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Synopsis

60-month follow-up of Long Limb vs. Standard Limb Roux-en-Y gastric bypass for type 2 diabetes and obesity: the LONG LIMB RCT

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Abstract

Background: Roux-en-Y gastric bypass is an established treatment option for type 2 diabetes and obesity. However, the optimal lengths for the small intestinal limbs remain controversial with variation in practice. A longer biliopancreatic limb length of 150 cm ('Long Limb') was hypothesised to better improve glycaemia compared to the standard Roux-en-Y gastric bypass with a biliopancreatic limb of 50 cm ('Standard Limb'). The aim of the trial was to evaluate the short-term mechanistic outcomes and the long-term clinical outcomes and safety of Long Limb versus Standard Limb Roux-en-Y gastric bypass.

Methods: We undertook a prospective double-blinded randomised controlled parallel group clinical trial across two sites in London. Participants were randomly assigned (1 : 1) to Long Limb or Standard Limb Roux-en-Y gastric bypass with a fixed alimentary limb of 100 cm. Mixed-meal tolerance tests and a hyperinsulinaemic-euglycaemic clamp were used to measure postprandial gut hormone response, glucose tolerance and insulin sensitivity. The primary outcome for the mechanistic study was the secretion of active glucagon-like peptide-1 at 2 weeks after intervention. Secondary outcomes were insulin sensitivity and fasting/postprandial glucose and insulin concentrations. Clinical outcomes, including HbA1c, number of glucose-lowering medications, weight loss, blood pressure and low-density lipoprotein cholesterol, and adverse events, were collected up to 60 months postoperatively to assess the durability of postoperative weight and glycaemic improvements.

Results: Of the 53 participants randomised, 48 completed the 12-month mechanistic investigation (Standard Limb 24, Long Limb 24) and 38 completed the 60-month follow-up (Standard Limb 18, Long Limb 20). The 24- to 60-month extension study coincided with two waves of the COVID-19 pandemic. There was no difference between the Standard Limb and Long Limb groups for postprandial active glucagon-like peptide-1 secretion (70 ± 32 pmol/L vs. 70 ± 19 pmol/L, respectively; $p = 0.43$), hepatic insulin sensitivity (3.4 ± 0.9 µmol/kg/min vs. 3.4 ± 1.4 µmol/kg/min, respectively; $p = 0.94$) and peripheral insulin sensitivity (29.0 ± 9.1 µmol/kg/min vs. 29.2 ± 9.9 µmol/kg/min, respectively; $p = 0.98$) at 2 weeks post intervention. There was no difference between the Standard Limb and Long Limb groups at 60-month follow-up for glycaemic remission (33% vs. 45%, respectively; $p = 0.52$), percentage total weight loss (27 ± 9% vs. 26 ± 8%, respectively; $p = 0.34$), systolic blood pressure (127 ± 11 mmHg vs. 125 ± 14 mmHg, respectively; $p = 0.63$) and low-density lipoprotein cholesterol (2.0 ± 1.0 mmol/L vs. 2.4 ± 1.0 mmol/L, respectively; $p = 0.27$).

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Conclusion: In conclusion, this study has demonstrated the substantial clinical benefit of Roux-en-Y gastric bypass to people living with type 2 diabetes and obesity; however, this trial did not demonstrate a clinical rationale for the elongation of the biliopancreatic limb of Roux-en-Y gastric bypass to 150 cm to enhance metabolic outcomes for type 2 diabetes and obesity.
Limitations: Although the surgical procedures were designed according to United Kingdom clinical practice at the time of study inception, there is substantial variation in practice internationally. Our original investigation was powered for mechanistic outcomes and is not powered to detect differences in clinical outcomes. Lastly, the loss of participants to follow-up may have limited our statistical power to detect significant differences in the clinical outcomes. We therefore cannot derive definitive conclusions on the relative clinical efficacy of the two variants of Roux-en-Y gastric bypass.
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SYNOPSIS

This report summarises a study that was undertaken to establish the mechanisms behind and long-term clinical outcomes resulting from a modified Roux-en-Y gastric bypass (RYGB) operation on glucose control in people living with type 2 diabetes (T2D) and obesity (body mass index or BMI ≥ 30 kg/m^2). An extension to our original study was granted to observe if improvements in glycaemia and clinical outcomes are sustained up to 60 months following the modified RYGB, and these results are presented for the first time in this synopsis.

Enhancing Roux-en-Y gastric bypass for type 2 diabetes

Roux-en-Y gastric bypass reduces the size of the stomach and bypasses the duodenum and proximal jejunum. The anatomical rearrangements of RYGB result in three intestinal sections or 'limbs': the 'alimentary limb', through which food enters the small intestine; the 'biliopancreatic limb', which includes the bypassed sections of duodenum and proximal jejunum, through which the biliopancreatic secretions flow; and the 'common limb', in which food and biliopancreatic secretions mix (*Figure 1*).

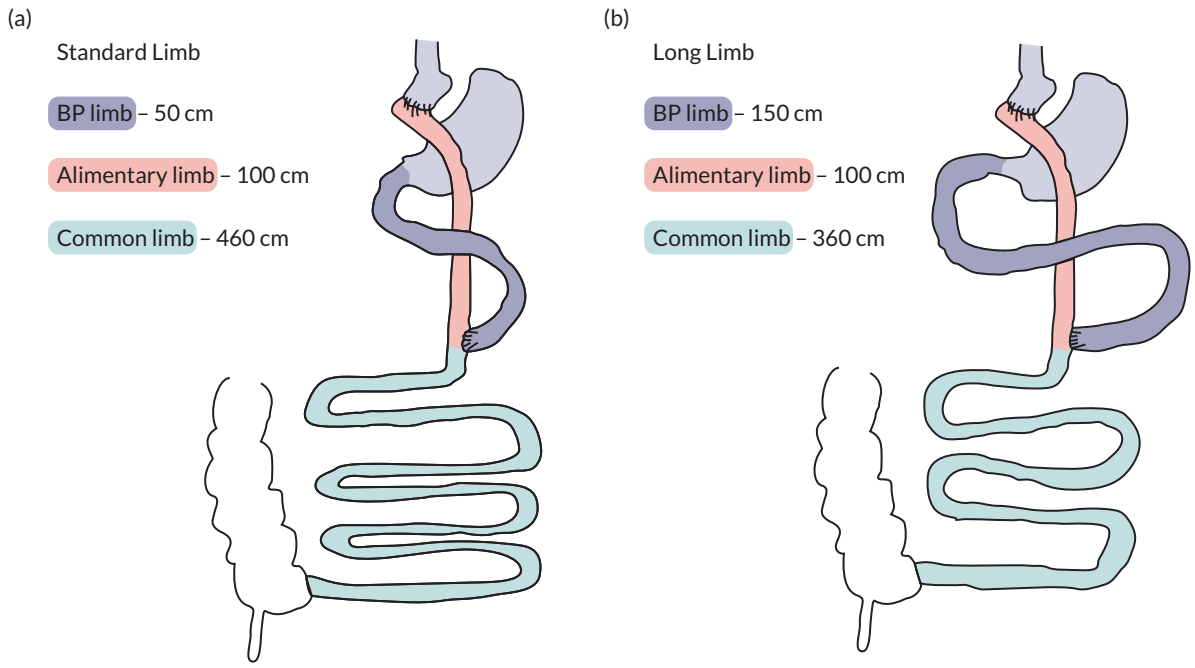

FIGURE 1 Schematic drawing of the Standard Limb and the Long Limb RYGB. (a) Standard Limb; (b) Long Limb. BP limb, biliopancreatic limb.

The dramatic and immediate glucose-lowering effects of bariatric operations indicate that the intestine is a central regulator of glucose homeostasis. Bariatric surgical procedures that bypass the upper gastrointestinal tract, such as RYGB and biliopancreatic diversion, result in better improvements in glycaemia than bariatric surgical procedures that maintain intestinal continuity and this has led to the concept of metabolic surgery.[1] The rate of T2D remission is greater after biliopancreatic diversion than after RYGB, even when weight loss after both procedures is the same.[2] Biliopancreatic diversion has a longer small intestinal bypass than RYGB, and as a result nutrients reach the lower small intestine faster and in a less-digested state. Clinical studies indicate that a longer small intestinal bypass has a weight loss-independent effect on glucose lowering,[3,4] possibly via potentiation of the postprandial secretion of the incretin hormone glucagon-like peptide 1 (GLP-1) which, at least in part, drives early (earlier than 3 months postoperatively) postprandial insulin secretion after surgery.[5] Also, biliopancreatic diversion causes greater improvement in insulin sensitivity compared to RYGB even when weight loss is matched at 20%.[2] Unfortunately, the biliopancreatic diversion operation has the distinct disadvantage of a substantially higher risk of developing severe macro and micronutrient deficiencies, which has limited its use.

The 'Long Limb Roux-en-Y gastric bypass'

To improve the glucose-lowering effects of RYGB while avoiding the risk of complications entailed by biliopancreatic diversion, we devised a 'Long Limb RYGB' as a hybrid operation that combines the design of Standard Limb RYGB with a longer biliopancreatic limb (*Figure 1*). Full details of the proposed study, statistical analysis plan and a detailed step-by-step standard operating procedure for the Long Limb RYGB and Standard Limb RYGB have previously been published in *Efficacy and Mechanism Evaluation*.[6]

Our original investigation was a mechanistic study that compared the effects of Standard Limb RYGB with a biliopancreatic limb of 50 cm versus a Long Limb RYGB with a biliopancreatic limb of 150 cm on the primary mechanistic outcome of postprandial GLP-1 responses to a mixed-meal test 2 weeks after RYGB.[6,7] Secondary mechanistic outcomes included insulin sensitivity measured by the gold standard euglycaemic-hyperinsulinaemic clamp. Clinical outcomes were glycated haemoglobin (HbA1c), glycaemic remission, percentage weight loss and number of medications. The hypothesis was that Long Limb RYGB is a better treatment for T2D because of enhanced postprandial GLP-1 stimulation, insulin secretion and insulin sensitivity.

Short-term mechanistic outcomes

To increase the generalisability of our findings, participants were enrolled from two sites that used a surgical approach which was consistent between surgeons and in line with a pre-agreed standard operation procedure. The trial was prospectively registered with the ISRCTN (International Standard Randomised Controlled Trial Number) registry as ISRCTN 15283219. The short-term (12-month) results of our trial were published in *Diabetes Care*.[7] Fifty-three participants were recruited into the Long Limb study between August 2015 and November 2017. Twenty-seven participants were randomised to Standard Limb and 26 to Long Limb RYGB. For anatomical reasons, one patient in the Standard Limb group underwent a vertical sleeve gastrectomy and one patient in the Long Limb group underwent a one-anastomosis gastric bypass, and thus were excluded from analysis. After dropouts resulting from failure to complete mechanistic visits and loss to follow-up, 24 participants completed the 12-month mechanistic visit in the Long Limb group and 24 in the Standard Limb group (*Figure 2*). Both interventions were associated with a greater than threefold increase in postprandial GLP-1 secretion during a mixed-meal test; however, there was no difference between the groups (treatment effect −8 pmol/l, 95% CI −25 to +9 pmol/l; $p = 0.34$).[6,7] Both operations were associated with a marked improvement in fasting and total postprandial glucose concentrations (area under the curve) at the mixed-meal tolerance test, and profound improvements in hepatic and peripheral insulin sensitivity measured by a euglycaemic-hyperinsulinaemic clamp, but there were no between-group differences.[6,7] Consistent with these changes in glucose metabolism, at the 12-month mark, both the Long Limb and Standard Limb RYGB were equally successful in improving HbA1c and all but one participant in the trial was in remission from T2D, that is, HbA1c in the non-diabetic range (< 48 mmol/mol) without glucose-lowering medications.[6,7] Subsequent to closure of the trial, it was observed that seven patients in the Standard Limb group restarted glucose-lowering medications versus one from the Long Limb group. An extension to our trial was therefore granted to follow up patients up to 60 months postoperatively to observe if there is a clinically significant difference in the long-term metabolic impact of Long versus Standard Limb RYGB.

Longitudinal follow-up coincided with the COVID-19 pandemic

Previous studies reporting on glycaemic remission in participants receiving a long biliopancreatic limb RYGB have reported findings 24 and 60 months postoperatively but these studies were single-site, non-randomised observational studies and they were not performed in

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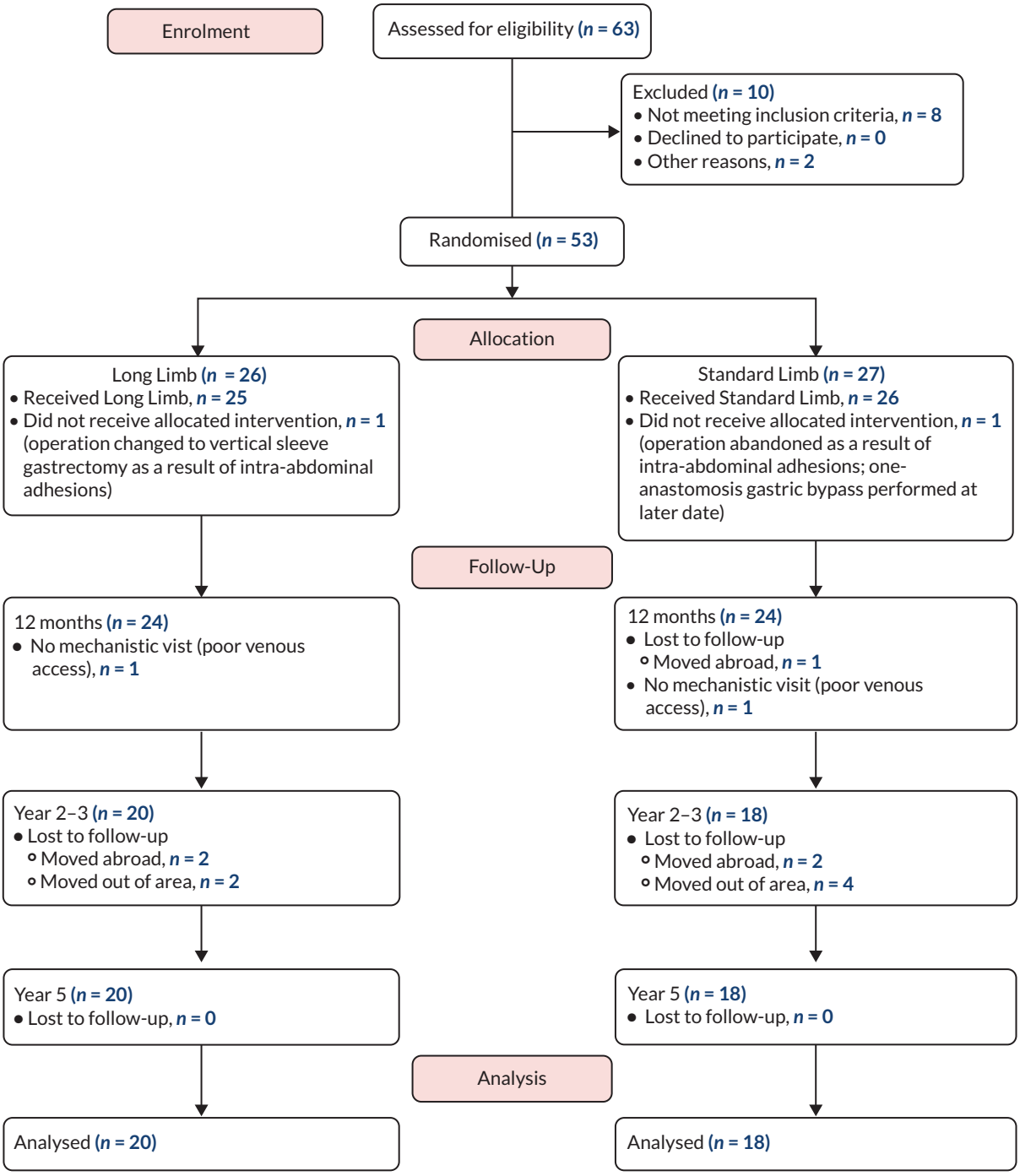


FIGURE 2 The Consolidated Standards of Reporting Trials (CONSORT) flow diagram. The as-treated population included 20 patients in Long Limb and 18 patients in Standard Limb.

people with T2D.[8,9] We designed our trial to specifically enable the longitudinal follow-up of participants because long-term RCT data in patients with T2D and obesity receiving a long biliopancreatic limb RYGB is lacking. In our extension study (Protocol Ref No: 15/LO/0813, Version 2.0), we planned to repeat a mixed-meal tolerance test 24 months after surgery plus annual clinical visits until 60-month follow-up. Unfortunately, the 24-month mixed-meal tolerance test plus clinical follow-up visit and 36-month clinical follow-up visit of our extension study coincided with the first wave of the COVID-19 pandemic, lockdown and restrictions. Therefore, the 24- and 36-month follow-up visits were combined. When it was safe to do so, we completed the mixed-meal tolerance tests in 15 patients in the Standard Limb group and 17 patients in the Long Limb group and collected clinical outcome data in 18 patients in the Standard Limb group and 20 in the Long Limb group.

Heightened anxiety from the COVID-19 pandemic resulted in four participants in the Long Limb group and six participants in the Standard Limb group permanently moving out of London to rural areas of the UK (*Figure 2*). The 48-month clinical follow-up visit in our trial coincided with the second wave of the COVID-19 pandemic and lockdown and it was not safe for participants to attend for their clinical study visit. Participants were therefore reviewed for their 60-month clinical visit when COVID-19 lockdown and restrictions had subsided.

Extended follow-up results

Glucose tolerance and insulin secretion at 24–36 months

Compared to the preoperative time point, there were reductions in mean fasting plasma glucose to the non-diabetic range in the Standard Limb group (mean ± SD: 6.4 ± 2.0 mmol/L) and Long Limb group (6.3 ± 1.4 mmol/L). At the 24- to 36-month postoperative visit, total postprandial glucose concentrations, assessed by area under the curve (AUC) at the mixed-meal tolerance test, were significantly reduced compared to baseline for both groups but there was no between-group difference (*Table 1*, *Figures 3* and *4*). Total AUC of postprandial insulin concentration did not change either within or between groups from baseline to 24- to 36-month follow-up (*Table 1*, *Figures 5* and *6*).

Glycaemic control and weight loss

Although there were no significant differences in the mean HbA1c concentrations between the trial groups at any time point during the 60-month study, both groups demonstrated a clinically important reduction in HbA1c in the first year that was maintained up to 60 months postoperatively (*Figure 7*). At 12-month follow-up, the mean HbA1c concentration was 47 ± 10 mmol/mol in the Standard Limb group (n = 24) while the Long Limb group (n = 24) had a mean HbA1c of 41 ± 5 mmol/mol. At 24- to 36-month follow-up, the mean HbA1c concentration in both groups was 45 ± 7 mmol/mol for the Standard Limb group (n = 18) and 44 ± 7 mmol/mol in the Long Limb group (n = 20). At 60-month follow-up, the mean HbA1c was 45 ± 8 mmol/mol for the Standard Limb group (n = 18) and 44 ± 7 mmol/mol for the Long Limb group (n = 20).

There was also a concomitant reduction in the number of glucose-lowering medications in both trial groups with no between-group difference during the 60-month follow-up period (*Table 2*). At baseline, participants were using a median of 3 (interquartile range, IQR 2–3) glucose-lowering medications in both trial groups, and at 60-month follow-up participants were using a median of 0 (IQR 0–1) glucose-lowering medications. Eight participants were using insulin at baseline and there were no participants that were using insulin at 60 months postoperatively.

TABLE 1 Glucose and insulin responses during the mixed-meal tolerance test preoperatively at 24–36 months postoperatively

		Time point, median (IQR)			
Outcome	**Trial group**	**Preoperatively**	**24–36 months postoperatively**	**Odds ratio (95% CI)**	***p*-value**
Glucose peak (mmol/L)	Standard Limb	15.3 (13.2–17.2)	11.0 (9.1–13.3)	1	
	Long Limb	14.4 (11.4–17.5)	11.2 (9.0–12.9)	1.02 (0.86 to 1.18)	0.79
Glucose AUC (mmol·min/l)	Standard Limb	2828 (2450–3172)	1447 (1179–1716)	1	
	Long limb	2647 (2103–3221)	1378 (1098–1659)	1.07 (0.92 to 1.22)	0.71
		Time point, mean (SD)			
Outcome	**Trial group**	**Preoperatively**	**24–36 months postoperatively**	**Treatment effect (95% CI)**	***p*-value**
Insulin peak (mU/l)	Standard Limb	29 (14)	65 (31)	0	
	Long Limb	28 (16)	67 (30)	−3.1 (−7.8 to 1.6)	0.69
Insulin AUC (mU·min/l)	Standard Limb	5281 (2464)	4679 (1110)	0	
	Long Limb	5128 (2833)	4785 (1363)	−110 (−198 to 88)	0.81

Notes
Continuous data are presented as mean (SD) when normally distributed or a median (IQR) when non-normally distributed.
Data were analysed using analysis of covariance with adjustment of between-group differences (treatment effect or odds ratio).
AUC – area under the curve calculated from time point 0 to 120 minutes.

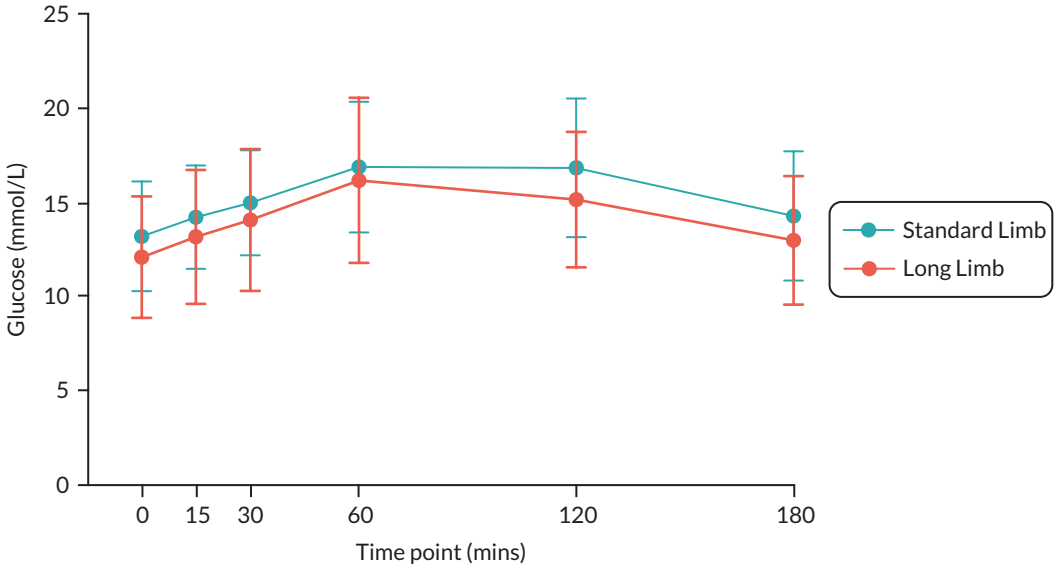


FIGURE 3 Preoperative plasma glucose excursion during the mixed-meal tolerance test (n = 24 per group). Data were plotted as means (SDs).

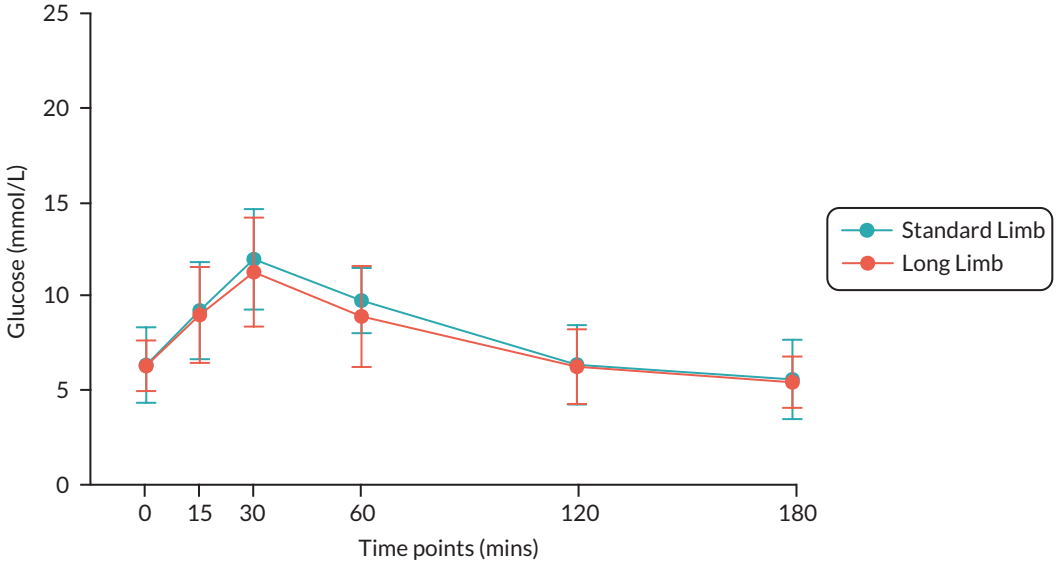


FIGURE 4 Plasma glucose concentrations during the mixed-meal tolerance test at 24–36 months postoperatively (n = 15, Standard Limb, n = 17, Long Limb). Data were plotted as means (SDs).

The most up-to-date American Diabetes Association consensus definition of glycaemic remission in T2D from 2021 is a HbA1c ≤ 48 mmol/mol without glucose-lowering medications for ≥ 3 months.[10] Using this definition there was no significant difference between the trial groups in the percentage of participants achieving glycaemic remission at 60 months (Standard Limb 33% vs. Long Limb 45%; p = 0.52) (*Figure 8*). The mean HbA1c for those in glycaemic remission in the Standard Limb group (n = 6) was 41 ± 5 mmol/mol and Long Limb group (n = 9) was 41 ± 5 mmol/mol at 60-month follow-up. Patients who were not in glycaemic remission were uniformly taking glucose-lowering medications, and for these individuals the adjusted HbA1c was calculated to estimate what the HbA1c would be without medications. The mean-adjusted HbA1c was 65 ± 10 mmol/mol for the Long Limb group (n = 11) and 67 ± 10 mmol/mol for the Standard Limb group (n = 12) at the 60-month follow-up; this was not significantly different between the groups. When comparing Standard Limb and Long Limb patients in glycaemic remission (n = 15) versus Standard Limb and Long Limb patients who were not in remission (n = 23), there were no between-group differences in baseline characteristics such as age, ethnicity, BMI, duration of T2D, preoperative HbA1c and the preoperative number of glucose-lowering medications (*Table 3*). There was also

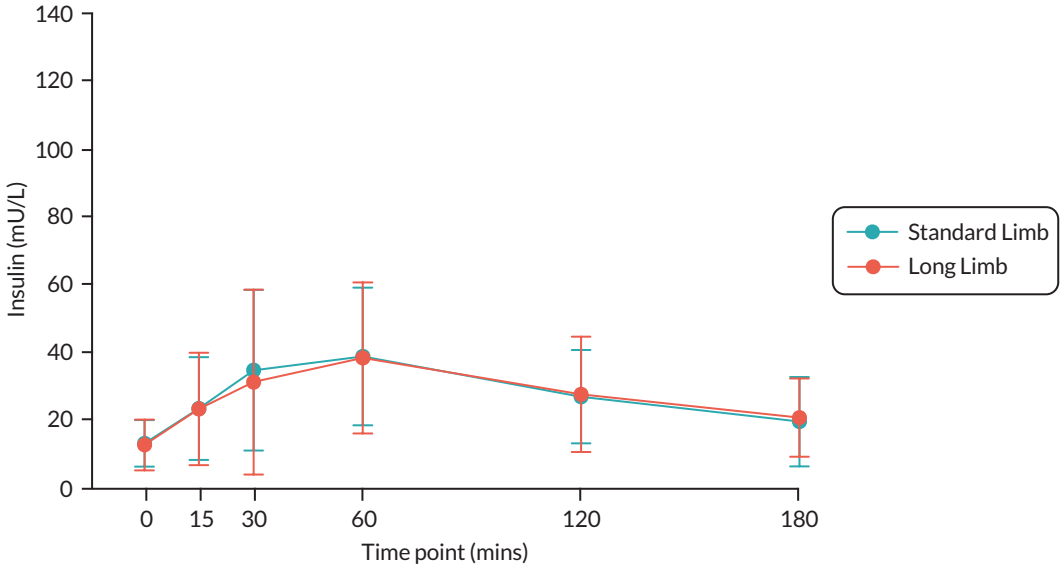


FIGURE 5 Preoperative serum insulin excursion during the mixed-meal tolerance test (n = 24 per group). Data were plotted as means (SDs).

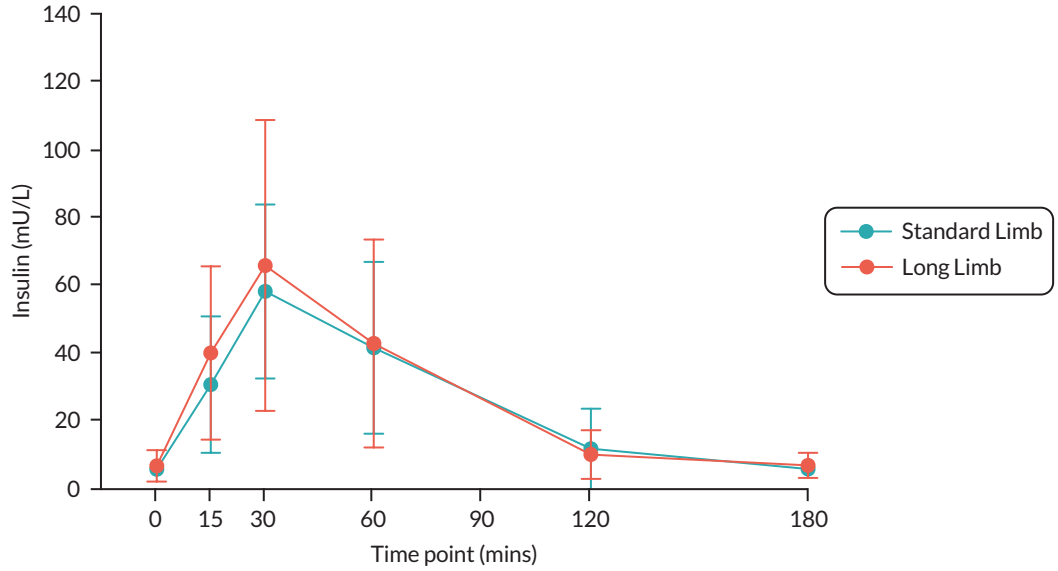


FIGURE 6 Serum insulin concentrations during the mixed-meal tolerance test at 24–36 months postoperatively (n = 15, Standard Limb, n = 17, Long Limb) Data were plotted as means (SDs).

no difference in postoperative weight loss in patients achieving glycaemic remission compared to patients who did not achieve glycaemic remission for the Standard Limb group (29 ± 8% vs. 24 ± 6%, respectively; p = 0.43) and the Long Limb group (26 ± 7% vs. 20 ± 7%, respectively, p = 0.3). The weight loss trajectories of those that did and did not achieve glycaemic remission are presented in *Figures 9* and *10*, respectively.

There was no difference in weight loss between the trial groups at any time point during our investigation (*Figure 11*). Percentage total body weight losses at 12, 24–36 and 60 months were 30 ± 10%, 28 ± 8% and 27 ± 9%, respectively for the Standard Limb group and 28 ± 10%, 26 ± 9% and 26 ± 8%, respectively for the Long Limb group. There were two patients in the Standard Limb group and two patients in the Long Limb group that were taking semaglutide at the 1mg dose prescribed for T2D at 60-month follow-up. Weight loss at 60 months remained similar after excluding these participants (Standard Limb group 26 ± 10%, Long Limb group 25 ± 9%). The clinical characteristics of Standard Limb and Long Limb patients with < 20% weight loss (n = 8) versus > 20% weight loss (n = 26) are presented in *Table 4*, and patients taking semaglutide were excluded from this analysis. There was no between-group difference in postoperative weight

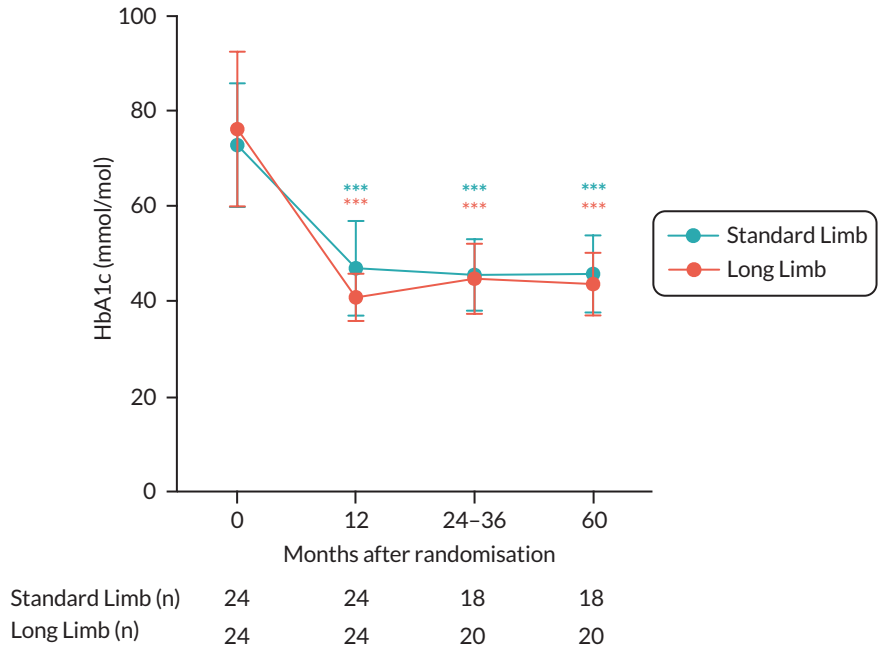


FIGURE 7 HbA1c levels (mmol/mol) at baseline (0 months) and at 12-, 24- to 36- and 60-month follow-up. Data are plotted as means (SDs). *n* in each trial group is denoted below 0, 12, 24–36 and 60 months. ***$p < 0.001$ vs. baseline.

loss in patients achieving < 20% weight loss (Standard Limb 12 ± 3% vs. Long Limb 11 ± 4%, $p = 0.67$) and > 20% weight loss (Standard Limb 29 ± 7% vs. Long Limb 28 ± 7%, $p = 0.53$). The weight loss trajectory of patients with < 20% weight loss ($n = 8$) is presented in *Figure 12*.

Cardiovascular risk factors: blood pressure and low-density lipoprotein cholesterol

There were no differences in systolic blood pressure between the groups at any time point during the 60-month follow-up (*Figure 13*). Systolic blood pressure at baseline and 60-month follow-up for the Standard Limb group was respectively 135 ± 13 mmHg and 127 ± 11 mmHg, and for the Long Limb group 135 ± 14 mmHg and 125 ± 14 mmHg, respectively. There was a significant reduction in diastolic blood pressure within both groups at 24–36 months ($p < 0.05$) and 60 months ($p < 0.05$) (*Figure 14*). Diastolic blood pressure at baseline, 24–36 months and 60 months for the Standard Limb group was respectively 77 ± 10 mmHg, 62 ± 10 mmHg, 63 ± 7 mmHg, and Long Limb group was 78 ± 10 mmHg, 69 ± 7 mmHg, 69 ± 7 mmHg. The median number of blood pressure-lowering medications taken by both groups at baseline and at 60-month follow-up were 2 (IQR 1–2) and 1 (IQR 0–1), respectively (*Table 2*).

There were no significant within- or between-group differences in low-density lipoprotein (LDL) cholesterol during at any time during the study (*Figure 15*). LDL cholesterol values at baseline and 60-month follow-up for the Standard Limb group were respectively 2.4 ± 1 mmol/L and 2.0 ± 1 mmol/L, and for the Long Limb group 2.9 ± 1 mmol/L and 2.4 ± 1 mmol/L. The median number of lipid-lowering medications for both groups at baseline and at 60-month follow-up was 1 (0–1) (*Table 2*).

Safety outcomes

The safety profile of both operations was similar throughout the extension study with no signal for increased malabsorption of macro and micronutrients in the Long Limb group (*Table 5*).

Discussion

This is the first double-blinded RCT comparing standard RYGB to a modified RYGB with a long biliopancreatic limb performed in the UK. We report on the 60-month clinical outcomes in a multi-ethnic British cohort with T2D and obesity. Despite disruption from the COVID-19 pandemic, follow-up at 60 months was obtained in 80% of our participants.

The findings of this study are in line with two previous clinical studies in which a longer biliopancreatic limb showed no additional benefit for reduction of HbA1c or glycaemic remission in T2D in the short[8] and long term.[8,11] A short-term study that kept the alimentary limb length constant in 93 people with obesity and T2DM reported that there was no difference in fasting plasma glucose or HbA1c between their versions of Standard Limb (biliopancreatic limb 50–75 cm) and Long Limb RYGB (biliopancreatic limb 100–150 cm) at 24-month follow-up, but they reported that a higher proportion of patients

TABLE 2 Medication usage in participants at 0, 12, 24–36 and 60 months in the Standard and Long Limb Roux-en-Y gastric bypass groups

	Standard Limb				Long Limb			
	0 months (*n* = 24)	12 months (*n* = 24)	24–36 months (*n* = 18)	60 months (*n* = 18)	0 months (*n* = 24)	12 months (*n* = 24)	24–36 months (*n* = 20)	60 months (*n* = 20)
Diabetes medications								
Biguanides	92% (22)	0	38% (7)	44% (8)	92% (22)	1	40% (8)	35% (7)
SGLT2 inhibitors	54% (13)	0	11% (2)	6% (1)	58% (14)	1	20% (4)	10% (2)
GLP-1 receptor agonists	38% (9)	0	0	11% (2)	17% (4)	0	5% (1)	20% (4)
DPP-4 inhibitors	29% (7)	0	6% (1)	6% (1)	54% (13)	1	0	0
Sulphonylureas	54% (13)	0	6% (1)	0	50% (12)	0	0	0
Insulin	17% (4)	0	0	0	17% (4)	0	0	0
Lipid-lowering medications								
Statins	71% (17)	67% (16)	67% (12)	72% (13)	75% (18)	54% (13)	50% (10)	55% (11)
Fibrates	4% (1)	4% (1)	0	0	8% (2)	8% (2)	5% (1)	0
Antihypertensive medications								
ACE inhibitors	50% (12)	42% (10)	38% (7)	40% (8)	50% (12)	30% (7)	20% (4)	35% (7)
ARBs	17% (4)	13% (3)	22% (4)	22% (4)	25% (6)	17% (4)	15% (3)	10% (1)
CCBs	30% (7)	13% (3)	11% (2)	17% (3)	25% (6)	21% (5)	20% (4)	30% (6)
Alpha-blocker	8% (2)	4% (1)	0	6% (1)	8% (2)	0	5% (1)	5% (1)
Thiazide-like diuretics	8% (2)	0	0	6% (1)	21% (5)	4% (1)	0	0
Diuretics	8% (2)	8% (2)	0	0	0	0	0	0
Beta-blocker	13% (3)	8% (2)	0	0	4% (1)	0	0	0

ACE, angiotensin converting enzyme; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide 1; SGLT-2, sodium-glucose co-transporter-2.

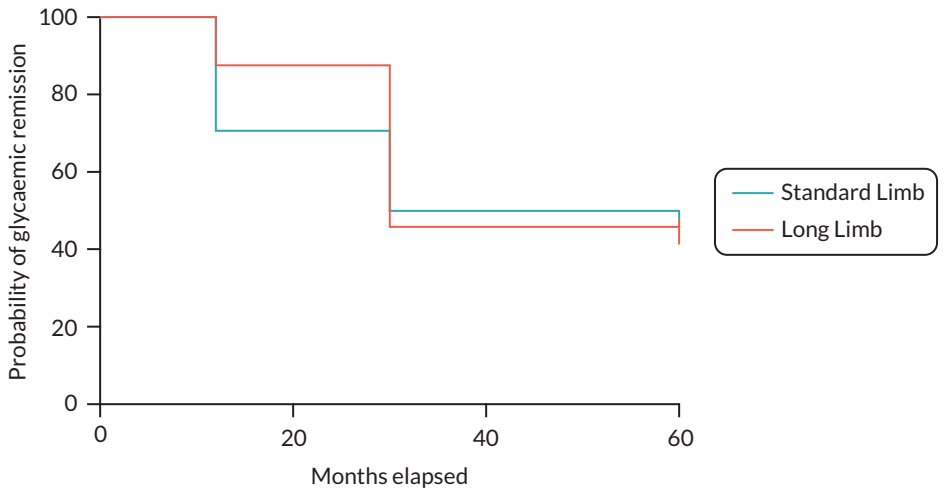


FIGURE 8 Kaplan–Meier curve of probability of diabetes remission (%) from baseline to 60-month follow-up in both trial groups.

TABLE 3 Baseline clinical characteristics of patients in diabetes remission vs. patients not in diabetes remission

	Diabetes remission		No diabetes remission		
	Standard Limb group (*n* = 6)	Long Limb group (*n* = 9)	Standard Limb group (*n* = 12)	Long Limb group (*n* = 11)	Remission vs. no remission, mean difference (95% CI)
Sex, female	4 (67%)	6 (67%)	6 (50%)	7 (63%)	N/A
Ethnicity					
Caucasian	5 (83%)	6 (67%)	10 (83%)	7 (64%)	N/A
South Asian	0 (0%)	2 (22%)	1 (9%)	3 (27%)	N/A
Afro-Caribbean	1 (17%)	1 (11%)	1 (9%)	1 (9%)	N/A
Age	54 (7)	48 (5)	48 (10)	50 (6)	N/A
Preoperative BMI (kg/m^2)	38 (1)	38 (5)	43 (3)	43 (9)	−5 (−10 to 1)
Duration of T2D (years), median (IQR)	7 (5–8)	5 (3–9)	8 (4)	7 (5–8)	N/A
Number of glucose-lowering medications preoperatively, median (IQR)	2 (2–3)	2 (2–3)	3 (2–3)	3 (2–3)	N/A
Insulin therapy preoperatively, (*n*)	1 (16%)	1 (11%)	2 (16%)	2 (18%)	N/A
Preoperative HbA1c (mmol/mol)	69 (9)	72 (20)	76 (15)	72 (12)	−3 (−10 to 4)

Notes
Categorical data are presented as n (percentage) or number (percentage).
Continuous data are presented as a mean (SD) when normally distributed or a median (IQR) when non-normally distributed.
Diabetes remission is defined as HbA1c < 48 mmol/L without glucose-lowering therapy for at > 3 months.

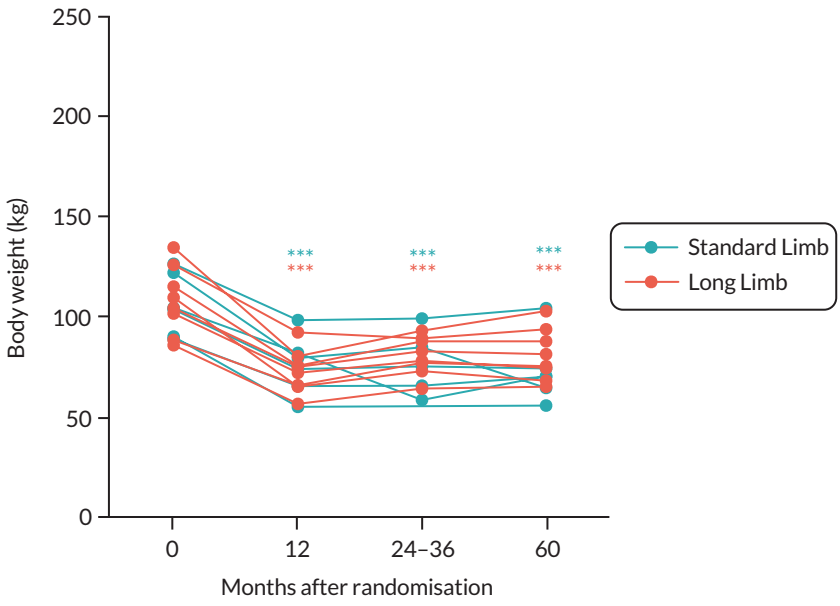


FIGURE 9 Weight loss trajectories at baseline (0 months) and at 12-, 24- to 36- and 60-month follow-up in participants that achieved glycaemic remission in the Standard Limb group (*n* = 6) and Long Limb group (*n* = 9). ***p < 0.001 vs. baseline.

receiving Long Limb RYGB achieved T2D remission (defined differently as fasting plasma glucose < 5.5 mmol/L and HbA1c < 42 mmol/mol without glucose-lowering therapy) versus Standard Limb RYGB (95% vs. 75%, respectively, p = 0.005).[8] However, this was a non-randomised retrospective cohort study. A long-term prospective study with over 7-year follow-up reported that RYGB with a long biliopancreatic limb (200 cm) and short alimentary limb (60 cm) had similar rates of T2D remission (HbA1c in the normal range without glucose-lowering medications)

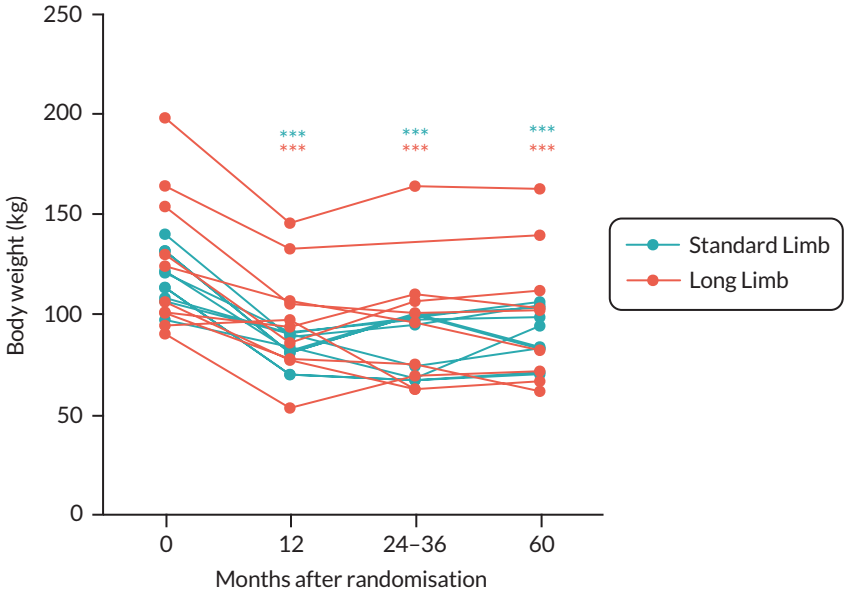


FIGURE 10 Weight loss trajectories at baseline (0 months) and at 12-, 24- to 36- and 60-month follow-up in participants that did not achieve glycaemic remission in the Standard Limb group (n = 12) and Long Limb group (n = 11). ***p < 0.001 vs. baseline.

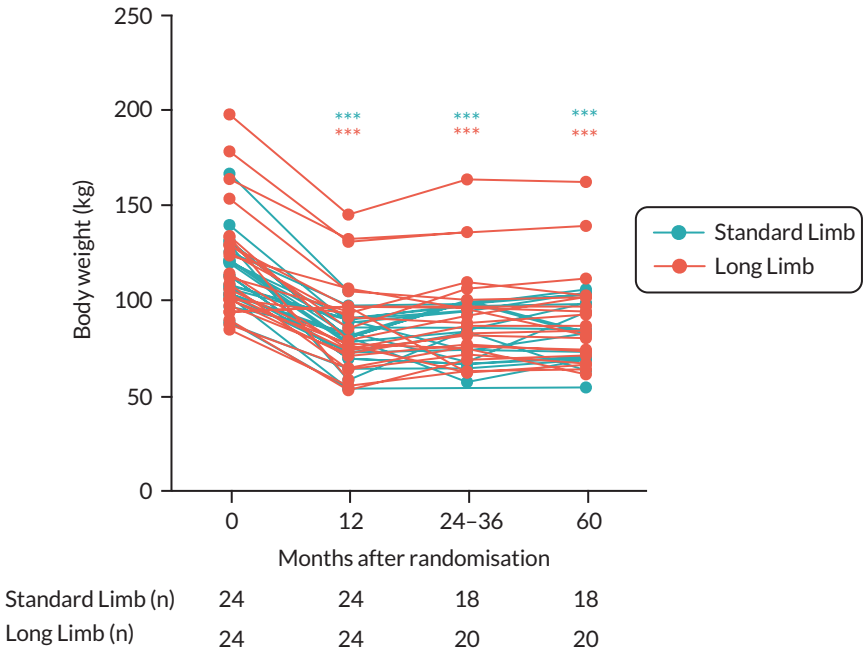


FIGURE 11 Body weight (kg) at baseline (0 months) and at 12-, 24- to 36- and 60-month follow-up. Data for individual participants are plotted. n in each trial group is denoted below 0, 12, 24–36 and 60 months. ***p < 0.001 vs. baseline.

compared to standard limb RYGB (biliopancreatic limb 60 cm, alimentary limb 150 cm) but looser stools were more frequently reported in the long biliopancreatic limb group. However, 80% of the original 187 participants with obesity, 20% of whom also had T2DM at baseline, were lost to follow-up at 7 years and therefore these long-term results are vulnerable to reporting bias.[11]

A retrospective case-control mechanistic study that kept the alimentary limb constant at 120 cm, using their versions of Standard Limb RYGB (biliopancreatic limb 87.8 ± 20.5 cm) versus Long Limb RYGB (which was longer with a biliopancreatic limb of 200 cm), reported that there were no between-group differences in postprandial concentrations of glucose and insulin during a mixed-meal test (MMT) 4 years after surgery, similar to our MMT results at 24–36 months. It should be noted that this cohort of patients did not have T2D unlike our study.[12]

There are two clinical studies reporting an improvement in glycaemia with a long biliopancreatic RYGB. A 3-year prospective study that recruited 94 people with T2D

TABLE 4 Baseline clinical characteristics of participants with < 20% weight loss and > 20% weight loss

	< 20% weight loss		> 20% weight loss		
	Standard Limb group (*n* = 4)	Long Limb group (*n* = 4)	Standard Limb group (*n* = 14)	Long Limb group (*n* = 16)	< 20% weight loss vs. > 20% weight loss, mean difference (95% CI)
Sex, female	3 (75%)	3 (75%)	10 (71%)	11 (69%)	N/A
Ethnicity					
Caucasian	3 (75%)	3 (75%)	12 (86%)	12 (81%)	N/A
South Asian	1 (25%)	1 (25%)	1 (7%)	3 (19%)	N/A
Afro-Caribbean	0 (0%)	1 (11%)	1 (7%)	0 (0%)	N/A
Age	52 (8)	44 (5)	49 (10)	43 (8)	N/A
Preoperative BMI (kg/m^2)	43 (4)	43 (6)	41 (5)	42 (7)	2 (−1 to 5)
Duration of T2D (years), median (IQR)	8 (7–9)	10 (7–14)	7 (6–8)	8 (6–9)	N/A
Number of glucose-lowering medications, median preoperatively (IQR)	3 (2–3)	3 (2–3)	3 (2–3)	3 (2–3)	N/A
Insulin therapy preoperatively, (*n*)	1 (25%)	1 (25%)	2 (14%)	2 (13%)	N/A
Preoperative HbA1c (mmol/mol)	74 (12)	76 (8)	69 (8)	71 (9)	9 (−1 to 19)

Notes
Categorical data are presented as *n* (percentage) or number (percentage).
Continuous data are presented as a mean (SD) when normally distributed or a median (IQR) when non-normally distributed.

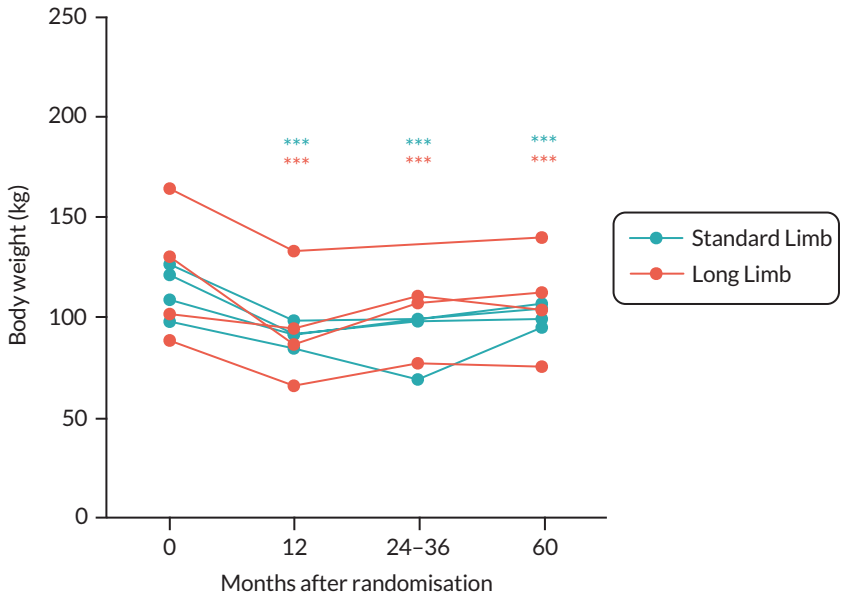
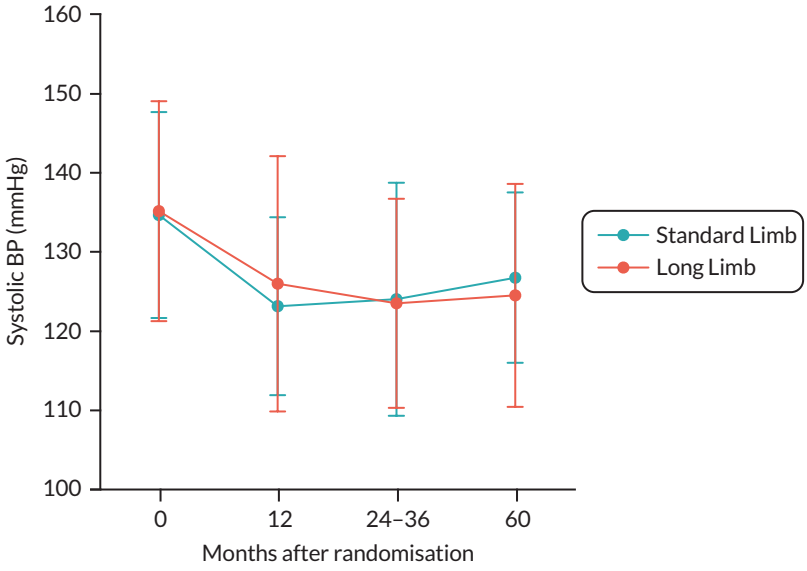


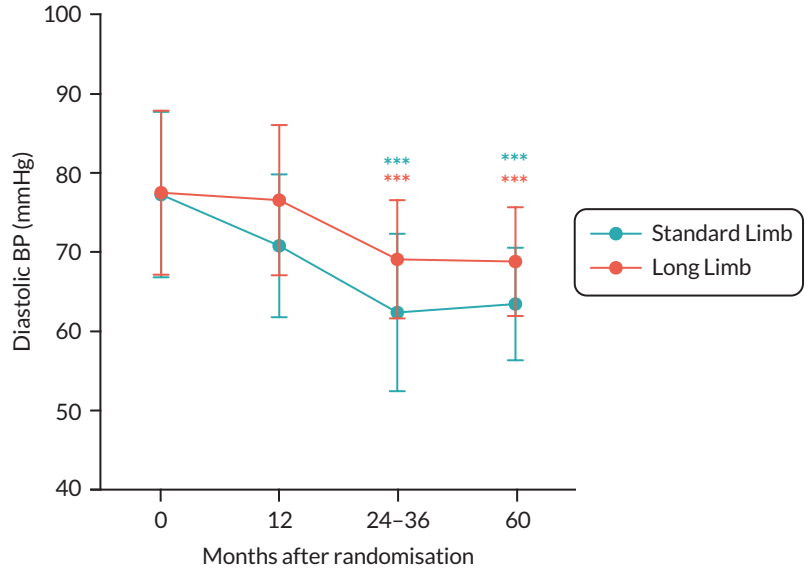
FIGURE 12 Weight loss trajectories at baseline (0 months) and at 12-, 24- to 36- and 60-month follow-up in participants that did not achieve > 20% total body weight loss in the Standard Limb group (*n* = 4) and Long Limb group (*n* = 4). *n* in each trial group is denoted below 0, 12, 24–36 and 60 months. ***p < 0.001 vs. baseline.

and obesity who underwent a long biliopancreatic limb RYGB (200 cm) with an alimentary limb of 120 cm reported that 100% of participants achieved T2D remission (achievement of non-diabetic glycaemia off medications); however, only 43% of participants reached 3 years of follow-up.[13] A retrospective analysis of 671 patients and 10-year follow-up also reported that 80% of patients receiving a long biliopancreatic limb RYGB (200 cm) achieved T2D remission compared to RYGB with a biliopancreatic limb of 60 cm.[14] However, this



Standard Limb (n)	24	24	18	18
Long Limb (n)	24	24	20	20

FIGURE 13 Measurement of systolic blood pressure at 0, 12, 24–36 and 60 months in both trial groups. Data are plotted as means (standard error of mean). *n* in each trial group is denoted below 0, 12, 24–36 and 60 months. *** $p < 0.001$ vs. baseline.



Standard Limb (n)	24	24	18	18
Long Limb (n)	24	24	20	20

FIGURE 14 Measurement of diastolic blood pressure at 0, 12, 24–36 and 60 months in both trial groups. Data are plotted as means (standard error of mean). *n* in each trial group is denoted below 0, 12, 24–36 and 60 months. *** $p < 0.001$ vs. baseline.

study was retrospective in nature and T2D remission was not defined.

Our prospective randomised and double-blinded study with 80% follow-up at 5 years is more robust than the previous prospective studies, where > 50% of patients have been lost to follow-up and non-randomised, and retrospective studies in avoiding confounding from baseline differences.

Both trial groups in our study demonstrated a reduction in postprandial glucose concentrations during mixed-meal tolerance test comparing baseline and 24–36 months without a corresponding reduction in postprandial insulin concentrations, although there was a tendency towards lower levels. We have previously shown that both trial groups experienced an improvement in hepatic and peripheral insulin sensitivity, assessed by the gold standard

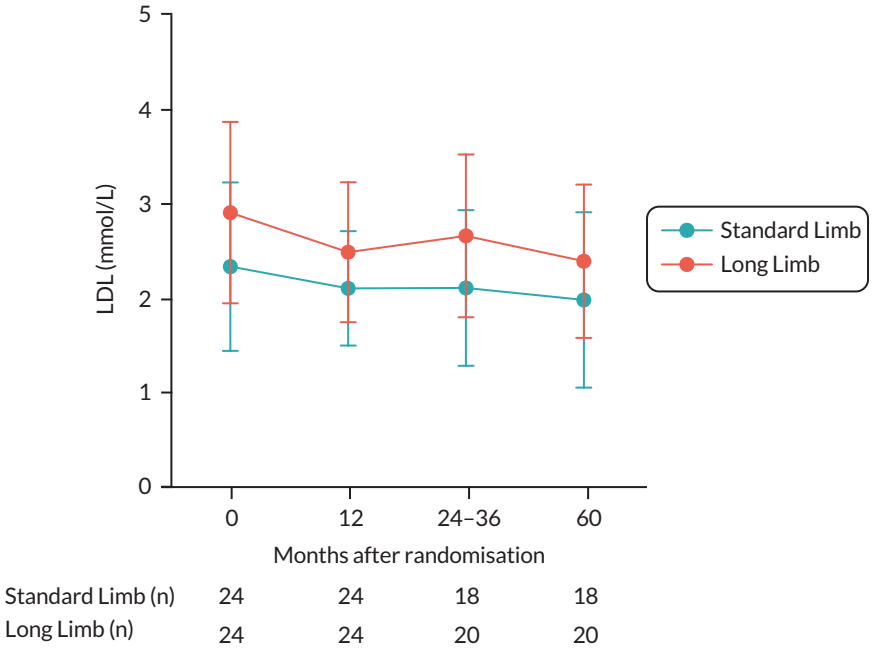


FIGURE 15 Measurement of LDL at 0, 12, 24–36 and 60 months in both trial groups. Data are plotted as means (standard error of mean). *n* in each trial group is denoted below 0, 12, 24–36 and 60 months. *** $p < 0.001$ vs. baseline. LDL, low-density lipoprotein cholesterol.

TABLE 5 Postoperative adverse events and complications during the 5-year follow-up

Adverse event	Long Limb RYGB *n* = 24	Standard Limb RYGB *n* = 24
Cardiovascular	0	0
Gastrointestinal		
Anastomotic stricture	1	0
Anastomotic ulcer	0	1
Perioperative bleeding	2	0
Gallstones	1	0
Abdominal pain	1	0
Laparotomy for purulent peritonitis	1	0
Gastritis	1	0
Diarrhoea	1	2
Constipation	5	7
Infections		
Would infection	4	2
Pneumonia	4	2
Viral tonsillitis	1	0
Soft tissue and musculoskeletal		
Incisional hernia	1	0
Limb fracture	0	1
Nutritional and metabolic		

TABLE 5 Postoperative adverse events and complications during the 5-year follow-up (*continued*)

Adverse event	Long Limb RYGB *n* = 24	Standard Limb RYGB *n* = 24
Intravenous treatment for dehydration	0	1
Acute kidney injury	0	2
Anaemia	5	5
Vasovagal	1	3
Hypoglycaemic episode	2	3
Adverse event leading to hospitalisation	5 (in 3 participants)	4 (in 4 participants)
Clavien-Dindo classification of complications (grades)		
I	17	20
II	14	9
IIIa	0	0
IIIb	0	0
IV	0	0
V	0	0
Total	31	29

Notes
Clavien-Dindo classification:
- Grade I: any deviation from the normal postoperative course not requiring surgical, endoscopic or radiological intervention. This includes the need for certain drugs (e.g. antiemetics, antipyretics, analgesics, diuretics and electrolytes), treatment with physiotherapy and wound infections that are opened at the bedside.
- Grade II: complications requiring drug treatments other than those allowed for grade I complications; this includes blood transfusion and total parenteral nutrition (TPN).
- Grade III: complications requiring surgical, endoscopic or radiological intervention.
  - Grade IIIa: intervention not under general anaesthetic.
  - Grade IIIb: intervention under general anaesthetic.
- Grade IV: life-threatening complications; this includes central nervous system complications (e.g. brain haemorrhage, ischaemic stroke, subarachnoid haemorrhage) that require intensive care, but excludes transient ischaemic attacks (TIAs).
  - Grade IVa: single-organ dysfunction (including dialysis).
  - Grade IVb: multiorgan dysfunction.
- Grade V: death of the patient.

euglycaemic-hyperinsulinaemic clamp, 12 months after surgery,[1,2] and our findings suggest that this phenomenon persists to at least 24–36 months.

The results of our study are also in keeping with several other clinical studies in which a Long Limb RYGB showed no additional benefit in terms of weight loss at 12 months,[15] 24 months[16] and 60 months,[17,18] systolic and diastolic blood pressure at 24 months,[14] 48 months[19] and 60 months,[11,17] and LDL cholesterol at 48 months.[19] Similar to our study, a within-group reduction in diastolic blood has been observed for both Standard Limb and Long Limb RYGB at 48-month follow-up but there was no difference between the groups.[19] The long-term safety profile of both procedures was also similar, with no signal for excess malabsorption of macro or micronutrients in the Long Limb group.

Taken together, the results of our study and that of previous research suggest that Long Limb RYGB is equivalent to Standard Limb RYGB in terms of efficacy and safety in the medium and long term for people with T2D and obesity. Although there are no other RCTs comparing Standard Limb RYGB to Long Limb RYGB with 60-month outcome data, there are at least four other RCTs performed in the USA,[20,21] Taiwan,[21] Italy[22] and Brazil[23] that have reported 60-month clinical outcomes in people with T2D and obesity undergoing Standard Limb RYGB.

The profound and durable reductions in glycaemia in our multi-ethnic British cohort are consistent with previous 60-month RCTs involving people with T2D and obesity undergoing standard RYGB surgery. Diabetes remission in our trial was defined as a HbA1c ≤ 48 mmol/mol with no glucose-lowering medications for ≥ 3 months, which

is the most up-to-date definition recommended by the American Diabetes Association in 2021.[10] There are three other RCTs in people with T2D and obesity that underwent Standard Limb RYGB reporting glycaemic remission at 60-month follow-up using a HbA1c of ≤ 48 mmol/mol, but in those studies their definition required that patients were not taking glucose-lowering medications for ≥ 12 months. Two of these single-site RCTs reported diabetes remission in 39%[20] and 42%[22] in US and Italian populations respectively, which is similar to our trial. The third RCT investigated an intensive lifestyle intervention plus medical therapy with and without RYGB in people with T2D and obesity and they reported a diabetes remission rate of 16% at 60 months after RYGB surgery in two sites in Taiwan and the USA. In that RCT, however, the primary outcome was a triple end-point of a HbA1c < 53 mmol/mol, systolic blood pressure < 130 mmHg and LDL cholesterol < 2.6 mmol/L.[21] In all three RCTs,[20–22] like our trial, there was a reduction in the use of glucose-lowering medications during the 60-month follow-up. A single-site RCT in Brazil investigating best medical therapy with and without standard RYGB found that 60% of patients with T2D and obesity achieved a HbA1c ≤ 48 mmol/mol 60 months after RYGB, but there was a more liberal use of glucose-lowering therapy in cases of T2D relapse after RYGB, and the median number of antidiabetic medications at 60 months in the RYGB group was higher at 3 (2–4).[23]

Weight loss was also durable in both trial groups and comparable to previous RCTs which have reported weight loss of 22%,[21] 23%[20,23] and 28%[22] at 60-month follow-up in people with T2D and obesity receiving standard RYGB surgery. However, the two-site RCT conducted in the USA and Taiwan reported the least weight loss of 22%[21] and their cohort of patients had a higher baseline HbA1c of 82 mmol/mol compared to the baseline HbA1c in this trial (73 mmol/mol). The single-site RCT in Italy (baseline HbA1c 70 mmol/mol) reported weight loss of 28%.

Our 60-month cardiovascular risk factor outcomes are similar to other RCTs in people with T2D and obesity receiving Standard Limb RYGB. There was a numerical reduction in LDL cholesterol of 0.4–0.5 mmol/L at 60-month follow-up in both trial groups and this magnitude of reduction is consistent with the three RCTs[21–23] that reported LDL cholesterol at 60-month follow-up. In all these studies including ours, patients were either at or close to the National Institute for Health and Care Excellence LDL cholesterol target of < 2.0 mmol/L at baseline, and levels well below this target were achieved at 60-month follow-up by the trial participants in the aforementioned studies. One RCT reported no change in LDL cholesterol concentrations at 60 months; however, in this trial, only 20% of patients were taking lipid-lowering therapy at the 60-month follow-up[20] which contrasts with the reported 40–70% of patients taking lipid-lowering medications in the aforementioned RCTs and the present trial.[21–23]

Neither RYGB variant in our trial was associated with a statistically significant reduction in systolic blood pressure at the 60-month follow-up and this finding is consistent with other RCTs.[20–23] There do however appear to be differences across RCTs in the percentage of patients on antihypertensive therapy 60 months after RYGB. Like the RCT conducted in a Brazilian cohort, > 60% of our patients were on antihypertensive therapy while other RCTs have reported rates of < 50%.[20–22] Interestingly, in our study and the RCT in Brazil, there was a significant reduction in diastolic blood pressure 60 months after RYGB. Many patients in our trial and the RCT in Brazil that experienced T2D relapse after RYGB were given SGLT-2 inhibitors, GLP-1 receptor analogues or a combination of the two, and these medications have a favourable impact on diastolic blood pressure.[24,25] These drugs were not approved at the time of the other RCTs,[20–22] and this may explain the difference in diastolic blood pressure.

The medium- and long-term findings of our trial are strengthened by the study design including the double-blinded randomised approach, the measurement of the entire length of the small intestine during surgery and the robust way of ensuring that the surgical approach was consistent between surgeons and in line with a pre-agreed standard operation procedure. We also had a dedicated research team to conduct the extension study and their hard work achieved 80% follow-up at 60 months notwithstanding two national lockdowns due to the COVID-19 pandemic.

Limitations of this study are that the biliopancreatic limb was elongated to a fixed length of 150 cm. We also defined Standard Limb RYGB as one with a biliopancreatic limb of 50 cm and an alimentary limb of 100 cm based on the popularity of this design in surgical practice. However, there is substantial variation in practice internationally. Another limitation is that our original investigation was an experimental medicine study with mechanistic outcomes and not a clinical trial. It was not powered to detect differences in clinical outcomes and therefore we cannot derive definitive conclusions on the relative clinical efficacy of the two variants of RYGB. Lastly, we achieved 80% follow-up at 60 months, and loss to follow-up may have limited our statistical power to detect differences in the clinical outcomes.

Patient and public involvement

Aim

Patient and public involvement (PPI) was undertaken to ensure that our research priorities aligned with the voices of people living with T2D and obesity so that our findings would be directly beneficial to patients.

Methods

We worked closely and developed an active relationship with PPI representatives from the application process to dissemination of results: Ms Georgina Hayman, the lead of the British Obesity Surgery Patient Association (BOSPA) West London branch and Dr Shamil Chandaria, Patron of the National Obesity Forum, an independent charity supporting patients and healthcare professionals. Ms Danielle Neal, the communications and public and patient involvement (PPI) officer, NIHR North West London approached the Diabetes Research Network PPI group. Involving a diverse range of people with lived experience of T2D and obesity alongside the charity sector directly informed considerations around study design, development, creation of patient information resources, study management and writing and dissemination of findings.

Results of patient and public involvement input

Patient and public involvement directly impacted our research. All three PPI representatives contributed to the development of the grant application, starting from its design, the choice of research topics and dissemination of the study findings through their organisations. The Trial Steering Committee and researchers conducting the day-to-day running of the trial and obtained feedback from patients to optimise the conduct of the trial to make it more acceptable. Numerous minor and major modifications were made to the way the clinical and mechanistic assessments and follow-up were performed as a result of this feedback. This helped the trial immensely with recruitment and retention. Only one patient dropped out of the trial.

Discussion of patient and public involvement input

During the early course of the project the lead for BOSPA conducted patient support groups throughout our study. These support groups were invaluable and served to support patients following their operations and acted as an avenue for the patient voice to be heard. Patients were so excited about contributing to this important study that many refused to accept the allocated reimbursement at the end of the trial.

Reflections and critical perspective

The involvement of patients and PPI representatives was key at all stages of our study. The study team's open dialogue with our participants during our extension study ensured that adherence was not impacted by the COVID-19 pandemic. Participants told us they wanted to attend their follow-up visits but did not want to travel via public transport although at the time this was allowed. We listened to our participants and organised taxis to and from the clinical research facility which allowed our research to continue during the COVID-19 pandemic when it was safe to do so. Listening to our participants through a formal PPI session at the end of the extension trial provided the research team with invaluable insight into the participant experience of research. Our participants enjoyed the mechanistic study visits because it helped them develop a deeper understanding of their T2D and obesity. They also enjoyed the clinical follow-up visits because it offered the opportunity to better understand how RYGB can improve T2D and obesity. Maintaining PPI throughout our trial has not only been invaluable to the research team but also for our participants. Our PPI session at the end of the extension trial helped us realise that our research has brought participants together through similar lived experiences so much so that friendships between our participants have formed. These friendships act as an important source of social support for people living with T2D and obesity. Two of our participants have explained to us that RYGB has transformed their lives for the better and they would like to be patient advocates for RYGB.

Equality, diversity and inclusion

In our study, 15% of participants were South Asian, 8% were Black British (Caribbean) and 77% were White European. It is estimated that T2D affects 8% of the South Asian population and 8% of the Black British population in the UK.[26] In our study, we had a higher number of people from the South Asian community compared to national data because the prevalence of type 2 diabetes in this ethnic group is higher in the local communities surrounding the two recruiting sites in North West and South London used in this study. Our local data suggest that ~15% of the South Asian community have T2D in North West and South London. The rates of South Asian and black ethnic groups in our study are higher than previous RCTs involving people with T2D and obesity undergoing RYGB surgery.[20–23] In our trial, 64% of our participants were women and this is similar to the 70% of women in the UK undergoing bariatric surgery.[27] The percentage of female participants in our study is also aligned with other previous RCTs involving people with T2D and obesity undergoing RYGB surgery.[20–23] Hence,

our study is representative of the types of patients that would be expected to undergo metabolic surgery for T2D and obesity in the UK, and would be expected to be more representative than studies from other countries.[13,14]

Impact and learning

Should further trials on modifying the small intestinal limbs of RYGB be planned, we recommend using ratios of limbs to the entire small intestine length in order to account for variability in total small intestinal length in humans.

Research recommendations

The common limb is the site of small intestinal glucose absorption following RYGB.[28] There is evidence to suggest that a modified RYGB with a long alimentary limb and a short common channel may enhance the already powerful glucose-lowering effects of RYGB[28–30] and future trials should consider this design. Interrogating intestinal remodelling and its impact on postoperative glucose metabolism could also be considered by taking small intestinal biopsies intraoperatively and then endoscopically postoperatively.

Our work adds to the large body of evidence that RYGB is an effective treatment for long-term glucose control and weight loss. However, like previous long-term RCTs involving people with T2D and obesity undergoing RYGB, we found that there were responders and non-responders in terms of glycaemic remission and weight loss.[20–23] Just over 1 in 2 of our trial patients experienced T2D relapse after RYGB and approximately 1 in 5 did not have > 15% weight loss, a figure which is considered clinically significant for glycaemic remission in T2D.[31] Non-responders to RYGB for T2D and obesity will require additional treatment with pharmacotherapy. A subsequent question that needs addressing with future trials is the additive benefits of RYGB and best current medical therapy to include GLP-1 receptor agonists, GLP-1/GIP receptor agonists and SGLT-2 inhibitors. Perhaps a combinational approach may slow the progression of T2D and reduce the associated morbidity and mortality in the long term.

Conclusion

In conclusion, this extension study has demonstrated the substantial clinical benefit of RYGB to people living with T2D and obesity. However, this trial did not demonstrate a clinical rationale for the elongation of the biliopancreatic limb of RYGB to 150 cm to enhance metabolic outcomes for T2D and obesity.

Additional information

CRediT contribution statement

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Tina Mazaheri: Project administration, Formal analysis, Writing – reviewing and editing.

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Harvinder Chahal: Methodology, Writing – reviewing and editing.

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Belén Pérez-Pevida: Project administration, Formal analysis, Writing – reviewing and editing.

Ameet Patel: Investigation.

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Dr Paul Bassett was the trial statistician.

Dr Victoria Salem is an independent researcher from Imperial College London and was responsible for the randomisation of trial patients.

Patient data statement

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that they are stored and used responsibly.

Data-sharing statement

Data are archived at the National Institute for Health Research Imperial Clinical Research Facility. All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

Ethics statement

The trial was approved by the West London Research Ethics Committee (reference number 15/LO/0813) and registered in the International Standard Randomised Controlled Trial registry (as ISRCTN 15283219) on 29 June 2015. Written informed consent was obtained from all patients prior to participation in the trial.

Information governance statement

Imperial College London is committed to handling all personal information in line with the UK Data Protection Act (2018) and the General Data Protection Regulation (EU GDPR) 2016/679. Under the Data Protection legislation, Imperial College London is the Data Controller, and you can find out more about how we handle personal data, including how to exercise your individual rights and the contact details for our Data Protection Officer here: https://www.imperial.ac.uk/admin-services/secretariat/information-governance/data-protection/contact-us/.

Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/MYWG6289.

Primary conflicts of interest: Stephen Bloom and Tricia Tan are shareholders in, and consultants for, Zihipp Ltd., an Imperial College spinout company that is developing gut hormone analogues for the treatment of obesity. Francesco Rubino declares that he is a shareholder in Metabolic Health International Ltd and London Metabolic and Bariatric Surgery Ltd.

Department of Health and Social Care disclaimer

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Study registration

Current Controlled Trials ISRCTN15283219.

Publications

Miras AD, Kamocka A, Tan T, Pérez-Pevida B, Chahal H, Moorthy K, *et al.* Long limb compared with standard limb Roux-en-Y gastric bypass for type 2 diabetes and obesity: the LONG LIMB RCT. *Efficacy Mech Eval* 2021;**8**:1–54.

Miras AD, Kamocka A, Pérez-Pevida B, Purkayastha S, Moorthy K, Patel A, *et al.* The effect of standard versus longer intestinal bypass on GLP-1 regulation and glucose metabolism in patients

with type 2 diabetes undergoing Roux-en-Y gastric bypass: The long-limb study. *Diabetes Care* 2021;**44**:1082–90.

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This synopsis provides an overview of the research award Are gut hormone changes why the long-limb gastric bypass is more effective than the standard-limb gastric bypass in improving type 2 diabetes mellitus? Extended Follow-up. Other articles published as part of this thread are: [LINKS to other articles]. For more information about this research please view the award page (https://www.fundingawards.nihr.ac.uk/award/NIHR130639)

About this synopsis

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List of abbreviations

BMI	body mass index
GIP	glucose-dependent insulinotropic peptide
GLP-1	glucagon-like peptide-1
LDL	low-density lipoprotein cholesterol
RYGB	Roux-en-Y gastric bypass surgery
T2D	type 2 diabetes

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