HEALTH CARE UTILIZATION AND COSTS OF BARIATRIC SURGERY PATIENTS WITH VS. WITHOUT COMORBID OBSTRUCTIVE SLEEP APNEA

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TITLE: Health Care Utilization and Costs of Bariatric Surgery Patients with vs. without Comorbid Obstructive Sleep Apnea

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LAY ABSTRACT

Obstructive sleep apnea (OSA) is underrecognized and a good proportion of patients with OSA are undiagnosed. To reduce the risk of peri-operative complications related to undiagnosed OSA, patients planned to undergo bariatric surgery are screened for OSA. To understand the performance of OSA screening practices, using a province-wide registry, the proportion of patients diagnosed with OSA within patients who underwent publicly-funded bariatric surgery in Ontario between 2010 and 2016 was measured at 47%. Furthermore, to understand the effect of OSA screening practices on peri-operative costs and longer-term health care costs, health care utilization and costs were compared between patients with OSA and matched patients without OSA in the 30 days and 1 year post-bariatric surgery. Total health care costs per patient were 1% lower in patients with OSA compared to patients without OSA, and this difference was driven by lower hospitalization-related costs.

ABSTRACT

Obstructive sleep apnea (OSA) is underrecognized. Between 10% and 69% of pre-operative patients have undiagnosed OSA [1-3]. To reduce the risk of peri-operative complications related to undiagnosed OSA, patients planned to undergo bariatric surgery are screened for OSA [4, 5].

To understand the OSA detection rate with screening practices, the prevalence of OSA within patients who underwent publicly funded bariatric surgery in Ontario between 2010 and 2016 was measured. Secondly, to understand the effect of OSA screening practices on peri-operative and longer-term health care costs, health care utilization and costs were compared between patients with OSA and matched patients without OSA in the 30 days post-bariatric surgery, as well as in the 1 year post-bariatric surgery.

The Ontario Bariatric Registry (OBR) linked to the ICES health administrative databases were used [6, 7]. A diagnosis of OSA was identified if recorded in the OBR at time of initial bariatric consultation, or if recorded in ICES databases from the bariatric surgery admission records. Costs were calculated based on the "Guidelines on Person-Level Costing Using Administrative Databases in Ontario" using ICES costing algorithms [8].

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The overall prevalence of OSA was 47% (95% CI 46% to 47%). Total health care costs per patient, in the 30-day post-operative period, were 1% lower (95% CI 1% to 1%, $p < 0.001$) in patients with OSA compared to matched patients without OSA. Similarly, at 1 year post-bariatric surgery, total health care costs per patient, were 1% lower (95% CI 1% to 1%, $p < 0.001$) in patients with OSA compared to matched patients without OSA. At 30 days and 1 year, this difference was driven by lower hospitalization-related costs.

OSA screening practices at surgical centers in our network led to similar rates of OSA detection as reported in the literature. However, the literature suggests that screening practices lead to missed OSA diagnoses. Further study is required to understand the reduced post-bariatric surgery costs in patients with OSA compared to matched controls without OSA; and, we postulate that missed OSA diagnoses may be a contributor.

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LIST OF ALL ABBREVIATIONS AND SYMBOLS

ADGs: Aggregated Diagnosis Groups

ADP: Assistive Devices Program Database

AHI: apnea hypopnea index

BMI: body mass index

CAD: coronary artery disease

CIHI: Canadian Institute for Health Information

CIHI-DAD: Canadian Institute for Health Information Discharge Abstract Database

COPD: chronic obstructive pulmonary disease

CPAP: continuous positive airway pressure

ED: emergency department

GLMM: generalized linear mixed model

HCD: Home Care Database

HTN: hypertension

ICD: International Classification of Disease

ICES: Institute for Clinical Evaluative Sciences

MOHLTC: Ministry of Health and Long Term Care

NACRS: National Ambulatory Care Reporting System

NB: negative binomial

NIS: Nationwide Inpatient Sample

OBR: Ontario Bariatric Registry

OMI: Ontario Marginalization Index

OSA: obstructive sleep apnea

PSG: polysomnogram

RPDB: Registered Persons Database

T2DM: type II diabetes mellitus

DECLARATION OF ACADEMIC ACHIEVEMENT

Dr. Vanessa Martelli is an ICES student and practicing Respirologist and Sleep Medicine specialist. She was responsible for: study conception and design, analysis and interpretation of results, and manuscript preparation.

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INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by recurrent reduction in breathing during sleep caused by transient upper airway collapse, which may lead to excessive daytime sleepiness, impaired quality of life, as well as an increased risk of cardiovascular disease (1). To diagnose OSA, an in-laboratory polysomnogram (PSG) or a home sleep study, which measure the frequency of respiratory events during sleep, i.e., the apnea hypopnea index (AHI), is required (2). Risk factors for developing OSA include: age, male sex, menopause, obesity, smoking, as well as genetic factors and race (due to their relationship with craniofacial features) (1). The following anthropometric measures have been associated with an increased risk for OSA: weight, body mass index (BMI), neck circumference, waist:hip ratio, and skin-fold thickness (3). In a secondary analysis of a dietary weight loss trial including 180 patients, a 5% to 10% reduction in weight was associated with an approximately 40% reduction in AHI (4). Although, in women, the incidence of OSA is thought to increase significantly post-menopause due to hormonal changes, this diagnosis should also be considered in pre-menopausal women. In a study of morbidly obese women with a mean age of 40 years (range 21 to 62 years), 93% were found to have OSA (5). In men and women, after age 60, evidence has shown that there is no longer a relationship between BMI and OSA severity (6).

In high-income countries, the prevalence of OSA in the general population has been estimated at 10% in women and 20% in men (1). However, the true prevalence may be higher than what has been estimated, as it is agreed upon that a high proportion of OSA remains undiagnosed (7). In a single center U.S.A. study of 1,118 pre-operative ambulatory patients, a screening protocol led to a new diagnosis of OSA in 10% of these patients (8). In a prospective Canadian study in which all pre-operative ambulatory patients without a pre-existing OSA

diagnosis underwent a sleep study (708 total), 69% were found to have undiagnosed OSA (9). In a randomly selected sample of 793 participants from a region of Australia, with the following characteristics: mean age 54 years, 48% male, mean BMI 27 kg/m^2 and 97% European ancestry, 15% were found to have previously undiagnosed moderate or severe OSA (10).

Given that obesity is a significant risk factor for OSA, it is expected that the prevalence of OSA in the bariatric surgery population is higher compared to the general population. In a U.S.A.- based registry in which all 290 patients being evaluated for bariatric surgery underwent an in-laboratory PSG, the prevalence of OSA was 78% overall, and rose to 95% in patients with a BMI greater than 60 kg/m^2 (11). Similarly, in a multicenter study conducted in Finland, all patients being evaluated for bariatric surgery underwent a home sleep study, and the prevalence of OSA was 71% overall (60% in females and 90% in males) (12). Similarly to the general population, OSA is underdiagnosed in the bariatric surgery population. In the aforementioned Finnish study, only one third of the included patients had been diagnosed with OSA prior to being referred for bariatric surgery (12). In a prospective cohort study of ten U.S.A. surgical centers (including 2,458 patients), not all patients underwent a sleep study; and, there was significant variation in the frequency of OSA testing in the 12 months preceding bariatric surgery (median: 18%, range: 5% to 71%) (13). This study found an overall OSA prevalence of 53% (based on sleep study results if a study was completed, or self-report) (13).

Given that OSA may be associated with an increased risk of peri-operative complications, American and international guidelines recommend screening bariatric surgery patients for OSA using validated questionnaires (either the Berlin Questionnaire or the STOP-Bang Questionnaire) (7, 14-16). Because of limited resources, a diagnostic sleep study is not the recommended standard for all patients being evaluated for bariatric surgery (15, 16). Although Canadian

authors contributed to the international guideline, there are currently no Canadian guidelines on OSA screening in the bariatric surgery population.

By definition, a screening test does not diagnosis disease, but rather identifies patients who should undergo further evaluation for a specific condition (17). Traditionally, screening tests are studied in terms of their ability to lead to early identification of asymptomatic disease and therefore improved outcomes (17). The STOP-Bang Questionnaire and the Berlin Questionnaire are referred to as screening tools, although they do not diagnose early asymptomatic disease. The STOP-Bang Questionnaire was developed in Canada to assist surgeons and anesthetists in determining which patients should have increased peri-operative monitoring or even a delay in surgery due to increased risk from untreated OSA (7). These screening tools were desirable because wait times for diagnostic sleep studies are in excess of several months, which would delay surgeries (7). The predictive ability of the STOP-Bang questionnaire has been evaluated in obese surgical patients, with a score of ≥ 3 having the following characteristics: to predict all OSA: sensitivity 91%, specificity 28%; to predict moderate/severe OSA: sensitivity 95%; specificity 20% (18). In patients being evaluated for bariatric surgery, the Berlin questionnaire was found to have a sensitivity of 86% and a specificity of 77% for the diagnosis of OSA (16). Although these screening tools have good test characteristics, some false negative results will occur, leading to undiagnosed OSA in patients undergoing surgery.

There is currently no published data on the prevalence of diagnosed OSA in patients undergoing bariatric surgery across the province of Ontario, Canada. Measuring OSA prevalence in patients who underwent bariatric surgery in Ontario, and comparison with the reported prevalence in other jurisdictions, would inform on the performance of OSA screening

practices in this province. Medically necessary care, including bariatric surgery, is covered in Ontario by a single payer public health care system. The Ontario Bariatric Registry (OBR), which was established in 2010 and prospectively collects data on all patients referred for publicly funded bariatric surgery within the province, represents a unique opportunity to generate information on the prevalence of OSA in Canadian patients undergoing bariatric surgery (19).

Furthermore, there is currently no published Canadian data on health care costs in patients with OSA in the context of post-bariatric surgery, both in the immediate (30 days) and longer term (1 year). Health administrative data can be leveraged to fill this void. Health administrative data are collected by governmental institutions or health systems for the purposes of accountability and planning (20). Although these data were not originally designed to be used for research purposes, organizations such as the Institute for Clinical Evaluative Sciences (ICES) in Ontario (the largest province in Canada), have utilized this data to perform studies on health care utilization, health policy and social determinants of health (21). This has been possible through data linkage of multiple governmental data repositories, as well as linkage to disease-specific registries and country- or province-wide health surveys (21). Furthermore, ICES-derived cohorts consist of population-level cohorts for certain chronic diseases (asthma, chronic obstructive pulmonary disease, diabetes, etc.) which are defined by a combination of physician billing diagnostic codes and International Classification of Disease (ICD) diagnosis codes recorded during hospitalizations or emergency department (ED) visits, and validated via chart review of physician records (21-23). Health administrative databases have also been used in health economic studies to measure cost of illness and cost-effectiveness of therapies, using validated costing algorithms (20). The World Health Organization has published guidelines for the systematic description of financial flows related to health care (24).

The published literature includes mixed evidence regarding the effect of OSA on post-bariatric surgery outcomes. Surgical outcomes, in turn, affect health care utilization and costs in the 30 days post-bariatric surgery. In a study of patients who underwent bariatric surgery in a single surgical center in Poland, treated OSA patients had a shorter post-operative hospital stay and a lower rate of post-operative pneumonia in comparison to untreated OSA patients or patients with a STOP-Bang score of ≥ 3 who had not undergone a sleep study (25). In addition, there were two deaths in the night of the second postoperative day in the untreated/undiagnosed group (25). In contrast, in a study of 1,050 hospitals and 91,028 patients undergoing bariatric surgery (from a U.S.A. all-payers' database), regression analysis showed that OSA compared to non-OSA was associated with decreased mortality, reduced length of stay and reduced total hospitalization costs (26). That being said, OSA was associated with an increased risk of emergent endotracheal intubation and need for invasive mechanical ventilation (26). In this study, protocols for increased peri-operative monitoring and OSA treatment status were not reported (26).

In the 1 year post-bariatric surgery, OSA may affect health care utilization and costs. The following data suggests that OSA treatment leads to reduced health care utilization and costs over a longer term. A study conducted within a health organization in Israel measured health care costs of patients with OSA in the two years prior to OSA diagnosis, in comparison to matched controls without OSA, including: number of days in hospital, number of ambulatory visits, number of ED visits, number of primary care visits, number of specialist visits and prescription drugs (27). This study showed that before OSA diagnosis, patients with OSA have higher health care costs compared to controls (2.2 fold higher in those aged ≤ 65 years of age), and this difference was driven by higher costs secondary to physician visits and prescription

drugs (27). Although OSA treatment is considered cost-effective, it is uncertain whether, patients with diagnosed OSA have increased or reduced health care utilization and costs compared to matched controls without OSA (28).

In summary, OSA is common, and a significant proportion of patients with OSA presenting for bariatric surgery evaluation may be undiagnosed at the time of initial consultation. Because untreated OSA may lead to increased perioperative complications, it is recommended that patients being evaluated for bariatric surgery be screened for OSA using questionnaires or other measures; however, the standard of care does not require all patients to undergo a sleep study, which may lead to underdiagnosis of OSA. To understand the performance of OSA screening practices in Ontario, Article 1 measures the prevalence of OSA in patients who underwent publicly funded bariatric surgery in Ontario overall, as well as by surgical center.

Furthermore, there is uncertainty regarding the effect of current screening practices' OSA diagnosis rate on peri-operative outcomes, and, in turn, health care utilization and costs in the peri-operative period. Article 2 measures health care utilization and costs in the 30 days post-bariatric surgery in patients with OSA compared to matched controls without OSA. Lastly, although OSA treatment is considered cost-effective, it is uncertain whether health care utilization and costs of patients with diagnosed OSA are higher than patients without OSA in the longer term. Therefore, Article 2 compares health care utilization and costs in the 1 year post-bariatric surgery in patients with OSA compared to matched controls without OSA. One year was chosen to capture the effect of diagnosed OSA rather than weight loss.

ARTICLE 1: Prevalence of Obstructive Sleep Apnea in Bariatric Surgery Patients: a Population-Based Study

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Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by recurrent reduction in breathing during sleep caused by transient upper airway collapse, which may lead to excessive daytime sleepiness, impaired quality of life, as well as an increased risk of cardiovascular disease (1). Risk factors for developing OSA include: age, male sex, menopause, obesity, smoking, as well as genetic factors and race (due to their relationship with craniofacial features) (1). OSA is diagnosed using an in-laboratory polysomnogram (PSG) or a home sleep study (2). The prevalence of OSA in the general population of high-income countries has been estimated at 10% in women and 20% in men (1). It is agreed upon that a high proportion of OSA remains undiagnosed; and, therefore, the true prevalence may be higher than what has been estimated (7).

Given that obesity is a significant risk factor for OSA, the prevalence of OSA in the bariatric surgery population is higher compared to the general population. In a U.S.A.- based registry in which all patients being evaluated for bariatric surgery underwent an in-laboratory PSG, the prevalence of OSA was 78% overall, and rose to 95% in patients with a body mass index (BMI) greater than 60 kg/m^2 (11). Similarly, in a multicenter study conducted in Finland in which all patients being evaluated for bariatric surgery underwent a home sleep study, the prevalence of OSA was 71% overall (60% in females and 90% in males); and only one third of these patients had been diagnosed with OSA prior to being referred for bariatric surgery (12). In

a prospective cohort study of ten U.S.A. surgical centers (including 2,458 patients), there was significant variation in the frequency of OSA testing in the 12 months preceding bariatric surgery (median: 18%, min: max: 5%: 71%) (13). In this study, the overall prevalence of OSA (based on sleep study results if a study was completed, or self-report) was 53% (13).

Given that OSA may be associated with an increased risk of peri-operative complications, international guidelines recommend screening bariatric surgery patients for OSA using validated questionnaires (either the Berlin Questionnaire or the STOP-Bang Questionnaire) (7, 14, 15). Because of limited resources, a diagnostic sleep study is not the recommended standard for all patients being evaluated for bariatric surgery (15, 16). There is currently no published data on the prevalence of diagnosed OSA in patients undergoing bariatric surgery across the province of Ontario, Canada.

Thus, OSA is common, and a significant proportion of patients with OSA presenting for bariatric surgery evaluation may be undiagnosed at the time of initial consultation. Because untreated OSA may lead to increased perioperative complications, it is recommended that patients being evaluated for bariatric surgery be screened for OSA using questionnaires or other measures; however, the standard of care does not require all patients to undergo a sleep study. In order to better understand the performance of current OSA screening practices, the objectives of this study were to: (i) measure the prevalence of OSA in patients who underwent publicly funded bariatric surgery in Ontario, Canada; and (ii) compare OSA prevalence between Ontario bariatric surgical centers to identify whether there may be varying effectiveness in OSA screening practices.

Methods

Study Design

This was a cross-sectional population-based study using the Ontario Bariatric Registry (OBR) linked to the Institute for Clinical Evaluative Sciences (ICES) health administrative databases. Ethics approval was obtained from the Hamilton Integrated Research Ethics Board, Hamilton, Ontario, Canada.

Setting and Participants

Patients who underwent publicly funded bariatric surgery in Ontario between January 2010 and December 2016 (most recent data available) were included. Non-Ontario residents and patients with a history of previous bariatric surgery were excluded. The Ontario Bariatric Network consists of 10 surgical centers of excellence across the province.

Data Sources

The OBR was established in 2010 and includes all patients referred for publicly funded bariatric surgery within the province of Ontario, Canada (19). ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement (21). For the purpose of this study, ICES databases accessed included: the Registered Persons Database (RPDB); the OHIP database; the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD); and the National Ambulatory Care Reporting System (NACRS). These datasets were linked using unique encoded identifiers and analyzed at ICES.

Variables

The following baseline characteristics were recorded in the OBR at the time of initial bariatric consultation: sex, BMI and current smoker; and the following characteristics were recorded at the time of surgery: age and surgery type.

ICES administrative databases were used to derive several variables to describe our population. First, the Ontario Marginalization Index (OMI), developed by Public Health Ontario in 2006 and shown to be associated with health outcomes, was used as a measure of social inequality (29). The OMI uses home address and 2016 census data to generate a score for each of the following four dimensions of social inequality: residential instability, material deprivation, dependency, and ethnic concentration (29). These four scores can then be incorporated into a summary score (1 to 5, with a higher score indicating a higher level of social inequality, Appendix Figures 2 & 3) (29).

Johns Hopkins Aggregated Diagnosis Groups (ADGs) were obtained from the Johns Hopkins ACG® system version 10, a widely used measure of morbidity burden based on International Classification of Disease (ICD) diagnosis codes (30). A count of major ADGs (labeled as such due to their very high expected resource use) was conducted for each patient (Appendix Figure 1) (30).

Comorbid asthma, chronic obstructive pulmonary disease (COPD), type II diabetes mellitus (T2DM) and hypertension (HTN) were identified using ICES-derived cohorts, which are defined using health administrative data via validated algorithms, and updated annually (21). Comorbid coronary artery disease (CAD) and anxiety or depression were defined based on either physician billings, in-patient hospital records or emergency department (ED) / ambulatory care records housed at ICES (21).

Defining Patients with OSA

A diagnosis of OSA is recorded in the OBR if present at the time of initial bariatric consultation. All patients are screened for OSA symptoms prior to undergoing surgery; however, it is not standard for all patients being evaluated for surgery to undergo a sleep study. Because many patients are diagnosed with OSA between the time of initial consultation and the time of surgery, a diagnosis of OSA was identified if recorded in the OBR at time of initial bariatric consultation; or, if recorded in ICES health administrative databases (based on in-patient hospital records or ED / ambulatory care records) in the five years leading up to the surgery (including the bariatric surgery admission records).

Statistical Methods

Using the aforementioned OSA definition, the prevalence of OSA was calculated within all patients having undergone publicly funded bariatric surgery in Ontario from 2010 to 2016. In addition, OSA prevalence was calculated for each individual surgical center, and comparison was made using Pearson chi-square test with Yates continuity correction. Lastly, to inform whether a difference in OSA prevalence across surgical centers was secondary to different populations or varying effectiveness of screening practices, patient characteristics were compared between surgical centers by calculating the standardized difference, which represents the difference in means or proportions divided by the standard error. A standardized difference greater than 0.2 (absolute value) was considered a significant difference (31). Surgical centres were deidentified using a letter designation. Statistical analysis was performed using R software (version 3.6.2).

Results

Study Population

A total of 18,074 patients underwent publicly funded bariatric surgery in Ontario from January 2010 to December 2016 (Table 1). The mean age of patients was 45 years and the majority (83%) were female. Regarding comorbidity burden, most patients had three or less major ADGs. The most common major comorbidity was anxiety or depression (58%), with only about 10% of patients having comorbid HTN, T2DM or CAD, and 3% with chronic lung disease (asthma or COPD).

Prevalence of Obstructive Sleep Apnea

The overall prevalence of OSA was 47% (95% CI 46% to 47%) (Table 2). 63% of OSA diagnoses were recorded in the OBR at the time of initial bariatric consultation, and the remainder were identified using ICES in-patient hospital records or ED / ambulatory care records in the five years leading up to the surgery (including the bariatric surgery admission records).

Comparison between Ontario Surgical Centres

OSA prevalence differed across surgical centers from 21% to 66%, and was significantly different in seven out of the ten surgical centers. Table 3 summarizes the characteristics of patients who underwent bariatric surgery by surgical center. Overall, patient characteristics were similar across centers. The patient population who underwent bariatric surgery at center A had a significantly lower mean BMI (small effect size, with a standardized mean difference of -0.21). Patients who underwent surgery at center H had a significantly lower mean OMI summary score (small effect size, with a standardized mean difference of -0.22).

Discussion

The prevalence of OSA in the bariatric surgery population reported in the literature varies from 35% to 94% (16). We estimated a prevalence of 47% (95% CI 46% to 47%). OSA was the second most common major comorbidity in this patient population, after anxiety or depression.

The variability in the reported prevalence in the literature is likely dependent on the OSA screening and testing practices employed, with studies in which all patients being evaluated for bariatric surgery are tested reporting a higher prevalence compared to studies in which only patients who screen positive are tested. For example, in a U.S.A.- based registry in which all patients being evaluated for bariatric surgery underwent an in-laboratory PSG, the prevalence of OSA was 78% overall (11). Similarly, in a single center U.S.A. study and a multicenter study conducted in Finland in which all patients being evaluated for bariatric surgery underwent a home sleep study, the prevalence of OSA was 71% and 77%, respectively (12, 32). In contrast, in studies in which patients were screened for OSA based on routine practices, the measured OSA prevalence was lower. In a study of ten U.S.A. surgical centers (including 2,458 patients), in which there was significant variation in the frequency of OSA testing, the overall prevalence of OSA (based on sleep study results if a study was completed, or self-report) was 53% (13). The Nationwide Inpatient Sample included 91,028 patients who underwent bariatric surgery at 1,050 hospitals with different OSA screening practices, and recorded an OSA prevalence of 36% (26). The overall OSA prevalence measured in our study resembles that reported in other studies in which not all patients being evaluated for bariatric surgery routinely undergo a sleep study. Therefore, OSA screening practices at surgical centers in our network led to similar rates of OSA detection as reported in the literature.

OSA may be associated with an increased risk of peri-operative complications (15). It is uncertain whether, with current OSA screening practices, missed OSA diagnoses lead to adverse outcomes. The predictive ability of the STOP-Bang questionnaire has been evaluated in obese surgical patients, with a score of ≥ 3 having the following characteristics: to predict all OSA: sensitivity 91%, specificity 28%; to predict moderate/severe OSA: sensitivity 95%; specificity 20% (18). In patients being evaluated for bariatric surgery, the Berlin questionnaire was found to have a sensitivity of 86% and a specificity of 77% for the diagnosis of OSA (16). Given that the sensitivity of these OSA screening questionnaires likely increases with increasing OSA severity, it is possible that missed OSA diagnoses consist of patients with milder sleep disordered breathing, which may be less likely to predispose to peri-operative complications.

It has been reported in the general population that a high proportion of OSA remains undiagnosed (7). In our study, about two thirds of patients with OSA were already diagnosed at the time of initial bariatric consultation. In the aforementioned multicenter study of bariatric surgery patients conducted in Finland, one third of the included patients with OSA were diagnosed prior to initial bariatric consultation (12). In a study conducted in the Netherlands, only 13% of patients with OSA were diagnosed prior to their initial bariatric consultation (33). These differences may be related to accessibility of sleep studies.

In our study, OSA prevalence differed across surgical centers from 21% to 66%, and was significantly different in seven out of the ten surgical centers. In order to verify whether the difference measured was secondary to differences in the patient populations seen at each surgical center, patient characteristics were compared. Patients who underwent bariatric surgery at center A had a significantly lower mean BMI (small effect size, with a standardized mean difference of -0.21), and this may partially explain why the lowest prevalence of OSA was measured at this

center. Although patients who underwent surgery at center H had a significantly lower mean OMI summary score (indicating lower social inequality), this, in isolation, would not explain the lower OSA prevalence in comparison to the rest of the group. Overall, it is felt that patient characteristics were similar across surgical centers; and, therefore, the differences in OSA prevalence measured may be secondary to varying effectiveness of OSA screening practices. As aforementioned, there has been variability in the measures of OSA prevalence reported in the literature within the bariatric surgery population, which is likely secondary to differing OSA screening and testing practices employed.

A major strength of this study is that it included all patients who underwent publicly funded bariatric surgery within the province of Ontario from 2010 and 2016; and, as such, is population-based, thereby reducing selection bias related to its observational nature. Furthermore, data from the prospectively collected bariatric registry had few missing values. An important limitation is the following. Given that OSA is recorded in the OBR only at time of initial consultation, ICES health administrative databases were used to capture OSA diagnoses between initial bariatric consultation and time of surgery, including records from the bariatric surgery hospitalization itself. Although patients diagnosed with OSA and recommended positive airway pressure therapy and/or a monitored setting in the peri-operative period were likely reliably documented in the bariatric surgery admission record, those considered to have mild OSA, for whom therapy and/or monitoring was not recommended, may not have been accurately captured.

Furthermore, the international consensus guideline on peri-operative management of OSA in bariatric surgery patients was published in 2017, whereas our study includes data from

surgeries that took place between 2010 and 2016 (16). Future directions of this work are to validate these findings using more recent data.

Conclusion

In keeping with studies conducted in other jurisdictions, a significant proportion of patients presenting for bariatric surgery evaluation in Ontario have undiagnosed OSA; and, therefore, a protocol for evaluation of OSA in this patient population remains important. The overall prevalence of OSA measured within the Ontarian population who underwent bariatric surgery between 2010 and 2016 was found to be 47%. This percentage is in keeping with other literature in which patients undergo sleep study testing based on pre-test probability for OSA; however, is lower compared to literature in which all patients undergo sleep study testing regardless of OSA screening questionnaire results. OSA prevalence varied across individual surgical centers, despite similar patient characteristics, indicating possible varying effectiveness of OSA screening practices. Further studies are required to determine whether, with current screening practices, missed OSA diagnoses lead to adverse outcomes.

Tables and Figures

Table 1: Characteristics of Patients Having Undergone Publicly Funded Bariatric Surgery in Ontario between 2010 and 2016

Variable	Statistic
N	18,074
Age (years, mean, SD)	45 (10)
Sex	
Female (n, %)	14,947 (83%)
BMI (kg/m^2, median, IQR)	47.0 (42.5 to 52.5)
Missing (n, %)	56 (0.3%)
Current smoker (n, %)	680 (4%)
OMI summary score (mean, SD)	3 (0.8)
Missing (n, %)	148 (1%)
Number of major ADGs	
Mean (SD)	2 (1.4)
0 (n, %)	2,939 (16%)
1 (n, %)	5,046 (28%)
2 (n, %)	4,615 (26%)
3 (n, %)	3,009 (17%)
4 (n, %)	1,596 (9%)
5 (n, %)	612 (3%)
6 (n, %)	212 (1%)
7 (n, %)	39 (0.2%)
8 (n, %)	6 (0.03%)
Major comorbidities	
Asthma (n, %)	473 (3%)
COPD (n, %)	592 (3%)
T2DM (n, %)	2,085 (12%)
HTN (n, %)	2,133 (12%)
CAD (n, %)	1,696 (9%)
Anxiety or depression (n, %)	10,418 (58%)
Surgery type	
Duodenal switch (n, %)	34 (0.1%)
Gastric bypass (n, %)	15,403 (85%)
Sleeve gastrectomy (n, %)	2,312 (13%)
Missing (n, %)	325 (2%)

Table 2: Percentage of Patients with OSA by Surgical Center

Surgical Center	N OSA	% (95% CI)	p-value*
Overall	8,438	47% (46% to 47%)	NA
A	83	21% (17% to 25%)	**< 0.001**
B	296	50% (46% to 54%)	0.07
C	351	39% (35% to 42%)	**< 0.001**
D	386	41% (38% to 44%)	**< 0.001**
E	591	42% (40% to 45%)	**< 0.001**
F	1,261	53% (51% to 55%)	**< 0.001**
G	1,634	66% (64% to 68%)	**< 0.001**
H	932	33% (32% to 35%)	**< 0.001**
I	1,355	48% (46% to 50%)	0.06
J	1,549	46% (44% to 47%)	0.15

* Comparison was made between selected center vs. overall minus selected center, using Pearson chi-square test with Yates continuity correction.

Table 3: Comparison of Patient Characteristics by Surgical Center

	Overall	A	Stand. diff. *	B	Stand. diff. *	C	Stand. diff. *	D	Stand. diff. *	E	Stand. diff. *
Age (yrs, mean, SD)	45 (10)	46 (11)	0.02	46 (11)	0.04	46 (11)	0.06	46 (11)	0.06	45 (11)	0.00
Sex											
Female (n, %)	14,947 (83%)	346 (87%)	0.12	509 (87%)	0.11	732 (81%)	-0.06	757 (81%)	-0.05	1,181 (84%)	0.05
BMI (kg/m^2, mean, SD)	48.1 (7.9)	46.5 (6.7)	**-0.21**	47.6 (8.0)	-0.07	48.3 (8.3)	0.02	48.4 (8.5)	0.03	48.1 (7.8)	0.00
Missing (n, %)	56 (0.3%)	0 (0%)		0 (0%)		3 (0.3%)		4 (0.4%)		8 (0.6%)	
OMI summary score (mean, SD)	3.0 (0.8)	3.1 (0.7)	0.08	3.0 (0.7)	0.02	3.1 (0.7)	0.08	3.1 (0.7)	0.09	3.1 (0.7)	0.03
Missing (n, %)	148 (1%)	11 (3%)		2 (0.3%)		11 (1%)		9 (1%)		31 (2%)	
Number of major ADGs (mean, SD)	1.9 (1.4)	1.8 (1.4)	-0.08	2.0 (1.5)	0.10	2.0 (1.4)	0.05	2.0 (1.5)	0.05	1.9 (1.4)	0.01
Major comorbidities											
Asthma (n, %)	473 (3%)	9 (2%)	-0.02	11 (2%)	-0.05	27 (3%)	0.02	24 (3%)	0.00	35 (2%)	-0.01
COPD (n, %)	592 (3%)	9 (2%)	-0.06	19 (3%)	0.00	35 (4%)	0.03	33 (4%)	0.01	54 (4%)	0.04
T2DM (n, %)	2,085 (12%)	29 (7%)	-0.13	78 (13%)	0.06	105 (12%)	0.00	118 (13%)	0.04	135 (10%)	-0.06
HTN (n, %)	2,133 (12%)	26 (7%)	-0.17	72 (12%)	0.01	107 (12%)	0.00	117 (13%)	0.02	194 (14%)	0.07
CAD (n, %)	1,696 (9%)	16 (4%)	-0.19	66 (11%)	0.07	109 (12%)	0.09	96 (10%)	0.03	106 (8%)	-0.07
Anxiety or depression (n, %)	10,418 (58%)	190 (48%)	-0.20	327 (56%)	-0.04	584 (64%)	0.14	624 (67%)	0.19	813 (58%)	0.01

* Comparison was made between selected site vs. total minus selected site. Standardized difference represents the difference in means or proportions divided by standard error; imbalance defined as absolute value greater than 0.20 (small effect size).

Table 3 (cont'd.): Comparison of Patient Characteristics by Surgical Center

	Overall	F	Stand. diff. *	G	Stand. diff. *	H	Stand. diff. *	I	Stand. diff. *	J	Stand. diff. *
Age (yrs, mean, SD)	45 (10)	45 (11)	-0.08	45 (10)	0.00	45 (10)	0.00	44 (11)	-0.11	46 (10)	0.11
Sex											
Female (n, %)	14,947 (83%)	1,962 (82%)	-0.01	2,058 (84%)	0.03	2,295 (82%)	-0.02	2,354 (84%)	0.04	2,753 (81%)	-0.06
BMI (kg/m^2, mean, SD)	48.1 (7.9)	47.9 (8.0)	-0.04	48.7 (7.9)	0.09	48.0 (7.7)	0.02	48.0 (7.9)	-0.02	48.2 (7.9)	0.01
Missing (n, %)	56 (0.3%)	5 (0.2%)		6 (0.2%)		17 (0.6%)		9 (0.3%)		3 (0.1%)	
OMI summary score (mean, SD)	3.0 (0.8)	3.1 (0.8)	0.18	3.0 (0.8)	-0.13	2.9 (0.8)	**-0.22**	3.1 (0.8)	0.04	3.1 (0.7)	0.04
Missing (n, %)	148 (1%)	22 (1%)		9 (0.4%)		16 (1%)		13 (0.5%)		24 (0.7%)	
Number of major ADGs (mean, SD)	1.9 (1.4)	1.9 (1.4)	0.04	1.8 (1.4)	-0.09	1.9 (1.4)	-0.04	1.9 (1.4)	0.00	1.9 (1.4)	0.03
Major comorbidities											
Asthma (n, %)	473 (3%)	76 (3%)	0.04	45 (2%)	-0.06	73 (3%)	0.00	70 (2%)	-0.01	103 (3%)	0.03
COPD (n, %)	592 (3%)	66 (3%)	-0.03	70 (3%)	-0.03	86 (3%)	0.01	90 (3%)	0.00	130 (4%)	0.04
T2DM (n, %)	2,085 (12%)	275 (12%)	0.00	283 (11%)	0.00	329 (12%)	0.01	314 (11%)	-0.01	419 (12%)	0.03
HTN (n, %)	2,133 (12%)	283 (12%)	0.00	288 (12%)	0.00	234 (8%)	-0.12	376 (13%)	0.06	436 (13%)	0.04
CAD (n, %)	1,696 (9%)	193 (8%)	-0.05	159 (6%)	-0.12	244 (9%)	-0.03	319 (11%)	0.08	388 (11%)	0.09
Anxiety or depression (n, %)	10,418 (58%)	1,533 (64%)	0.16	1,307 (53%)	-0.11	1,550 (55%)	-0.05	1,672 (60%)	0.05	1,818 (53%)	-0.10

* Comparison was made between selected site vs. total minus selected site. Standardized difference represents the difference in means or proportions divided by standard error; imbalance defined as absolute value greater than 0.20 (small effect size).

ARTICLE 2: Health Care Utilization and Costs of Bariatric Surgery Patients with vs. without Comorbid Obstructive Sleep Apnea in Ontario, Canada

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Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by recurrent reduction in breathing during sleep caused by transient upper airway collapse, which may lead to excessive daytime sleepiness, impaired quality of life, as well as an increased risk of cardiovascular disease (1). Risk factors for developing OSA include: age, male sex, menopause, obesity, smoking, as well as genetic factors and race (due to their relationship with craniofacial features) (1). OSA is diagnosed using an in-laboratory polysomnogram (PSG) or a home sleep study (2). The prevalence of OSA in the general population of high-income countries has been estimated at 10% in women and 20% in men (1). Given that obesity is a significant risk factor for OSA, the prevalence of OSA in the bariatric surgery population is higher, with estimates ranging from 35% to 94% (16).

There is mixed evidence regarding the effect of OSA on peri-operative outcomes and, in turn, the effect of OSA on health care utilization and costs in the peri-operative period. In a study of patients who underwent bariatric surgery in a single surgical center in Poland, treated OSA patients (compared to untreated OSA patients or patients with a STOP-Bang score of ≥ 3 who had not undergone a sleep study) had a shorter post-operative hospital stay and a lower rate of post-operative pneumonia (25). In addition, there were two deaths in the night of the second postoperative day in the untreated/undiagnosed group (25). In contrast, in a study using data from a U.S.A. all-payers' database (including 1,050 hospitals and 91,028 patients undergoing

bariatric surgery), regression analysis identified that OSA was associated with decreased mortality, reduced length of stay and reduced total hospitalization costs (26). That being said, OSA was associated with an increased risk of emergent endotracheal intubation and need for invasive mechanical ventilation (26). This study did not report OSA treatment status (26). There is no Canadian data on the effect of OSA on post-bariatric surgery health care costs in the peri-operative period.

In the 1 year post-bariatric surgery, OSA may affect post-bariatric surgery health care utilization and costs. The following data suggests that OSA treatment leads to reduced health care utilization and costs over a longer term. A study conducted in Israel measured health care costs of patients with OSA in the two years prior to OSA diagnosis, in comparison to matched controls without OSA, including: number of days in hospital, number of ambulatory visits, number of emergency department (ED) visits, number of primary care visits, number of specialist visits and prescription drugs (27). This study showed that before OSA diagnosis, patients with OSA have higher health care costs compared to controls (2.2 fold higher in those aged $\leq$ 65 years of age), and this difference was driven by higher costs for physician visits and prescription drugs (27). Although OSA treatment is considered cost-effective, it is uncertain whether, patients with diagnosed OSA have increased or reduced health care utilization and costs compared to matched controls without OSA (28).

Thus, there is uncertainty regarding the effect of OSA on peri-operative health care costs, as well as the longer-term effect of diagnosed OSA on health care utilization and costs. The objectives of this study were to: (i) compare health care utilization and costs between bariatric surgery patients with vs. without OSA at 30 days post-surgery; and (ii) compare health care

utilization and costs between bariatric surgery patients with vs. without OSA at 1 year post-surgery. One year was chosen to capture the effect of diagnosed OSA rather than weight loss.

Methods

Study Design

This was a population-based cohort study using the Ontario Bariatric Registry (OBR) linked to the Institute for Clinical Evaluative Sciences (ICES) health administrative databases. Ethics approval was obtained from the Hamilton Integrated Research Ethics Board, Hamilton, Ontario, Canada.

Setting and Participants

Patients who underwent publicly funded bariatric surgery in Ontario between January 2010 and December 2016 (most recent data available) were included. Non-Ontario residents and patients with a history of previous bariatric surgery were excluded.

Data Sources

The OBR was established in 2010 and includes all patients referred for publicly funded bariatric surgery within the province of Ontario, Canada (19). ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement (21). Databases accessed included: the Assistive Devices Program Database (ADP); the Registered Persons Database (RPDB); the OHIP database; the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD); the National Ambulatory Care Reporting System (NACRS) and the Home Care Database (HCD). These datasets were linked using unique encoded identifiers and analyzed at ICES.

Variables

The following baseline characteristics were recorded in the OBR at the time of initial bariatric consultation: sex, body mass index (BMI) and current smoker; and the following characteristics were recorded at the time of surgery: age and surgery type. The Ontario Marginalization Index (OMI), described previously, was used as a measure of social inequality (29). As described previously, a count of major Johns Hopkins Aggregated Diagnosis Groups (ADGs) was conducted for each patient (30). As described previously, the following major comorbidities were recorded: asthma, chronic obstructive pulmonary disease (COPD), type II diabetes mellitus (T2DM), hypertension (HTN), coronary artery disease (CAD) and anxiety or depression. A diagnosis of OSA was identified if recorded in the OBR at time of initial bariatric consultation; or, if recorded in ICES health administrative databases (based on in-patient hospital records or ED / ambulatory care records) in the five years leading up to the surgery (including the bariatric surgery admission records).

Health care utilization and costs were measured prior to surgery (for propensity score matching), 30 days and 1 year post bariatric surgery. The perspective used was that of the single payer public health care system in the province of Ontario, Canada. ICES houses health administrative data from the Canadian Institute for Health Information (CIHI) and the Ministry of Health and Long Term Care (MOHLTC), which include health care utilization data for all Ontario residents, including: hospital admissions, ED visits, ambulatory care visits, same day surgery, physician billings (visits and procedures) and home care visits (21). Costs not captured include all hospital-administered drug costs, as well as out-patient prescription medication costs for those who do not qualify for public drug insurance (individuals under the age of 65 not receiving social assistance).

Costs were calculated based on the "Guidelines on Person-Level Costing Using Administrative Databases in Ontario" using ICES costing algorithms (20). Costs per encounter are derived either from service-specific cost data (e.g. physician billings, diagnostic tests or home care services) or micro-level costing (20). Micro-level costing is performed using health care utilization data (number of hospitalizations, length of stay, number of ED visits, etc.) factored with a case-mix system, which categorizes patients into groups based on major diagnoses and interventions received for each visit, to determine resource utilization intensity (20). Costs were measured in 2018 Canadian dollars.

Outcome Measures

The primary outcome was total health care costs per patient at 30 days and 1 year post-bariatric surgery.

Secondary outcomes were the following health care utilization measures (at 30 days and 1 year post-surgery): number of hospitalizations per patient, length of stay per patient, number of ED visits per patient, total number of physician visits per patient, number of generalist visits per patient, number of specialist visits per patient, and number of home care visits per patient. In addition, secondary outcomes included dividing health care costs per patient into those related to: hospitalizations, ED visits, physician visits (including generalist vs. specialist) and home care visits.

Statistical Methods

In order to control for confounding, propensity score matching was used (34). Nearest neighbour matching (1:1), with replacement, keeping all members of the OSA group and selected matching members of the non-OSA group, was performed. The propensity score was calculated using logistic regression with the following potential confounders included as covariates: age,

sex, BMI, current smoker, OMI summary score, count of major ADGs, major comorbidities (asthma, COPD, T2DM, HTN, CAD, anxiety or depression), total health care costs in three years prior to surgery, number of hospitalizations in one year prior to surgery, number of days in hospital in one year prior to surgery and number of ED visits in one year prior to surgery. The adequacy of propensity score matching was assessed using visual inspection of the propensity score distribution graph, as well as the standardized difference per covariate, with greater than 0.1 considered a significant difference.

After balanced groups were created by propensity score matching, mean and median health care utilization and costs at 30 days and 1 year post-bariatric surgery were calculated for the group with OSA vs. the matched group without OSA. The effect of OSA on health care utilization was analyzed in the following manner. Health care utilization consists of count data, and we expected to see a skewed data distribution. Therefore, in order to fit the assumptions of the model, depending on data distribution, a negative binomial (NB) regression model or, if an important proportion of zeroes was present due to non-consumption of health care services, a zero-inflated NB regression model was used. A NB regression model estimates an incidence rate ratio that is interpreted as the odds of the outcome (hospitalization, ED visit, etc.) within a time frame in patients with compared to without the exposure (OSA) (35). A zero-inflated NB regression model is considered a 2-part model, and generates two incidence rate ratios per exposure. The binomial model (with logit link) predicts the odds of a value of zero for the outcome, and the negative binominal model (with log link) predicts the odds of an additional count of the outcome (35). Zero-inflated models assume that excessive zeroes are due to a subpopulation who are not at risk for the outcome, i.e. low health care users (35). To take into account sampling with replacement, matching weights were included in the regression model.

Clustering caused by matching was considered by using cluster-robust variance to estimate the standard error, with matching stratum membership as the clustering variable.

The effect of OSA on health care costs was analyzed in the following manner. Health care costs consist of continuous data, and we expected to find a skewed data distribution. Therefore, in order to fit the assumptions of the model, a generalized linear mixed model (GLMM) with log link and gamma-distributed errors or, if an important proportion of zeroes was present due to non-consumption of health care services, a zero-inflated GLMM with the same parameters was used. A GLMM estimates a coefficient that is interpreted as the relative difference in cost in patients with compared to without the exposure (OSA) (26). A zero-inflated GLMM is considered a 2-part model, and generates two coefficients per exposure. The binomial model (with logit link) predicts the odds of a value of zero for the outcome, and the GLMM (with log link) estimates a coefficient, i.e., the relative difference in cost in patients with compared to without the exposure (36). Matching stratum membership was used as the clustering variable and matching weights were included in the regression model.

The percentage of patients that were dropped from the models due to a missing variable was 1%. Statistical analysis was performed using R software (version 3.6.2).

Results

Study Population

A total of 18,074 patients underwent publicly funded bariatric surgery in Ontario from January 2010 to December 2016. Table 4 summarizes characteristics of patients with vs. without comorbid OSA for the entire sample, prior to propensity score matching. Patients diagnosed with OSA were older; more likely to be male; had a higher BMI; a higher burden of

comorbidities; and increased health care utilization and associated costs prior to surgery. After propensity score matching, patient characteristics were balanced between patients with vs. without OSA (standardized difference < 0.1) (Table 5, Appendix Figures 4 & 5).

Total Health Care Costs per Patient at 30 Days Post-Bariatric Surgery

Based on regression analysis, total health care costs per patient, in the 30-day post-operative period, were 1% lower (95% CI 1% to 1%; $p < 0.001$; mean: $ 13,753.00 [SD $ 7,842.94] vs. mean: $ 14,007.00 [SD $ 8,918.13]) in patients with OSA compared to matched patients without OSA (Table 7).

Health Care Utilization and Costs per Patient at 30 Days Post-Bariatric Surgery

At the timeframe of 30 days post-bariatric surgery, patients with OSA had a 7% increased (95% CI 5% to 9%, $p < 0.001$) odds of requiring a physician visit (Table 6). There was no statistically significant difference found with regards to number of hospitalizations, length of stay, ED visits or home care services between patients with vs. without OSA.

Based on regression, costs related to hospitalizations in the 30-day post-operative period were 2% lower (95% CI 2% to 2%; $p < 0.001$) in patients with vs. without OSA (Table 7). Costs incurred by physician visits were 6% higher (95% CI 4% to 9%; $p < 0.001$) in patients with OSA. No statistically significant differences were observed for 30-day costs related to ED visits or home care services.

Total Health Care Costs per Patient at 1 Year Post-Bariatric Surgery

Based on regression analysis, total health care costs per patient, in the 1 year post-operative period, were 1% lower (95% CI 1% to 1%; $p < 0.001$; mean: $ 17,698.00 [SD $ 13,588.13] vs. mean: $ 18,150.00 [SD $ 19,841.23]) in patients with OSA compared to matched patients without OSA (Table 9).

Health Care Utilization and Costs per Patient at 1 Year Post-Bariatric Surgery

At 1 year post-bariatric surgery, patients with OSA had a 7% lower (95% CI 4% to 9%, $p < 0.05$) odds of a one day increase in hospitalization duration (Table 8). In addition, patients with OSA had a 6% increased (95% CI 3% to 8%, $p < 0.001$) odds of requiring a physician visit. There was no statistically significant difference found with regards to number of hospitalizations, ED visits or home care services between patients with vs. without OSA.

Based on regression, costs per patient related to hospitalization in the 1-year post-operative period were 3% lower (95% CI 3% to 3%; $p < 0.001$) in patients with vs. without OSA (Table 9). Costs incurred by physician visits were 6% higher (95% CI 3% to 9%; $p < 0.001$) in patients with OSA.

Discussion

Within the 30-day post-bariatric surgery period, patients with OSA had lower total health care costs per patient compared to matched patients without OSA, and this difference was driven by lower hospitalization-related costs. At 1 year post-bariatric surgery, patients with OSA continued to have lower total health care costs per patient compared to matched patients without OSA. This is the first study measuring health care costs post-bariatric surgery in the Canadian context.

The majority of patients had a single hospitalization during the 30-day post-operative period, which would have been the bariatric surgery hospitalization itself. There was no difference in the number of hospitalizations per patient or length of stay per patient between patients with vs. matched patients without OSA; and, therefore, the difference in hospitalization costs was secondary to increased resource utilization intensity (i.e. interventions such as

diagnostic tests, procedures, level of monitoring, etc.) between the two groups. Based on practice guidelines, patients in our study with a diagnosis of OSA would have been receiving OSA treatment in a monitored setting in the perioperative period, although some patients with very mild OSA may not have been recommended treatment (16). It has previously been reported in the literature that patients with OSA have lower total health care costs within 30 days post-bariatric surgery. In the Nationwide Inpatient Sample (NIS, U.S.A. all-payers' database including 1,050 hospitals and 91,028 patients undergoing bariatric surgery), regression analysis showed that OSA was associated with reduced mortality, reduced length of stay and reduced total hospitalization costs in the adjusted analysis (26). OSA treatment status was not reported in this study (26). The authors postulated that OSA may be a protective factor due to ischemic preconditioning, i.e., the ability of short periods of ischemia to make the myocardium more resistant to subsequent myocardial infarction (26, 37).

Although some authors postulate that OSA may be cardioprotective, the literature shows convincing evidence that undiagnosed, untreated or suboptimally treated OSA increases the risk of respiratory complications in the peri-operative setting. The aforementioned NIS study also showed an increased risk of emergent endotracheal intubation and need for invasive mechanical ventilation in patients with OSA (26). In a study of patients who underwent bariatric surgery in a single surgical center in Poland, treated OSA patients (compared to untreated OSA patients or patients with a STOP-Bang score of ≥ 3 who had not undergone a sleep study) had a shorter post-operative hospital stay and a lower rate of post-operative pneumonia (25). In addition, there were two deaths in the night of the second postoperative day in the untreated/undiagnosed group (25). From a Canadian perspective, in a retrospective matched cohort study of 480 surgical patients (not exclusively bariatric surgery) at a single center in Ontario, patients with OSA (49%

of whom used continuous positive airway pressure (CPAP) post-operatively) had a higher rate of respiratory complications, and an increased rate of admission to intensive care unit (38). Furthermore, in comparison to patients with OSA alone, patients with OSA and hypercapnia (from obesity hypoventilation syndrome or chronic lung disease) are at further increased risk of respiratory failure and increased hospital length of stay (39).

In a separate publication, our group reported on the difference in OSA prevalence measured within the bariatric surgery population depending on OSA screening and testing practices employed. More specifically, we summarized that the prevalence of OSA reported in the bariatric surgery literature differs between studies in which all patients undergo a sleep study vs. studies in which patients undergo testing based on screening protocols by approximately 30%. Therefore, although the OSA prevalence measured in our study was 47%, the true prevalence may be closer to 77%. Thus, we postulate that the increased 30-day postoperative hospitalization costs in the group labeled as "No OSA" may in fact be the effect of missed OSA diagnoses. The predictive ability of the STOP-Bang questionnaire has been evaluated in obese surgical patients, with a score of ≥ 3 having the following characteristics: to predict all OSA: sensitivity 91%, specificity 28%; to predict moderate/severe OSA: sensitivity 95%; specificity 20% (18). In patients being evaluated for bariatric surgery, the Berlin questionnaire was found to have a sensitivity of 86% and a specificity of 77% for the diagnosis of OSA (16). Given that the sensitivity of these OSA screening questionnaires likely increases with increasing OSA severity, it is possible that missed OSA diagnoses consist of patients with milder sleep disordered breathing, which may be less likely to predispose to peri-operative complications and increased health care services use in the 30-day post-operative period. Further study is required to better understand the reason for decreased health care service use in patients with OSA in the 30-day

post-bariatric surgery period compared to matched patients without OSA. In addition to the previously described hypothesis that treated OSA is cardioprotective, we postulate that increased health care use in the "No OSA" group may be secondary to undiagnosed OSA in this group.

At 30 days and 1 year post-bariatric surgery, patients with OSA had increased physician visits (to both general practitioners and specialists) compared to matched patients without OSA. Previous studies have looked at health care utilization and costs of patients with OSA compared to controls. A study conducted within a health organization in Israel showed patients with OSA have higher health care costs compared to matched controls (2.2 fold higher in those aged ≤ 65 years), and this difference was driven by higher costs for physician visits and prescription drugs (27). A study from Manitoba, Canada using health administrative databases measured increased physician billings in patients with OSA compared to matched controls (40). In keeping with previous studies, our study showed that patients diagnosed with OSA have increased physician visits compared to matched controls.

At 1 year post-bariatric surgery, patients with OSA continued to have lower total health care costs compared to matched patients without OSA. This difference was driven by reduced hospitalization-related costs in patients with OSA, which was contributed to by reduced average length of stay in this group; and, potentially, as was described within the 30-day post-operative period, reduced resource utilization intensity while in hospital. Previously published literature has shown a difference in health care utilization and costs depending on OSA treatment adherence, suggesting that OSA treatment reduces health care costs. In a study of 543 patients from a sleep practice in California U.S.A., in an adjusted analysis, patients with high adherence to OSA treatment had lower total health care costs (including physician visits, hospitalizations, ED visits, drugs and tests) at 3 years compared to those with low adherence (41). In a study of

1,098 patients from a sleep practice in North Carolina U.S.A., in an adjusted analysis, patients with high adherence to OSA treatment had lower total health care costs (including hospitalizations and ED visits only) at 18 months compared to patients with low adherence (42). However, previously published literature has not shown reduced health care costs over a 1 year period in patients with OSA compared to matched controls without OSA. As already mentioned, possible hypotheses to explain this include OSA being cardioprotective via ischemic preconditioning, or undiagnosed OSA in the "No OSA" group secondary to current OSA screening practices.

An additional hypothesis to explain the reduced health care costs related to hospitalizations in patients with OSA at 1 year post-bariatric surgery is the following. We showed that patients with OSA have increased physician visits in the 1 year post-bariatric surgery, and preventative care likely reduces the need for acute care. In a study of a U.S.A. representative sample using claims data, it was found that patients with better continuity of primary care had lower hospitalization rates and total health care costs (43). Furthermore, in the Canadian context, in a study of urban residents of the province of Manitoba, results suggested that ambulatory care visits reduce hospitalizations in patients with higher socioeconomic status (44).

A major strength of this study is that it included all patients who underwent publicly funded bariatric surgery within the province of Ontario from 2010 and 2016; and, as such, is population-based, thereby reducing selection bias related to its observational nature. Furthermore, data from the prospectively collected bariatric registry had few missing values; and ICES health administrative databases include the entirety of health care utilization within the province's single public payer health care system.

In addition to strengths, there are also limitations to using health administrative databases. Firstly, given that OSA is recorded in the OBR only at time of initial consultation, ICES health administrative databases were used to capture OSA diagnoses between initial bariatric consultation and time of surgery, including records from the bariatric surgery hospitalization itself. Although patients diagnosed with OSA and recommended positive airway pressure therapy and/or a monitored setting in the peri-operative period were likely reliably documented in the bariatric surgery admission record, those considered to have mild OSA, for whom therapy and/or monitoring were not recommended, may not have been accurately captured. Secondly, information on OSA severity, as well as OSA therapy was not available. Thirdly, although propensity score matching is a validated method to address confounding, in observational studies, there is a risk of confounding from unknown/unmeasured variables. Lastly, given the single-payer health care system, the health administrative data used to measure health care utilization and costs is complete; however, an important category of costs not captured are drug costs. Furthermore, based on the "Guidelines on Person-Level Costing Using Administrative Databases in Ontario", when service-specific cost data are not available, costs are estimated using algorithms, rather than directly measured.

Conclusion

Patients with OSA had lower 30-day post-bariatric surgery total health care costs per patient compared to matched patients without OSA, a difference which was likely driven by reduced resource utilization intensity during the bariatric surgery hospitalization. Previous authors have hypothesized that this difference is secondary to cardioprotection from ischemic preconditioning secondary to OSA. Given that we have previously described the likelihood of

undetected OSA in patients who underwent bariatric surgery, we postulate that the difference in health care costs measured in this study may be secondary to costs related to undiagnosed OSA in the "No OSA" group. At 1 year post-bariatric surgery, patients with OSA continued to have reduced total health care costs per patient compared to matched patients without OSA. This difference was secondary to reduced hospitalization related costs and reduced length of stay, despite increased physician visits. This suggests that increased preventative care through ambulatory visits may reduce acute care costs.

Tables and Figures

Table 4: Comparison of Patients having Undergone Bariatric Surgery, with vs. without OSA

	Patients with OSA	Patients without OSA	P-value*
N, %	8,438 (47%)	9,636 (53%)	NA
Age (years, mean, SD)	48 (10)	43 (11)	**< 0.001**
Sex Female (n, %)	6,296 (75%)	8,651 (90%)	**< 0.001**
BMI (kg/m^2, median, IQR)	48.1 (43.4 to 53.8)	47.2 (42.0 to 51.3)	**< 0.001**
Current smoker (n, %)	321 (4%)	359 (4%)	0.81
OMI summary score (mean, SD) Missing (n, %)	3.0 (0.8) 70 (1%)	3.0 (0.8) 78 (1%)	0.08
Number of major ADGs (mean, SD)	2.0 (1.5)	1.8 (1.4)	**< 0.001**
Major comorbidities Asthma (n, %) COPD (n, %) T2DM (n, %) HTN (n, %) CAD (n, %) Anxiety or depression (n, %)	 226 (3%) 343 (4%) 1,126 (13%) 1,055 (13%) 988 (12%) 4,868 (58%)	 247 (3%) 249 (3%) 959 (10%) 1,078 (11%) 708 (7%) 5,550 (58%)	 0.66 **< 0.001** **< 0.001** **0.006** **< 0.001** 0.91
Total health care cost per patient in 3 years prior to surgery (CAN $; mean, SD; median, IQR)	10,423.00 (14,061.00) 6,580.00 (4,113.00 to 11,707.00)	8,011.00 (10,353.00) 5,160.00 (3,044.00 to 9,508.00)	**< 0.001**
Number of hospitalizations per patient in 1 year prior to surgery (mean, SD; median, min to max)	0.09 (0.30) 0 (0 to 5)	0.07 (0.30) 0 (0 to 8)	**< 0.001**
Number of days in hospital per patient with ≥ 1 hospitalization in 1 year prior to surgery (days; mean, SD; median, IQR)	4.1 (6.0) 2.0 (1.0 to 5.0)	4.1 (10.9) 2.0 (1.0 to 4.0)	0.54
Number of ED visits per patient in 1 year prior to surgery (mean, SD; median, IQR)	1.0 (5.6) 0 (0 to 1)	0.8 (3.4) 0 (0 to 1)	0.95

* Student's t-test used for normally distributed continuous variables; Pearson chi-square test with Yates continuity correction used for categorical variables; and Wilcoxon rank-sum test used for non-normally distributed continuous variables.

Table 5: After Propensity Score Matching - Comparison of Patients having Undergone Bariatric Surgery, with vs. without OSA

	Patients with OSA	Patients without OSA	Std. difference *
N	8,356	8,356	NA
Age (years, mean, SD)	48 (10)	48 (10)	0.03
Sex Female (n, %)	 6,243 (75%)	 6,348 (76%)	 0.03
BMI (kg/m^2, median, IQR)	48.1 (43.4 to 53.8)	48.1 (43.3 to 53.9)	0.01
Current smoker (n, %)	313 (4%)	264 (3%)	0.03
OMI summary score (mean, SD)	3.0 (0.8)	3.1 (0.8)	0.01
Number of major ADGs (mean, SD)	2.0 (1.4)	2.1 (1.4)	0.00
Major comorbidities Asthma (n, %) COPD (n, %) T2DM (n, %) HTN (n, %) CAD (n, %) Anxiety or depression (n, %)	 222 (3%) 340 (4%) 1,119 (13%) 1,037 (12%) 977 (12%) 4,830 (58%)	 205 (2%) 320 (4%) 1,115 (13%) 1,086 (13%) 1,022 (12%) 4,904 (59%)	 0.01 0.01 0.00 0.02 0.02 0.02
Total health care cost per patient in 3 years prior to surgery (CAN $; mean, SD; median, IQR)	10,425.00 (14,093.00) 6,585.00 (4,115.00 to 11,689.00)	10,257.00 (15,293.00) 6,095.00 (3,552.00 to 11,361.00)	0.01
Number of hospitalizations per patient in 1 year prior to surgery (mean, SD; median, min to max)	0.09 (0.3) 0 (0 to 5)	0.09 (0.3) 0 (0 to 4)	0.00
Number of days in hospital per patient with ≥ 1 hospitalization in 1 year prior to surgery (days; mean, SD; median, IQR)	4.1 (6.0) 2.0 (1.0 to 5.0)	3.9 (4.7) 2.0 (1.0 to 5.0)	0.00
Number of ED visits per patient in 1 year prior to surgery (mean, SD; median, IQR)	1.0 (5.6) 0 (0 to 1)	0.9 (3.6) 0 (0 to 1)	0.02

* A standardized difference greater than 0.1 was considered a significant difference.

Table 6: Effect of OSA on Health Care Utilization per Patient at 30 Days Post-Bariatric Surgery

	No OSA	OSA	IRR (95% CI)	p-value
Number of hospitalizations per patient (mean, SD; median, IQR)	1.1 (0.3) 1 (1 to 1)	1.1 (0.3) 1 (1 to 1)	1.00 (0.98 to 1.04)	0.21
Length of stay (days; (mean, SD; median, IQR)	2.8 (6.1) 2 (2 to 2)	2.7 (3.3) 2 (2 to 3)	0.96 (0.94 to 0.98)	0.15
Number of ED visits per patient (mean, SD; median, IQR)	0.2 (0.6) 0 (0 to 0)	0.2 (0.6) 0 (0 to 0)	count: 1.05 (0.97 to 1.13) zero: 1.02 (0.86 to 1.21)	0.23 0.86
Number of physician visits per patient (mean, SD; median, IQR)				
Total	8.6 (9.2) 6 (5 to 9)	9.2 (9.1) 7 (5 to 10)	1.07 (1.05 to 1.09)	**< 0.001**
Generalist	1.7 (2.3) 1 (0 to 2)	1.9 (2.4) 1 (0 to 3)	1.12 (1.08 to 1.16)	**< 0.001**
Specialist	6.9 (8.5) 5 (4 to 7)	7.3 (8.4) 5 (4 to 8)	1.06 (1.03 to 1.08)	**0.003**
Home care service visits per patient (mean, SD; median, IQR)	0.5 (2.7) 0 (0 to 0)	0.5 (2.7) 0 (0 to 0)	count: 0.91 (0.87 to 1.13) zero: 0.73 (0.89 to 1.18)	0.91 0.73

Table 7: Effect of OSA on Health Care Costs per Patient at 30 Days Post-Bariatric Surgery

	No OSA	OSA	Coefficient (95% CI)	p-value
Hospitalization costs per patient (CAN$; mean, SD; median, IQR)	10,122.00 (8,265.17) 9,047.00 (8,376.00 to 9,717.00)	9,799.00 (6,866.44) 8,592.00 (7,673.00 to 9,717.00)	0.98 (0.98 to 0.98)	**<0.001**
ED visit costs per patient (CAN$; mean, SD; median, IQR)	94.75 (271.67) 0.00 (0.00 to 0.00)	99.47 (286.35) 0.00 (0.00 to 0.00)	gamma: 1.01 (0.96 to 1.07) zero: 0.97 (0.90 to 1.05)	0.62 0.51
Physician visit costs per patient (CAN$; mean, SD; median, IQR)				
Total	467.90 (1,007.42) 214.00 (137.00 to 380.00)	482.30 (973.51) 240.00 (155.00 to 410.00)	1.02 (1.02 to 1.02)	**<0.001**
Generalist	37.11 (101.68) 6.00 (0.00 to 43.00)	38.21 (73.71) 11.00 (0.00 to 45.00)	1.15 (1.08 to 1.22)	**<0.001**
Specialist	430.80 (972.53) 181.00 (126.00 to 340.00)	444.00 (956.19) 205.00 (130.00 to 364.00)	1.02 (1.02 to 1.02)	**< 0.001**
Home care costs per patient (CAN$; mean, SD; median, IQR)	65.36 (324.09) 0.00 (0.00 to 0.00)	61.45 (310.14) 0.00 (0.00 to 0.00)	gamma: 0.96 (0.88 to 1.04) zero: 1.02 (0.89 to 1.17)	0.33 0.75
Total costs per patient (CAN$; mean, SD; median, IQR)	14,007.00 (8,918.13) 12,527.00 (11,544.00 to 14,100.00)	13,753.00 (7,842.94) 12,238.00 (11,445.00 to 13,812.00)	0.99 (0.99 to 0.99)	**<0.001**

Table 8: Effect of OSA on Health Care Utilization per Patient at 1 Year Post-Bariatric Surgery

	No OSA	OSA	IRR (95% CI)	p-value
Number of hospitalizations per patient (mean, SD; median, IQR)	1.3 (0.8) 1 (1 to 1)	1.2 (0.7) 1 (1 to 1)	0.99 (0.97 to 1.02)	0.35
Length of stay (days; (mean, SD; median, IQR)	3.7 (10.5) 2 (2 to 3)	3.5 (6.2) 2 (2 to 3)	0.93 (0.91 to 0.96)	**0.05**
Number of ED visits per patient (mean, SD; median, IQR)	1.2 (2.3) 0 (0 to 2)	1.2 (2.1) 0 (0 to 2)	count: 0.96 (0.91 to 1.01) zero: 0.99 (0.92 to 1.06)	0.14 0.75
Number of physician visits per patient (mean, SD; median, IQR)				
Total	34.9 (40.0) 24 (14 to 42)	36.9 (36.4) 26 (16 to 36)	1.06 (1.03 to 1.08)	**<0.001**
Generalist	13.8 (17.8) 9 (5 to 16)	14.8 (20.5) 10 (5 to 17)	1.07 (1.04 to 1.10)	**<0.01**
Specialist	21.0 (31.8) 13 (7 to 24)	22.1 (26.2) 14 (8 to 27)	1.05 (1.02 to 1.08)	**0.02**
Home care service visits per patient (mean, SD; median, IQR)	3.5 (23.5) 0 (0 to 0)	3.3 (22.0) 0 (0 to 0)	count: 0.94 (0.79 to 1.12) zero: 0.99 (0.89 to 1.11)	0.56 0.85

Table 9: Effect of OSA on Health Care Costs per Patient at 1 Year Post-Bariatric Surgery

	No OSA	OSA	Coefficient (95% CI)	p-value
Hospitalization costs per patient (CAN$; mean, SD; median, IQR)	11,718.00 (16,948.77) 9,528.00 (8,476.00 to 10,800.00)	11,186.00 (10,841.88) 9,046.00 (8,142.00 to 10,647.00)	0.97 (0.97 to 0.97)	**<0.001**
ED visit costs per patient (CAN$; mean, SD; median, IQR)	425.00 (837.07) 0.00 (0.00 to 522.00)	401.10 (1,733.13) 0.00 (0.00 to 536.20)	gamma: 0.97 (0.94 to 1.01) zero: 1.02 (0.96 to 1.08)	0.12 0.62
Physician visit costs per patient (CAN$; mean, SD; median, IQR)				
Total	1,848.80 (2,648.67) 1,013.00 (501.80 to 2,121.80)	1,891.90 (2,403.37) 1,130.00 (582.80 to 2,270.20)	1.03 (1.02 to 1.04)	**<0.001**
Generalist	287.90 (526.52) 141.00 (41.00 to 344.00)	292.80 (697.28) 142.00 (47.00 to 342.00)	1.04 (1.00 to 1.09)	0.07
Specialist	1,560.80 (2,451.96) 794.50 (362.00 to 1,766.20)	1,599.00 (2,168.21) 895.00 (431.00 to 1,887.00)	1.03 (1.02 to 1.04)	**<0.001**
Home care costs per patient (CAN$; mean, SD; median, IQR)	318.60 (1,974.21) 0.00 (0.00 to 0.00)	290.40 (1,534.55) 0.00 (0.00 to 0.00)	gamma: 1.01 (0.92 to 1.11) zero: 1.00 (0.90 to 1.11)	0.78 0.96
Total costs per patient (CAN$; mean, SD; median, IQR)	18,150.00 (19,841.23) 14,468.00 (12,742.00 to 17,833.00)	17,698.00 (13,588.13) 14,303.00 (12,702.00 to 17,590.00)	0.99 (0.99 to 0.99)	**<0.001**

DISCUSSION AND CONCLUSIONS

Based on literature review, OSA prevalence in the bariatric surgery population has been reported at 35% to 94% (16). Our study measured an overall prevalence of 47% (95% CI 46% to 47%) within all patients who underwent publicly funded bariatric surgery in Ontario from 2010 to 2016. After anxiety or depression, OSA was the second most common major comorbidity in patients who underwent bariatric surgery.

The variability in the reported prevalence in the literature is likely secondary to the OSA screening and testing practices employed. Studies in which all patients being evaluated for bariatric surgery were tested for OSA reported a higher OSA prevalence compared to studies in which only patients who screen positive are tested. For example, in a U.S.A.- based registry in which all patients being evaluated for bariatric surgery underwent an in-laboratory polysomnogram (PSG), OSA prevalence was 78% (11). Similarly, in a single center U.S.A. study and a multicenter study conducted in Finland in which all patients being evaluated for bariatric surgery underwent a home sleep study, the prevalence of OSA was 71% and 77%, respectively (12, 32). In contrast, studies in which patients were screened for OSA based on routine practices resulted in a lower OSA prevalence. In a study of ten U.S.A. surgical centers (including 2,458 patients), in which there was significant variation in the frequency of OSA testing, the overall prevalence of OSA (based on sleep study results if a study was completed, or self-report) was 53% (13). The Nationwide Inpatient Sample included 91,028 patients who underwent bariatric surgery at 1,050 hospitals in the U.S.A. with different OSA screening practices, and recorded an OSA prevalence of 36% (26). The overall OSA prevalence measured in our study resembles that reported in other studies in which not all patients being evaluated for

bariatric surgery routinely undergo a sleep study. Therefore, OSA screening practices at surgical centers in our network led to similar rates of OSA detection as reported in the literature.

Given that OSA may be associated with an increased risk of peri-operative complications, guidelines recommend screening bariatric surgery patients for OSA using validated questionnaires (either the Berlin Questionnaire or the STOP-Bang Questionnaire) (7, 14, 15). Because of limited resources, a diagnostic sleep study is not the recommended standard for all patients being evaluated for bariatric surgery (15, 16). It is uncertain whether, with current OSA screening practices, missed OSA diagnoses lead to adverse outcomes, and, in turn, increased health care utilization and costs in the 30-day post-operative period. The predictive ability of the STOP-Bang questionnaire has been evaluated in obese surgical patients (18). The following test characteristics have been measured for a score of ≥ 3: to predict all OSA: sensitivity 91%, specificity 28%; to predict moderate/severe OSA: sensitivity 95%; specificity 20% (18). In patients being evaluated for bariatric surgery, the Berlin questionnaire was found to have a sensitivity of 86% and a specificity of 77% for the diagnosis of OSA (16). If the sensitivity of these OSA screening questionnaires increases with increasing OSA severity, missed OSA diagnoses would consist primarily of patients with milder sleep disordered breathing, which may be less likely to predispose to peri-operative complications. Furthermore, these two screening questionnaires are not always concordant. In a single center study conducted in the U.S.A. of 14,962 pre-operative patients, 24% were classified as high risk for OSA based on the Berlin Questionnaire and 42% were considered high risk for OSA based on the STOP-Bang Questionnaire (45). Although patients with already diagnosed OSA or who screened high risk based on the STOP-Bang had a higher rate of ICU admission, the proportion of planned vs. unplanned ICU admissions was unknown (45). There was no significant difference in 30-day

mortality in patients with diagnosed OSA or high risk for OSA compared to those without OSA, and it was postulated that this could be because of protocols for increased peri-operative monitoring of patients with OSA leading to prevention of complications (45).

It has been reported in the general population that a high proportion of OSA remains undiagnosed (7). In our study, two thirds of patients with OSA were already diagnosed at the time of initial bariatric consultation. In the aforementioned multicenter study of bariatric surgery patients conducted in Finland, prior to initial bariatric consultation, one third of the included patients with OSA were already diagnosed (12). In a study conducted in the Netherlands, only 13% of patients with OSA were diagnosed prior to their initial bariatric consultation (33). These differences may be related to accessibility of sleep studies. Analysis of Ontario health administrative data from 2006 to 2013 measured a median wait time between primary care referral to diagnostic sleep study of 449 days at hospital-based sleep clinics, and 361 days at community-based sleep clinics (46). In Ontario, OSA diagnosis is made almost exclusively by in-laboratory polysomnogram because home sleep studies are currently not funded by the public health care system. This wait time may partially explain why OSA is underdiagnosed, and also highlights the need for alternative pathways to diagnose OSA in patients awaiting surgery.

In our study, OSA prevalence differed across surgical centers from 21% to 66%, and was significantly different in seven out of the ten surgical centers. To determine whether the difference measured was secondary to differences in the patient populations seen at each surgical center, patient characteristics were compared. Patients who underwent bariatric surgery at center A had a significantly lower mean BMI (small effect size, with a standardized mean difference of -0.21), and this may partially explain why the lowest prevalence of OSA was measured at this center. Although patients who underwent surgery at center H had a significantly lower mean

OMI summary score (indicating lower social inequality), this, in isolation, would not explain the lower OSA prevalence in comparison to the rest of the group. Overall, patient characteristics were similar across surgical centers; and, therefore, it can be postulated that the differences in OSA prevalence measured may be secondary to varying effectiveness of OSA screening practices. As previously mentioned, literature review has shown variability in OSA prevalence reported within the bariatric surgery population, which is likely secondary to differing OSA screening and testing practices employed.

There is uncertainty whether current OSA screening and testing practices are sufficient to prevent peri-operative complications related to untreated OSA. Our study showed that, within the 30-day post-bariatric surgery period, patients with OSA had lower hospitalization-related costs compared to matched patients without OSA. Patients with OSA also had lower total heal care costs per patient at 30 days, and this was driven by the lower hospitalization-related costs. The majority of patients had a single hospitalization during the 30-day post-operative period, which would have been the bariatric surgery hospitalization itself. There was no difference in the number of hospitalizations per patient or length of stay per patient between patients with vs. matched patients without OSA. Therefore, the difference in hospitalization costs was secondary to increased resource utilization intensity (i.e. interventions such as diagnostic tests, procedures, level of monitoring, etc.) between the two groups. Based on practice guidelines, patients included in our study with a diagnosis of OSA would have been receiving OSA treatment in the perioperative setting, with the exception of some patients with very mild OSA may not have been recommended treatment (16). Similar findings have been reported previously in the literature. In the Nationwide Inpatient Sample (NIS) including 91,028 patients undergoing bariatric surgery (U.S.A. all-payers' database including 1,050 hospitals), a regression analysis showed that OSA

was associated with reduced mortality, reduced length of stay and reduced total hospitalization costs in the adjusted analysis (26). OSA treatment status was not reported in this study (26). The authors postulated that OSA may be a protective factor due to ischemic preconditioning, i.e., short periods of ischemia leading to the myocardium becoming more resistant to myocardial infarction (26, 37). In a single center study conducted in the U.S.A. of 14,962 pre-operative patients, patients with already diagnosed OSA had shorter surgery-related hospital lengths of stay compared to patients without OSA and patients who screened high risk based on questionnaires; however, data on the proportion of patients treated with positive airway pressure therapy was not available (45).

Although some authors postulate that OSA may be cardioprotective, there is convincing evidence that undiagnosed, untreated or suboptimally treated OSA increases the risk of respiratory complications in the peri-operative setting. The aforementioned NIS study also showed an increased risk of emergent endotracheal intubation and need for invasive mechanical ventilation in patients with OSA (26). In a study of patients who underwent bariatric surgery in a single surgical center in Poland, treated OSA patients (compared to untreated OSA patients or patients with a STOP-Bang score of ≥ 3 who had not undergone a sleep study) had a shorter post-operative hospital stay and a lower rate of post-operative pneumonia (25). In addition, there were two deaths in the night of the second postoperative day in the untreated/undiagnosed group (25). In a retrospective matched cohort study of 480 surgical patients at a single center in Ontario, patients with OSA (49% of whom used continuous positive airway pressure (CPAP) post-operatively) had a higher rate of respiratory complications, and an increased rate of admission to intensive care unit (38). In a study of 3,452 elective surgery patients conducted at three sites in Italy, before a standardized protocol for anesthesia management of high risk for

OSA patients was in place, patients classified as high risk for OSA based on a STOP-Bang score of ≥ 5 had a higher rate of peri-operative complications, difficult intubation and difficult mask ventilation compared to those classified as low risk (47). Moreover, in comparison to patients with OSA alone, patients with OSA and hypercapnia (from obesity hypoventilation syndrome or chronic lung disease) are at an even higher risk of respiratory failure and increased hospital length of stay (39).

As already mentioned, there is a difference in OSA prevalence measured within the bariatric surgery population depending on OSA screening and testing practices employed. More specifically, we summarized that the prevalence of OSA reported in the bariatric surgery literature differs between studies in which all patients undergo a sleep study vs. studies in which patients undergo testing based on screening protocols by approximately 30%. Therefore, although the OSA prevalence measured in our study was 47%, the true prevalence may be closer to 77%. Thus, we postulate that the increased 30-day postoperative hospitalization costs in the group labeled as "No OSA" may in fact be the effect of missed OSA diagnoses. In a study conducted in a tertiary hospital in India, 182 elective non-cardiac surgery patients without a previous diagnosis of OSA completed the STOP-Bang Questionnaire as well as a portable sleep study (48). 39% were diagnosed with OSA based on the sleep study, 12% of which were not identified using a STOP-Bang Questionnaire cut-off of ≥ 3 (48). All patients were monitored with continuous pulse oximetry for 24 hours post-surgery; however, they were not treated with positive airway pressure therapy (48). In an adjusted analysis, patients with untreated OSA had an increased risk of pneumonia or sepsis, respiratory failure and myocardial infarction or heart failure at seven days post-surgery, compared to those without OSA (48). Further study is

required to better understand the effect of missed OSA diagnoses on peri-operative outcomes and, in turn, health care utilization and costs in the 30 days post-bariatric surgery.

At 30 days and 1 year post-bariatric surgery, patients with OSA had increased physician visits (to both general practitioners and specialists) compared to matched patients without OSA. Previous studies have reported health care utilization and costs of patients with OSA compared to controls. A study conducted within a health organization in Israel showed patients with OSA have higher health care costs compared to matched controls without OSA (2.2 fold higher in those ≤ 65 years of age), and this difference was driven by higher costs related to physician visits and prescription drugs (27). A study using health administrative data from Manitoba, Canada measured increased physician billings in patients with OSA compared to matched controls (40). In keeping with previously reported findings, our study measured increased physician visits in patients with OSA compared to matched patients without OSA.

At 1 year post-bariatric surgery, patients with OSA continued to have lower total health care costs per patient compared to matched patients without OSA. This difference was secondary to reduced hospitalization-related costs in patients with OSA, which was contributed to by reduced average length of stay in this group; and, potentially, as was described within the 30-day post-operative period, reduced resource utilization intensity while in hospital. Previous studies have shown a difference in health care utilization and costs depending on OSA treatment adherence, suggesting that OSA treatment reduces health care costs. In a study of 543 patients from a sleep practice in California U.S.A., the adjusted analysis showed that patients with high OSA treatment adherence had lower total health care costs (including physician visits, hospitalizations, ED visits, drugs and tests) at three years compared to patients with low treatment adherence (41). In a study of 1,098 patients from a sleep practice in North Carolina

U.S.A., the adjusted analysis showed that patients with high OSA treatment adherence had lower total health care costs (including hospitalizations and ED visits only) at 18 months compared to those with low adherence (42). To our knowledge, this is the first study to show reduced health care costs over a one year period in patients with OSA compared to matched controls without OSA. As already mentioned, possible hypotheses to explain this include OSA being cardioprotective via ischemic preconditioning, or undiagnosed OSA in the "No OSA" group in the context of current OSA screening practices.

The following is an additional hypothesis to explain the reduced health care costs related to hospitalizations in patients with OSA at 1 year post-bariatric surgery. We showed that patients with OSA have increased physician visits in the 1 year post-bariatric surgery, and previously reported studies have shown that preventative care likely reduces the need for acute care. In a study using claims data of a representative U.S.A. sample, patients with better continuity of primary care were found to have lower hospitalization rates and total health care costs (43). In the Canadian context, in a study of urban residents of the province of Manitoba, results suggested that ambulatory care visits reduce admissions to hospital in patients with higher socioeconomic status (44).

A major strength of this study is that it included all patients who underwent publicly funded bariatric surgery within the province of Ontario from 2010 and 2016; and, as such, is population-based. This reduces selection bias related to the study's observational nature. Furthermore, data from the prospectively collected bariatric registry had few missing values; and, ICES health administrative databases capture the entirety of health care utilization in Ontario's single public payer health care system.

In addition to strengths, there are limitations to using health administrative datasets. Firstly, given that a diagnosis of OSA is recorded in the OBR only at time of initial consultation, ICES health administrative databases were used in order to include OSA diagnoses made between the initial bariatric consultation and the time of surgery (including records from the bariatric surgery hospitalization itself). Although patients diagnosed with OSA and recommended positive airway pressure therapy and/or a monitored setting in the peri-operative period were likely reliably recorded in the bariatric surgery admission record, those considered to have mild OSA, for whom therapy and/or monitoring were not recommended, may not have been accurately documented. Secondly, it is important to mention that information on OSA severity, as well as adherence to OSA therapy were not available. Thirdly, although propensity score matching is a validated method to address confounding in observational studies, there remains a risk of confounding from unknown or unmeasured variables. Fourthly, given the single-payer health care system, health administrative data used to measure health care utilization and costs are complete; however, an important cost category not captured in the ICES datasets are costs related to prescription drugs. In addition, based on the "Guidelines on Person-Level Costing Using Administrative Databases in Ontario", if service-specific cost data are not available, costs are estimated using algorithms, rather than directly measured. Furthermore, the international consensus guideline on peri-operative management of OSA in bariatric surgery patients was published in 2017, whereas our study includes data from surgeries that took place between 2010 and 2016 (16). Future directions of this work are to validate these findings using more recent data.

In summary, in keeping with studies conducted in other jurisdictions, a significant proportion of patients referred for bariatric surgery in Ontario have undiagnosed OSA.

Therefore, a protocol for evaluation of OSA in this patient population remains important. We measured an overall prevalence of OSA within the Ontarian population who underwent bariatric surgery between 2010 and 2016 to be 47%. This percentage is in keeping with previously reported studies in which patients undergo OSA testing based on pre-test probability for OSA; however, is lower compared to the prevalence reported in studies in which all patients undergo OSA testing regardless of OSA screening questionnaire results. Despite similar patient characteristics, OSA prevalence varied across individual surgical centers, which was suggestive of varying effectiveness of OSA screening practices.

Patients with OSA had lower 30-day post-bariatric surgery total health care costs per patient compared to matched patients without OSA. This difference was likely secondary to reduced resource utilization intensity during the bariatric surgery hospitalization. Previous authors have hypothesized that this difference is secondary to cardioprotection from ischemic preconditioning secondary to OSA. Given that we have previously described the likelihood of undetected OSA in patients who underwent bariatric surgery, we postulate that this difference may be secondary to increased resource utilization related to undiagnosed OSA in the "No OSA" group. Therefore, current OSA screening practices may be insufficient at preventing peri-operative complications related to OSA in the bariatric surgery population, and further study is required on this topic.

At 1 year post-bariatric surgery, patients with OSA continued to have reduced total health care costs per patient compared to matched patients without OSA. This difference was secondary to reduced hospitalization related costs and reduced length of stay, despite increased physician visits. Once more, this difference may be secondary to cardioprotection from ischemic preconditioning or undiagnosed OSA in the "No OSA" group. An additional hypothetical

explanation would be that increased preventative care through ambulatory visits reduces acute care costs. Further study is required to understand the effects of OSA on health care utilization and costs in the longer term.

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APPENDICES

Article 1 – Supplementary Results

Appendix Figure 1 illustrates the frequency of each major ADG within patients who underwent bariatric surgery in Ontario from 2010 to 2016, as well as a description of the ADGs considered major, with an accompanying example.

Article 2 – Supplementary Methods

The OMI summary score should be used only if all four dimensions are similarly correlated with the outcome of interest. This was verified used total health care costs at 1 year post surgery as the outcome measure (Appendix Figures 2 & 3).

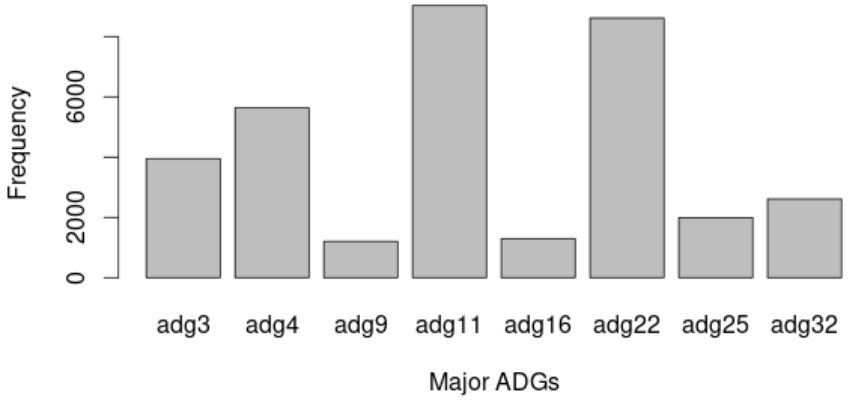
The following propensity score matching yielded the best balance between groups: nearest neighbour matching (1:1), with replacement, keeping all members of the OSA group and selected matching members of the non-OSA group (Appendix Figures 4 & 5). The following additional propensity score matching methods were trialed. Nearest neighbour matching (1:1) without replacement yielded less unmatched control units; however, covariates were unbalanced (Appendix Figures 6 & 7). Nearest neighbour matching (1:1) without replacement and with a caliper of 0.25 yielded relatively balanced groups; however, treated units went unmatched (Appendix Figures 8 & 9).

Article 2 – Supplementary Results

To inform regression model selection, distribution of outcome measures was visualized using histograms (Appendix Figure 10). In order to quantify model goodness of fit, residual

deviance and dispersion parameter were calculated (Appendix Tables 1 to 4). Although overall, model goodness of fit was good, some models were less ideal.

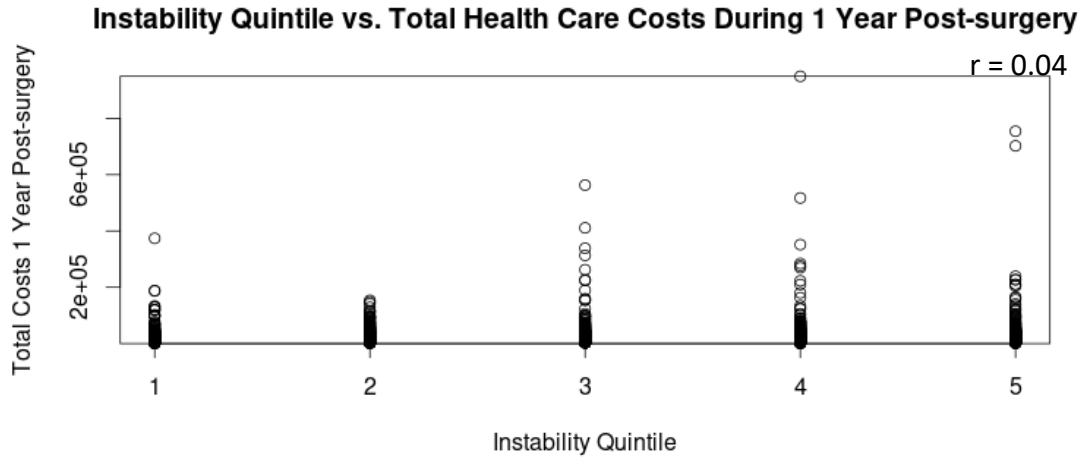
Appendix Figure 1: Bar Plot of Major ADGs in Patients who Underwent Bariatric Surgery in Ontario from 2010 to 2016



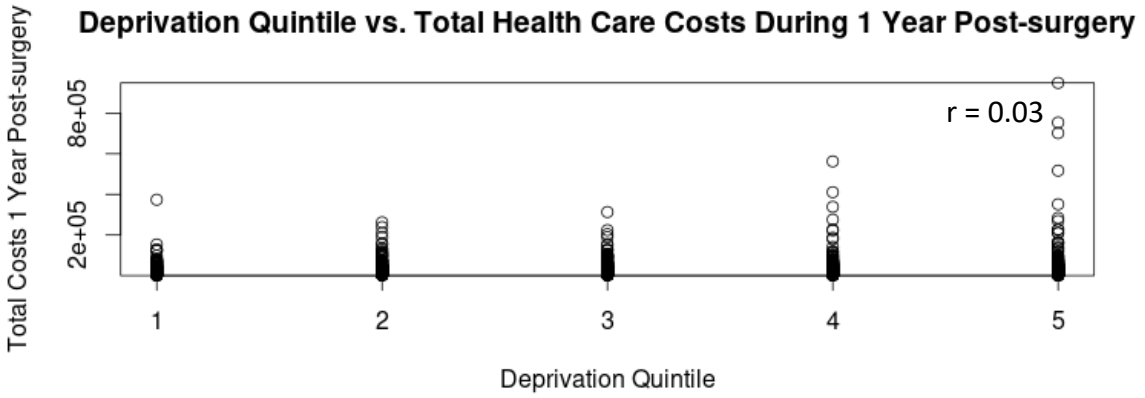
Adult Major ADGs	Examples
3: Time limited major	Bowel obstruction
4: Time limited major primary infection	Septic arthritis
9: Likely to recur progressive	Cerebral thrombosis
11: Chronic medical unstable	Sickle-cell anemia
16: Chronic specialty unstable-orthopedic	Spinal stenosis
22: Injuries/adverse effects major	Intracranial injury
25: Psychosocial recurrent or persistent, unstable	Schizophrenia
32: Malignancy	Breast cancer

Appendix Figure 2: Correlation between each Dimension of the Ontario Marginalization Index and Total Health Care Costs at 1 Year Post-surgery

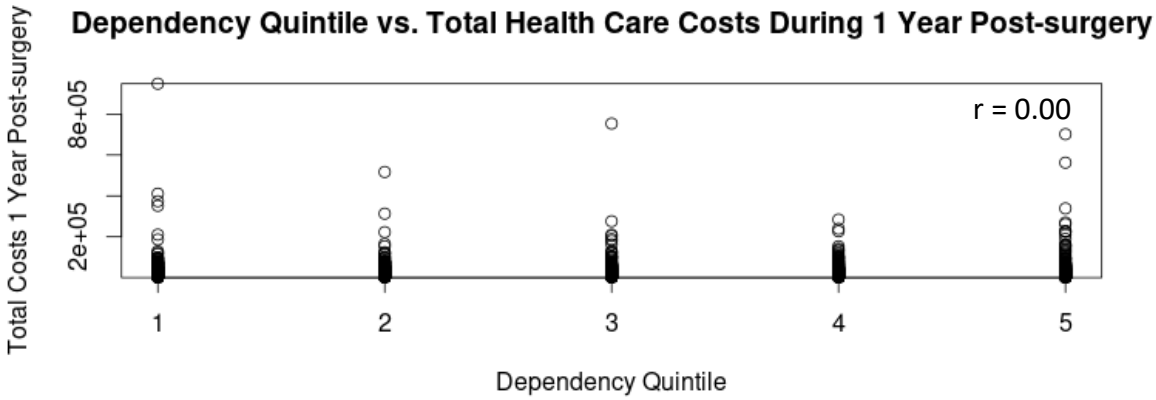
A)



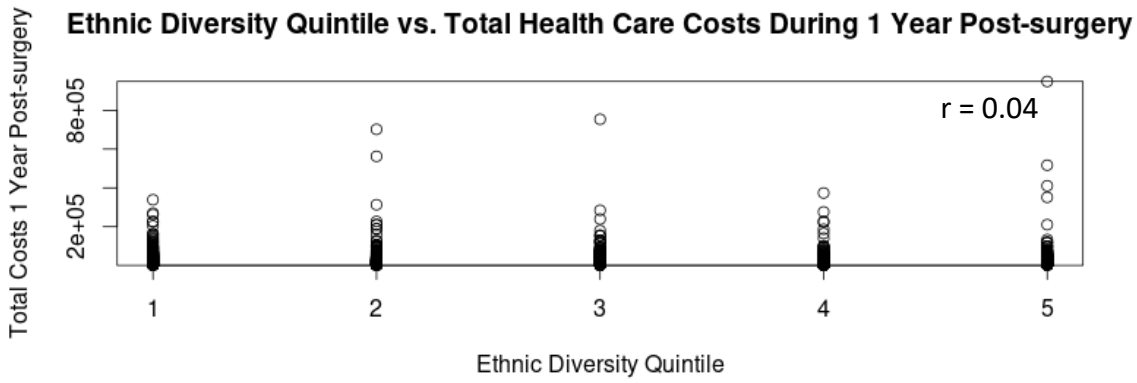
B)



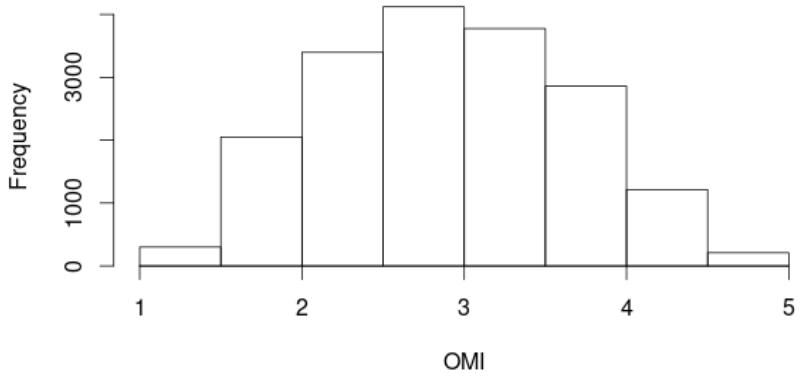
C)



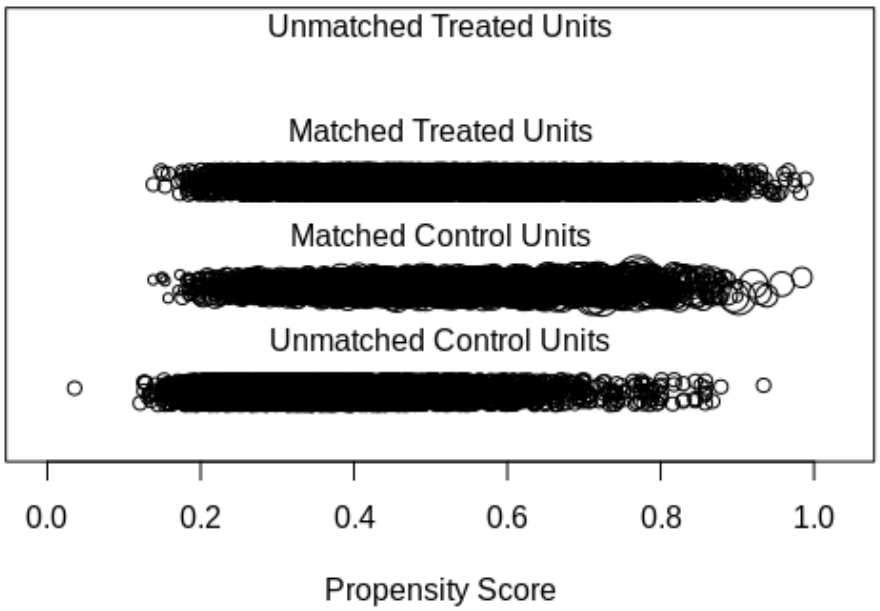
D)



Appendix Figure 3: Histogram of Ontario Marginalization Index Summary Score

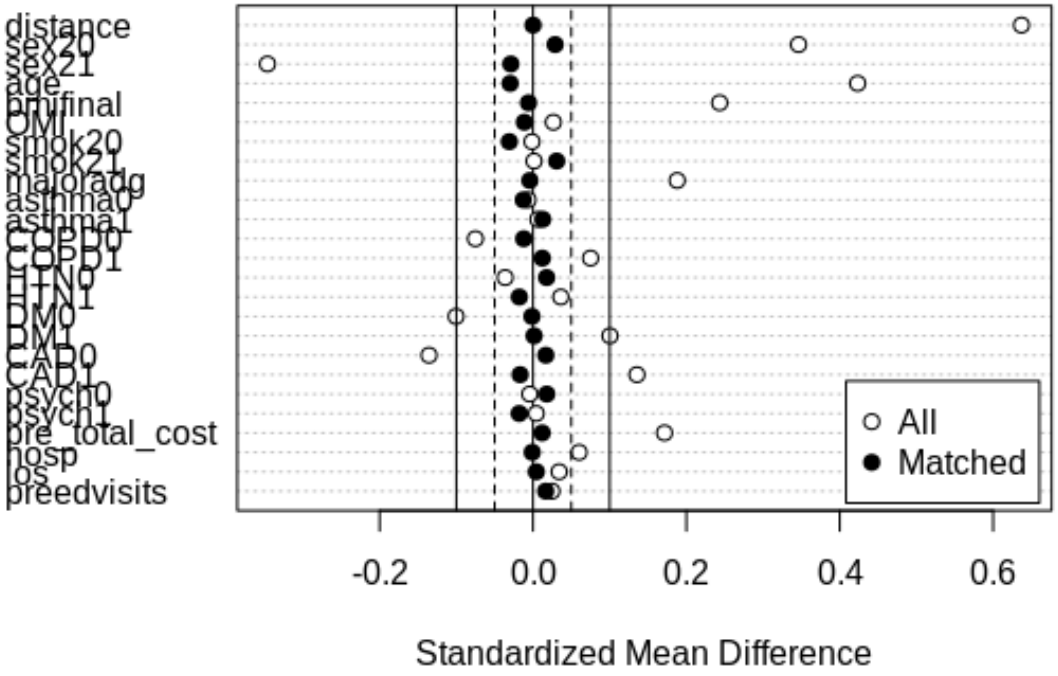


Appendix Figure 4: Distribution of Propensity Scores (Selected Method)

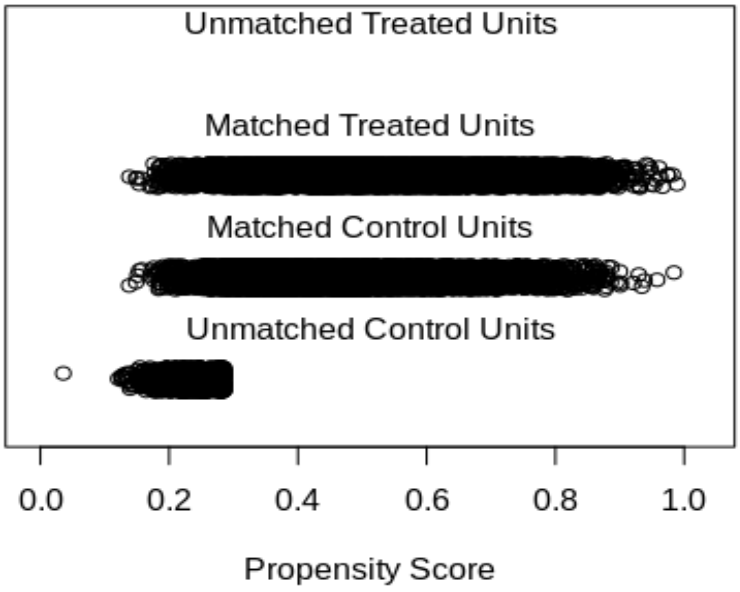


N matched treated (OSA) units = 8,356
N unmatched treated (OSA) units = 0
N matched control (no OSA) units = 4,355
N unmatched control (no OSA) units = 5,160

Appendix Figure 5: Standardized Mean Difference Using All vs. Matched Patients (Selected Method)

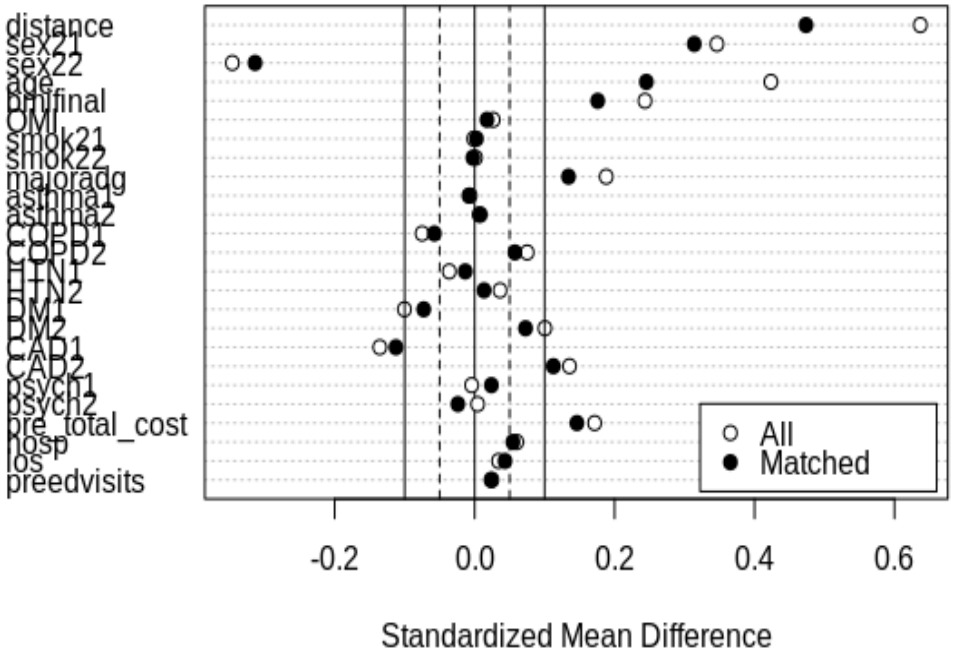


Appendix Figure 6: Distribution of Propensity Scores (Alternative Method 1)



N matched treated (OSA) units = 8,356
N unmatched treated (OSA) units = 0
N matched control (no OSA) units = 8,356
N unmatched control (no OSA) units = 1,159

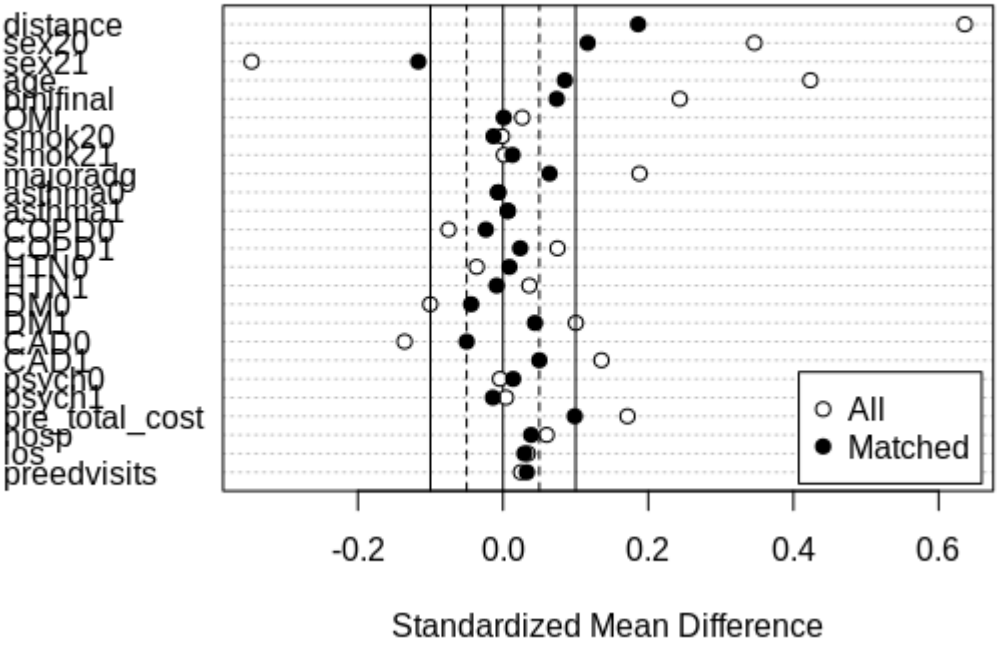
Appendix Figure 7: Standardized Mean Difference Using All vs. Matched Patients (Alternative Method 1)



Appendix Figure 8: Distribution of Propensity Scores (Alternative Method 2)

N matched treated (OSA) units = 7,279
N unmatched treated (OSA) units = 1,077
N matched control (no OSA) units = 7,279
N unmatched control (no OSA) units = 2,236

Appendix Figure 9: Standardized Mean Difference Using All vs. Matched Patients (Alternative Method 2)



Appendix Table 1: Regression Analysis of Effect of OSA on Average Health Care Utilization per Patient at 30 Days Post-Bariatric Surgery

	IRR (95% CI)	p-value	Goodness of Fit
Number of hospitalizations per patient	1.00 (0.98 to 1.04)	0.21	Residual deviance 881 (16710 DF) Dispersion parameter: 0.07
Length of stay	0.96 (0.94 to 0.98)	0.15	Residual deviance 12625 (16710 DF) Dispersion parameter: 4.97
ED visits per patient	count: 1.05 (0.97 to 1.13) zero: 1.02 (0.86 to 1.21)	0.23 0.86	Log-likelihood -10140 (5 DF) Dispersion parameter: 1.09
Physician visits per patient Total	1.07 (1.05 to 1.09)	**< 0.001**	Residual deviance 16831 (16710 DF) Dispersion parameter: 2.14
Generalist	1.12 (1.08 to 1.16)	**< 0.001**	Residual deviance 18054 (16710 DF) Dispersion parameter: 1.32
Specialist	1.06 (1.03 to 1.08)	**0.003**	Residual deviance 16830 (16710 DF) Dispersion parameter: 2.48
Home care services per patient	count: 0.91 (0.87 to 1.13) zero: 0.73 (0.89 to 1.18)	0.91 0.73	Log-likelihood -6082 (5 DF) Dispersion parameter: 0.99

Appendix Table 2: Regression Analysis of Effect of OSA on Average Health Care Costs per Patient at 30 Days Post-Bariatric Surgery

	Coefficient (95% CI)	p-value	Goodness of Fit
Hospitalization costs per patient	0.98 (0.98 to 0.98)	**<0.001**	Residual deviance 315690 (16708 DF) Dispersion parameter: 0.09
ED visit costs per patient	gamma: 1.01 (0.96 to 1.07) zero: 0.97 (0.90 to 1.05)	0.62 0.51	Residual deviance 59338 (16706 DF) Dispersion parameter: 0.35
Physician visit costs per patient Total	1.02 (1.02 to 1.02)	**<0.001**	Residual deviance 279346 (16708 DF) Dispersion parameter: 0.06
Generalist	1.15 (1.08 to 1.22)	**<0.001**	Residual deviance 120400(16708 DF) Dispersion parameter: 4.76
Specialist	1.02 (1.02 to 1.02)	**< 0.001**	Residual deviance 279279 (16708 DF) Dispersion parameter: 0.06
Home care services costs per patient	gamma: 0.96 (0.88 to 1.04) zero: 1.02 (0.89 to 1.17)	0.33 0.75	Residual deviance 20489 (16706 DF) Dispersion parameter: 0.38
Total costs per patient	0.99 (0.99 to 0.99)	**<0.001**	Residual deviance 320338(16708 DF) Dispersion parameter: 0.06

Appendix Table 3: Regression Analysis of Effect of OSA on Average Health Care Utilization per Patient at 1 Year Post-Bariatric Surgery

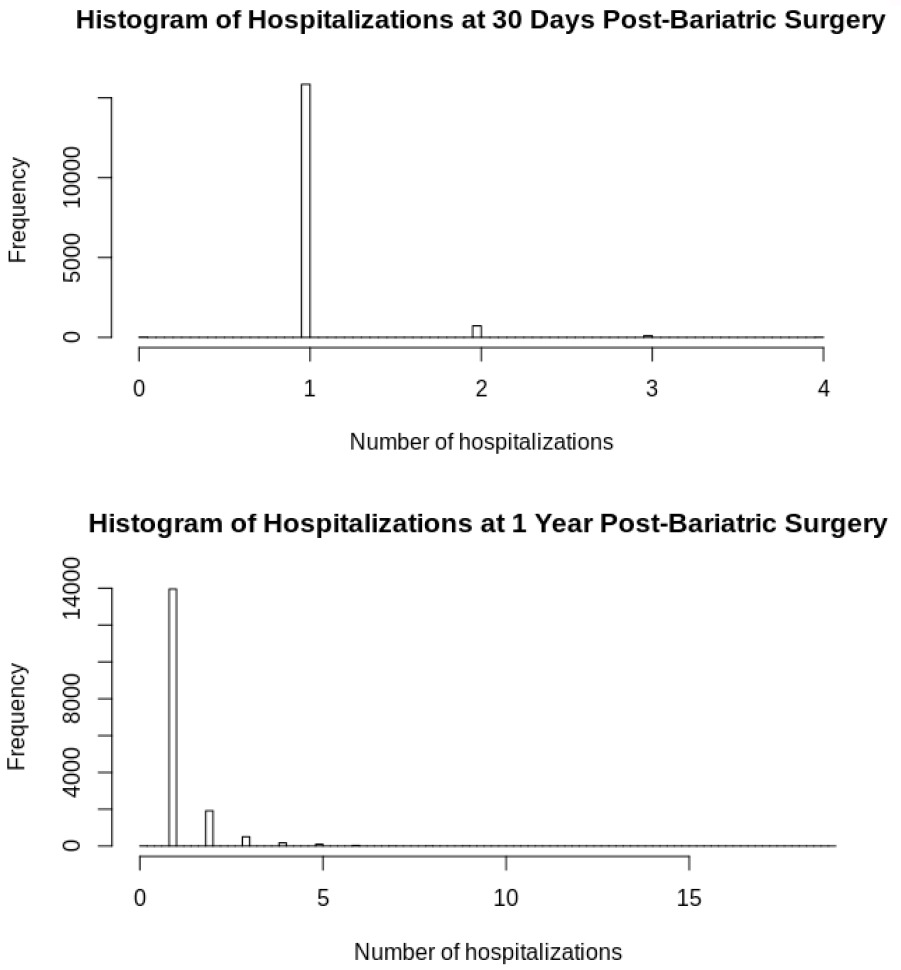
	IRR (95% CI)	p-value	Goodness of Fit
Number of hospitalizations per patient	0.99 (0.97 to 1.02)	0.35	Residual deviance 4513 (16710 DF) Dispersion parameter: 0.42
Length of stay	0.93 (0.91 to 0.96)	**0.05**	Residual deviance 14910 (16710 DF) Dispersion parameter: 6.72
ED visits per patient	count: 0.96 (0.91 to 1.01) zero: 0.99 (0.92 to 1.06)	0.14 0.75	Log-likelihood -25070 (5 DF) Dispersion parameter: 2.09
Physician visits per patient Total	1.06 (1.03 to 1.08)	**<0.001**	Residual deviance 18023 (16710 DF) Dispersion parameter: 1.86
Generalist	1.07 (1.04 to 1.10)	**<0.01**	Residual deviance 18567 (16710 DF) Dispersion parameter: 2.04
Specialist	1.05 (1.02 to 1.08)	**0.02**	Residual deviance 18265 (16710 DF) Dispersion parameter: 2.27
Home care services per patient	count: 0.94 (0.79 to 1.12) zero: 0.99 (0.89 to 1.11)	0.56 0.85	Log-likelihood -12040 (5 DF) Dispersion parameter: 1.29

Appendix Table 4: Regression Analysis of Effect of OSA on Average Health Care Costs per Patient at 1 Year Post-Bariatric Surgery

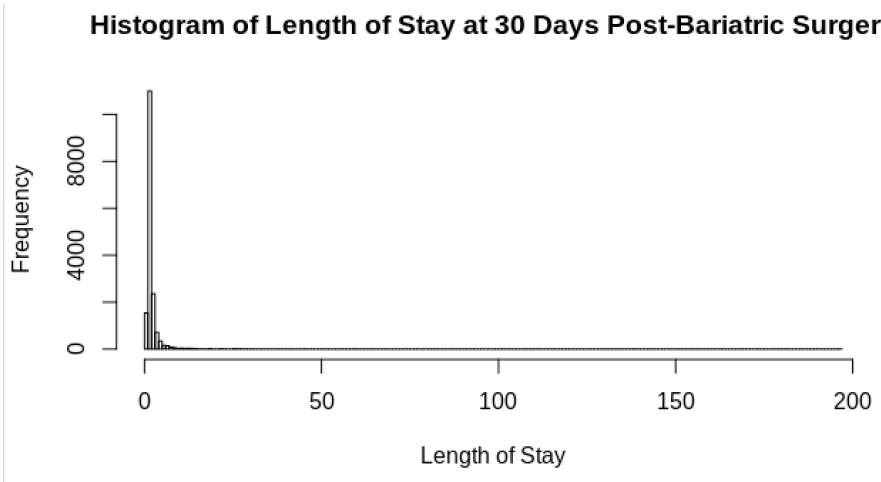
	Coefficient (95% CI)	p-value	Goodness of Fit
Hospitalization costs per patient	0.97 (0.97 to 0.97)	**<0.001**	Residual deviance 323559 (16708 DF) Dispersion parameter: 0.13
ED visit costs per patient	gamma: 0.97 (0.94 to 1.01) zero: 1.02 (0.96 to 1.08)	0.12 0.62	Residual deviance 150080 (16706 DF) Dispersion parameter: 0.55
Physician visit costs per patient Total	1.03 (1.02 to 1.04)	**<0.001**	Residual deviance 296821(16708 DF) Dispersion parameter: 0.11
Generalist	1.04 (1.00 to 1.09)	0.07	Residual deviance 219015 (16708 DF) Dispersion parameter: 3.88
Specialist	1.03 (1.02 to 1.04)	**<0.001**	Residual deviance 278166 (16708 DF) Dispersion parameter: 0.10
Home care services costs per patient	gamma: 1.01 (0.92 to 1.11) zero: 1.00 (0.90 to 1.11)	0.78 0.96	Residual deviance 38443 (16706 DF) Dispersion parameter: 0.40
Total costs per patient	0.99 (0.99 to 0.99)	**<0.001**	Residual deviance 337698(16708 DF) Dispersion parameter: 0.12

Appendix Figure 10: Verifying Assumptions of Regression Models

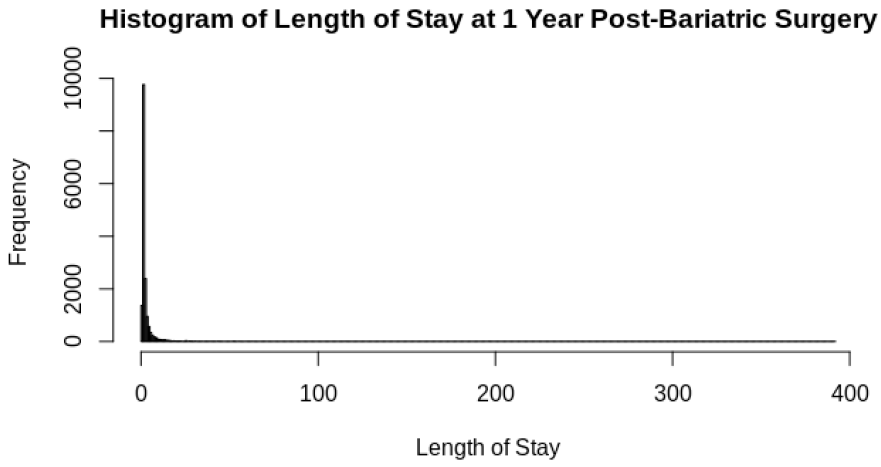
A. Hospitalizations



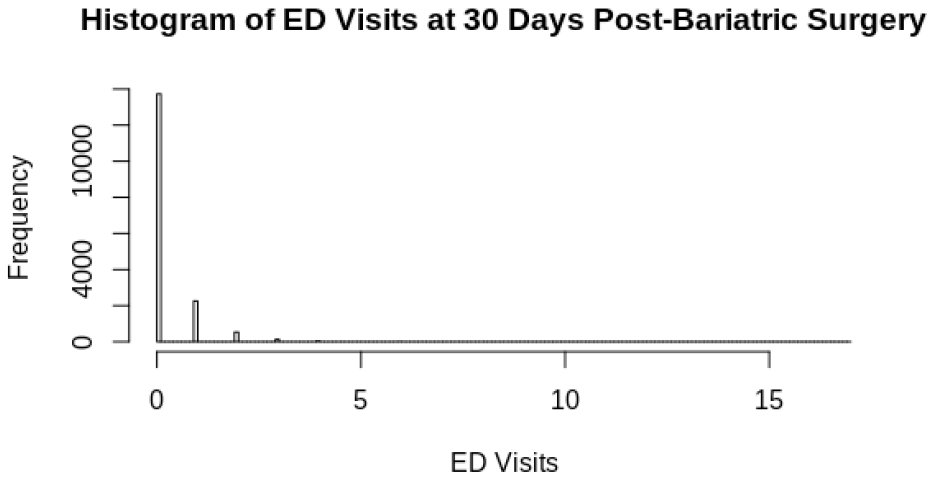
B. Length of Stay

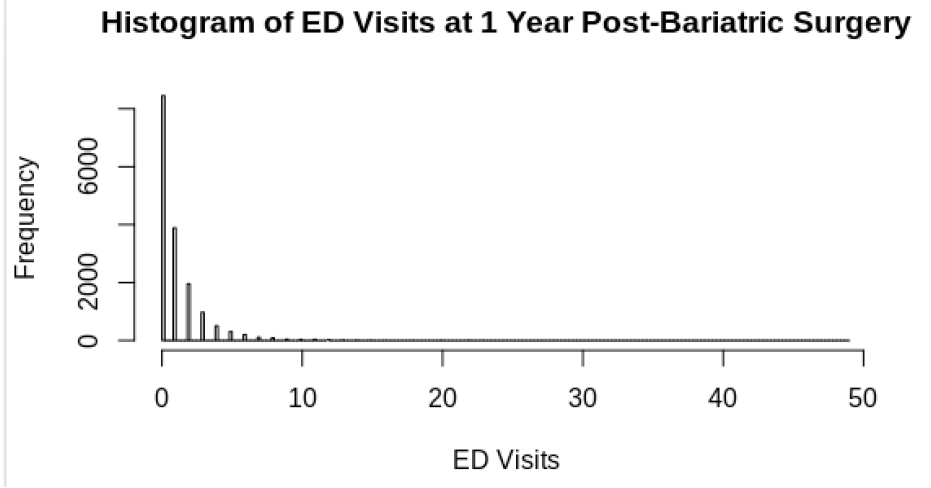


Appendix Figure 10 (cont'd.): Verifying Assumptions of Regression Models



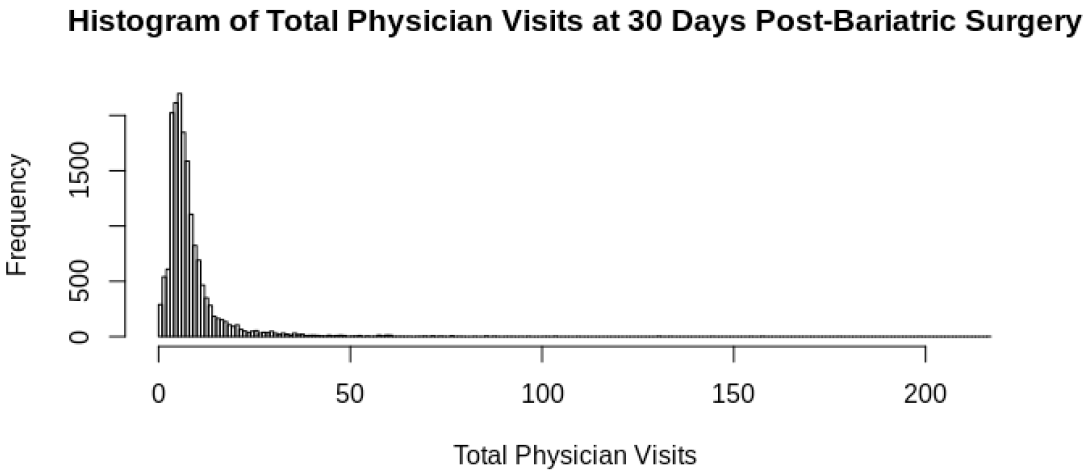
C. ED Visits

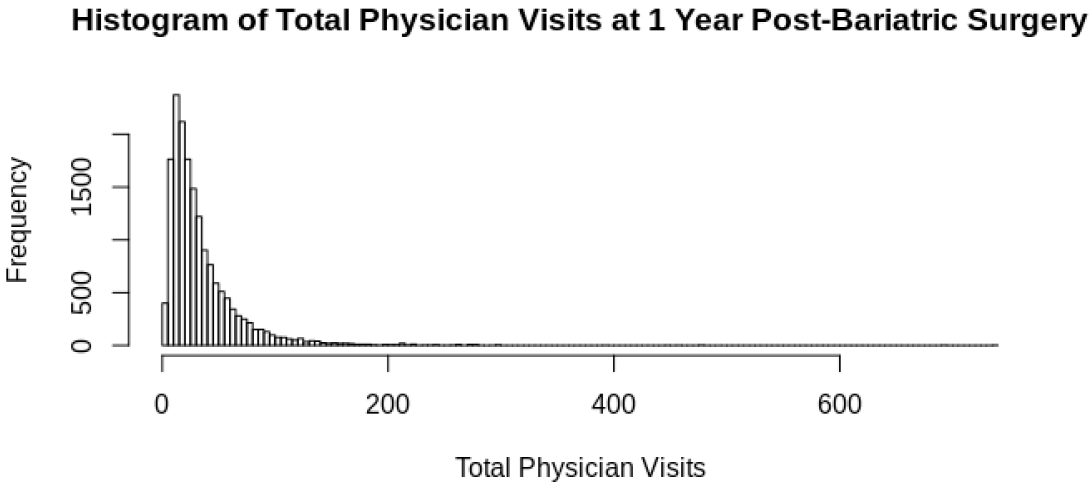




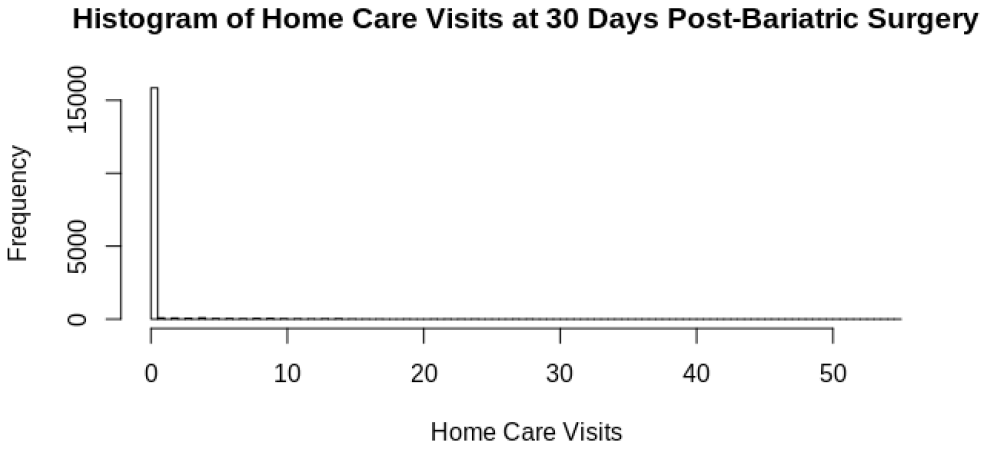
Appendix Figure 10 (cont.d): Verifying Assumptions of Regression Models

D. Physician Visits

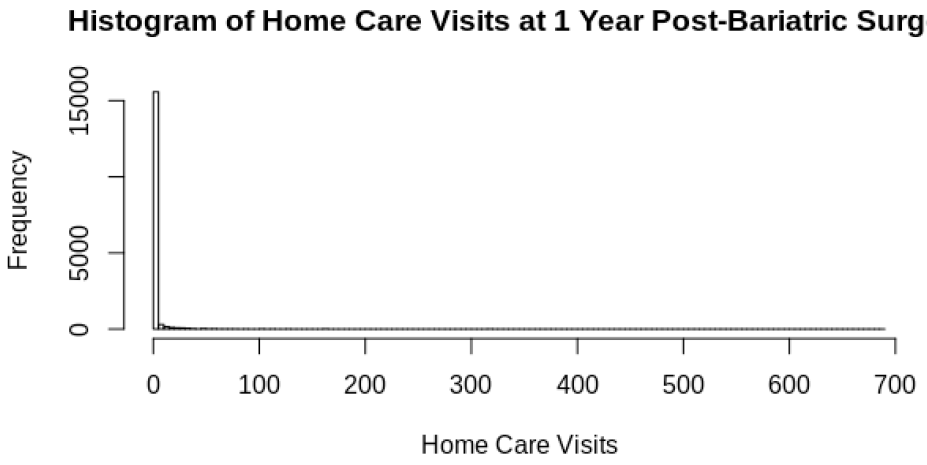




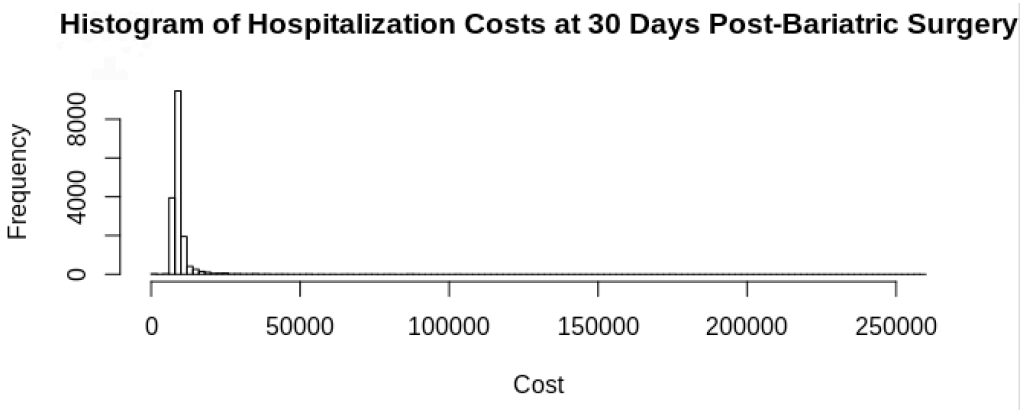
E. Home Care Visits

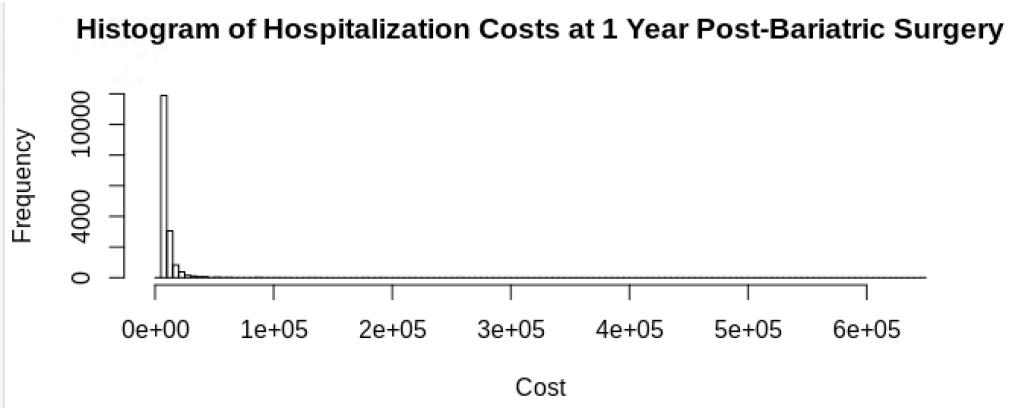


Appendix Figure 10 (cont'd.): Verifying Assumptions of Regression Models



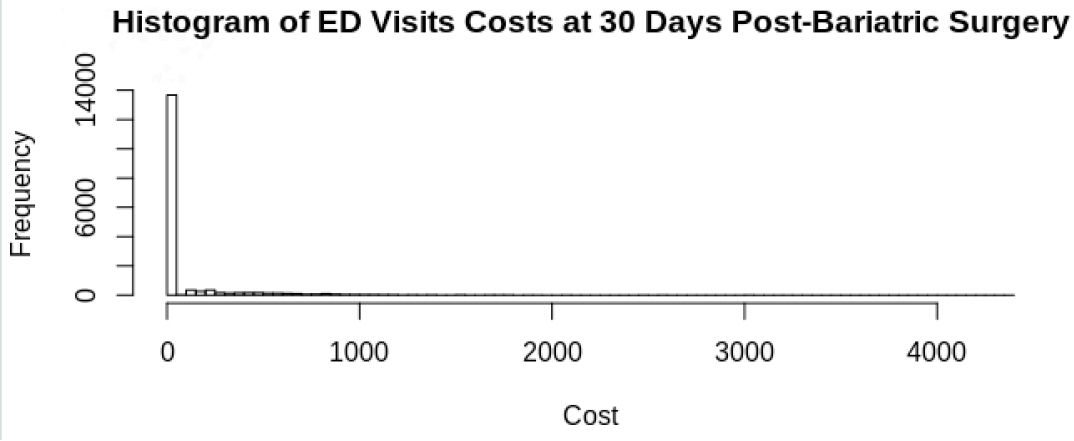
F. Hospitalization Costs

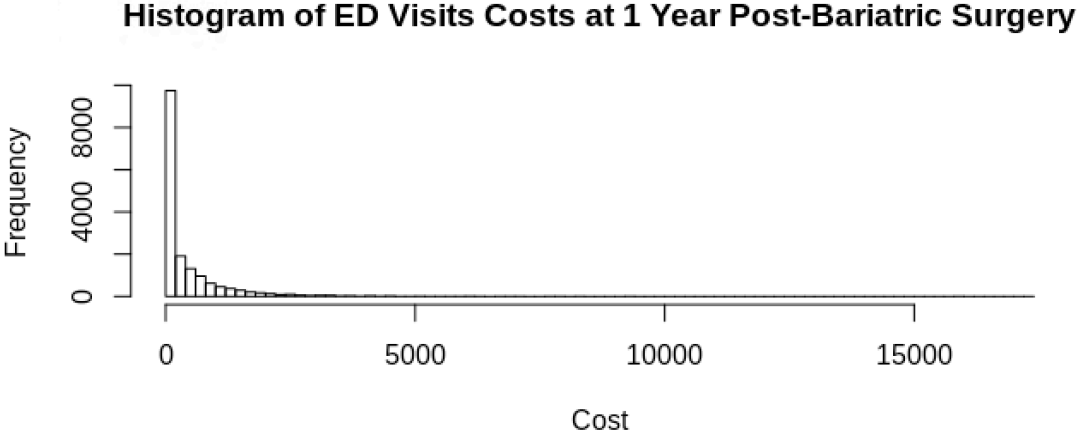




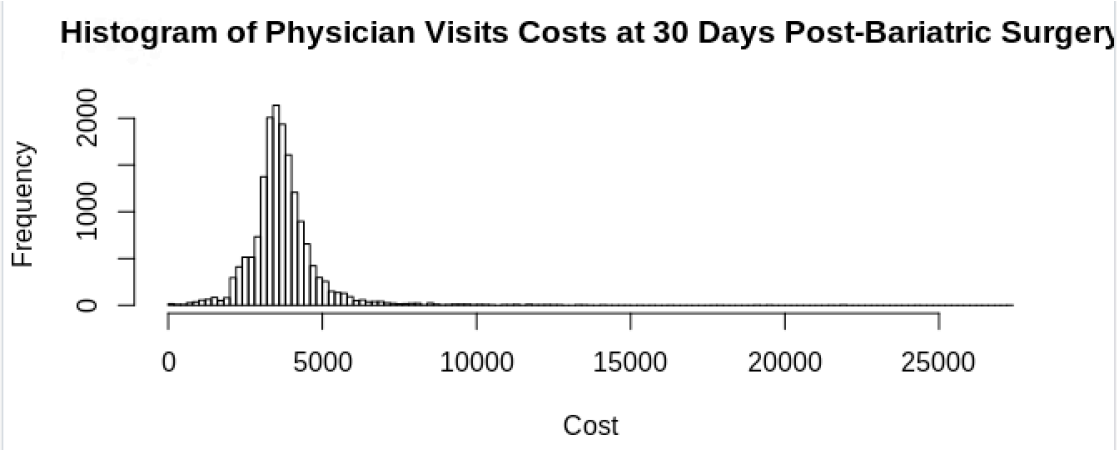
Appendix Figure 10 (cont'd.): Verifying Assumptions of Regression Models

G. ED Visits Costs

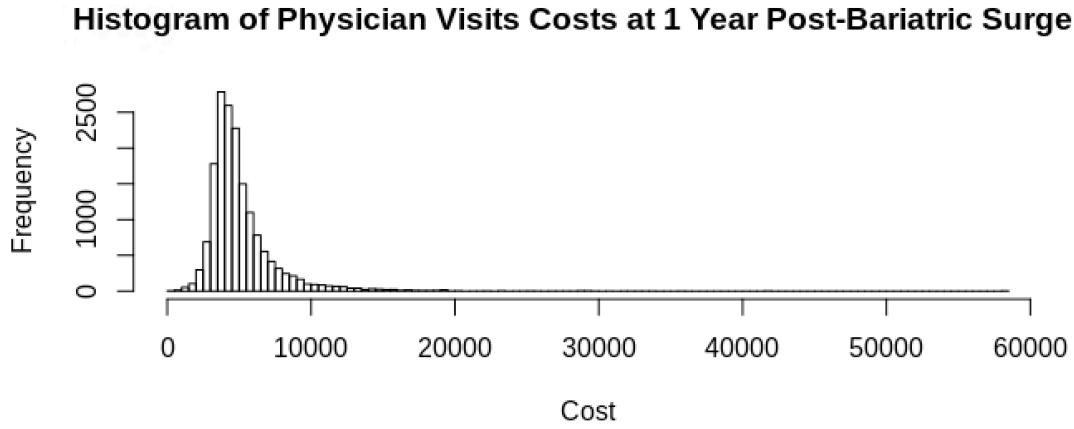




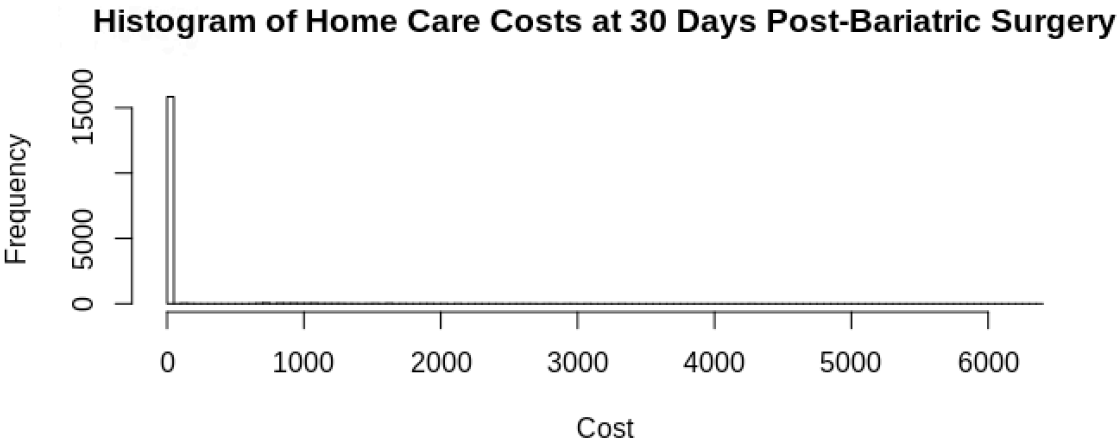
H. Physician Visits Costs

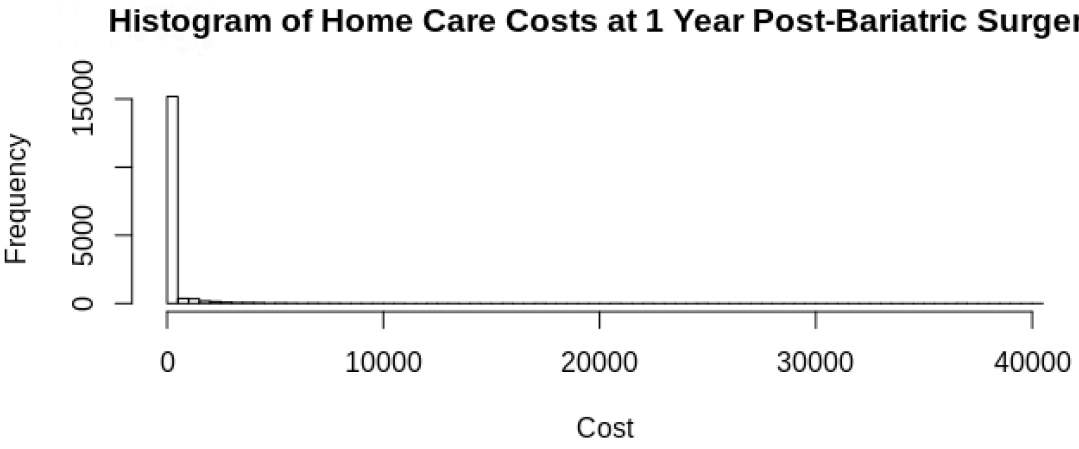


Appendix Figure 10 (cont'd.): Verifying Assumptions of Regression Models



I. Home Care Costs





Appendix Figure 10 (cont'd.): Verifying Assumptions of Regression Models

J. Total Costs