Medication use before and after bariatric surgery: 5-year results from a randomised controlled trial of banded Roux-en-Y gastric bypass versus sleeve gastrectomy in patients with obesity and type 2 diabetes

James Tan, Talat Nur, Bronwen Jones, Rinki Murphy, David Kim, Richard Cutfield, Lindsay D Plank, Michael Booth

ABSTRACT

AIM: Bariatric surgery is an effective tool for weight loss and for improving weight related co-morbidities. Changes in medication usage after a silastic ring laparoscopic Roux-en-Y gastric bypass (SR-LRYGB) compared with laparoscopic sleeve gastrectomy (LSG) are unknown.

METHODS: This was a single-centre, double-blind, randomised controlled trial. Patients were randomised to either SR-LRYGB or LSG. A medication history was obtained at regular follow-up intervals, and mean numbers of prescribed medications were analysed over 5 years. Poisson regression and generalised estimating equations were used to test for statistically significant changes in usage.

RESULTS: After eight patients were lost to follow-up, data from 52 patients in each group were available for analysis. There was no difference between the SR-LRYGB or LSG groups in the number of medications prescribed, with the exception of oral glucose-lowering medications, where there was a greater decrease after SR-LRYGB compared to LSG (79% vs 55% respectively) from baseline to 5 years. At 5 years, total medication prescribed was down 10% from pre-operative levels. Prescribed insulin decreased by 72%, and cardiovascular medication decreased by 56% compared to baseline. Prescriptions for analgesia increased by 50%, psychiatric medications by 133% and proton-pump inhibitors by 81%.

CONCLUSION: Both SR-LRYGB and LSG reduced requirement for diabetic and cardiovascular medications, but increased requirement for nutritional supplementation, analgesia and psychiatric medications. There was a greater reduction in oral anti-diabetic medication prescriptions following SR-LRYGB compared to LSG, but no other difference in medication usage between surgical groups was found.

It is well established that bariatric surgery is a successful tool for weight loss, and results in improvements in weight-related comorbidities. The Roux-en-Y gastric bypass has been performed for over 50 years with good long-term results; however, the sleeve gastrectomy is now the most commonly performed bariatric operation in New Zealand,[1] partly due to good long-term results achieved following surgery but with relative simplicity of the operation compared to the gastric bypass, and partly due to a different side effect profile.

It has been shown that bariatric surgery results in significant changes in medication usage for some obesity-related comorbidities,[2–4] but these studies have been limited by their lack of blinding. It is also not known what effect different bariatric operations have on medication usage.

In addition to side effects, the cost of medications places a significant financial burden on healthcare systems, and thus any reduction in medication requirements is likely to be beneficial for both patients and healthcare systems.

The aim of the present study was to identify if patients with type 2 diabetes and obesity who underwent bariatric surgery had a reduction in medication usage following surgery, and if so, if there was a difference between those who underwent a silastic ring laparoscopic Roux-en-Y gastric bypass (SR-LRYGB) versus laparoscopic sleeve gastrectomy (LSG).

Methods

A prospective, double-blind, randomised controlled trial was undertaken at our institution between 2011 and 2015. The protocol[5] and results

of the primary outcome of this trial[6] have been published.

Participants were eligible for inclusion if they were aged between 20–55 years, had type 2 diabetes for at least 6 months' duration, a BMI of 35–65kg/m^2 for at least 5 years, were suitable for either of the two surgical procedures, able to provide written informed consent and committed to follow-up. Exclusion criteria included C-peptide <350pmol/L, type 1 diabetes or secondary diabetes, chronic pancreatitis, oral steroid therapy, current smokers and those not suitable for general anaesthesia.

After induction of anaesthesia, patients were randomised 1:1 to either SR-LRYGB or LSG using computer generated codes, with stratification according to age category (20–29, 30–39, 40–55), BMI category (35–44.9, 45–54.9, 55–65), ethnicity (Māori, Pacific peoples, NZ European/other), duration of diabetes diagnosis (<5, 5–10 and >10 years) and the presence of insulin therapy.

Both operations were performed using identical incisions with a four-port laparoscopic technique. For LSG, a sleeve was fashioned starting 2cm proximal to the pylorus using serial applications of an Echelon Flex 45 stapler (Ethicon) over a 36 Fr oro-gastric bougie. For SR-LRYGB, a lesser curve-based gastric pouch was fashioned over a 32 Fr oro-gastric tube, with a 50cm biliopancreatic limb, 100cm antecolic Roux limb with a hand-sewn single layer gastrojejunostomy over a 32 Fr oro-gastric tube. A 6.5cm silastic ring was then secured around the gastric pouch 2–3cm above the gastrojejunostomy anastomosis. Mesenteric defects were closed.

Immediately following surgery, all medications for diabetes, hypertension, lipid-lowering therapies and aspirin were ceased, except in those patients for whom aspirin or lipid-lowering agents were used for secondary prevention, and for patients with microalbuminuria, angiotensin converting enzyme-inhibitor/angiotensin receptor blockers were not stopped. All patients were commenced on a multivitamin (Centrum Plus, Pfizer New Zealand) twice daily, containing 200mg elemental calcium and 600IU vitamin D3, and proton-pump inhibitor (PPI) (pantoprazole, 20mg once daily).

Prior to discharge, patients were reviewed by an endocrinologist who was blinded to the surgical procedure. Anti-hypertensive treatment was restarted if the mean post-operative blood pressure was greater than 150/90mmHg. Anti-diabetic treatment was restarted if the mean post-operative capillary glucose was greater than 12mmol/L.

Patients were followed up at 3, 6, 9, 12, 18, 24, 36, 48 and 60 months post-operatively. During follow-up, patients were reviewed by an endocrinologist and were actively considered for adjustment (cessation, dose adjustment or initiation) of anti-diabetics, anti-hypertensive and other cardio-protective medications (statins and aspirin/anti-platelets) on the basis of clinical profile, including blood pressure measurements, HbA1c level, urinary microalbumin level and cardiovascular risk, as per a pre-defined protocol.[5]

A medication history was obtained at each follow-up appointment. In the event of a patient missing a follow-up appointment, electronic dispensing records were accessed where available to obtain the medication history for that time point. If data from more than two time points was unavailable, that patient was considered lost to follow-up and excluded from the study. Medications that were only taken on an as-required basis were excluded, as were short course prescriptions (e.g., antibiotics). Topical treatments such as ointments and eyedrops were excluded.

Statistical methods

Medication usage was analysed as the average number of medications prescribed per class, not dosage. For analysis, medication classes were grouped into categories. Categories are described in Appendix 1. For each medication class or category, analysis was performed using Poisson regression and generalised estimating equations. If there was no statistical difference between the time profiles for the two groups, the overall time effect was reported and changes in usage were provided for the pooled groups. Two-sided p values <0.05 were considered to indicate statistical significance. Analysis was performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Results

After excluding patients not meeting inclusion criteria (n=90) and those who refused to participate (n=17), there were 114 patients who were randomised to either LSG (n=58) or SR-LRYGB (n=56). At 5 years, one patient had died in each group, and after the removal of those who were lost to follow-up (LSG: n=5; SR-LRYGB: n=3) there were 52 participants in each group. Baseline characteristics for the two groups were similar (Table 1), as was prevalence of baseline medication usage by indication (Table 2).

For all classes and categories of medications,

there was no difference found in medication prescribed over time between the SR-LRYGB and LSG groups (p >0.05), with the exception of the oral anti-diabetic medication group, where there was a significant surgery group/time interaction (p=0.036).

A statistically significant reduction (38%) in total medication prescribed was seen over the first 3 post-operative months (mean number of regular medications per patient = 5.0 pre-operatively, versus 3.1 at 3 months), but by 5 years this increased to approach baseline levels (10% reduction, mean number of medications = 4.5) (Figure 1). There was no difference between the two surgical groups (p=0.66).

Prescriptions for oral anti-diabetic medications reduced by 93% on average at 3 months after surgery (mean number per patient = 1.2 pre-operatively, versus 0.1 at 3 months), and increased slowly thereafter over the 5-year follow-up period to reach a mean of 0.5 for the LSG group and 0.3 for the SR-LRYGB group (Figure 2).

There was an 84% reduction in insulin prescribed at 3 months post-operatively (mean number of insulin types per patient = 0.31 pre-operatively, versus 0.05 at 3 months), with rates rising slightly over the 5-year follow-up period to reach a 72% reduction at 5 years (Figure 3). Of the 25 patients on insulin pre-operatively, only five remained on

Table 1: Baseline characteristics of patients.

Characteristic	Laparoscopic silastic ring Roux-en-Y gastric bypass (n=52)	Laparoscopic sleeve gastrectomy (n=52)
Age—year	47.9±5.8	46.5±6.4
Female sex—no. (%)	31 (60)	25 (48)
Ethnicity—no. (%)		
NZ European	31 (60)	37 (71)
Māori	10 (19)	8 (15)
Pacific peoples	6 (12)	1 (2)
Other	5 (10)	6 (12)
Duration of diabetes—no. (%)		
<5 years	24 (46)	23 (44)
5–10 years	11 (21)	15 (29)
>10 years	17 (33)	14 (27)
Insulin usage—no. (%)	15 (29)	10 (19)
HbA1c—mmol/mol	63.8±18.3	60.7±11.4
Body weight—kg	123.2±21.9	125.4±24.4
BMI (kg/m^2) —no. (%)		
35–44.9	41 (79)	37 (71)
45–54.9	7 (13)	13 (25)
55–65	4 (8)	2 (4)

Plus-minus values are means ± SD.

Table 2: Proportion of patients on medication at baseline.

Medication class	Laparoscopic silastic ring Roux-en-Y gastric bypass (n=52) no. (%)	Laparoscopic sleeve gastrectomy (n=52) no. (%)
Oral anti-diabetic	47 (90)	43 (83)
Insulin	15 (29)	10 (19)
All cardiovascular	46 (88)	46 (88)
Anti-hypertensive	39 (75)	36 (69)
Anti-platelet	19 (37)	19 (37)
Lipid-lowering	37 (71)	31 (60)
All psychiatric	10 (19)	8 (15)
Anti-depressant	10 (19)	8 (15)
Proton-pump inhibitors	10 (19)	12 (23)
Analgesics	5 (10)	3 (6)
Gout	6 (12)	5 (10)
Nutritional supplementation	13 (25)	16 (21)

insulin after 3 months, increasing to eight patients at 5 years.

Cardiovascular medication prescriptions, including anti-hypertensives (Figure 4), anti-platelets (Figure 5) and lipid-lowering agents (Figure 6), decreased by 72% after 3 months (mean number of cardiovascular medications per patient = 2.2 pre-operatively, versus 0.6 at 3 months). Over the 5-year follow-up period, there was a gradual increase in cardiovascular medication prescriptions (mean number per patient = 1.0 at 5 years), but this was still a 56% reduction compared to baseline (Figure 7).

PPI prescriptions more than doubled post-operatively (mean number of PPIs per patient = 0.21 pre-operatively, versus 0.50 at 3 months), with rates dropping back to baseline levels by 6 months (mean number = 0.21 at 6 months), then rising gradually to reach an 81% increase from baseline at 5 years (mean number = 0.39 at 5 years). PPI prescriptions at 5 years were slightly higher in the sleeve group, but this was not statistically significant (Figure 8).

From 1-year post-operative, there was a trend for increased psychiatric medication prescriptions continuing until 5 years after surgery, at which time there was a 133% increase in the prescription of psychiatric medications (including anti-depressants [Figure 9], anti-psychotics, hypnotics and sedatives) compared to pre-operative levels (mean number per patient = 0.23 pre-operatively versus 0.54 at 5 years) (Figure 10).

Prescriptions for analgesics trended upwards from 3 years post-operatively, increasing by 50% compared to pre-operatively after 5 years (mean number per patient = 0.10 pre-operatively and 0.15 at 5 years) (Figure 11).

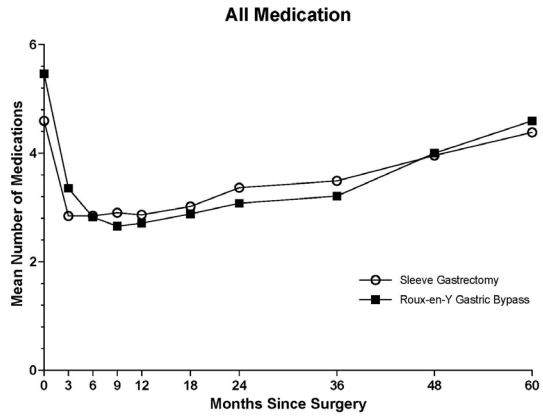
Nutritional supplementation prescriptions increased post-operatively (mean number of nutritional supplements per patient = 0.36 pre-operatively versus 1.24 at 3 months) but stabilised out to 5 years (mean number = 1.33 at 5 years), an increase of 273% on pre-operative levels (Figure 12).

There was no change in gout (Figure 13) or respiratory medication (Figure 14) prescriptions before and after surgery.

Discussion

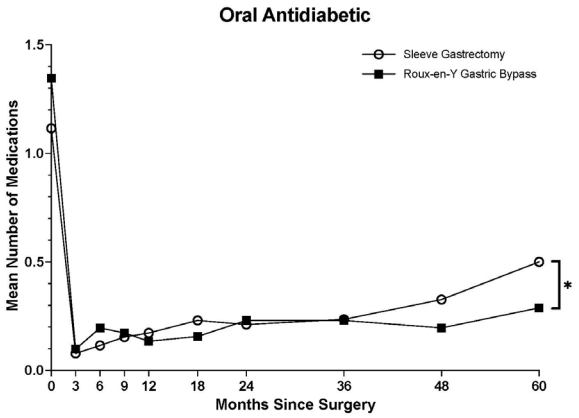
Medication usage among people with obesity

Figure 1: All medication prescriptions following surgery.



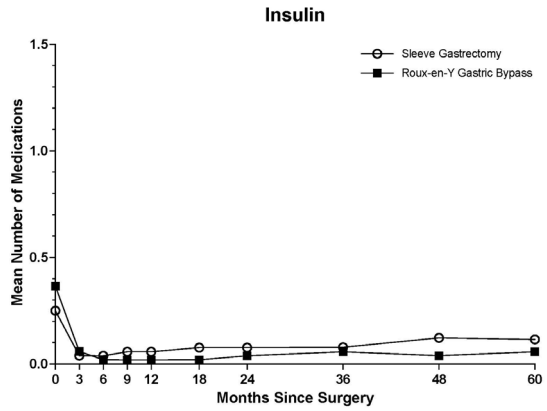
Overall time effect p <0.0001.

Figure 2: Oral anti-diabetic medication prescriptions following surgery.



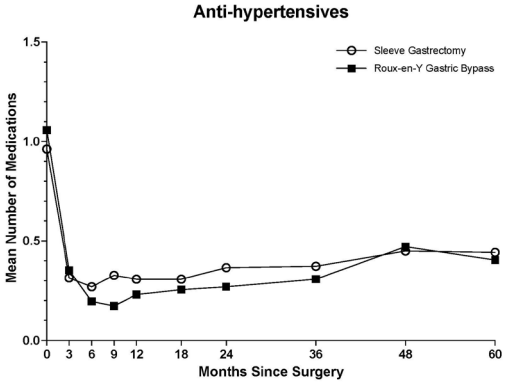
*Surgery group/time interaction p=0.036. Time effects: sleeve gastrectomy, p=0.008; gastric bypass, p=0.0002.

Figure 3: Insulin prescriptions following surgery.



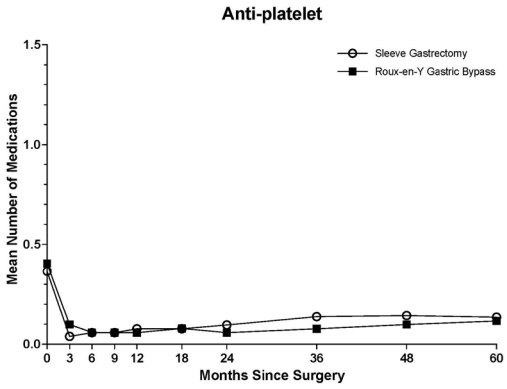
Overall time effect p=0.009.

Figure 4: Anti-hypertensive prescriptions following surgery.



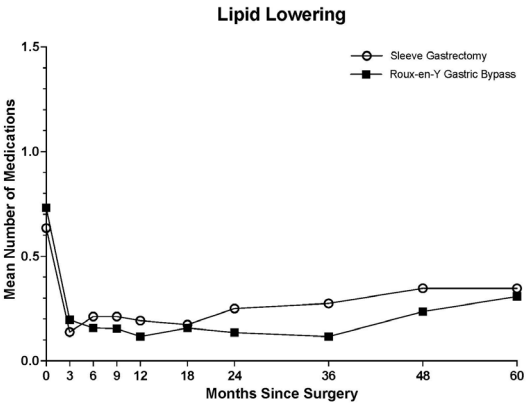
Overall time effect p <0.0001.

Figure 5: Anti-platelet prescriptions following surgery.



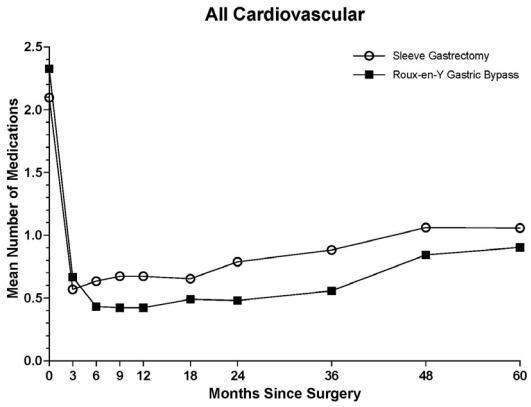
Overall time effect p=0.001.

Figure 6: Lipid-lowering prescriptions following surgery.



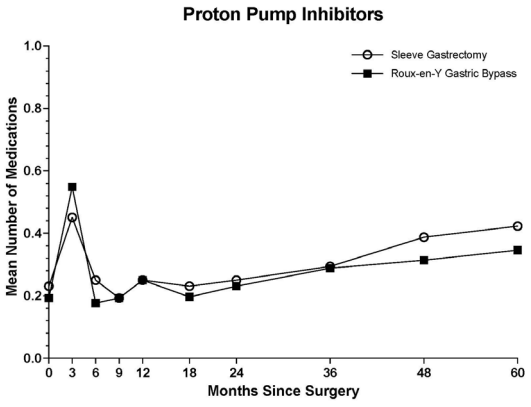
Overall time effect p <0.0001.

Figure 7: All cardiovascular medication prescriptions following surgery.



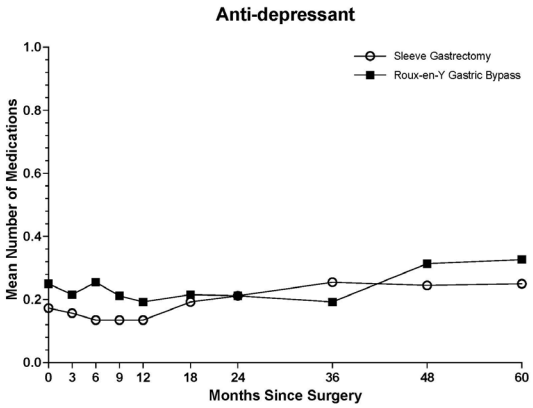
Overall time effect p <0.0001.

Figure 8: Proton-pump inhibitor prescriptions following surgery.



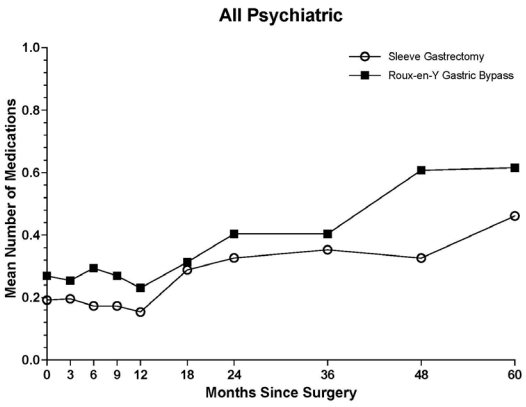
Overall time effect p <0.0001.

Figure 9: Anti-depressant prescriptions following surgery.



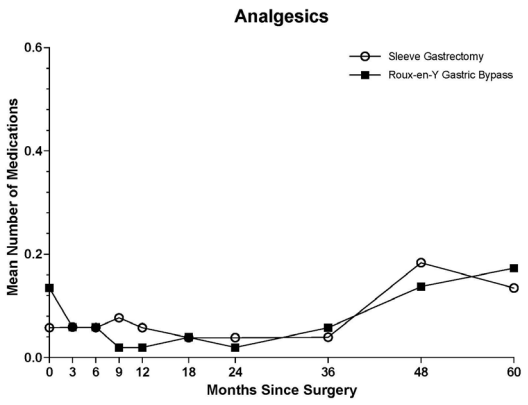
Overall time effect p=0.008.

Figure 10: All psychiatric medication prescriptions following surgery.



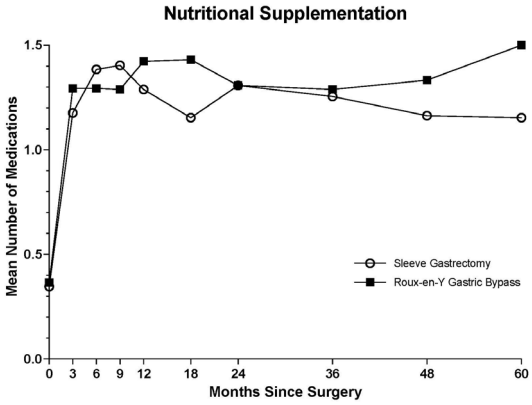
Overall time effect p <0.0001.

Figure 11: Analgesic medication prescriptions following surgery.



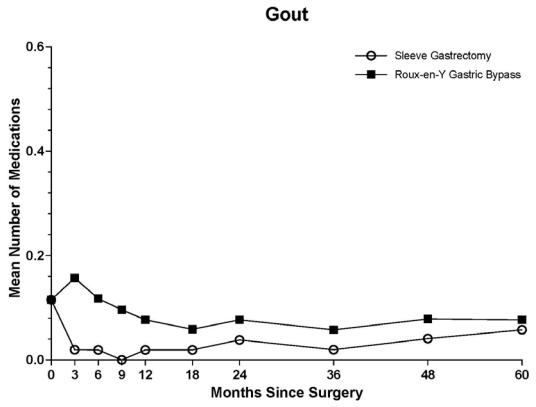
Overall time effect p=0.028.

Figure 12: Nutritional supplementation prescriptions following surgery.



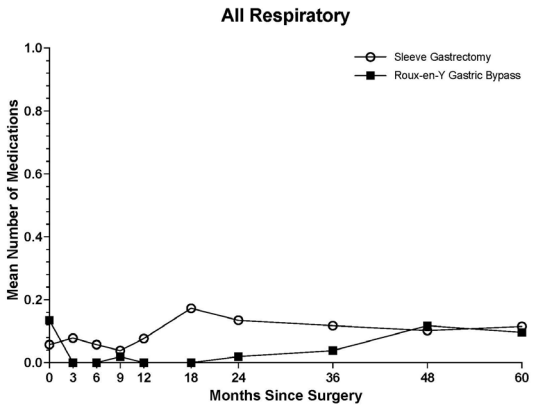
Overall time effect p <0.0001.

Figure 13: Gout medication prescriptions following surgery.



Overall time effect p=0.381.

Figure 14: All respiratory medication prescriptions following surgery.



Overall time effect p=0.081.

and type 2 diabetes changes significantly after both SR-LRYGB and LSG. Immediately post-operatively, total medication prescriptions decreased by 39%. This is largely due to a reduction in anti-diabetic medication (both oral and insulin) and cardiovascular risk-reducing medication (including anti-hypertensives, anti-platelets and lipid-lowering medication) requirements. The reduction in diabetic medication is not surprising given the improvements in glycaemic control that were seen at 1 year[7] and 5 years post-operatively among the same cohort of patients,[6] and the diabetes remission following bariatric surgery that has been shown in meta-analyses.[8] Oral anti-diabetic medication was the only class of medications for which there was a difference between the SR-LRYGB and LSG groups, where there was a higher requirement for oral anti-diabetic medication in those who had LSG compared to SR-LRYGB. However, the trial was powered to detect a difference in diabetes remission, not overall medication differences, and therefore the lack of statistical significance between the two trial groups with regards to medication usage could be related to being underpowered for this purpose.

The reduced requirement for oral anti-diabetic medication at 5 years in the SR-LRYGB compared to LSG suggests a benefit in the SR-LRYGB in terms of diabetic control in accordance with the results from the 5-year analysis of this cohort.[6] The mechanism of action of bariatric surgery on weight and diabetes is complex and multifactorial, and involves changes in gut hormones, bile acids and altered gut microbiota. These changes are possibly more beneficial following the SR-LRYGB compared to the LSG, which could account for the greater reduction in oral anti-diabetic medication usage in the SR-LRYGB group compared to the LSG group.[9] A recent systematic review and meta-analysis comparing LSG with laparoscopic Roux-en-Y gastric bypass revealed a paucity of data from randomised controlled trials to draw long term conclusions,[10] further highlighting the need for more studies in this area.

Cardiovascular medication prescriptions dropped significantly following bariatric surgery and, while rates slowly increased over time, usage rates were approximately half that of pre-operative levels. Overall, there are limited studies on cardiovascular events following bariatric surgery. However, a prospective, non-randomised controlled intervention trial comparing outcomes in obese type 2 diabetics who had bariatric surgery versus a control group who did not have surgery demonstrated a significant reduction in myocardial infarction incidence among the group who had bariatric surgery.[11] Cardiovascular risk after bariatric surgery is likely lower than pre-operatively, although validated risk prediction equations have not been developed for this population on which to base decisions on cardiovascular medication prescribing. It appears that cardiovascular medication usage is reduced on the basis of targeted risk factors (blood pressure, lipids, diabetes) improving.

The dramatic spike in PPI prescriptions immediately post-operatively is attributable to the fact that patients were discharged on a PPI after surgery for protection against ulceration. The reasons for the long-term trend towards increasing PPI prescriptions in both surgical groups are less clear.

Other studies have shown that gastro-oesophageal reflux disease symptoms can be worsened following a sleeve gastrectomy,[12] possibly due to anatomical changes which result in increased pressure within the sleeve. This could explain the increased requirement in the LSG group. For patients in the SR-LRYGB group, potential reasons for increasing PPI requirements include the development of anastomotic ulceration or reflux symptoms that may be attributable to the silastic ring.

Psychiatric medication prescriptions, including anti-depressants, anti-psychotics, sedatives and hypnotics, changed significantly throughout the 5-year follow-up period, with patients taking more than double the number of medications from these classes at 5 years. This was an unexpected finding, as bariatric surgery often results in an improvement in psychological health; a recent review of the long-term effects of bariatric surgery on depression and anxiety suggests that bariatric surgery is associated with long-term reductions in anxiety and depressive symptoms.[13] We would have therefore expected a reduction in the need for psychiatric medications. It is possible that patients may have improved psychiatric symptoms despite an increased requirement for medication, and further studies in this field are needed.

While the absolute number was small, there was an increase in analgesia prescriptions over the 5-year follow-up period following bariatric surgery. This is despite bariatric surgery and subsequent weight loss usually resulting in improvements in pain and physical functioning.[14] While our sample size precluded analysis of analgesic medication use by individual class, other studies have evaluated opioid use before and after bariatric surgery and have found opioid requirements increase after bariatric surgery.[15,16] The authors of those studies suggested that possible reasons for persistent opioid requirement despite weight loss included tolerance to opioids and more pain sensitivity in obese patients, which persists after bariatric surgery.[15]

The dramatic increase in nutritional supplementation after surgery was expected, as all patients were discharged on lifelong multivitamin supplementation to prevent nutritional deficiencies.

Overall, our study has provided an interesting insight into medication changes following SR-LRYGB and LSG, but we do appreciate there are some limitations. First, medication usage is only a surrogate marker for medical comorbidities, and further studies evaluating long-term outcomes following bariatric surgery, especially in the areas of cardiovascular events, psychiatric health and chronic pain would be useful. A further limitation is that of medication compliance, although this issue is not unique to our study. Our analysis was based on prescribed medication, but it is known that patient adherence with prescribed medication is often poor. A large review of medication compliance for the treatment of diabetes, hypertension and dyslipidaemia revealed that only 63% of patients continue with medication beyond 1 year, and patients only take their medication 72% of the time.[17] Finally, our study is further limited by the lack of non-operated controls. Future research would benefit from including such a group for drawing comparisons.

In summary, bariatric surgery is an effective tool for reducing the requirements for diabetic and cardiovascular medication in type 2 diabetic patients with obesity, but results in increased requirements for nutritional supplementation, PPIs, analgesia and psychiatric medication. Respiratory and gout medication usage is unchanged following surgery. The type of operation performed did not affect medication usage except for oral anti-diabetic medication, which had a greater reduction following SR-LRYGB compared to LSG.

COMPETING INTERESTS
This study was funded primarily through the Waitematā District Health Board. Additional funding for blood sample storage and a research nurse salary was provided by Johnson & Johnson (New Zealand), Covidien (New Zealand), Auckland Medical Research Foundation and Obex (New Zealand).

AUTHOR INFORMATION
Dr James Tan: Department of Surgery, North Shore Hospital, Te Whatu Ora – Waitematā, Shakespeare Road, Takapuna, Auckland 0622, New Zealand.
Dr Talat Nur: Department of Surgery, North Shore Hospital, Te Whatu Ora – Waitematā, Shakespeare Road, Takapuna, Auckland 0622, New Zealand.
Ms Bronwen Jones: Department of Surgery, North Shore Hospital, Te Whatu Ora – Waitematā, Shakespeare Road, Takapuna, Auckland 0622, New Zealand.
Prof Rinki Murphy: Department of Medicine, Faculty of Medical and Health Sciences, The University of Auckland, M&HS Building 507, 28 Park Ave, Grafton, Auckland 1023, New Zealand.
Dr David Kim: Department of Endocrinology, North Shore Hospital, Te Whatu Ora – Waitematā, Shakespeare Road, Takapuna, Auckland 0622, New Zealand.
Dr Richard Cutfield: Department of Endocrinology, North Shore Hospital, Te Whatu Ora – Waitematā, Shakespeare Road, Takapuna, Auckland 0622, New Zealand.
Assoc Prof Lindsay D Plank: Department of Surgery, Faculty of Medical and Health Sciences, The University of Auckland, M&HS Building 507, 28 Park Ave, Grafton, Auckland 1023, New Zealand.
Mr Michael Booth: Department of Surgery, North Shore Hospital, Te Whatu Ora – Waitematā, Shakespeare Road, Takapuna, Auckland 0622, New Zealand.

CORRESPONDING AUTHOR
Dr James Tan: Bariatric Surgeon, Department of Surgery, Hastings Hospital, Te Whatu Ora – Te Matu a Māui Hawke's Bay, 210 Omahu Road, Camberley, Hastings 4120, New Zealand. Ph: +64 6 878 8109.
E: James.Tan@hbdhb.govt.nz

URL
https://nzmj.org.nz/journal/vol-137-no-1594/medication-use-before-and-after-bariatric-surgery-5-year-results-from-a-randomised-controlled-trial-of-banded-roux-en-y-gastric-

REFERENCES
1. Australia and Aotearoa New Zealand Bariatric Surgery Registry. Bariatric Surgery Registry 2022 Annual Report [Internet]. Melbourne VIC (AU): Central Clinical School, Monash University; 2023 [cited 2024 Jan 1]. Available from: https://www.monash.edu/__data/assets/pdf_file/0018/3351042/Bariatric-Surgery-Registry-Annual-Report-2022_web.pdf
2. 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):1646-56. doi: 10.1007/s11695-009-9960-1.
3. Kennedy AL, Nelson T, Pettine S, et al. Medication use following bariatric surgery: factors associated with early discontinuation. Obes Surg. 2014;24(5):696-704. doi: 10.1007/s11695-013-1131-8.
4. Gesquiere I, Aron-Wisnewsky J, Foulon V, et al. Medication cost is significantly reduced after Roux-en-Y gastric bypass in obese patients. Obes Surg. 2014;24(11):1896-903. doi: 10.1007/s11695-014-1325-8.
5. Murphy R, Evennett NJ, Clarke MG, et al. Sleeve gastrectomy versus Roux-en-Y gastric bypass for type 2 diabetes and morbid obesity: double-blind randomised clinical trial protocol. BMJ Open. 2016;6(7):e011416. doi: 10.1136/bmjopen-2016-011416.
6. Murphy R, Plank LD, Clarke MG, et al. Effect of Banded Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy on Diabetes Remission at 5 Years Among Patients With Obesity and Type 2 Diabetes: A Blinded Randomized Clinical Trial. Diabetes Care. 2022;45(7):1503-1511. doi: 10.2337/dc21-2498.
7. Murphy R, Clarke MG, Evennett NJ, et al. Laparoscopic Sleeve Gastrectomy Versus Banded Roux-en-Y Gastric Bypass for Diabetes and Obesity: a Prospective Randomised Double-Blind Trial. Obes Surg. 2018;28(2):293-302. doi: 10.1007/s11695-017-2872-6.
8. 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. doi: 10.1016/j.amjmed.2008.09.041.
9. Pucci A, Batterham RL. Mechanisms underlying the weight loss effects of RYGB and SG: similar, yet different. J Endocrinol Invest. 2019;42(2):117-128. doi: 10.1007/s40618-018-0892-2.
10. Lee Y, Doumouras AG, Yu J, et al. Laparoscopic Sleeve Gastrectomy Versus Laparoscopic Roux-en-Y Gastric Bypass: A Systematic Review and Meta-analysis of Weight Loss, Comorbidities, and Biochemical Outcomes From Randomized Controlled Trials. Ann Surg. 2021;273(1):66-74. doi:

10.1097/SLA.0000000000003671.
11. Romeo S, Maglio C, Burza MA, et al. Cardiovascular events after bariatric surgery in obese subjects with type 2 diabetes. Diabetes Care. 2012;35(12):2613-7. doi: 10.2337/dc12-0193.
12. DuPree CE, Blair K, Steele SR, Martin MJ. Laparoscopic sleeve gastrectomy in patients with preexisting gastroesophageal reflux disease : a national analysis. JAMA Surg. 2014;149(4):328-34. doi: 10.1001/jamasurg.2013.4323.
13. Gill H, Kang S, Lee Y, et al. The long-term effect of bariatric surgery on depression and anxiety. J Affect Disord. 2019;246:886-894. doi: 10.1016/j.jad.2018.12.113.
14. King WC, Chen JY, Belle SH, et al. Change in Pain and Physical Function Following Bariatric Surgery for Severe Obesity. JAMA. 2016;315(13):1362-71. doi: 10.1001/jama.2016.3010.
15. Raebel MA, Newcomer SR, Reifler LM, et al. Chronic use of opioid medications before and after bariatric surgery. JAMA. 2013;310(13):1369-76. doi: 10.1001/jama.2013.278344.
16. King WC, Chen JY, Belle SH, et al. Use of prescribed opioids before and after bariatric surgery: prospective evidence from a U.S. multicenter cohort study. Surg Obes Relat Dis. 2017;13(8):1337-1346. doi: 10.1016/j.soard.2017.04.003.
17. Cramer JA, Benedict A, Muszbek N, et al. The significance of compliance and persistence in the treatment of diabetes, hypertension and dyslipidaemia: a review. Int J Clin Pract. 2008;62(1):76-87. doi: 10.1111/j.1742-1241.2007.01630.x.

Appendix

Appendix 1: Medication categories.

Category	Examples
Oral anti-diabetic	Alpha-glucosidase inhibitors Biguanide Dipeptidyl peptidase-4 (DPP-4) inhibitors Glucagon-like peptide-1 (GLP-1) receptor agonists Sodium-glucose co-transporter 2 (SGLT-2) inhibitors Sulfonylurea Thiazolidinediones
Psychiatric	Anti-depressants Anti-psychotics Hypnotics Sedatives Stimulants
Analgesics	Anti-convulsant (e.g., gabapentin) Anti-migraine Non-steroidal anti-inflammatory drugs Opiates Paracetamol
Cardiovascular	Anti-anginal Anti-arrhythmic Anti-coagulation Anti-hypertensives Anti-platelets Diuretics Lipid-lowering
Nutritional supplementation	Iron supplementation Multivitamins Vitamin B12 Vitamin D
Gout	Allopurinol Colchicine
Respiratory	Inhalers