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Long-term impact of weight loss for people with overweight but not obesity, and with type 2 diabetes: 10-year outcomes of a randomized trial of gastric band surgery

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Abstract

Aim: Randomized trials reporting 5-year outcomes have shown bariatric surgery to induce diabetes remission and improve cardiovascular risk. However, the longer-term effects of surgery are uncertain, with only one randomized trial reporting 10-year diabetes outcomes in people with obesity. We aimed to compare 10-year diabetes outcomes of people who are overweight but not obese, randomly assigned to receive either multidisciplinary diabetes care, or multidisciplinary diabetes care combined with gastric band (GB) surgery.

Methods: Between 2009 and 2011, 51 adults were randomized. After 5 years, they were discharged to receive community care and reassessed after 10 years. The primary outcome was diabetes remission, defined as glycated haemoglobin (HbA1c) <6.5% (48 mmol/mol) without glucose-lowering medication.

Results: Forty-one participants (20 medical and 21 GB) completed the 10-year assessment. The median (Q1, Q3) weight loss in the GB group was 9.8 (6.7, 16.3)% at 10 years compared with 5.6 (3.4, 7.6)% in the medical group (median difference 4.2%; $p = .008$). Diabetes remission occurred in five GB participants and no medical participants (relative risk 0.76, 95% CI: 0.55-0.93, $p = .048$). GB participants used fewer glucose-lowering medications at 10 years but HbA1c, fasting glucose, calculated cardiovascular risk, quality-of-life and incident diabetes complications did not differ significantly between the groups.

Conclusion: When compared with medical care, GB surgery achieved greater weight loss and modestly increased the likelihood of diabetes remission. However, it did not improve HbA1c, cardiovascular risk or quality of life.

KEYWORDS
adjustable gastric band, bariatric surgery, diabetes remission, overweight, type 2 diabetes, weight loss

Abbreviations: BMI, body mass index; BPD, biliopancreatic diversion; GB, gastric band; GLP, glucagon-like peptide; GP, general practitioner; HbA1c, glycated haemoglobin; MDC, multidisciplinary medical care; QoL, quality of life; SGLT, sodium-glucose cotransport.

Registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12609000286246.

1 | INTRODUCTION

Randomized trials involving people with type 2 diabetes have shown that weight loss through lifestyle modification,[1,2] pharmacotherapy[3] or bariatric surgery[4] improves glucose control, incidence of diabetes remission, cardiovascular risk and quality of life over a 1-5-year time frame. Whether the weight loss described in these studies can endure over longer time frames to ultimately protect against serious diabetes complications and premature death is uncertain. Observational studies of individuals with obesity followed for up to 24 years have reported substantial, sustained weight loss following bariatric surgery to be associated with a lower risk of diabetes vascular complications[5] and death.[6-8] However, unmeasured differences between surgery and control groups in these studies may have confounded their findings, highlighting a need for higher-quality evidence to confirm or refute them.

Two randomized trials comparing the effects of medical care and sleeve gastrectomy, Roux-en-Y gastric bypass (RYGB) or biliopancreatic diversion (BPD) on diabetes outcomes have reported 5-year outcomes.[9,10] In these trials, the mean diabetes duration was over 5 years and mean body mass index (BMI) exceeded 35 kg/m^2. When compared with medical care, bariatric surgery induced over 19% weight loss after 5 years. This was associated with higher rates of diabetes remission, decreased use of glucose-lowering medication and

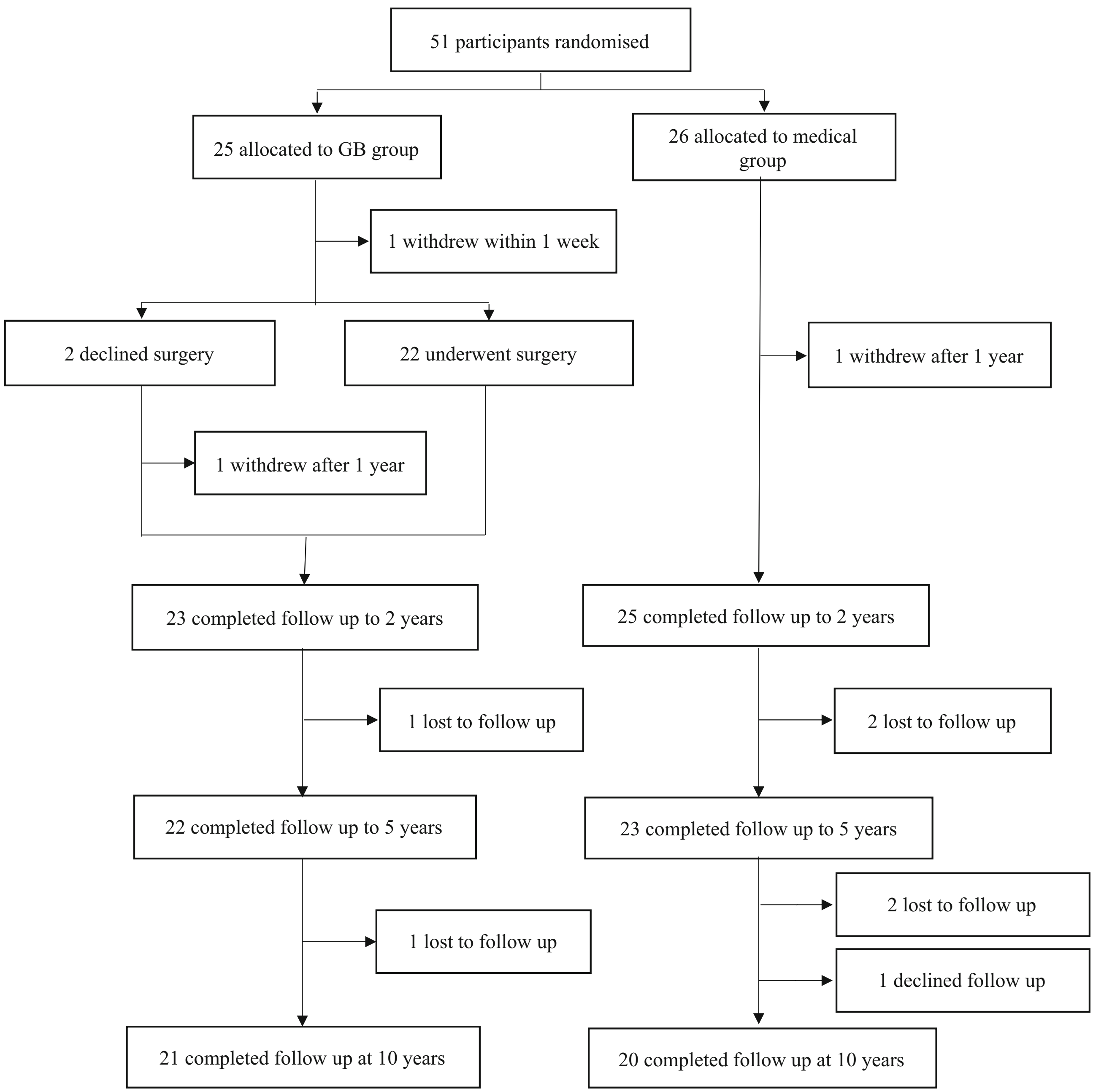

FIGURE 1 Consort diagram. GB, gastric band

improved glycated haemoglobin (HbA1c) and quality of life. Longer-term outcomes are less certain, with only one of these trials reporting 10-year data for RYGB or BPD in 55 adults with obesity. It showed bariatric surgery induced 25% weight loss at 10 years associated with increased incidence of diabetes remission, lower use of glucose-lowering medication, a decrease in HbA1c of 1% (10 mmol/mol), improved quality of life and a lower incidence of diabetes vascular complications.[11] The only other randomized trial of weight loss reporting 10-year outcomes is the Look AHEAD study of intensive lifestyle intervention compared with usual care. It involved 5145 participants whose mean age, diabetes duration and BMI were 59 years, 5 years and 36 kg/m^2, respectively. It showed that lifestyle intervention achieved 2.5% body weight loss relative to a control group at 10 years, which was associated with modest improvements in HbA1c and cardiac risk factors but no difference in the incidence of cardiovascular events.[2]

Gastric band (GB) surgery has a favourable safety profile and induces significant, sustained weight loss in people who are overweight and obese without altering incretin hormones that influence glucose metabolism.[12,13] These characteristics make GB surgery the ideal tool for determining the effect of long-term weight loss through decreased calorie intake in combination with medical care for glucose control and other diabetes outcomes, particularly in people who are overweight but not obese who may not wish to consider more hazardous RYGB or BPD surgery. In 2009, we commenced a randomized trial of GB surgery in this population and showed that surgery caused durable weight loss relative to control of 12% at 2 years and 8% at 5 years. This was associated with improved rates of diabetes remission, lower cardiovascular risk and increased quality of life.[14,15] We now report 10-year trial outcomes to contribute to our understanding of the impact of sustained weight loss on diabetes outcomes for individuals whose BMI is between 25 and 30 kg/m^2.

2 | MATERIALS AND METHODS

The study design and interventions were reported previously.[14] Inclusion criteria included age between 18 and 65 years, BMI 25-30 kg/m^2 and diabetes duration less than 5 years. Diabetes at baseline was defined as one or more of HbA1c >6.5% (48 mmol/mol), fasting glucose ≥7.0 mmol/L and 2-h glucose following 75 g oral glucose ≥11.1 mmol/L. Participants were recruited between November 2009 and June 2011 and randomized 1:1 to receive multidisciplinary diabetes care (MDC) or GB surgery combined with MDC for 5 years and

TABLE 1 Baseline characteristics

	GB group n = 21	Medical group n = 20	*p*-value
Age (years)	53 (50, 57)	55 (50, 59)	.401
Men	4 (19)	6 (30)	.484
Weight (kg)	80 (75, 89)	82 (73, 93)	.782
Body mass index (kg/m^2)	29.5 (28.7, 29.8)	29.4 (27.7, 29.9)	.670
Waist circumference (cm)	100 (95, 104)	101 (96, 104)	.861
Fasting glucose (mmol/L)	7.4 (6.1, 8.3)	7.5 (6.6, 10.7)	.481
HbA1c (%)	7.0 (6.4, 7.3)	7.1 (6.6, 8.5)	.267
HbA1c (mmol/mol)	53 (46, 56)	54 (49, 69)	.267
Diabetes duration (years)	1.5 (0.6, 4.0)	3.0 (1.4, 5.0)	.128
Diabetes treatment			
Metformin	13 (62)	18 (90)	.067
Sulphonylurea	3 (14)	4 (20)	.697
DPP-4 inhibitor	1 (5)	3 (15)	.343
GLP agonist	0	1 (5)	.488
Insulin	4 (19)	1 (5)	.343
HOMA-B	88 (59, 113)	76 (41, 121)	.544
HOMA-IR	2.25 (1.76, 3.71)	2.33 (1.95, 3.28)	.985
Systolic blood pressure (mmHg)	130 (115, 142)	130 (120, 138)	.995
Diastolic blood pressure (mmHg)	80 (73, 88)	84 (80, 87)	.355
Total cholesterol (mmol/L)	4.5 (4.2, 5.4)	4.5 (3.8, 6.0)	.902
Triglycerides (mmol/L)	1.3 (1.0, 2.3)	1.8 (1.4, 2.3)	.150
High-density lipoprotein cholesterol (mmol/L)	1.2 (0.9, 1.5)	1.1 (0.9, 1.3)	.723
Low-density lipoprotein cholesterol (mmol/L)	2.5 (2.3, 3.7)	2.7 (2.1, 3.7)	.641

Note: Data are presented as median (Q1, Q3) and n (%).
Abbreviations: DPP-4, dipeptidyl peptidase-4; GB, gastric band; GLP, glucagon-like peptide; HbA1c, glycated haemoglobin.

then diabetes care by their general practitioner. MDC involved review by a diabetes specialist every 3-6 months and by a dietician and diabetes educator on two occasions in the first year and as required thereafter. Monash University Human Research Ethics Committee gave approval for participants to undergo a clinical examination and have blood tests more than 10 years after their randomization visit. All participants provided written informed consent to attend follow-up assessments, which were performed between February 2020 and November 2021.

A single physician (JMW) interviewed all participants in person or by telephone and each subsequently attended a community optometrist or ophthalmologist for eye examination. COVID restrictions during the study required some participants to consult their GP for measurement of weight, waist circumference and blood pressure. Pathology endpoints were measured by accredited pathology providers in the community.

The primary outcome of the original study[14] was diabetes remission, defined as fasting glucose <7.0 mmol/L and glucose 2 h after 75 g oral glucose <11.1 mmol/L. However, because of logistical and ethical considerations, in this study we adopted consensus criteria for diabetes remission as HbA1c <6.5% (48 mmol/mol) without use of glucose-lowering medication for the preceding 3 months.[16] The primary outcome was assessed by modified intention to treat. Comparison of baseline characteristics of the 41 participants reported in this analysis to the 10 participants who withdrew before 10 years is presented in Table S1.

Other outcomes were weight loss, blood pressure, waist circumference, medication use, HbA1c, fasting glucose, medication usage, lipid profile, diabetes complications and quality of life. Complications were ascertained from medical history and eye examination reports and corroborated with supporting documentation where necessary. Macrovascular complications were defined as stroke, myocardial infarction and symptomatic peripheral vascular disease. Microvascular complications were diabetic retinopathy, albuminuria, symptomatic neuropathy and neuropathic foot ulcer. Beta cell function (HOMA-B) and insulin resistance (HOMA-IR) were calculated from fasting glucose and C-peptide using the homeostatic model.[17]

Quality of life composite scores for physical and mental health as well as health utility were measured using the SF-36 survey, as previously described.[15] The 10-year coronary heart disease risk was calculated using Framingham equations.[18] Medication costs were obtained from the 2022 Australian Pharmaceutical Benefits Schedule and are presented in Australian dollars (AUD). Tolerability of the GB was assessed by asking GB participants if they were pleased to have had GB surgery.

Baseline, 2-, 5- and 10-year data were complete for all 41 participants who underwent the year 10 assessment. Analyses used Prism software (version 9.4.0). Group differences were determined using Fisher's exact test and Mann-Whitney U-tests for categorical and continuous data respectively. Correlation analyses used Spearman's test. Analyses to determine the association between weight loss and the trial outcomes excluded one medical participant with suboptimal glucose control [HbA1c at year 10 8.8% (73 mmol/mol)] who lost 37% body weight attributed to recurrent foot sepsis, anorexia and immobility.

3 | RESULTS

Between 2009 and 2011, 51 participants were randomized: 25 to the GB group and 26 to the medical group. At 10 years, 21 GB and 20 medical participants returned for assessment, including one GB participant who had declined GB surgery (Figure 1). The baseline characteristics of the two treatment groups did not differ significantly (Table 1).

Figure 2A shows the time course of weight loss in the two groups. Weight loss following GB surgery was maximal at 2 years and endured out to 10 years. In the medical group, significant weight loss was not observed over the first 5 years; however, at 10 years, significant weight loss of 4.7 (3.1, 5.9) kg or 5.6 (3.4, 7.6)% had occurred ($p = .006$ and .009, respectively; Table 2). This included one medical

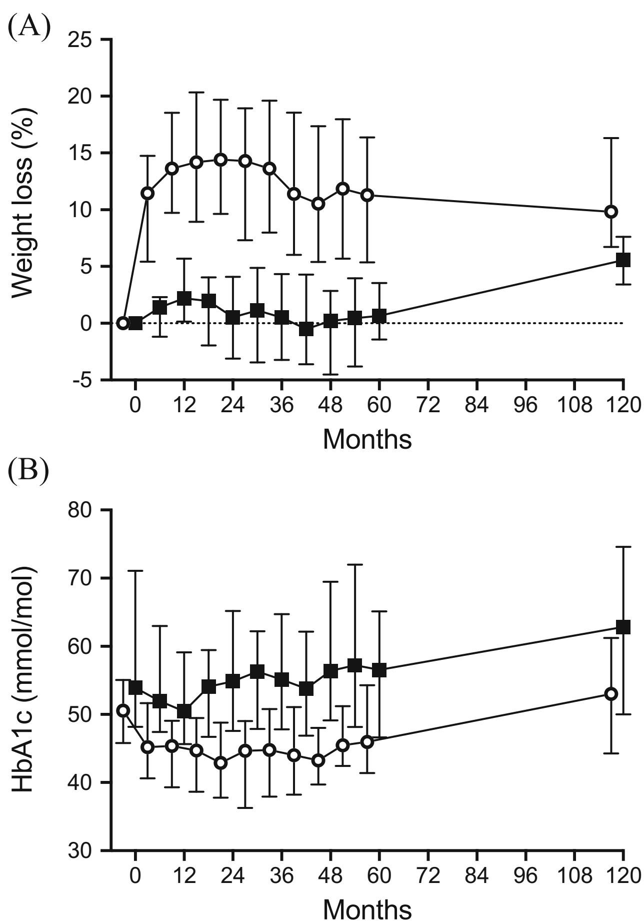

FIGURE 2 Weight and glycated haemoglobin (HbA1c) for the 41 participants who completed the 10-year assessment. Median (Q1, Q3) (A) percentage weight loss and (B) HbA1c over 10 years for the gastric band (open circles) and medical (filled squares) groups are presented as median with interquartile range

participant whose weight loss of 28 kg (37%) was attributed to catabolic effects of recurrent foot sepsis and another who attained 19 kg (17%) weight loss through lifestyle modification between years 5 and 10. After 10 years, the median (Q1, Q3) weight loss in the GB group of 8.5 (5.4, 13.1) kg or 9.8 (6.7, 16.3)% was significantly greater than that of the medical group [4.7 (3.1, 5.9) kg or 5.6 (3.4, 7.6)%], equating to a median difference (95% CI) between the groups of 3.9 (1.2-7.4) kg or 4.3 (1.5-9.4)% of baseline body weight (p = .006 and .008, respectively). This was substantially lower than the median difference of 10.6 (4.8-13.6)% observed at 5 years. When data from the entire study population were analysed, weight loss did not correlate with diabetes remission. Furthermore, the median percentage weight loss of 9.7 (7.1, 20.4) for the five remitters was comparable with the 9.8 (6.6, 15.7)% weight loss seen in the other 16 GB participants (p = .660).

Five (24%) participants in the GB group and none in the medical group achieved diabetes remission at 10 years, defined as HbA1c

TABLE 2 Outcomes at 10 years

	GB group n = 21	Medical group n = 20	*p*-value
Diabetes remission	5/21	0/20	.048
HbA1c (%)	7.0 (6.2, 7.8)	7.9 (6.7, 9.0)	.143
HbA1c (mmol/mol)	53 (44, 61)	63 (50, 75)	.143
Diabetes treatment			
Metformin	14 (67)	20 (100)	.009
Sulphonylurea	3 (14)	10 (50)	.020
DPP-4 inhibitor	4 (19)	3 (15)	>.999
GLP agonist	3 (14)	3 (15)	>.999
SGLT inhibitor	3 (14)	14 (70)	<.001
Insulin	1 (5)	4 (20)	.184
HOMA-B	54 (39, 80)	56 (38, 64)	.537
HOMA-IR	1.79 (1.28, 3.28)	2.01 (1.25, 2.85)	.932
Fasting glucose (mmol/L)	7.6 (6.5, 10.6)	8.9 (7.6, 10.6)	.274
Weight (kg)	71 (63, 79)	77 (68, 89)	.262
Weight loss (kg)	8.5 (5.4, 13.1)	4.7 (3.1, 5.9)	.006
Percentage weight loss (%)	9.8 (6.7, 16.3)	5.6 (3.4, 7.6)	.008
Change in waist (cm)	5.5 (0.0, 12.0)	2.5 (-2.0, 8.0)	.373
Systolic blood pressure (mmHg)	129 (121, 136)	127 (117, 140)	.565
Diastolic blood pressure (mmHg)	80 (74, 90)	77 (71, 80)	.267
Total cholesterol (mmol/L)	4.2 (3.3, 5.3)	4.0 (3.4, 4.9)	.771
Triglycerides (mmol/L)	1.4 (1.1, 2.0)	1.8 (1.3, 2.7)	.125
High-density lipoprotein cholesterol (mmol/L)	1.2 (1.0, 1.7)	1.1 (0.8, 1.3)	.030
Low-density lipoprotein cholesterol (mmol/L)	2.0 (1.3, 2.7)	1.9 (1.4, 2.9)	.877
10-year coronary artery disease risk score	16.3 (10.6, 26.0)	20.9 (14.1, 37.6)	.144
Diabetes medication cost/month ($)	11.00 (0.00, 48.00)	66.00 (53.50, 105.30)	<.001
Number of diabetes medications	1 (0, 2)	3 (2, 3)	<.001
CV medication cost/month ($)	34.00 (20.00, 43.50)	44.50 (21.13, 67.00)	.074
Number of CV medications	2 (1, 3)	2 (1, 3)	.371
Complications – total	15/63	13/60	.832
Macrovascular complications	3/21	2/20	>.999
Microvascular complications	9/21	8/20	>.999
Cataracts	3/21	3/20	>.999
QoL physical composite score	50.44 (45.56, 58.10)	47.89 (41.16, 55.41)	.218
QoL mental composite score	53.97 (45.40, 58.86)	52.28 (44.00, 59.28)	.990
Health utility	0.81 (0.66, 0.85)	0.72 (0.64, 0.85)	.664

Note: Data are presented as median (Q1, Q3) and n (%).
Abbreviations: CV, cardiovascular; DPP-4, dipeptidyl peptidase-4; GB, gastric band; GLP, glucagon-like peptide; QoL, quality of life; HbA1c, glycated haemoglobin; SGLT, sodium-glucose cotransport.

<6.5% (48 mmol/mol) without use of glucose-lowering medication for the preceding 3 months.[16] All five of these participants had also been in remission at years 2 and 5. The relative risk of diabetes following surgery after 10 years was 0.76 (95% CI: 0.55-0.93, $p = .048$). However, in a sensitivity analysis of the entire study population that assumed none of the four missing GB participants and two of the six missing medical participants entered diabetes remission at 10 years, surgery was not associated with a significantly lower relative risk of diabetes (0.87, 95% CI: 0.65-1.11; $p = .417$).

The HbA1c of the medical group showed progressive deterioration after 1 year whereas in the GB group HbA1c was lower than baseline for the first 5 years and then increased between years 5 and 10 (Figure 2B). At 10 years, the HbA1c of the GB group of 7.0 (6.2, 7.7)% [53 (44, 61) mmol/mol] was lower than that of the medical group 7.9 (6.7, 9.0)% [63 (50, 75) mmol/mol]. However, in contrast to values obtained during the first 5 years of the study, this difference was not statistically significant ($p = .143$; Table 2).

Other 10-year outcomes for the GB and medical groups are presented in Table 2. Despite no significant difference in HbA1c between the groups, GB participants used significantly fewer glucose-lowering medications, with significantly less use of metformin, sulphonylureas and sodium-glucose cotransport (SGLT) inhibitors. This equated to a median monthly cost saving of AUD$55. Four individuals within the GB group ceased insulin use within 12 months following band insertion and remained on oral glucose-lowering agents alone. One GB participant commenced insulin between years 5 and 10. In the context of equivalent use of blood pressure- and lipid-lowering drugs by both groups, GB surgery increased high-density lipoprotein cholesterol concentration at 10 years [1.2 mmol/L (1.0, 1.7) vs. 1.1 mmol/L (0.8, 1.3); $p = .030$], but had no significant impact on blood pressure or other lipid measures, reflected by comparable 10-year coronary artery disease risk scores. Consistent with this, the incidence of diabetes-related vascular complications was similar in each group. Finally, the superior weight loss of the GB group did not translate into improved measures of physical or mental quality of life, or of health utility.

The unexpected weight loss observed in the medical group prompted us to explore if this might be explained by differential use of two glucose-lowering medications that promote weight loss: SGLT inhibitors and glucagon-like peptide (GLP) agonists. SGLT inhibitors became government-subsidized in 2014 and were first prescribed in this study in November 2014. At 10 years, significantly more medical group participants were taking SGLT inhibitors (14 of 20 compared with three of 21 GB participants; $p = .001$). In contrast, use of GLP agonists was similar, with three participants in each group injecting a GLP agonist at 10 years. The 13 medical participants who used an SGLT inhibitor at 10 years lost 5.6 (2.7, 7.3)% body weight compared with 6.2 (3.0, 22.1)% for the seven who did not ($P = .547$), noting that the latter subgroup included the two participants whose substantial weight loss was attributed to other factors.

Correlation analyses to identify factors associated with diabetes remission in all 41 participants revealed that none of the measures presented in Table 1 and neither baseline beta cell function nor 10-year weight loss was significantly associated with diabetes remission at 10 years. In addition, only one of the outcomes presented in Table 2, high-density lipoprotein cholesterol, was significantly associated with 10-year weight loss ($R = 0.42$, $p = .007$).

Each GB participant had their band adjusted a median of 20 (12, 28) times, with 80% of adjustments occurring during the first 5 years. Three participants were dissatisfied with their GB. One underwent explant in year 9 because of symptoms of gastro-oesophageal reflux associated with a gastric pouch at a cost of AUD $4000, one had experienced intermittent swallowing difficulties throughout the study and one was planning explant surgery for band slippage. Of the remaining 17 GB participants who had GB surgery, 15 were pleased to have been randomized to receive surgery and two were undecided.

4 | DISCUSSION

In this randomized trial involving individuals with type 2 diabetes who were overweight but not obese, GB surgery decreased the need for glucose-lowering medication and induced clinically significant weight loss over 10 years, with five of the 21 participants entering early and sustained diabetes remission. Weight loss was significantly greater in the GB compared with the medical control group throughout the 10 years of this study. However, the medical group experienced clinically significant weight loss over the final 5 years, which decreased the difference in weight loss between groups from 10.6% at year 5 to 4.3% at year 10. In contrast to our findings at 5 years,[15] the superior weight loss observed in the GB group at 10 years was not associated with improved HbA1c, cardiovascular risk, quality of life or health utility. Furthermore, the rate of incident diabetes complications was similar in each group, although the overall number of events was low.

Type 2 diabetes is a chronic disease caused by irreversible pancreatic beta cell failure.[19] While effective treatment of hyperglycaemia has been shown to protect against long-term diabetes complications,[20] subsequent work showed the critical importance of blood pressure- and lipid-lowering therapies to mitigate their risk.[21] The initial reports of high rates of diabetes remission following bariatric surgery raised the possibility that dramatic improvements in glucose control conferred by surgery could deliver equally dramatic improvements in long-term outcomes.[22] While questioned at the time,[23] these benefits were duly reported in observational cohorts showing bariatric surgery to be associated with lower mortality[6,7] and lower rates of diabetes complications,[5] leading to the incorporation of bariatric surgery into type 2 diabetes treatment guidelines.[24] These guidelines nonetheless highlighted significant uncertainty surrounding the long-term impact of bariatric surgery and the need for better evidence, which is now particularly relevant given the more recent evidence that SGLT inhibitors and GLP agonists promote weight loss and protect against diabetes complications and mortality.[25,26] To date only one other randomized controlled trial of bariatric surgery for diabetes has reported 10-year outcomes.[11] This study by Mingrone et al. reported the effects of either gastric bypass or BPD surgery compared with medical care in people with obesity (mean BMI 44 kg/m^2) and reported surgery induced 25%

weight loss relative to the medical group and durable diabetes remission in 38% of participants. Participants who underwent surgery experienced clinically significant improvements in HbA1c and quality of life, and had a lower rate of diabetes complications, primarily because of incident albuminuria and neuropathy in the medical group. BPD surgery in this study was associated with a greater risk of serious adverse events and nutrient deficiencies. In our study, the population was leaner, the bariatric surgery procedure was not anticipated to alter incretin hormone release, and the difference in weight between surgical and medical groups was smaller. Together these differences may explain the lower rate of sustained diabetes remission following surgery in our study, as well as the lack of significant differences in glucose control, quality of life and incident diabetes complications after 10 years. In addition, in the Mingrone trial, only 20% of the medical group participants were treated with SGLT inhibitors compared with 70% in our study. SGLT inhibitors induce durable weight loss and prevent incident albuminuria in type 2 diabetes populations,[26] raising the possibility that greater use of this drug class in the Mingrone trial may have improved weight outcomes and prevented diabetes complications, thereby diminishing the reported benefits of surgery.

SGLT inhibitors are now recommended as a second-line glucose-lowering medication after metformin for the treatment of type 2 diabetes[27] and recent innovation in GLP agonists has shown the newer weekly injectable formulations deliver vastly improved weight outcomes for individuals with type 2 diabetes who are overweight or obese.[28] Both 10-year bariatric surgery trials commenced well before this new therapeutic era and their long-term impact should be considered in the current therapeutic context when weighing up the potential benefits of surgery for people with type 2 diabetes.

Although GB surgery was associated with improved rates of diabetes remission at 10 years, this effect was modest and neither weight loss nor baseline beta cell function predicted it. The lack of correlation with weight loss may be because of type II error given the relatively small number of patients in remission at 10 years. However, Mingrone et al. also noted no relationship between weight loss and diabetes remission despite a 38% rate of diabetes remission at 10 years,[11] indicating possible roles for other unmeasured factors, such as different diets and levels of physical activity,[1] in attaining remission after bariatric surgery.

A key issue in the field is whether bariatric surgery improves diabetes outcomes beyond glucose control in the longer term. The Swedish Obese Subjects observational cohort-controlled study of 603 people with type 2 diabetes suggested that GB or bypass surgery performed between 1987 and 2001 prevented the development of both micro- and macrovascular diabetes complications over a 15-year time frame.[5] With the caveat that the small number of vascular events observed in our study and the study of Mingrone et al.[11] limit our ability to test these findings in a randomized trial setting, it is notable that GB surgery in people who are overweight but not obese did not afford vascular protection whereas more substantial weight loss following gastric bypass or BPD surgery in people with obesity did. Possible reasons for this discrepancy include differences in the populations studied and study methodologies, the much greater percentage weight loss overserved in the Mingrone et al. study and, potentially, beneficial effects of enhanced incretin release following bypass and BPD procedures.[13] When the two bariatric surgery trials are considered together with the Look AHEAD trial finding that weight loss of 2.5% body weight relative to the control group was not associated with protection from cardiovascular events,[2] our findings raise the possibility that greater than 5% weight loss is needed to confer cardiovascular protection. This is supported by a post hoc analysis of the Look AHEAD trial that reported 10% weight loss through intensive lifestyle intervention was associated with a 21% risk of a cardiovascular event[29] and accords with our previous study of people with obesity that showed that 7% weight loss was required to resolve metabolic syndrome in the majority of participants.[30]

Economic analyses based primarily on observational datasets conclude that bariatric surgery is a cost-effective intervention for people with type 2 diabetes who are overweight.[31-33] These analyses assume surgery improves quality of life, decreases medical costs and prevents glucose-dependent diabetes complications over many decades. Our previous cost-effectiveness analysis concluded that, over 10 years, the incremental cost-effectiveness ratio of GB surgery of people with type 2 diabetes who were overweight but not obese was US$29 000 per quality-adjusted life year.[33] This conclusion assumed GB surgery would improve health utility by 0.08, lower HbA1c by 0.7% (8 mmol/mol) and save US$1600 in medication costs each year. While these assumptions appear to have been valid during the first 5 years of our trial,[15] our 10-year data showed no difference in health utility and lesser improvements in HbA1c and medication costs. Therefore, longer-term incremental cost-effectiveness ratio estimates for this population will almost certainly need to be revised upward.

In addition to limitations mentioned above, we acknowledge that the unavoidable open-label nature of this study may have biased some outcomes, particularly diabetes complications, which depended on the medical history provided by each participant. Between years 5 and 10, we did not provide regular multidisciplinary medical care. While this may have affected treatment outcomes, it is worth noting that similar numbers of participants in each group were referred by their GP to a diabetes specialist between years 5 and 10, so any consequences of non-specialist diabetes care will probably have affected both groups equally. In addition, lockdowns associated with the COVID-19 pandemic in Melbourne may have had direct adverse effects on participant mental health and required many to have anthropometric assessment in the community rather than in the clinic research unit. These unavoidable issues may have confounded quality of life assessments and decreased the accuracy of weight, waist and blood pressure measurements. Our focus on a population with BMI <30 kg/m^2 limits applicability of our findings to people with obesity, who would probably seek weight loss surgery. Finally, GB surgery is now uncommonly performed, which limits the generalizability of our findings to the modern era. However, because GB surgery induces weight loss without altering abdominal anatomy, we contend that our findings could be used to predict the impact of comparable weight loss strategies, including lifestyle approaches[1] and adjustable gastric balloon.[34]

In summary, when compared with medical care, GB surgery for people who are overweight but not obese with type 2 diabetes induces sustained weight loss, and in a minority, diabetes remission. However, in contrast to its effects at 5 years, after 10 years GB surgery did not improve HbA1c or quality of life and was not associated with protection from incident diabetes complications.

AUTHOR CONTRIBUTIONS

J.M.W. and P.E.O. devised the study. P.B., W.A.B. and P.E.O. performed GB surgery and oversaw postsurgical follow-up. J.M.W. and J.P. arranged participant assessments and collated the data with Q.Y.D.Q., who with J.M.W. analysed the data and drafted the manuscript, which all authors reviewed and edited. J.M.W. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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CONFLICT OF INTEREST STATEMENT

No potential conflicts of interest relevant to this article were reported.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/dom.14992.

DATA AVAILABILITY STATEMENT

De-identified data from this study will be made available to other researchers upon reasonable request to the corresponding author, John M Wentworth.

ETHICS STATEMENT

This study was sponsored by the Monash University Centre for Obesity Research and Education and approved by Monash University Human Research Ethics Committee. All participants provided written informed consent.

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SUPPORTING INFORMATION

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

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