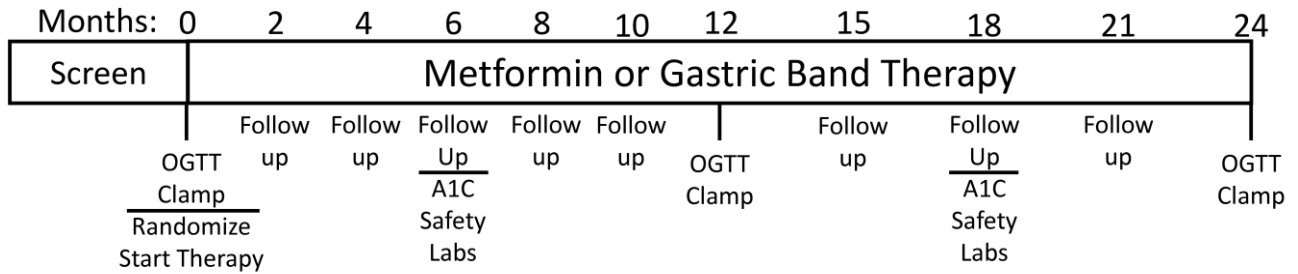
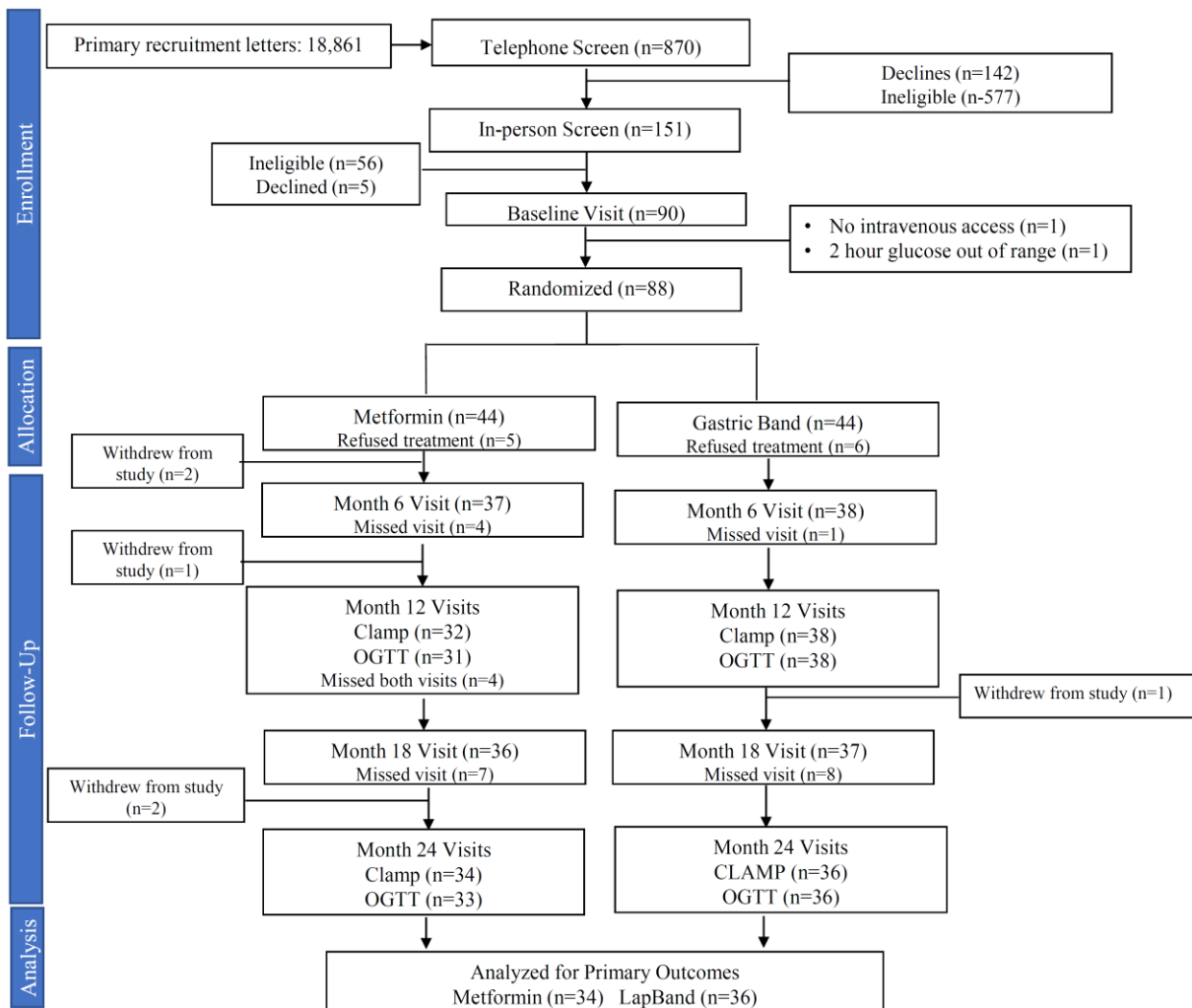


SUPPLEMENTARY DATA

Supplementary Figure 1. Overview of Study Design. Procedures are described in text.

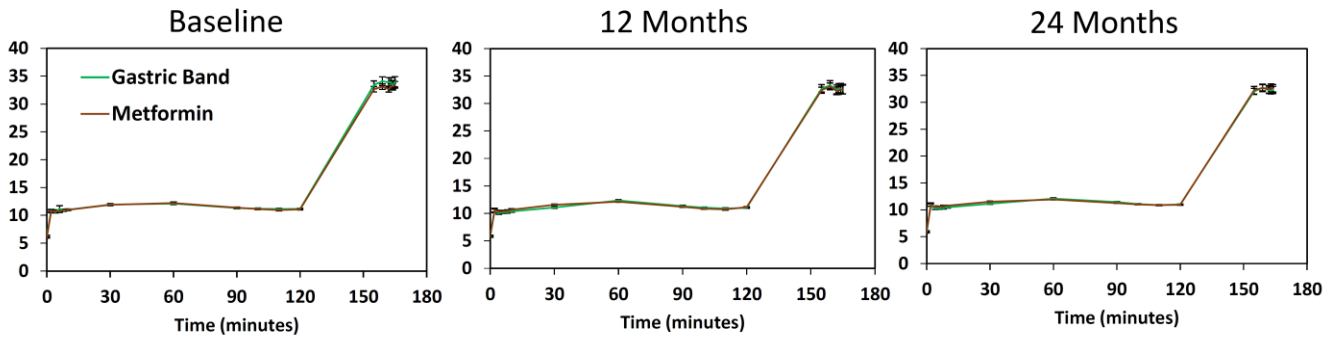


Supplementary Figure 2. Consort diagram of enrollment and progress through the study.



SUPPLEMENTARY DATA

Supplementary Figure 3. Plasma glucose levels during glucose clamp studies at baseline, 12 and 24 months. Glucose was injected at t=0 minutes to raise plasma glucose to ~11.1 mmol/L. An infusion of glucose was used to clamp plasma glucose at ~11.1 mmol/L until 120 minutes, then raise plasma glucose to >25 mmol/L over at least 30 min, when arginine (5 grams) was injected. Primary outcomes were assessed during steady state (100-120 minutes) and maximal response (five minutes after arginine injection) periods. Data are mean \pm se.



SUPPLEMENTARY DATA

Supplementary Table 1. Impact of treatments on secondary clamp outcomes*

Clamp Secondary Outcomes	Gastric Band (n=36)			Metformin (n=34)			Intergroup P-value †	
	Baseline	24 Months	P-value ‡	Baseline	24 Months	P-value ‡	Baseline	24-Month
Acute [‡] C-peptide response to glucose (ACPRg; nmol/L) adjusted for M/I [§]	0.43 (0.31, 0.59)	0.59 (0.44, 0.78)	0.014	0.48 (0.34, 0.66)	0.48 (0.35, 0.65)	0.33	0.65	0.17
Acute [‡] insulin response to glucose (AIRg; pmol/L) adjusted for M/I [§]	167 (121, 221)	213 (164, 270)	0.015	178 (129, 236)	187 (141, 242)	0.12	0.77	0.45
Maximum [¶] insulin response (AIRmax; pmol/L) adjusted for M/I [§]	3029 (2485, 3692)	2569 (2154, 3063)	0.30	2916 (2379, 3575)	2468 (2059, 2958)	0.045	0.79	0.69
Steady-state [#] insulin (pmol/L)	591 (454, 770)	404 (313, 520)	<0.0001	492 (375, 645)	432 (333, 561)	0.022	0.34	0.02
Steady-state [#] glucose infusion rate (mmol/kg/min)	0.19 (0.16, 0.23)	0.19 (0.16, 0.22)	0.90	0.16 (0.13, 0.20)	0.18 (0.15, 0.21)	0.39	0.29	0.96
Clinical Glucose Status**			0.018			0.033	0.46	0.63
Normal (n, %)	0 (0%)	8 (22%)		0 (0%)	5 (15%)			
IGT (n, %)	18 (50%)	16 (45%)		20 (59%)	15 (44%)			
Diabetes (n, %)	18 (50%)	12 (33%)		14 (41%)	14 (41%)			

Abbreviations: IGT=impaired glucose tolerance

* Data presented are geometric means (95% CI) from 70 individuals who had data on primary outcomes at 24 months or n (%) for categorical variables

† P-value testing for difference between groups at baseline and 24-months after adjusting for baseline value of the variable

‡ P-value testing for change within group

§ M/I is defined as mean glucose infusion rate divided by mean insulin concentration at steady state (100, 110, 120 min) during glucose clamp

‖ Mean incremental plasma concentration curve for first 10 min above concentrations before glucose injection to initiate glucose clamp

¶ AIRmax is acute insulin release, maximal, defined as mean incremental insulin response above concentrations before arginine injection

Mean of measurements made at 100, 110, 120 min during glucose clamp at ~200 mg/dl

** By American Diabetes Association Criteria

SUPPLEMENTARY DATA

Supplementary Table 2. Impact of treatments on cardiovascular and hepatic outcomes*

	Gastric Band (n=36)			Metformin (n=34)			Intergroup P-value [†]	
	Baseline	24 Months	P-value [‡]	Baseline	24 Months	P-value [‡]	Baseline	24-Month
Systolic BP (mmHg)	127.1 ± 10.5	124.8 ± 11.3	0.19	126.4 ± 10	128.9 ± 11.6	0.26	0.79	0.08
Diastolic BP (mmHg)	78.3 ± 7.5	76.4 ± 7.6	0.11	75.9 ± 8.1	77.6 ± 8.0	0.26	0.23	0.15
Total cholesterol (mmol/L)	4.5 ± 0.7	4.4 ± 0.8	0.55	4.5 ± 0.9	4.5 ± 1.1	0.84	0.92	0.57
LDL cholesterol (mmol/L)	2.7 ± 0.7	2.5 ± 0.7	0.40	2.7 ± 0.8	2.6 ± 0.9	0.49	0.87	0.80
HDL cholesterol (mmol/L)	1.2 ± 0.3	1.3 ± 0.3	0.001	1.2 ± 0.3	1.3 ± 0.3	0.004	0.74	0.30
VLDL cholesterol (mmol/L)	0.60 (0.29, 1.24)	0.50 (0.24, 1.05)	0.007	0.56 (0.24, 1.32)	0.59 (0.27, 1.3)	0.44	0.67	0.009
Total triglycerides (mmol/L)	1.32 (0.62, 2.68)	1.09 (0.52, 2.3)	0.007	1.23 (0.52, 2.89)	1.28 (0.58, 2.82)	0.43	0.47	0.009
Alanine aminotransferase (U/L)	26.1 ± 15.2	16.1 ± 6.3	0.001	26.7 ± 12.4	22.1 ± 9.1	0.04	0.85	0.001

Abbreviations: BP=blood pressure; LDL= low-density lipoprotein; HDL=high-density lipoprotein; VLDL=very low-density lipoprotein

* Data presented are mean ± se for normally distributed variables, geometric means (95% CI) for skewed variables, from 70 individuals who had data on primary outcomes at 24 months.

[†] P-value testing for difference between groups at baseline and 24-month after adjusting for baseline value of the variable

[‡] P-value testing for change within group

SUPPLEMENTARY DATA

Supplementary Table 3. Number (%) of individuals with adverse events

	All (n=88)	Gastric Band (n=44)	Metformin (n=44)
Stomach Discomfort/Pain	11 (13%)	---	11 (25%)
Diarrhea	3 (3%)	---	3 (7%)
Breast Cancer*	2 (2%)	2 (5%)	---
Port Revision/Replacement	2 (2%)	2 (5%)	---
Protracted Vomiting/Band Slippage*	2 (2%)	2 (5%)	---
Depression and GI issues	1 (1%)	---	1 (2%)
Heartburn	1 (1%)	---	1 (2%)
Nausea	1 (1%)	---	1 (2%)
Lack of Energy	1 (1%)	---	1 (2%)
Upper GI for Dysphagia	1 (1%)	1 (2%)	---
Laparoscopic Cholecystectomy*	1 (1%)	1 (2%)	---
Motor Vehicle Accident*	1 (1%)	---	1 (2%)
Elective Gastric Sleeve Surgery*	1 (1%)	---	1 (2%)

* Serious Adverse Events

SUPPLEMENTARY DATA

APPENDIX

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