

LSE

THE LONDON SCHOOL
OF ECONOMICS AND
POLITICAL SCIENCE ■

LSE Research Online

Helen Booth, Omar Khan, Toby Prevost, Marcus Reddy, Alex Dregan, Judith Charlton, Mark Ashworth, [Caroline Rudisill](#), Peter Littlejohns and Martin C. Gulliford

Incidence of type 2 diabetes after bariatric surgery: population-based matched cohort study

**Article (Published version)
(Refereed)**

Original citation:

Booth, Helen, Khan, Omar, Prevost, Toby, Reddy, Marcus, Dregan, Alex, Charlton, Judith, Ashworth, Mark, Rudisill, Caroline, Littlejohns, Peter and Gulliford, Martin C. (2014) *Incidence of type 2 diabetes after bariatric surgery: population-based matched cohort study*. [The Lancet Diabetes & Endocrinology](#). ISSN 2213-8587 (In Press) DOI: [10.1016/S2213-8587\(14\)70214-1](https://doi.org/10.1016/S2213-8587(14)70214-1)

© 2014 The Authors. Published by [Elsevier Ltd.](#)

Open Access article distributed under the terms of [CC BY 3.0](#).

This version available at: <http://eprints.lse.ac.uk/60130/>

Available in LSE Research Online: November 2014

LSE has developed LSE Research Online so that users may access research output of the School. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LSE Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain. You may freely distribute the URL (<http://eprints.lse.ac.uk>) of the LSE Research Online website.

Incidence of type 2 diabetes after bariatric surgery: population-based matched cohort study

Helen Booth, Omar Khan, Toby Prevost, Marcus Reddy, Alex Dregan, Judith Charlton, Mark Ashworth, Caroline Rudisill, Peter Littlejohns, Martin C Gulliford



Summary

Background The effect of currently used bariatric surgical procedures on the development of diabetes in obese people is not well defined. We aimed to assess the effect of bariatric surgery on development of type 2 diabetes in a large population of obese individuals.

Methods We did a matched cohort study of adults (age 20–100 years) identified from a UK-wide database of family practices, who were obese (BMI ≥ 30 kg/m²) and did not have diabetes. We enrolled 2167 patients who had undergone bariatric surgery between Jan 1, 2002, and April 30, 2014, and matched them—according to BMI, age, sex, index year, and HbA_{1c}—with 2167 controls who had not had surgery. Procedures included laparoscopic gastric banding (n=1053), gastric bypass (795), and sleeve gastrectomy (317), with two procedures undefined. The primary outcome was development of clinical diabetes, which we extracted from electronic health records. Analyses were adjusted for matching variables, comorbidity, cardiovascular risk factors, and use of antihypertensive and lipid-lowering drugs.

Findings During a maximum of 7 years of follow-up (median 2.8 years [IQR 1.3–4.5]), 38 new diagnoses of diabetes were made in bariatric surgery patients and 177 were made in controls. By the end of 7 years of follow-up, 4.3% (95% CI 2.9–6.5) of bariatric surgery patients and 16.2% (13.3–19.6) of matched controls had developed diabetes. The incidence of diabetes diagnosis was 28.2 (95% CI 24.4–32.7) per 1000 person-years in controls and 5.7 (4.2–7.8) per 1000 person-years in bariatric surgery patients; the adjusted hazard ratio was 0.20 (95% CI 0.13–0.30, $p < 0.0001$). This estimate was robust after varying the comparison group in sensitivity analyses, excluding gestational diabetes, or allowing for competing mortality risk.

Interpretation Bariatric surgery is associated with reduced incidence of clinical diabetes in obese participants without diabetes at baseline for up to 7 years after the procedure.

Funding UK National Institute for Health Research.

Copyright © Booth et al. Open Access article distributed under the terms of CC BY.

Introduction

Obesity is an increasing worldwide health problem.¹ Treatment of obesity with lifestyle or behavioural approaches is generally associated with only small reductions in bodyweight that are typically not sustained.^{2,3} Bariatric surgical interventions for obesity have been associated with substantial weight loss, decreased morbidity, and improvements in quality of life.^{4,5} Despite the escalating use of bariatric surgery,⁶ the evidence base supporting use of these procedures for obesity and obesity-associated morbidity is scant. In a systematic review,⁷ only 11 high-quality trials were identified (with 796 participants). Similarly, little evidence is available on the long-term effects of bariatric surgery. The Swedish Obese Subjects (SOS) study,⁸ which provides the best evidence for long-term effects so far, was initiated more than 20 years ago and the surgical procedures used might not reflect current practice. Most reported studies have been done in specialist centres and outcomes achieved might not be typical of routine practice.

The possible effect of bariatric surgery on type 2 diabetes is of particular importance because 3% of

severely obese individuals develop diabetes every year.⁹ Data show that bariatric surgery might contribute to resolution of existing type 2 diabetes.^{10,11} Evidence is scarcer for whether bariatric surgery for weight loss in obese patients without diabetes prevents future development of diabetes. In the SOS study,⁹ 1658 patients without diabetes were followed up over a 15-year period, with a 76% reduction in the incidence of diabetes after bariatric surgery. However, most participants in the SOS study had vertical banded gastroplasty—an operation that is not undertaken widely nowadays because of the high frequency of weight regain.

Participants in research studies often undergo intensive follow-up that might not be typical of care provided in routine clinical practice. The aim of our study was to recruit a population-based cohort of patients and matched controls, drawn from a database of primary care electronic health records, to provide a pragmatic assessment of the effect of bariatric surgery on the development of clinical diabetes in obese individuals receiving routine clinical care.

Lancet Diabetes Endocrinol 2014

Published Online
November 3, 2014
[http://dx.doi.org/10.1016/S2213-8587\(14\)70214-1](http://dx.doi.org/10.1016/S2213-8587(14)70214-1)
See Online/Comment
[http://dx.doi.org/10.1016/S2213-8587\(14\)70218-9](http://dx.doi.org/10.1016/S2213-8587(14)70218-9)

Department of Primary Care and Public Health Sciences, King's College London, London, UK (H Booth MSc, Prof T Prevost PhD, A Dregan PhD, J Charlton MSc, M Ashworth DM, Prof P Littlejohns MD, Prof M C Gulliford FFPH); NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust, London, UK (H Booth, Prof T Prevost, A Dregan, Prof M C Gulliford); Department of Surgery, Whittington Hospital, London, UK (O Khan FRCS); Department of Surgery, St George's Hospital, London, UK (M Reddy FRCS); and Department of Social Policy, London School of Economics and Political Science, London, UK (C Rudisill PhD)

Correspondence to: Dr Martin Gulliford, Department of Primary Care and Public Health, King's College London, London SE1 3QD, UK martin.gulliford@kcl.ac.uk

For the study protocol see http://www.nets.nihr.ac.uk/_data/assets/pdf_file/0005/81806/PRO-12-5005-12.pdf

Methods

Participants

We selected participants from the Clinical Practice Research Datalink (CPRD). This database includes electronic health records for more than 5 million individuals currently registered for primary care at more than 680 family practices in the UK.¹² The size and geographical distribution of family practices, and the age and sex of individuals included in the database, are broadly representative of the UK population, enabling selection of population-based controls. The high quality of CPRD diagnostic and prescription information has been reported elsewhere.¹³

From the CPRD database we identified a cohort of obese individuals without diabetes who had undergone bariatric surgery before April 30, 2014, using medical codes for laparoscopic gastric banding, gastric bypass, or sleeve gastrectomy. We defined the date on which the first code was recorded as the index date. We excluded participants who had bariatric surgery less than 1 year after the start of the electronic health record, because this record might have indicated a procedure undertaken before their registration at the family practice. We also excluded patients younger than 20 years at the index date, those with either no BMI record before surgery or a last recorded BMI value less than 30 kg/m², individuals with a record for gastric band removal before the index date, and patients with diabetes diagnosed on or before the index date. The most recent BMI value was not always recorded immediately before surgery and might not have provided an accurate assessment of the degree of preoperative obesity.

We obtained matched controls for comparison from a cohort of 103 502 obese individuals without diabetes, sampled from the CPRD, who did not have bariatric surgery and were not older than the maximum age of the bariatric surgery patients. We defined the index date for controls as the date of the earliest BMI record on which the patient attained their highest BMI category. We matched controls for age, BMI, sex, index year, and highest measured HbA_{1c} category (<6%, 6·0% to <6·5%, and not known). We did nearest neighbour matching without replacement¹⁴ using the `psmatch2` command in Stata version 13 (College Station, TX, USA).

We analysed data that were fully anonymised. The CPRD Independent Scientific Advisory Committee gave scientific and ethics approval for the study (ISAC 13_089).

Procedures

We recorded baseline characteristics of bariatric surgery patients and matched controls. We identified new diagnoses of clinical diabetes from prospective electronic health records, obtaining data for medical diagnoses, drug prescriptions, and HbA_{1c} values. We judged patients to have a diagnosis of clinical diabetes if a medical code for diabetes was recorded, if insulin or oral hypoglycaemic drugs were prescribed, or if an HbA_{1c} value of 6·5% or

higher was recorded (WHO criteria).¹⁵ Oral hypoglycaemic drugs included sulfonylureas, metformin, acarbose, dipeptidyl-peptidase-4 inhibitors, glitazones, and glinide drugs. We coded women with recorded diagnoses of polycystic ovary syndrome, who were prescribed diabetes drugs but were never diagnosed with diabetes, as non-diabetic. We took the date of the earliest medical, therapeutic, or test event as the date of diabetes diagnosis. We included all new diagnoses of diabetes because different diabetes phenotypes cannot always be distinguished clearly in clinical practice. However, we analysed new cases of diabetes according to codes for type 1 diabetes, for prescription of insulin within 6 months of the diagnosis date, and for diagnoses of gestational diabetes.

The index BMI was the most recently recorded value before the index date. We identified records for smoking status, blood pressure, and cholesterol and used the most recently recorded value before the index date for the baseline value. We identified concomitant depression, coronary heart disease, and stroke with medical codes.^{16–18}

Statistical analysis

To assess diabetes onset, we used a time-to-event framework, using a Cox proportional hazards model. We classed failure as a new diagnosis of diabetes. We censored records at the end of a participant's registration, the last date of CPRD data collection, or death, and we censored follow-up after 7 years when only a few participants remained. We adjusted models for: matching variables (age, sex, BMI, HbA_{1c}, and index year); prevalent coronary heart disease, stroke, and previous diagnosis of depression; smoking status; total cholesterol greater than 5 mmol/L; blood pressure higher than 140/90 mm Hg; and use of statins and anti-hypertensive drugs before surgery. Quadratic terms for age and BMI did not improve goodness of fit. We used indicator variables for missing data for blood pressure and cholesterol. We evaluated the proportional hazards assumption with no evidence that it was violated. To allow for clustering of responses by family practice, we used robust variance estimates.

We did several sensitivity analyses. We used the unmatched cohort of 103 502 obese patients without diabetes for comparison. Using the matched cohort, we excluded participants diagnosed with diabetes within 12 months of the index date, then we excluded patients diagnosed with gestational diabetes. We also assessed the effect of competing risk on mortality.¹⁹ We used Stata version 13 for all analyses.

Role of the funding source

The funder 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 the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Jan 1, 2002, and April 30, 2014, 4793 obese patients in the CPRD database had undergone bariatric surgery. We excluded 1324 individuals whose procedure was first recorded less than 1 year after the start of their electronic health record, 14 people younger than 20 years at the index date, and 401 patients with either no BMI record before surgery or BMI values lower than 30 kg/m² before surgery. A further 878 people were excluded who had a diagnosis of diabetes before the date of their surgery, and nine individuals were excluded who underwent gastric band removal before the index date. Therefore, we included 2167 obese patients without diabetes who had bariatric surgery. We matched these patients according to age, BMI, sex, index year, and HbA_{1c} category with 2167 controls who did not have surgery. Median duration of follow-up was 2.8 years (IQR 1.3–4.5), with a maximum of 7 years of follow-up.

The type of bariatric surgery was classified according to the procedure recorded on the index date. 1053 (49%) patients received laparoscopic gastric banding, 795 (37%) had gastric bypass procedures, and 317 (15%) underwent sleeve gastrectomy; two people had codes for more than one type of procedure on the index date.

Baseline values were those most recently recorded before the index date (table 1). Bariatric surgery patients and controls were generally well matched for age, sex, and BMI; index BMI was 40 kg/m² or higher for about 60% of all participants. 1198 (55%) bariatric surgery patients and 701 (32%) controls had previously been diagnosed with depression before the index date ($p < 0.0001$). Bariatric surgery patients were more likely to have elevated blood pressure or raised total cholesterol values and to be treated with anti-hypertensive or lipid-lowering drugs (table 1).

The figure shows the incidence of diabetes in bariatric surgery patients during the 7 years after the procedure and in matched controls. 38 new diagnoses of diabetes were made in bariatric surgery patients and 177 were made in controls (table 2). None of the participants was recorded as having type 1 diabetes. Three controls and one bariatric surgery patient with diabetes were treated with insulin within 6 months of the diabetes diagnosis date. Ten controls and three bariatric surgery patients had gestational diabetes and were excluded in the sensitivity analysis. By the end of 7-year follow-up, 4.3% (95% CI 2.9–6.5) of bariatric surgery patients and 16.2% (13.3–19.6) of matched controls had developed diabetes (table 2). Incidence of diabetes was 28.2 (95% CI 24.4–32.7) diagnoses per 1000 person-years in controls and 5.7 (4.2–7.8) per 1000 person-years in bariatric surgery patients (table 3).

Compared with controls, the unadjusted hazard ratio for development of diabetes in bariatric surgery patients was 0.20 (95% CI 0.14–0.30; $p < 0.0001$). Multivariable adjustment for baseline characteristics (including matching variables [ie, age, BMI, sex, index year, and HbA_{1c}

category]; comorbid cardiovascular disease and depression; smoking; and hypertension, high blood cholesterol, and associated treatment) had a negligible effect on the size of

	Bariatric surgery patients (n=2167)	Matched controls (n=2167)	p value
Women	1812 (84%)	1878 (87%)	Matched
Age (years)	44.4 (10.1)	44.6 (14.1)	Matched
BMI (kg/m ²)	43.0 (8.1)	43.2 (8.6)	Matched
BMI category			Matched
Obese (30–34.9 kg/m ²)	339 (16%)	332 (15%)	..
Severe obesity (35–39.9 kg/m ²)	535 (25%)	551 (24%)	..
Very severe obesity (≥ 40 kg/m ²)	1293 (60%)	1284 (59%)	..
Index year			Matched
2002–05	84 (4%)	113 (5%)	..
2006–08	483 (22%)	442 (20%)	..
2009–11	979 (45%)	1014 (47%)	..
2012–14	621 (29%)	598 (28%)	..
HbA _{1c} category			Matched
<6.0% (<42 mmol/mol)	208 (10%)	195 (9%)	..
6.0% to <6.5% (42 to <48 mmol/mol)	54 (2%)	50 (2%)	..
Not recorded	1905 (88%)	1922 (89%)	..
Coronary heart disease	60 (3%)	58 (3%)	0.847
Stroke	20 (1%)	26 (1%)	0.381
Previous depression diagnosis	1198 (55%)	701 (32%)	<0.0001
Current smoker	372 (17%)	386 (18%)	0.590
Blood pressure recorded >140/90 mm Hg*	581 (27%)	464 (21%)	0.0002
Total cholesterol recorded >5 mmol/L*	845 (39%)	387 (18%)	<0.0001
Treatment for hypertension	906 (42%)	519 (24%)	<0.0001
Lipid-lowering treatment	270 (12%)	183 (8%)	<0.0001

Data are number of people (%) or mean (SD). *591 (27%) controls and 18 (1%) bariatric surgery patients had missing values for blood pressure and 1466 (68%) controls and 557 (26%) bariatric surgery patients had missing values for cholesterol.

Table 1: Baseline characteristics

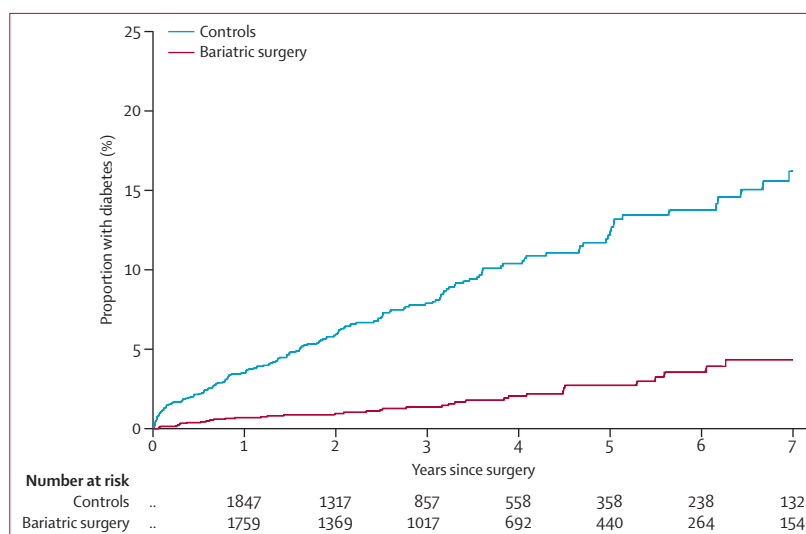


Figure: Incidence of type 2 diabetes in patients undergoing bariatric surgery and in matched controls during 7 years of follow-up

the estimated hazard ratio. The fully adjusted hazard ratio for bariatric surgery was 0·20 (0·13–0·30; $p < 0·0001$). After allowing for bariatric surgery, baseline characteristics were generally not associated with the risk of developing diabetes, except for an increased hazard associated with raised baseline HbA_{1c} (appendix p 1).

See Online for appendix

Table 3 shows the incidence of diabetes and hazard ratios for development of diabetes by subgroup. The effect

Year	Bariatric surgery patients		Matched controls	
	Diabetes diagnoses (n)	Proportion with diabetes* (95% CI)	Diabetes diagnoses (n)	Proportion with diabetes* (95% CI)
1	14	0·7% (0·4–1·2)	73	3·5% (2·8–4·4)
2	4	1·0% (0·6–1·5)	41	5·9% (5·0–7·1)
3	5	1·4% (0·9–2·1)	23	7·9% (6·7–9·3)
4	6	2·1% (1·4–3·0)	20	10·4% (8·8–12·2)
5	4	2·7% (1·9–4·0)	10	12·4% (10·5–14·7)
6	3	3·6% (2·4–5·2)	5	13·8% (11·6–16·3)
7	2	4·3% (2·9–6·5)	5	16·2% (13·3–19·6)

*Calculated from time-to-event data and not from aggregate figures shown in columns to left.

Table 2: New diabetes diagnoses during up to 7 years of follow-up

of bariatric surgery was generally similar in men and women and across age groups. No interaction was noted between bariatric surgery and age. The effect of bariatric surgery was also similar for index periods between 2002 and 2014, even though gastric banding accounted for 96% (81 of 84) of procedures in the earliest period and only 24% (148 of 621) in the latest. However, an interaction was noted between bariatric surgery and increasing BMI ($p = 0·0819$). In the fully adjusted model, which included adjustment for index year and the other covariates, hazard ratios were slightly lower for both gastric bypass and sleeve gastrectomy compared with laparoscopic gastric banding ($p = 0·0714$), although every type of procedure was associated with a lower incidence of diabetes compared with controls. Only a few patients were included in some subgroups: laparoscopic gastric banding was associated with 30 new diagnoses of diabetes, gastric bypass with six, and sleeve gastrectomy with two.

The association of bariatric surgery with decreased incidence of diabetes was robust in several sensitivity analyses. When the entire comparison cohort of 103 502 obese individuals without diabetes was used for reference (rather than selected matched controls), the adjusted hazard ratio for the effect of bariatric surgery on development of diabetes was 0·16 (95% CI 0·11–0·22; $p < 0·0001$). Diagnosis of diabetes might be more likely soon after the index date because of heightened medical surveillance. However, when patients with diabetes diagnosed within the first year after the index date were excluded, the adjusted hazard ratio was 0·20 (0·12–0·32; $p < 0·0001$). Exclusion of individuals who had gestational diabetes gave an adjusted hazard ratio of 0·19 (0·13–0·30; $p < 0·0001$). In a competing risks analysis, allowing for the competing risk of death, the adjusted hazard ratio was 0·20 (0·13–0·31, $p < 0·0001$). Analyses that used only clinical criteria (ie, medical diagnoses and drug prescriptions) and not HbA_{1c} for diagnosis of diabetes gave similar results (data not shown).

Discussion

In a large population-based cohort of obese patients undergoing bariatric surgery by contemporary methods, the risk of developing type 2 diabetes was reduced by 80% over a maximum of 7 years of follow-up compared with controls who did not undergo surgery. Our study is perhaps the first large-scale pragmatic study to assess the effect of current bariatric surgical procedures on diabetes incidence in the context of usual care settings (panel). Even in patients seen in routine clinical practice, our results show that modern bariatric surgical procedures have particular effectiveness for diabetes prevention in obese patients.

An effect of bariatric surgery on incidence of diabetes was noted in both men and women and across all ages. Gastric bypass and sleeve gastrectomy were associated with slightly lower relative hazards for diabetes than was laparoscopic gastric banding, but we caution against

	Diabetes incidence per 1000 person-years (95% CI)		Adjusted hazard ratio* (95% CI)	p value
	Bariatric surgery patients	Controls		
All participants	5·7 (4·2–7·8)	28·2 (24·4–32·7)	0·20 (0·13–0·30)	<0·0001
Sex				
Men	6·8 (3·2–14·3)	38·5 (26·7–55·4)	0·17 (0·06–0·46)	0·0004
Women	5·5 (3·9–7·8)	26·8 (22·8–31·5)	0·21 (0·13–0·33)	<0·0001
Baseline BMI category (kg/m ²)				
30–34·9	6·1 (2·9–12·9)	15·7 (9·7–25·2)	0·39 (0·11–1·42)	0·1469
35–39·9	5·9 (3·2–10·9)	22·1 (16·0–30·5)	0·24 (0·12–0·49)	<0·0001
≥40	5·5 (3·6–8·4)	35·0 (29·3–41·7)	0·15 (0·09–0·25)	<0·0001
Age group (years)				
20–34	1·7 (0·4–7·0)	17·3 (11·8–25·2)	0·14 (0·03–0·63)	0·0102
35–54	6·3 (4·4–9·3)	26·3 (21·1–32·7)	0·21 (0·13–0·34)	<0·0001
≥55	7·0 (3·5–14·1)	42·1 (33·3–53·2)	0·18 (0·08–0·38)	<0·0001
Type of procedure†				
Laparoscopic gastric banding	7·3 (5·1–10·5)	24·9 (20·2–30·6)	0·29 (0·18–0·48)	<0·0001
Gastric bypass	3·2 (1·4–7·1)	33·3 (26·0–42·7)	0·10 (0·04–0·25)	<0·0001
Sleeve gastrectomy	2·9 (0·7–11·7)	31·7 (21·4–47·0)	0·07 (0·01–0·30)	0·0003
Index period				
2002–05	3·8 (1·0–15·3)	29·7 (18·9–46·5)	0·12 (0·03–0·52)	0·0045
2006–08	8·3 (5·4–12·9)	25·8 (19·7–33·9)	0·32 (0·18–0·57)	<0·0001
2009–11	4·2 (2·5–7·3)	28·2 (22·6–35·4)	0·14 (0·06–0·31)	<0·0001
2012–14	4·4 (1·4–13·7)	32·4 (22·5–46·6)	0·10 (0·03–0·36)	<0·0001

*Adjusted for age, sex, BMI, coronary heart disease, stroke, depression, smoking status, elevated total cholesterol, high blood pressure, HbA_{1c} category, use of antihypertensive drugs and statins, and year of procedure.

Table 3: Effect of bariatric surgery on risk of diabetes by age group, sex, BMI, and type of procedure

drawing firm conclusions concerning the comparative effectiveness of different procedures from a non-randomised study because selection for different procedures might be associated with the underlying risk of developing diabetes, and some of the subgroup analyses were based on small numbers of outcome events.

Previous studies of bariatric surgery and prevention of type 2 diabetes include the SOS study⁹ and several case series (panel).^{20–22} In the SOS study,⁹ 69% of patients underwent vertical banded gastroplasty, 19% underwent banding, and 12% received gastric bypass surgery. The incidence of diabetes in bariatric surgery patients and controls and the relative risk reduction associated with bariatric surgery were both very similar to those recorded in our study. Our findings, therefore, are important confirmation from a population-based sample that intervention with current surgical procedures can reduce the incidence of diabetes.

Our study had the strengths of a large population-based sample with prolonged follow-up and prospective documentation of clinical diabetes in primary care. However, we acknowledge several limitations. First, we identified three major procedures used in bariatric surgery in the UK; however, some surgical techniques are done less frequently, such as the duodenal switch, which we did not include. Second, controls did not receive standardised non-surgical intervention for obesity and, during the study period, intensive multimodal weight loss programmes in primary care were rare. Third, ascertainment of diabetes outcomes was comprehensive, and diagnoses noted in CPRD records are generally valid.¹³ However, we were not able to document cases of subclinical diabetes that might have been confirmed by testing all patients for evidence of hyperglycaemia. We excluded women in whom antidiabetes drugs were prescribed for polycystic ovary syndrome, but some other prescriptions might have been for diabetes prevention or other indications rather than treatment of clinical diabetes. Fourth, bodyweight and other relevant measures were not recorded consistently during the period of study. Preoperative BMI category might have been misclassified and we were unable to relate differences in diabetes incidence to changes in bodyweight, although we should point out that the effects of bariatric surgery are not mediated entirely by changes in bodyweight.²³ We noted that weight reductions after surgery accorded with those of previous reports. Fifth, access to bariatric surgery is currently limited in the UK; thus, people receiving surgery represent a highly selected group. Sixth, the higher prevalence of previous diagnoses of depression in surgical patients compared with controls suggests that obese individuals with depression were more likely to be referred for surgery, possibly with the belief that weight loss might improve their depressive symptoms. Seventh, patients who received surgery might have been more adherent than controls to other diabetes prevention advice, including diet or exercise. However, we noted that

Panel: Research in context

Systematic review

We searched Scopus, Web of Science, PubMed, Medline, and Embase for studies published in English up to Sept 26, 2014, with the keywords: “diabetes”, “bariatric surgery”, “prevention”, and “incidence”. We retrieved no randomised controlled trials in which the incidence of diabetes after bariatric surgery was reported.⁷ We identified four cohort studies in which the development of diabetes after bariatric surgery was assessed,^{9,20–22} none of which were population based. The largest cohort was in the Swedish Obese Subjects (SOS) study,⁹ which comprised 1658 participants, with 69% receiving vertical banded gastroplasty, 19% gastric banding, and 12% gastric bypass from 1987 onwards. Other studies were smaller, with fewer than 300 participants; two only included people with prediabetes.^{20,22} All four studies suggested reduced occurrence of diabetes after bariatric surgery.

Interpretation

In our population-based cohort of 2167 patients who had bariatric surgery between 2002 and 2014—including laparoscopic adjustable gastric banding, gastric bypass, and sleeve gastrectomy—and 2167 controls matched for age, sex, and BMI, the incidence of diabetes was reduced after bariatric surgery, with an adjusted hazard ratio of 0.20 (95% CI 0.13–0.30). The association of bariatric surgery with reduced diabetes incidence was seen in both men and women, across age groups, and after different types of surgical procedure. In people with severe obesity, bariatric surgical procedures in current use could be effective at reducing the incidence of clinical diabetes for up to 7 years.

people who received surgery were more likely to be prescribed antihypertensive drugs or statins, which can sometimes be associated with diabetes. Eighth, controls had missing values for blood pressure and plasma cholesterol more frequently than did bariatric surgery patients, suggesting medical surveillance was decreased in this group. Differential medical surveillance might have made detection of diabetes or prediabetes more likely in patients considered for surgery, leading to possible exclusion bias in patients receiving surgery. However, the higher proportion of bariatric surgery patients on antihypertensive or lipid-lowering treatment might suggest selection bias in the opposite direction. Ninth, we included relevant confounders (such as hypertension and hyperlipidaemia) in our analysis, but misclassification and missing values could lead to residual bias. In a non-randomised study, residual confounding from unmeasured genetic, social, or environmental variables is a concern. However, we fitted several different models and did sensitivity analyses that showed the main findings of the study were robust. Finally, nearest neighbour matching gave a comparison group that was not exactly matched for key variables.

However, covariate adjustment had little effect and very similar results were obtained when the entire source cohort was used for reference. A method of analysis that did not allow for matching might give slightly wider CIs and larger p values than a matched analysis,²⁴ but our results did not raise concerns about statistical error.

Our findings, together with those of previous studies,²⁵ suggest that bariatric surgery could be a highly effective method for prevention of diabetes in patients with severe obesity. How should surgery for obesity be integrated into strategies for control of obesity and prevention of diabetes in the population at risk? Further research is needed to understand the outcomes of different levels of uptake of obesity surgery, and the long-term effects for patients who receive current surgical procedures for obesity.

Contributors

MCG, TP, MA, CR, MR, OK, PL, and AD designed the study. TP advised on the design and implementation of the data analysis, together with other authors. JC, HB and MCG did the data analysis. HB and MCG wrote the report. OK, MR, PL, CR, and MA contributed to interpretation of results. All authors commented on and approved the report. MCG is guarantor.

Declaration of interests

We declare no competing interests.

Acknowledgments

This research was funded by the UK National Institutes for Health Research (NIHR) Health Services and Delivery Research programme. AD, TP, and MCG are supported by the NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the UK National Health Service, NIHR, or the Department of Health (England). This study is based in part on data from the Clinical Practice Research Datalink (CPRD) obtained under licence from the UK Medicines and Healthcare products Regulatory Agency (MHRA); however, the interpretation and conclusions contained in this report are those of the authors alone.

References

- 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.
- Dombrowski SU, Knittle K, Avenell A, Araujo-Soares V, Sniehotta FF. Long term maintenance of weight loss with non-surgical interventions in obese adults: systematic review and meta-analyses of randomised controlled trials. *BMJ* 2014; **348**: g2646.
- Avenell A, Broom J, Brown TJ, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. *Health Technol Assess* 2004; **8**: iii–182.
- Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007; **357**: 741–52.
- Picot J, Jones J, Colquitt JL, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technol Assess* 2009; **13**: 215–357.
- Burns EM, Naseem H, Bottle A, et al. Introduction of laparoscopic bariatric surgery in England: observational population cohort study. *BMJ* 2010; **341**: c4296.
- Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. *BMJ* 2013; **347**: f5934.
- Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. *J Intern Med* 2013; **273**: 219–34.
- Carlsson LMS, Peltonen M, Ahlin S, et al. Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. *N Engl J Med* 2012; **367**: 695–704.
- Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *Am J Med* 2009; **122**: 248–56.e5.
- Sjöström L, Peltonen M, Jacobson P, et al. Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. *JAMA* 2014; **311**: 2297–304.
- Williams T, van Staa T, Puri S, Eaton S. Recent advances in the utility and use of the general practice research database as an example of a UK primary care data resource. *Ther Adv Drug Safety* 2012; **3**: 89–99.
- Herrett E, Thomas SL, Schoonen WM, Smeeth L, Hall AJ. Validation and validity of diagnoses in the general practice research database: a systematic review. *Br J Clin Pharmacol* 2010; **69**: 4–14.
- Abadie A, Imbens GW. Large sample properties of matching estimators for average treatment effects. *Econometrica* 2006; **74**: 235–67.
- WHO. Use of glycated haemoglobin (HbA1c) in the diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. 2011. http://www.who.int/diabetes/publications/report-hba1c_2011.pdf (accessed Sept 4, 2014).
- Bhattarai N, Charlton J, Rudisill C, Gulliford MC. Coding, recording and incidence of different forms of coronary heart disease in primary care. *PLoS One* 2012; published online Jan 19. <http://dx.doi.org/10.1371/journal.pone.0029776>.
- Gulliford MC, Charlton J, Ashworth M, Rudd AG, Toschke AM, for the eCRT Research Team. Selection of medical diagnostic codes for analysis of electronic patient records: application to stroke in a primary care database. *PLoS One* 2009; published online Sept 24. <http://dx.doi.org/10.1371/journal.pone.0007168>.
- Bhattarai N, Charlton J, Rudisill C, Gulliford MC. Prevalence of depression and utilization of health care in single and multiple morbidity: a population-based cohort study. *Psychol Med* 2013; **43**: 1423–31.
- Fine RJ, Gray JP. A proportional hazards model for the sub-distribution of a competing risk. *J Am Statist Assoc* 1999; **94**: 496–509.
- Long SD, O'Brien K, MacDonald KG Jr, et al. Weight loss in severely obese subjects prevents the progression of impaired glucose tolerance to type II diabetes: a longitudinal interventional study. *Diabetes Care* 1994; **17**: 372–75.
- Pontiroli AE, Folli F, Paganelli M, et al. Laparoscopic gastric banding prevents type 2 diabetes and arterial hypertension and induces their remission in morbid obesity: a 4-year case-controlled study. *Diabetes Care* 2005; **28**: 2703–09.
- Wentworth JM, Hensman T, Playfair J, et al. Laparoscopic adjustable gastric banding and progression from impaired fasting glucose to diabetes. *Diabetologia* 2014; **57**: 463–68.
- Courcoulas AP, Christian NJ, Belle SH, et al. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA* 2013; **310**: 2416–25.
- Austin PC. Comparing paired vs non-paired statistical methods of analyses when making inferences about absolute risk reductions in propensity-score matched samples. *Stat Med* 2011; **30**: 1292–301.
- Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes: a systematic review and meta-analysis of different intervention strategies. *Diabetes Obes Metab* 2014; **16**: 719–27.