## SURGEON AND HOSPITAL VOLUME OUTCOMES IN BARIATRIC SURGERY:

### A POPULATION-LEVEL STUDY FROM QUEBEC, CANADA

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## ABSTRACT

**Background**: Bariatric surgery is the cornerstone in the treatment of severe obesity. There is evidence that outcomes after bariatric surgery are correlated with the cumulative frequency of patients treated by surgeons and their surgical units, hereinafter defined as surgical volume. However, this relationship is not clearly established for each procedure, including the most commonly performed sleeve gastrectomy (SG).

**Objective**: To evaluate the influence of surgeon and hospital volume on postoperative morbidity after bariatric surgery in the province of Quebec, Canada; and to identify surgeon volume (SV) and hospital volume (HV) thresholds to improve clinical outcomes.

Methods: All patients who underwent bariatric surgery in Quebec, Canada, between 2007 and 2012 were identified from provincial administrative datasets. After stratification by procedure, multilevel cross-classified logistic regression was used to quantify the effects of annual SV and HV on a composite 90-day postoperative outcome. The volumes were calculated using the number of procedures performed the year prior to the surgery. The 90-day composite morbidity outcome was defined as occurrence of shock, initiation of dialysis, macrovascular events, venous thromboembolic events, reintubation, prolonged intensive care admission, prolonged hospital admission (≥7 days), intra-abdominal sepsis, reoperation, readmission or death. Receiver operating characteristic (ROC) curve analysis was used to identify a value for SV or HV which most likely predicted the occurrence or absence of complications in a univariate logistic regression. These values were then used as volume categories in multilevel regressions. Effect measures are reported as odds ratio (OR) with 95% confidence intervals (CI) and as absolute risk reduction (ARR). The respective area under the curve (AUC) statistic is reported for each ROC.

Results: 8,271 patients underwent bariatric surgery in Quebec during the study period. These procedures were performed by 42 surgeons in 18 institutions. The frequencies of patients by procedure were as follows: 821 underwent Roux-en-Y gastric bypass (RYGB) 1,802 SG, and 1,810 had biliopancreatic diversion with duodenal switch (BPD-DS). For the RYGB group, 175 (21%) experienced morbidity outcomes. An increase in 10 cases per year for the SV was associated with for a reduction in odds of complications of 0.82 (95%CI: 0.71-0.94) in the multilevel model. An increase in 10 cases per year for the HV was associated with an OR of 0.86 (95%CI: 0.77-0.96) when adjusting for both patient and surgeon levels. Annual thresholds of 21 RYGBs for SV and 25 cases for HV were identified (AUC=0.60 and 0.61, respectively). Using the SV threshold, 368 RYGBs were performed by high-volume surgeons and being in the high SV category translated into an ARR of 12.5% for morbidity. Using the calculated HV threshold, 448 RYGBs were done in a high-volume center and ARR for composite outcomes was 9.5%. For the SG group, 227 (13%) experienced the outcome. An increase in 10 cases per year for the SV was associated with OR for complications of 0.99 (95%CI: 0.93-1.06) when adjusting for patient and hospital levels. Moreover, an increase in 10 cases per year for the HV was associated with OR of 0.99 (95%CI: 0.97-1.01) when adjusting for patient and surgeon levels. Annual thresholds of 17 SGs for SV and 139 for HV were identified (AUC=0.52, 0.60 respectively) but were not associated with significant improvement in outcome in the fully adjusted model. In the BPD-DS group, 460 (25%) developed the 90-day composite morbidity. SV and HV thresholds were not calculated for BPD-DS since 97% of these procedures were performed in a single centre.

**Conclusion**: SV and HV are significant independent predictors of 90-day composite morbidity after RYGB procedures. However, such associations could not be demonstrated for SG. This

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study further supports establishment of minimum SV and HV requirements for more complex bariatric procedures such as RYGB. However, the role of volume targets in SG remains unclear.

## Résumé

**Mise en contexte**: La chirurgie bariatrique est une composante importante dans le traitement de l'obésité. Les risques de complications à la suite d'une chirurgie bariatrique sont surtout liés au volume opératoire du chirurgien et de l'hôpital. Cependant, cette relation n'est pas clairement démontrée pour la gastrectomie pariétale (GP), considérée moins complexe.

**Objectifs** : Cette étude évalue l'effet du volume opératoire du chirurgien et de l'hôpital sur les complications post-opératoires au Québec. S'il y a lieu, un seuil de volume minimal significatif et unique à chaque procédure sera identifié.

Méthodologie : Les données administratives du système de santé québécois ont été utilisées afin d'identifier les individus ayant subi une chirurgie bariatrique entre 2007 et 2012. Après stratification par procédure, une régression logistique multi-niveaux est utilisée pour évaluer l'effet du volume opératoire sur un résultat composite de complications à 90 jours. Le volume chirurgical du chirurgien et de l'hôpital est calculé pour chaque procédure, grâce à la somme de l'année précédente. Le résultat composite est défini par l'occurrence d'un choc, de dialyse, d'un événement macrovasculaire ou thromboembolique, de ré-intubation, d'admission aux soins intensifs prolongée, d'admission prolongée à l'hôpital (≥7 jours), de septicémie intra-abdominale, de ré-opération, de réadmission ou de mortalité. La fonction d'efficacité du récepteur (ROC) est utilisée afin d'identifier les volumes chirurgicaux permettant la meilleure prédiction d'une complication, en utilisant une régression logistique univariée. Ces valeurs sont ensuite utilisées dans une régression similaire incluant les autres prédicteurs. Les résultats sont exprimés en *odds ratio* (OR), avec un intervalle de confiance à 95% (IC) et réduction du risque absolu (RRA).

Résultats : Le taux de mortalité post-opératoir est de 0.22% sur les 8271 individus inclus dans la cohorte, avec un taux de complication composite de 14%. Pour la dérivation gastrique (DG), en contrôlant, au niveau du patient et de l'hôpital, l'augmentation annuelle de 10 cas du volume opératoire du chirurgien est associée à une réduction des complications, avec un odds ratio (OR) de 0.82 (IC 95% 0.71-0.94). Le volume hospitalier est également associé à une réduction des complications (OR 0.86, 0.77-0.96), avec ajustement au niveau des caractéristiques du patient et du chirurgien. Pour la GP, l'augmentation du volume du chirurgien ou de l'institution est associée à des OR de 0.99 (0.93-1.06) et 0.99 (0.97-1.01), respectivement. En utilisant le CRO et une spline, un seuil de 21 cas par année par chirurgien est identifié. Un seuil de 25 cas par an est aussi identifié en tant que volume minimal institutionnel. Pour la GP, des seuils de 17 cas annuels pour le chirurgien, et 139 pour l'hôpital ont été identifiés, mais ne résultent pas en une amélioration significative dans le modèle ajusté. Concernant la dérivation biliopancréatique, 460 patients (25%) ont développé une complication à 90 jours. L'effet du volume chirurgical n'a donc pas pu être évalué, étant donné que 97% des cas ont été effectués à une seule institution, au courant de la période d'étude. Conclusion : Les volumes annuels du chirurgien et de l'hôpital sont associés avec le risque de complications post-opératoires de la DG. Cependant, une telle association n'a pu être démontrée avec la GP, malgré une tendance vers de meilleurs résultats lors d'un plus haut volume. Cette étude supporte l'utilisation de seuils minimaux de volumes opératoire pour la DG, mais le rôle d'une telle mesure pour la GP demeure incertain.

## PREFACE

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# LIST OF ABBREVIATIONS/ACRONYMS

AGB	Adjustable Gastric Band
AIC	Akaike Information Criterion
ARR	Absolute Risk Reduction
ASMBS	American Society for Metabolic and Bariatric Surgery
AUC	Area Under the Curve
BAR-HARM	BARiatric HospitAl stay, Readmission, and Mortality rates score
BMI	Body Mass Index
BPD-DS	Biliopancreatic Diversion with Sleeve Gastrectomy
CCI	Charlson Comorbidity Index
CI	Confidence Interval
CPD	Chronic Pulmonary Disease
DAG	Directed Acyclic Graph
DALY	Disability Adjusted Life Years
DM	Diabetes Mellitus
DVT	Deep Venous Thrombosis
GBD	Global Burden of Disease
GLP-1	Glucagon-Like Peptide
HTN	Hypertension
HV	Hospital Volume
ICD	International Classification of Disease
ICU	Intensive Care Unit

INSPQ	Institut national de la santé publique du Québec
LOS	Length Of Stay
MBSAQIP	Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program
MI	Myocardial Infarction
MSSS	Ministère de la Santé et Service Sociaux
OR	Odds Ratio
OSA	Obstructive Sleep Apnea
RAMQ	Régie de l'Asssurance Maladie du Québec
ROC	Receiver Operator Characteristic
RR	Risk Ratio
RYGB	Roux-en-Y Gastric Bypass
SD	Standard Deviation
SES	Socio-Economic Status
SG	Sleeve Gastrectomy
SSLR	Stratum-Specific Likelihood Ratios
SV	Surgeon Volume
VPC	Variance Partition Coefficients
VTE	Venous Thromboembolism
WHO	World Health Organisation

## **1** INTRODUCTION

Obesity is a growing problem in Quebec, Canada and worldwide (1, 2). In 2015, it was estimated that 40% of Americans had a body mass index (BMI) above  $30 \text{kg/m}^2$  (3). In Canada, one in four are considered obese (4). Obesity is associated with several comorbidities responsible for decrease in life expectancy and quality of life (1, 5). In addition to the impact on individual's health, obesity is associated with a severe economic burden both in direct healthcare cost and loss of productivity (6, 7).

The efficacy of bariatric surgery, also known as metabolic surgery or weight loss surgery, in addressing the problem of severe obesity has been repeatedly demonstrated. Multiple studies, including randomized control trials, have revealed the positive impact of various bariatric procedures in improving comorbidities and survival when compared to medical management alone (8-10). As a result and despite different initiatives to address obesity as a major public health issue, health care systems continue to struggle to improve access to bariatric surgery. In Quebec, the approach has been to increase the number of centres with bariatric programs including in rural and underserved areas of the province. On the contrary, in Ontario, the neighbouring province, bariatric surgery is centralized to a handful of institutions which are accredited centres of excellence.

Furthermore, multiple factors influence outcomes after surgery. On a system level, studies in various fields of surgery have shown a relationship between an institution's or a surgeon's cumulative frequency of surgical procedures (hereinafter designated as surgical volume) and postoperative outcomes (11). In the field of bariatric surgery, these studies often combine several types of procedures from old cohorts including outdated procedures or use methodology that is

prone to bias (12, 13). Therefore, the generalizability of such studies to inform modern minimally invasive surgical practice is limited.

I therefore sought to evaluate the influence of surgeon and hospital volume on postoperative morbidity after bariatric surgery using the population-level data from the province of Quebec, which is at the forefront of bariatric surgery in Canada and provides the most access to various types of bariatric surgery in the country. In addition, I aimed to identify surgeon volume (SV) and hospital volume (HV) thresholds that could be used as targets to improve surgical outcomes.

## **2 REVIEW OF LITERATURE**

#### 2.1 **OBESITY**

#### 2.1.1 Burden of disease

According to the World Health Organization (WHO), overweight and obesity are defined by abnormal or excessive fat accumulation that may impair health (14). Common indices to measure obesity include waist circumference, waist-to-height ratio and BMI. Of those, BMI is most commonly used in clinics and research programs for ease of use and because of its proven strong association with relevant health outcomes (5, 15-17). It is defined as the weight (kilogram) divided by the squared height (meter). The WHO classifies the ranges of BMI as normal (18.5-24.99), overweight ( $\geq$ 25), obese class I (30-34.99), obese class II (35-39.99) and obese class III ( $\geq$ 40) with increasing associated risk for comorbidities (18). There is evidence of association between high BMI and at least 20 disease processes such as cardiovascular disease, diabetes mellitus, esophageal cancer, colorectal cancer, liver cancer, pancreatic cancer, and others (1, 17). The result is a significantly diminished life expectancy of 3.3 to 13.7 years for an elevated BMI

(1, 19, 20). In the 2017 study from the Global Burden of Disease Obesity Collaborative (GBD), high BMI contributed to 4 million deaths per year representing 7.1% of all-cause mortality (1). This increase in mortality was mainly driven by cardiovascular disease totalling 41% of obesity-related death followed by diabetes. The same study also highlighted the disability adjusted life years (DALYs) loss due to high BMI to be at 120 million which represents 4.9% of DALYs from any cause among adults globally (1).

Obesity is a significant public health issue worldwide and locally. It is estimated that 107.7 million children and 603.7 million adults were obese worldwide in 2015. Obesity prevalence has doubled in 73 countries from 1980 including Canada (1). In the United States alone, the prevalence of obesity reached 39.8% of the whole population for 2015-2016 with some subgroups such as non-Hispanic black having age-adjusted prevalence as high as 54.8% (3). Canada is not far behind with data from 2015 showing an estimated 28.1%, or more than one in four adults, suffering from obesity with an additional 36% being overweight (21). In Quebec, the obesity level is reported to be lower than the national average at 22.8% (22). Moreover, the burden of obesity varies with geography. For instance, in Quebec, there is a higher prevalence of obesity in rural regions such as Côte-Nord (28.2%), Gaspésie (28.1%) and Abitibi-Témiscamingue (28.0%). Larger cities, such as Montreal and Quebec City, tend to have lower rates of obesity, 19.9% and 21.6% respectively (22).

#### 2.1.2 Risk factors

Obesity is a complex disease with multiple risk factors both at the individual and at the population level. These factors can explain the variation in risk between individuals within a population and must therefore be accounted for in studies on the subject. Understanding these

factors also allows for better public health and individual interventions aimed at reducing the burden and consequences of the disease.

#### 2.1.2.1 Sex

Worldwide, there is a small but consistent trend towards females having a higher prevalence of obesity in all age brackets (1). The age-standardized prevalence of obesity estimated by the GBD collaborative using survey data provided by Statistics Canada, is 19.79% [17.18 - 22.59] in males and 20.77% [18.71 – 23] in females (1). Studies looking directly at gender and obesity convey a more complex story. First, there is a biological difference between males and females. Women, starting from young age but more significantly after puberty, develop greater adipose stores than men. This difference exists even after controlling for BMI and stems, among other causes, from hormonal influences (23). Body fat distribution is also different, with females accumulating more subcutaneous fat compared to visceral fat (24). On the other hand, males tend to accumulate more visceral fat, which is associated with worse health outcomes compared with females with similar BMI (16, 25). Secondly, aside from biological sex, gender can have an important influence on obesity. Gender is a social construct associated with differences in norms and behaviors. Applying a gender approach to obesity highlights the difference in perception of weight, weight bias internalisation and eating disorders. Boswell et al. found that females are more likely to have weight bias internalisation through being more exposed to weight-based stigmatisation and more internalisation of their experiences (26). The result is a higher correlation to binge eating disorder, weight cycling and other psychiatric issues than their male counterpart. This has consequences on weight itself but also on response and adherence to treatment, such as bariatric surgery (26).

#### 2.1.2.2 Genetics

Genome-wide association studies estimate that heritability could account for more than 20% in BMI variation. However, studies on the subject are only able to identify a fraction of that variation (27-29). In total, the NHGRI-EBI Catalog of published genome-wide association studies currently contains 968 single-nucleotide polymorphisms associated with obesity with a p-value of less than 5 x 10<sup>-8</sup> (30). These studies and others highlight the fact that most of the genetic causes of obesity are still unknown. A large component of the BMI variability is therefore not solely explained by genetic factors but rather by the interaction between the latter and environmental influences, which can be modified by individuals and public health policies. Key examples are the effect modification by smoking (28) or by physical activity (31) on genetic predispositions for obesity.

#### 2.1.2.3 Physical activity

Physical activity, or lack thereof, is a key player in development of obesity. Several studies demonstrate a strong correlation between physical activity and BMI (32, 33). In a cohort study by Mozaffarian et al., healthy non-obese individuals were followed over time and their habits recorded (34). For any level of initial physical activity, and with other variables controlled for, individuals gained less weight over time if they had a positive increase in physical activity. In this study, the absolute level of physical activity was not associated with change in weight. On the other hand, increase in time spent watching television had a strong correlation with increase in weight (34). The Sedentary Behavior Research Network defines a sedentary behaviour as "any waking behavior characterized by an energy expenditure  $\leq 1.5$  metabolic equivalents, while in a sitting, reclining or lying posture" (35). These behaviours have been associated with increased risk of obesity (36), cardiovascular disease (37-39) and mortality (39, 40).

#### 2.1.2.4 Diet

Diet plays a significant role in the development of obesity and its health consequences. The amount and source of calories have an influence on weight and obesity. In a recent systematic review from the Cochrane Collaborative using the pooled analysis of 53,647 participants in 24 studies, lower proportion of energy from fat appeared to be associated with lower weight, BMI and waist circumference correlated with usual fat diet (41). The cut-off used in these studies was a maximal amount of 30% of energy from fat. Moreover, adherence to a named diet was associated with weight loss at 6 and 12 months with only minimal variation between the different diets (42). In a recent meta-analysis including a meta regression of 48 randomized controlled trials on weight loss from diet, named diets with low carbohydrate or low-fat intake resulted in significant weight loss at 6 and 12 months with a mean loss of 7.27kg and 7.25kg, respectively. There was also significant effect modification from behavioral support and exercise (43). Increased portion size, fast food and soft drinks are all associated with increased rates of obesity and have been targets for public health interventions aiming at reducing obesity rates in at-risk populations (44-47).

#### 2.1.2.5 Societal factor

On a broader societal term, there are several factors affecting obesity rates in the population. The main themes involve access and availability of healthy and unhealthy food items, social support and material conditions. In developed countries, lower income is associated with higher risk of obesity. However, financial status itself may be more an indicator of nutritional uncertainty and access to healthy foods and habits. Studies have found that people with greater access to supermarkets have lower BMIs and rates of obesity compared with similar-income households whose members have to travel long distances to shop for groceries (48, 49).

Interestingly, the link between income and obesity might not be in the expected direction. A recent systematic review and meta-analysis provided stronger evidence towards obesity leading to lower income than the opposite causal direction (50). This effect would be mainly mediated through stigmatisation with resulting increase in job insecurity, discrimination and higher burden of mental health (51, 52). Socioeconomic status (SES) is also associated with surgical outcome in other fields of surgery (53-55). Patients in the lowest income strata have higher rates of complications and mortality following operative interventions independent of other patient factors (53). In the field of obesity surgery, no study has demonstrated such effect. However, SES was not shown to be associated with weight loss following bariatric surgery in a recent study on the subject (56).

#### 2.1.3 Management

The Obesity Canada Clinical Practice Guidelines on the management and prevention of obesity in adults and children recommends a progressive approach to obesity management (57). First, the diagnosis of obesity should be confirmed by clinical evaluation of the patient with measurements of BMI and/or waist circumference. Clinical and laboratory investigation should then be done in patients with BMI above 25kg/m<sup>2</sup> to screen for metabolic syndrome and treat if necessary. Patients should also be screened for depression, eating and other mood disorders. These diagnoses are more prevalent in obese individuals and affect the management of obesity. Finally, before any interventions are suggested, the readiness to change, motivation and barriers to weight loss should be assessed. With the patient, a plan including lifestyle modification should be devised with realistic goals such as 5-10% body weight loss at a slow but consistent rate of 0.5 to 1kg per week for 6 months. The recommended lifestyle modification program should include a diet with caloric reduction of 500 to 1000 kilocalories per day and an increase in physical activity by initially 30 minutes 3-5 times a week up to 60 minutes on most days. Patients should be followed by a nutrition and exercise health professional. Cognitive-behavior therapy for associated psychiatric comorbidities should also be initiated, if indicated.

#### 2.1.3.1 Medical management

In patients with moderate obesity who fail lifestyle interventions, the next step in management can include pharmacological agents aimed at inducing weight loss and improving comorbidities. As of 2019, there are only three medications available to prescribers for weight loss with Health Canada approval. Orlistat is a lipase inhibitor which decreases the breakdown and absorption of fat. (58) This medication therefore reduces the caloric absorption from meals and induces behavioral changes in the patients due to fat intolerance. At 1 year, the mean weight loss is 2.6kg [95% Confidence interval (CI): 2.16-3.04] with odd ratio (OR) of >10% weight loss of 2.40 [95%CI: 2.08-2.78] relative to placebo (59). The second is a combination medication including both an antidepressant (dopamine and norepinephrine-reuptake inhibitor) and an opioid antagonist: Bupropion and Naltrexone. Despite its mechanism of weight loss not being fully understood, this medication is associated with 1-year weight loss of 4.95kg [95%CI: 5.54-4.36] compared to diet alone. It is also well tolerated (59). Lastly, Liraglutide has received approval for weight loss in 2015. This is a glucagon-like peptide-1 (GLP-1) receptor agonist which acts to increases glucose-dependent insulin secretion, slows gastric emptying, and decreases food intake. Initially designed to help manage diabetes (Victoza®), it was rebranded with dose adjustment (Saxenda®) for weight loss and therefore is well suited for obese patients with metabolic syndrome including diabetes mellitus. It is associated with 1-year mean weight loss of 5.24kg [95%CI: 4.87-5.60] compared with diet alone and superior weight loss than Orlistat in direct comparison within randomized studies (59, 60).

#### 2.1.4 Bariatric surgery

For the more severe cases of obese patients with BMI above 40kg/m<sup>2</sup> or above 35kg/m<sup>2</sup> in the presence of metabolic comorbidities, bariatric surgery is indicated (57, 61). The idea of surgery as a treatment for obesity is not new. The first described results of such procedures included 10 patients who underwent bypass of the small intestine by performing a jejuno-colic shunt and was published in 1961. However, this study cites discussions by Kremen et al. on the consequences of small intestine bypass on dogs as the idea behind performing small intestine bypass procedures as early as 1956 (62). This proposed procedure eventually gave rise to the jejuno-ileal bypass which was performed more widely during the 1970s. This procedure induced weight loss through significant malabsorption but also several complications such as fat-soluble vitamin deficiencies, diarrhea, nephrolithiasis, renal failure and liver failure (63). Several other procedures have come and gone as the bariatric surgery community attempted to minimize complications but inadvertently introduced new ones. Such procedures include the vertical banded gastroplasty, gastric plication and the original biliopancreatic diversion (64).

To achieve weight loss, surgeries are thought to use two main mechanisms. The first is referred to as "restriction". Restrictive procedures yield weight loss by decreasing the number of calories a patient can consume in one sitting. The second mechanism is "malabsorption". Weight loss is induced by decreasing the number of calories absorbed by the gastrointestinal tract for a similar amount of nutritional intake. In addition to these changes in feeding habits, surgeries are associated with hormonal changes involved in the regulation of satiety and glucose metabolism such as increase in GLP-1, decrease in gastric inhibitory polypeptide and ghrelin. However, the exact mechanism of weight loss after bariatric surgery is not completely understood but includes several other mechanisms including bile salt signaling, changes in small bowel microbiome,

leptin levels, and changes in gastric mechanoreceptor feedback, cholecystokinin and oxyntomodulin (65-69).

Several types of bariatric surgery have been proposed and modified over the last few decades. However, four procedures have withstood the test of time and are widely performed worldwide. These include the Roux-en-Y gastric bypass (RYGB), the biliopancreatic diversion with duodenal switch (BPD-DS), the SG and the adjustable gastric band (AGB) even though in fading numbers worldwide due to its poor long-term surgical outcomes (70). Most of these procedures are now performed exclusively in a minimally invasive fashion with laparoscopic or robotic platforms (71).

#### 2.1.4.1 Roux-en-Y gastric bypass (RYGB)

Inspired by a procedure developed for gastric ulcers, a partial gastrectomy with Billroth II reconstruction, the gastric bypass was introduced in the 1960s by Mason et al. The procedure was progressively modified towards its final form with a Roux-en-Y reconstruction in order to prevent bile reflux (72). By convention, RYGB consists of creating a small gastric pouch (5-7cm long), at least 100cm of alimentary limb while bypassing 50-100cm of biliopancreatic limb with a Roux-en-Y reconstruction. The result is restriction through the small capacity of the gastric pouch and malabsorption from the bypassed segment. The advent of laparoscopy meant this procedure could now be performed without a large incision resulting in less incisional hernias, wound and pulmonary complications without increased risk of anastomotic leaks or mortality (73, 74). Multiple studies have demonstrated the effectiveness and safety of RYGB. The use of RYGB has been associated with sustained weight loss beyond 5 years of follow up and improvement in comorbidities including diabetes and hypertension (8, 42, 75). Along with other bariatric surgeries, RYGB was associated with decreased in all-cause mortality in a population-

based study (76). In 2017, it accounted for 17.8% of procedures performed in the USA and is the second most common bariatric surgery performed in North America (70, 77).

#### 2.1.4.2 Biliopancreatic diversion with duodenal switch (BPD-DS)

The biliopancreatic diversion was first described by Scopinaro et al. in 1979. First performed in Italy, this new weight loss surgery consisted of a distal gastrectomy with over sowing of the duodenal stump and transection of the ileum with varying length for the Roux-en-y reconstruction (78). Building on those results, the procedure was modified by surgeons in Quebec City, Canada, by lengthening the common channel and performing a partial gastrectomy to preserve the pylorus with stapling of the duodenum (79). In the following years, the procedure was improved with the duodenum divided instead of occluded to become the current BPD-DS (80). The procedure was then adapted and performed by laparoscopy carrying the advantage of lower wound complication and faster recovery with similar benefits and morbidity profile (81). It is the procedure associated with the highest weight loss and best resolution of comorbidities including diabetes (8). However, given the significant malabsorption behind these impressive results, patients are at risk of severe protein malnutrition and vitamin deficiencies especially fatsoluble ones, which warrant close follow up and lifelong supplementation (8, 82, 83). These concerns along with technical challenges and complexity of BPD-DS as a surgical procedure, have limited its use worldwide and in the United State of America where it now represents only 0.7% of cases annually (70, 77).

#### 2.1.4.3 Adjustable Gastric Band (AGB)

Following the principle of the older vertical banded gastroplasty, the AGB was introduced and marketed as less invasive than other surgeries and is a completely reversible restrictive procedure. In performing AGB, a silicone band containing a balloon is fitted around the fundus

of the stomach using laparoscopy and is connected to a subcutaneous reservoir. The surgeon can adjust the volume of the band in follow up visits in order to increase restriction, enhance weight loss or minimize side effects such as vomiting or dysphagia. Several clinical trials demonstrated the efficacy of this surgery at inducing weight loss and resolution of comorbidities, despite the lesser success when compared to sleeve gastrectomy and RYGB (8, 84). The laparoscopic AGB accounted for nearly half of procedures performed in 2008 before falling out of favor to less than 2% in 2017 given its inferiority and recognition of long-term complications such as erosion and slippage (77, 85, 86).

#### 2.1.4.4 Sleeve gastrectomy (SG)

As the restrictive part of the BPD-DS, SG was performed as a stand-alone procedure initially for the first of the two-stage approach to surgical management of the super-obese patients (BMI >50kg/m<sup>2</sup>). In these patients, significant weight loss was induced prior to performing the malabsorptive portion of the surgery. Given these findings, simplicity and safety of the procedure, and poor long-term outcomes from AGB, SG began to gain popularity as a primary procedure obviating the need for the second stage BPD-DS for many patients. From less than 10% of bariatric surgeries in 2009, SG has become the dominant procedure in the USA over the last 5 years representing nearly 70% of all primary bariatric procedure performed (70, 77). Studies have compared SG to RYGB and have demonstrated similar rates of complication and weight loss up to 5 years of follow up (87, 88). However, one of the major concerns with this procedure is the development or worsening of gastroesophageal reflux disease and possible increase in Barrett's esophagus or even esophageal adenocarcinoma (89, 90). This remains an area of active study.

#### **2.2 EFFECT OF SURGICAL VOLUMES IN SURGERY**

In bariatric surgery, as in many other specialized surgical fields, there are many factors influencing outcomes of a procedure. Primarily, there are patient-specific factors, such as age, sex, body habitus, comorbidities, laboratory findings, e.g., albumin, hemoglobin A1c, and many others that can influence surgical outcomes. There are also procedure-specific factors. Every surgical procedure has pitfalls and unique benefits, which have to be factored in in the surgeon's decision to choose the most appropriate procedure for a given patient. The surgeon's experience and technical skills are also important factors, which are difficult to quantify and adequately account for in studies on surgical management of a disease. The surgeon's annual volume has been proposed as a proxy for several surgeon-specific factors. It is easily measurable and thus, it can become a useful target for quality improvement and has been the subject of several studies in various fields of surgery(11, 12). However, the surgeon's true experience encompasses several other aspects than simply their annual surgical volume, such as specific training in the form of fellowships or additional courses, quality of training and mentoring, total number of procedures performed, access to senior colleagues, ongoing senior mentorship, and their technical skills. In the field of bariatric surgery, Birkemeyer et al. published a study in 2013 using video recordings of procedures from trained bariatric surgeons (91). These recordings were rated for quality and perceived skills by peers and the outcomes of the patients were analyzed and compared. The results demonstrated a clear association between the perceived skill of a surgeon and the outcomes of the respective patients. Surgeons classified in the top quartile of skills experienced less surgical and medical complications than those in the other quartiles. This relationship was driven by the lower number of acute obstructions, bleeding, infections, renal failure and all-cause mortality for the highest skilled surgeons (91). Interestingly, a follow up study published in 2016

did not find an association between the surgeon's skill level and several long-term outcomes, including resolution of comorbidities and weight loss (92). The authors of the latter study explained the contradictory findings as a demonstration of several other factors driving the eventual long-term success or failure as opposed to the surgeon's skills alone (92).

Patient outcomes are also associated with several factors at the institutional level. This can include the type of hospital establishment, source of payment for care being public or private, the geographic location of the institution, and the annual volume of surgeries performed at the specific centre. Similar to SV, HV is also shown to influence postoperative mortality and complication (11).

The conceptual framework behind the volume-outcome relationship hinges on the complexity of patient and procedure selection as a function of comorbidity and severity, surgeon's skills, skills of other physicians and allied health care professionals, as well as hospital processes including continuous education and staff training (93). All these factors plausibly contribute to influence outcomes at an institution. Higher volume centres tend to have access to more subspecialized services including interventional endoscopy and radiology, intensive care units (ICUs), larger blood banks, and adequately staffed multidisciplinary bariatric teams with psychiatrist(s), nutritionist(s), physiotherapist(s) among others. The hospital staff, from the personal care attendant to the radiologist, are more exposed to this specific patient population. By themselves however, these assets present in high volume centres may not necessarily require a given annual volume to result in better outcomes(94). They likely reflect quality improvement measures, processes of care, and expertise that could be transferred or made accessible to lower volume centres via telemedicine, training or transfer agreements.

The influence of surgeon and hospital volume is recognized in several fields of surgery. A landmark study on the subject, published by Birkmeyer et al. (11), evaluated the effect of HV on outcomes after 14 cardiovascular or oncologic procedures using Medicare data from the USA. Annual HV was separated by quintiles and the results showed an incremental decrease in mortality with each increasing quintile. This effect was still present when adjusting for covariates including age, sex, socio-economical status (SES) and Charlson Comorbidity Index (CCI). Similar studies have since expanded on these findings to various fields of surgery with a trend towards more complex procedures having a stronger association between volume and better outcomes (95).

#### 2.2.1 Volume outcome in bariatric surgery

The relationship between surgeon and hospital volume with outcomes after bariatric surgery has also been explored in the last 20 years. Several studies have attempted to quantify and explain these relationships using mainly smaller prospective cohort studies as well as larger retrospective studies using administrative databases. Several of these studies are explored in this section to provide a narrative review of the body of literature on the subject.

There is a systematic review on the relationship between volume and outcomes in the field of bariatric surgery. Published in 2012 in the Annals of Surgery, this systematic review included 24 original articles published up to April 2011 (12). On the subject of SV and outcome, 13 studies were identified. They all demonstrated evidence of improvement in outcomes for the higher volume surgeons. This included 4 cohorts studies comparing low to high volume groups using different cut-offs for volume. Most of these studies used in-hospital mortality as the outcome of interest and did not account for the inter-hospital variation. The cut-offs were set arbitrarily between 20 and 50 cases either as total SV or annual volume. Meta-analysis was not feasible

given the heterogeneity in the studies with different designs, thresholds and types of surgery. The included studies mostly consisted of open and laparoscopic RYGB and a now obsolete open vertical banded gastroplasty or combined all types of surgery when looking at SV.

The study from Smith et al., using data from the Longitudinal Assessment of Bariatric Surgery cohort, a prospectively collected database from 33 surgeons in 9 accredited centres of excellence also revealed a decrease in rate of complications with increase in SV for RYGB (96). The composite outcome was defined as death, deep venous thrombosis (DVT), pulmonary embolism, reoperation, non-discharge at 30 days and readmission within 30 days. Compared to surgeons with 0-24 annual cases, the surgeons in the higher volume groups had a lower risk of complications with an adjusted relative risk for 25-49, 50-99 and >100 surgeries at 0.61 (95%CI: 0.30-1.25), 0.41 (95%CI: 0.22-0.79) and 0.35 (95%CI: 0.16-0.76), respectively. These RRs were obtained from a multilevel Poisson regression with adjustment for procedure, BMI, obstructive sleep apnea (OSA), DVT, and surgeon's experience prior to entry in the cohort. The authors' interpretation was that the volume to outcome relationship is one that is linear and did not suggest a specific volume threshold (96).

In a study by Flum et al. published in 2005 using Medicare data from 1997 to 2005, SV was associated with a decrease in odds of death (97). This study, using a logistic regression model with age, sex, SV quartiles, and CCI revealed a protective mortality OR of 0.8 (95%CI: 0.8-0.9) for an increase of a quartile in surgical volume. Interestingly, the difference in outcome from low to high SV was greater in older patients who are arguably more vulnerable and at risk for postoperative complications. The 90 days mortality for patients older than 65 years old operated by surgeons with less than 15 bariatric cases annually was 13.8% compared to 1.1% in the higher volume quartile. In patients <65 years old, the mortality rate at 90 days was 3.0% in the lowest

volume quartile compared to 1.8% in highest quartile (97). These results prompted the authors to conclude that higher risk group patients would benefit the most from referral to higher volume surgeons. However, again the SV was calculated by combining all types of bariatric procedures performed including vertical banded gastroplasty and not by specific procedure, which in terms of experience gained, equates a purely restrictive case e.g. vertical banded gastroplasty to a more complex bypass-type case e.g. BPD-DS (97). Since the publication of the systematic review by Zevin et al., several more recent studies were published on the subject. However, the same methodological limitations are repeatedly seen and do not permit drawing firm conclusions on the subject (98-106).

A large study of 32,000 patients using data from the Nationwide Inpatient Sample from 2005-2007 assessed the effect of HV on severe complications after both laparoscopic and RYGB, AGB and all procedures combined (98). The main result of this study was a positive association between specific or total volumes and outcomes. The authors compared incremental values to dichotomize the dataset and found significant association for all values with no specific inflection point identified. In consequence, the authors questioned the validity of minimal case load for accreditations based on arbitrary numbers, which may miss the underlying processes towards improving quality of care. A more recent study analysing the same database from 2006 to 2010 included only laparoscopic procedures and RYGB and SG only. It used the arbitrary threshold of 50 combined cases per year for HV and found an increase in mortality (OR=2.5 [95% CI: 1.3-4.8]) and serious morbidity (OR=1.2 [95% CI: 1.1-1.4]) (99). Both of these studies did not account for SV or clustering in their respective analysis. Given their use of inpatient databases, these studies also fail to capture morbidity and mortality seen after discharge; thus, greatly limiting the conclusions. A study investigating RYGB in the state of Pennsylvania between 1999 and 2003 used a matrix approach to assess the effect of surgeon and hospital volume independently (100). Despite including patients with open approach to their procedures, the finding of this study demonstrated the independent contribution of both HV and SV. For example, patients treated by surgeons with high annual volumes in centres with also high annual volumes had lower odds of 30-day mortality than patients treated by similar surgeons but in hospitals with lower annual volume (OR=0.30, p=0.01, CI not provided). The opposite situation where a surgeon with high annual volume from a low-volume hospital is compared to a surgeon with a low annual volume in a low-volume hospital did not result in improvement of outcomes (OR=0.89, [95%CI: 0.49-1.64]). This study used 30-day mortality in their analysis, however, which in the modern era of bariatric surgery is a poor outcome measurement given the low rate of such events. Moreover, in another study using the inpatient database from 12 states, hospitals were stratified by combined volume of laparoscopic AGB and laparoscopic RYGB. The result of the analysis of 446,127 patients from 2006 to 2011 revealed higher complication rates among patients operated in low-volume centres with OR of 1.39 (95%CI: 1.07-1.80) in the most recent period of the study after adjusting for patient but not surgeon-level variables (101).

Using the Bariatric Outcomes Longitudinal Database, a group from North Carolina investigated the effect of surgical volume on SG and RYGB outcomes (102, 103). Surgeons were classified as low and high-volume using an arbitrary threshold of 50 cases of the procedure of interest per year. At the time of writing this thesis, this is the only published study looking at volume outcomes after SG (102). In all, 16,547 SGs were performed by 87 higher annual volume surgeons and 649 with lower experience surgeons. There was a significantly lower complication rate in the high-volume group (5.6% vs 7.0%, p < 0.001) as well as lower reoperations and

readmissions. Interestingly, SG-specific volume had a greater influence on complication rates, readmissions and reoperations than the surgeon's RYGB volume. Therefore, the authors suggest that procedure-specific volumes should be used over overall bariatric volumes as a measure for accreditation or further research in the field (102). The similar approach to laparoscopic RYGB yielded similar results with OR for 30-day complications of 0.81 (95% CI: 0.75-0.87) and even 30-day mortality difference with OR of 0.50 (95% CI: 0.27-0.91) (103). However, both these studies have significant limitations that affect the interpretation of such impressive differences. The main flaws are that HV is not accounted for. In addition, the statistical models used do not address clustering of surgeons within institutions which could have a large effect on the estimates. Therefore, one cannot conclude if the effect measure is due to surgeons' differences or institutional variation.

Alami et al. compared 85 patients with laparoscopic RYGB from a high-volume teaching hospital to 55 patients in a low-volume veterans affair hospital centre (104). These surgeries were all performed by a single surgeon practicing in both centres. There were significant differences between the samples of patients in the 2 centres with a higher percentage being male and older age in the low-volume centre, 85.5%, 51 years compared to 15.3%, 44 years of age in the high-volume centre. There were no differences in early complications or reoperations between groups. There were also no differences between late complications and weight loss at one year. The authors concluded that in context of close collaboration to centres of excellence, well established multidisciplinary teams and similar patient selection and postoperative care, assigning minimum caseloads for institutions is not justified (104). This study highlights the concept that HV by itself is likely not causally involved with better or worse outcomes but rather an indicator of other quality improvement targets that are more important in reducing

complications in bariatric surgery. Therefore, in this system where the hospital is closely related to a centre of excellence, a low-volume centre benefits from the expertise of high-volume surgeons and institutional processes needed to maintain a high-quality surgical care. With the evidence previously described demonstrating a more robust association between SV and outcomes than from HV, such a model with expert bariatric surgeons performing procedures in lower volume associated institutions might provide a solution that meets demands from the population to have care in proximity of their residence while ensuring high-quality surgical care.

A recent study from Brunaud et al. published in 2018 using the French nation-wide database, assessed the effect of HV with postoperative complications and need for reoperations (105). The authors identified 184,322 patients from 606 institutions. After adjusting for age, sex, BMI class, Elixhauser comorbidity and calendar year in a logistic regression model, centres with volumes >200 cases per year had a lower reoperation rate at 3 and 6 months for RYGB and SG (105). However, this study had significant flaws that weakened the authors' conclusion that highvolume centres are truly superior to lower volume centres. First, SV was unaccounted for in the study. Given the previously presented literature and the clustering of high-volume surgeons in high-volume institutions, it is difficult to agree with authors of the above-mentioned study that the relationship described is truly from HV. Also, there is an issue with multiple comparisons. Multiple primary outcomes were explored including length of stay (LOS), ICU stay, reoperation during initial admission, at 1 month, 3 months and 6 months for three types of surgeries as well as for all procedures between 3 categories of surgical volume (105). This results in 56 different ORs presented, which increases substantially the chance of finding a significant association at the conventional 5% alpha level. Moreover, the authors' conclusions are solely based on two statistically significant ORs reported among many that were calculated. Several studies on the
subject suffer from similar shortcomings. The study by Nguyen et al. published in 2004 evaluating outcomes of patients who underwent RYGB in 93 academic centres with various surgical volumes, also fails to account for SV when assessing outcomes. The results also demonstrate a reduction in perioperative morbidity and mortality, 30-day readmission and shorter LOS (106).

Therefore, considering the evidence available, summarized in table 1, there seems to be an influence from both SV and HV on complications after bariatric surgery. However, due to the significant limitations from the methodologies and data available to researchers, the true effect of each component still remains unknown. This is especially true for SG which has even less and lower quality data available.

Despite these shortcomings, the body of literature on the subject has informed healthcare policy and quality improvement programs. The American College of Surgeons and the American Society for Metabolic and Bariatric Surgery (ASMBS) quality improvement program (MBSAQIP) standard manual mandate an annual volume of 50 stapled bariatric procedures to maintain a "Comprehensive Center" accreditation and 25 bariatric procedures annually for a "Low Acuity Center". In order to be accredited, a centre must have at least one "Metabolic and Bariatric-Verified Surgeon" with an average of 25 cases per year over a period of 3 years. These guidelines are used widely in the United States and recognized by insurance companies where payment is tied to the certification. On the other hand, in the province of Ontario, Canada, bariatric centres of excellence need to perform a minimum of 120 cases per year with at least 2 surgeons each performing more than 50 cases per year. Fulfilment of these volume-based criteria are required along with the need to have access to ICU, 24-hour surgical coverage, along with medical, psychiatric and multidisciplinary support for bariatric patients (107).

Table 1. Summary of manuscript on bariatric volume outcome thresholds

Study	Thresholds	Threshold value	Findings	Major limitations
Smith et al. (2010)	Arbitrary	Procedure specific SV (RYGB): Groups 0-24, 25-49, 50-99, ≥100	Risk of complication decreased by annual volume when adjusting for clustering and selected covariate. RR of complication 0-24: (ref) 25-49: 0.61 (95%CI: 0.30-1.25), 50-99: 0.41 (95%CI: 0.22-0.79) $\geq$ 100: 0.35 (95%CI: 0.16-0.76)	-
Flum et al. (2005)	Median and quartile	All procedures SV: Quartile 1: 14 Median: 36 Quartile 3: 70	Highest quartile of volume was associated with decrease risks of mortality (1.1% vs 9.3%). Odds of death is 1.6 times higher for patients of surgeon with lower volume (less than the median). Concluded on continuous improvement.	Combined all types of surgery for SV assessment. Open surgery limits external validity No adjustment for HV or clustering
Gould et al. (2011)	Arbitrary	All procedure HV: 25, 50, 75, 100, 125, 150, 175 & 200	HV of ≤100 adjusted OR of 1.22 (95%:1.01-1.49) Concluded on continuous improvement.	No adjustment for SV or clustering.
Jafari et al. (2013)	Arbitrary	All procedure HV: <50, 50-125, >125	HV <50 compared to >125 associated with OR of 1.55 (95%CI: 1.23-1.95) for serious complications	No adjustment for SV or clustering.
Torrente et al. (2013)	Arbitrary	Procedure specific (RYGB) SV: <50, ≥50 HV: <125, ≥300	Comparing low SV & HV to high SV and HV, OR of 0.30 (95%CI: 0.15-0.60)	Limited external validity given population of open bypass
Varban et al. (2015)	Arbitrary based on ASMBS	All procedures (RYGB & AGB): HV <50 or ≥125	OR of serious complication in low HV vs high HV of 1.55 (95%CI: 1.23-1.95) in RYGB for 2006-2007	No adjustment for SV or clustering.
Celio et al. (2016)	Arbitrary	SG SV: <50, ≥50 RYGB SV: <50, ≥50	OR for SG of 30-day complication (0.80, 95%CI: 0.64-0.92), reoperation (0.69, 95%CI: 0.52-0.90) and readmission (0.73, 95%CI: 0.61-0.88) for high volume surgeons. SG volume is more closely associated to SG outcomes then RYGB volume.	No adjustment for HV or clustering
Celio et al. (2017)	Arbitrary	Procedure specific SV (RYGB): <50, ≥50	OR of 30-day readmission (0.85, 95%CI: 0.77-0.94), reoperation (0.82, 95%CI: 0.72- 0.93) and mortality (0.50, 95%CI: 0.27- 0.91) for high volume surgeons	No adjustment for HV or clustering
Alami et al. (2005)	No thresholds	High volume vs low volume hospital by the same surgeon	No difference in early post-operative complication or early reoperation rate	-
Brunaud et al. (2018)	Arbitrary	HV <100, 100-199, ≥200	Decreased reoperation rate after RYGB in high volume centers (≥200 vs <100) at 1- month aOR 0.71 (95%CI: 0.56-0.89) "Threshold of 200 bariatric cases per year should be evaluated for further validation or adjustments"	No adjustment for SV or clustering. Multiple comparison.
Nguyen et al. (2004)	Arbitrary	HV <50, 50-99, ≥100	In-hospital mortality lower in high volume centers (0.3% vs 1.2%, p<0.01)	Lack of regression adjustment including clustering and surgeon's volume

#### **2.3 BARIATRIC SURGERY IN QUEBEC**

In the province of Quebec, there are currently no set standards with regards to quality and surgical volumes. Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program certification is also voluntary.

The latest policy statement for organisation of bariatric surgery in Quebec dates back to 2009 (108). It followed the recommendation of an expert panel from 2005, which due to the established benefits of bariatric surgery, advised the government to increase access to surgery throughout the province, establish criteria for performing the procedures tied into quality improvement programs, and launch a provincial registry. The report titled "L'organisation de la chirurgie bariatrique au Québec: Plan d'action" covers the landscape of bariatric surgery in Quebec with 8 centres performing a total of 840 cases in 2008-2009. The goal was to increase the volume to 3,000 procedures per year by 2011-2012. To achieve this, volume from already existing centres was to be increased with the designation of 2 centres as centres of excellence. The AGB became covered under the provincial insurance and 4 new centres were to gained privileges in bariatric surgery to improve coverage of certain regions. The last aspect of this document involves ensuring the success of bariatric surgery through the implantation of a provincial registry to facilitate quality improvement province-wide (108). These measures were partially implemented after 2009. However, the registry was never implemented, and the volume objectives were not fully met. In 2011-2012, only 1,894 procedures were performed and it took until 2014-2015 to surpass the objective of 3,000 cases per year (4). On the other hand, new nondesignated centres started performing bariatric surgery while others that were assigned to, never did, which essentially did not address the issue of differential access to bariatric surgery in certain geographic regions within the province of Quebec.

In a recent study published in 2018, via an online survey, we explored the state of bariatric surgery in the province of Quebec and investigated various practices, training and resources available to all surgeons performing bariatric surgery in all bariatric centres in Quebec (109). We surveyed 46 surgeons from 15 centres with a response rate of 87%. We found that only 35% of Quebec bariatric surgeons had completed a 1-year additional training in the field of bariatric surgery in the form of fellowship and 74% performed more than 50 bariatric procedures per year. All surgeons performed SG, 55% perform at least 1 RYGB per year, and 34% carried out at least 1 BPD-DS per year (109). Another interesting finding of this study was the high level of stated support (70%) for the establishment of a centralized referral system for bariatric surgery within the province. Furthermore, the surgeons also believed that referral for bariatric surgery should be based on patient's geographical convenience (93%), patient's preference in procedure (78%), surgical waitlist at a given centre (50%), and multidisciplinary capabilities of the centres (55%)(109). A similar model has been established in the province of Ontario in 2009, which has successfully increased the number of referrals and as a consequence access to surgery across all geographical regions (110).

# **3 OBJECTIVES**

The primary objective of this study was to evaluate the influence of SV and HV on postoperative morbidity after bariatric surgery in the province of Quebec, Canada. As secondary objectives, I aimed to identify minimum SV and HV thresholds associated with improved outcomes.

# **4 METHODS**

This is a population-level retrospective cohort study based on the linkage of administrative healthcare data from the province of Quebec, Canada. Quebec is the second most populous province with an estimated population of 8,394,034 (2). All citizens of Quebec are covered by a single payer health system which insures all hospitalization and physician costs for more than 97% of permanent residents in the province.

#### 4.1.1 Data source

The Régie d'assurance maladie du Québec (RAMQ) is the government body in charge of claim reimbursements to physicians in the universal single payer healthcare system in the province of Quebec. The database maintained by this governmental institution includes information on 97% of the population that lives in the province (111). Billing information is provided by the near totality of 45,978 physicians, surgeons, and other health providers for publicly reimbursed activities. The claims covered by RAMQ include both inpatient and outpatient visits as well as physician-entered acts based on the International Classification of Diseases, 9<sup>th</sup> revision-Clinical Modification (ICD9-CM) diagnosis codes. Vitals statistics are provided by RAMQ including month and year of birth, death as well as a 3-character postal code associated with an individual.

The second part of the dataset is provided by the Ministère de la Santé et Service Sociaux (MSSS). It is the branch of the government in charge of funding and administration of the public healthcare system in the province. It maintains an administrative record on the activities at the institutions it manages. This includes records of every in-hospital visit including diagnostic and procedure codes. These codes are derived from hospital discharge summaries and procedure notes. It also includes information on emergency room visits, admission dates, ICU stay and

diagnostic tests. Codes are included in ICD9-CM format until 2006 after which International Classification of Diseases, 10<sup>th</sup> revision (ICD10) format was also added.

Data from both RAMQ and MSSS databases were linked using a denominalized and encrypted 10-digit number as a unique identifier for each subject, the respective surgeon/healthcare provider, and institution in the study cohort.

#### 4.1.2 Study population

I identified all patients aged 18 and older who underwent bariatric surgery in the province of Quebec, Canada from January 1, 2006 to December 31, 2012. This allowed for capture of information on the pre and post-2009 era when changes were made to increase access to bariatric surgery in Quebec, chiefly the increase in the bariatric surgical centres.

The RAMQ and MSSS databases provided records on all patients who had undergone bariatric surgery during the study period (the list of different bariatric surgeries is provided in Appendix 1). The ICD9-CM diagnosis codes for obesity (278.0; 278.9) were used to identify subjects that had the index surgery for treatment of their obesity from both the RAMQ and the MSSS datasets. For each study subject, the data was extracted from 1 year prior to the index surgery date up to December 31, 2017. After merging datasets, the duplicate entries were eliminated.

In an attempt to identify the subjects that underwent the selected surgeries for the treatment of their obesity, individuals who in addition to obesity codes, had alternate ICD9-CM diagnosis codes associated with their procedure codes were excluded. These alternate diagnoses included malignancies of the gastrointestinal tract, malignancies with metastatic potential to the stomach or neighboring organs, benign tumours of the stomach, peptic ulcer disease and gastrointestinal hemorrhage. In addition, some patient had missing, or additional diagnoses associated with the

index procedure such as biliary colic or hiatal hernia which can be addressed at the same time as a bariatric surgery. All uncertain cases were reviewed individually to ensure obesity was the only possible indication for the procedure (Appendix 1, 2, and 3).

Using the unique surgeon and institution identifiers, the number of bariatric cases performed in the year prior were used to calculate the annual SV and HV. Thus, the respective numbers from the first year (2006) of the study period were used for calculation of the volumes for year 2007 and consequently censored from the volume-outcome analysis. Therefore, the final study cohort includes all patients who underwent bariatric surgery for the treatment of morbid obesity in the province of Quebec from January 01, 2007 to December 31, 2012.

#### 4.1.3 Time frame and variable

The data was analysed on a per-patient basis with time zero defined as the index date associated with the bariatric surgery code (Appendix 1). Exposure and baseline covariates were extracted from the datasets using diagnosis codes during the 1 year prior to the index date. The outcome variables were extracted from index date until December 31, 2017. Calendar year in which the bariatric procedures were performed is used as a patient specific-variable in the statistical analysis to address the presence or absence of any time-period effect.

#### 4.1.4 Outcomes

The primary outcome was defined as occurrence of 90-day postoperative morbidity and mortality after the index bariatric surgery. The time of mortality was extracted using the month and year provided in the RAMQ datasets. Thus, given that the exact day was not available, the date of death was defined as the 15<sup>th</sup> of the month to minimize misclassification. To improve accuracy, the occurrence of individual morbidity was documented if the respective ICD9-CM/10 and/or

RAMQ physician billing codes were present in datasets. The detailed list of ICD9-CM/10 and RAMQ billing codes used is provided in Appendix 4. Several clinically relevant individual postoperative complications were considered and included: non-hemorrhagic shock, need for *de novo* hemodialysis, venous thromboembolism (VTE), macrovascular events comprising of acute myocardial infarction and/or cerebrovascular accident, hemorrhage, postoperative infection or leak (using codes such as postoperative infection or peritonitis in the immediate postoperative period, including a subcategory for leaks requiring operative management), pneumonia, prolonged ventilation defined as the presence of billing codes for managing a ventilated patient for more than 2 consecutive days following surgery, reintubation defined as use of ventilation billing codes for a period of at least 1 day following a time window of more than a day without ventilation, reintervention with endoscopy, reintervention with radiology corresponding to Clavien Dindo IIIa complications, reoperation, prolonged hospital admission in accordance with the ASMBS definition of  $\geq$ 7 days, and unplanned ICU admission defined as at least 2 days in the ICU or any admission longer than 3 days (112).

Moreover, the individual complications were combined to create 3 *a priori* selected composite outcomes based on literature available from other administrative databases in the field of bariatric surgery (113). The first composite outcome was *any complication*, which was defined simply as the presence of any individual postoperative complication. Second aggregate outcome was *composite complication*, which was defined as the presence of any of the following complications: bleeding, VTE, pneumonia, macrovascular events, postoperative infection/leaks, shock, need for *de novo* hemodialysis, reintubation, prolonged intubation, prolonged admission (≥7 days), and mortality. This outcome is also inspired by the "major complication" category in the ASMBS standard reporting manual (114-116). Lastly, *serious complication* which included

events categorized as more severe and life-threatening and consisted of ICU admission, shock, need for *de novo* hemodialysis, VTE, acute myocardial infarction, reintubation and mortality. Finally, an attempt to better represent the spectrum of complication was made by using a scoring system for postoperative complications. An already validated scoring system exists in the surgical outcomes literature called the HARM score (117). It consists of a zero to eleven score with a maximum of 5 points for LOS, 1 for readmission and 5 in the event of mortality. This score originally developed for colorectal surgery was later adapted to bariatric surgery with modification of the LOS points (BAR-HARM) (118). In a similar fashion, using the Quebec data, the score was adapted for this study with new quintiles for LOS (Qc-BAR-HARM) (Appendix 5).

#### 4.1.5 Main exposures

The two main variables of interest for this project are the yearly surgeon and hospital-specific surgical volumes. Using the unique surgeon and institution identifiers, the number of bariatric cases performed in the year prior to the index surgery date were used to calculate the annual SV and HV. Thus, yearly SVs and HVs may vary between patients of the same surgeon or hospital. This allows for the surgical volume to change through the years as a surgeon or institution increase or decrease their yearly bariatric surgical numbers reflecting the true surgical experience of a surgeon/centre at the index date as opposed to a set projection over a year. Furthermore, the calculated surgical volumes are procedure-specific, which is more representative of the experience of a surgeon/centre in various procedures that cannot really be painted with the same complexity brush e.g. AGB versus BPD-DS.

#### 4.1.6 Covariates

Several covariates are associated to both outcomes after bariatric surgery and possibly to the exposure variables. These variables were collected from the period corresponding to the one year prior to the index surgery date.

Patients' age was estimated by subtracting the birth year and month from the date of the index surgery. This was analysed both as continuous, mean-centered and in age categories. These were selected to divide the patients in the most equal groups possible (18-29, 30-44, 45-59, 60 and more). Patient's sex was obtained as a binary variable directly from the demographic information provided in the datasets.

To capture the SES of the individuals in the study cohort, ecological level data was applied to every individual using the 3-character postal codes provided by RAMQ. The data was extracted from an index developed by the "Institut national de la santé publique du Québec" (INSPQ). Created from the data available from the 2011 Canadian Census, the Deprivation Index (French: Indice de défavorisation) is a score divided in two components (119, 120). The social component uses information on the proportion of individuals living alone, proportion of lone parent families and proportion of separated, divorced or widowed individuals. The material component involves the average income, proportion of individuals without high school diploma and proportion of employed individuals. This data is used to calculate a score unique to every census sub-division which corresponds to an area smaller than a full 6-character postal code. The information is available to researchers as a program or spreadsheet used to attach social and material quintiles by municipality and postal codes. Given that the postal codes available for the study cohort are 3 characters each, a median of the quintile value on the 6-character sub-division was obtained and attached to the patient's individual data and used as a proxy for SES. To assess and account for baseline comorbidities of patients, CCI was extracted using the original method by Deyo et al. using ICD9-CM diagnosis codes (121). For ICD10 derived diagnoses, the modification published by Quan et al. was used (122). Individual comorbidities were classified using the Elixhauser method (third version) and adapted to the RAMQ-specific ICD9-CM codes and when appropriate, the Quan et al. modification for ICD10 codes were applied (122, 123). To help improve the accuracy of capturing individual diagnoses, specific billing codes from RAMQ associated with certain diagnoses were added to the tables. The complete list of codes is included in Appendix 6. The included comorbidity covariates were CCI score (numerical), diabetes mellitus (DM), hypertension (HTN), anemia, chronic pulmonary disease (CPD) and depression. Hemodialysis was extracted uniquely from physician billing codes. Furthermore, information on dyslipidemia, OSA, non-alcohol steatohepatitis, gastroesophageal reflux disease and smoking were also collected however, accuracy of these diagnoses in the RAMQ and MSSS datasets are not verified from previous research.

#### 4.1.7 Statistical Analysis

Descriptive statistics representing counts, frequency, median (interquartile range) and mean (standard deviation) were obtained for the various variables described above. The study cohort was stratified based on the type of procedure. However, more detailed analyses especially assessment of surgical volume-outcomes were performed only for SG and RYGB, primarily because these procedures account for >95% of all bariatric surgeries performed yearly in North America (70). Furthermore, as per our previous survey study (109), AGB has been practically abandoned in Quebec and is currently clinically irrelevant. Also as per descriptive analysis of the study cohort, >97% of BPD-DS in Quebec is performed in a single institution rendering its volume-outcome findings less generalizable.

#### 4.1.7.1 Selection of patient-level covariates

Several clinically relevant covariates were selected *a priori* to be used in the predictive model based on previous published studies. These included basic demographic information associated with success of bariatric surgery such as age, sex, and SES. Age was used as a centered continuous variable to facilitate interpretation of the intercept. Despite the assumption of linearity, this approach was thought to be superior to the use of age categories given the loss of information associated with wide age categories required to capture the data. A measure of comorbidity at time of surgery is an important variable to account for in surgical cohort studies. Two different approaches were used to capture the preoperative risk of the patient in terms of comorbidities: 1) CCI as a combined score, or 2) individual comorbidities defined by the Elixhauser method. Since the individual comorbidities are included in the CCI score, they were compared separately to avoid double counting and collinearity.

#### 4.1.7.2 Addressing clustering by surgeons and hospitals

To account for clustering of both surgeon and hospital volumes, a multilevel cross-classified logistic regression was used. Patient-level data is used as a fixed effect with higher order levels for surgeon then hospital. In contrast to a hierarchical model where each group is included within a higher order group, a cross-classified multilevel model allows surgeons to be associated with multiple hospitals. For each of these procedures, a model was constructed with 2 levels (patient and surgeon or hospital) and then 3 levels (patient, surgeon, and hospital). Fixed effect covariates defined *a priori* were then added and the effect of SV was expressed as OR tested in the model controlling for hospital-level variation. The opposite situation was then tested for the effect of HV while controlling for surgeon-level variation. For the sensitivity analysis using the BAR-HARM score as a continuous outcome, a 2-level linear regression was used to extract relative

risk ratios (RRs) from increase in 10 cases annually for SV or HV. Finally, a full 3-level model was used to assess the influence of SV and HV while accounting for both surgeon and hospital variation with the random effect in the models. For these multilevel models, variation partition coefficients (VPC) are calculated. This measure represents a percentage of the variation in outcome attributed to differences within a level of the model such as variation between surgeons or between hospitals.

#### 4.1.7.3 Selecting meaningful surgical volume thresholds

After evaluating the effect of both SV and HV using continuous variables, different methods were used based on procedure type to identify meaningful volume thresholds for SG and RYGB. These were then compared in the 2-level models against the composite outcomes. Absolute risk reduction (ARR) were also calculated between the high and low volume groups.

#### 4.1.7.3.1 Standard cut-off

The current cut-offs used by the ASMSB are 25 stapling bariatric cases annually per surgeon and 50 per institution. This will be referred to as the standard cut-off (124).

#### 4.1.7.3.2 Median

Another method used is to simply divide the data set in two equal groups using the median. This arbitrary number reflects the data available to the researcher but is very efficient for statistical analysis because of the two equal sized groups.

### 4.1.7.3.3 Stratum-specific likelihood ratios (SSLR)

To identify more meaningful thresholds, a variation of the receiver operating characteristic (ROC) curve called the SSLR can be used. This technique first described in 1993 and recently applied by a group to several orthopedic surgical outcomes research, uses a standard ROC curve

to derive SSLR with 95%CIs (125-128). Stratum with overlapping CIs are then combined sequentially until overlaps are no longer present. This results in 2 or more strata with different likelihood of the outcomes. The limits of these strata can then be used as cut-offs for surgical volumes (125).

# 4.1.7.3.4 Traditional ROC

The ROC curve is usually used in diagnostic studies to visualize and calculate a cut-off to maximize the sensitivity and specificity of a test. In order to use this method, sensitivity and specificity is calculated for a given threshold using a 2x2 table. This table is built with the number of true positive, false positive, true negative and false negative for a given threshold (Figure 1).

	Free of complication	Presence of complication
Above selected threshold	True Positive (TP)	False Positive (FP)
Below selected threshold	False Negative (FN)	True Negative (TN)

Figure 1. 2x2 table for ROC curve analysis to investigate surgical volume-outcome relationship

A ROC curve is calculated with the goal of minimizing the misclassification using various thresholds. A threshold value is found using either the maximum Youden index value or closest

to left upper corner methods. The area under the curve (AUC) provides information on how good the model can correctly classify the outcome.

#### 4.1.7.3.5 Splines

Cubic splines are smoothed curves used to visualize non-linear data. It has been used to identify thresholds in various studies by visually identifying inflection points on the fitted curve (129, 130). Each data point is placed on a scatter plot with the SV or HV as X-axis and the absence or presence of the postoperative complication as 0 or 1 on the Y-axis. A binomial smooth spline is then computed to express a function of the rate of the outcome at a given surgical volume value with associated CIs. The number of nodes is varied to avoid overfitting and minimize the uncertainty. Inflection points for change in slope of the spline function are then visually identified and defined as a possible threshold. The identified thresholds were then used in the corresponding 2-level models to evaluate the association between surgical volumes and outcome.

#### 4.1.7.4 Sensitivity analysis

As a sensitivity analysis, a modified score is compared which will not include mortality. Postoperative mortality may be due to the patient's risk factors and a failure to rescue from a complication. Therefore, postoperative complications should be detectable independent of the mortality outcome. As previously described, an alternative outcome was also developed labelled "serious complication" consisting only of more consequential disease status.

For the sensitivity analyses for both SV and HV, the full predictive models were tested with three definitions of surgical volume: 1) procedure-specific, 2) stapled procedure, and 3) any procedure. Models were compared using Akaike information criterion (AIC). The model with the

best fit should indicate which volume measurement better predicts the surgical volume-outcome relationship.

Statistical analysis was performed using STATA version 12 (StataCorp LP) and R (R Foundation for Statistical Computing). *Lme4* and *blme* packages were used for regressions and figures were produced using the *ggplot2* package. Inference was based on a two-sided 5% level for all the statistical analyses.

#### 4.1.8 Ethical considerations

Ethics approval was obtained at the institution-level from the Ethics Review Board of McGill University Health Centre (#2017-3028). In accordance to Quebec laws, the "Commission d'accès à l'information" (CAI) also granted approval for the use of the administrative datasets for research purposes with several measures to maintain the patient data confidentiality. All patients were assigned an anonymous unique identification number prior to the delivery of the encrypted data to the research team. Providers and institutions are also given a unique and anonymous identification number to protect the patients' and providers' confidentiality.

# **5 Results**

## 5.1 COHORT DESCRIPTION

After inclusion and exclusion criteria were applied, the study cohort included 8,271 patients who underwent bariatric surgery in Quebec for the treatment of their morbid obesity during the study period (January 01, 2007 - December 31, 2012). The flowchart for the construction of the study cohort is provided in Figure 2.



Figure 2. Flowchart corresponding to the construction of the study cohort

Among all procedures performed during the study period, AGB was most frequently performed with 3,838 procedures (46%). SG was the second most commonly performed with 1,802 operations (22%) followed by BPD-DS and RYGB at 1,810 (22%), and 821 (10%) procedures, respectively. There was a change in popularity of procedures throughout the study period with a steady increase in the use of SG. Frequency of AGB peaked by 2010-2011 with a subsequent decline until the end of the study period. There was an overall increase in the total number of bariatric surgeries performed during the study period specifically after year 2009, reflecting the increase in both number of bariatric centres and surgeons performing them (Figure 3).



Figure 3. Distribution of different bariatric procedures over time during the study period

The mean age of subjects at the time of surgery was 44 (SD=11) years old with 28% male (N=2,283). This trend was observed for all types of surgery with males representing from 24 to 32% of patients. The mean SES for the patients in each surgical group were also similar for both social and material indices (Table 1). The patients who underwent AGB were healthier at baseline with a higher proportion of patients having a CCI <2 (89%). They also had less frequent diagnosis of DM (25%). On the contrary, patients who underwent RYGB had a higher frequency of metabolic burden from their obesity with 37% suffering from DM and 25% from HTN. The detailed list of baseline characteristics of the study cohort is provided in Table 1.

Table 2. Baseline descriptive characteristics of the study cohort

	Cohort	AGB	SG	RYGB	BPD-DS
	N=8,271	N=3,838	N=1,802	N=821	N=1,810
Age - Mean (SD)	44 (11)	43 (11)	46 (11)	43 (10)	44 (10)
Age category <sup>*</sup> - N (%)					
18-29	881 (11)	461 (12)	149 (8)	90 (11)	181 (10)
30-44	3,561(43)	1,663 (43)	727 (40)	395 (48)	776 (43)
45-59	3,203(39)	1,428 (37)	736 (41)	295 (36)	744 (41)
> 60	626(8)	461 (12)	190 (11)	41 (5)	109 (6)
Sex - N (%)					
Male	2,283 (28)	954 (25)	553 (31)	194 (24)	582 (32)
SES <sup>†</sup> - Mean (SD)					
Social <sup>‡</sup>	2.93 (1.05)	2.95 (1.03)	2.96 (1.04)	3.12 (1.06)	2.78 (1.07)
Material <sup>§</sup>	3.22 (1.09)	3.23 (1.08)	3.15 (1.10)	3.26 (1.01)	3.24 (1.14)
CCI - N (%)					
≤1	7,222 (87)	3,430 (89)	1,532 (85)	699 (85)	1,561 (86)
2	700 (8)	282 (7)	161 (9)	92 (11)	165 (9)
3+	349 (4)	126 (3)	109 (6)	30 (4)	84 (5)
DM - N (%)	2,525 (31)	971 (25)	594 (33)	300 (37)	660 (36)
HTN - N (%)	1,801 (22)	812 (21)	399 (22)	208 (25)	382 (21)
Anemia - N (%)	221 (3)	91 (2)	48 (3)	21 (3)	61 (3)
CPD <sup>¶</sup> - N (%)	1,203 (15)	546 (14)	254 (14)	147 (18)	256 (14)
Surgery period - N (%)					
2007-09	3,170 (38)	1,420 (37)	301 (17)	421 (51)	1,028 (57)
2010-12	5,101 (62)	2418 (63)	1,501 (83)	400 (49)	782 (43)

**SD:** Standard deviation, **AGB**: Adjustable gastric band, **SG**: Sleeve gastrectomy, **RYGB**: Roux-en-Y gastric bypass, **BPD-DS**: Biliopancreatic diversion with duodenal switch, **SES**: Socioeconomic status, **CCI**: Charlson comorbidity index, **DM**: Diabetes mellitus, **HTN**: Hypertension, **CPD**: Chronic pulmonary disease.

\* Age categories were constructed using rounded quartile value to distribute the group in equal sized groups.

<sup>†</sup> SES was obtained using ecological level data expressed by quintile of the postal code of residence of the individuals compared to the Canadian population.

‡ Social index was based on the component of the deprivation index extracted from census information for the proportion of individuals living alone, proportion of lone parent families and proportion of separated, divorced or widowed individuals.

§ Material index was based on the component of the deprivation index extracted from the average income, proportion of individuals without high school diploma and proportion of employed individuals.

¶ CPD included asthma, obstructive sleep apnea and chronic obstructive pulmonary disease.

In total, 42 bariatric surgeons were identified operating in 18 different institutions. The median annual volume of surgeons was 35 cases per year (58). The surgeon's experience varied from a single case in a year up to a maximum of 259 bariatric procedures. The median number of procedures for the institutions was 45 cases per year. The smaller centres had years with a single bariatric case performed while the highest volume centres had a median of 374 bariatric cases per year. Overall, the 3 highest volume centres performed 65% of all procedures in Quebec during the study period.

Among the various bariatric surgeries, SG was the procedure performed in the most centres (N=15, 83%) and by the most surgeons (N=33, 79%). There was a trend towards an increase in individual volumes by both centres and surgeons over the years demonstrating a time-period effect (Figure 4). This trend was not visualized for RYGB among various institutions and surgeons (Figure 5). During the study period, only 4 centres performed BPD-DS with 97% of cases performed at a single high-volume institution (Figure 6). Given this finding, I elected to forgo any further evaluation of volume-outcome relationship for BPD-DS.



Each dot represents a patient operated in the described year. Each color represents a hospital in which the procedure was performed

Figure 4. Annual hospital volume of SG per institution by calendar year



Each dot represents a patient operated in the described year. Each color represents a hospital in which the procedure was performed





Each dot represents a patient operated in the described year. Each color represents a hospital in which the procedure was performed

Figure 6. Annual hospital volume of BPD-DS per institution by calendar year

For RYGB and SG, higher volume surgeons were clustered in high volume centres. However, because some surgeons performed surgeries in more than one institution and most centres had surgeons with different case-volumes, it was possible to analyze specifically the interplay between surgeon and centre volumes.

In terms of postoperative morbidity, 21% of the study cohort experienced at least one complication within the first 90 days after surgery. However, AGB had the lowest frequency of 90-day complications (13%) compared to both RYGB and BPD-DS having frequencies of 33% and 32%, respectively. The frequency of composite complications was 14% for the study cohort but varied significantly according to the procedure. AGB had the lowest rate with 7.1%, followed by SG (13%), RYGB (21%), and then BPD-DS (25%) (p < 0.01). 90-day operative mortality was 0.22% (N=18). The operative mortality rate was both low and comparable between all procedure types ranging from 0.10% after AGB to 0.39% after SG (p=0.137).

	Cohort	AGB	SG	RYGB	BPD-DS
Complication - Count (%)	N=8,271	N=3,838	N=1,802	N=821	N=1,810
Unplanned ICU stay <sup>*</sup>	177 (2.1)	23 (0.60)	56 (3.1)	68 (8.3)	30 (1.7)
Shock	66 (0.80)	13 (0.34)	25 (1.4)	11 (1.3)	17 (0.94)
Hemodialysis <sup>†</sup>	68 (0.82)	14 (0.36)	21 (1.2)	9 (1.1)	24 (1.3)
Acute MI	24 (0.29)	8 (0.21)	7 (0.39)	1 (0.12)	8 (0.44)
Reintubation <sup>‡</sup>	83 (1.0)	13 (0.34)	27 (1.5)	18 (2.2)	25 (1.4)
Prolonged intubation <sup>§</sup>	63 (0.76)	7 (0.18)	20 (1.1)	18 (2.2)	18 (0.99)
Hemorrhage	210 (2.5)	25 (0.65)	55 (3.1)	34 (4.1)	96 (5.3)
Abdominal sepsis/leak	398 (4.8)	78 (2.0)	90 (5.0)	80 (9.7)	150 (8.3)
Required surgery <sup>¶</sup>	193 (2.3)	47 (1.2)	46 (2.6)	26 (3.2)	74 (4.1)
VTE <sup>#</sup>	266 (3.2)	133 (3.5)	35 (1.9)	40 (4.9)	58 (3.2)
Pneumonia	105 (1.3)	21 (0.55)	31 (1.7)	19 (2.3)	34 (1.9)
Stroke	9 (0.11)	5 (0.13)	2 (0.11)	0	2 (0.11)
Prolonged admission**	408 (4.9)	14 (0.36)	58 (3.2)	77 (9.4)	259 (14)
Readmission	714 (8.6)	182 (4.7)	166 (9.2)	113 (14)	253 (14)
Reoperation <sup>††</sup>	345 (4.2)	70 (1.8)	68 (3.8)	53 (6.5)	154 (8.5)
Therapeutic endoscopy <sup>‡‡</sup>	327 (4.0)	54 (1.4)	73 (4.1)	65 (7.9)	135 (4.5)
Interventional radiology <sup>§§</sup>	133 (1.6)	41 (1.1)	42 (2.3)	15 (1.8)	35 (1.9)
Transfer to other institution $^{\P}$	178 (2.2)	112 (2.9)	34 (1.9)	14 (1.7)	18 (0.99)
Any complication	1712 (21)	508 (13)	346 (19)	273 (33)	585 (32)
Composite complication <sup>##</sup>	1134 (14)	272 (7.1)	227 (13)	175 (21)	460 (25)
Serious complication***	488 (5.9)	167 (4.4)	108 (6.0)	105 (13)	108 (6.0)
Mortality	18 (0.22)	4 (0.10)	7 (0.39)	3 (0.37)	4 (0.22)

Table 3. Distribution of postoperative complications up to 90 days after bariatric surgery

AGB: Adjustable gastric band, SG: Sleeve gastrectomy, RYGB: Roux-en-Y gastric bypass, BPD-DS: Biliopancreatic diversion with duodenal switch, ICU: Intensive care unit, MI: Myocardial infarction, VTE: Venous thromboembolic event.

\* Defined as any ICU stay beyond the first two postoperative days.

*† De novo* hemodialysis was defined as at least one dialysis session in an individual not previously dialysed.

‡ Reintubation was defined when ventilation was needed postoperatively after 24 hours without ventilatory support.

§ Prolonged intubation was defined as ongoing postoperative ventilatory support beyond 48 hours.

¶ Abdominal sepsis/leak including peritonitis which required surgical exploration and drainage of abscess.

# VTE included both deep venous thrombosis and pulmonary embolism.

\*\* Prolonged admission was defined as LOS >7 days after the index procedure.

†† Reoperations included all the operative codes in the 90-day postoperative period e.g. operations for management of abdominal sepsis/leak, bleeding and bowel obstructions.

‡‡ Therapeutic endoscopy was defined as need for upper endoscopy for anastomotic dilation or other interventions e.g. stent placement.

§§ Interventional radiology was defined as any radiologic-guided procedure from a list including percutaneous drainage, feeding tube placement or inferior vena cava filter placement.

¶¶ Transfer to another institution excluded transfers to a long-term care facility or a rehabilitation centre. ## Composite complication was defined as occurrence of any of the following complications: shock, hemodialysis, acute MI, reintubation, prolonged intubation, abdominal sepsis leak, VTE, pneumonia, stroke, prolonged admission, readmission and reoperation.

\*\*\* Serious complication was defined as occurrence of any of the following complications: Unplanned ICU admission, shock, hemodialysis, acute MI, reintubation, VTE.

There was an overall decrease in postoperative complication rates irrespective of the procedure

type and throughout the study period. In 2007, the frequency of postoperative complications was

27.3%, this estimate continued to decrease yearly to 17.8% in 2012. (Figure 7)



Figure 7. Evolution of 90-day postoperative complications throughout the study period

#### **5.2** UNIVARIATE ANALYSIS

For SG, in univariate logistic regression analysis, an increment of 10 cases in SV was associated with a decrease in crude odds of developing the composite complication outcome (OR=0.90, 95%CI: 0.84-0.97) (Table 3). For RYGB, this crude relationship was also observed with a higher effect size (OR=0.81, 95%CI: 0.73-0.90) (Table 4). Furthermore, a higher annual procedurespecific HV (10 more RYGBs) was associated with a decrease in the odds of developing the composite outcome after RYGB (OR=0.84, 95%CI: 0.77-0.91) (Table 4). For SG, this crude association between higher HV and decreased composite complications was observed but with a very small effect size (OR=0.98, 95%CI: 0.96-0.99) (Table 3). For both SG and RYGB, the protective effect of respective 10-case increments annually in both SV and HV against composite complications was found to be higher in the later time period of 2010-2012 (OR=0.54, 95%CI: 0.43-0.67; OR=0.88, 95%CI: 0.63-1.23, respectively). Among other risk factors after SG, age (OR=1.05, 95%CI: 1.04-1.06), DM (OR=1.58, 95%CI: 1.27-1.96) and anemia (OR=2.25, 95%CI: 1.33-3.77) were found to be significant predictors (Table 3). On the other hand, for RYGB, only HTN was found to be an independent predictor in univariate analysis (OR=1.53, 95%CI: 1.06-2.20) (Table 4).

Table 4. Univariate predictors of 90-day composite complications after SG

Variable	OR (95% CI)
Age <sup>*</sup>	1.05 (1.04 – 1.06)
Sex (Male)	1.11(0.89 - 1.39)
$SES^{\dagger}$ (Social) <sup>‡</sup>	1.03(0.90 - 1.17)
SES <sup>†</sup> (Material) <sup>§</sup>	$1.01 \ (0.89 - 1.14)$
CCI	
≤1	0 (ref)
2	1.54(0.98 - 2.35)
3+	1.17(0.64 - 2.00)
DM	1.58 (1.27 – 1.96)
HTN	1.23 (0.95 – 1.57)
Anemia	2.25 (1.33 – 3.77)
CPD <sup>¶</sup>	1.20(0.89 - 1.61)
Time period (2010-2012)	0.54 (0.43 - 0.67)
SV (Procedure-specific)	0.90 (0.84 - 0.97)
SV (Stapled procedure) <sup>#</sup>	0.95(0.90 - 1.00)
SV (Any procedure)	0.96 (0.91 – 1.01)
HV (Procedure-specific)	0.98(0.96 - 0.99)
HV (Stapled procedure) <sup>#</sup>	0.97 (0.96 - 0.98)
HV (Any procedure)	0.97(0.96 - 0.98)

SG: Sleeve gastrectomy, OR: Odds ratio, CI: Confidence interval, SES: Socioeconomic status, CCI: Charlson comorbidity index, DM: Diabetes mellitus, HTN: Hypertension, CPD: Chronic pulmonary disease, SV: Surgeon volume, HV: Hospital volume.

\* Age was used as a continuous variable centered at the median age in the cohort expressed in years.

<sup>†</sup> SES was obtained using ecological level data expressed by quintile of the postal code of residence of the individuals compared to the Canadian population.

‡ Social index was based on the component of the deprivation index extracted from census information for the proportion of individuals living alone, proportion of lone parent families and proportion of separated, divorced or widowed individuals.

§ Material index was based on the component of the deprivation index extracted from the average income, proportion of individuals without high school diploma and proportion of employed individuals.

proportion of individuals without high school diploma and proportion of employed individuals

¶ CPD included asthma, obstructive sleep apnea and chronic obstructive pulmonary disease.

# Stapled procedures include all bariatric surgeries except for adjustable gastric band.

Table 5. Univariate predictors of 90-day composite complications after RYGB

Variable	OR (95% CI)
Age <sup>*</sup>	1.02(1.00-1.03)
Sex (Male)	0.80(0.53 - 1.19)
$SES^{\dagger} (Social)^{\ddagger}$	1.19(0.97 - 1.46)
SES <sup>†</sup> (Material) <sup>§</sup>	1.12(0.91 - 1.39)
CCI	
<u>≤1</u>	0 (ref)
2	0.77(0.42 - 1.33)
3+	1.57(0.67 - 3.40)
DM	1.13(0.80 - 1.60)
HTN	1.53 (1.06 – 2.20)
Anemia	2.33(0.91 - 5.63)
CPD <sup>¶</sup>	1.03(0.66 - 1.58)
Time period (2010-2012)	0.88(0.63 - 1.23)
SV (Procedure-specific)	0.81(0.73 - 0.90)
SV (Stapled procedure) <sup>#</sup>	0.95(0.88 - 1.01)
SV (Any procedure)	0.98(0.95 - 1.00)
HV (Procedure-specific)	0.84(0.77 - 0.91)
HV (Stapled procedure) <sup>#</sup>	0.99(0.95 - 1.01)
HV (Any procedure)	0.99(0.98 - 1.00)

**RYGB**: Roux-en-Y gastric bypass, **OR**: Odds ratio, **CI**: Confidence interval, **SES**: Socioeconomic status, **CCI**: Charlson comorbidity index, **DM**: Diabetes mellitus, **HTN**: Hypertension, **CPD**: Chronic pulmonary disease, **SV**: Surgeon volume, **HV**: Hospital volume.

\* Age was used as a continuous variable centered at the median age in the cohort expressed in years.

<sup>†</sup> SES was obtained using ecological level data expressed by quintile of the postal code of residence of the individuals compared to the Canadian population.

‡ Social index was based on the component of the deprivation index extracted from census information for the proportion of individuals living alone, proportion of lone parent families and proportion of separated, divorced or widowed individuals.

§ Material index was based on the component of the deprivation index extracted from the average income, proportion of individuals without high school diploma and proportion of employed individuals.

¶ CPD included asthma, obstructive sleep apnea and chronic obstructive pulmonary disease.

# Stapled procedures include all bariatric surgeries except for adjustable gastric band.

# 5.3 MULTILEVEL ANALYSIS

## 5.3.1 SG

For SG, the 2-level logistic regression model including both patient and surgeon's level variables

resulted in a VPC of 3.3% corresponding to an OR=0.99 (95%CI: 0.93-1.06) for an annual

increment of 10 cases of HV (Table 5). Looking into the contribution of variation between

hospital and postoperative complications, the 2-level model accounting for both patient and hospital-level variables resulted in a VPC of 1.2% for inter-hospital variability and an OR=0.99 (95%CI: 0.97-1.01) for 10-cases increment in SV (Table 5). The cross-classified 3-level model accounting for differences at patient, surgeon and hospital levels, yielded a variance of 4.0% explained by the surgeon-level differences and a 2.2% variability explained by inter-hospital differences (Table 5). Consequently, after 3-level multivariable adjustment accounting for variation between hospitals and surgeons due to random effect, the ORs associated with increasing the volume of SG by 10 cases per year for each surgeon was 1.00 (95%CI: 0.90-1.10) and 0.99 (95%CI: 0.96-1.03) for each hospital, respectively (Table 5 and Figure 8).

Table 6. Multilevel regression model accounting for inter-surgeon and hospital variability after SG

Models	2-level		2-level		3-level cross-classified		
	Patient <sup>*</sup> and hospital		Patient <sup>*</sup> and surgeon		Patient <sup>*</sup> , surgeon and hospital		pital
	$\mathbf{VPC}^{\dagger}$	OR (SV) <sup>‡</sup>	$\mathbf{VPC}^{\dagger}$	OR (HV)§	$\mathbf{VPC}^{\dagger}$	OR (SV) <sup>‡</sup>	OR (HV)§
Surgeon	-	-	3.3	0.99 (0.93–1.06)	4.0	1.00 (0.00, 1.10)	0.00 (0.06 1.02)
Hospital	1.2	0.99 (0.97–1.01)	-	-	2.2	1.00 (0.90–1.10)	0.99 (0.90–1.03)

SG: Sleeve gastrectomy, VPC: Variance partition coefficient, OR: Odds ratio, SV: Surgeon volume, HV: Hospital volume.

\* The included patient characteristics were age (median centered), CCI, SES (both social and material indices), and time period.

<sup>†</sup> VPC corresponds to the percentage of variation in the outcome attributed to differences between surgeons or hospital.

‡ OR (SV) is the odds ratio of complication associated with a 10-case incremental increase of SV.

§ OR (HV) is the odds ratio of complication associated with a 10-case incremental increase of HV.

Variable	Patient & Hospital level	Patient & Surgeon level
	OR (95%CI)	OR (95%CI)
Age <sup>*</sup>	1.02(1.00-1.03)	1.02(1.00-1.03)
Sex (Male)	0.86(0.63 - 1.18)	0.86(0.62 - 1.17)
$SES^{\dagger}$ (Social) <sup>‡</sup>	1.03 (0.90 - 1.18)	1.03(0.90 - 1.18)
SES <sup>†</sup> (Material) <sup>§</sup>	$1.01 \ (0.89 - 1.14)$	1.00(0.88 - 1.14)
CCI		
≤1	0 (ref)	0 (ref)
2	1.48(0.94 - 2.31)	1.53(0.97 - 2.41)
3+	1.09(0.60 - 1.96)	1.09(0.60 - 1.96)
Time period (2010-2012)	0.60 (0.40 - 0.85)	0.66 (0.43 – 1.00)
SV (Procedure-specific)	0.99(0.93 - 1.06)	_
HV (Procedure-specific)	-	0.99(0.97 - 1.01)

Table 7. Adjusted predictors for composite complications after SG based on 2-level regression analysis

SG: Sleeve gastrectomy, OR: Odds ratio, CI: Confidence interval, SES: Socioeconomic status, CCI: Charlson comorbidity index, SV: Surgeon volume, HV: Hospital volume.

\* Age was used as a continuous variable centered at the median age in the cohort expressed in years.

<sup>†</sup> SES was obtained using ecological level data expressed by quintile of the postal code of residence of the individuals compared to the Canadian population.

‡ Social index was based on the component of the deprivation index extracted from census information for the proportion of individuals living alone, proportion of lone parent families and proportion of separated, divorced or widowed individuals.

§ Material index was based on the component of the deprivation index extracted from the average income, proportion of individuals without high school diploma and proportion of employed individuals.

## Random effect component of surgeons

#### Random effect component of institution





Each line corresponds to an intercept for each surgeon or institution in the random effect component of a model adjusted with fixed effect for age, sex, SES, CCI, surgeon's volume, hospital volume and period

Figure 8. Visual representation of random effect component of the multilevel logistic regression model for SG

#### 5.3.2 RYGB

For RYGB, a 2-level model with patient and surgeon levels revealed a VPC of 12% while controlling for HV (OR=0.86, 95%CI: 0.77-0.96) (Table 7). The opposite model including patient and hospital-level variables, revealed a VPC of 19% while controlling for SV (OR=0.82, 95%CI: 0.71-0.94). The cross-classified 3-level model accounting for differences at the patient, surgeon and hospital levels showed a VPC of 22% for inter-hospital variability and 2.5% for inter-surgeon differences (Table 7). After 3-level multivariate adjustment, both surgeon and hospital volumes were found to have non-significant ORs of 0.81 (95%CI: 0.63-1.03) and 0.98 (95%CI: 0.83-1.17), respectively (Table 7 and Figure 9).

Table 8. Multilevel regression model accounting for inter-surgeon and hospital variability after RYGB

Models	2-level		2-level		3-level	cross-classified	
	Patient	* and hospital	Patient	* and surgeon	Patient	*, surgeon and hos	pital
	$VPC^{\dagger}$	OR (SV) <sup>‡</sup>	$VPC^{\dagger}$	OR (HV)§	$\mathbf{VPC}^{\dagger}$	OR (SV) <sup>‡</sup>	OR (HV)§
Surgeon	-	-	12%	0.86 (0.77-0.96)	2.5	0.81(0.62, 1.02)	0.08(0.82, 1.17)
Hospital	19	0.82 (0.71-0.94)	-	-	22	0.01 (0.03–1.03)	0.90 (0.03-1.17)

**RYGB**: Roux-en-Y gastric bypass, **VPC**: Variance partition coefficient, **OR**: Odds ratio, **SV**: Surgeon volume, **HV**: Hospital volume.

\* The included patient characteristics were age (median centered), CCI, SES (both social and material indices), and time period.

<sup>†</sup> VPC corresponds to the percentage of variation in the outcome attributed to differences between surgeons or hospital.

‡ OR (SV) is the odds ratio of complication associated with a 10-case incremental increase of SV.

§ OR (HV) is the odds ratio of complication associated with a 10-case incremental increase of HV.

Variable	Patient & Hospital level	Patient & Surgeon level	
	OR (95%CI)	OR (95%CI)	
Age*	1.02(1.00-1.04)	1.02(1.00-1.04)	
Sex (Male)	0.81(0.52 - 1.25)	0.81 (0.53 – 1.26)	
SES <sup>†</sup> (Social) <sup>‡</sup>	1.06 (0.89 – 1.25)	1.06 (0.90 – 1.26)	
SES <sup>†</sup> (Material) <sup>§</sup>	1.09(0.91 - 1.31)	1.10(0.92 - 1.32)	
CCI			
≤1	0 (ref)	0 (ref)	
2	0.60(0.33 - 1.10)	0.61 (0.33 – 1.11)	
3+	1.24(0.51-2.97)	1.24(0.52 - 2.97)	
Time period (2010-2012)	0.82(0.57 - 1.18)	0.79 (0.53 – 1.17)	
SV (Procedure-specific)	0.82 (0.71 - 0.94)	-	
HV (Procedure-specific)	-	0.86 (0.77 – 0.96)	

Table 9. Adjusted predictors for composite complications after RYGB based on 2-level regression analysis

**RYGB**: Roux-en-Y gastric bypass, **OR**: Odds ratio, **CI**: Confidence interval, **SES**: Socioeconomic status, **CCI**: Charlson comorbidity index, **SV**: Surgeon volume, **HV**: Hospital volume.

\* Age was used as a continuous variable centered at the median age in the cohort expressed in years.

<sup>†</sup> SES was obtained using ecological level data expressed by quintile of the postal code of residence of the individuals compared to the Canadian population.

‡ Social index was based on the component of the deprivation index extracted from census information for the proportion of individuals living alone, proportion of lone parent families and proportion of separated, divorced or widowed individuals.

§ Material index was based on the component of the deprivation index extracted from the average income, proportion of individuals without high school diploma and proportion of employed individuals.

## Random effect component of surgeons

# Random effect component of institutions





Each line corresponds to an intercept for each surgeon or institution in the random effect component of a model adjusted with fixed effect for age, sex, SES, CCI, surgeon's volume, hospital volume and period

Figure 9. Visual representation of random effect component of the multilevel logistic regression model for RYGB

## **5.4** THRESHOLD ANALYSIS

### 5.4.1 SG

Thresholds for minimum number of surgeries performed per year by a surgeon to reduce postoperative complications were calculated for SG. The traditional ROC method resulted in 2 possible thresholds at 17 cases (Youden: Sensitivity 29.1%, specificity 78.9%) and 32 cases (Closest top left: Sensitivity 60.9%, specificity 42.6%). The SSLR technique also yielded 17 cases per year. As previously mentioned for stapled bariatric procedures, the ASMBS standard threshold is set at 25 cases per year. Visually, using a spline graph, there is a gradual improvement in outcomes with the higher SG volumes especially when annual SV was  $\geq$ 50 cases per year (Figure 10). The model's best fit was obtained with the 17-case threshold (AIC=1361.2) which was superior when compared to the 25-case (AIC=1366.3) and 32-case cut-off (AIC=1367.5).



Figure 10. Spline regression of composite complications based on annual SV for SG Using the 17-case threshold in an unadjusted model resulted in an OR of 0.64 (95%CI: 0.47-0.88) for the high-volume group and the composite complications. In the 2-level model accounting for patient characteristics and variability between hospitals, the adjusted OR of composite complications was 0.71 (95%CI: 0.51-1.00) for the high SV group (Table 9). For HV, the threshold obtained using traditional ROC was 139 cases with sensitivity of 50.6% and specificity of 61.3%. Visually, using splines, a visual threshold of 80 SGs is observed (Figure 11). The ASMBS standard cut-off of 50 stapling cases is also added. These various thresholds were used in the full model accounting for both patient and surgeon levels and compared based on AIC. The threshold of 139 cases per centre showed the best fit (AIC=1357.8) compared to 80 (AIC=1360.1) and 50 (AIC=1360.7).



Figure 11. Spline regression of composite complications based on annual HV for SG

The crude OR for postoperative composite complications was 0.62 (95%CI: 0.47-0.83) for the high-volume hospital group in the unadjusted model. Using the threshold of 139 cases per centre per year in the 2-level regression model accounting for patient's characteristics and surgeon's variability resulted in adjusted OR of 0.69 (95%CI: 0.49-1.00) for the high-volume institutions.

Table 10. Adjusted effect measure for surgeon and hospital volumes on composite complications after SG using dichotomous volume categories

Variable	Patient & Hospital level OR (95%CI)	Patient & Surgeon level OR (95%CI)
SV (High ≥17 cases)	0.71 (0.51 - 1.00)	-
HV (High $\geq$ 139 cases)	-	0.69(0.49 - 1.00)

SG: Sleeve gastrectomy, OR: Odds ratio, CI: Confidence interval, SV: Surgeon volume, HV: Hospital volume.

In terms of SV of RYGB, both traditional ROC and SSLR methods yielded the same threshold of 21 cases per year with a sensitivity of 69.9% and specificity of 48.8%. This threshold approximately corresponded to the inflection point on the spline graph (Figure 12). As previously mentioned in the methods, the standard cut-off set by ASMBS is 25 stapling bariatric cases annually per surgeon.



Figure 122. Spline regression of composite complications based on annual SV for RYGB

In the unadjusted model, the threshold of 21 cases per year resulted in a crude OR of 0.35 (95%CI: 0.21-0.59) for composite complications when comparing high-volume surgeons to the low-volume group. Moreover, using this threshold, 368 RYGBs were performed by high-volume surgeons and being in the high-SV category translated into an ARR of the 12.5% for the composite morbidity. In the adjusted 2-level model accounting for variation between hospital

and patient characteristics, the adjusted OR of composite complications was 0.35 (95%CI: 0.21-0.59) for the high-volume surgeons (Table 10).

The HV cut-off was calculated at 25 cases per year using the traditional ROC method with a sensitivity 57.6% and specificity of 56.6% for correctly classifying absence of composite complications. This corresponded to the approximate inflection point for composite complications on the spline curve (Figure 13). The ASMBS standard cut-off was set at 50 cases/year. I found that there was a better model fit for the 25-case cut-off (AIC=843.6) than the 50-case cut-off (AIC=847.4). However, only 2 centres exceeded the threshold of 50 RYGBs per year during the study period.



Figure 13. Spline regression of composite complications based on annual HV for RYGB

The unadjusted OR for high HV (≥25 cases per year) and composite complications was 0.57 (95%CI: 0.4-0.79). This threshold categorized 448 RYGBs to have been done in a high-volume

centre resulting in an ARR for composite morbidity of 9.5%. Using the 25-case threshold and

after adjustment in the 2-level logistic regression model accounting for patient characteristics and

variation between surgeons, the adjusted OR for composite complications was 0.63 (95%CI:

0.41-0.99).

Table 11. Adjusted effect measure for surgeon and hospital volumes on composite complications after RYGB using dichotomous volume categories

Variable	Patient & Hospital level OR (95%CI)	Patient & Surgeon level OR (95%CI)
SV (High $\geq$ 21 cases)	0.35 (0.21 - 0.59)	-
HV (High $\geq$ 25 cases)	-	0.63 (0.41 - 0.99)

RYGB: Roux-en-Y gastric bypass, OR: Odds ratio, CI: Confidence interval, SV: Surgeon volume, HV: Hospital volume.

# 5.5 SENSITIVITY ANALYSIS

For accreditation purposes, the ASMBS utilizes the number of stapled bariatric cases as a mean to account for surgical volume. 2-level logistic regression models using three various ways to define surgical volumes (procedure-specific, stapled procedure, and any bariatric procedure) were compared for SG and RYGB. Models using procedure-specific volumes had a better fit when comparing AIC for both SG and RYGB (Table 11).

Table 12. Comparison of multivariate predictive models for using various definitions of surgical volume

	Procedure-specific	Stapled procedure	Any procedure
SG			
AIC <sub>SV</sub>	1367.8	1368.2	1366
$OR_{SV} (95\% CI)^*$	0.99 (0.93 – 1.06)	1.02 (0.95 - 1.10)	1.04(0.98 - 1.10)
AIC <sub>HV</sub>	1361.1	1361.3	1361.7
$OR_{HV} (95\% CI)^{\dagger}$	0.99(0.97 - 1.01)	1.00(0.98-1.01)	1.00(0.99 - 1.02)
RYGB			
AIC <sub>SV</sub>	817.4	825.4	820.9
$OR_{SV} (95\% CI)^*$	0.82 (0.71 – 0.94)	1.01 (0.91 – 1.11)	0.96 (0.92 - 1.01)
AIC <sub>HV</sub>	824.2	831.3	828.4
$OR_{HV} (95\% CI)^{\dagger}$	0.86 (0.77 – 0.96)	1.00(0.96 - 1.04)	0.98(0.96 - 1.00)
Using the same predictors, alternative outcomes were compared. The "composite complication

outcome without mortality" showed a better fit than the "composite complication" outcome

based on AIC but with similar effect of surgical volume on the modified outcome (Table 12).

An even better fit was observed with "serious complication" outcome (Table 12). However, the

effect of surgical volume moved towards the null in RYGB with wider 95%CIs. Finally, surgical

volume was predictive of a significant decrease in the postoperative complication score as

defined by the Quebec modification of the BAR-HARM score (Table 12).

	<b>Composite</b> complication	Modified composite complication <sup>*</sup>	Serious complication	BAR-HARM score <sup>†</sup>
SG	<b>_</b>	FF		
AIC <sub>SV</sub>	1367.8	1355.5	810.5	5202.65
$OR_{SV}^{\ddagger}$	0.99 (0.93-1.06)	0.99 (0.93-1.06)	0.96 (0.87-1.06)	
RR <sub>sv</sub> §				0.88 (0.86-0.90)
$AIC_{HV}$	1361.1	1349.0	808.6	5221.43
$\mathrm{OR}_{\mathrm{HV}}^{\P}$	0.99 (0.97-1.01)	0.99 (0.97-1.02)	0.97 (0.94-1.00)	
$\mathrm{RR}_{\mathrm{HV}}^{\#}$				0.96 (0.95-0.96)
RYGB				
AIC <sub>SV</sub>	817.4	813.5	608.4	2566.84
$OR_{SV}^{\ddagger}$	0.82 (0.71-0.94)	0.81 (0.70-0.93)	0.92 (0.78-1.09)	
RR <sub>sv</sub> §				0.85 (0.81-0.91)
$AIC_{HV}$	824.2	820.7	611.8	2474.59
$\mathrm{OR}_{\mathrm{HV}}^{\P}$	0.86 (0.77-0.96)	0.86 (0.77-0.96)	0.92 (0.80-1.05)	
$\mathrm{RR}_{\mathrm{HV}}^{\#}$				0.92 (0.88-0.96)

Table 13.	Comparison	of multivariate	predictive	models for SV	′ and HV	′ using various	outcome measures
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**BAR-HARM**: Bariatric-Hospital stay, Readmission, and Mortality, SG: Sleeve gastrectomy, AIC: Akaike information criterion, SV: Surgeon volume, OR: Odds ratio, RR: Risk ratio, HV: Hospital volume, RYGB: Roux-en-Y gastric bypass.

\* Modified composite complication is defined as occurrence of any of the previously defined composite complications except for mortality.

SG: Sleeve gastrectomy, AIC: Akaike information criterion, SV: Surgeon volume, OR: Odds ratio, CI: Confidence interval, HV: Hospital volume, RYGB: Roux-en-Y gastric bypass.

<sup>\*</sup>  $OR_{SV}$  is derived from 2-level logistic regression models for composite complication outcome with a random effect for hospitals and fixed effect for patients' age, sex, CCI, SES, time period and SV in increment of 10 cases annually as defined by the group.

 $<sup>\</sup>dagger$  OR<sub>HV</sub> is derived from 2-level logistic regression models for composite complication outcome with a random effect for surgeons and fixed effect for patients' age, sex, CCI, SES, time period and HV in increment of 10 cases annually as defined by the group.

<sup>†</sup> BAR-HARM score consists of 0-10 score with a maximum of 5 points for LOS, 1 for readmission and 5 in the event of mortality was originally developed for colorectal surgery (HARM score) and was later adapted to bariatric surgery with modification of the LOS points (Appendix 5).

 $\ddagger$  OR<sub>SV</sub> is derived from 2-level logistic regression models for composite complication outcome with a random effect for hospital and fixed effect for patients' age, sex, CCI, SES, time period and SV in increment of 10 cases annually. § RR<sub>SV</sub> is derived from risk ratio associated to an increase in 10 cases of hospital procedure specific volume in a 2level linear regression models with same respective fixed and random effect components as the OR<sub>SV</sub>.

 $\P$  OR<sub>HV</sub> is derived from 2-level logistic regression models for composite complication outcome with a random effect for surgeon and fixed effect for patients' age, sex, CCI, SES, time period and HV in increment of 10 cases annually. # RR<sub>HV</sub> is derived from risk ratio associated to an increase in 10 cases of hospital procedure specific volume in a 2-level linear regression models with same respective fixed and random effect components as the OR<sub>HV</sub>.

# **6 DISCUSSION**

### 6.1 SUMMARY OF MAIN FINDINGS

#### 6.1.1 Main analysis

This population-based study confirms the safety of bariatric surgery in Quebec and within a Canadian public healthcare system with low 90-day mortality for AGB, SG, RYGB, and BPD-DS comparable to trial data(131). Given the very low occurrence of postoperative death, mortality rates could not be reliably compared between procedures.

In terms of 90-day morbidity after RYGB, our results add to the existing knowledge that hospital and surgeon's volumes are directly associated with surgical outcomes and complications. Increases in surgical volume was associated with reduction in the composite outcome when controlling for patient and hospital or surgeon-level variability. Volume thresholds were determined for both surgeons (21 cases/year) and hospitals (25 cases/year). Moreover, the use of population-level data allowed for calculation of population level effect measures. A surgeon in the high-volume group had a 12.5% absolute risk reduction for composite complications after RYGB. This estimate is not only statistically important but also underscores the clinical

significance of the volume-outcome relationship as more complications translate into prolonged LOS, additional interventions, possible transfer between institutions, and eventual increase in healthcare cost and loss of productivity at the society level.

Our results also demonstrate that using procedure-specific volume benchmarks as opposed to lumping restrictive with bypass-type procedures in one group (stapled procedures or any procedure) adds the necessary granularity to differentiate these very technically different procedures and is superior in predicting risk of postoperative complications. A surgeon whose bariatric practice primarily entails high volumes of SG but only occasional RYGB and rare BPD-DS may exhibit low risk of complications after SG but higher complication rates for the bypasstype procedures likely due to the unique technical aspects of each procedure. Moreover, dissociating the effect of SV and HV on postoperative outcomes is difficult given the strong correlation between these two variables. To address this situation, I used a multilevel regression model to isolate the effect of surgeon and hospital volume and found that a larger variance in outcomes was explained by the HV (VPC 19%) than the surgeon-level parameters (VPC 12%). However, SV showed a larger effect size on the 2-level model (accounting for patient characteristics and inter-hospital parameters) and was nearly statistically significant in the 3level model accounting also for the difference between surgeons. It therefore appears that while both parameters are important, SV may play a more vital role than HV in terms of postoperative outcomes and morbidity-profile after bariatric surgery. These findings corroborate the available literature on the subject as was already discussed in the background section of this dissertation (12, 98, 101). In addition, I found that when using procedure-specific volumes, a higher annual SV for RYGB was 18% (up to 29%) protective against occurrence of composite complications after surgery. Table 11 further highlights how procedure-specific volumes likely represent better

targets for centre/surgeon accreditation processes versus grouping bariatric surgeries into stapled procedures or even less granular fashion by treating all surgeries the same (any procedure).

On the other hand, for SG the effect of surgical volume for both surgeons and hospitals did not reveal a large influence on 90-day postoperative composite complications. While in univariate analysis, increases in both SV and HV were linked to a significant decrease in composite complications, after accounting for confounding including that from the period effect, the association disappeared. In the full model, the time period (late: 2010-2012 versus early: 2007-2009) was significantly associated with a decrease in postoperative complications after SG, which was only introduced in Quebec as a stand-alone procedure during the onset of the study period circa 2006/2007. This period effect for SG can also be seen in Figures 3 and 4 by the rise in its popularity over the years represented by increases in both SG-specific SV and HV. Therefore, calendar year in the study period represented a significant confounder to the relationship between surgical volume and outcomes. This time-period effect is likely representative of all North America or worldwide and not just Quebec, given the rise in popularity of SG as a stand-alone procedure in the mid to late 2000's. (132) Our findings differ from those of recent studies on SG volume and outcomes including the study published by Celio et al. using the Bariatric Outcomes Longitudinal Database in 2016 which reported a significant decrease in complications for surgeons performing more than 50 SGs on the year of the study (102). This study also found that SG volume was a better predictor of complications after bariatric surgery than the volume of RYGB (102). However, their study did not account for hospital level variability when looking at the volume-outcome relationship, which may bias the findings in an unknown direction from the null. Further research validating our findings with

more recent data also including metabolic outcomes are needed to assess the true difference in outcomes after SG performed by low versus high-volume surgeons or centres.

In Quebec, BPD-DS is a very common procedure. Given the lack of high-quality large studies on this procedure, it would have been interesting to perform the same procedure-specific analysis for BPD-DS. However, 97% of such cases were performed at a single institution with a very high annual surgical volume averaging 292 BPD-DS per year during the study period. Hence, the absence of a reliable/representative low-volume group did not allow for further meaningful and generalizable analyses for the BPD-DS subgroup While both RYGB and BPD-DS are bypass-type procedures and their respective technical complexities are more elaborate compared to SG or AGB, yet they are also not fully comparable and ideally should not be lumped together. Furthermore, BPD-DS is associated with greatest weight loss and remission of DM and is recommended for cases of extreme obesity (9, 133). Given the absence of information on exact BMI values in our datasets, grouping of BPD-DS patients with those from other procedures may introduce selection bias that cannot be appropriately accounted for. That said, our population-level data demonstrated that BPD-DS remains a safe procedure when performed in a high-volume centre.

### 6.1.2 Threshold analysis

Demonstrating a relationship between surgeon or institutional volumes in bariatric surgery and postoperative outcomes, although important, may not be enough to affect healthcare policies. An ideal minimal surgical case-load would be one which once implemented leads to a decrease in morbidity and mortality while maintaining beneficial outcomes. The cut-off needs to be validated in the population for which it will be used and should be realistically achievable by enough operating centres and surgeons not to unfairly decrease access to care. It would

preferably represent a value unique to each procedure, near an inflection point where lower values would have significant increase in morbidity yet higher values would only be associated to small improvement in outcomes. Several assumptions are involved in finding such a threshold. First assumption is that complication rates are strongly associated with surgical volume. Secondly, there needs to be a change in the rate of improvement in outcomes with increased surgical volumes. In other words, among higher surgical volume conditions, there should be a plateauing of the improvement in outcomes for any added increments in surgical volumes (Figure 14).



Figure 144. Optimal selection process for annual surgical volume thresholds

Similar frameworks have been advocated for accreditation standards including those suggested by the MBSAQIP (124). However, most thresholds put forth in the literature have some limitations which this study attempted to mitigate. Most studies on surgical volume-outcome relationship use arbitrary cut-offs to divide the data into groups of lower and higher volumes (11). This is done by using values from the data distribution such as median or quintiles. One of the first landmark papers on the subject by Birkmeyer et al. published in the New England Journal of Medicine in 2002 used quintiles of surgical volume to identify the effect of HV on mortality. The results found improvement in mortality outcomes with higher hospital surgical volumes for several higher-risk procedures (11). For instance, in pancreatic resection, when comparing very high (>16 cases) to very low annual volume centres (<2 cases - 20% mortality rate) there was a statistically significant adjusted mortality benefit (11). The major issue with such approach in assigning surgical volume thresholds is the lack of generalizability of the finding to other populations, given that the cut-offs chosen depended completely on the volumes seen in the study sample size as opposed to an unbiased *true* value or one that is obtained from the entire population at risk. Furthermore, when more than one procedure can be offered for the treatment of a given pathology like morbid obesity and metabolic syndrome, it is unknown which procedure would be the best intervention. Therefore, the use of median or quartiles are good means to show evidence of volume-outcome relationships but its use for changing policy or establishing benchmarks should be done with caution. Other studies have tried to use other methods in determining surgical thresholds (126). One such method uses SSLR to identify meaningful cut-offs to separate the data, which allows for minimizing loss of information from a single cut-point for surgical volumes (126, 128). In our study, the use of the SSLR technique for both SG and RYGB procedures resulted in a single cut-off for the respective SV and HV. These cut-offs also corresponded to the same volume thresholds found using a traditional ROC curve. This method was cumbersome to apply requiring multiple steps of combining values and

recalculating the associated CIs until overlap was no longer found to yield the same result as the software-based approach to the use of ROC curves.

Despite the extra attempts to identify more reliable thresholds rather than arbitrary ones, the cutoffs did tend to approach the median of surgical volumes for each procedure. This may be explained by the degree at which surgical volume truly predicts postoperative complications in an unadjusted model. In a model where surgical volume was independent of complications, the estimated volume threshold would equal the median with sensitivity of 50%, specificity of 50%, and AUC of 0.5. Therefore, the capacity of surgical volume to correctly classify a patient as having a postoperative complication or being complication-free is reflected in the ROC model. Moreover, several other patient-level factors are influential in the occurrence of postoperative complications. For RYGB procedure, the identified cut-off for SV of 21 cases/year was very close to the median SV at time of procedure of 22 cases, and HV threshold of 25 cases/year which also approximated the median of 30 cases. On the contrary, given the higher surgical volume of SG performed among various centres, the estimated thresholds were higher for HV (139 cases/year) compared to the median annual HV of 191 cases. In either scenario, our SGvolume threshold is much higher than what is recommended by ASMBS (only 50 stapled bariatric cases) (134). Looking at the distribution of the complication rate versus the institutional surgical volume, this observed difference seems to demonstrate that there might still be ongoing improvement in complication rates past the first 50 with benefits up to 150 cases/year (Figure 11). It is difficult to draw any conclusions given these higher thresholds for SG. On one hand, recommendations for various centres to perform more than 150 SG/year might limit access to surgery by decreasing the number of centres providing such services. On the other hand, the long-term success after bariatric surgery is intricately involved with the postoperative

multidisciplinary care provided and more surgeries may lower 90-day morbidity but the lack of adequate multidisciplinary support negatively impacts long-term outcomes (109). Nevertheless, I found that after adjusting for covariates and potential predictors, the influence from both surgeon and hospital SG-volumes were no longer independently associated with composite complications further minimizing the value of a meaningful threshold for SG. This example also highlights the procedure-specific approach to outcomes and assignment of meaningful threshold such as the case for RYGB as a more complex bypass-type procedure where only smaller volumes of surgery are performed in fewer centres compared to SG. Looking at the graphic distribution of postoperative complications versus annual HV of RYGB (Figure 13), one could interpret a possible continued benefit to higher HVs above 75 cases per year. However, due to the paucity of patients that would be in this category, this study does not allow for evaluation of this hypothesis. Despite an attempt to move away from arbitrary thresholds, the obtained cut-off values for SV and HV are limited by the distribution of patients and are representative of the spectrum of practice in the province of Quebec. One should therefore be careful in using these values outside of the population studied. Subsequently, minimal case volumes or thresholds derived from reliable population-level data such as those from our study may be more useful when benchmarking standards and discussing quality improvement measures and accreditation processes.

#### 6.1.3 Sensitivity analysis

The choice of a clinically relevant outcome can be a difficult one to make in population-based studies. Previous work on bariatric surgical volume used mortality as the study outcome which is difficult to use in modern day bariatric surgery given the very low postoperative death rate irrespective of procedure type (11, 12). Among possible outcomes, a definition based on ASMBS

major complications was used given its clinical relevance and availability of information in our databases (114). The goal was to maximize the sensitivity in detecting an abnormal postoperative course from individual complications such as reoperation for peritonitis or hemorrhage as well as indirect proxies for complications such as prolonged LOS or need for reintubation. In addition, I used a more restrictive aggregate endpoint in terms of postoperative complications (serious complication), which encompassed only direct codes for severe complications. Finally, a score was adapted to the local data to better capture the spectrum of complications (BAR-HARM) (118). Unfortunately, this simple score appeared to be heavily weighed on by LOS. This results in the models using this outcome predicting LOS and not complications. Sensitivity analysis performed by evaluating various outcome measures using the full 2-level models actually showed that when compared by AIC, the models showed a better fit in estimating the influence of SV and HV when serious complication was used as an aggregate outcome followed by the modified composite outcome which excluded mortality (Table 12). The influence of surgical volume (SV and HV) no longer was statistically significant for serious postoperative complications even after RYGB. This finding may be explained by the relatively small number of serious complications at 13% (N=105) compared to the more frequent composite complications. The BAR-HARM score was associated with surgical volumes for both SG and RYGB. Therefore, it appears that surgical volume is also associated with a shorter LOS. However, it is difficult to compare the model based on BAR-HARM (continuous variable) with the rest of the 3 outcome measures (dichotomous variables) given the use of linear regression versus the logistic regression, respectively.

### 6.2 EXPLAINING THE SURGICAL VOLUME-OUTCOME RELATIONSHIP

There are multiple theories that attempt to explain the relationship between surgical volume and operative complications and mortality (135, 136). In case of morbid procedures such as cardiac surgery or pancreatic and esophagus resections a mortality difference is observed among centres with different surgical volumes, and the excess mortality observed after similar complications in low-volume institutions is explained by the concept of failure to rescue (135). Complications are bound to happen despite access to the best surgeons and institutions and may depend predominantly on patient-level characteristics. However, once a given complication occurs, its prompt recognition and management may dictate the success or failure to rescue a patient from possible mortality following a severe complication. This concept of rescue following a complication is thought to be highly correlated to quality of surgical care. In a study looking at high risk cancer surgery, Ghaferi et al. found that low-volume centres did not experience significantly higher complication rates; however, their failure to rescue patients from complications was much higher and accounted for the observed differences in inter-hospital mortality (137). In bariatric surgery, given the very low postoperative mortality rates, assessment of the influence of surgical volume on failure to rescue following a complication using Quebec's population-level data was neither possible nor clinically warranted.

Beside annual SV, the cumulative surgical volume is also used as an indirect proxy for the respective skills and expertise of a bariatric surgeon. In a recent study by Doumouras et al., the cumulative volume of RYGB by Ontario surgeons was associated with shorter operative times and a decrease in all-cause morbidity even beyond 500 cases (136). The method used to assess SV in the aforementioned study partially accounts for the learning curve effect (136). A surgeon who starts performing a new procedure will initially have low volumes until enough experience

is gathered by the increasing number of cases performed transforming the provider into a highvolume surgeon. Therefore, complications occurring during the acute and early phase of the learning curve will be counted accurately as being from a low-volume surgeon. However, the effect of cumulative volume beyond the first year is not captured and may represent an unmeasured confounder in the annual volume-outcome relationship described in our study for RYGB. Aside from the cumulative experience of a surgeon, other aspects of experience are also known to have an effect on outcomes and are not capture by the databases used in our study. These include dedicated fellowship training and/or additional training which are associated with shorter learning curves and complications (138, 139). Higher surgical volumes may also be associated with different use of more challenging techniques and procedures (140, 141).

Many other processes can account for improvement in complication rates following surgery which are likely more established in higher-volume centres. Standardization of postoperative care for bariatric patients as well as implementation of evidence-based early recovery after surgery have been shown to improve clinical outcomes in several recent studies (142-144). Aside from volume objectives, these various means of improving quality of surgical care are rooted in certification and accreditation of different centres worldwide and may explain the reduction in complications observed after their implementation. Moreover, this effect was observed in a recent study using propensity score matching to compare centres of excellence to non-certified centres in Germany (145). In the matched analysis based on patient's characteristics, certified centres had less postoperative complications and mortality when compared to non-certified centres (0.43% to 0.14%, p<0.001).

This increase in standards associated to accreditation and higher volume can take many forms. In this study by Javanainen et al., the institution learning curve resulted in changes in protocol and

utilisation of resources(146). Initially, patients were heavily medicalised with ICU initial stay and maintenance of monitoring means including arterial cannula, drains and bladder catheter. Progressively, patients were de-medicalised and recovered instead on the ward with early mobilization, decreased use on intravenous medication and increased use of CPAP and incentive spirometry. The later patients, with the gain in institutional experience and increased use of ERAS interventions saw a significant decrease in pulmonary complications with OR of 0.32 (95%CI: 0.14-0.74)(146). Targets of such ERAS protocols can be numerous, however, several aspects of these protocols lack robust evidence or are extrapolated from other types of major abdominal surgery (147).

Other possible means to explain the volume-outcome relationship in surgery have been explored in other fields of medicine but not directly in the context of bariatric surgery. In a review of the subject, Mesman et al. explored the intermediary steps involved in published studies on the subject (94). Three main categories were identified: compliance to evidence-based processes of care, level of specialization and hospital level factors. Examples of increase compliance involve perioperative processes of care such as in a study from Hollenbeck B et al. which found high volume hospital to have higher rate of preoperative cardiac testing, arterial monitoring and continent diversions for cystectomy in bladder cancer. Patients in the low volume hospital had increased mortality (4.9% vs 3.5%) with 23% of the volume-effect explained by these difference in process of care measures such as prophylactic antibiotics and appropriate VTE prophylaxis with increase HV and, in a multilevel model, an association with those processes and a composite outcome for complications(149). Both these studies support the concept that part of the benefit of high-volume centers are through increase use of evidence-based processes of care.

Several studies also demonstrated decreased morbidity and mortality from surgical interventions performed by more subspecialized surgeons associated with higher volume centers in the case of hepatectomies and ovarian cancer treatments (150-152). Finally, hospital level factors was found in one study on colon cancer surgery to replace the hospital volume as the most significant predictor of post-operative mortality with OR of 0.75 (95%CI: 0.62-0.89). This predictor was defined by the presence of solid organ transplantation and cardiac surgery programs within the institution (153). The explanation for this strong association is the necessity for these centers to have access to high level intensive care unit, interventional radiology, urgent cardiac catherization and an array of medical specialist facilitating management of any complications thus rescuing the patient from its complication (153).

Despite the stated advantages of specialization of care in surgery, including bariatric surgery, it raises concerns over limiting the access to surgery by decreasing the number of hospitals allowed to provide a given service and increasing the distance needed to travel. Studies from the USA have shown that the implementation of accreditation standards did in fact not significantly affect access to care (154, 155). In a recent study from Virginia investigating the effect of distance travelled by patients, remote patients (>1 hour) did not have worse perioperative outcomes, however, they were at a higher risk for lower compliance and decreased long-term survival. Moreover, the survival difference was hypothesized to be originating from a decrease in both access to preventative medicine and comprehensive follow up after bariatric surgery (156). This study is the only one available in the literature linking distance travelled to long-term outcomes after bariatric surgery (156). This can serve as a warning for possible harm in limiting the expertise in bariatric surgery follow up for more rural locations within the province of Quebec. Possible solutions may include certifying rural bariatric centres but keeping them associated to

tertiary centres or similar to what is established in the province of Ontario, institute multidisciplinary teams in remote regions which ensure work up of patients and follow up after bariatric surgery is performed in an urban high-volume centre (142).

## 6.3 LIMITATIONS

Unfortunately, detailed information on some important variables specific to bariatric surgery and morbidly obese patients were not readily available from the obtained datasets since the data is mainly gathered for administrative and remunerative purposes. Some of these main variables are exact BMI values and weight parameters. Thus, while patients included in the study cohort clearly had BMIs greater than 40 kg/m<sup>2</sup> due to the presence of the respective billing (5513) and ICD9-CM codes, I could not fully account for the influence from various levels of obesity given that BMI is linked to both complications after bariatric surgery as well as mortality irrespective of bariatric surgery (157). It is therefore unknown if higher-volume surgeons or centres treat a different patient population with higher BMIs compared to their lower-volume counterparts. However, if such unmeasured bias was to be present, it is likely to influence the effect measures towards the null.

Bariatric surgeries captured during our study period were performed either in an open approach by laparotomy or via minimally invasive approach by laparoscopy. In terms of other minimally invasive approaches, there are no centres performing robotic bariatric surgery or endoluminal therapies for obesity treatment in Quebec. Contrary to the large incision required for open surgery, laparoscopic approach involves smaller incisions and offers the benefit of less operative pain, faster recovery and the potential for lower complications including VTEs and woundrelated adverse events (158). The billing code specific to laparoscopic approach for bariatric

surgery (5011) was introduced only midway during the study period and prior to 2010 its absence in the respective datasets did not necessarily equate with an open surgery, which would possibly introduce misclassification bias. Therefore, it was not considered as a reliable mean to classify the approaches to these procedures in this dataset. Given the association of surgical approach with postoperative complications and possibly with surgical volumes by a surgeon or a centre, the distribution of open and laparoscopic surgeries could be considered in the causal relationship between surgical volume and outcome. One hypothesis being that a low-volume surgeon might be less comfortable with the higher level of skills required for laparoscopic bariatric surgery especially in the absence of extra fellowship training and might perform more open surgeries. This would therefore mean that surgical approach as a variable does not meet the definition of a confounder since open surgery might be involved in the causal pathway by which less experienced surgeons are associated to higher complications (Figure 15). Adjusting for surgical approach would therefore control for the effect of the exposure of interest and should not be done if the goal is to assess the effect along this causal pathway.





Additionally, given the nature of administrative datasets, there is risk of misclassification of exposure, outcomes and covariates due to inaccurate coding of diagnosis and/or billing information. Regarding exposure, given the completeness of the billing information for Quebec surgeons, annual surgical volumes are very accurate. However, some cases may not be captured via the usual billing codes. In the event of a surgery surpassing 4 hours in anesthesia time, a surgeon may decide to cite other codes that would not allow for differentiation of the specific bariatric procedure performed. This would include cases more likely to be complex or associated with intraoperative complications. Covariates are also subject to misclassification with sensitivity of administrative database varying widely depending on the diagnosis. Some important and prevalent comorbidities associated with morbidly obese patients such as obstructive sleep apnea, are not reliably derived from administrative datasets. Several scores exist to help predict the influence of comorbidities on overall survival in either disease-specific fashion such as the Ranson Criteria in pancreatitis, or a general portray of comorbidity status such as CCI. The CCI is by far the most widely used in the literature since its publication in 1987 (159). The main advantage of this scoring system is that it is not unique to a specific disease state and has been validated in several patient populations (160-163). Most importantly, CCI has also been widely used as a means to account for baseline comorbidities in studies using administrative dataset (164, 165). Various methods have been investigated to extract the information used to calculate the score using ICD9-CM codes from large administrative datasets. Two popular examples are the codes derived from Deyo et al. and Dartmouth Manitoba (121, 166, 167). Deyo et al. adapted the CCI index to a study cohort of Medicare patient undergoing lumbar spine surgery and similar to the original chart-based CCI score, patients with higher scores had higher in-hospital complications, LOS and 6-week mortality (121). In a study using

the same RAMQ datasets as the ones used in our study, Wilchesky et al. validated Deyo's approach in obtaining CCI scores by cross-validation with the information obtained from chart reviews of 14,980 patients (168). They demonstrated high specificity on all 18 disease conditions included in CCI when cross-linked data from RAMQ's medical services claims and physician billing information over a 1-year period were used (168). Sensitivity for identifying individual conditions was low varying between 8.7 %-11.24% in case of hemiplegia but up to 62.6%-65.56% for DM. However, the aggregate CCI score was a perfect match in 44% of patients and within 1 point in over 70% of cases when using the administrative datasets compared to the chart review (168). An important finding was the use of both medical services and physician billings, improved the accuracy of the score over using billing information alone. Therefore, this approach was used in our study and was even supplemented by cross linkage of data with yet another dataset from MSSS which includes hospital discharge summaries and procedure notes, in order to increase accuracy. Furthermore, CCI is also validated in administrative databases using ICD10 diagnostic codes. Stavem et al., found a high correlation between CCI score derived using ICD10 codes and that from individual chart reviews which reliably predicted 30-day and 1-year mortality in patient admitted to the ICU (165). However, in the field of bariatric surgery, CCI has not been evaluated very well. Moreover, there are limited studies validating the use of CCI as a predictor of mortality after bariatric surgery. In a study from Australia published in 2007, the authors used administrative data on 12,062 patients having undergone bariatric surgery to assess postoperative complications and mortality (169). In a multivariate logistic regression, CCI was shown as an independent predictor of both mortality and complications. The relative contribution of CCI was small however, and only accounted for 5.3% of the variability in the model (169).

Another technique to assess the effect of comorbidities using population-level administrative datasets in a disease-specific context is the use of Elixhauser comorbidity analysis (170). This technique first published in 1998 by Elixhauser et al., uses ICD9-CM codes to identify 30 comorbidity variables associated with prolonged LOS and mortality in general hospital patient population (170). In another study published in 2007, a bariatric-specific predictive model using Elixhauser comorbidity analysis was developed using the National Hospital Discharge Survey as the training dataset and the National Inpatient Survey as the validation dataset for the proposed model (171). Using a logistic regression model for occurrence of the outcome (morbidity and mortality) and via a backward selection process, 6 variables were included in the predictive model including age, sex (male), anemia, complicated DM, CPD, HTN and depression. This limited model (Elixhauser method) performed superior to CCI in predicting postoperative mortality and demonstrated a higher C-Index of 0.72 compared to CCI (0.52) (171). However, there are several limitations in the methodology used in the aforementioned study both in variable selection process in the construction of the model as well as the assessment of the model's fitness. Moreover, their study did not propose a formal score rather provided a list of covariates that should be included in survival models in order to appropriately risk-adjust for baseline comorbidities in patients after bariatric surgery.

Proper recording of outcomes is also at risk of misclassification when large datasets are studied. The main advantage of using the RAMQ database is accurate recording of vital statistics and administrative type information such as LOS or transfer to other institutions. When possible, validated ICD9-CM/10 codes were used to detect complications such as acute respiratory infections (172). Moreover, I used aggregate complications such as composite or serious complications in order to increase the accuracy to detect the desired study outcome.

Furthermore, as previously discussed in the background section, SES can have a significant role in the obesity epidemic as well as postoperative compliance and complications after bariatric surgery. In our study, while in the full multilevel logistic regression models, I attempted to account for SES, the respective detailed information on patients' material and social factors was not available from the datasets. Ecological data was therefore applied to each patient using the Deprivation Index as explained in the methodology section, which may expose this covariate to the ecological fallacy with the assumption that all individuals within a region have the same SES which may not be accurate.

Finally, there are also statistical limitations to the analysis performed. Several of the more complex multilevel analyses yielded random effects of zero. These models were tested both in STATA and R using the *lme4* package and yielded similar results. Models with random effect variance of zero are coined: "Singular models". Several causes are known to result in such a problem with multilevel models. The most common, and most likely cause in our study, is a small number of random effect levels. For instance, in the model used for BPD-DS, only 4 centres account for HVs with 1 of them accounting for 97% of all surgeries performed, hence the reason why I refrained from carrying out the respective procedure-specific analysis. In such a context, the paucity of data points in various combinations makes the estimation of a random effect to address the variance between the different centres impossible. This yields a value of zero i.e. a singular model. There are several suggested means to address singular models proposed in the literature. After identification, one can simply drop the covariate and the level, include the level as a fixed effect categorical variable, or even use a weakly informative prior to run a Bayesian model and obtain an *a posteriori* estimate of the effect (173-175). I utilized these approaches as exploratory analyses. However, one should carefully use these techniques as they

might result in overfitting of models. Our results should therefore be carefully interpreted. In the more robust scenarios, where model singularity was not an issue, the Bayesian approach to multilevel modelling resulted in similar estimates of random effect variance and fixed-effect coefficients.

# 7 CONCLUSION

Annual surgeon and hospital surgical volumes are significant predictors of short-term complications 90 days after RYGB. However, a similar association was not identified for the SG after accounting for the period effect and patient characteristics. Our study supports the establishment of minimum procedure-specific volume requirements for more complex (bypasstype) bariatric surgeries like RYGB. However, the role of volume targets for SG remains unclear. Future research on the subject should aim at understanding the intermediate between higher surgical volumes and better outcome with the aim of improving quality of surgical care independent of the surgical volumes performed. At both surgeon and institutional levels, local data collection and quality improvement programs should aim at identifying short comings of a given program and address them through training, implementation of care pathways and close collaboration with expert centres regardless of the surgical volumes.

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## 9.1 APPENDIX 1 - RAMQ PROCEDURE CODES FOR BARIATRIC SURGERY

RAMQ Code	Type of surgery
5305	AGB
5355	SG
5114*	Partial or subtotal gastrectomy with or
	without vagotomy
5306	RYGB
5308	BPD-DS

**RAMQ**: Régie d'assurance maladie du Québec; **AGB**: Adjustable gastric band; **SG**: sleeve gastrectomy; **RYGB**: Roux-en-Y gastric bypass; **BPD-DS**: Biliopancreatic diversion with duodenal switch. \*Prior to 2010, the billing code 5114 was also used for SG, this code was subsequently replaced with 5355 exclusively for SG procedure in treatment of morbid obesity. As a result, to increase our detection of SG before 2010, 5114 billing code was included for data extraction.

## 9.2 APPENDIX 2 - EXCLUSION CRITERIA

If the following code was present in the year prior to index case

ICD9-CM diagnostic code	Description
151	Malignant neoplasm of stomach
1510	Malignant neoplasm of cardia
1511	Malignant neoplasm of pylorus
1512	Malignant neoplasm of pyloric antrum
1513	Malignant neoplasm of fundus of stomach
1514	Malignant neoplasm of body of stomach
1515	Malignant neoplasm of lesser curvature of stomach, unspecified
1516	Malignant neoplasm of greater curvature of stomach, unspecified
1518	Malignant neoplasm of other specified sites of stomach
1519	Malignant neoplasm of stomach, unspecified site
2111	Benign neoplasm of stomach
2302	Carcinoma in situ of stomach
2352	Neoplasm of uncertain behavior of stomach, intestines, and rectum

## 9.3 APPENDIX 3 - EXCLUSION CRITERIA - NON MALIGNANT

If the following code was associated to the index procedure

Category	ICD9-CM	Description		
	151	Malignant neoplasia stomach		
	152	Malignant neoplasia duodenum		
	1469	Malignant oropharynx		
	1509	Malignant neoplasm of esophagus, unspecified site		
	1510	Malignant neoplasm of cardia		
	1511	Malignant neoplasm of pylorus		
	1512	Malignant neoplasm of pyloric antrum		
	1513	Malignant neoplasm of fundus of stomach		
	1514	Malignant neoplasm of body of stomach		
	1515	Malignant neoplasm of lesser curvature of stomach, unspecified		
	1516	Malignant neoplasm of greater curvature of stomach, unspecified		
	1518	Malignant neoplasm of other specified sites of stomach		
	1519	Malignant neoplasm of stomach, unspecified site		
	1520	Malignant neoplasm of duodenum		
	1528	Malignant neoplasm of other specified sites of small intestine		
	1529	Malignant neoplasm of small intestine, unspecified site		
	1531	Malignant neoplasm of transverse colon		
	1532	Malignant neoplasm of descending colon		
	1533	Malignant neoplasm of sigmoid colon		
	1534	Malignant neoplasm of cecum		
Malignancy	1536	Malignant neoplasm of ascending colon		
	1538	Malignant neoplasm of other specified sites of large intestine		
	1539	Malignant neoplasm of colon, unspecified site		
	1540	Malignant neoplasm of rectosigmoid junction		
	1541	Malignant neoplasm of rectum		
	1549	Tumeur maligne rectum, jonction recto-sigmoïdienne, anus - sans précision		
	1552	Malignant neoplasm of liver not specified as primary or secondary		
	1559	Tumeur maligne du foie et des voies biliaires intrahépatiques - sans précision		
	1569	Malignant neoplasm of biliary tract, part unspecified site		
	1570	Malignant neoplasm of head of pancreas		
	1571	Malignant neoplasm of body of pancreas		
	1572	Malignant neoplasm of tail of pancreas		
	1579	Malignant neoplasm of pancreas, part unspecified		
	1598	Malignant neoplasm of other sites of digestive system and intra- abdominal organs		
	1599	Malignant neoplasm of ill-defined sites within the digestive organs and peritoneum		
	1629	Malignant neoplasm of bronchus and lung, unspecified		
	1639	Malignant neoplasm of pleura, unspecified		
	1719	Malignant neoplasm of connective and other soft tissue, site unspecified		
	1739	Unspecified malignant neoplasm of skin, site unspecified		
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	1809	Malignant neoplasm of cervix uteri, unspecified site		
	1820	Malignant neoplasm of corpus uteri, except isthmus		
	1830	Malignant neoplasm of ovary		
	1849	Malignant neoplasm of female genital organ, site unspecified		
	1872	Malignant neoplasm of glans penis		
	1889	Malignant neoplasm of bladder, part unspecified		
	1890	Malignant neoplasm of kidney, except pelvis		
	1952	Malignant neoplasm of abdomen		
	1975	Secondary malignant neoplasm of large intestine and rectum		
	1976	Secondary malignant neoplasm of retroperitoneum and peritoneum		
	1977	Malignant neoplasm of liver, secondary		
	1990	Disseminated malignant neoplasm without specification of site		
	1991	Other malignant neoplasm without specification of site		
	2008	Other named variants of lymphosarcoma and reticulosarcoma, unspecified site, extranodal and solid organ sites		
	2019	Hodgkin's disease, unspecified type, unspecified site, extranodal and solid organ sites		
	2028	Other malignant lymphomas, unspecified site, extranodal and solid organ sites		
	2029	Other and unspecified malignant neoplasms of lymphoid and histiocytic tissue, unspecified site, extranodal and solid organ sites		
	2302	Carcinoma in situ of stomach		
	2303	Carcinoma in situ of colon		
	2352	Neoplasm of uncertain behavior of stomach, intestines, and rectum		
	2355	Neoplasm of uncertain behavior of other and unspecified digestive organs		
	2389	Neoplasm of uncertain behavior, site unspecified		
	2390	Neoplasm of unspecified nature of digestive system		
	2398	Neoplasms of unspecified nature, other specified sites		
	2399	Neoplasm of unspecified nature, site unspecified		
	1578	Tumeur maligne du pancréas - autres		
	5642	Postgastric surgery syndromes		
	5792	Blind loop syndrome		
	6869	Unspecified local infection of skin and subcutaneous tissue		
	7832	Loss of weight		
Complication of surgery	9583	Infection post-traumatique d'une plaie, non classée ailleurs		
	9609	Intoxication par antibiotiques - sans précision		
	9982	Perf.ou déchirure acc.relative à intervention chirurgicale sf 6206-996- 664-665		
	9986	Fistule postopératoire persistante		
	9989	Compl.dues à des actes chirurgicaux, sai, non cl.aill.sauf 6694		
	5602	Volvulus		
GI disorder	5603	Impaction of intestine, unspecified		
	5609	Unspecified intestinal obstruction		

	5621	Diverticulosis of colon (without mention of hemorrhage)		
	5641	Irritable bowel syndrome		
	5651	Anal fistula		
	5690	Anal and rectal polyp		
	5692	Stenosis of rectum and anus		
	5694	Other specified disorders of rectum and anus		
	5718	Other chronic nonalcoholic liver disease		
	5733	Hepatitis, unspecified		
	2859	Anemia, unspecified		
	2879	Unspecified hemorrhagic conditions		
Hemorrhage	4590	Hemorrhage, unspecified		
	5780	Hematemesis		
	5789	Hemorrhage of gastrointestinal tract, unspecified		
	5770	Acute pancreatitis		
Pancreatic diagnosis	5771	Chronic pancreatitis		
	5772	Cyst and pseudocyst of pancreas		
	5400	Acute appendicitis with generalized peritonitis		
	5409	Acute appendicitis without mention of peritonitis		
Peritonitis	5672	Peritonitis (acute) generalized		
	5679	Unspecified peritonitis		
	5689	Unspecified disorder of peritoneum		
	8659	Traumatisme de la rate - sans précision		
	8691	Internal injury to unspecified or ill-defined organs with open wound into cavity		
Trauma	8798	Open wound(s) (multiple) of unspecified site(s), without mention of complication		
	9598	Traum.aut.et sai aut.local.précis., y compris local.mult. sauf 9590-9597		
	9599	Traumatismes, autres et sans précision, localisation non précisée		
	5310	Acute gastric ulcer with hemorrhage, without mention of obstruction		
	5311	Acute gastric ulcer with perforation, without mention of obstruction		
	5312	Acute gastric ulcer with hemorrhage and perforation, without mention of obstruction		
	5313	Acute gastric ulcer without mention of hemorrhage or perforation, without mention of obstruction		
	5314	Chronic or unspecified gastric ulcer with hemorrhage, without mention of obstruction		
Ulcer diasease	5315	Chronic or unspecified gastric ulcer with perforation, without mention of obstruction		
	5317	Chronic gastric ulcer without mention of hemorrhage or perforation, without mention of obstruction		
	5319	Gastric ulcer, unspecified as acute or chronic, without mention of hemorrhage or perforation, without mention of obstruction		
	5320	Acute duodenal ulcer with hemorrhage, without mention of obstruction		
	5321	Acute duodenal ulcer with perforation, without mention of obstruction		
	5324	Chronic or unspecified duodenal ulcer with hemorrhage, without mention of obstruction		

	5325	Chronic or unspecified duodenal ulcer with perforation, without	
	5327	Chronic duodenal ulcer without mention of hemorrhage or perforation, without mention of obstruction	
	5329	Duodenal ulcer, unspecified as acute or chronic, without hemorrhage or perforation, without mention of obstruction	
	5331	Acute peptic ulcer of unspecified site with perforation, without mention of obstruction	
	5334	Chronic or unspecified peptic ulcer of unspecified site with hemorrhage, without mention of obstruction	
	5339	Peptic ulcer of unspecified site, unspecified as acute or chronic, without mention of hemorrhage or perforation, without mention of obstruction	
	5349	Gastrojejunal ulcer, unspecified as acute or chronic, without mention of hemorrhage or perforation, without mention of obstruction	
	5350	Acute gastritis, without mention of hemorrhage	
	5354	Other specified gastritis, without mention of hemorrhage	
	5355	Unspecified gastritis and gastroduodenitis, without mention of hemorrhage	
	5359	Gastrite et duodénite - sans précision	
	5360	Achlorhydria	
	5368	Dyspepsia and other specified disorders of function of stomach	
	5369	Unspecified functional disorder of stomach	
	5370	Acquired hypertrophic pyloric stenosis	
	5373	Other obstruction of duodenum	
	5374	Fistula of stomach or duodenum	
Upper GI disorder	5378	Other specified disorders of stomach and duodenum	
	5379	Unspecified disorder of stomach and duodenum	
	5589	Other and unspecified noninfectious gastroenteritis and colitis	
	7505	Congenital hypertrophic pyloric stenosis	
	7507	Other specified anomalies of stomach	
	7508	Other specified anomalies of upper alimentary tract	
	7519	Unspecified anomaly of digestive system	

# 9.4 APPENDIX 4 - OUTCOME DEFINITIONS

Condition	ICD-9 diagnosis	ICD-10 diagnosis	Billing code (RAMQ)	Description
Shock	7855			Shock, non-traumatic
		T81.1		Postoperative shock
		R57.2		Septic Shock
		R57.1		Hypovolemic shock
Dialysis	V451			Post-operative hemodialysis
		Z49.X		Care involving dialysis

			15041-15047,	Hemodialysis (if not previously
DE	41 8 37		15722	present pre-op)
PE	415.X	126.X		Pulmonary embolism
Stroke	434.X, 436.X	I63.X, I64		Cerebral infarction
Acute MI	410.X	I21, I22		Acute Myocardial infarction
			4601-4607, 4611, 4612, 4022, 4608	Coronary artery bypass grafting
			9302, 20520, 20523	intervention
Cardiac complications	997.1			Complications cardiaques, sauf 4294
(includes MI)		I46		Cardiac arrest
Intubation			900	Care of ventilated patient
			182, 912, 926, 927, 928, 940,	Supplement for intubated patient
			990, 991, 9362, 15231, 15696, 15756, 15757, 41029, 41030	(presence of code after a grace period of 1 day post op or 1 day without intubation codes)
Ventilation >48h				Intubation code >2 consecutive days
Hemorrhage	998.1	T81.0		Hemorrhage and hematoma complicating a procedure
Postoperative Infection / leak	998.5			Infection postopératoire, sauf 9993-6743-9966
	567.X	K65.X		Peritonitis
		T81.4		Infection following a procedure
		T81.83		Post operative leak
			1005	Incision et drainage d'un abcès
			5080	Drainage abces sous-phrenique ou intra-abdominal
			5084	Drainage d'abcès de la paroi abdominale
DVT	451.X, 453.X	I80.1-9		Deep venous thrombosis (upper and lower limbs)
Pneumonia	997.3; 481-2; 482.0-4;	J13, J14, J15.X, J18.X, J69.0		Pneumonia

	482.8-9;	
	485-6	
Reintervention		
(Endoscopy)		
Reintervention		See specific tables
(Radiology)		
Reoperation		

# Reoperation

Billing code	Description
5010	Diagnostic laparoscopy
5077	Diagnostic laparotomy
5080	Sub-diaphragmatic, intraabdominal abscess drainage
5084	Abdominal wall abscess drainage
5054, 5462, 5471, 5488, 5469, 5466, 5459, 5460,	Various hernia repair codes
5287, 5224, 5521	Esophagectomy
5357	Repair of esophageal rupture
5023	Gastrostomy or duodenostomy
5114	Partial gastrectomy
5205, 4235, 4250, 4166, 4251	Splenectomy and splenic repairs
5527	Gastric band removal
5373, 5375, 5376	Revision or repair of gastro-enterostomy
5027, 5238, 5029, 5038, 5030	Ileostomy or colostomy creation
5090, 5039	Bowel anastomosis
5136, 5165, 5166, 5140,	
5152, 5141, 5142, 5154,	Bowel resection with or without anastomosis
5164, 5231	
5389, 5387	Primary repair of bowel injury
5384, 5385, 8386	Bowel obstruction

# **Reintervention (Endoscopy)**

Billing code	Description
Post operative day 1 and beyon	d
691	Diagnostic upper endoscopy
Post operative day 0 and beyon	d
20135	Diagnostic upper endoscopy in ICU or acute care setting
874	Therapeutic endoscopy (dilation, polyp, hemostatic control,
	and other techniques)
562	Endoscopic dilation of stenosis under fluoroscopy

390	Percutaneous endoscopic gastrostomy
304	Endoscopic feeding tube placement
548	Esophageal stent placement
20040	Rigid esophagoscopy
692, 9337	Other endoscopy (ERCP, etc.)

#### **Reintervention (Radiology)**

Billing code	Description
9436, 9437, 9438, 9355	Angioembolization for bleeding, pseudoaneurysm coiling
9446	Embolectomy
9448	Inferior vena cava filter placement (check valeu)
435, 9449, 9450, 9451, 9452,	Various biliary interventions
9453, 9454, 9455,	
9456, 9457	Percutaneous gastrostomy and enterostomy
9458, 416, 854	Percutaneous nephrostomy and double J
9472, 20075, 9474	Percutaneous drainage catheter placement

### **Unplanned ICU admission:**

## ICU stay of more than 2 days (MSSS data). The MSSS data does not allow to date the ICU stay within the dates of the admission. The issues with this variable are patients kept in ICU post operatively for observation given other comorbidities. This would count as complication however could still be "planned". With this limitation acknowledged, >48h in ICU would be considered abnormal hence counted as "unplanned ICU admission"

#### **Composite outcome**

Presence of any of the following complications:

- 1. Bleeding,
- 2. VTE,
- 3. Pneumonia,
- 4. Acute MI,
- 5. AKI requiring dialysis,
- 6. Abdominal sepsis / leak
- 7. Stroke,
- 8. Shock,

- 9. Unplanned reintubation,
- 10. Prolonged ventilation (>48h),
- 11. Prolonged hospitalisation,
- 12. Reoperation,
- 13. Mortality.

### Serious outcome

Presence of any of the following complications:
1. ICU admission
2. Shock
3. AKI requiring dialysis
4. VTE
5. Acute MI
6. Reintubation
7. Mortality

## 9.5 APPENDIX 5 - QC-BAR-HARM SCORE

## Length of stay categories

LOS Categories	Original HARM score	BAR-HARM score	Based on Quebec data (Qc-BAR-HARM)
		Days	
0	1-3	<1	0
1	4	1	1
2	5	2	2
3	6	3	3
4	7-8	4-8	4-5
5	+9	+9	+6

#### Score calculation

Score = LOS (0 - 5) + discharge status  $(0 - 1) \ge 5$  + readmission (0 - 1)

Where:

- LOS is the category of length of stay
- Discharge status is dead (1) or alive (0)

• Readmission, yes (1) or no (0)

## Distribution of score across patients





# 9.6 APPENDIX 6 - ICD AND BILLING CODE USED FOR IDENTIFICATION OF

#### COVARIATE

Condition	ICD9-CM diagnosis	ICD10 diagnosis	Billing code (RAMQ)	Description
Diabetes	250.0– 250.9*	E0800 – E139		Diabetes mellitus

	-	-	343, 20534	Initiation or verification of diabetes treatment
	-	-	16030	Visit, non insulin dependent type II diabetic
	-	-	9329	Visit, verification insulin therapy
Hypertension	401.0– 401.9*	I10, I11.1- I13.x, I15.X	-	Hypertension
Dyslipidemia	272.0- 272.4	E7800, E7801 ,E781-5	-	Hypercholesterolemia and related disease
Obstructive sleep apnea	786.0, 786.9	-	-	Symptoms from respiratory system and thorax
(OSA)	-	G4730, G4733, G4736	-	Sleep apnea unspecified, obstructive or from other condition
NACII	-	-	8472, 8475	Sleep study
NASH	571.5	-	-	mention of alcohol
	571.8	-	-	alcoholic
	-	K7581	-	Nonalcoholic steatohepatitis (NASH)
GERD	530, 530.1	-	-	Esophageal disease, esophagitis unspecified
	-	K210, K219	-	disease with / without esophagitis
	-	-	-	and Proton pump inhibitors)
Smoking	-	Z72.0, Z87.891, F17, O99.3	-	Various Tobacco use or nicotine dependency
	-	-	15161	Billing for smoking cessation counselling
Anemia	280.1- 281.9, 285.9	D50.8, D50.9, D51.x- D53.x	-	Deficiency anemia
Depression	300.4, 301.1, 309.0, 309.1, 311	F20.4, F31.3- F31.5, F32.x, F33.x, F34.1,	-	Depression

		F41.2, F43.2		
Chronic pulmonary disease	490–492.8, 493.00– 493.91, 494.x– 505.x, 506.4	I27.8, I27.9, J40.x–J47.x, J60.x–J67.x, J68.4, J70.1, J70.3		Chronic pulmonary disease (Elixhauser definition)
Chronic kidney disease on dialysis	V451	Z49.X		Post-operative hemodialysis Care involving dialysis
			15041-15047, 15722	Hemodialysis