Study[12] who underwent sleeve gastrectomy in New South Wales (NSW), Australia, between 1 January 2006 and 31 December 2015. The dispensing patterns of government-subsidized prescription medications were reviewed from 12 months before sleeve gastrectomy to the 24 months post-surgery. All medication dispenses were analyzed on the basis of their Anatomical Therapeutic Chemical (ATC) classification levels (1st to 5th levels).

2.2 | Data sources

The 45 and Up Study is a large-scale study conducted by the Sax Institute, which recruited over 267,000 participants aged 45 years and older across NSW (approximately 10% of the state's population in this age group). The study was designed to be representative of the NSW population aged 45 years and over. Details about the study are documented elsewhere.[12] In brief, participants were randomly sampled from the general population of NSW using the Services Australia (formerly Medicare Australia) enrollment database. Baseline surveys were then distributed to participants between January 2006 and December 2008, with written consent sought for further follow-up including additional surveys and routine linkage of their health records in whole-population administrative health databases. The mean time from survey completion to bariatric surgery was 4.5 years (SD = 2.2 years). Individuals needed to be a resident of NSW (postcode recorded as NSW in Medicare). The overall response rate was estimated to be 17.9%.

Participants' survey data used for this study included body mass index (BMI), age, gender, education level, and income and were linked to five administrative health datasets. These included the NSW Admitted Patient Data Collection (APDC) (which records all public and private hospital separations in NSW) from July 2001 to December 2017. Linked admitted patient data contain details of principal and secondary diagnoses coded using the International Classification of Diseases 10th Revision—Australian Modification (ICD-10-AM)[13] and all surgical procedures performed (coded using the Australian Classification of Health Interventions).[14] Mortality data (details of all registered deaths and coded causes of death from Register of Births, Deaths and Marriages Death Registrations and Cause of Death Unit Record File) from July 2001 to December 2017.

In addition, Medicare Benefits Schedule (MBS) data (comprising inpatient care provided outside the public hospital setting and outpatient and primary health care services subsidized by the Australian Government e.g., general practitioner and psychiatrist consultations) and Pharmaceutical Benefits Scheme (PBS) data (which records data for each pharmaceutical product that is subsidized by the Australian Government and supplied by PBS-approved pharmacies) were linked to the dataset. Medicare Benefits Schedule and PBS data were obtained from July 2004 to December 2017. Linkage to the PBS and MBS administrative datasets was undertaken by the Sax Institute using a unique identifier and deterministic methods. Linkage to the NSW administrative datasets was undertaken by the NSW Center for Health Record Linkage using probabilistic techniques.[15]

2.3 | Study cohort

All individuals from the 45 and Up Survey were included if identified as having primary sleeve gastrectomy recorded in APDC (public hospital data only) (Table S1) or MBS data (public hospital, private hospital or private clinic) (Table S2) after study entry. A lookback period in the APDC and MBS data to July 2001 was implemented to exclude participants with sleeve gastrectomy recorded prior to recruitment to the 45 and Up Study (Table S3).

Participants were excluded if their first sleeve gastrectomy after the baseline survey was a revisional procedure, or if individuals had a non-diabetic or non-obesity related primary ICD-10-AM diagnosis for surgery admission, as these surgeries were likely used for indications other than the management of obesity. Patients who did not have a full 24 months post-surgery follow-up in the PBS dataset (i.e., their sleeve gastrectomy was after 01/01/2016, or if individuals died within 2 years of surgery) were excluded. The selection of the cohort from all 45 and Up Study participants is shown in Figure 1.

3 | OUTCOMES

The main outcome variables of interest were the number of, and change in, total dispenses in the 24 months following surgery compared with the 12 months prior to surgery. All dispensing information was obtained from the PBS dataset, and all medications were reviewed on the basis of their different ATC (Anatomical Therapeutic Chemical) classification levels (1st to 5th levels).[16]

All ATC levels in which a prescription medication was dispensed in the 12 months prior to sleeve gastrectomy were included in the analysis. Medication data were then classified into three broad groups; (i) gastrointestinal medications (drugs for peptic ulcers, propulsives, antiemetics and antinauseants), (ii) metabolic and cardiorespiratory medications (diabetes, selected hormonal preparations, blood and blood-forming organs, selected cardiovascular medicines, selected respiratory medicines) and (iii) medications for the musculoskeletal and nervous systems (anti-inflammatories, anti-rheumatics, analgesics). Specific ATC codes for these medications are presented in Tables 1–3, respectively.

3.1 | Statistical analysis

All data cleaning, data management and statistical analysis were completed using R (version 4.1.3).[17]

Descriptive statistics were performed for demographic characteristics examined at the time of completion of the 45 and Up Study survey. These characteristics included self-reported age, gender, BMI, highest education level attained, income, and age at surgery (Table 4). Categorical variables are summarized using frequencies and proportions. Continuous variables with normal distributions are presented as means with standard deviations (SD); continuous variables

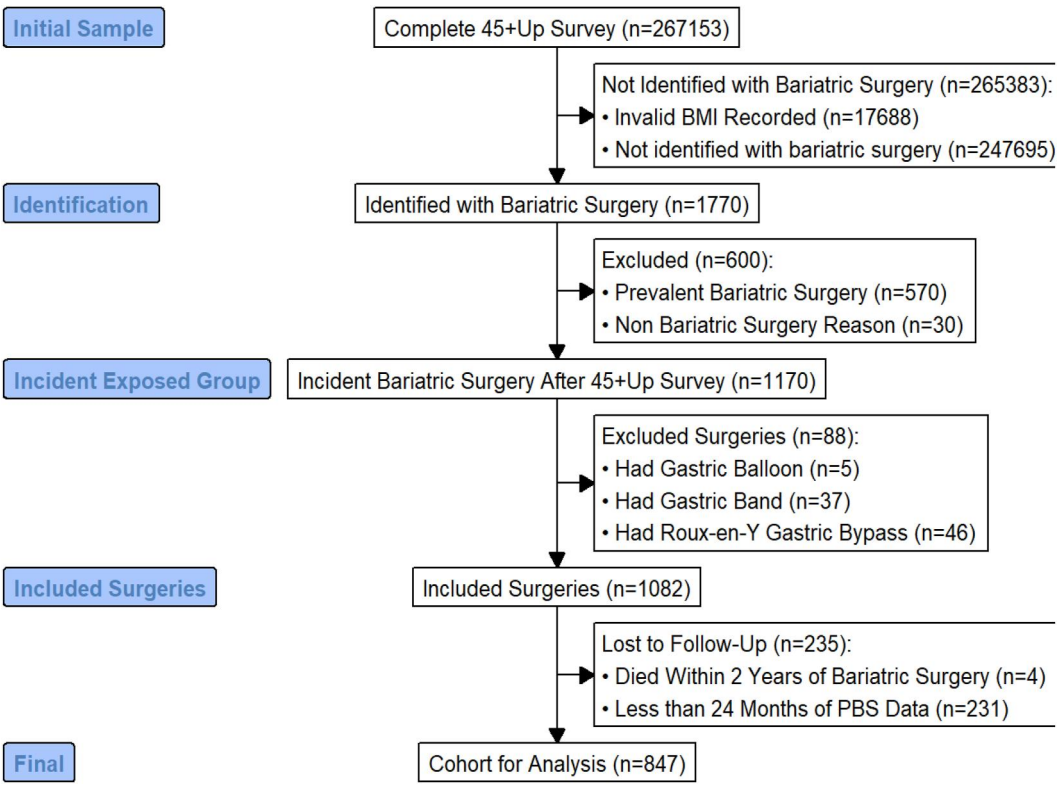

FIGURE 1 Flowchart illustrating the inclusion and exclusion criteria.

TABLE 1 Changes in gastrointestinal medications over time.

	12 Months before		12 Months after				13–24 Months after			
	People	Dispenses	People		Dispenses		People		Dispenses	
ATC group	*n*	*n*	*n*	% Change	*n*	% Change	*n*	% Change	*n*	% Change
A—Alimentary tract and metabolism										
A02B—Drugs for treatment of peptic ulcer	290	2145	218	−24.83	1629	−24.06	167	−42.41	1401	−34.69
A03F—Propulsives	28	67	13	−53.57	38	−43.28	9	−67.86	25	−62.69
A04—Antiemetics and antinauseants	31	47	10	−67.74	19	−59.57	8	−74.19	18	−61.70

with non-normal distributions are presented as medians and interquartile ranges.

The number of patients who had a dispensed prescription medicine and the number of dispenses were analyzed in each time a pre-post period for each specified ATC level of interest. The change in the number of people who had a dispensing and the number of dispenses were examined in the 12 months following surgery and 13–24 months following surgery, compared to the 12 months prior to surgery.

The total number of dispenses and the number of unique medications dispensed in each time period are presented as mean (SD), and medians with (1st and 3rd quartiles). Crude statistical comparisons were made using the dependent sample *t*-tests, comparing the 12 months prior to surgery and the 12 and 24 months post-surgery.

Interrupted time-series analysis was performed for the number of individuals with a dispensed medication in each specific ATC class per month, with the date of sleeve gastrectomy being the breakpoint. When the probability of dispensing medication in an ATC class was likely affected by the sleeve gastrectomy (i.e., use of analgesics for short-term post-surgical pain management) the month before and after surgery were excluded from the analysis.

Ethics approval for the 45 and Up Study was provided by the University of NSW Human Research Ethics Committee (HREC). This analysis was approved by the NSW Population and Health Services Ethics Committee (2019/ETH01569) and the University of Tasmania HREC (H0017293).

4 | RESULTS

4.1 | Participant characteristics

Characteristics of the 847 patients who were identified with sleeve gastrectomy, after completion of the 45 and Up Study survey, with a full 24-month follow-up in the PBS dataset, are shown in Table 4. The majority of patients were female (76.9%) and the mean age was 57.2 years (SD = 5.71 years). The average (SD) BMI was 37.5 (5.7) kg/m^2. Comorbidities of the participants were calculated based on the Treatment Risk comorbidity index, which means at least two prescriptions within a diagnosis group, within the 12 months prior to surgery.

The cohort was compared to individuals excluded from this analysis (data not shown), due to insufficient PBS follow-up, death within 2 years of surgery, or different surgery types (i.e., gastric balloon, gastric band, or Roux-en-Y gastric bypass). No significant differences were found in terms of age at surgery, gender, BMI, education, or income self-reported in the 45 and Up Study survey.

4.2 | Medication use

The total number of unique medications dispensed per patient (based on 7-digit ATC code), and the total number of dispensings per patient, in each time period examined are presented in Table 5.

When examining the difference in the average number of unique medications dispensed per patient, there was a slight increase from 12 months before surgery to 12 months after surgery. However, a statistically significant decrease was observed in the average number of unique medications dispensed per individual during the period of 13–24 months post-surgery in contrast to the year preceding the surgery, from 5.30 to 4.66 ($p = 0.004$) respectively, which corresponds to a 12.1% reduction.

The total number of dispenses per person significantly reduced from pre-surgery levels in the 12 months following surgery; from 26.4 to 22.3 dispenses, corresponding to a 15.9% reduction in dispenses of all prescription medications per person in the year post-surgery. Medication dispensing then remained steady in the 13–24 months following surgery ($p = 0.003$).

4.3 | Therapeutic categories

Compared with the year before sleeve gastrectomy, medication dispensing decreased significantly across the three therapeutic categories examined (gastrointestinal, metabolic and cardiorespiratory, and musculoskeletal and nervous systems) in the 24 months post sleeve gastrectomy, both in terms of the number of individuals who were dispensed these medications and the total number of dispenses, except for opioids (N02A—Opioids and N02AA—Natural Opium Alkaloids).

4.3.1 | Gastrointestinal medications

Changes in selected gastrointestinal medications post-operatively are shown in Table 1. The proportion of patients who were

TABLE 2 Changes in metabolic and cardiorespiratory medications over time.

	12 Months before		12 Months after				13–24 Months after			
	People	Dispenses	People		Dispenses		People		Dispenses	
ATC group	*n*	*n*	*n*	% Change	*n*	% Change	*n*	% Change	*n*	% Change
Medications for metabolic disorders										
A—Alimentary tract and metabolism										
A10—Drugs used in diabetes	184	1925	123	−33.15	998	−48.16	113	−38.59	1025	−46.75
A10A—Insulins and analogs	65	349	43	−33.85	130	−62.75	43	−33.85	123	−64.76
A10B—Blood glucose lowering drugs, excluding insulins	165	1576	104	−36.97	854	−45.81	91	−44.85	870	−44.80
H—Systemic hormonal preparations										
H03—Thyroid therapy	62	142	56	−9.68	132	−7.04	53	−14.52	118	−16.90
Medications for cardiovascular disease										
B—Blood and blood forming organs										
B01A—Antithrombotic agents	118	504	54	−54.24	376	−25.40	34	−71.19	306	−39.29
B01AA—Vitamin K antagonists	18	221	12	−33.33	150	−32.13	10	−44.44	121	−45.25
B01AA03—Warfarin	18	221	12	−33.33	150	−32.13	10	−44.44	121	−45.25
B01AB—Heparin group	87	121	22	−74.71	53	−56.20	6	−93.10	19	−84.30
B01AC—Platelet aggregation inhibitors excluding heparin	30	153	19	−36.67	104	−32.03	12	−60.00	86	−43.79
B03—Antianemic preparations	15	28	9	−40.00	22	−21.43	3	−80.00	9	−67.86
C—Cardiovascular system										
C01—Cardiac therapy	31	226	22	−29.03	162	−28.32	23	−25.81	171	−24.34
C02—Antihypertensives	32	244	20	−37.50	115	−52.87	9	−71.88	80	−67.21
C02A—Antiadrenergic agents, centrally acting	18	129	10	−44.44	66	−48.84	5	−72.22	41	−68.22
C02C—Antiadrenergic agents, peripherally acting	13	89	9	−30.77	26	−70.79	3	−76.92	17	−80.90
C03—Diuretics	102	331	48	−52.94	163	−50.76	34	−66.67	140	−57.70
C03B—Low-ceiling diuretics, excluding thiazides	25	65	11	−56.00	26	−60.00	7	−72.00	18	−72.31
C03C—High-ceiling diuretics	59	139	23	−61.02	58	−58.27	16	−72.88	52	−62.59
C03D—Potassium-sparing agents	19	104	15	−21.05	65	−37.50	12	−36.84	57	−45.19
C07—Beta blocking agents	91	521	75	−17.58	460	−11.71	60	−34.07	411	−21.11
C08—Calcium channel blockers	102	805	72	−29.41	527	−34.53	47	−53.92	413	−48.70
C09—Agents acting on the renin-angiotensin system	351	3225	274	−21.94	2192	−32.03	210	−40.17	2045	−36.59
C10—Lipid modifying agents	313	3073	271	−13.42	2278	−25.87	230	−26.52	2212	−28.02
Medications for respiratory disease										
R—Respiratory system										
R03—Drugs for obstructive airway diseases	169	880	88	−47.93	511	−41.93	79	−53.25	533	−39.43
R03A—Adrenergics, inhalants	153	663	77	−49.67	367	−44.65	69	−54.90	378	−42.99
R03B—Drugs for obstructive airway diseases, inhalants	48	209	25	−47.92	124	−40.67	22	−54.17	138	−33.97

dispensed a medication for the treatment of peptic ulcers (A02B) reduced from 34.2% to 19.7% ($p < 0.001$) in the two years following surgery. This resulted in a 42.4% relative reduction in patients who dispensed these medications from 12 months prior to surgery and a relative reduction of total dispenses of 34.7% across this time period.

TABLE 3 Changes in musculoskeletal and nervous system medications over time.

	12 Months before		12 Months after				13–24 Months after			
	People	Dispenses	People		Dispenses		People		Dispenses	
ATC group	*n*	*n*	*n*	% Change	*n*	% Change	*n*	% Change	*n*	% Change
H—Systemic hormonal preparations										
H02—Corticosteroids for systemic use	61	153	20	−67.21	80	−47.71	17	−72.13	75	−50.98
M—Musculoskeletal system										
M01—Anti-inflammatory and anti-rheumatic products	192	979	121	−36.98	591	−39.63	103	−46.35	542	−44.64
M01A—Anti-inflammatory and anti-rheumatic products	192	938	116	−39.58	564	−39.87	99	−48.44	519	−44.67
M01C—Specific anti-rheumatic agents	9	41	7	−22.22	27	−34.15	6	−33.33	23	−43.90
M04—Anti-gout preparations	21	77	17	−19.05	67	−12.99	15	−28.57	74	−3.90
M04A—Anti-gout preparations	21	77	17	−19.05	67	−12.99	15	−28.57	74	−3.90
M05—Drugs for treatment of bone diseases	16	123	12	−25.00	86	−30.08	10	−37.50	78	−36.59
N—Nervous system										
N02—Analgesics	218	1326	152	−30.28	1092	−17.65	129	−40.83	1311	−1.13
N02A—Opioids	153	770	91	−40.52	600	−22.08	78	−49.02	759	−1.43
N02AA—Natural opium alkaloids	106	372	57	−46.23	336	−9.68	47	−55.66	430	15.59
N02AB—Phenylpiperidine derivatives	6	20	1	−83.33	14	−30.00	1	−83.33	13	−35.00
N02AE—Oripavine derivatives	13	71	1	−92.31	26	−63.38	2	−84.62	48	−32.39
N02AJ—Opioids in combination with non-opioid analgesics	25	55	6	−76.00	19	−65.45	3	−88.00	4	−92.73
N02AX—Other opioids	44	218	22	−50.00	103	−52.75	12	−72.73	102	−53.21
N02B—Other analgesics and antipyretics	103	478	66	−35.92	364	−23.85	52	−49.51	324	−32.22
N02C—Antimigraine preparations	13	78	10	−23.08	63	−19.23	8	−38.46	64	−17.95
N03A—Antiepileptics	25	174	16	−36.00	132	−24.14	14	−44.00	132	−24.14
N03AX12—Gabapentin	3	16	2	−33.33	12	−25.00	1	−66.67	6	−62.50

Note: There were no recorded dispenses for Pregabalin (N03AX16) in the 12 months prior to sleeve gastrectomy.

Greater reductions from pre-surgery levels were seen in the dispensing of propulsives (A03F) and antiemetics and antinauseants (A04) in the first 12 months following surgery, with a 53.6% and 67.7% reduction in participants dispensed these medications, respectively. Such medications include proton pump inhibitors, H2 receptor antagonists, but also somewhat lesser-used agents such as sucralfate and prostaglandins.

4.3.2 | Diabetes medications

The proportion of patients who dispensed all metabolic and cardiorespiratory medications examined in the 2 years following sleeve gastrectomy reduced compared with the 12 months prior to surgery (Table 2). In the first and second year post-surgery, the proportion of patients receiving medication for diabetes (A10) significantly reduced from 21.7% to 13.3% ($p < 0.001$), respectively, compared with pre-surgery levels. This represented a 38.6% relative reduction in patients receiving these medications after 24 months post-surgery compared with the 12 months prior to surgery and included a relative reduction of 46.8% in dispenses.

4.3.3 | Cardiorespiratory medications

Compared to pre-surgery levels, the proportion of patients who received a lipid modifying agent (C10), significantly reduced from 37.0% to 27.1% ($p < 0.001$), in the 24 months post-surgery. This reduction represented a 26.5% relative reduction from the 12 months preceding surgery and was associated with a corresponding relative reduction of 28.0% in the total number of dispenses.

The proportion of patients receiving an anti-thrombotic agent (B01A) reduced from 13.9% to 4.0% ($p < 0.001$) in the 24 months post-surgery. This was a 71.1% relative reduction from the

TABLE 4 Participant characteristics.

	Overall (n = 847)
Age at surgery	
Mean (SD)	57.2 (5.71)
Age group at surgery	
45–49	86 (10.2%)
50–54	266 (31.4%)
55–59	229 (27.0%)
60–64	181 (21.4%)
65–69	71 (8.4%)
70+	14 (1.6%)
Gender	
Male	196 (23.1%)
Female	651 (76.9%)
BMI at 45 and up survey	
Mean (SD)	37.5 (5.66)
Median [Q1–Q3]	37.1 [33.7–41.6]
BMI category at 45 and up survey	
Overweight (<29.9)	85 (10.1%)
Obese I (30.0–34.9)	204 (24.1%)
Obese II (35.0–39.9)	274 (32.3%)
Obese III (>40.0)	284 (33.5%)
Education at 45 and up survey	
No school certificate	82 (9.7%)
School or intermediate certificate	169 (20.0%)
Higher school or leaving certificate	73 (8.6%)
Trade or apprenticeship	55 (6.5%)
Certificate or diploma	238 (28.1%)
University degree or higher	227 (26.8%)
Income at 45 and up survey	
<$5000	11 (1.3%)
$5000–$9999	12 (1.4%)
$10000–$19999	37 (4.4%)
$20000–$29999	53 (6.3%)
$30000–$39999	49 (5.8%)
$40000–$49999	70 (8.3%)
$50000–$69999	132 (15.6%)
>$70000	339 (40.0%)
Missing	144 (17.0%)
Comorbidities identified prior to index bariatric surgery	
GORD	319 (37.7%)
Hyperlipidemia	270 (31.9%)
Depression	242 (28.6%)
Hypertension	207 (24.4%)
Ischemic heart disease	133 (15.7%)
Diabetes	120 (14.2%)
Pain	99 (11.7%)
Chronic airways disease	74 (8.7%)

Abbreviation: GORD, gastro-oesophageal reflux disease.

12 months preceding surgery and was accompanied by a relative reduction of 39.3% in total dispenses.

The proportion of patients who were dispensed a medication for the agents acting on the renin-angiotensin system (RAS) reduced from 41.4% to 24.7% ($p < 0.001$) in the 2 years following surgery. This resulted in a 40.4% relative reduction in patients who dispensed these medications from 12 months prior to surgery and a relative reduction of total dispenses of 36.6% across this time period.

Figure 2 shows the temporal trends, from interrupted time-series analysis, pre- and post sleeve gastrectomy in the usage of medications for the treatment of diabetes (ATC class—A10), agents acting on the RAS (ATC class—C09), lipid modifying agents (ATC class—C10), medications for obstructive airway disease (ATC class—R03), anti-inflammatory products (ATC class—M01A) and opioids (N02A). The months pre- and post-surgery were not included in the model to avoid dispensing directly around, and likely related to, the time of surgery.

4.3.4 | Musculoskeletal and nervous system medications

From 12 months pre-surgery to 24 months post-surgery, there was a significant reduction in the proportion of patients receiving an anti-inflammatory and/or a disease-modifying anti-rheumatic drug (M01) from 22.6% to 12.1% ($p < 0.001$) (Figure 2). This represented a relative reduction of 46.3% in patients who dispensed M01 medications and corresponded to a relative reduction of 44.6% in total dispenses.

The reduction in opioid medication (N02A) dispensing varied post-operatively. The proportion of patients who were dispensed an opioid reduced from 18.1% pre-surgery to 9.2% ($p < 0.001$) in the 2 years post-surgery, resulting in a 49.0% relative reduction. However, the number of dispenses of these medicines per individual increased from 5.0 dispenses (770/153) pre-surgery to 9.7 (759/78) by 24 months post-surgery ($p < 0.001$).

4.4 | Nervous system

Figure 2 demonstrates the effect of sleeve gastrectomy on the usage of anti-inflammatory and anti-rheumatic products (ATC

TABLE 5 Summary of all medication dispenses.

	12 months before	12 months after	13–24 months after	*p*-value (comparison 12 months before to 13–24 months after)
Number of unique medications per participant				
Mean (SD)	5.30 (5.19)	5.34 (5.18)	4.66 (4.56)	0.004
Median [Q1–Q3]	4 [1.00–8.00]	4.00 [1.00–8.00]	3.00 [1.00–7.00]	
Total number of dispenses per participant				
Mean (SD)	26.4 (29.7)	22.3 (26.0)	22.2 (25.8)	0.003
Median [Q1–Q3]	15.0 [3.00–41.0]	12.0 [3.00–33.5]	13.0 [2.00–33.0]	

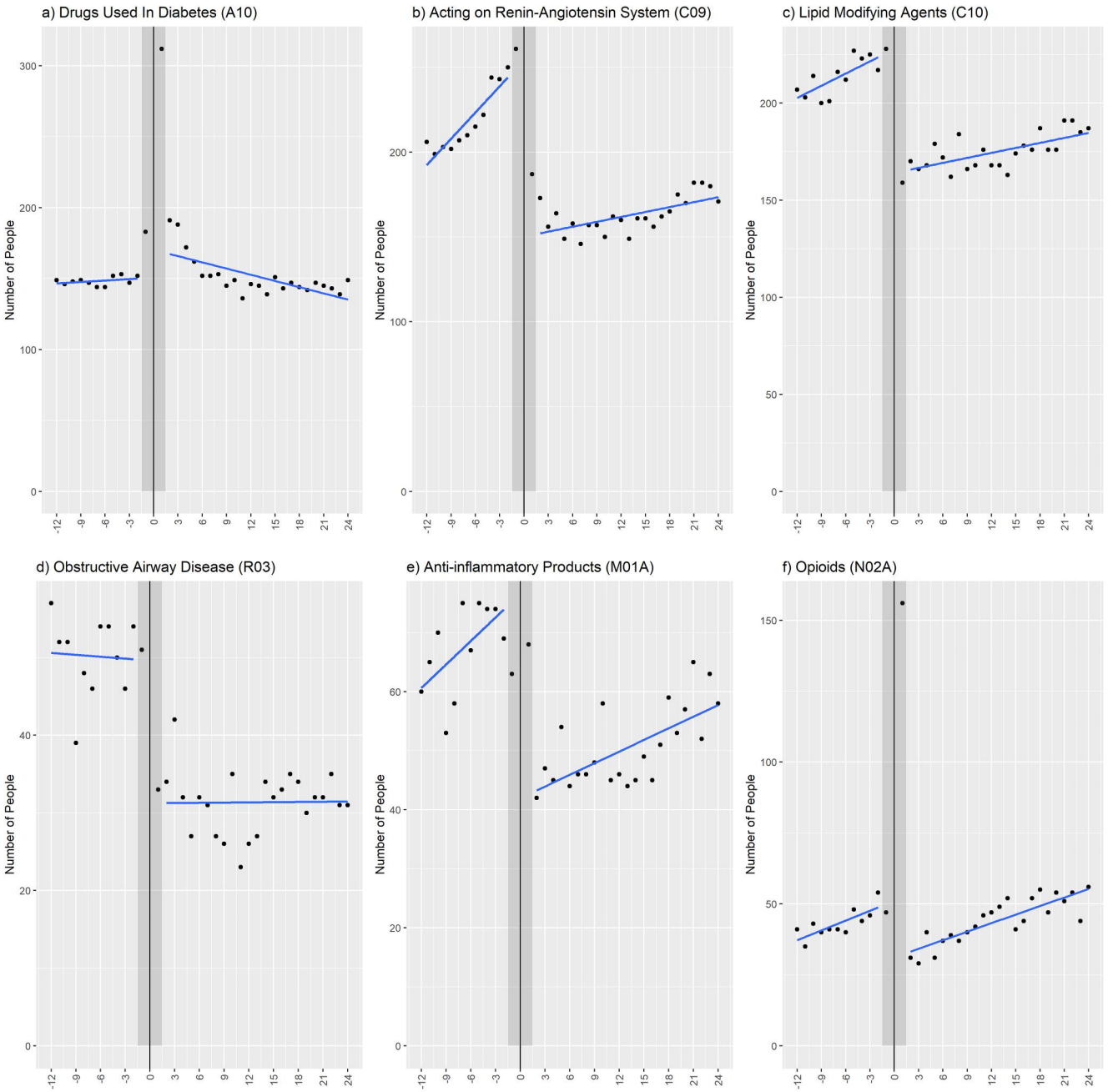

FIGURE 2 Dispenses of A10, C09, C10, R03, M01A, N02A.

class—M01A), and opioids (ATC class—N02). An initial reduction is seen in the monthly dispenses of M01A, after a significant increase pre-operatively. However, this reduction is not maintained, with monthly dispenses increasing steadily in the 24 months post-operatively.

There was an initial statistically significant reduction in opioid dispenses (N02A) in the 12 months the following surgery; however, this reduction was not continued and returned to pre-surgery levels by 24 months post-surgery. While the proportion of patients who were dispensed an opioid decreased significantly from 18.1% to 9.2% ($p < 0.001$) in the 2 years following surgery, resulting in a 49.0% relative reduction from the 12 months prior to surgery, the reduction in total dispenses did not occur. The number of dispenses per individual who had increased dispense, from 5.0 dispenses (770/153) prior to surgery to 9.7 (759/78) ($p < 0.001$) in the 2 years following surgery.

5 | DISCUSSION

In this study, there was a significant reduction in mean annual pharmaceutical dispensing in the 2 years following sleeve gastrectomy relative to the year of surgery. The most substantial reductions in the number of patients dispensed medicines and the total number of dispenses were observed in medications used to treat obesity-related diseases, specifically diabetes, cardiovascular disease, respiratory disease and musculoskeletal disorders. The reduction in medication use observed in this study is consistent with the known benefits of substantive weight loss, which has been shown to improve glycemic control, blood pressure, lipid levels, and joint pain, among other obesity-related comorbidities.[18,19] However, this is one of the first studies to quantify the level of change in pharmacotherapy required to manage such conditions following sleeve gastrectomy.

When examining the difference in the number of unique medications dispensed, there was a significant decrease between 12 months before surgery and 24 months after surgery. As the recovery from surgery progresses, the need for certain medications may diminish or cease altogether and resolve or improve the underlying health condition/s, leading to a decrease in the number of unique medications being prescribed and dispensed.[20]

Arguably, as patients living with obesity consider sleeve gastrectomy, a greater effort is invested in identifying and optimizing obesity-related complications prior to surgery. The reduction post-operatively does not appear to be due to reduced contact between the patient and general practitioner but could be due to the general practitioner becoming more confident to de-prescribe in the second year following surgery.

In addition to the changes observed in the number of unique medications dispensed, the impact of sleeve gastrectomy on obesity-related complications before and after surgery should be considered. Peptic ulcers, characterized by mucosal erosion in the gastric lining, can arise within the stomach and are usually caused by *Helicobacter pylori* (H.pylori) and nonsteroidal anti-inflammatory drugs (NSAIDs).[21] Patients who are morbidly obese have higher rates of H. pylori infections and NSAIDs.[22] Following sleeve gastrectomy, there may be a reduction in gastric acid secretion due to the anatomical modification. The decrease in acid production as a result of the surgery subsequently alleviates the irritative effects on the gastric mucosa, leading to a reduction in the occurrence of peptic ulceration. Post-operative patients often experience weight loss and improved overall health, which can alleviate symptoms, mitigate pain, and reduce the necessity for medications that might otherwise contribute to ulcerogenesis, leading to a decrease in peptic ulcer medication.

The RAS is a complex hormonal system that plays an important role in regulating blood pressure, fluid balance and electrolyte homeostasis.[23] Hyperactivity of the RAS is associated with obesity and many obese individuals have high blood pressure.[23,24] With the sleeve gastrectomy associated weight loss, patients may experience a reduction in blood pressure, which may require a reduction in or discontinuation of RAS medications. Ongoing medication management after weight loss will need to be maintained as blood pressure control is influenced by multiple factors.

With the weight loss associated with a sleeve gastrectomy, insulin sensitivity and glycemic control can be improved as the body becomes more efficient in utilizing insulin25 The surgery can also alter the production and release of various gut hormones involved in glucose regulation, such as glucagon-like peptide 1 and peptide YY.[26] These hormones play a role in appetite control, satiety and blood sugar regulation. The increased release of these hormones can contribute to improved glycemic control and reduced reliance on diabetes medication. Also, beta-cell function in the pancreas may improve with the associated weight loss and metabolic changes.[27] As a result of these metabolic improvements and weight loss associated with sleeve gastrectomy, the cardiovascular risk profile of individuals with obesity can be significantly reduced, leading to a decreased need for anti-thrombotic agents and improvements in lipid levels.[28]

The increase in opioid dispenses certainly bears some scrutiny. The use of opioids in chronic non-cancer pain is well-established and effective.[29] Prescribers tend to offer simple analgesics such as paracetamol and then add non-acetylsalicylate non-steroidal anti-inflammatory agents (NA-NSAIDs). However, the prescription of NA-NSAIDs is frequently resisted in patients following gastric surgery because of concerns as to their safety profile, particularly relating to the risk of inflammation and ulceration in the gastric remnant.[30] It is generally anticipated that weight loss surgery would result in reduced pain and reduced opioid use. However, studies have shown an increase in postsurgical chronic opioid use irrespective of pre-surgery chronic pain and/or depression diagnoses.[31] Additionally, increased pain sensitivity and lower pain detection thresholds in people living with obesity and chronic pain were identified. Recent research has also demonstrated an association between chronic use of opioids and lower socioeconomic status.[32]

This study has several strengths, including the comprehensive 45 and Up Study baseline survey, which was completed by participants and allowed for their follow-up across Australia due to the linked MBS and PBS data. A "wash-out" period was included prior to the 45

and Up Study survey completion to identify participants who had undergone previous sleeve gastrectomy, ensuring that analysis was conducted only on those with sleeve gastrectomy. The study also analyzed medication reduction based on more granular ATC classes than previous research.

There are several limitations to consider for this study. Participants with an "invalid" BMI, as recorded over 50 or deemed implausible (6.6% of total responses), were excluded from the analysis. The study only included participants who resided in NSW during 2006–2008 and those who moved to NSW after this time were not included in the analysis of sleeve gastrectomy outcomes. While the response rate of 17.9% in our study may introduce some potential bias, the strategic oversampling in rural areas, the cohort design emphasizing long-term follow up, and the impracticality of comparing to non-respondents due to unavailable medical histories collectively mitigate this concern, supporting the robustness and validity of our findings. The sample included only those aged 45+ years and therefore the generalizability to younger patients is uncertain. However, the majority of chronic health conditions investigated are more prevalent after reaching middle age. As well, the 24-month follow up is a limitation as Figure 2 shows a gradual rise in medication use post surgery, spanning various medications except those targeting diabetes and obstructive pulmonary disease. This study will provide significant insights for health practitioners with patients identified as high risk of developing these conditions, particularly those who may require pharmacotherapy as an integral component of their treatment.

6 | CONCLUSION

In summary, this study analyzed medication changes in the 2 years after sleeve gastrectomy in patients aged 45 years and over. Results indicated a significant reduction in overall medication usage, in terms of unique medications and total dispenses, in the 2 years following surgery compared to the year before the procedure. The greatest reductions were observed in medication categories targeting gastrointestinal issues, diabetes, cardiovascular disease, and respiratory disease, as well as anti-inflammatory and anti-rheumatic medications. In contrast, an increase in opioids requires further research to determine the causal factors. Further analysis is required to determine the predictors of medication reduction, including the identification of patients who cease medications altogether. Additionally, the extent to which reductions are maintained in the longer-term should be explored.

ACKNOWLEDGMENTS

We would like to thank the participants from the 45 and Up Study.

Open access publishing facilitated by The University of Western Australia, as part of the Wiley - The University of Western Australia agreement via the Council of Australian University Librarians.

CONFLICT OF INTEREST STATEMENT

We have no conflicts of interest to disclose.

ORCID

Gina Arena https://orcid.org/0000-0002-6956-3472
Michelle Kilpatrick https://orcid.org/0000-0001-6039-9154
Alison Venn https://orcid.org/0000-0001-7090-1398
David B. Preen https://orcid.org/0000-0002-2982-2169

REFERENCES

1. Adair T, Lopez AD. The role of overweight and obesity in adverse cardiovascular disease mortality trends: an analysis of multiple cause of death data from Australia and the USA. *BMC Med*. 2020;18(1):199. https://doi.org/10.1186/s12916-020-01666-y
2. Hruby A, Hu FB. The epidemiology of obesity: a big picture. *Pharmacoeconomics*. 2015;33(7):673-689. https://doi.org/10.1007/s40273-014-0243-x
3. Xia Q, Campbell JA, Ahmad H, Si L, de Graaff B, Palmer AJ. Bariatric surgery is a cost-saving treatment for obesity-A comprehensive meta-analysis and updated systematic review of health economic evaluations of bariatric surgery. *Obes Rev*. 2020;21(1):e12932. https://doi.org/10.1111/obr.12932
4. O'Brien PE, Hindle A, Brennan L, et al. Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. *Obes Surg*. 2019;29(1):3-14. https://doi.org/10.1007/s11695-018-3525-0
5. Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*. 2007;357(8):741-752. https://doi.org/10.1056/nejmoa066254
6. Peeters A, O'Brien PE, Laurie C, et al. Substantial intentional weight loss and mortality in the severely obese. *Ann Surg*. 2007;246(6):1028-1033. https://doi.org/10.1097/sla.0b013e31814a6929
7. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. *N Engl J Med*. 2017;376(7):641-651. https://doi.org/10.1056/nejmoa1600869
8. Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. *JAMA*. 2012;307(1):56-65. https://doi.org/10.1001/jama.2011.1914
9. Sjöström L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med*. 2004;351(26):2683-2693. https://doi.org/10.1056/nejmoa035622
10. Peterli R, Wölnerhanssen BK, Peters T, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial. *JAMA*. 2018;319(3):255-265. https://doi.org/10.1001/jama.2017.20897
11. Musella M, Berardi G, Velotti N, Schiavone V, Vitiello A. Ten-year results of laparoscopic sleeve gastrectomy: retrospective matched comparison with laparoscopic adjustable gastric banding-Is there a significant difference in long term? *Obes Surg*. 2021;31(12):5267-5274. https://doi.org/10.1007/s11695-021-05735-w
12. 45 Up Study Collaborators. Cohort profile: the 45 and up study. *Int J Epidemiol*. 2007;37(5):941-947. https://doi.org/10.1093/ije/dym184
13. World Health Organization. *The International Statisitcal Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM)*. National Centre for Classification in Health; 2006.

14. Australian Consortium for Classification Development. *Australian Classification of Health Interventions (ACHI)*. Indepent Hospital Pricing Authority; 2018.
15. Centre for Health Record Linkage. Enabling a Better Undersanding of Health and Wellbeing by Linking Multiple Sources of Data; 2023. Accessed May 11, 2023. https://www.cherel.org.au/
16. World Health Organization. Anatomical Therapeutic Chemical Classification System; 2023. Accessed June 1, 2023. https://www.who.int/tools/atc-ddd-toolkit/atc-classification
17. R Core Team. R: A Language and Environment for Statistical Computing; 2022. https://www.R-project.org/
18. Tan MMC, Jin X, Taylor C, et al. Long-term trajectories in weight and health outcomes following multidisciplinary publicly funded bariatric surgery in patients with clinically severe obesity (>3 associated comorbidities): a nine-year prospective cohort study in Australia. *J Clin Med*. 2022;11(15):4466. https://doi.org/10.3390/jcm11154466
19. Koliaki C, Liatis S, le Roux CW, Kokkinos A. The role of bariatric surgery to treat diabetes: current challenges and perspectives. *BMC Endocr Disord*. 2017;17(1):50. https://doi.org/10.1186/s12902-017-0202-6
20. Lorico S, Colton B. Medication management and pharmacokinetic changes after bariatric surgery. *Can Fam Physician*. 2020;66(6):409-416.
21. Makola D, Peura DA, Crowe SE. Helicobacter pylori infection and related gastrointestinal diseases. *J Clin Gastroenterol*. 2007;41(6):548-558. https://doi.org/10.1097/mcg.0b013e318030e3c3
22. Loke SS, Li WC. Peptic ulcer disease associated with central obesity. *J Personalized Med*. 2022;12(12):1968. https://doi.org/10.3390/jpm12121968
23. de Kloet AD, Krause EG, Woods SC. The renin angiotensin system and the metabolic syndrome. *Physiol & Behav*. 2010;100(5):525-534. https://doi.org/10.1016/j.physbeh.2010.03.018
24. Ramalingam L, Menikdiwela K, LeMieux M, et al. The renin angiotensin system, oxidative stress and mitochondrial function in obesity and insulin resistance. *Biochim Biophys Acta, Mol Basis Dis*. 2017;1863(5):1106-1114. https://doi.org/10.1016/j.bbadis.2016.07.019
25. Kashyap SR, Gatmaitan P, Brethauer S, Schauer P. Bariatric surgery for type 2 diabetes: weighing the impact for obese patients. *Cleve Clin J Med*. 2010;77(7):468-476. https://doi.org/10.3949/ccjm.77a.09135
26. Larraufie P, Roberts G, McGavigan A, et al. Importat role of the GLP-1 axis for glucose homeostasis after bariatric surgery. *Cell Rep*. 2019;26(6):1399-1408. https://doi.org/10.1016/j.celrep.2019.01.047
27. Liu T, Zou X, Ruze R, Xu Q. Bariatric Surgery: targeting pancreatic β cells to treat type II diabetes. *Front Endocrinol*. 2023;14:1031610. https://doi.org/10.3389/fendo.2023.1031610
28. Srinivasan M, Thangaraj SR, Arzoun H, Thomas SS, Mohammed L. The impact of bariatric surgery on cardiovascular risk factors and outcomes: a systematic review. *Cureus*. 2022;14(3):e23340. https://doi.org/10.7759/cureus.23340
29. Busse JW, Wang L, Kamaleldin M, et al. Opioids for chronic noncancer pain: a systematic review and meta-analysis. *JAMA*. 2018;320(23):2448-2460. https://doi.org/10.1001/jama.2018.18472
30. Abou Zeid H, Kallab R, Najm MA, et al. Safety and efficacy of non-steroidal anti-inflammatory drugs (NSAIDs) used for analgesia after bariatric surgery: a retrospective case-control study. *Obes Surg*. 2019;29(3):911-916. https://doi.org/10.1007/s11695-018-3608-y
31. Nagar VR, Birthi P. Implications of bariatric surgery on chronic pain and opioid use. *J Pain Palliat Care Pharmacother*. 2015;29(1):51-53. https://doi.org/10.3109/15360288.2014.997851
32. Wallén S, Szabo E, Palmetun-Ekbäck M, et al. Impact of socioeconomic status on new chronic opioid use after gastric bypass surgery. *Surg Obes Relat Dis*. 2023;19(12):1375-1381. https://doi.org/10.1016/j.soard.2023.06.005

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Arena G, Kitsos A, Hamdorf JM, et al. Evaluation of prescription medication changes following sleeve gastrectomy surgery. *Obes Sci Pract*. 2024;e742. https://doi.org/10.1002/osp4.742