Web additional material

Table S1. Panel A: Additional anthropometric and biochemical data at baseline and 5 years. Panel B: Additional prevalence and remission data for CV risk factors at baseline and 5 years.

Per protocol data (crossovers excluded). See below, for definitions and thresholds used. RYGB, Roux-en-Y gastric bypass; SD, standard deviation; n, number of patients; CI, confidence interval; Apo A1, apolipoprotein A1; Apo B, apolipoprotein B; WCC, white cell count; ALP, alkaline phosphatase; Vitamin D, 25-hydroxyvitamin D; nd, not determined; nc, not calculable.

Panel A	***RYGB adolescents***							***Control adolescents***		***RYGB vs. Control adolescents***		
	Raw data				***Within group (RYGB Adolescents) mixed-model change***			***Raw data***		***Between group mixed-model difference***		
	Baseline		***5 years***		***Baseline to 5 years***			***5 years***		***5 years***		
Variable	**Mean (SD)**	**n**	**Mean**	**n**	**Mean change**	**95% CI**	**p-value**	**Mean (SD)**	**n**	**Mean difference**	**95% CI**	**p-value**
Apo A1 (g/L)	1·2 (0·2)	80	1·6 (0·3)	76	0·4	0·3 to 0·5	<0·001	1·2 (0·2)	38	0·34	0·2 to 0·4	<0·001
Apo B (g/L)	0·9 (0·2)	80	0·7 (0·2)	76	-0·15	-0·2 to 0·1	<0·001	1·0 (0·2)	38	-0·24	-0·3 to -0·2	<0·001
WCC ($x10^9$/L)	8·2 (1·7)	77	5·8 (1·2)	31	-2·25	-2·8 to -1·7	<0·001	8·4 (1·9)	20	-2·57	-3·5 to -1·6	<0·001
Bilirubin (µmol/L)	9·6 (5·3)	75	7·1 (4·0)	76	-2·4	-3·4 to -1·3	<0·001	7·9 (4·3)	40	-0·8	-2·4 to 0·8	0·331
Albumin (g/L)	40·1 (3·8)	78	39·0 (3·7)	72	-1·1	-2·1 to -0·2	0·019	39·2 (4·5)	38	-0·3	-1·9 to 1·4	0·767
ALP (µkat/L)	1·7 (0·6)	80	1·2 (0·3)	75	-0·5	-0·6 to -0·4	<0·001	1·2 (0·3)	38	0·0	-0·1 to 0·2	0·470
Sodium (mmol/L)	140·6 (2·4)	78	140·6 (2·1)	74	0·11	-0·6 to 0·8	0·748	139·8 (2·7)	42	0·82	-0·1 to 1·8	0·093
Potassium (mmol/L)	4·1 (0·3)	77	3·9 (0·3)	75	-0·12	-0·2 to 0·0	0·003	4·1 (0·3)	41	-0·18	-0·3 to -0·1	0·005
Creatinine (µmol/L)	61·5 (9·3)	80	61·9 (9·2)	72	0·35	-1·9 to 2·6	0·775	62·0 (11·5)	40	-0·03	-4·2 to 4·2	0·988
Iron (µmol/L)	13·1 (5·2)	77	15·0 (9·1)	76	1·86	-0·5 to 4·2	0·118	14·1 (6·2)	38	0·91	-2·0 to 3·8	0·533
Ferritin (pmol/L)	135·8 (90·4)	65	54·8 (59·3)	75	-72·84	-101·7 to -44·0	<0·001	210·4 (170·8)	31	-155·61	-217·5 to -93·7	<0·001
Vitamin B12 (pmol/L)	315·2 (95·9)	74	323·8 (238·6)	74	15·17	-45·9 to 76·2	0·628	304·8 (112·4)	31	18·96	-49·0 to 87·0	0·582
Vitamin D (nmol/L)	52·0 (19·0)	33	43·5 (20·6)	73	-8·62	-16·0 to -1·2	0·022	49·4 (22·4)	35	-5·87	-14·7 to 3·0	0·192
Calcium (mmol/L)	2·3 (0·1)	78	2·3 (0·1)	72	-0·04	-0·1 to 0·0	<0·001	2·3 (0·1)	39	-0·05	-0·1 to 0·0	0·011
Parathyroid hormone (pmol/L)	nd	0	7·2 (3·6)	75	nc	nc	nc	5·2 (2·0)	37	2·01	1·0 to 3·1	<0·001

Table S2. Additional prevalence and remission data for CV risk factors at baseline and 5 years.

Per protocol data (crossovers excluded). See below, for definitions and thresholds used. RYGB, Roux-en-Y gastric bypass; n, number of patients; CI, confidence interval; WCC, white cell count; ALP, alkaline phosphatase; Vitamin D, 25-hydroxyvitamin D; nc, not calculable; *number in resolution calculation lower than number positively identified at baseline owing to missing data.

Panel B	***RYGB adolescents***						**p-value**	***Control adolescents***		**p-value**
	Baseline		**5 years**		**Resolution**		**RYGB Baseline vs. 5 years**	**5 years**		**RYGB 5 years vs. Controls 5 years**
Variable	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**		**n**	**% (95% CI)**	
Elevated WCC	7/77	9·1 (3·7 to 17·8)	0/31	0·0 (0·0 to 11·2)	1/1*	100·0 (2·5 to 100·0)	1·000	4/20	20·0 (5·7 to 43·7)	0·019
Low Albumin	2/78	2·6 (0·3 to 9·0)	9/72	12·5 (5·9 to 22·4)	1/1*	100·0 (2·5 to 100·0)	0·021	4/38	10·5 (2·9 to 24·8)	1·000
Elevated ALP	0/80	0·0 (0·0 to 4·5)	0/75	0·0 (0·0 to 4·8)	nc	nc	nc	0/38	0·0 (0·0 to 9·3)	nc
Elevated creatinine	1/80	1·3 (0·0 to 6·8)	0/72	0·0 (0·0 to 5·0)	1/1	100·0 (2·5 to 100·0)	1·000	0/40	0·0 (0·0 to 8·8)	nc
Vitamin D insufficiency	16/33	48·5 (30·8 to 66·5)	46/73	63·0 (50·9 to 74·0)	4/16	25·0 (7·3 to 52·4)	0·267	20/35	57·1 (39·4 to 73·7)	0·674
Vitamin D deficiency	4/33	12·1 (3·4 to 28·2)	20/73	27·4 (17·6 to 39·1)	2/4	50·0 (6·8 to 93·2)	0·065	7/35	20·0 (8·4 to 36·9)	0·482
Low Vitamin B12	1/74	1·4 (0·0 to 7·3)	16/73	21·9 (13·1 to 33·1)	0/1	0·0 (0·0 to 97·5)	<0·001	2/31	6·5 (0·8 to 21·4)	0·051
Low ferritin	5/65	7·7 (2·5 to 17·0)	50/75	66·7 (54·6 to 77·1)	2/4*	50·0 (6·8 to 93·2)	<0·001	3/31	9·7 (2·0 to 25·8)	<0·001
Low iron	15/76	19·7 (11·5 to 30·5)	22/76	28·9 (19·1 to 40·5)	7/12*	58·3 (27·7 to 84·8)	0·093	10/38	26·3 (13·4 to 43·1)	0·828

Table S3. Details of quality of life outcomes from SF-36 questionnaire.

Panel A shows data from SF-36 (short-form 36 questionnaire) scores. Asterisks indicate significant improvement between baseline and 5 years among RYGB adolescents. Panel B shows data from SF-36 Physical and Mental Component Scores and OP-14 (obesity-related problem scale) scores. A higher score in SF-36 domains indicates better function, whereas a higher OP-14 score indicates greater dysfunction. Both panels show data at baseline and 5 years after Roux-en-Y gastric bypass (RYGB) and panel A also shows data from control patients at 5 years following conservative management (CON) for adolescent severe obesity.

	RYGB adolescents					**Control adolescents**	**RYGB vs. CON, 5 years**		
Variable	**BL, mean (SD)**	**5 years, mean (SD)**	**Mean change**	**95% CI**	**p-value**	**5 years, mean (SD)**	**Mean difference**	**95% CI**	**p-value**
Generic QoL (SF-36)									
Physical functioning	72·1 (22·4)	84·4 (21·2)	13·5	8·1 to 19·0	<0·001	75·9 (23·4)	8·8	-0·0 to 17·6	0·051
Physical role functioning	75·9 (24·6)	83·9 (25·2)	11·2	4·0 to 18·3	0·002	71·3 (30·9)	13·5	2·2 to 24·8	0·020
General health perceptions	53·8 (23·4)	64·8 (22·7)	12·4	6·5 to 18·3	<0·001	56·2 (26·6)	8·7	-1·1 to 18·5	0·080
Bodily pain	67·7 (26·8)	67·6 (30·0)	2·1	-5·2 to 9·3	0·575	71·6 (27·5)	-3·1	-14·0 to 7·9	0·579
Vitality	48·4 (18·6)	50·8 (23·0)	3·8	-2·2 to 9·9	0·211	54·8 (27·2)	-3·5	-13·6 to 6·6	0·497
Mental health	65·6 (21·0)	68·1 (21·8)	4·1	-1·7 to 9·9	0·166	63·5 (27·0)	5·1	-4·7 to 15·0	0·305
Social role functioning	77·1 (25·7)	79·5 (26·1)	3·3	-2·7 to 9·4	0·285	72·8 (29·8)	7·5	-3·5 to 18·6	0·180
Emotional role functioning	75·2 (30·7)	80·7 (27·5)	6·3	-1·2 to 13·8	0·099	73·1 (33·4)	8·3	-3·9 to 20·6	0·180
Physical component score	44·1 (9·5)	48·3 (10·3)	5·2	2·5 to 7·9	<0·001	45·7 (10·0)	-2·9	-6·9 to 1·0	0·137
Mental component score	41·6 (12·2)	44·7 (12·1)	0·7	-2·5 to 3·9	0·658	42·9 (15·4)	-2·3	-7·9 to 3·4	0·427
Obesity-specific QoL (OP-14)									
OP-14 scale score	49·1 (26·4)	37·4 (28·8)	-13·0	-19·6 to -6·4	<0·001	45·1 (34·9)	-7·9	-20·7 to 4·5	0·218

Figure S1. Patient flow chart.

RYGB, Roux-en-Y gastric bypass (RYGB); *One patient decided against surgical treatment on the day of surgery.

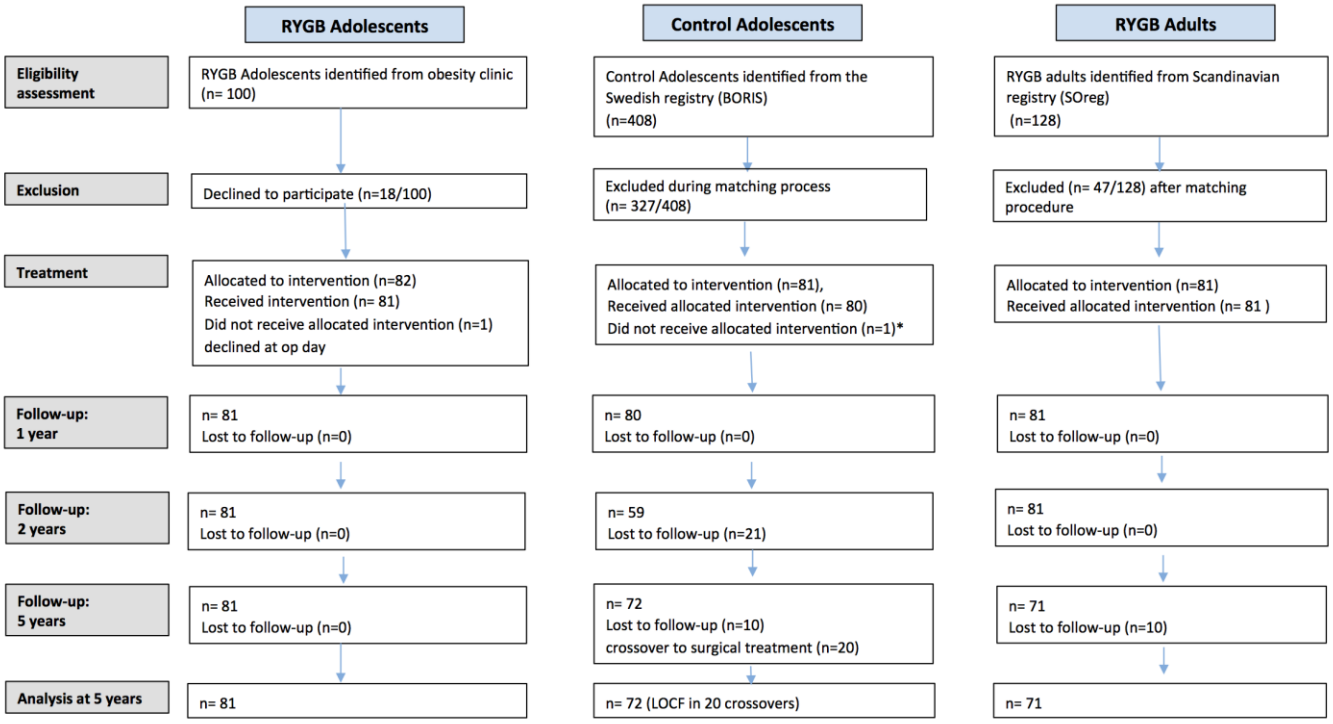


Figure S2 – Biochemical and blood pressure data curves from baseline to 5 years.

Means within the adolescent RYGB group are presented as point markers with 95% confidence bars. HbA1c, glycated haemoglobin; hsCRP, high-sensitivity C-reactive protein; HDL, high-density lipoprotein; LDL, low-density lipoprotein; syst, systolic; diast, diastolic.

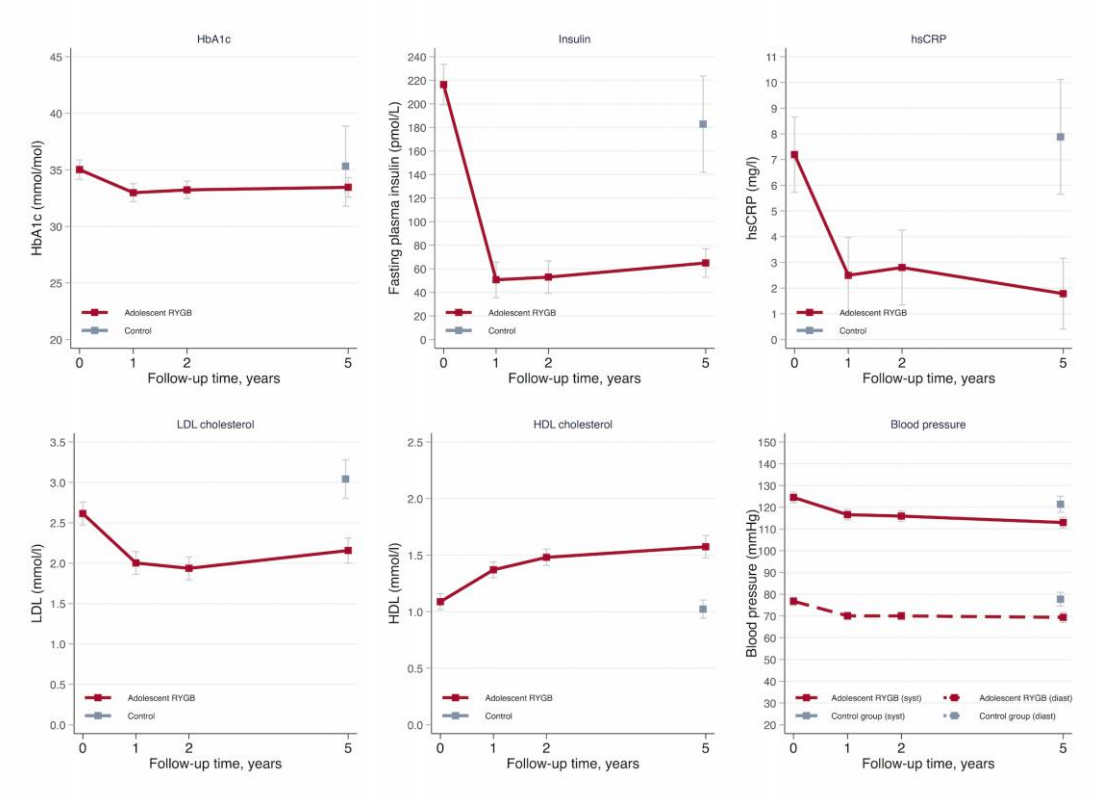
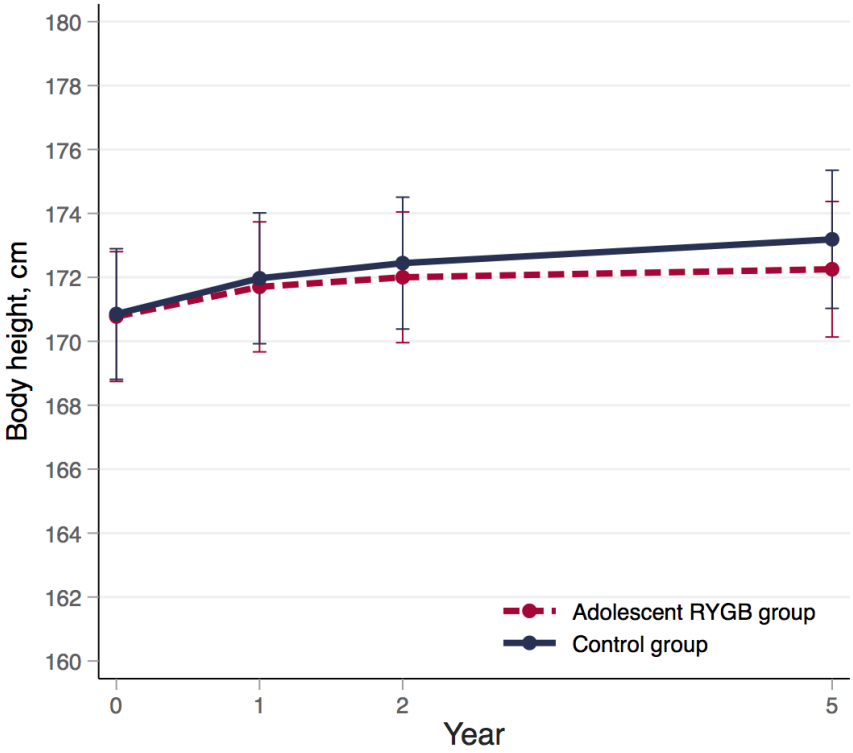


Figure S3 – Body height from baseline to 5 years for adolescents with severe obesity undergoing Roux-en-Y gastric bypass or conservative treatment.

Means are presented as point markers with 95% confidence bars.



Definitions and thresholds:

Type 2 diabetes mellitus (T2DM) was defined in accordance with ADA criteria,[1] i.e. fasting blood glucose (FBG) of ≥7 mmol/L (≥126 mg/dL), HbA1c of ≥45 mmol/mol (≥6·5%), or the existence of a prior medical record of T2DM.

Remission of T2DM was defined in accordance with ADA criteria,[2] i.e., FBG <7·0 mmol/L (<126 mg/dL), HbA1C <45 mmol/mol (<6·5%), fasting capillary glucose <6·1 mmol/L (<110 mg/dL) in combination with the absence of diabetes medication.

Disturbed glucose homeostasis was defined in accordance with ADA criteria,[1] i.e. FBG ≥5·5 mmol/L but <7 mmol/L (≥100 mg/dL but <126 mg/dL), HbA1c of ≥39 mmol/mol (≥5·7%) but <45 mmol/mol (<6·5%), fasting capillary glucose ≥6·1 mmol/L but <7·0 mmol/L (≥100 but <110 mg/dL), in the absence of medication use for T2DM.

Remission of disturbed glucose homeostasis was defined in accordance with ADA criteria,[2] i.e., FBG <5·5 mmol/L (<100 mg/dL), HbA1c <39 mmol/mol (<5·7%), fasting capillary glucose <5·5 mmol/L (<100mg/dL) in the absence of medication use for T2DM.

Dyslipidaemia was defined as use of lipid lowering medications (LLM), or fasting triglycerides (TG) ≥1·47 mmol/L (≥130 mg/dL), or low density lipoprotein cholesterol (LDL-C) ≥3·37 mmol/L (≥130 mg/dL), or high density lipoprotein cholesterol (HDL-C) ≥1·04 mmol/L (<40mg/dL).
Remission of dyslipidaemia was defined in subjects <21 years of age as no use of LLM, and fasting TG ≥1·47 mmol/L (<130 mg/dL), and LDL-C <3·37 mmol/L (<130 mg/dL), and HDL-C ≥1·04 mmol/L (≥40 mg/dL).
In subjects ≥21 years of age, remission was defined as no use of LLM, and fasting TG <2·26 mmol/L (<200 mg/dL), and LDL-C <4·14 mmol/L (<160 mg/dL), and HDL-C ≥1·04 mmol/L (≥40 mg/dL) if male or ≥1·29 mmol/L (≥50 mg/dL) if female.

Elevated blood pressure (BP) was defined according to cutoffs used to define hypertension. However, in the absence of multiple, separated measurements, and in concordance with existing literature in this field[16], the term elevated BP was used, rather than hypertension.
Elevated BP was defined in subjects <18 years of age as use of BP medications, or systolic (SBP) or diastolic BP (DBP) ≥95th percentile for age, sex and height. In subjects ≥18 years of age, the definition was use of BP medications, or SBP ≥140 mmHg or DBP ≥90 mmHg.
Remission of elevated BP was defined as no use of BP medications and SBP <140 mmHg and DBP <90 mmHg, since all subjects were ≥18 years of age.

Inflammation was defined as high sensitivity C-reactive protein (hsCRP) ≥2 mg/L (≥19 nmol/L).
Remission of inflammation was defined as hsCRP <2 mg/L (<19 nmol/L).

Anaemia was defined as haemoglobin <100 g/L if female, or <110 g/L, if male. Low haemoglobin was defined as <120 but ≥100 g/L if female, or <130 but ≥110 g/L if male.

Additional measures:

Parameter	Abnormality threshold
Fasting plasma insulin	≥139 pmol/L
Vitamin D (25 hydroxyvitamin D)	<50 nmol/L (insufficiency); <30 nmol/L (deficiency)
Vitamin B12	<145 pmol/L
Ferritin	<45 pmol/L (boys); <22·5 pmol/L (girls)
Iron	<9 μmol/L
Creatinine	≥90 μmol/L
Aspartate transaminase	≥0·7 μkat/L
Alanine transaminase	≥0·7 μkat/L
Albumin	<35 g/L
Alkaline phosphatase	≥6·5 μkat/L
Apo A1	≤1·0 g/L
Apo B	>0·9 g/L

Web additional material references

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes care* 2012; **35 Suppl 1**: S64-71.

2. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? *Diabetes care.* 2009; 1;**32**(11):2133-5.

3. Inge TH, Courcoulas AP, Jenkins TM, et al. Weight Loss and Health Status 3 Years after Bariatric Surgery in Adolescents. *The New England journal of medicine* 2016; **374**(2): 113-23.