Original article

# Obesity surgery and risk of cancer

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**Background:** Obesity increases the risk of several types of cancer. Whether bariatric surgery influences the risk of obesity-related cancer is not clear. This study aimed to uncover the risk of hormone-related (breast, endometrial and prostate), colorectal and oesophageal cancers following obesity surgery.

**Methods:** This national population-based cohort study used data from the Hospital Episode Statistics database in England collected between 1997 and 2012. Propensity matching on sex, age, co-morbidity and duration of follow-up was used to compare cancer risk among obese individuals undergoing bariatric surgery (gastric bypass, gastric banding or sleeve gastrectomy) and obese individuals not undergoing such surgery. Conditional logistic regression provided odds ratios (ORs) with 95 per cent confidence intervals.

**Results:** In the study period, from a cohort of 716 960 patients diagnosed with obesity, 8794 patients who underwent bariatric surgery were matched exactly with 8794 obese patients who did not have surgery. Compared with the no-surgery group, patients who had bariatric surgery exhibited a decreased risk of hormone-related cancers (OR 0·23, 95 per cent c.i. 0·18 to 0·30). This decrease was consistent for breast (OR 0·25, 0·19 to 0·33), endometrium (OR 0·21, 0·13 to 0·35) and prostate (OR 0·37, 0·17 to 0·76) cancer. Gastric bypass resulted in the largest risk reduction for hormone-related cancers (OR 0·16, 0·11 to 0·24). Gastric bypass, but not gastric banding or sleeve gastrectomy, was associated with an increased risk of colorectal cancer (OR 2·63, 1·17 to 5·95). Longer follow-up after bariatric surgery strengthened these diverging associations.

**Conclusion:** Bariatric surgery is associated with decreased risk of hormone-related cancers, whereas gastric bypass might increase the risk of colorectal cancer.

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## Introduction

Obesity, defined as a BMI over 30 kg/m$^2$, is an increasing global health problem[1]. Since 1980 the prevalence of obesity has nearly doubled, and currently more than half a billion of the world's adult population are obese[2]. Obesity increases the risk of overall mortality and of certain cancer types, as well as cardiovascular, respiratory and liver diseases[3]. Hormone-related cancer (breast, endometrium and prostate), colorectal cancer and oesophageal cancer have all been associated with obesity[4]. Obesity (bariatric) surgery is the only evidence-based treatment that offers substantial and long-lasting weight reduction in severely obese individuals[5]. The use of bariatric surgery has increased in England and elsewhere during the past three decades[6], and is presently among the most commonly performed gastrointestinal operations globally, with approximately 468 609 laparoscopic operations a year[7].

Bariatric surgery has gained support from studies[5,8,9] showing improved long-term survival and improvements in diabetes and cardiovascular conditions compared with rates in unoperated obese individuals. However, there is limited knowledge on how bariatric surgery influences cancer risk, and the existing studies[10–14] show conflicting results.

Three dominating bariatric surgery procedures – gastric bypass, gastric banding and sleeve gastrectomy – have different mechanisms. Gastric bypass is restrictive (reduced gastric reservoir), malabsorptive (as the small gastric reservoir drains into the small bowel so that the nutrient stream is diverted away from the gastric fundus and antrum, the

duodenum and proximal jejunum), and mediates hormonal changes (promoting early satiety and suppressing hunger). Gastric banding is restrictive (limiting the gastric reservoir, provoking early satiety and slowing down emptying from the pouch, thereby decreasing food intake). Sleeve gastrectomy is also restrictive, it reduces the gastric reservoir by narrowing the width of the stomach.

This study aimed to compare the risk of five types of cancer (breast, endometrial, prostate, colorectal and oesophageal) in obese individuals who have undergone bariatric surgery with matched obese individuals who have not had such surgery.

## Methods

This study was based on a nationwide English population-based cohort of patients over the age of 17 years who were diagnosed with obesity between 1 April 1997 and 31 March 2012. Data were derived from the Hospital Episode Statistics (HES) database[15]. Patients with obesity were identified using the ICD-10 code E66. Patients were tracked through HES using their unique identifier to ascertain all cohort members who underwent bariatric surgery. The HES was also used to identify study participants who developed cancer. All patients were followed through the entirety of the HES or until death as defined by the Office for National Statistics database. HES captures all patients treated in public sector hospitals and the minority of patients treated in privately funded institutions. All diagnostic and procedural codes were verified nationally and locally.

Surgical procedures were identified using OPCS fourth revision codes for gastric bypass (G281–G283, G288–G289, G310–G316, G318–G325, G328–G332, G335–G336, G338–G339), gastric banding (G301–G304, G308–G309) and sleeve gastrectomy (G284, G285). Within the study interval, 171 patients underwent intragastric balloon procedures, and two patients had a duodenal switch procedure alone and were excluded from the analysis. The incidence of breast, endometrial, prostate, colorectal and oesophageal cancers in patients who underwent bariatric surgery (exposed group) was compared against propensity-matched obese individuals who did not have such surgery (control group). The five studied cancer types were identified with ICD-10 codes for breast cancer (C50, D05), endometrial cancer (C54, D070), prostate cancer (C61, D075), colorectal cancer (C18–C20, D010–D012) and oesophageal cancer (C15, D001). Cancer outcomes were further compared for the different bariatric procedures; gastric bypass, gastric banding and sleeve gastrectomy.

Permission and ethical approval for the comparison of anonymized administrative data was obtained from the National Information Governance Board for Health and Social Care in England.

### Propensity matching and statistical analysis

Propensity scores were calculated with a logistic regression model predicting the dependent variable of bariatric surgery or not. Co-variables included in the model were sex, age (each year), Charlson Co-morbidity Index (categorical score 0–9) and duration of study period (continuous variable in months). Patients who underwent bariatric surgery (exposed group) were matched, with exact propensity scores, on a one-to-one basis with patients in the obese study cohort who did not undergo bariatric surgery (control group). The length of the study period was defined as the time from first diagnosis of obesity in both groups to the final day of the study period or death, whichever occurred first. Patients diagnosed with cancer earlier than their entry into the cohort were excluded before matching. Each patient who underwent bariatric surgery (exposed) was matched with a no-surgery patient (unexposed) for length of study period and date of diagnosis. The matched control patients were then assigned an intervention date, according to the surgery date of their exposed matched pair. If one of the pair died (a few cases only), follow-up of their matched pair was truncated to the date of death. Thus the length of follow-up for each exposed and control pair was the same. In both groups, cancers that developed between the date of diagnosis of obesity and the intervention date were excluded. Patients in the bariatric surgery group and their matched comparison subject in the control group were tracked from the intervention date until the end of follow-up, to identify those who developed the studied cancers.

To estimate the relative risk of developing cancer following bariatric surgery $2 \times 2$ contingency tables were created. The columns corresponded to whether the patient had undergone bariatric surgery (and its subtypes) or not (controls), and the rows corresponded to whether the patient developed the studied cancers or not: hormonal overall, breast (women only), endometrial (women only), prostate (men only), colorectal and oesophageal. $\chi^2$ analysis was used to calculate odds ratios (ORs) with 95 per cent confidence intervals of developing cancer in the bariatric surgery group. To avoid detection bias, patients in both groups diagnosed with cancer within 1 year of the intervention date were excluded from the $\chi^2$ analysis. To identify whether bariatric surgery was more protective in older patients, a subgroup analysis including all patients over the age of 40 years was performed. This included

contingency tables and $\chi^2$ analyses for bariatric surgery overall and all the studied cancers. These categorical variables are presented as percentages, and continuous variables as median (i.q.r.) values.

Kaplan–Meier plots were created for visual comparison of disease-free survival, from overall hormonal cancers and colorectal cancer, in the bariatric surgery group and in the subset of patients who had a gastric bypass. Disease-free survival in these groups was compared using the log rank test. In addition, Cox regression models were used to investigate how the relative risk of developing overall hormonal cancer and colorectal cancer in the bariatric surgery and gastric bypass groups changed over time. Cox regression models were created at less than 1, 5, 10 and 15 years after surgery, providing hazard ratios (HRs) with 95 per cent confidence intervals. The dependent variable was cancer or not, and, as the groups were matched for available relevant co-variables, the only co-variable included was whether the patient was an exposed or a control patient.

All statistical analyses were performed using the statistical software SPSS® version 24 (IBM, Armonk, New York, USA).

## Results

The entire study cohort included 716 960 patients diagnosed with obesity during the study interval, of whom 9102 (1·3 per cent) underwent bariatric surgery. Of these, 308 patients were excluded as there were no exact matches among the unoperated cohort. Thus, 8794 operated patients and the same number of exactly matched unoperated patients remained for final analysis. For both groups, the median age was 42 years, the median length of follow-up was 55 months, 7069 (80·4 per cent) were women and 5697 (64·8 per cent) had a co-morbidity score of zero (*Table 1*). Of the operated patients, 4978 (56·6 per cent) underwent gastric bypass, 2957 (33·6 per cent) underwent gastric banding and 859 (9·8 per cent) had a sleeve gastrectomy.

**Table 1** Characteristics of study participants with obesity in control and bariatric surgery groups

| | Control ($n = 8794$) | Bariatric surgery ($n = 8794$) |
|---|---|---|
| Age at diagnosis (years)* | 42 (35–50) | 42 (35–50) |
| Duration of follow-up (months)* | 55 (30–94) | 55 (30–94) |
| Sex ratio (M : F) | 1725 : 7069 | 1725 : 7069 |
| Charlson Co-morbidity Index | | |
| 0 | 5697 (64·8) | 5697 (64·8) |
| 1 | 2438 (27·7) | 2438 (27·7) |
| 2 | 555 (6·3) | 555 (6·3) |
| 3 | 86 (1·0) | 86 (1·0) |
| 4 | 15 (0·2) | 15 (0·2) |
| 5 | 2 (0·0) | 2 (0·0) |
| 9 | 1 (0·0) | 1 (0·0) |

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.).

**Table 2** Risk of breast, endometrial, prostate, colorectal and oesophageal cancer in control and bariatric surgery groups

| | Control ($n = 8794$†) | Bariatric surgery ($n = 8794$†) | Odds ratio* |
|---|---|---|---|
| Breast cancer (women only) | 239 (3·4) | 61 (0·9) | 0·25 (0·19, 0·33) |
| Endometrial cancer (women only) | 84 (1·2) | 18 (0·3) | 0·21 (0·13, 0·35) |
| Prostate cancer (men only) | 27 (1·6) | 10 (0·6) | 0·37 (0·17, 0·76) |
| Hormone-related cancers | | | |
| Overall | 318 (3·6) | 75 (0·9) | 0·23 (0·18, 0·30) |
| Men | 27 (1·6) | 10 (0·6) | 0·37 (0·17, 0·76) |
| Women | 291 (4·1) | 65 (0·9) | 0·22 (0·17, 0·28) |
| Colorectal cancer | | | |
| Overall | 16 (0·2) | 35 (0·4) | 2·19 (1·21, 3·96) |
| Men | 6 (0·3) | 9 (0·5) | 1·50 (0·53, 4·23) |
| Women | 10 (0·1) | 26 (0·4) | 2·61 (1·26, 5·41) |
| Oesophageal cancer | | | |
| Overall | 8 (0·1) | 4 (0·0) | 0·50 (0·15, 1·66) |
| Men | 5 (0·3) | 4 (0·2) | 0·80 (0·21, 2·98) |
| Women | 3 (0·0) | 0 (0·0) | 0·14 (0·01, 2·77) |

Values in parentheses are percentages unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals. †Includes 7069 women and 1725 men.

**Table 3** Risk of breast, endometrial, prostate, colorectal and oesophageal cancer in control and gastric bypass groups

| | Control ($n = 4978$†) | Gastric bypass ($n = 4978$†) | Odds ratio* |
|---|---|---|---|
| Breast cancer (women only) | 129 (3·2) | 29 (0·7) | 0·22 (0·15, 0·33) |
| Endometrial cancer (women only) | 50 (1·3) | 4 (0·1) | 0·08 (0·03, 0·22) |
| Prostate cancer (men only) | 18 (1·8) | 4 (0·4) | 0·22 (0·07, 1·65) |
| Hormone-related cancers | | | |
| Overall | 181 (3·6) | 30 (0·6) | 0·16 (0·11, 0·24) |
| Men | 18 (1·8) | 4 (0·4) | 0·22 (0·07, 1·65) |
| Women | 163 (4·1) | 26 (0·7) | 0·15 (0·10, 0·23) |
| Colorectal cancer | | | |
| Overall | 8 (0·2) | 21 (0·4) | 2·63 (1·17, 5·95) |
| Men | 3 (0·3) | 6 (0·6) | 2·01 (0·50, 8·04) |
| Women | 5 (0·1) | 15 (0·4) | 3·01 (1·09, 8·28) |
| Oesophageal cancer | | | |
| Overall | 7 (0·1) | 2 (0·0) | 0·29 (0·06, 1·38) |
| Men | 4 (0·4) | 2 (0·2) | 0·50 (0·09, 2·73) |
| Women | 3 (0·1) | 0 (0) | 7·01 (0·36, 135·67) |

Values in parentheses are percentages unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals. †Includes 3986 women and 992 men.

### Bariatric surgery and risk of hormone-related cancers

The risk of the three studied hormone-related cancers together was decreased following bariatric surgery (OR

**Table 4** Risk of breast, endometrial, prostate, colorectal and oesophageal cancer in control and gastric banding groups

| | Control ($n = 2957$†) | Gastric banding ($n = 2957$†) | Odds ratio* |
|---|---|---|---|
| Breast cancer (women only) | 94 (3·9) | 29 (1·2) | 0·30 (0·20, 0·46) |
| Endometrial cancer (women only) | 30 (1·2) | 13 (0·5) | 0·43 (0·22, 0·83) |
| Prostate cancer (men only) | 6 (1·2) | 6 (1·2) | 1·00 (0·32, 3·12) |
| Hormone-related cancers | | | |
| Overall | 118 (4·0) | 41 (1·4) | 0·34 (0·23, 0·48) |
| Men | 6 (1·2) | 6 (1·2) | 1·00 (0·32, 3·12) |
| Women | 112 (4·6) | 35 (1·4) | 0·30 (0·21, 0·44) |
| Colorectal cancer | | | |
| Overall | 6 (0·2) | 10 (0·3) | 1·67 (0·61, 4·60) |
| Men | 1 (0·2) | 1 (0·2) | 1·00 (0·06, 16·03) |
| Women | 5 (0·2) | 9 (0·4) | 1·80 (0·60, 5·38) |
| Oesophageal cancer | | | |
| Overall | 0 (0) | 2 (0·1) | 5·00 (0·24, 104·27) |
| Men | 0 (0) | 2 (0·4) | 5·00 (0·24, 104·80) |
| Women | 0 (0) | 0 (0) | – |

Values in parentheses are percentages unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals. †Includes 2436 women and 521 men.

**Table 5** Risk of breast, endometrial, prostate, colorectal and oesophageal cancer in control and sleeve gastrectomy groups

| | Control ($n = 859$†) | Sleeve gastrectomy ($n = 859$†) | Odds ratio* |
|---|---|---|---|
| Breast cancer (women only) | 16 (2·5) | 3 (0·5) | 0·18 (0·05, 0·63) |
| Endometrial cancer (women only) | 4 (0·6) | 1 (0·2) | 0·25 (0·03, 2·23) |
| Prostate cancer (men only) | 3 (1·4) | 0 (0) | 7·10 (0·36, 138·31) |
| Hormone-related cancers | | | |
| Overall | 19 (2·2) | 4 (0·5) | 0·21 (0·07, 0·61) |
| Men | 3 (1·4) | 0 (0) | 7·10 (0·36, 138·31) |
| Women | 16 (2·5) | 4 (0·6) | 0·25 (0·08, 0·74) |
| Colorectal cancer | | | |
| Overall | 2 (0·2) | 4 (0·5) | 2·01 (0·37, 10·97) |
| Men | 2 (0·9) | 2 (0·9) | 1·00 (0·14, 7·17) |
| Women | 0 (0) | 2 (0·3) | 0·20 (0·01, 4·16) |
| Oesophageal cancer | | | |
| Overall | 1 (0·1) | 0 (0) | 3·00 (0·12, 73·84) |
| Men | 1 (0·5) | 0 (0) | 3·01 (0·12, 74·41) |
| Women | 0 (0) | 0 (0) | – |

Values in parentheses are percentages unless indicated otherwise; *values in parentheses are 95 per cent confidence intervals. †Includes 647 women and 212 men.

0·23, 95 per cent c.i. 0·18 to 0·30). This was a consistent finding across all three hormonal cancers studied, with an OR of 0·25 (0·19 to 0·33) for breast cancer, 0·21 (0·13 to 0·35) for endometrial cancer and 0·37 (0·17 to 0·76) for prostate cancer (*Table 2*). The subgroup analysis of patients aged over 40 years demonstrated similar results: OR 0·23 (0·17 to 0·32) for breast cancer, 0·21 (0·13 to 0·36) for endometrial cancer and 0·34 (0·16 to 0·73) for prostate cancer (*Table S1*, supporting information).

Gastric bypass was associated with the largest risk reduction of all three studied hormone-related cancers (OR 0·16, 95 per cent c.i. 0·11 to 0·24), but gastric banding (OR 0·34, 0·23 to 0·48) and sleeve gastrectomy (OR 0·21, 0·07 to 0·61) were also associated with strongly decreased risks (*Tables 3–5*). Again, the finding was consistent across all three cancer types, although gastric bypass was the only obesity surgery procedure associated with a significant reduction in the risk of prostate cancer (*Table 3*).

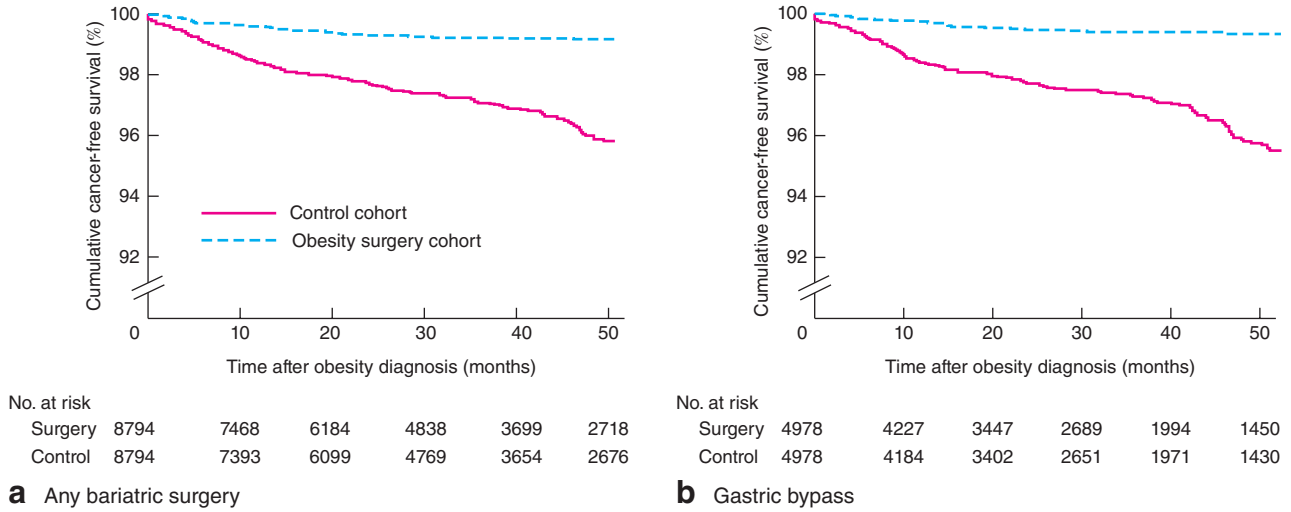


**Fig. 1** Kaplan–Meier curves of freedom from hormone-related cancer following **a** any bariatric surgery and **b** gastric bypass *versus* the control unoperated cohort. **a** $P < 0·001$, **b** $P < 0·001$ (log rank test)

**Table 6** Risk of hormone-related cancer (breast, endometrial and prostate) and colorectal cancer at 1, 5, 10 and 15 years after bariatric surgery and gastric bypass

| | Hazard ratio | |
|---|---|---|
| Time after surgery (years) | Hormone-related cancer | Colorectal cancer |
| Bariatric surgery* | | |
| ≤ 1 | 0·46 (0·30, 0·69) | 1·51 (0·25, 9·03) |
| ≤ 5 | 0·23 (0·17, 0·30) | 2·13 (1·11, 4·13) |
| ≤ 10 | 0·22 (0·17, 0·29) | 2·00 (1·10, 3·64) |
| ≤ 15 | 0·23 (0·18, 0·30) | 2·19 (1·21, 3·96) |
| Gastric bypass | | |
| ≤ 1 | 0·28 (0·15, 0·51) | 1·00 (0·14, 7·13) |
| ≤ 5 | 0·19 (0·13, 0·29) | 2·64 (1·03, 6·74) |
| ≤ 10 | 0·17 (0·11, 0·25) | 2·25 (0·98, 5·17) |
| ≤ 15 | 0·16 (0·11, 0·24) | 2·64 (1·17, 5·96) |

Values in parentheses are 95 per cent confidence intervals. *Gastric bypass, gastric banding or sleeve gastrectomy.

Kaplan–Meier analysis of freedom from hormone-related cancers following any bariatric surgery showed a steadily divergent curve from the unoperated control (*Fig. 1a*), and this pattern was strengthened following gastric bypass (*Fig. 1b*). The HR for hormone-related cancer within 1 year in the bariatric surgery group was 0·46 (95 per cent c.i. 0·30 to 0·69). This halved within 5 years to 0·23 (0·17 to 0·30) and remained at a similarly decreased level until the end of the study period (*Table 6*). There was a similar finding in the gastric bypass group, although the HRs were further decreased: within 1 year the HR was 0·28 (0·15 to 0·51), which decreased to 0·19 (0·13 to 0·29) within 5 years and 0·16 (0·11 to 0·24) within 15 years (*Table 6*).

## Bariatric surgery and risk of colorectal cancer

Patients undergoing bariatric surgery had a greater than twofold increased risk of developing colorectal cancer compared with unoperated patients (OR 2·19, 95 per cent c.i. 1·21 to 3·96) (*Table 2*). The risk of patients over 40 years developing colorectal cancer was greater following bariatric surgery (OR 2·43, 1·31 to 4·55) (*Table S1*, supporting information). When analysing the bariatric procedures individually, gastric bypass was the only procedure that increased the risk of colorectal cancer (OR 2·63, 1·17 to 5·95) (*Table 3*).

Kaplan–Meier analysis of freedom from colorectal cancer following any bariatric surgery and gastric bypass is shown in *Fig. 2*. The colorectal cancer curves demonstrated an initial latency period during which there was no change in the incidence of colorectal cancer between the comparison groups (*Fig. 2a*). However, after this initial period the curves diverged, with an increasing incidence of colorectal cancer in the surgery cohort. This difference was strengthened in the gastric bypass group (*Fig. 2b*).

This finding was consolidated by the Cox regression analysis, which for the bariatric surgery cohort showed no clear change in risk within 1 year (HR 1·51, 95 per cent c.i. 0·25 to 9·03), but increasing HRs in the surgery group within 5 years (HR 2·13, 1·11 to 4·13) and within 15 years of the operation (HR 2·19, 1·21 to 3·96) (*Table 6*).

A similar, but more pronounced, pattern was seen following gastric bypass surgery. Within 1 year the HR was 1·00 (95 per cent c.i. 0·14 to 7·13), increasing to 2·64

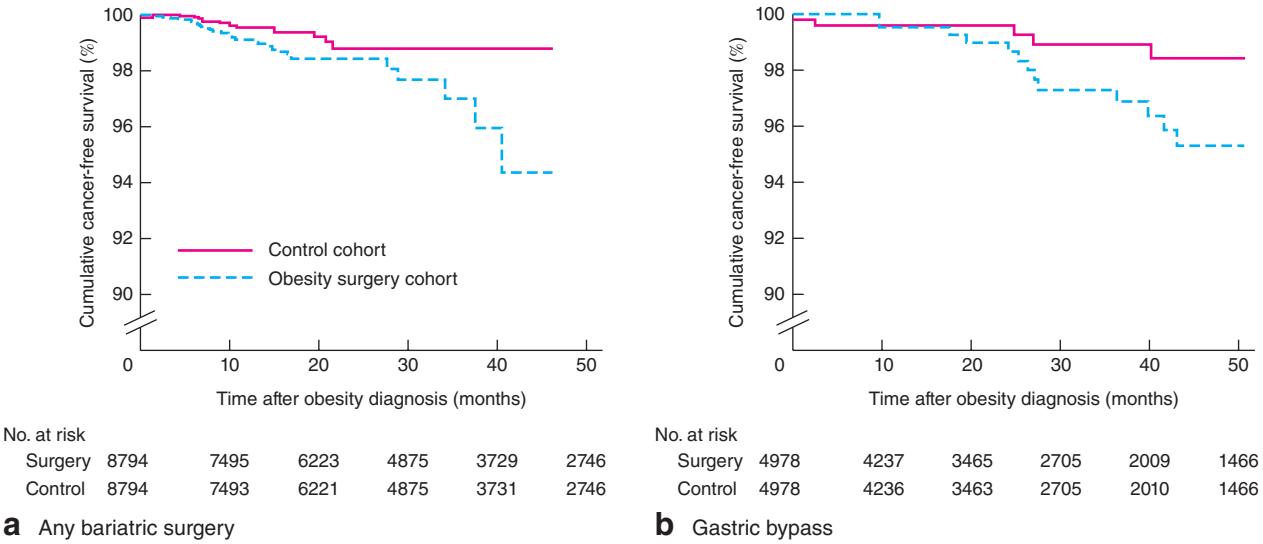


**Fig. 2** Kaplan–Meier curves of freedom from colorectal cancer following **a** any bariatric surgery and **b** gastric bypass *versus* the control unoperated cohort. **a** $P = 0·021$, **b** $P = 0·008$ (log rank test)

(1·03 to 6·74) within 5 years and 2·64 (1·17 to 5·96) within 15 years (*Table 6*).

### Bariatric surgery and risk of oesophageal cancer

The overall incidence of oesophageal cancer was low in both the bariatric surgery and control groups (*Table 2*). None of the bariatric procedures demonstrated a significant change in risk for oesophageal cancer, although the odds ratio following gastric bypass was low (*Table 3*). The incidence of oesophageal cancer was too low to perform a time-dependent analysis as described for the other cancer types.

## Discussion

This study indicates that bariatric surgery using gastric bypass, gastric banding or sleeve gastrectomy is associated with a substantial reduction in the risk of hormone-related cancers of the breast, endometrium and prostate. Interestingly, gastric bypass was also associated with an increased risk of colorectal cancer.

It is important to consider the validity of this study when interpreting the findings. The population-based design with propensity matching of unoperated obese individuals, the large sample size and the completeness of follow-up are among the methodological strengths. A weakness is that, in the HES database, obesity was coded only as a co-morbidity, and exact weight and BMI data were not available. This introduces a potential source of bias, as the allocation of patients for bariatric surgery is commonly based on the absolute BMI and the presence of medical co-morbidities in the UK, which did evolve during the study period[16]. However, as the direction of change in hormone-related and colorectal cancer were opposite and strong, an underlying difference in BMI or co-morbidity between the comparison groups is unlikely to be the primary driver for the changes in cancer incidence observed. Furthermore, changes in BMI or medical co-morbidity status following surgery could not be assessed and thus it was not possible to make a correlation between BMI changes after surgery and cancer risk. However, gastric bypass and sleeve gastrectomy have been shown[17,18] to result in more weight loss compared with gastric banding, and these procedures had the strongest influence on hormone-related cancer risk.

Obese individuals may have concomitant maladaptive social or behavioural patterns, including tobacco-smoking, high alcohol intake and low physical activity, all of which are potential confounding factors that are not coded in HES and therefore not included in the propensity matching[4]. However, the propensity matching for sex, age, co-morbidity and length of follow-up created a similar control group.

Although the sample size was large, the statistical power for assessing the risk of oesophageal cancer was low due to the low incidence of this cancer. Moreover, there was a lack of tumour histology within the data set. Thus, oesophageal squamous cell carcinoma, which is not associated with obesity, was included in the analysis, which could have diluted potential associations with the obesity-related adenocarcinoma of the oesophagus.

There was a fivefold reduction in the incidence of hormone-related cancers following bariatric surgery, particularly in patients who had undergone gastric bypass or sleeve gastrectomy. However, it must also be noted that there was a threefold reduction in the incidence of hormone-related cancers after gastric banding. Some previous publications[10–14] have also demonstrated associations between bariatric surgery and hormone-related cancers, but the evidence has been conflicting. Importantly, the present study included 56·6 per cent of patients receiving a gastric bypass, a much greater proportion than in previously conducted studies, potentially increasing the percentage weight loss and anticancer effects within the bariatric surgery cohort.

Modulation of the levels of sex hormones (oestrogens and androgen) can reduce the risk of hormone-dependent tumours[14]. The mechanism of reduced risk of breast and endometrial cancer following bariatric surgery may be due to a decrease in oestrogen levels and an increase in sex hormone-binding globulin, thus removing the neoplastic driver[19]. Regarding endometrial cancer specifically, it has been suggested that endometrial hyperplasia can be counteracted by bariatric surgery[20]. Bariatric surgery can also normalize the serum testosterone level and possibly reduce the risk of prostate cancer[21], which might help explain the results of the present study regarding this cancer.

Interestingly, there was a greater than twofold increased risk of colorectal cancer following gastric bypass. This finding parallels the results observed in a Swedish study[22], which demonstrated a twofold increased risk of colorectal cancer at 10 years or more after bariatric surgery. In line with these results are the findings of increased proliferation of the rectal mucosa and increased biomarker levels after gastric bypass surgery[23], as well as the finding that an inflammatory environment stimulates hyperproliferation of the bowel mucosa following bariatric surgery[24]. Research has also suggested that metabolic changes following gastric bypass surgery may be at least partially mediated by changes in the gut microbiome following gastrointestinal reconstruction[25,26]. There is a need for

further investigation to understand better the biological mechanism and interplay with the gut microbiome underpinning this observed increase in colorectal cancer following Roux-en-Y gastric bypass surgery. Whether colonoscopy surveillance may be considered after gastric bypass requires more research to establish the association and to evaluate benefits against costs of any such surveillance. Nevertheless, the available research taken together may indicate a role for prompt colonoscopy in patients who present with bowel symptoms following gastric bypass surgery.

There are potential mechanisms by which gastric bypass may reduce the incidence of oesophageal adenocarcinoma[27]. These include the antireflux component of the procedure, which may alter the well established causal link between obesity and reflux and oesophageal adenocarcinoma[28,29]. In addition, sex hormone exposure may play a role in the aetiology of oesophageal adenocarcinoma[30]. However, in the present study bariatric surgery did not alter the risk of oesophageal cancer, although the statistical power was low, leaving a risk of type II error, and the inclusion of squamous cell carcinoma might have diluted associations with adenocarcinoma.

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## Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.