Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity (AMOS): a prospective, 5-year, Swedish nationwide study

Torsten Olbers, Andrew J Beamish, Eva Gronowitz, Carl-Erik Flodmark, Jovanna Dahlgren, Gustaf Bruze, Kerstin Ekbom, Peter Friberg, Gunnar Göthberg, Kajsa Järvholm, Jan Karlsson, Staffan Mårild, Martin Neovius, Markku Peltonen, Claude Marcus

Summary

Background Severe obesity in adolescence is associated with reduced life expectancy and impaired quality of life. Long-term benefits of conservative treatments in adolescents are known to be modest, whereas short-term outcomes of adolescent bariatric surgery are promising. We aimed to compare 5-year outcomes of adolescent surgical patients after Roux-en-Y gastric bypass with those of conservatively treated adolescents and of adults undergoing Roux-en-Y gastric bypass, in the Adolescent Morbid Obesity Surgery (AMOS) study.

Methods We did a nationwide, prospective, non-randomised controlled study of adolescents (aged 13–18 years) with severe obesity undergoing Roux-en-Y gastric bypass at three specialised paediatric obesity treatment centres in Sweden. We compared clinical outcomes in adolescent surgical patients with those of matched adolescent controls undergoing conservative treatment and of adult controls undergoing Roux-en-Y gastric bypass. The primary outcome measure was change in BMI over 5 years. We used multilevel mixed-effect regression models to assess longitudinal changes. This trial is registered with ClinicalTrials.gov, number NCT00289705.

Findings Between April, 2006, and May, 2009, 100 adolescents were recruited to the study, of whom 81 underwent Roux-en-Y gastric bypass (mean age 16·5 years [SD 1·2], bodyweight 132·8 kg [22·1], and BMI 45·5 kg/m² [SD 6·1]). 80 matched adolescent controls and 81 matched adult controls were enrolled for comparison of outcomes. The change in bodyweight in adolescent surgical patients over 5 years was –36·8 kg (95% CI –40·9 to –32·8), resulting in a reduction in BMI of –13·1 kg/m² (95% CI –14·5 to –11·8), although weight loss less than 10% occurred in nine (11%). Mean BMI rose in adolescent controls (3·3 kg/m², 95% CI 1·1–4·8) over the 5-year study period, whereas the BMI change in adult controls was similar to that in adolescent surgical patients (mean change –12·3 kg/m², 95% CI –13·7 to –10·9). Comorbidities and cardiovascular risk factors in adolescent surgical patients showed improvement over 5 years and compared favourably with those in adolescent controls. 20 (25%) of 81 adolescent surgical patients underwent additional abdominal surgery for complications of surgery or rapid weight loss and 58 (72%) showed some type of nutritional deficiency; health-care consumption (hospital attendances and admissions) was higher in adolescent surgical patients compared with adolescent controls. 20 (25%) of 81 adolescent controls underwent bariatric surgery during the 5-year follow-up.

Interpretation Adolescents with severe obesity undergoing Roux-en-Y gastric bypass had substantial weight loss over 5 years, alongside improvements in comorbidities and risk factors. However, gastric bypass was associated with additional surgical interventions and nutritional deficiencies. Conventional non-surgical treatment was associated with weight gain and a quarter of patients had bariatric surgery within 5 years.

Funding Swedish Research Council; Swedish Governmental Agency for Innovation Systems; National Board of Health and Welfare; Swedish Heart and Lung Foundation; Swedish Childhood Diabetes Foundation; Swedish Order of Freemasons Children's Foundation; Stockholm County Council; Västra Götaland Region; Mrs Mary von Sydow Foundation; Stiftelsen Göteborgs Barnhus; Stiftelsen Allmänna Barnhuset; and the US National Institute of Diabetes, Digestive, and Kidney Diseases (National Institutes of Health).

Introduction

Severe obesity in adolescence is a life-threatening and life-shortening disease,[1,2] leading to a multitude of other disorders.[3,4] As the mean age of obesity onset has decreased,[5] the onset of related diseases—most notably, type 2 diabetes—has shifted increasingly towards childhood.[6] Type 2 diabetes is substantially more aggressive when it occurs in childhood, with medical treatments failing earlier and a shorter time to requirement for insulin therapy.[6] Obesity amplifies cardiovascular risk factors in childhood,[7] leading to a poor prognosis in this population,[8,9] with few effective therapeutic options available.[10]

The prevalence of adolescent obesity has now reached 5–10% in high-income countries.[5,11,12] Non-surgical programmes remain the main treatment for adolescents with severe obesity, although their effectiveness is slight and insufficient for long-term reduction of obesity-related

Lancet Diabetes Endocrinol 2017

Published Online
January 5, 2017
http://dx.doi.org/10.1016/S2213-8587(16)30424-7

See Online/Articles
http://dx.doi.org/10.1016/S2213-8587(16)30315-1

See Online/Comment
http://dx.doi.org/10.1016/S2213-8587(16)30425-9

Department of Gastrosurgical Research (T Olbers PhD, A J Beamish MD, E Gronowitz PhD), **Department of Paediatrics** (J Dahlgren PhD, E Gronowitz), **Department of Health and Care Sciences** (S Mårild PhD), **and Department of Paediatric Surgery, Queen Silvia Children's Hospital** (G Göthberg PhD), **Sahlgrenska University Hospital, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden; Department of Research, Royal College of Surgeons of England, London, UK** (A J Beamish); **Childhood Obesity Unit, Skåne University Hospital, Malmö, Sweden** (C-E Flodmark PhD, K Järvholm PhD); **Clinical Epidemiology Unit, Department of Medicine, Solna, Karolinska University Hospital, Stockholm, Sweden** (G Bruze PhD, M Neovius PhD); **Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden** (K Ekbom PhD, C Marcus PhD); **Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska University Hospital, University of Gothenburg, Gothenburg, Sweden** (P Friberg PhD); **Department of Psychology, Lund University, Lund, Sweden** (J Karlsson PhD, K Järvholm); **and National Institute for Health and Welfare, Helsinki, Finland** (M Peltonen PhD)

Correspondence to:
Dr Torsten Olbers, Department of Gastrosurgical Research, Institute of Clinical Sciences, University of Gothenburg, Sahlgrenska University Hospital, Gothenburg 41 345, Sweden
torsten.olbers@gu.se

Research in context

Evidence before this study

We searched PubMed between Feb 14, 1956, and Feb 13, 2006, with the terms "adolescent" OR "child*" AND "gastric bypass" AND "obesity", with no restrictions on language. Of 246 items returned, we identified six relevant retrospective case series, dating as far back as 1975, comprising between four and 39 patients who were genetically normal and undergoing Roux-en-Y gastric bypass. However, prospective and systematic assessments of the risks and benefits of this procedure in adolescents were scarce. Within the limited case series, a mean BMI reduction of 20 kg/m² was reported at least 1 year after Roux-en-Y gastric bypass, but fewer than 45 patients had follow-up to 5 years or longer. Several adolescents showed improvement in obesity-related metabolic variables after surgery—eg, glucose homoeostasis, lipidaemia, and blood pressure. However, inherent limitations of small series render these results of limited reliability and generalisability. Most studies included few participants and had a retrospective design, many using suboptimum methods of follow-up without requiring clinic attendance; yet, minor-to-moderate complications were fairly common.

Added value of this study

Since we began our study, several prospective studies have been published from the USA, Europe, Saudi Arabia, and Australia, reporting outcomes up to 3 years after surgery, most notably the Teen-LABS study. Our prospective study reports similar improvements in BMI and cardiometabolic status to these other studies, and advances knowledge and understanding of the outcomes of Roux-en-Y gastric bypass among adolescents with severe obesity into the long term (>5 years). Furthermore, in our study, outcomes were compared in adolescents undergoing Roux-en-Y gastric bypass concurrently with those in a group of contemporary, matched, adolescent controls undergoing conventional treatment and in a group of contemporary matched adults undergoing Roux-en-Y gastric bypass, embedding the observed results within the context of the existing understanding of adult outcomes. Moreover, our study adds data from several national registries, expanding outcomes to include health-care consumption.

Implications of all the available evidence

The present study shows that adolescents with severe obesity had substantial weight loss alongside improvements in comorbidities and risk factors, over 5 years after Roux-en-Y gastric bypass. It has been demonstrated widely in adults that Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric banding are safe and effective in achieving and maintaining weight loss and substantial metabolic health gains, often inducing remission of type 2 diabetes or prediabetes, dyslipidaemia, and hypertension. However, bariatric surgery in adolescents presents many challenges. Targeted strategies need to be developed to diminish weight regain and avoid nutritional deficiencies in adolescents undergoing surgery and to reduce the need for additional surgery. The published literature is now sufficiently mature to consider formal integration of bariatric surgery into treatment pathways for adolescents with severe obesity. However, assessment of adolescents for surgery should be embedded within formal programmes incorporating all other available obesity treatments, led by a multidisciplinary team capable of undertaking physical and psychosocial assessments of the individual patient. Provision must also be made for long-term follow-up and management, with concern for surgical and nutritional adverse events, avoidance of weight regain, and continuous psychological support when needed, knowing that these patients are a vulnerable group.

health hazards.[13] However, surgery is increasingly recommended[14] and done in adolescents,[15] and robust outcomes have been reported up to 3 years after surgery.[16–18]

The Adolescent Morbid Obesity Surgery (AMOS) study is a Swedish, nationwide, prospective, non-randomised controlled study.[17] Our aim was to compare outcomes in a group of adolescents with severe obesity over 5 years after Roux-en-Y gastric bypass or conservative treatment with a group of matched adult controls undergoing Roux-en-Y gastric bypass.

Methods

Study design and participants

We assessed for surgical eligibility all adolescents who presented with severe obesity to one of three specialised paediatric obesity treatment units in Sweden: Sahlgrenska University Hospital, Gothenburg; Children's Hospital, Karolinska University Hospital, Stockholm; and Skåne University Hospital, Malmö. Inclusion criteria were: age 13–18 years; BMI 40 kg/m² or higher, or 35 kg/m² or higher with comorbidity (eg, type 2 diabetes, dyslipidaemia, metabolic syndrome); pubertal Tanner stage III or higher; height growth velocity beyond peak; and at least 1 year in a formal, conventional, weight loss programme. Exclusion criteria were: severe psychiatric disorder; ongoing drug abuse; obesity secondary to brain injury; and syndromic or monogenic obesity (we sequenced the melanocortin 4 receptor in >50% of patients based on clinical suspicion).

We identified a group of adolescents from the Swedish Childhood Obesity Treatment Register (BORIS)[13] who had received conservative treatment for obesity. This registry did not include detailed formal data about individuals' compliance with conventional treatment. We sequentially matched adolescent controls from this group with adolescent surgical patients to ensure that

mean values for baseline BMI, age, and sex in controls moved closer to mean values within the surgical group as much as was possible with each additional control. We ensured the date an adolescent surgical patient underwent Roux-en-Y gastric bypass was within 1 month of baseline weight for the corresponding adolescent control.

We also matched adolescent surgical patients with a group of adult controls aged 35–45 years with severe obesity undergoing Roux-en-Y gastric bypass at Sahlgrenska University Hospital, Gothenburg. We used the same inclusion and exclusion criteria for adult controls as we did for adolescent surgical patients.[17] We matched adult controls with adolescent surgical patients according to BMI and sex.

We did the AMOS study according to the Declaration of Helsinki with the approval of the Gothenburg regional ethics committee (523–04). Written consent for study participation was obtained at the first study attendance from all patients, their carers, or both. Informed consent for surgery was obtained from all surgical patients, their carers, or both.

Procedures

The laparoscopic gastric bypass procedure incorporated an antecolic, antegastric Roux-en-Y construction with a linearly stapled gastrojejunostomy,[19] without closure of mesenteric windows. All surgical procedures for adolescent patients were done at Sahlgrenska University Hospital by one of two skilled bariatric surgeons, assisted by a paediatric surgeon. The same surgical team (excluding the paediatric surgeon) delivered Roux-en-Y gastric bypass for adult controls in an identical setting, to maximise comparability with adolescent surgical patients. Within the pragmatic study design, conventional treatment of adolescent controls was non-standardised; it was delivered as an individualised treatment by the multidisciplinary team according to Swedish standards.[17] This treatment focused on achieving behaviour change through regular clinical contact to deliver education, raising awareness among adolescents and their carers of the effect of their obesity and how to achieve a healthier lifestyle.[13,20,21]

We used the term disturbed glucose homoeostasis in response to incomplete data for fasting blood glucose levels. We outlined this term by adding a fasting capillary glucose criterion to the American Diabetes Association (ADA) definition of impaired fasting glucose, or prediabetes,[22] as follows: fasting capillary glucose 6·1 mmol/L or higher but less than 7·0 mmol/L (≥110 mg/dL but <126 mg/dL); fasting blood glucose 5·5 mmol/L or higher but less than 7·0 mmol/L (≥100 mg/dL but <126 mg/dL); HbA_{1c} 39 mmol/mol or higher but less than 45 mmol/mol (≥5·7% but <6·5%); and an absence of diabetes medication. We also diagnosed type 2 diabetes and its remission according to ADA definitions, with remission ascertained with the following criteria: fasting blood glucose less than 7·0 mmol/L (<126 mg/dL); HbA_{1c} less than 45 mmol/mol (<6·5%); fasting capillary glucose less than 6·1 mmol/L (<110 mg/dL); and an absence of diabetes medication.[22] Other definitions and remission criteria are provided in the appendix (pp 6, 7).

See Online for appendix

We assessed adolescent surgical patients preoperatively and at 2 months, 6 months, 1 year, 2 years, and 5 years after surgery. We measured bodyweight, height, and blood pressure and did biochemical analyses and quality-of-life assessments preoperatively and at 1 year, 2 years, and 5 years after surgery. Procedures for blood sampling and handling have been described previously.[17] To measure health-related quality of life, we used a Swedish version of the short form-36 health survey version 2 (SF-36), which was validated for use in adolescents.[23] We used the obesity-related problems scale (OP-14) to assess psychosocial problems related to bodyweight and body shape.[24] We sought information about use of drugs or alcohol from adolescent surgical patients and caregivers at recruitment. We prescribed adolescent patients a daily multivitamin and mineral supplement (including 200 µg folic acid), vitamin B12 (cobalamin 1 mg/day), and calcium carbonate or vitamin D (1 g/800 IU per day). We also gave female surgical patients iron supplements (Fe^{2+} 100 mg/day).

We measured bodyweight and height of adolescent controls at baseline and 1 year, 2 years, and 5 years after recruitment. At 5 years, we invited adolescent controls to attend a study visit for biochemical analyses and quality-of-life data collection. Between years 2 and 5, adolescents were followed up predominantly in the community. In

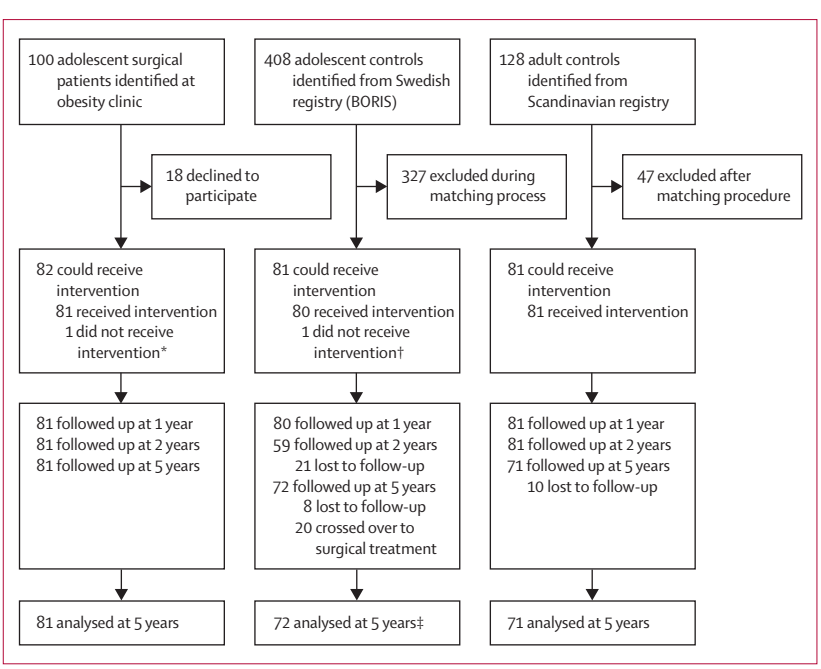

Figure 1: **Study profile**
*One patient decided against surgical treatment on the day of surgery. †One patient received surgical treatment instead of the control intervention. ‡Last-observation-carried-forward assumption used for crossovers.

accordance with Swedish convention, systematic medical treatment for cardiovascular risk factors in youth—eg, dyslipidaemia or hypertension—was not common practice.

We measured bodyweight and height in adult controls prospectively at inclusion and 1 year after surgery. We obtained bodyweight data at 2 years and 5 years after surgery from measurements taken at a community health-care centre, when available, and self-reported measurements otherwise.

We assessed data for surgical complications at 30 days in adolescent surgical patients at the 2-month follow-up visit and, thereafter, complications were prospectively

	Adolescent surgical patients		Adolescent controls		Adult controls	
	Baseline (n=81)	5 years (n=81)	Baseline (n=80)	5 years (n=72)	Baseline (n=81)	5 years (n=71)
Sex						
Male	28 (35%)	28 (35%)	35 (44%)	30 (42%)	28 (35%)	23 (32%)
Female	53 (65%)	53 (65%)	45 (56%)	42 (58%)	53 (65%)	48 (68%)
Age (years)	16·5 (1·2)	21·9 (1·2)	15·8 (1·2)	20·9 (1·3)	39·7 (2·9)	44·7 (2·9)
Male	16·6 (1·3)	22·0 (1·4)	15·9 (1·2)	21·0 (1·2)	40·2 (3·5)	45·2 (3·5)
Female	16·5 (1·1)	21·9 (1·1)	15·7 (1·3)	20·8 (1·3)	39·5 (2·6)	44·5 (2·6)
Height (cm)	171 (9)	172 (9)	171 (9)	173 (10)	171 (11)	171 (11)
Male	178 (10)	180 (9)	178 (8)	180 (8)	182 (9)	182 (9)
Female	167 (6)	168 (6)	166 (8)	167 (8)	165 (7)	165 (7)
Bodyweight (kg)	133 (22)	96 (22)	124 (21)	124 (32)	127 (20)	90 (18)
Male	147 (23)	109 (26)	135 (20)	132 (27)	142 (17)	102 (17)
Female	125 (17)	89 (17)	115 (17)	118 (34)	120 (17)	85 (16)
BMI (kg/m^2)	45·5 (6)	32·3 (6)	42·2 (5)	41·7 (10)	43·5 (5)	31·0 (6)
Male	46·7 (6)	33·3 (7)	43·0 (5)	40·8 (8)	43·1 (6)	31·1 (6)
Female	44·8 (6)	31·8 (6)	41·6 (5)	42·3 (12)	43·7 (5)	31·0 (6)

Data are mean (SD) or number of participants (%).

***Table 1*: Baseline and 5-year characteristics**

	Adolescent surgical patients						Adolescent controls at 5 years		Between-group mixed-model difference (surgical *vs* control adolescents) at 5 years	
	Baseline		5 years		Within-group mixed-model change from baseline to 5 years		Mean (SD)	n	Mean (95% CI)	p value
	Mean (SD)	n	Mean (SD)	n	Mean (95% CI)	p value				
Height (cm)	170·8 (9·3)	81	172·3 (9·4)	81	1·48 (0·9 to 2·1)	<0·0001	173·0 (10·0)	53	−0·75 (−4·2 to 2·7)	0·67
Bodyweight (kg)	132·8 (22·1)	81	96·0 (22·2)	81	−36·8 (−40·9 to −32·8)	<0·0001	133·3 (28·9)	53	−37·21 (−46·4 to −28·0)	<0·0001
BMI (kg/m^2)	45·5 (6·1)	81	32·3 (6·3)	81	−13·14 (−14·5 to −11·8)	<0·0001	44·6 (9·5)	53	−12·26 (−15·2 to −9·3)	<0·0001
HbA_{1c} (mmol/mol)*	35·1 (3·9)	80	33·5 (3·8)	65	−1·56 (−2·5 to −0·6)	0·002	35·3 (10·6)	37	−1·8 (−5·4 to 1·8)	0·32
Fasting plasma glucose (mmol/L)	5·1 (0·5)	80	4·8 (0·4)	36	−0·33 (−0·5 to −0·1)	0·001	5·2 (0·7)	18	−0·45 (−0·8 to −0·1)	0·009
Fasting capillary glucose (mmol/L)	5·6 (0·5)	78	5·2 (0·5)	73	−0·35 (−0·5 to −0·22)	0·001	5·8 (2·4)	16	−0·6 (−1·8 to 0·6)	0·34
Fasting plasma insulin (pmol/L)	216·7 (122·4)	79	65·0 (34·2)	75	−151·42 (−173·3 to −129·5)	<0·0001	182·8 (122·6)	37	−117·81 (−158·3 to −77·3)	<0·0001
Triglycerides (mmol/L)	1·3 (0·6)	80	0·9 (0·3)	76	−0·39 (−0·5 to −0·3)	<0·0001	1·4 (0·8)	41	−0·47 (−0·7 to −0·2)	<0·0001
LDL cholesterol (mmol/L)	2·6 (0·7)	81	2·2 (0·7)	76	−0·46 (−0·6 to −0·3)	<0·0001	3 (0·8)	41	−0·88 (−1·2 to −0·6)	<0·0001
HDL cholesterol (mmol/L)	1·1 (1·1)	81	1·6 (0·5)	75	0·49 (−0·4 to 0·6)	<0·0001	1·0 (0·3)	42	0·55 (0·4 to 0·7)	<0·0001
Systolic blood pressure (mm Hg)	124·6 (12·3)	78	113·2 (10·7)	72	−11·55 (−14·0 to −9·1)	<0·0001	121·4 (11·4)	40	−8·18 (−12·5 to −3·8)	<0·0001
Diastolic blood pressure (mm Hg)	76·9 (9·8)	78	69·4 (9·9)	72	−7·4 (−10·2 to −4·6)	<0·0001	77·7 (10·0)	40	−8·28 (−12·2 to −4·4)	<0·0001
High-sensitivity C-reactive protein (mg/L)	7·2 (5·9)	75	1·8 (2·2)	77	-5·41 (−7·4 to −3·5)	<0·0001	7·9 (6·9)	39	−6·09 (−8·3 to −3·9)	<0·0001
Alanine aminotransferase (μkat/L)	0·6 (0·4)	80	0·3 (0·2)	76	−0·35 (−0·4 to −0·3)	<0·0001	0·4 (0·3)	42	−0·16 (−0·3 to −0·1)	<0·0001
Aspartate aminotransferase (μkat/L)	0·5 (0·2)	80	0·4 (0·2)	76	−0·09 (−0·1 to −0·0)	0·002	0·4 (0·2)	41	−0·04 (−0·1 to 0·0)	0·25
Haemoglobin (g/L)	139·3 (12·3)	78	127·7 (17·4)	77	−11·69 (−15·6 to −7·8)	<0·0001	141·9 (14·4)	42	−14·17 (−20·1 to −8·3)	<0·0001

Per-protocol data (crossovers excluded). *To convert mmol/mol to %, (0·0915 × mmol/mol) + 2·15.

***Table 2*: Anthropometric, biochemical, and blood pressure data at baseline and 5 years**

recorded in the electronic case record file. We did a complementary retrospective survey of medical records to capture missing data up to the 5-year follow-up visit. Moreover, we retrieved data for inpatient care (admissions and hospital days) and hospital-based outpatient care visits from the Swedish national patient register and prescription drug costs from the prescribed drug register.

Outcomes

The primary outcome of our study was change in BMI across the 5-year study period. Predetermined secondary outcomes were: anthropometric measurements, serum measures of cardiometabolic diseases, risk factors and nutrition (glucose homoeostasis, lipid status, blood pressure, inflammatory markers, liver enzymes, haemoglobin, ferritin, vitamin B12, and vitamin D), and quality of life. Additional secondary outcomes reported were: psychosocial health, adverse events, and health-care consumption.

Statistical analysis

We present descriptive statistics as mean (SD). To assess longitudinal changes, we fitted multilevel mixed-effect regression models to the data. In analyses, we considered observations nested within individuals, and we calculated SD by taking into account repeated measurements. We expressed changes over time with 95% CIs. We assessed underlying assumptions for the mixed models by analyses of residuals.

For control crossovers, we used the last-observation-carried-forward assumption for anthropometric data, and we excluded crossovers from analyses for all other variables. We estimated sex-adjusted and age-adjusted mean differences for 5-year accumulated hospital days, visits for outpatient care, and prescription drug costs using linear regression, with 95% CIs generated by non-parametric bootstrapping not requiring additional assumptions.

All p values are two-tailed and we judged p values less than 0·05 as significant. We used Stata (version 12.1) for all statistical analyses.

This trial is registered with ClinicalTrials.gov, number NCT00289705.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results

Between April, 2006, and May, 2009, 100 adolescents who presented to one of the three study centres with severe obesity were assessed for surgery. 19 individuals declined surgery and the remaining 81 adolescents underwent Roux-en-Y gastric bypass (figure 1). 80 adolescent controls and 81 adult controls were recruited for comparison of outcomes. Mean follow-up was 5·0 years (SD 0·3). All 81 adolescent surgical patients were followed up for 5 years, with 72 (90%) of 80 adolescent controls and 71 (88%) of 81 adult controls completing 5-year follow-up. 100% of the cohorts were followed up in national health-care registries.

Baseline and 5-year demographic and anthropometric characteristics of patients and controls are presented in table 1. At baseline, adolescent surgical patients were older than adolescent controls and had significantly higher BMI. Both groups had a lower proportion of male than female participants, but the sex difference between patients and controls was not significant. The change in height over 5 years for adolescent patients and controls is shown in the appendix (p 5).

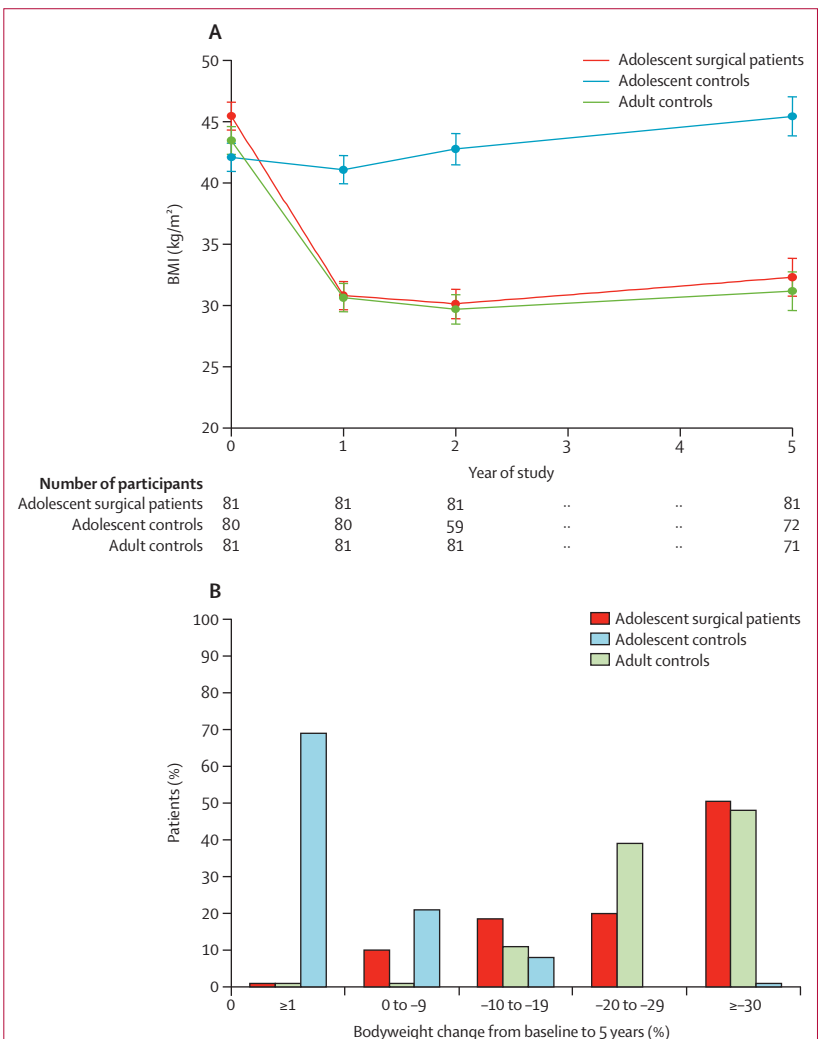

Figure 2: **Change in BMI (A) and bodyweight (B) from baseline to 5 years**
Data for adolescent controls are presented using the last-observation-before-surgery-carried-forward assumption for crossovers who underwent surgery within the follow-up period. Data points in (A) are the mean value and error bars show the 95% CI.

Psychosocial impairment—eg, depressive or anxiety disorder—was reported in adolescent surgical patients, and 25 (31%) had a neuropsychiatric diagnosis (specific diagnoses unavailable). 13 (16%) individuals had previously shown self-destructive behaviour, and 33 (41%) had been previously treated in a paediatric psychiatry outpatient department. These data are unavailable for adolescent and adult controls.

Mean BMI change across 5 years was –13·1 kg/m² (95% CI –14·5 to –11·8) in adolescent surgical patients (table 2), compared with 3·3 kg/m² (1·1–4·8) in adolescent controls, and –12·3 kg/m² (–13·7 to –10·9) in adult controls (figure 2A). 58 (72%) of 81 adolescent surgical patients, five (7%) of 72 adolescent controls, and 54 (76%) of 71 adult controls reached a BMI of less than 35 kg/m² after 5 years. Moreover, after 5 years, 30 (37%) of 81 adolescent surgical patients, two (3%) of 72 adolescent controls, and 31 (44%) of 71 adult controls no longer had obesity (BMI <30 kg/m²). Most adolescent surgical patients (55/81 [69%]) and adult controls (60/71 [85%]) achieved 20% or greater total bodyweight loss, but most adolescent controls (50/72 [69%]) gained bodyweight (figure 2B). Adolescents (surgical patients and control) were more likely than adults to have suboptimum weight loss (p=0·035). Mean weight regain between a nadir observed at 2 years and follow-up at 5 years was similar in adolescent surgical patients and adult controls (figure 2A).

20 (25%) of 80 adolescent controls had bariatric surgery between 2 years and 5 years of follow-up, having reached adult eligibility. This group had a median weight gain of 19·6 kg (range –1·1 to 53·5) from baseline until surgery, compared with a 7·3 kg increase (range –26·8 to 60·4) in the 60 adolescent controls who did not have surgery over 5 years of follow-up.

All measures of glucose homoeostasis improved across 5 years in adolescent surgical patients (table 2; appendix p 4). At baseline, three (4%) of 81 adolescent surgical patients had type 2 diabetes, all of whom were in remission 5 years after surgery (table 3). Disturbed glucose homoeostasis was noted at baseline in 22 (27%) adolescent surgical patients, which normalised in 18 (86%) individuals at 5 years, although two new cases arose after 5 years, resulting in a total of six (8%) cases at 5 years after surgery (table 3). Fasting plasma insulin levels decreased significantly, from 216·7 pmol/L at baseline to 65·0 pmol/L at 5 years (table 2). Meanwhile, in adolescent controls, the prevalence of disturbed glucose homoeostasis was 16% (7/44) at 5 years, and one new case of type 2 diabetes was reported (table 3).

56 (69%) of 81 adolescent surgical patients had dyslipidaemia at baseline, decreasing to 11 (15%) of 76 at 5 years (table 3). Notably, all cases of increased LDL or triglycerides resolved across 5 years. The 5-year prevalence of dyslipidaemia in adolescent controls was 73% (30/41;

	Adolescent surgical patients						p value*	Adolescent controls		p value†
	Baseline		5 years		Resolution‡			5 years		
	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)		n/N	% (95% CI)	
Type 2 diabetes	3/81	3·7 (0·8–10·4)	0/79	0·0 (0·0–4·6)	3/3	100·0 (29·2–100·0)	0·25	1/44	2·3 (0·1–12·0)	0·37
Disturbed glucose homoeostasis	22/81	27·2 (17·9–38·2)	6/79	7·6 (2·8–15·8)	18/21§	85·7 (63·7–97·0)	0·001	7/44	15·9 (6·6–30·1)	0·098
Increased HbA_{1c}	10/80	12·5 (6·2–21·8)	6/65	9·2 (3·5–19·0)	5/8§	62·5 (24·5–91·5)	0·73	6/37	16·2 (6·2–32·0)	0·35
Impaired fasting plasma glucose	16/80	20·0 (11·9–30·4)	0/36	0·0 (0·0–9·7)	13/13§	100·0 (75·3–100·0)	0·003	2/18	11·1 (1·4–34·7)	0·11
Raised fasting plasma insulin	56/79	70·9 (59·6–80·6)	3/76	3·9 (0·8–11·1)	49/52§	94·2 (84·1–98·8)	<0·0001	17/37	45·9 (29·5–63·1)	<0·0001
Dyslipidaemia	56/81	69·1 (57·9–78·9)	11/76	14·5 (7·5–24·4)	43/52§	82·7 (69·7–91·8)	<0·0001	30/41	73·2 (57·1–85·8)	<0·0001
Increased LDL cholesterol	13/81	16·0 (8·8–25·9)	0/76	0·0 (0·0–4·7)	13/13	100·0 (75·3–100·0)	<0·0001	9/41	22·0 (10·6–37·6)	<0·0001
Increased triglycerides	25/80	31·3 (21·3–42·6)	0/76	0·0 (0·0–4·7)	22/22§	100·0 (84·6–100·0)	<0·0001	10/41	24·4 (12·4–40·3)	<0·0001
Decreased HDL cholesterol	41/81	50·6 (39·3–61·9)	11/75	14·7 (7·6–24·7)	28/37§	75·7 (58·8–88·2)	<0·0001	27/42	64·3 (48·0–78·4)	<0·0001
Raised blood pressure	12/78	15·4 (8·2–25·3)	2/72	2·8 (0·3–9·7)	12/12	100·0 (73·5–100·0)	0·013	4/39	10·3 (2·9–24·2)	0·18
Raised systolic blood pressure	11/78	14·1 (7·3–23·8)	0/72	0·0 (0·0–5·0)	11/11	100·0 (71·5–100·0)	0·001	2/39	5·1 (0·8–17·3)	0·12
Raised diastolic blood pressure	4/78	5·1 (1·4–12·6)	2/72	2·8 (0·3–9·7)	4/4	100·0 (39·8–100·0)	0·69	4/39	10·3 (2·9–24·2)	0·18
Increased high-sensitivity C-reactive protein	65/75	86·7 (76·8–93·4)	19/77	24·7 (15·6–35·8)	45/61§	73·8 (60·9–84·2)	<0·0001	32/39	82·1 (66·5–92·5)	<0·0001
Increased liver enzymes	25/81	30·9 (21·1–42·1)	4/76	5·3 (1·5–12·9)	23/25	92·0 (74·0–99·0)	<0·0001	8/44	18·2 (8·2–32·7)	0·03
Increased alanine aminotransferase	24/80	30·0 (20·3–41·3)	2/76	2·6 (0·3–9·2)	23/24	95·8 (78·9–99·9)	<0·0001	7/42	16·7 (7·0–31·4)	0·01
Increased aspartate aminotransferase	9/80	11·3 (5·3–20·3)	4/76	5·3 (1·5–12·9)	9/9	100·0 (66·4–100·0)	0·27	3/41	7·3 (1·5–19·9)	0·7
Anaemia	8/78	10·3 (4·5–19·2)	25/77	32·5 (22·2–44·1)	5/7§	71·4 (29–96·3)	0·002	3/42	7·1 (1·5–19·5)	0·001

Per-protocol data (crossovers excluded). Definitions and thresholds in the appendix (pp 6, 7). *Difference between surgical patients at baseline and at 5 years. †Difference between surgical patients and controls at 5 years. ‡Resolution of cardiometabolic comorbidity (appendix pp 6, 7). §Number in resolution calculation lower than baseline denominator owing to missing data.

Table 3: **Prevalence and remission of cardiovascular risk factors at baseline and 5 years**

table 3). Blood pressure was raised in 12 (15%) of 78 adolescent surgical patients at baseline, which returned to normal in all cases at 5 years, although two incident cases led to a prevalence of 3% (table 3). The 5-year prevalence of increased blood pressure in adolescent controls was 10% (4/39). High-sensitivity C-reactive protein, a marker of inflammation, was amplified in 65 (87%) of 75 adolescent surgical patients at baseline, reducing to 19 (25%) of 77 across 5 years. In adolescent controls, high-sensitivity C-reactive protein was raised in 32 (82%) of 39 individuals at 5 years (table 3). Alanine aminotransferase concentration was increased in 25 (31%) of 80 adolescent surgical patients at baseline, returning to normal in 23 (92%) cases at 5-year follow-up, although two additional incident cases arose (table 3). Aspartate aminotransferase concentration was also increased at baseline in nine (11%) of 80 adolescent surgical patients, normalising in all cases across 5 years (table 3). The prevalence of anaemia in the adolescent surgical group rose from 10% (8/78) to 32% (25/77) across 5 years, whereas in adolescent controls it was 7% (3/42) at 5 years (table 3).

Data for other biochemical variables at baseline and at 5-year follow-up in adolescent patients and controls are presented in the appendix (pp 1, 2). After 5 years of follow-up, the prevalence of vitamin D insufficiency was 63% (46/73) in adolescent surgical patients and 57% (20/35) in adolescent controls. Low amounts of ferritin, iron, or both were present in 18 (24%) of 76 adolescent surgical patients at baseline, increasing to 51 (66%) of 77 at 5 years, compared with 12 (29%) of 42 adolescent controls at 5 years (data at baseline not obtained for controls). One (1%) of 74 adolescent surgical patients had a low amount of vitamin B12 at baseline, increasing to 16 (22%) of 73 after 5 years of follow-up; the prevalence of vitamin B12 deficiency after 5 years of follow-up was 6% (2/31) in adolescent controls (appendix p 2).

Data for quality-of-life outcomes are presented in the appendix (p 3). At 5-year follow-up, significant improvements were recorded among adolescent surgical patients in the physical component summary score on SF-36 (mean change 5·2, 95% CI 2·5–7·9). Moreover, three of the eight health domains showed pronounced changes, all of which are within the physical domain (figure 3): physical functioning (mean change 13·5, 95% CI 8·1–19·0), physical role functioning (11·2, 4·0–18·3), and general health perceptions (12·4, 6·5–18·3). Physical role functioning was also significantly better among adolescent surgical patients than adolescent controls (mean difference 13·5, 95% CI 2·2–24·8; appendix p 3). Weight-related psychosocial problems, measured using OP-14, were significantly improved after 5 years of follow-up (mean difference –13·0, 95% CI –19·6 to –6·4).

Across the 5-year study period, 20 (25%) adolescent surgical patients had 21 additional abdominal surgical interventions, excluding plastic surgery (table 4).

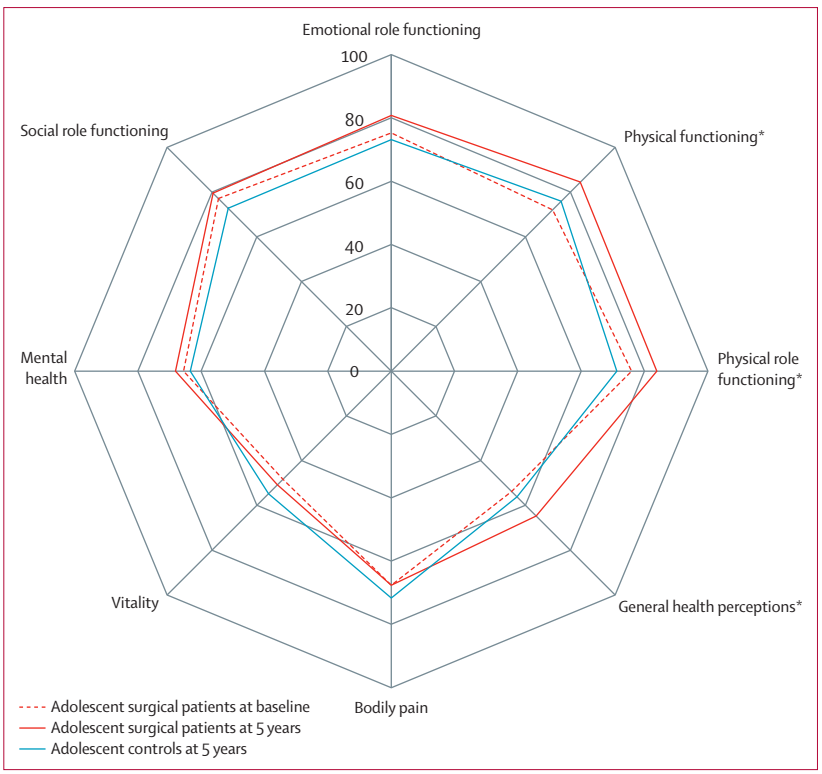

Figure 3: **Polar chart showing quality-of-life outcomes**
Data are scores from the short-form 36 questionnaire (SF-36). *Significant improvement between baseline and 5 years among adolescent surgical patients.

11 procedures were for acute intestinal obstruction and nine were for symptomatic gallstones. No deaths occurred across 5 years of follow-up. Some patients and their caregivers withheld information about substance misuse, even before surgery. We could not obtain valid data about adverse events and reoperation in adult controls.

Over 5 years of follow-up, including the index admission, adolescent surgical patients accumulated a mean of 16·1 hospital days (95% CI 10·1–22·0), compared with 2·8 days (1·5–4·1) for adolescent controls (mean difference 13·0, 95% CI 7·4–18·6). The mean number of in-hospital days related to admissions for surgical procedures, including the index surgery, was 6·5 days (95% CI 4·5–8·6) for adolescent surgical patients compared with 1·6 days (0·9–2·2) for adolescent controls (mean difference 5·0, 95% CI 2·7–7·2). The mean number of outpatient visits was also higher for adolescent surgical patients than for adolescent controls (14·6 [95% CI 11·8–17·3] *vs* 10·0 [8·3–11·7]; mean difference 4·9, 95% CI 1·3–8·4). Mean total prescription drug costs over 5 years were similar for adolescent patients and controls (US$2317 [95% CI 1394–3239] *vs* $2701 [328–5073]; mean difference –611, 95% CI –3252 to 2030).

Discussion

In our study, most adolescents undergoing Roux-en-Y gastric bypass for severe obesity had substantial weight

	Number of patients (%)
Serious adverse events	
All surgery	20/81* (25%)
Laparoscopy (small bowel obstruction)†	11/81 (14%)
Cholecystectomy (gallstones)	9/81 (11%)
Laparotomy (severe abdominal pain)	1/81 (1%)
Blood or iron transfusion (severe anaemia)‡	2/81 (2%)
Observation and investigation only (abdominal pain)	9/81 (11%)
Psychiatric assessment (drug abuse)§	6/81 (7%)
Other adverse outcomes	
Anaemia	25/77 (32%)
Vitamin D deficiency	20/73 (30%)
Low vitamin B12	16/73 (22%)
Low ferritin or iron	51/77 (66%)
Assessment by eating disorder team¶	1/81 (1%)

Serious adverse events entailed admission to hospital. Other adverse events did not need admission. Definitions and thresholds are provided in the appendix (pp 6, 7). *21 procedures in 20 patients; †Obstruction caused by internal herniation or adhesions. ‡Anaemia requiring admission for iron therapy or blood transfusion. §Narcotic abuse requiring medical referral or intervention. ¶Individual was referred for assessment but was never diagnosed with an eating disorder.

Table 4: **Adverse outcomes in adolescents after Roux-en-Y gastric bypass during the 5-year study period**

loss, metabolic improvement, reduction in the chronic inflammatory state, and enhancement of quality of life, which remained 5 years after surgery. The bypass procedure resulted in a mean 28% weight loss after 5 years, which is comparable with the 28% reduction after 3 years reported in the Teen-LABS study.[16] Rapid weight reduction during the first year was followed by modest weight regain between 2 and 5 years. The matched adult controls, who had Roux-en-Y gastric bypass surgery at the same centre, had a similar mean weight reduction to the adolescent surgical patients, but adolescent controls undergoing conventional treatment had progressive weight gain. However, we noted greater variability in long-term weight outcome in adolescent surgical patients than in adults, which could indicate greater phenotypical heterogeneity, an augmented need for postoperative support to optimise outcomes, or both.

We and others have previously reported that metabolic risk factors and comorbid conditions improve substantially in adolescents with severe obesity 2–3 years after gastric bypass surgery.[16–18] In our study, these positive trends remained after 5 years. We noted amelioration of disturbed glucose homoeostasis, dyslipidaemia, and high blood pressure. We also recorded a substantial reduction in high-sensitivity C-reactive protein after surgery, suggesting improvement of the chronic inflammatory state, which contributes to development of cardiovascular comorbidity.[25,26] At 5 years, metabolic risk factors—eg, dyslipidaemia and increased liver enzyme concentrations—were more prevalent in adolescent controls than surgical patients, although direct comparison between the two adolescent groups was affected by crossover of controls to undergo Roux-en-Y gastric bypass during follow-up. Since individuals with the most severe weight gain had surgery during follow-up, the control group became progressively healthier across the follow-up period.

Gastric bypass surgery is associated with an inherent risk of developing vitamin and mineral deficiencies, owing to impairment of absorption and decreased food intake.[27] Therefore, nutritional supplements were prescribed, according to Scandinavian clinical standards at that time. At 5 years after surgery, we noted a concerning prevalence of iron deficiency, associated low haemoglobin levels, and vitamin D insufficiency. Poor compliance with supplementation, as noted previously in similar populations, might have contributed to this outcome.[17] Supplementation is an important area for improvement, and present guidance suggests adopting aggressive supplementation (eg, high doses of vitamin D) and use of highly effective compounds (eg, calcium citrate rather than calcium carbonate). Regular access to long-term follow-up between 2 years and 5 years might have ameliorated nutritional deficiencies.

Psychosocial impairment is highly prevalent in adolescents with severe obesity,[28] as recorded at baseline in our study.[17,29] Adolescent surgical patients had improvements over 5 years in obesity-related psychosocial problems and in self-reported quality of life—most notably, in participants' perceived general health and physical function. Improvements did not, however, occur across all aspects of quality of life, which should be communicated to patients and their families preoperatively to manage expectations. Specific attention must also be paid to identifying and helping individuals at risk of self-harm and suicide in this vulnerable group.

The accumulated in-hospital stay across 5 years was longer in adolescent surgical patients than in adolescent controls, which is in line with expectations in view of the primary procedure and incidence of complications and remedial interventions in the surgical group.[30] Thus, obesity-related comorbid diseases recorded in adolescent controls did not augment the need for in-hospital treatments within 5 years of follow-up. Despite including routine prescribed nutritional supplementation, the observed costs of medication were no greater in adolescent surgical patients than in controls.

The number of additional procedures undertaken in adolescent surgical patients was higher than that reported within the Teen-LABS study,[16] mainly because of a high frequency of intra-abdominal herniation associated with non-closure of mesenteric defects.[31] Furthermore, the number of cholecystectomy procedures for gallstones was high in our study, presumably a result of substantial and rapid weight loss.[32] However, rates of small bowel obstruction and cholecystectomy were similar in Swedish

adults undergoing the Roux-en-Y gastric bypass.[31,33] Recent advances in practice have enabled reduction in the incidence of both internal herniation and gallstone formation by performing primary closure of mesenteric defects[31] and ursodeoxycholic acid prophylaxis,[33] suggesting that the rate of additional surgery can be reduced by more than 50%.[31,33]

The overall risk-to-benefit analysis for gastric bypass must take into account not only existing and imminent health implications for young people with severe obesity but also the failure of other treatments to achieve sustainable improvements.[10,13] Although a few (3%) adolescent controls succeeded in reaching normal bodyweight after 5 years, most (90%) failed to reverse their obesity and two-thirds (69%) actually gained weight. With most controls gaining weight across 5 years, delaying surgery until adulthood—and thereby prolonging exposure to cardiometabolic risk factors—likely increases the risk of development or progression of comorbid diseases.[7]

The strengths of our study include good rates of retention throughout follow-up, particularly considering that the population under study was comprised of adolescents and the 5-year follow-up period. Surgical procedures in adolescents and adults were done by surgeons at one centre, using a standardised and well recognised technique,[19] refined over thousands of procedures in adults. Adult controls had an almost identical treatment pathway to adolescent surgical patients, minimising bias related to the treatment. Swedish health-care registries guarantee accurate quantification of postoperative health care and medication use.

The limitations of our study include the non-randomised setting and use of a pragmatic, non-standardised, conservative treatment. However, to the best of our knowledge, only one long-term study has been published of a specific conservative treatment of obesity including adolescents, in which participants achieved only modest weight loss and almost 40% of participants were lost to follow-up across 5 years.[34] A randomised controlled trial would have reduced the potential for selection bias; however, without safety and efficacy data, we judged this design challenging. Many bodyweight datapoints for adult controls were self-reported, although evidence from a population of overweight adults shows that self-reporting bodyweight data leads to under-reporting by only 0·8–0·9 kg,[35] allaying our concerns. There was also some attrition in patient numbers with respect to laboratory and quality-of-life measures. A 25% crossover to surgery among adolescent controls during follow-up limited comparability with adolescent surgical patients. Because of the limited size of the study population and, therefore, the low number of adverse events, adjustment was done for age and sex alone. Roux-en-Y gastric bypass was the only surgical procedure undertaken, because sleeve gastrectomy was novel at the time, although this method has been used in later adolescent series.[16,36] Finally, although our study is nationwide, caution should be exercised in generalisation to other populations and regions.

In conclusion, Roux-en-Y gastric bypass results in substantial weight loss, frequent resolution of cardiometabolic comorbidity, and improvement in quality of life into the long term in adolescents with severe obesity. By contrast, non-surgical treatment can lead to further weight gain and surgery. The gastric bypass procedure was associated with additional surgical intervention and nutritional deficiencies. The literature base now seems sufficiently mature to consider formal integration of bariatric surgery into treatment pathways for adolescents with severe obesity. However, adolescent bariatric surgery must be done within appropriate specialist multidisciplinary programmes that are specifically designed to accommodate adolescent patients and provide long-term follow-up and support. Future challenges include refinement of indications and contraindications, identification of ideal target age groups, and optimisation of postoperative support. We must also closely monitor patients for potential long-term adverse effects of surgery, across decades rather than years.

Contributors

All authors contributed to study design and writing of the report, had full access to all data in the study, and approved the final version. TO and CM had the idea for the study; TO, CM, EG, AJB, GB, and MN contributed to data collection and analysis; C-EF, JD, KE, PF, GG, KJ, JK, and SM contributed to data collection; and MP contributed to data analysis.

Declaration of interests

TO has received consulting fees for participation in a global advisory board and a lecturing fee from Ethicon Endo-Surgery, unrelated to the present work; lecturing fees from AstraZeneca and Sanofi-Aventis, unrelated to the present work; and disposable surgical equipment from Ethicon Endo-Surgery, for use in study participants. KJ has received a lecturing fee from Nestlé, unrelated to the present work. MN has received consulting fees for participation in a scientific advisory committee from Itrim, a commercial provider of non-surgical weight-loss services, unrelated to the present work; research grants from Pfizer, Cambridge Weight Plan, Novo Nordisk, and AstraZeneca, unrelated to the present work; and lecturing and/or consulting fees from Pfizer, Sanofi-Aventis, Roche, and Strategic Health Resources, unrelated to the present work. CM has received consulting fees for participation in scientific advisory committees from Itrim, Oriflame Wellness, and Sigrid Therapeutics, unrelated to the present work; and a research grant from Novo Nordisk, unrelated to the present work. EG, C-EF, JD, GB, KE, PF, GG, JK, SM, and MP declare no competing interests.

Acknowledgments

We thank all participating adolescents, their families, and health-care staff who made this study possible. We thank Malin Werling and Hans Lönroth for invaluable contributions. TO, EG, KJ, AJB, C-EF, CM, KE, PF, JD, GG, GM, JK, and SM were supported by grants from Västra Götaland Region, the Swedish Research Council (521-2012-319 and 2013-3770 [to GB]), the Swedish Governmental Agency for Innovation Systems (2013-01339), the Mrs Mary von Sydow Foundation, the Swedish Heart and Lung Foundation, the Swedish Childhood Diabetes Foundation, Stockholm County Council, and the National Board of Health and Welfare. TO and CM were supported by grants from the Swedish Order of Freemasons Children's Foundation, Stiftelsen Göteborgs Barnhus, and Stiftelsen Allmänna Barnhuset. AJB has received funding from the Royal College of Surgeons of England in the form of a clinical research fellowship. MN was supported by a

grant from the Swedish Research Council. MN and GB were supported by an award from the US National Institute of Diabetes, Digestive, and Kidney Diseases (National Institutes of Health; number R01DK105948). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, nor any other funding body.

References

1 Neovius M, Sundstrom J, Rasmussen F. Combined effects of overweight and smoking in late adolescence on subsequent mortality: nationwide cohort study. *BMJ* 2009; **338:** b496.

2 van Dam RM, Willett WC, Manson JE, Hu FB. The relationship between overweight in adolescence and premature death in women. *Ann Intern Med* 2006; **145:** 91–97.

3 Juonala M, Magnussen CG, Berenson GS, et al. Childhood adiposity, adult adiposity, and cardiovascular risk factors. *N Engl J Med* 2011; **365:** 1876–85.

4 Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic risks and severity of obesity in children and young adults. *N Engl J Med* 2015; **373:** 1307–17.

5 Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384:** 766–81.

6 Shah AS, D'Alessio D, Ford-Adams ME, Desai AP, Inge TH. Bariatric surgery: a potential treatment for type 2 diabetes in youth. *Diabetes Care* 2016; **39:** 934–40.

7 Beamish AJ, Olbers T. Bariatric and metabolic surgery in adolescents: a path to decrease adult cardiovascular mortality. *Curr Atheroscler Rep* 2015; **17:** 53.

8 Olshansky SJ, Passaro DJ, Hershow RC, et al. A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med* 2005; **352:** 1138–45.

9 Twig G, Yaniv G, Levine H, et al. Body-mass index in 2·3 million adolescents and cardiovascular death in adulthood. *N Engl J Med* 2016; **374:** 2430–40.

10 Kelly AS, Barlow SE, Rao G, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. *Circulation* 2013; **128:** 1689–712.

11 NHS UK Data Service. Health Survey for England: child trend tables, 2013. Dec 10, 2014. http://content.digital.nhs.uk/catalogue/PUB16077 (accessed Dec 1, 2016).

12 Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States 2009–2010. *NCHS Data Brief* 2012; **82:** 1–8.

13 Danielsson P, Kowalski J, Ekblom O, Marcus C. Response of severely obese children and adolescents to behavioral treatment. *Arch Pediatr Adolesc Med* 2012; **166:** 1103–08.

14 Michalsky M, Reichard K, Inge T, et al. ASMBS pediatric committee best practice guidelines. *Surg Obes Relat Dis* 2012; **8:** 1–7.

15 Paulus GF, de Vaan LE, Verdam FJ, Bouvy ND, Ambergen TA, van Heurn LW. Bariatric surgery in morbidly obese adolescents: a systematic review and meta-analysis. *Obes Surg* 2015; **25:** 860–78.

16 Inge TH, Courcoulas AP, Jenkins TM, et al. Weight loss and health status 3 years after bariatric surgery in adolescents. *N Engl J Med* 2016; **374:** 113–23.

17 Olbers T, Gronowitz E, Werling M, et al. Two-year outcome of laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity: results from a Swedish Nationwide Study (AMOS). *Int J Obes* 2012; **36:** 1388–95.

18 O'Brien PE, Sawyer SM, Laurie C, et al. Laparoscopic adjustable gastric banding in severely obese adolescents: a randomized trial. *JAMA* 2010; **303:** 519–26.

19 Olbers T, Lonroth H, Fagevik-Olsen M, Lundell L. Laparoscopic gastric bypass: development of technique, respiratory function, and long-term outcome. *Obes Surg* 2003; **13:** 364–70.

20 Danielsson P, Bohlin A, Bendito A, Svensson A, Klaesson S. Five-year outpatient programme that provided children with continuous behavioural obesity treatment enjoyed high success rate. *Acta Paediatr* 2016; **105:** 1181–90.

21 Nowicka P, Pietrobelli A, Flodmark CE. Low-intensity family therapy intervention is useful in a clinical setting to treat obese and extremely obese children. *Int J Pediatr Obes* 2007; **2:** 211–17.

22 American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2012; **35** (suppl 1): S64–71.

23 Taft C, Karlsson J, Sullivan M. Performance of the Swedish SF-36 version 2.0. *Qual Life Res* 2004; **13:** 251–56.

24 Karlsson J, Taft C, Sjostrom L, Torgerson JS, Sullivan M. Psychosocial functioning in the obese before and after weight reduction: construct validity and responsiveness of the Obesity-related Problems scale. *Int J Obes Relat Metab Disord* 2003; **27:** 617–30.

25 Ross R. Atherosclerosis: an inflammatory disease. *N Engl J Med* 1999; **340:** 115–26.

26 Kobayashi S, Inoue N, Ohashi Y, et al. Interaction of oxidative stress and inflammatory response in coronary plaque instability: important role of C-reactive protein. *Arterioscler Thromb Vasc Biol* 2003; **23:** 1398–404.

27 Bal BS, Finelli FC, Shope TR, Koch TR. Nutritional deficiencies after bariatric surgery. *Nat Rev Endocrinol* 2012; **8:** 544–56.

28 Herget S, Rudolph A, Hilbert A, Bluher S. Psychosocial status and mental health in adolescents before and after bariatric surgery: a systematic literature review. *Obes Facts* 2014; **7:** 233–45.

29 Jarvholm K, Karlsson J, Olbers T, et al. Two-year trends in psychological outcomes after gastric bypass in adolescents with severe obesity. *Obesity* 2015; **23:** 1966–72.

30 Neovius M, Narbro K, Keating C, et al. Health care use during 20 years following bariatric surgery. *JAMA* 2012; **308:** 1132–41.

31 Stenberg E, Szabo E, Ågren G, et al. Closure of mesenteric defects in laparoscopic gastric bypass: a multicentre, randomised, parallel, open-label trial. *Lancet* 2016; **387:** 1397–404.

32 Johansson K, Sundström J, Marcus C, Hemmingsson E, Neovius M. Risk of symptomatic gallstones and cholecystectomy after a very-low-calorie diet or low-calorie diet in a commercial weight loss program: 1-year matched cohort study. *Int J Obes* 2014; **38:** 279–84.

33 Uy MC, Talingdan-Te MC, Espinosa WZ, Daez ML, Ong JP. Ursodeoxycholic acid in the prevention of gallstone formation after bariatric surgery: a meta-analysis. *Obes Surg* 2008; **18:** 1532–38.

34 Reinehr T, Kleber M, Lass N, Toschke AM. Body mass index patterns over 5 y in obese children motivated to participate in a 1-y lifestyle intervention: age as a predictor of long-term success. *Am J Clin Nutr* 2010; **91:** 1165–71.

35 Christian NJ, King WC, Yanovski SZ, Courcoulas AP, Belle SH. Validity of self-reported weights following bariatric surgery. *JAMA* 2013; **310:** 2454–56.

36 Alqahtani AR, Antonisamy B, Alamri H, Elahmedi M, Zimmerman VA. Laparoscopic sleeve gastrectomy in 108 obese children and adolescents aged 5 to 21 years. *Ann Surg* 2012; **256:** 266–73.