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Long-Term All-Cause and Cause-Specific Mortality for Four Bariatric Surgery Procedures

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Abstract

OBJECTIVE—This retrospective study incorporated long-term mortality results after different bariatric surgery procedures and for multiple age-at-surgery groups.

METHODS—Subjects with bariatric surgery (Surgery) and without (Non-surgery) were matched (1:1) for age, sex, BMI, and surgery date with a driver license application/renewal date. Mortality rates were compared by Cox regression, stratified by sex, surgery type, and age-at-surgery.

RESULTS—Subjects included 21,837 matched Surgery and Non-surgery pairs. Follow-up was up to 40 years (mean 13.2±9.5 years). All-cause mortality was 16% lower in Surgery compared to Non-surgery groups (hazard ratio, 0.84; 95% CI 0.79 to 0.90; p<0.001). Significantly lower mortality after bariatric surgery was observed for both females and males. Mortality after Surgery versus Non-surgery decreased significantly by 29%, 43%, and 72% for cardiovascular disease,

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cancer, and diabetes, respectively. The hazard ratio for suicide was 2.4 times higher in Surgery compared to Non-surgery subjects (95% CI 1.57–3.68; $p<0.001$), primarily in subjects with ages at surgery between 18–34 years.

CONCLUSIONS—Reduced all-cause mortality was durable for multiple decades, for multiple bariatric surgical procedures, for females and males, and irrespective of age at surgery. Rate of death from suicide was significantly higher in Surgery vs. Non-surgery subjects only in the youngest age-at-surgery subjects.

Keywords

Bariatric surgery; obesity; mortality; BMI

Introduction

Among United States adults, prevalence of severe obesity (body mass index (BMI) ≥ 35 kg/m^2) has doubled from 1999–2000 (4.7%) through 2017–2018 (9.2%).[1] Population studies observed that patients with severe obesity have increased risks of cardiometabolic diseases[2] and mortality[3]. While bariatric surgery is the most successful treatment for the severely obese population[4], it remains under-utilized.[5] Patients who have undergone bariatric surgery have demonstrated significant improvement in obesity-related comorbidity such as remission of type 2 diabetes mellitus and decreased long-term mortality when compared to non-surgical subjects with severe obesity,[4,6,7] stimulating intense interest in discovery of causal pathophysiologic mechanisms that may facilitate non-surgical treatment(s) of obesity.[8]

This retrospective study compared long-term mortality of bariatric surgical patients and matched non-surgical subjects identified from driver licenses. While mortality after gastric bypass surgery was previously reported from 1984 through 2002,[9] this study extends mortality follow-up through 2021. Additional gastric bypass patients and patients who had gastric banding, sleeve gastrectomy or duodenal switch from 1982 through 2021 have been included. Mortality outcomes were also analyzed stratified by sex, types of bariatric surgeries, and patients' ages at surgery.

Methods

This study was approved by the University of Utah's Resource for Genetic and Epidemiologic Research. Due to the deidentification, the study was considered non-human subjects research by the University Institutional Review Board (IRB #00095902). IRB approval was also obtained at Intermountain Healthcare.

Study aims.

The primary aim was to determine the association of all-cause and cause-specific mortality risk between bariatric surgical patients and matched non-surgical subjects identified from driver license applications or renewals. Secondary aims were to determine whether age at surgery influenced mortality outcomes and whether mortality rates differed between sexes and between surgical procedures, which included gastric bypass, gastric banding, sleeve gastrectomy and duodenal switch. Duodenal switch included single and double anastomosis procedure types and were primarily performed from 2010 through 2018.

Subjects.

Our study utilized information from the Utah Population Database (UPDB). The UPDB includes linked population-based information from Utah with statewide birth and death certificates, driver licenses and ID cards, and voter registration records. It also contains state-wide cancer registry records, and health facility records including inpatient discharge, ambulatory surgeries, and emergency claims. The UPDB creates and maintains links between the database and the medical records held by the two largest healthcare providers in Utah.

Patients who had undergone bariatric surgery in Utah between 1982 and 2018 were identified from three large bariatric surgical practices in Salt Lake City, Utah, USA and from medical records from the University of Utah and Intermountain Healthcare Enterprise Data Warehouses (EDWs), Salt Lake City, Utah, USA (Figure 1). Exclusion criteria are shown in Figure 1, and the counts in each line of the boxes represent the number of missing or non-qualifying records for that variable out of the total records listed in the box above. Each record could have multiple missing values (such as missing age and BMI) and would be counted multiple times so that the total counts within a box do not add up to the total in the preceding box. The qualifying bariatric surgery procedures were Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy, and bilio-pancreatic diversion with duodenal switch.

Non-surgical subjects were selected from Utah driver license records or ID cards. Since driver licenses are generally renewed every five years, there were multiple records to choose from for matching to the bariatric surgeries. Exclusions were made on a record basis (Figure 1) resulting in 694,909 qualifying records for matching to surgical patients in a 1:1 ratio. Matching variables were sex, BMI category, age category (18–19, 20–24, 25–29,…,75–80 years), and year of surgery, which was matched to year of driver license application or renewal (± 2 years). The subset of surgery and non-surgery subject pairs used in our prior study[9] were previously matched using microfilm records by 3 BMI categories (33–44, 45–54 and ≥55 kg/m^2). Because UPDB now has electronic records for the later years, adjusted BMI categories of 18.5–24.9; 25–29.9; 30–34.9; 35–39.9; 40–44.9; 45–49.9; and >=50 kg/m^2 were used for the additional surgery subjects in order to get even closer BMI matching. All controls were required to have never had bariatric surgery determined from the three large bariatric surgery registries, health facility records, or the EDWs. Clinical records were generally available only after 1995, and statewide coverage of clinical data was also not available, preventing the use of clinical data to be used to subset or correlate with the mortality data. As previously described,[9] self-reported heights and weights on driver licenses were corrected using sex-specific regression equations to address over-estimation of height and under-estimation of weight. Because these regression equations were developed using only subjects with a BMI≥33 kg/m^2, unadjusted, self-reported BMIs under 30 were excluded.

Statistical analyses.

Demographic characteristics between surgical patients and matched non-surgical subjects were compared using t-tests for continuous variables and chi-square tests for categorical variables. Unadjusted absolute death rates per 10,000 person years were calculated by sex and specific causes of death. Index date was defined as date of bariatric surgery or date of driver license application/renewal and set as July 1st if only year was known. All-cause mortality risks were estimated using Cox proportional hazard models, additionally adjusting for age at index year, index year, BMI, sex, whether Caucasian, whether Hispanic, and clustering by matched pairs. Cause-specific mortality risks were estimated using competing risk models.[10] All individuals were followed until death, last date known to reside in Utah, date of revision surgery, or December 31st, 2021, whichever occurred first. All records in UPDB, including the clinical data records, were used to determine continued residency in Utah during follow-up. There were 3,086 surgery patients and 2,715 non-surgery pairs who presumably moved after their last known residency date in Utah. The proportional hazards assumptions were checked using statistical tests and graphical diagnostics based on scaled Schoenfeld residuals. Analyses were stratified by sex, age at index date (<35, 35–44, 45–54, and 55–80), and surgical procedure. All causes of death were derived from primary causes of death as reported in Utah Death Certificates, except for Alzheimer’s disease and diabetes mellitus, which were derived from both primary and secondary causes of death and defined with ICD-9 and ICD-10 codes (Supplementary Appendix Tables 1 and 2). The P values and the 95% confidence Intervals are all 2-sided, and the criterion used for statistical significance was $p<0.05$. Statistical analyses were conducted using R version 4.1.0.[11] Finally, non-external deaths were defined as deaths related to diseases such as diseases of the heart, cancer, and diabetes, whereas external deaths were defined as deaths related to accidents, self-harm such as suicide, and related adverse effects. Deaths from all causes included combined non-external and external deaths.

Results

Table 1 indicates basic characteristics of the 21,837 matched surgical and non-surgical pairs. The majority of subjects were female (79%). The most common procedure utilized was Roux-en-Y gastric bypass (n=15,110; 69.2%), followed by gastric sleeve (n=3,050; 14.0%), adjustable gastric banding (n=2,629; 12.0%), and duodenal switch (n=1,048; 4.8%). Over 40 years (median=10.8, interquartile range, 5.0 to 19.1 years) there were 2,943 (13.5%) deaths for surgical patients and 3,181 (14.6%) deaths for non-surgical subjects. Death rates during the first year following index date were similar between groups, 111 deaths (0.5%) and 89 deaths (0.4%) in the surgical and nonsurgical groups, respectfully, $p=0.14$ (Table 1). Mean age at index date was 42.2 years (SD: 11.7 years) and 42.3 years (SD: 11.9 years, $p=0.60$, for surgical and non-surgical subjects, respectively. Although mean BMI was significantly different between groups, the difference was only 0.2 kg/m^2, indicating close BMI matching. Of the surgical and non-surgical subjects, 94.4% and 87.6% ($P<0.001$) were Caucasian, respectively, while 7.8% and 12.4% ($p<0.001$) of surgical and non-surgical subjects were Hispanic, respectively. Numbers of patients undergoing each type of bariatric surgery and year of surgery are shown in Supplementary Appendix Table 3. In addition, the numbers of subjects in each group meeting study inclusion and exclusion criteria are presented in Figure 1.

Distribution of deaths and death rates per 10,000 person years for all matched subjects and for sex-specific matched subjects are presented in Table 2. Rate of death from all causes was 16% lower in the surgery compared to non-surgery groups (hazard ratio (HR), 0.84; 95% confidence interval (CI), 0.79–0.90; P<0.001; Figure 2). Total mortality was also significantly lower for surgical than non-surgical subjects for both females (HR, 0.86; 95% CI, 0.80 – 0.93; P<0.001) and males (HR, 0.79; 95% CI, 0.69–0.90; P<0.001). Non-external deaths were lower among surgical versus non-surgical subjects for combined sexes (HR, 0.74; 95% CI, 0.69–0.80; P<0.001), females (HR, 0.76; 95% CI, 0. 70–0.83; P<0.001) and males (HR, 0.68; 95% CI, 0. 59–0.79; P<0.001; Figure 2). Death rates were significantly lower for surgical compared to non-surgical subjects (combined sexes) for diabetes (72% lower, P<0.001), major cardiovascular disease (29% lower, P<0.001), cancer (43% lower, P<0.001), and chronic lung disease (39% lower; P=0.04). However, deaths from chronic liver disease were significantly greater among surgical than non-surgery subjects (combined sexes) (83% higher, P=0.02). For combined sexes and for females and males, external-caused death rates were significantly greater in the surgery group compared to non-surgery group. Accidents and adverse effects were 92% higher (P=0.03) and suicide was 140% higher (P<0.001) (Figure 2). Suicide after bariatric surgery was also significantly greater for both females and males.

Figure 3 indicates relative mortality risk in the surgery patients compared with non-surgery subjects by age category at the time of surgery or driver license application/renewal. While the 18 through 34 and 35 through 44-year age categories were the only groups to have significantly greater risk for external causes of death (HR, 3.63; 95% CI, 2.37–5.59; P<0.001 and HR, 2.19; 95% CI, 1.46–3.31; P<0.001, respectively), only the 18 through 34-year group had significantly greater suicide mortality (HR, 5.08; 95% CI 1.97–13.09; P=0.001).

Except for the 18-to-34-year group, all age categories had significantly lower mortality from all causes of death for surgery compared to non-surgery subjects (Figure 3). Significantly greater all causes of death risk for surgical versus non-surgical subjects in the 18 through 34-year category appeared related to greater risk for external causes of death among surgical patients in this age group. Chronic liver disease death risk was significantly greater among surgery versus non-surgery subjects in the 18 through 34-year age category, but the number of deaths was small leading to large confidence intervals.

Analyses of mortality risk between surgical patients and non-surgical subjects were stratified by type of bariatric surgical procedure (Figure 4). Gastric bypass, gastric banding, and sleeve gastrectomy each showed significantly lower total mortality risk for surgical compared to non-surgical subjects: gastric bypass (HR, 0.85; 95% CI, 0.79–0.91; P<0.001); gastric banding (HR, 0.72; 95% CI, 0.55–0.94; P=0.017); and sleeve gastrectomy (HR, 0.49; 95% CI, 0.30–0.79; P=0.004). Patients undergoing duodenal switch were the fewest in number and these procedures were performed later in the follow-up time-period. Cancer, diabetes, and cardiovascular disease mortality were all significantly reduced after gastric bypass surgery. The number of deaths for other surgery procedures for cause-specific mortality were small, although diabetes mortality was significantly lower after sleeve gastrectomy.

Unadjusted Kaplan-Meier survival curves were estimated for non-external-, external-, and all-cause mortality risk by surgical and non-surgical subjects (Supplemental Figure 1). Restricted mean survival time for non-external deaths was 1.72 years longer (95% CI 1.35–2.09; P<0.001) for surgical compared to non-surgery subjects (Supplemental Figure 1a). Survival time for external deaths was 0.4 years less (95% CI, −0.56 to −0.25; P<0.001) for surgery patients versus non-surgery patients (Supplemental Figure 1b). Combined, survival time for all causes of death was 1.3 years (95% CI, 0.93–1.67; P<0.001) longer for surgery compared to non-surgery subjects (Supplemental Figure 1c).

Discussion

Advancing the understanding of clinical efficacy of bariatric surgery has focused on short- and long-term outcomes of obesity-related comorbidities, including type 2 diabetes mellitus (T2DM),[4,12–14] primary cardiovascular (CVD) risk factors,[15–17] CVD events such as myocardial infarction and stroke,[18–20] cancer,[21,22] as well as all-cause mortality.[7,9,23] Multiple association studies relating bariatric surgery and mortality outcomes have been reported, with wide-variation in study design pertaining to: subject number; control cohorts; mean follow-up; procedure type; age at surgery; clinical endpoints (i.e. life expectancy and death rates for all cause and cause specific); and presence or absence of prevalent diabetes.[3,6,24–36] Study type has been predominately retrospective in nature, with the Swedish Obesity Subjects (SOS) study prospectively studied.[7,23]

This 40-year retrospective Utah study extends the mortality risks after bariatric surgery from the previously reported matching of 7,925 surgical and non-surgical pairs to 21,837 matched pairs. This study now includes patients who had undergone the most common bariatric procedures performed today, doubling the number of previously reported gastric bypass patients (n = 15,110), and including 2,629 gastric banding, 3,050 sleeve gastrectomy, and 1,048 duodenal switch patients. Mortality benefits related to bariatric surgery were shown to remain durable for multiple decades following surgery, with a significant 16% lower all-causes of death for surgical versus matched non-surgical subjects, and in addition, a significant 14% and 21% reduction in all-cause mortality for female and male surgical patients, respectively, compared to non-surgical subjects. Previously reported results did not show reduced mortality among the male surgical population but were based on much smaller numbers of males. Further, improved cause-specific mortality (cardiovascular, diabetes, and cancer) was shown for surgical patients compared to matched non-surgical subjects. Cardiovascular and diabetes mortality risk was lower for both male and female surgical patients, and lower for cancer for female surgical patients compared to the respective non-surgical subjects. Finally, new to this study is a reported increase in deaths from cirrhosis of the liver, occurring primarily among the surgical patients who underwent bariatric surgery between ages 18 through 34 years. Clinical information concerning details of liver cirrhosis were not available, preventing us from further investigation of alcohol use, viral hepatitis, or fibrosis before or after baseline.

Surgical patients undergoing surgery between ages 35 to 44 years, 45 to 54 years and 55 to 80 years had significantly lower mortality from all causes of death compared to non-surgery subjects, suggesting bariatric surgery to be associated with a lower non-external mortality risk (i.e., cardiovascular disease and cancer). Significant results only in the older age groups should not imply patients necessarily postpone surgery until older age, as post-surgical complications have been shown to increase with increasing age at surgery and surgical postponement may result in worsened clinical status related to certain conditions such as orthopedic joint health. Finally, significantly improved all-cause mortality for surgical versus non-surgery subjects was shown for individual surgical procedures (gastric bypass, gastric banding, and sleeve gastrectomy).

Consistent with previous findings,[9] deaths related to external causes such as suicide and accidents were significantly greater (2.35 times) among bariatric surgery patients compared to matched non-surgical subjects, with most of this increased mortality risk occurring among patients who were ages 18 to 34 years at the time of surgery. Utah State mortality rates for suicide were 1.0/10,000 person-years for females and 3.6/10,000 for males ages 15–74 for the years 1999–2020.(https://ibis.health.utah.gov/) These rates are comparable to the non-surgical subjects of our study with severe obesity suicide rates of 1.3/10,000 person-years (female) and 2.9/10,000 person-years (male). The surgery group rates of 3.0 for females and 8.2/10,000 persons-years for males are clearly higher than the population as a whole.

As mentioned, among the youngest age group there was a significant increase in mortality from cirrhosis of the liver. Mitchell et al have reported that following certain bariatric surgery procedures there is increased disinhibition and impulsivity and increased rates of absorption of alcohol.[37] However, a recent study by Aminian, et al., retrospectively followed patients who underwent bariatric surgery (n=650) and non-surgery patients with obesity (n=508) who all had baseline biopsy-proven fibrotic nonalcoholic steatohepatitis (NASH) without cirrhosis.[38] After median follow-up of seven years, bariatric surgery was significantly associated with a lower risk of major adverse liver outcomes, with 5 surgical and 40 non-surgical patients experiencing the adverse liver outcomes.[38] Alcohol use and clinical liver disease details were not available in our study. One possibility that would explain these discrepant results includes that the increased mortality after bariatric surgery in our study was derived from those with possible liver cirrhosis at baseline, and once cirrhosis has occurred resolution is limited after surgery. Another possibility is that the risk estimates are unstable, despite the statistical significance, due to small sample sizes.

Recently reported mortality outcomes of the Swedish Obesity Subjects (SOS) study, with median follow-up of 20 to 24 years, reported a 23% lower mortality in the bariatric surgery group (n = 2007 patients) compared to the matched control group (HR, 0.77; 95% CI, 0.68 to 0.87; p<0.001). With 69%, 18%, and 13% of surgical patients undergoing vertical banded gastroplasty, banding, and gastric bypass, respectively, their results showed an unadjusted median life expectancy of 2.4 years greater than non-surgical matched controls (95% CI, 1.2 to 3.5; p<0.001). This reduction in mortality was similar to our Utah study in which risk from all causes of death was 16% lower among surgical patients compared to non-surgical subjects (HR, 0.84; 95% CI, 0.79–0.90; p<0.001), with a mean extended life expectancy for all causes of deaths of 1.3 years (95%CI, 0.93–1.67; P<0.001) The SOS study also reported a significantly reduced mortality of 30% and 23% for cardiovascular and cancer, respectively, for the surgery compared to non-surgical groups, similar to our Utah study which reported a significant 29% and 43% lower risk for major cardiovascular diseases and cancer, respectively, when comparing the two groups. Finally, as pointed out by SOS authors,[7] when considering populations who are at increased clinical risk such as patients with severe obesity, minimal gains in mean life expectancy (i.e., 1.3 years) are meaningful. Even with minimal benefits on overall mortality, studies have shown significantly increased quality of life after bariatric surgery.[13]

A recently published one-stage meta-analyses explored the association of bariatric surgery with long-term survival, including patients with and without diabetes prior to their surgery. The study, which included 174,772 participants from 16 matched cohort studies and one prospective controlled trial, reported that bariatric surgery was associated with a significantly reduced hazard rate of death of 49.2% (95% CI 46.3 to 51.9; $p<0.0001$), with a calculated mean life expectancy of 6.1 years (95% CI 5.2 to 6.9) longer among the surgical patients when compared to the usual care, non-surgical controls.[39] Further, Syn et al.,[39] performed subgroup analyses and reported that while surgical patients who did and did not have baseline diabetes had lower mortality rates when compared to non-surgical subjects, long-term mortality and survival was more favorable for the bariatric surgery patients who at surgery had diabetes compared to surgical patients without baseline presence of diabetes. Further evidence of improved long-term survival following bariatric surgery has recently been reported by Homberg et al., [40]. Investigators compared the all-cause mortality of patients in Sweden and Finland who had undergone gastric bypass with patients receiving sleeve gastrectomy. Among the 61,503 patients who were followed for a mean of 6.8 person-years, both bariatric surgical procedures had similar all-cause mortality over the entire study duration. Sub-group analyses suggested that patients presenting with diabetes status at time of surgery may have more favorable long-term mortality following gastric bypass when compared to sleeve gastrectomy.[40] Our retrospective study did not have clinical outcomes relating to whether patients and driver license subjects had baseline diabetes.

An important limitation of our study relates to the lack of clinical data at the time of bariatric surgery or application date, as well as absence of clinical surveillance throughout the study. For example, we don't know how much weight was lost after surgery and throughout the follow-up period or the degree of weight maintenance in the driver license subjects. The possibility that surgical and non-surgical subjects were similar in physical health status at surgery or at driver license application is supported by a long-term prospective study our group has conducted on a subset of these surgical patients.[13] At baseline of the prospective study, there were no significant differences in clinical endpoints, (smoking status, hypertension, diabetes, dyslipidemia, or sleep apnea) between patients undergoing bariatric surgery (n=420), patients seeking bariatric surgery but did not have surgery (n=415), and subjects randomly selected from the population who were severely obese and not seeking bariatric surgery (n=321).[41] Current smoking prevalence in that study was 8% in the surgical subjects compared with a northern Utah prevalence of 11% in persons ages ≥18 using data from the Behavioral Risk Factor Surveillance System (http://health.utah.gov/opha/OPHA_BRFSS.htm). The low state smoking prevalence and similar prevalence in subjects having bariatric surgery hopefully minimize bias from not having smoking data.

Further, at 12-years follow-up of our prospective study, with over 90% follow-up rate, the bariatric surgery group had sustained a mean change in body weight from baseline of −35 kg (−26.9%), while mean weight changes of the two non-surgical groups were −2.9 kg and 0 kg, respectively, minimizing the effects weight change might have over the follow-up period. Nevertheless, whether non-surgical subjects who were part of our mortality analysis were less likely to choose and participate in healthy lifestyle practices or were less likely to engage in medical screening and treatment compared to patients who underwent bariatric surgery remains in question.

Because some of the bariatric procedures were developed more recently, follow-up time of these procedures was much shorter than for gastric bypass surgery. Therefore, the numbers of deaths after these surgeries were smaller, resulting in wider confidence intervals around the hazard ratios. Hazard ratios were separately provided for each procedure to address this limitation.

Multiple methodological-related strengths are associated with our study, specifically extended length of follow-up and different bariatric surgery procedures. This study extends from near the time gastric bypass procedures began in the U.S. to approval and initiation of gastric banding, followed by the rise in gastric sleeve. Close matching of surgical patients to driver license subjects facilitated important physiologic and temporal alignment by which to compare mortality between groups, and the analyses of age at surgery provided unique insight into study results. Finally, the Utah Population Database strengthened the accuracy of mortality data extraction.

Conclusions

In conclusion, results of this study attest to the decades-long durability of bariatric surgery in reducing death from all causes and reducing deaths related to cardiovascular disease, cancer and diabetes when compared to matched subjects with severe obesity. In addition, favorable mortality outcomes were evident for major bariatric surgery procedures. Serious concern, however, continues to be exhibited regarding increased mortality following bariatric surgery in relation to suicide, accidents, and cirrhosis of the liver. This study showed the primary group associated with this untoward mortality outcome are patients choosing to have bariatric surgery between ages 18 to 34 years, suggesting this age group may require more aggressive pre-surgical psychological screening and post-surgery follow-up. Finally, with what appears to be an ever-increasing rise in percentage of individuals with severe obesity, coupled with the realization that in practicality bariatric surgery has limited treatment delivery, there remains an important research need to discover physiologic and biomolecular mechanisms leading to non-surgical treatment that result in weight loss and improved mortality similar to that achieved by bariatric surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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STUDY IMPORTANCE QUESTIONS

What is already known about this subject?

- Multiple retrospective studies and one prospective study (Swedish Obesity Subjects study) have reported lower all-cause mortality among patients who have undergone bariatric surgery when compared to BMI matched patients who have not undergone bariatric surgery. In addition to reduced all-cause mortality, studies have reported reduced cardiovascular-, cancer-, and diabetes-related death rates among bariatric surgery patients compared to matched non-surgery patients.
- Our group has previously reported on long-term mortality of Roux-en-Y gastric bypass patients compared to BMI-matched subjects identified from drivers licenses. This previous study was limited to only gastric bypass patients (approximately 7,000) and follow-up was conducted only to 2002.

What are the new findings in your manuscript?

- Current study extends follow-up up to 40 years and includes almost 22,000 surgical patients representing all four major types of bariatric procedures performed today.
- The younger age at surgery group in this study showed significantly increased risk for death from cirrhosis of the liver. Studies have noted increased disinhibition and impulsivity and increased rates of absorption of alcohol following some types of bariatric surgery, although a recent study showed lower risk of adverse liver outcomes after bariatric surgery. Further, lower all-cause mortality was reported for male bariatric surgery patients as well as female patients when compared to sex-matched non-surgical subjects.

How might your results change the direction of research or the focus of clinical practice?

- Reported findings of increased suicide rates among bariatric surgical patients who underwent surgery at younger ages (i.e., 18 to 34 years) may result in more aggressive pre-surgical psychological screening and post-surgery follow-up, especially among patients representing this age group.
- As a result of the decades-long durability of bariatric surgery in reducing death from all causes and reducing deaths related to cardiovascular disease, cancer and diabetes when compared to matched subjects with severe obesity, these findings may not only increase interest in bariatric surgery treatment for patients with severe obesity, but in addition, further stimulate important research related to the discovery of physiologic and biomolecular mechanisms leading to non-surgical treatment that result in weight loss and improved mortality similar to that achieved by bariatric surgery.

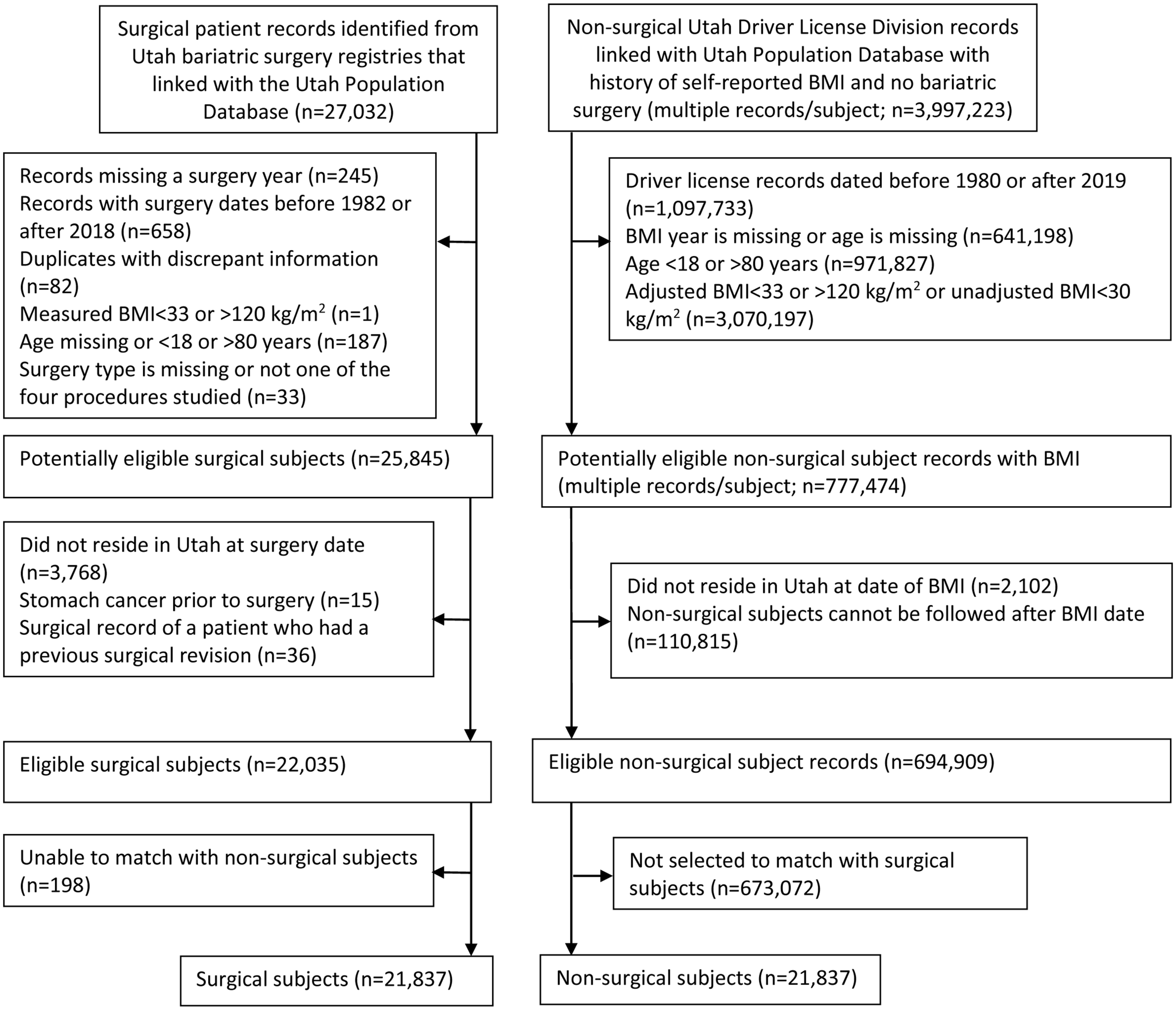

Figure 1.

Retrospective study design and exclusions.

Diagram indicating the exclusion criteria and number of exclusions for each variable listed. The counts in each line of the boxes represent the number of missing or non-qualifying data points out of the total records listed in the box above. Each record could have multiple missing values (such as missing age and BMI) and would be counted multiple times so that the total counts within a box do not add up to the total in the preceding box. This allows the counts to represent the amount of missing data for that variable.

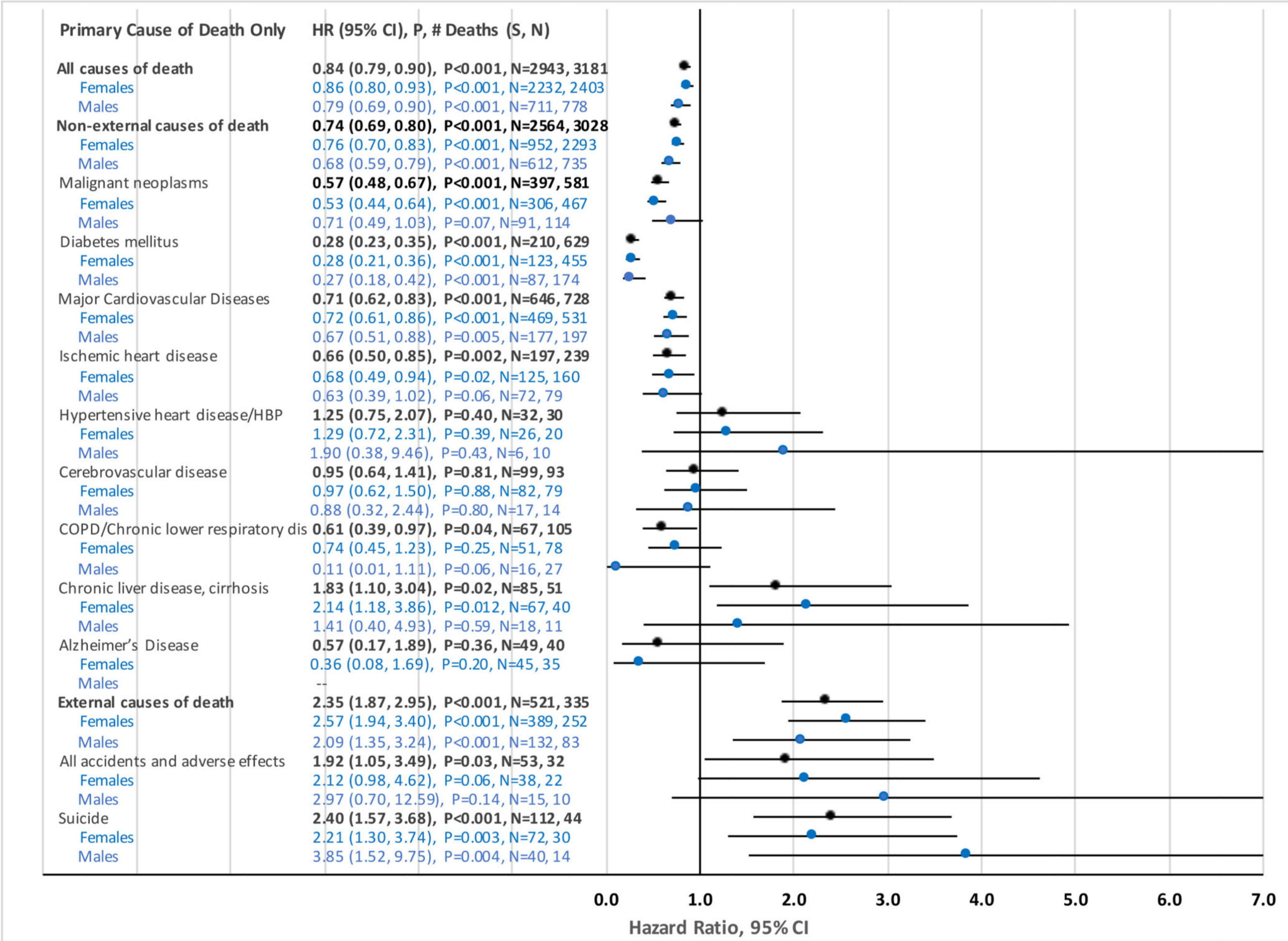

Figure 2.

Mortality risk of bariatric surgery patients compared to non-surgery driver license applicant subjects stratified by sex. S = Surgery Patients; N = Non-surgery Subjects

Non-external causes of death defined as Natural or Pending Investigation with specified codes listed under in the non-external causes of death categories (Supplementary Appendix Table 2).

External causes of death defined as Suicide or Homicide or Accident or Missing (NA) with specified codes listed under in the external causes of death categories (Supplementary Appendix Table 2).

All disease classifications were taken from the primary causes of death except diabetes and Alzheimer's disease, which also used secondary causes of death. Malignant neoplasms used codes defined in Supplementary Appendix Table 1.

Counts less than 11 are required by the Utah Department Health to be reported only as <11.

HR: hazard ratio; CI: confidence interval; S: surgery group; N: non-surgery group.

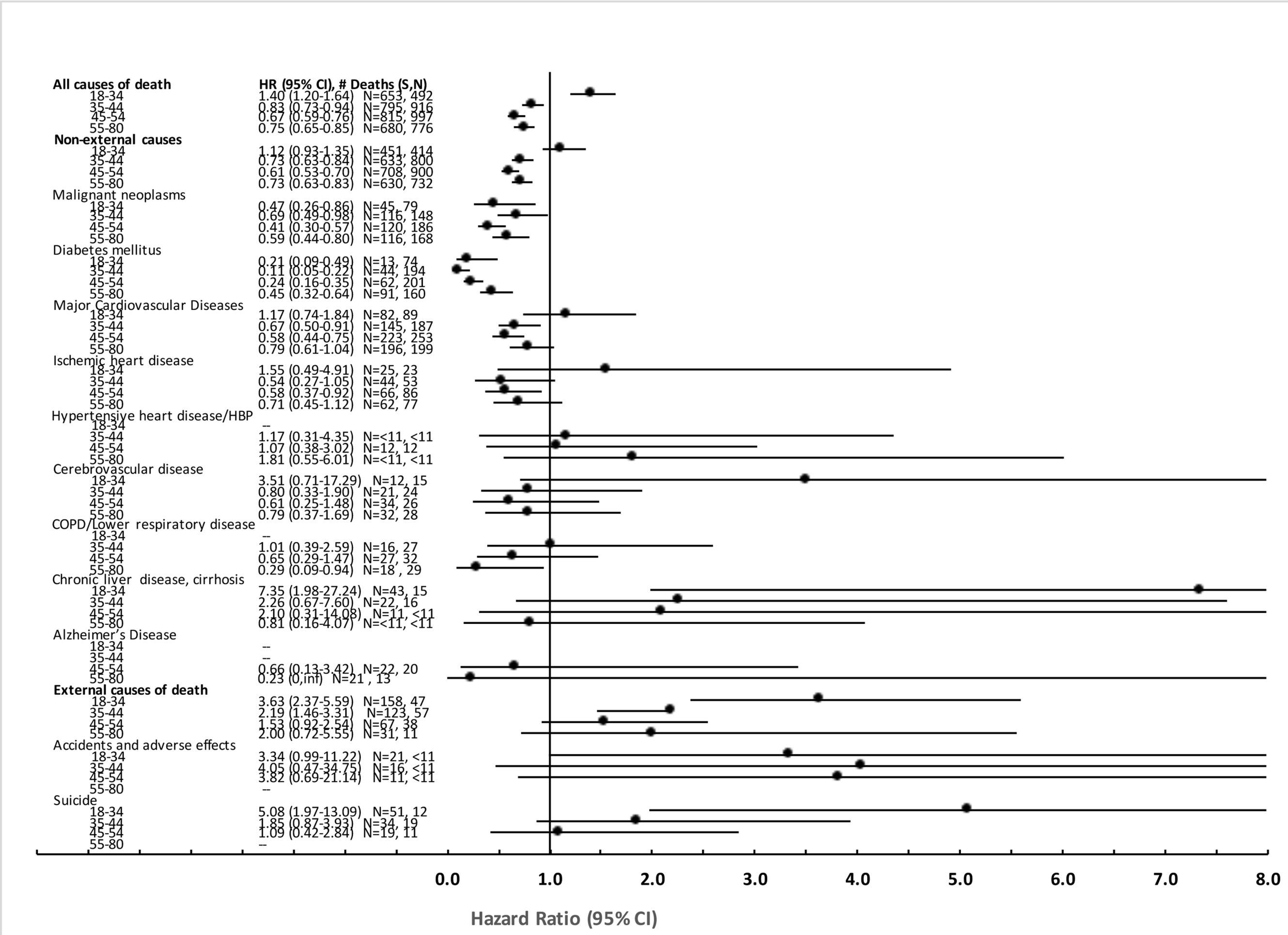

Figure 3.

Mortality risk of bariatric surgery patients compared to non-surgery driver license applicant subjects stratified by age category (years) at surgery. S = Surgery Patients; N = Non-surgery Subjects

Non-external causes of death defined as Natural or Pending Investigation with specified codes listed under in the non-external causes of death categories (Supplementary Appendix Table 2).

External causes of death defined as Suicide or Homicide or Accident or Missing (NA) with specified codes listed under in the external causes of death categories (Supplementary Appendix Table 2).

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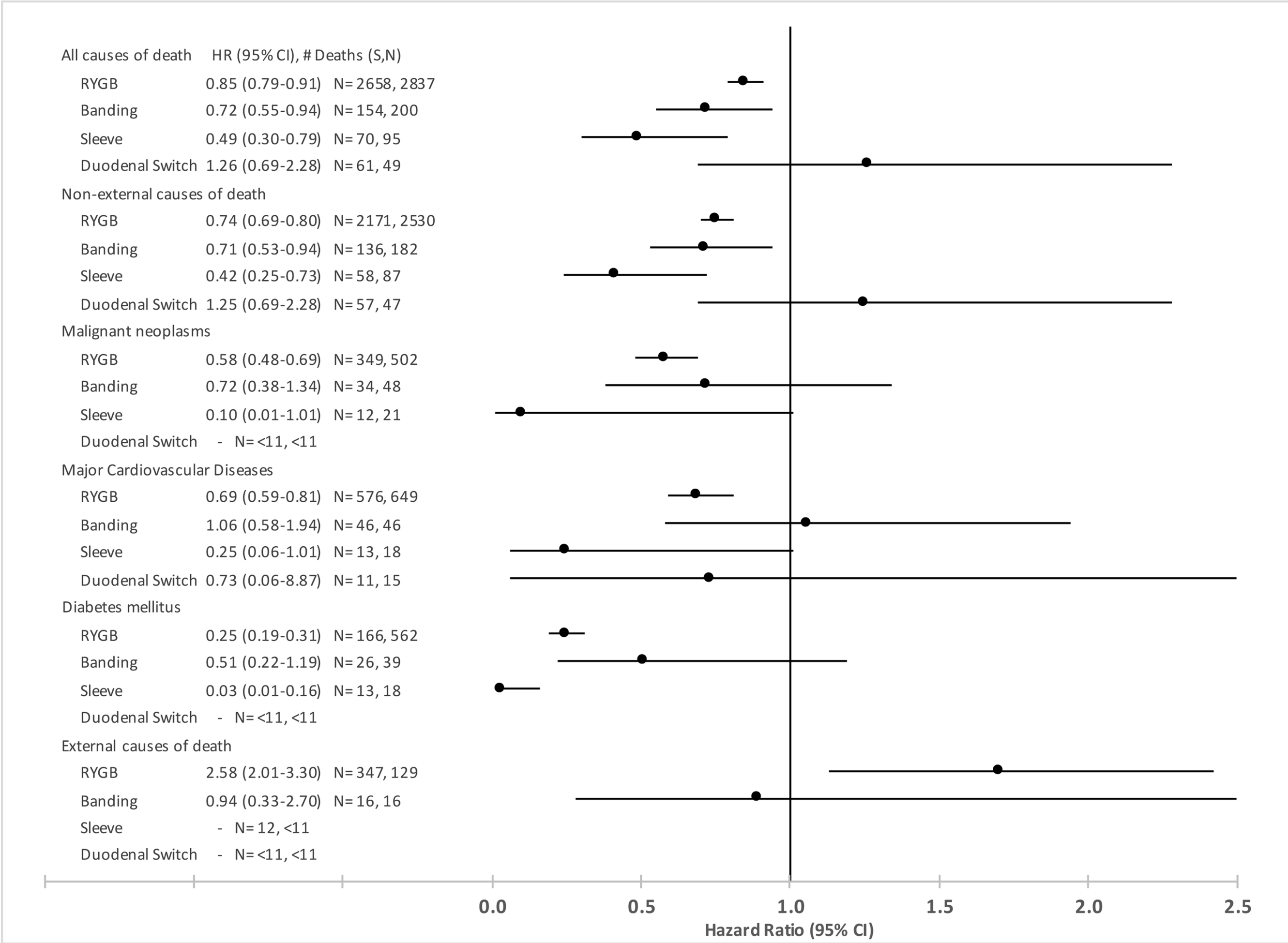

Figure 4.

Mortality risks of bariatric surgery patients compared to non-surgery driver license applicant subjects stratified by surgery type. S = Surgery Patients; N = Non-surgery Subjects

Non-external causes of death defined as Natural or Pending Investigation with specified codes listed under in the non-external causes of death categories (Supplementary Appendix Table 2).

External causes of death defined as Suicide or Homicide or Accident or Missing (NA) with specified codes listed under in the external causes of death categories (Supplementary Appendix Table 2).

All disease classifications were taken from the primary causes of death except diabetes and Alzheimer's disease, which also used secondary causes of death. Malignant neoplasms used codes defined in Supplementary Appendix Table 1.

Counts less than 11 are required by the Utah Department Health to be reported only as <11.

HR: hazard ratio; CI: confidence interval; S: surgery group; N: non-surgery group.

Table 1:

Characteristics of bariatric surgery patients and matched driver license subjects linked to Utah death certificates.

Characteristics	All matched subjects			All female matched subjects			All male matched subjects		
	Non-Surgery Group	**Surgery Group**	**p-value**	**Non-Surgery Group**	**Surgery Group**	**p-value**	**Non-Surgery Group**	**Surgery Group**	**p-value**
N	21837	21837		17271	17271		4566	4566	
Sex						-			-
- Female	17271 (79.1%)	17271 (79.1%)		-	-	-	-	-	-
- Male	4566 (20.9%)	4566 (20.9%)		-	-	-	-	-	-
Birth year	1962.4 (13.8)	1962.4 (13.8)	0.78	1962.4 (13.9)	1962.4 (13.9)	0.87	1962.2 (13.4)	1962.3 (13.4)	0.77
Age at index date (years)[1]	42.3 (11.9)	42.2 (11.7)	0.60	41.5 (11.7)	41.4 (11.5)	0.63	45.3 (12.2)	45.2 (12.1)	0.83
Index year[1]	2004.7 (10.2)	2004.6 (10.4)	0.75	2003.9 (10.4)	2003.9 (10.6)	0.71	2007.5 (9.0)	2007.5 (9.1)	0.98
BMI at index date (kg/m^2)[2]	46.2 (6.8)	46.0 (8.3)	0.003	45.8 (6.2)	45.3 (7.9)	<0.001	47.5 (8.5)	48.3 (9.2)	<0.001
Whether Caucasian			<0.001			<0.001			<0.001
- Yes	19136 (87.6%)	20625 (94.4%)		15229 (88.2%)	16339 (94.6%)		3907 (85.6%)	4286 (93.9%)	
- No	1729 (7.9%)	890 (4.1%)		1317 (7.6%)	663 (3.8%)		412 (9%)	227 (5%)	
- Unknown	972 (4.5%)	322 (1.5%)		725 (4.2%)	269 (1.6%)		247 (5.4%)	53 (1.2%)	
Hispanic			<0.001			<0.001			<0.001
- No	17600 (80.6%)	19397 (88.8%)		13896 (80.5%)	15259 (88.4%)		3704 (81.1%)	4138 (90.6%)	
- Yes	2708 (12.4%)	1700 (7.8%)		2204 (12.8%)	1399 (8.1%)		504 (11%)	301 (6.6%)	
- Unknown	1529 (7%)	740 (3.4%)		1171 (6.8%)	613 (3.5%)		358 (7.8%)	127 (2.8%)	
Type of surgery[3]			-			-			-
- RYGB	-	15110 (69.2%)		-	12288 (71.1%)		-	2822 (61.8%)	
- Banding	-	2629 (12%)		-	2045 (11.8%)		-	584 (12.8%)	
- Sleeve	-	3050 (14%)		-	2260 (13.1%)		-	790 (17.3%)	
- Duodenal Switch	-	1048 (4.8%)		-	678 (3.9%)		-	370 (8.1%)	
Censoring status in 2021[4]			0.001			0.007			0.062
- Alive	18656 (85.4%)	18894 (86.5%)		14868 (86.1%)	15039 (87.1%)		3788 (83%)	3855 (84.4%)	

Characteristics	All matched subjects			All female matched subjects			All male matched subjects		
	Non-Surgery Group	Surgery Group	p-value	Non-Surgery Group	Surgery Group	p-value	Non-Surgery Group	Surgery Group	p-value
- Died (Total)	3181 (14.6%)	2943 (13.5%)		2403 (13.9%)	2232 (12.9%)		778 (17%)	711 (15.6%)	
Died within the 1st year	89 (0.4%)	111 (0.5%)	0.14	49 (0.3%)	73 (0.4%)	0.037	40 (0.9%)	38 (0.8%)	0.91
Follow up time to death[5] (Mean (SD))	13.2 (9.5)	13.3 (9.8)	0.20	13.9 (9.8)	14.0 (10.1)	0.23	10.6 (8.0)	10.7 (8.3)	0.65
Follow up time to death[5] Median (IQR) and (Min, Max)	10.8 (5.0, 19.1) (0.0, 39.1)	11.0 (4.9, 19.4) (0.0, 39.6)		11.8 (5.3, 20.1) (0.0, 39.1)	11.9 (5.2, 20.6) (0.0, 39.6)		8.2 (4.4, 14.9) (0.0, 38.2)	8.2 (4.3, 15.1) (0.0, 38.8)	

[1]Index date is defined as date of bariatric surgery for surgical patients and date of DL applications for matching controls. If only index year is known, then index date is set as July 1st of that year.

[2]Unadjusted BMI for surgical patients and corrected self-reported BMI for matching non-surgical subjects.

[3]See Supplementary Appendix Table 3 for distribution of index year by bariatric surgery type

[4]Cause of death is defined as primary causes of death as recorded in Utah death certificates. Follow up time (years) is determined as time from index date to follow up date.

[5]Follow up date is determined 1) as the date that a person is considered to still live in Utah, or 2) when a surgical patient undergoes revision bariatric procedures, or 3) December 31st, 2021 (the last year UPDB received Utah death certificate records), or 4) death date, whichever occurred first.

Demographic characteristics between surgical patients and their matching controls were compared using t-tests for continuous variables and chi-square tests for categorical variables.

Table 2:

Distribution of Deaths and Death Rates per 10,000 Person-years for all Matched Surgical and Non-surgical Subjects and Sex-specific Matched Subjects.

Endpoint	All Matched Subjects				Matched Subjects, Female				Matched Subjects, Male			
	Non-Surgery Group (N = 21837)		Surgery Group (N = 21837)		Non-Surgery Group (N = 17271)		Surgery Group (N = 17271)		Non-Surgery Group (N = 4566)		Surgery Group (N = 4566)	
	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate	N	Rate
All causes of death [1]	3181	110.7	2943	101.4	2403	100.6	2232	92.5	778	160.5	711	145.4
Non-external causes of death [2]	2846	99.0	2422	83.4	2151	90.0	1843	76.4	695	143.3	579	118.4
Malignant neoplasms	581	20.2	397	13.7	467	19.5	306	12.7	114	23.5	91	18.6
Alzheimer's disease	40	1.4	49	1.7	35	1.5	45	1.9	<11	-	<11	-
Diabetes mellitus	629	21.9	210	7.2	455	19.0	123	5.1	174	35.9	87	17.8
Major Cardiovascular Diseases	728	25.3	646	22.3	531	22.2	469	19.4	197	40.6	177	36.2
- Ischemic heart disease	239	8.3	197	6.8	160	6.7	125	5.2	79	16.3	72	14.7
- Hypertensive heart disease	30	1.0	32	1.1	20	0.8	26	1.1	<11	-	<11	-
- Hypertension	20	0.7	37	1.3	16	0.7	29	1.2	<11	-	<11	-
- Cerebrovascular disease	93	3.2	99	3.4	79	3.3	82	3.4	14	2.9	17	3.5
Chronic obstructive pulmonary disease/ Chronic lower respiratory disease	105	3.7	67	2.3	78	3.3	51	2.1	27	5.6	16	3.3
Chronic liver disease cirrhosis	51	1.8	85	2.9	40	1.7	67	2.8	11	2.3	18	3.7
All other diseases	1085	37.7	1100	37.9	806	33.7	860	35.6	279	57.5	240	49.1
External causes of death [3]	153	5.3	379	13.1	110	4.6	280	11.6	43	8.9	99	20.2
Select accidents and adverse effects	32	1.1	53	1.8	22	0.9	38	1.6	<11	2.1	15	3.1
Suicide	44	1.5	112	3.9	30	1.3	72	3.0	14	2.9	40	8.2
All other external causes	77	2.7	214	7.4	58	2.4	170	7.0	19	3.9	44	9.0

[1] If Manner of Death and ICD codes are both missing, the death was included in the all causes of death row but excluded from all other rows. Therefore, the counts of non-external and external causes of death do not add up to the all causes of death counts.

[2] Determined by Manner of Death as Natural or Pending Investigation or Undetermined if Injured Purposely or Accidentally or Missing (NA) with specified codes listed under in the non-external causes of death categories (Supplementary Table 2)

[3] Determined by Manner of Death as Suicide or Homicide or Accident or Missing (NA) with specified codes listed under in the external causes of death categories (Supplementary Table 2)

All disease classifications were taken from the primary causes of death except diabetes and Alzheimer's disease, which also used secondary causes of death. Malignant neoplasms used codes defined in Supplementary Table 1.

Cells with less than 11 counts must be reported as less than 11 according to Utah Department of Health policy.