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Association between Severity of Obstructive Sleep Apnea and Health Care Utilization

by

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Abstract

Background: Patients with Obstructive Sleep Apnea (OSA) are suspected of being a heavy burden on health care resources. The purpose of this study was to determine the association between OSA severity and health care utilization. Predictors of increased health care utilization were also identified.

Subjects and Methods: A retrospective cohort study was conducted on patients referred for sleep testing from July 2005 to August 2007. Health care use prior to testing was determined from Alberta Health and Wellness administrative databases. Rates of health resource use were measured using negative binomial regression, with predictors of increased health care use determined using logistic regression.

Results: Among the 2149 subjects, OSA severity was not associated with health care utilization. Physician visits, hospitalizations, length of stay and emergency room visits were high amongst all OSA severity categories. Predictors of increased health care use included excessive sleepiness, age, sex, and desaturation profile.

Conclusions: Patients with OSA utilize a substantial amount of health care resources, although severity of OSA was not associated with increased health care use.

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Dedication

To my beautiful wife and best friend, Vanessa, who has always encouraged me to pursue my dreams. Your constant love and enthusiasm was key to the completion of this project.

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List of Abbreviations and Nomenclature

Abbreviations	Definition
AHCIP	Alberta Health Insurance Plan
AHI	Apnea-Hypopnea Index
BMI	Body Mass Index
CI	Confidence Interval
CIHI	Canadian Institute for Health Information
COPD	Chronic Obstructive Pulmonary Disease
CPAP	Continuous Positive Airway Pressure
ESS	Epworth Sleepiness Scale
ICD	International Classification of Diseases
IQR	Inter-quartile Range
OR	Odds Ratio
OSA	Obstructive Sleep Apnea
PHN	Provincial Health Number
PSG	Polysomnography
RCMP	Royal Canadian Mounted Police
RDI	Respiratory Disturbance Index
RR	Rate Ratio
SE	Standard Error

BACKGROUND

1.1. Obstructive Sleep Apnea:

Obstructive Sleep Apnea (OSA) is the most common sleep disorder with a prevalence of 24% among males and 9% among females (1). OSA is a condition characterized by repetitive periods of cessation of breathing during sleep, followed by arousal from sleep. This disorder is associated with excessive daytime sleepiness in 4% of males and 2% of women (1-3). It is also associated with an increased risk of depression and cardiovascular disorders such as hypertension, heart failure, arrhythmias, heart disease, and stroke (4-9). Because of the associated co-morbidities, OSA patients are believed to be heavy users of health care resources. Unfortunately, little research has been done to effectively assess this claim.

Obstructive sleep apnea can be effectively treated with continuous positive airway pressure (CPAP); however, this incurs a fixed cost for the initial diagnostic testing and subsequent treatment. Given the high prevalence of disease in the normal population, diagnosis and treatment of all patients with OSA would be extremely costly and unnecessary. In order to control costs, most jurisdictions have placed arbitrary limits on both access to diagnostic testing as well as CPAP funding. This results in no funding, unacceptably long waiting times, and inappropriate allocation of resources (10). Thus, the ability to identify patients with clinically relevant sequelae or increased health care utilization would allow health care planners to more effectively target funding towards 'at risk' patients.

1.2. Prevalence of OSA:

The prevalence of OSA is 24% among males and 9% among females (1). Despite the relatively high prevalence, approximately 80% of men and women with moderate to severe sleep apnea remain undiagnosed (11-14). Therefore the population prevalence of OSA is likely to be even higher. This is partly due to the fact that most family physicians are not trained in sleep medicine and routine assessment of sleep quality seldom occurs in the office setting.

Obesity has been well established as a risk factor for OSA in multiple population-based studies (1, 15, 16). It is estimated that more than half of the prevalence of OSA is attributable to excess body weight (15,16). In the United States in 2004, the estimated prevalence of adult obesity, as defined by a body mass index (BMI) $> 30 \text{ kg/m}^2$, was more than 30% (17). Associated health expenditures in obese individuals are 36% greater than people with normal body weights and approximately 7% of annual health expenditures in North America are related to obesity (18, 19). This is due to the increase in obesity related medical conditions such as diabetes mellitus and cardiovascular disease. In parallel, OSA has also been associated with a number of adverse health conditions including depression, hypertension, and diabetes (4-9, 20).

1.3. OSA and Associated Morbidity:

Published evidence suggests that patients with OSA experience increased morbidity (4-9). If left untreated, OSA may lead to a number of adverse consequences including cardiovascular disease (hypertension, heart failure, and arrhythmias), motor-vehicle accidents, and depression (4-9, 20, 21). A multi-center prospective cohort study

demonstrated that OSA was a risk factor for the development of systemic hypertension (6). This was the first study to show an association between OSA and high blood pressure. It was shown that moderate to severe OSA had an odds ratio (OR) for hypertension of 1.37 ($p=0.005$) after controlling for BMI, neck circumference, alcohol intake, smoking and gender. Further community-based studies have shown similar results (7, 9). A prospective analysis of the Wisconsin Sleep Cohort showed that an even slightly elevated Apnea-Hypopnea Index (AHI), ($0 < \text{AHI} < 5$ events per hour) was associated with a 42% (95% Confidence Interval (CI): 13, 78%) increased odds of developing hypertension over a 4-year follow-up period (7). Furthermore, a dose-response relationship was observed for more severe categories of OSA, with an odds ratio of 2.9 (95% CI: 1.5, 5.6) for an AHI of 15 or greater versus an AHI of zero events per hour.

OSA is also associated with cardiovascular outcomes including myocardial infarction and stroke. Case-control studies of patients assessed for OSA after myocardial infarction (MI) support an association between the two conditions, with an odds ratio ranging from 4.1 to 4.5 in men and women (22-24). A cross-sectional study on a large Spanish cohort referred to a sleep clinic showed that untreated patients with severe OSA had a significantly increased risk of fatal (OR: 2.87, 95% CI: 1.17, 7.51) and non-fatal (OR: 3.17, 95% CI: 1.12, 7.51) cardiovascular events compared to healthy participants (4). An additional study by Yaggi et al. also reported an association between severe OSA and a composite end point of stroke or death (5). After adjusting for patient demographics, smoking status, alcohol consumption and underlying co-morbidity, OSA patients were at increased risk of the development of this endpoint (Hazard Ratio, 1.97; 95% CI: 1.12, 3.48) compared to a control group with no OSA.

Untreated OSA has also been associated with increased motor vehicle accidents (21). The Wisconsin Sleep Cohort Study showed that patients with untreated OSA were three times more likely to be involved in a motor vehicle accident than population-based controls. Many studies have also found an association between depression and OSA (8, 25-28). Clinical studies have noted that depression is very prevalent among patients with OSA (approximately 20%) and some researchers believe increased health care use among OSA patients may be driven by underlying depression, rather than OSA alone (29).

Recently, cross-sectional associations have been reported between OSA and insulin resistance and glucose intolerance (20, 30-33). This relationship was independent of age and body mass index. A cross-sectional and longitudinal analysis in 1,387 participants of the Wisconsin Sleep Cohort showed that there was a greater prevalence of diabetes (as defined by physician diagnosis or a fasting glucose $\geq 126\text{mg/dl}$) in subjects with increasing levels of sleep-disordered breathing. The odds for having a physician diagnosis of diabetes mellitus with an AHI ≥ 15 events per hour versus an AHI < 5 events per hour was 2.30 (95% CI: 1.28, 4.11). Though not statistically significant, the odds of developing diabetes within a four-year period were 1.62 (95% CI: 0.67, 3.65) after adjusting for age, sex and body habitus (20).

1.4. An Overview of Health Care Utilization:

Health care utilization is commonly measured by health care consumed. This broad term often encompasses hospital stays, emergency department contacts, general practitioner contacts, specialist physician contacts, and other types of services within and outside the formal health care system. Health care use can be measured in a number of

ways (34). Two of the most common forms of measurement are self-reported health care utilization and the use of provincial administrative databases. Self-report of health care utilization is often collected through questionnaires, interviews or surveys. The most widely and readily available sources of self-reported health care utilization in Canada are national health surveys such as the National Population Health Survey or Canadian Community Health Survey (35). Survey data has its advantages in that they are easy to conduct and are relatively inexpensive. However, if data is required at a population level, the associated cost may be considerable. In addition, response rates to surveys decrease as the amount of information asked of a participant increases. This can be a limiting factor in the amount of information collected (36).

Secondly, health care utilization can be measured through the use of provincial administrative databases. These include individual patient level linkable information about health services related to physician claims for services, ambulatory care visits, as well as hospitalizations. Administrative data are a potentially valuable tool for chronic disease surveillance. They are relatively easy to access and process, significantly reduce the cost and time involved in primary data collection, and allow researchers to access population-based data that can be used to monitor a variety of diseases. Administrative data can also provide both cross-sectional and longitudinal information about disease prevalence and incidence for entire populations. However, because administrative data are collected for purposes of health system management and provider payment and not for chronic disease surveillance, it is important to assess their validity for the latter purpose. Issues of consistency and completeness continue to be one disadvantage

pertaining to administrative data. Fortunately, data quality continues to improve and subsequently, its use for health surveillance in Alberta continues to increase.

Both of these measures (survey and administrative data) provide different representations of actual utilization. One is based on respondent recall, with potential for under-reporting or over-reporting of utilization, and the other is based on data derived from records primarily used for administrative purposes. For the purposes of this study, we accessed administrative databases to derive health care utilization among patient referred for sleep diagnostic testing. Though both sources can provide detailed information at a patient-specific level, survey data cannot be linked to the exposure of interest (OSA).

There are many methods used to define health care utilization among subjects. It can simply be measured as the number of services provided to a patient, such as the number of physician visits or hospitalizations. More often, however, a variety of procedures and services are also of interest, and some measure of “cost” is assigned to each service so that resource intensity can be summed over all provided services. Because pricing systems are likely to vary among providers, it is common to adjust the charges by a facility’s “cost-to-charge” ratio. Yet, such an approach assumes that costs are actually known and that the relationship of costs to charges can be represented. Another approach is to summarize utilization by counting each unit of care, instead of using facility charges. For the purposes of this study, health care utilization was defined by summing the number of unique services and aspects of care, including the number of hospitalizations, length of stay in hospital, number of emergency room visits and number of outpatient physician visits, all within an 18-month period prior to sleep diagnostic testing. The

rationale for including each of these aspects of health care resource use is provided below.

1.4.1. Number of Hospitalizations:

OSA is associated with an increased risk of depression and cardiovascular disorders such as hypertension, heart failure, arrhythmias, heart disease, and stroke (4-9). As OSA severity increases, a patient may be at greater risk for a hospitalization for one or more of the co-morbid conditions mentioned above. For these reasons, we determined the number of all-cause hospitalizations within this ambulatory population. Hospitalizations are an excellent measure of health care utilization as they represent one of the largest costs to the health care system and require the largest amount of health care resources (37). The Canadian Institute for Health Information (CIHI) estimated that hospital expenditures accounted for 36.8% of all public-sector health expenditures (38). Number of hospitalizations is a commonly used measure of health care utilization as they can be used to compare admission rates within regions and between provinces. This is important from a health planning perspective as it provides administrators with valuable information on trends in health expenditure, which may help predict future health care use. Hospitalizations have also been used in the assessment of other chronic conditions such as Chronic Obstructive Pulmonary Disease (COPD), cardiovascular disease and diabetes (39-42). It should be noted that using hospitalization as a health resource outcome is limited in that it only represents a fraction of total health expenditure and does not include other hospital services such as rehabilitation and chronic care (37,43). Another limitation is the inability to attribute hospitalizations to the exposure of interest.

As a result, all-cause hospitalizations were identified and all available diagnostic and procedure codes were used to assess co-morbidity amongst these patients.

1.4.2. Length of Stay:

Hospital length of stay was determined based on the number of days in hospital for each subject within the 18-month period prior to sleep testing. This is an important outcome measure as health care expenditure and resource use is directly related to number of days a patient remains in hospital. As mentioned previously, there are a number of co-morbid conditions associated with OSA. It is likely that as OSA severity increases, the number of co-morbid conditions a patient presents with will increase (29). This may result in greater complications amongst those that do have a hospitalization and ultimately increase their hospital length of stay. Previous literature has shown that increased co-morbidity leads to greater length of stay in a number of chronic conditions (39, 44-48).

As mentioned previously, hospital stays account for a large proportion of total health expenditures. Therefore, cumulative health resource use will increase for every additional day spent in hospital (49). There are a number of factors that influence length of stay in hospital. This may include the number of beds within a hospital that are staffed and operational, current demand for vacant beds, and access to care outside of the hospital upon discharge (49). For example, a physician may discharge a patient earlier if demands for hospital beds are high or alternatively keep a patient in hospital longer until care outside of the hospital has been arranged.

With respect to reporting, we determined the number of days spent in hospital amongst those that had at least one hospitalization. We were also able to identify patients that had only one hospitalization, but remained in hospital for long periods of time. This can be a limitation to using length of stay as an outcome, as extended hospital stays within a small group of patients can significantly inflate reported rates.

1.4.3. Emergency Room visits:

Emergency room visits also require large amounts of health care resources and result in significant costs to the health care system (50). Unfortunately, there is limited data on emergency room visits amongst patients with OSA in North America. This is because not all provinces currently collect information on ambulatory care. As mentioned previously, OSA has been associated with increased risk of motor vehicle and occupational accidents (21, 51, 52) and is also associated with a number of cardiovascular conditions (4-9). The likelihood of presenting to the emergency room due to an accident or cardiovascular event may increase as OSA severity increases. Previous literature has shown an association between AHI and motor vehicle accidents (21).

Assessing emergency room visits amongst patients with OSA will be an important contribution to the current literature as there is limited data on this outcome. Unfortunately, we are limited in our ability to compare results for this measure of health resource use due to variability in reporting between provinces. For this study, we determined the number of emergency room visits within the 18-month period prior to sleep testing.

1.4.4. Number of Outpatient Physician Visits:

Physician visits are likely to be high within this population as many people with OSA have other pre-existing medical conditions such as depression, hypertension, and diabetes (4-9, 20-28). These conditions alone will result in a higher frequency of physician visits, as they are conditions that require close monitoring (38, 41). Previous studies in Manitoba have shown physician visits to be high amongst OSA patients (53-55). In the current literature, the mean rate of outpatient physician visits prior to sleep testing range from 7 to 9 visits per year (53-57). We focused on outpatient physician visits for all conditions as in-patient visits are influenced by a number of factors, and we were interested primarily in the ambulatory care use of these patients (49, 50).

1.5. Health Care Utilization Among Patients with OSA:

It is estimated that health care utilization among patients with OSA is twice that of age and gender matched controls (53-62). However, it remains unclear if OSA is an independent determinant of increased utilization. It is also unclear whether health care use increases with increasing severity of disease, or if other factors (such as the presence of depression or obesity) are confounding variables or effect modifiers. Health care programs are under tremendous economic pressure, as they attempt to serve a growing population within a limited budget. In 2003, funding for therapy for OSA was cut in Alberta due to lack of evidence that OSA was a significant health concern. However, growing evidence is showing that if left untreated, OSA incurs huge costs to the health care system (53-62).

Few studies have measured health care utilization and associated costs among patients with OSA. Kryger et al. (53) looked at health care utilization among 97 obese patients ($\text{BMI} > 35 \text{ kg/m}^2$) with severe OSA compared to age and gender matched controls. Health care utilization in this study was defined as total number of hospitalization days within a two-year period prior to diagnosis of OSA. During this two-year study period, patients with OSA spent more days in the hospital. OSA patients spent 251 nights in the hospital compared to 90 nights for the control group ($p < 0.001$). An additional study by Kryger et al. involving 181 OSA patients, demonstrated similar results. This 10 year follow-up study defined health care utilization as total number of hospitalization and total physician claims within the ten years prior to diagnosis of OSA. They concluded that length of stay amongst OSA patients was twice that of age and gender matched controls within the ten-year period (1,118 nights vs. 676 nights, $p < 0.001$). Total physician visits were also two times higher amongst OSA patients (109 visits vs. 60 visits, $p < 0.001$) (54). Though these studies provided the groundwork for studying OSA and its association with elevated health care use, both of the studies have been limited by small sample size and lack generalizability as only severe OSA patients were studied. Secondly, increased health care use in the OSA group may have been secondary to co-morbid conditions, including arterial hypertension and obesity, which were not controlled for in either of these studies.

A larger study by Smith et al. compared health care resource use among 773 patients with OSA and age, gender, geographic and physician-matched controls from the general population (55). Matching patients with OSA to controls by postal code was done to correct for socio-economic factors and distance to health care services. Matching for a

specific primary physician was done to minimize biases that could occur if patients and controls had different doctors. This relates to differences in referral patterns and billing practices amongst physicians. Health resources were defined by total physician visits, total number of nights spent in hospital, and outpatient surgeries in the five-year period prior to diagnosis. They found that OSA patients used 23 to 50% more resources than controls ($p < 0.001$). The mean number of hospital nights spent by OSA patients was 2.98 ± 0.24 (Standard Error (SE)) compared to 1.98 ± 0.20 (SE) for controls over the five-year period. OSA patients also had an average of 36.7 ± 1.1 (SE) physician visits compared to 29.9 ± 1.1 (SE) among controls within the same time period ($p < 0.001$). Though these differences in health care utilization were smaller than previous studies, the study was unable to statistically adjust for differences in BMI and co-morbidity profiles between cases and controls.

A recent case-control study by Tarasiuk et al. reported similar findings on a cohort of young (22-39 yrs) and middle-aged (40-64 yrs) adult males with OSA (58). Patients with OSA used almost twice the health care resources as age and gender matched controls in the five-year period prior to OSA diagnosis. Unfortunately, similar limitations exist within this study including the inability to adjust for the effect of BMI and underlying co-morbidity within controls.

Future studies should examine all OSA patients regardless of severity, and ideally, recruit from a community-based setting. This was attempted in a cross sectional study of 238 OSA patients by Kapur et al. (59). They determined a dose-response relationship between severity of OSA and the health care resource use: as OSA severity increased, healthcare utilization increased. In this study health care utilization was

defined as total number of inpatient hospital days and physician claims within the two-year period prior to diagnosis of OSA. They also estimated that untreated obstructive sleep apnea may cause \$3.4 billion in additional medical costs in the United States. This was determined by assigning costs to each medical care service used by the patient. Unfortunately, this study was also limited by its selection of only OSA patients from a tertiary setting, and did not take into account the costs associated with patients referred for testing but diagnosed as not having OSA. They were also unable to adjust for body mass index, as no height or weight measurements were taken on their control group.

A major limitation in all previous studies measuring health care use among OSA patients is the inability to control for body weight, an important potential confounder (63). Since obesity is common in patients with sleep apnea, obesity and its associated co-morbidities rather than OSA could account for differences in health care use. Another limitation is the use of community-based controls as a comparison group. This group is very different from OSA patients in that they are generally healthier, have lower body mass indexes, and access the health care system far less. No study has assessed the health care use and costs of patients referred for sleep testing that did not have OSA. All studies have excluded patients that were referred for assessment of OSA but did not have the disorder. In fact, this group is likely to have similar underlying co-morbid conditions and be similar in body mass index to patients with OSA.

In this study we utilized a cohort of all patients referred for sleep diagnostic testing (in both the community and tertiary setting). This allowed us to define severity of OSA among all patients, from no OSA to severe OSA. The collection of body mass index and associated co-morbidity data also allowed for the adjustment of potential

confounding variables, a major limitation in prior studies. We hypothesized that health care utilization is likely driven by a select group of subjects.

1.6. Self-Reported Co-morbidity versus Administrative Data:

Given the number of co-morbid conditions present among patients with OSA, to truly assess the economic burden that OSA itself may pose on the health care system, researchers must adjust for co-morbid conditions. Few studies have established if higher costs are due to the presence of these co-morbidities or due to the OSA itself and no study to date has performed a risk adjustment analysis to assess increased health care use in this population (63).

The use of self-reported data through questionnaires or interviews is one of the most common methods of assessing medical history and the presence of specific medical conditions. This method of determining co-morbidities is undertaken due to availability, efficiency, and the relatively low cost associated with the measure. However, the reliability and accuracy of this data is questionable and it has been suggested that the agreement between self-reported data and medical records vary depending on the conditions in question (64-70).

Studies have also assessed self-reported medical history against administrative databases (71-76). Susser et al. showed that agreement between the two sources was poor to fair (overall interclass correlation coefficient: 0.43; 95% CI: 0.40, 0.47). The interclass correlation coefficient is a measure of the agreement between two scores. In this case it related to scores on the Charlson Co-morbidity Index.

In light of this poor agreement between self-report and administrative data, research has shown that merging clinical data with administrative databases is an effective method of increasing the completeness and accuracy when measuring outcomes and adjusting for factors that may affect that outcome (77-79). In a study by Lix et al., they defined enhanced measures of chronic disease by comparing self-reported data from the Canadian Community Health Survey Cycle 1.1 to pre-defined administrative algorithms (79). They validated these comparisons by calculating kappa statistics, sensitivity, specificity, and positive and negative predictive values for each condition. The enhanced measure that was reported was based on an optimal balance of sensitivity and specificity.

There have been studies on morbidity and mortality measures among patients with various chronic conditions, including coronary heart disease and those undergoing coronary artery bypass graft surgery (80-82). However, there have been no studies to date that have used administrative data to aid in the measure of co-morbidity among patients with OSA. In this study, in which co-morbidities were determined by both self-report and administrative data sources, we were able to compare the two methods as a means of determining co-morbidity in a cohort of patients referred for OSA testing. The two methods were then combined to obtain an “enhanced” measure of co-morbidity. Ultimately, this provided a more complete measure of co-morbidity among this group and aided in the adjustment of these coexisting conditions in the assessment of health care burden associated with OSA.

1.7. Summary and Overview of Study:

In summary, there is a high prevalence of OSA in the general population. If left untreated, OSA is associated with substantial morbidity and elevated health care utilization. Unfortunately, in a time of limited health resources, treatment of all patients with OSA would be costly, and likely not feasible. Determining whether OSA of increasing severity is associated with increased health care utilization, and identifying predictors of increased health care utilization would allow more effective allocation of health care resources by focusing on patients at highest risk. Through the use of all severities of OSA (from no OSA to severe OSA) we will be able to adjust for obesity within this population; a major limitation of the studies conducted to date. Thus, the primary objective of this study was:

1) To determine if health care utilization increases with increasing severity of OSA.

Hypothesis: As OSA severity increases, there will be an increase in health care utilization.

Secondary Objectives:

2) To identify determinants of increased health care utilization among patients referred for sleep diagnostic testing.

Hypothesis: Increased health care utilization will be limited to patients with severe OSA and associated co-morbidities, including hypertension, diabetes and depression.

3) To assess the agreement between self-reported co-morbidity and administrative databases among patients referred for sleep diagnostic testing.

Hypothesis: Self-reported co-morbidity among patients referred for sleep diagnostic testing will have good agreement with administrative databases.

METHODS

2.1. Study Design:

This study is part of a larger longitudinal project assessing the effect of CPAP on health care utilization. Total follow-up time was based upon a three-year funding period. Thus, the objectives of the original study were to determine health care use 18-months prior to sleep testing and then 18-months after the initiation of CPAP therapy, amongst a cohort of patients referred for sleep testing. The present study relates to the first objective.

Our study utilized a retrospective cohort design employing prospective collection of clinical characteristics and diagnostic testing to identify study subjects. Prior health care use was determined retrospectively through administrative data. The exposure variable was OSA severity and outcomes were health care utilization for an 18-month period prior to sleep testing. As OSA is a chronic condition, any associated change in health care use was likely present many years prior to diagnosis. Therefore assessing health care use during this defined period was justified.

2.2. Study Population:

2.2.1. Sampling Frame and Inclusion Criteria:

The sampling frame included all adult patients (> 18 years old) referred to the Alberta Lung Association Sleep Center at the Foothills hospital and private home care facilities within the city of Calgary for sleep diagnostic testing during the time period from July 2005 to August 2007. Virtually all sleep diagnostic testing for Calgary and surrounding areas is conducted in these facilities. All patients who underwent

polysomnography (PSG) or ambulatory monitoring for the presence of OSA were asked to participate in the study. Some patients lived outside of Calgary itself, but were still included within the Calgary Health Region. The result was a sampling frame of approximately 1.2 million people.

2.2.2. Exclusion Criteria:

- a) Patients previously diagnosed with OSA and those who were referred but did not undergo diagnostic testing.
- b) Out-of-province patients. Due to the inability to monitor health service utilization from out of province patients, only patients with a valid Alberta Provincial Health Number (PHN) were included.

2.2.3. Study Period:

The study period and time frame for the assessment of physician visits (including respirologists, general internists, psychiatrists and general practitioners (GP's)), emergency room visits, hospitalizations and length of stay was the 18-month period prior to the patient's sleep diagnostic test. As mentioned previously, OSA is a chronic condition, and any associated change in health care use will likely be present many years prior to diagnosis. Therefore assessing health care use during this defined period is justified.

2.3. Study Variables and their Measurement:

2.3.1. Obstructive Sleep Apnea:

The exposure variable of interest was OSA. We used polysomnography (PSG) and ambulatory monitoring to identify OSA within participants. Although PSG is considered the ‘gold standard’ diagnostic test for OSA, an ambulatory monitoring device has proven to have excellent agreement, sensitivity and specificity with PSG. A previous study by Vazquez et al. quantified the agreement between the two test methods. The mean (2 standard deviations) of the differences between the Respiratory Disturbance Index (RDI) measurements for PSG and ambulatory monitoring was 2.18 (12.3)/hour. Using case criteria of 15 events/hour for RDI, the sensitivity and specificity was 98 percent and 88 percent respectively (83). In addition, the use of ambulatory monitoring has been validated as a clinical management tool (84, 85).

2.3.2. Diagnostic Testing:

As part of a unique public-private delivery model using inexpensive ambulatory monitoring, patients undergoing sleep diagnostic testing may be referred to the university based Alberta Lung Association Sleep Centre for polysomnography, or else referred for ambulatory monitoring through a variety of respiratory care companies (Respiratory Homecare Solutions, Respiratory Wellness Centre, VitalAire and Medigas). This results in a large number of primary care referrals for testing, including screening. As a consequence, the prevalence of OSA within the cohort is in keeping with community-based samples, and to a lesser degree resembles the general population.

Polysomnography:

Patients stayed in-laboratory for full overnight polysomnography. In-laboratory PSG data was recorded for approximately eight hours using a computerized polysomnographic system (Sandman Elite Version 8.0, Nellcor Puritan Bennett (Melville) Ltd, Kanata, Ontario, Canada). This included a standardized montage: three channel electroencephalograms (C4/A1, C3/A2, O1/A2), bilateral electro-oculograms (EOG), submental electromyogram (EMG), bilateral leg EMGs, and electrocardiography (ECG). Airflow was measured using a nasal pressure transducer (Braebon Medical Corp, Ontario, Canada). Respiratory effort was assessed by inductance plethysmography (Respirtrace Ambulatory Monitoring, Ardsley, New York, USA), and oxygen saturation was recorded using a finger probe.

Ambulatory Monitoring:

Patients are fitted with a Remmers Sleep Recorder (SagaTech Electronics Ltd, Calgary, Canada) at the Alberta Lung Association Sleep Centre or respiratory care company within the community. This is a take-home ambulatory monitoring device, which measures snoring, nocturnal oxygen saturation profile, respiratory airflow and body position. Patients sleep for approximately eight hours with this device and return it the following day for electronic download.

Definition of OSA severity

The respiratory disturbance index (RDI) was defined by the average number of apneas and hypopneas per hour of sleep. Apnea was defined as a cessation of airflow for

at least 10 seconds. Hypopnea was defined as an abnormal respiratory event lasting at least 10 seconds with at least a 30% reduction in thoracoabdominal movement or airflow as compared to baseline, and with at least a 4% oxygen desaturation.

Based on the sleep test results, we stratified patients by OSA severity based on the RDI into: no OSA (RDI <5 event/hr), mild OSA (RDI 5-14.9 events/hr), moderate OSA (RDI 15-29.9 events/hr) and severe OSA (RDI \geq 30 events/hr). Patients with an RDI <5 were considered the reference group (86, 87). This classification system is well accepted in both clinical practice and within the medical literature (88).

2.3.3. Determination of Co-morbidities and Clinical Characteristics:

As part of the Alberta Lung Association Sleep Center and private home-care facility protocol of the larger study, baseline clinical and demographic information was collected for all participants prior to sleep diagnostic testing. This included: age, sex, height, weight, BMI, neck circumference, and postal code. Each participant also completed the Epworth Sleepiness Scale (ESS). This is a validated, self-administered questionnaire that provides a measure of daytime sleepiness. It is an eight-question scale, scored out of 24 points. A subject who scores 10 points or greater is considered clinically sleepy and is encouraged to consult a sleep specialist (89).

In addition, the measurement of co-morbidity associated with OSA was determined through the use of a questionnaire administered by trained personnel within the clinics (Appendix 1). Patients were asked to self-report the presence or absence of specific co-morbidities and to provide a current list of medications. This list of conditions was derived from the Charlson Co-morbidity Index and the Elixhauser Co-morbidity

Index (48, 90). It included hypertension, asthma, depression, cardiac arrhythmia, myocardial infarction, chronic obstructive pulmonary disease, diabetes, heart failure, and stroke.

Self-Reported Co-morbidity

A specific co-morbid condition was considered present if it was self-reported based on the initial questionnaire administered to all subjects.

Administrative Data as a Measure of Co-morbidity

To compare the completeness of self-reported medical history, the International Classification of Diseases (ICD-9-CM and ICD-10) definitions for the nine specific co-morbidities were identified within the Alberta Health and Wellness administrative datasets. For the conditions of interest, the ICD-9-CM co-morbidity coding scheme derived by Elixhauser et al. (48) and the ICD-10 coding scheme developed by Quan et al. were utilized (91) (Table 1). When available, validated algorithms for defining these co-morbidities were used (Table 2) (92-97). For co-morbidities that did not have validated algorithms (specifically COPD, depression and cardiac arrhythmia), ICD-9-CM and ICD-10 diagnostic codes were identified within the ICD-9-CM and ICD-10 manuals developed by the World Health Organization (98, 99). Within the administrative datasets, the condition was considered present if the algorithm defining the condition was satisfied. For example, diabetes was considered present if there were two or more separate diagnostic codes identifying diabetes within the physician claims or one or more hospitalization diagnostic code identifying diabetes within the a two year period (96). For

co-morbidities that do not have a defined algorithm, such as depression, COPD and cardiac arrhythmia, they were considered present if at least one diagnostic code recorded for the condition within either the physician claims data or inpatient hospitalization data was recorded within the 18-month period prior to sleep diagnostic testing. All 3 diagnostic coding fields were used within the physician claims data and all 25 diagnostic codes within inpatient hospitalization data. Diagnostic type indicators in this data source allowed for the restriction of conditions to only those present prior to admission and therefore excluded any condition that developed while staying in hospital.

2.3.4. Health Care Utilization:

We assessed cumulative health care use incurred during the 18-month period prior to sleep diagnostic testing. Health care use was defined as the cumulative sum (counts) of each of outpatient physician visits, hospitalizations, length of stay in hospital, and emergency room visits within the defined period of 18 months. Rates and rate ratios were calculated for each variable to account for person-time in the denominator as not all patients had the same amount of follow-up.

Outpatient Physician Visits:

The timeframe for assessment of all outpatient physician visits was 18 months prior to sleep diagnostic testing for OSA. Given that OSA is a chronic and stable condition, we assumed that individuals diagnosed with OSA had this condition 18 months prior to overnight polysomnography or ambulatory testing. An outpatient physician visit was defined using the Alberta Health and Wellness data for the study

period. Our primary focus was outpatient physician visits for all conditions as physician billing codes are not always accurately linked to the reason for the specific medical visit (43). In addition, outpatient GP (general practitioner) visits and outpatient specialist visits (including respirologists, general internists and psychiatrists) were examined separately.

Hospitalizations:

The timeframe for the assessment of all-cause hospitalizations was also 18 months prior to sleep diagnostic testing. The rationale for this time frame is similar to that provided above for physician visits, in that OSA is a chronic condition likely to be present in the period 18 months before diagnosis. Therefore, hospitalizations within this time frame would be relevant.

Length of Stay in hospital:

Hospital length of stay was determined based on the total number of hospitalizations and duration of stay (in days) in hospital for each encounter for each subject within the 18-month period prior to sleep testing. This allowed us to identify patterns of hospitalization and account for patients that had been admitted several times, each within a few days of their last admission, and patients that have only had one hospitalization, but remained in hospital for long periods of time. This was important as these patients significantly skewed data on number of hospitalizations and average length of stay.

Emergency Room visits:

The timeframe for assessment of number of emergency room visits was also 18 months prior to sleep diagnostic testing. The rationale for this time frame is similar to that provided above.

2.4. Administrative Data Sources:

We linked the cohort of patients to Alberta Health and Wellness administrative data sources by the participant's unique Provincial Health Number (PHN). Data sources accessed from Alberta Health and Wellness included: Alberta Health Insurance Plan (AHCIP) Registry, Inpatient hospitalization abstracts prepared by Canadian Institute for Health Information (CIHI), Physician claims data and the Ambulatory Care Classification System (ACCS).

The AHCIP registry covers virtually all residents in the province except a small proportion of special population groups (i.e. members of the Armed Forces and Royal Canadian Mounted Police (RCMP), federal inmates, persons from other provinces during their first three months in Alberta – accounting for approximately 1% of the total population) (100).

The CIHI hospital inpatient data source contains details regarding hospitalizations including admission date, discharge date, length of stay, 25 diagnostic codes, and 10 procedure codes for each participant. These diagnostic and procedure codes were used in validating the self-reported medical history obtained from the baseline questionnaire.

The Alberta physician claims registry and ambulatory care registry contains information on physician services for patients covered by the provincial insurance

program. This file is updated daily and captures all individuals who visited fee-for-services physician. Virtually all residents from Alberta are under the provincial insurance program. Therefore, these claims capture nearly all physician visits on a fee-for-service basis. Physicians who are paid by salary are also required to “shadow bill”, thus claims should be complete, although the extent to which salaried physicians complete their claims has not been assessed in Alberta. These databases include information on all payments and dates of visits to health professionals. They include information on provider specialty, location and date for each consultation, and diagnostic code. In addition, this registry allowed the identification of the location of visits as either inpatient or outpatient. For the purposes of our study provider specialty was categorized as psychiatry, general practice, internal medicine, respiratory medicine and “other”.

2.5. Ethical Approval:

The study was approved by the Ethics Review Board of the University of Calgary (see Appendix 2).

2.6. Analysis:

2.6.1. Descriptive Statistics:

Patient demographics (age, BMI, neck circumference), Epworth Sleepiness Score, and data collected from the overnight polysomnography or ambulatory monitoring device (RDI, % time spent below 90% oxygen saturation) were described using mean and standard deviation for normally distributed variables. In cases of highly skewed or clearly non-normal distributions, the median and the inter-quartile range (IQR) were reported.

Means and proportions were compared using analysis of variance and X^2 tests respectively. In addition, proportions of patients presenting with specific co-morbidities, identified in the questionnaire, were calculated.

2.6.2. Primary Objective:

The association between OSA severity and health care use was determined by Poisson regression (also known as Poisson Log-Linear Regression). Rates of hospitalizations, length of stay, physician visits and emergency room visits, by OSA severity, were initially calculated. A Poisson Log-Linear regression model was fit for each dependent variable of healthcare utilization; total number of hospitalizations, outpatient physician visits, length of stay and emergency room visits separately. Regression models were assessed using backward selection techniques. To construct these models, an initial bivariate model was created to identify significant independent predictor ($p < 0.05$). Once these predictors were identified, a saturated multivariate model was then constructed using the significant predictors. In addition, relevant interaction terms were constructed. We developed further reduced models based on the presence or absence of effect modification and confounding by the specified independent predictors. Relevant interaction terms included: OSA severity x BMI and OSA severity x sex. The fit of each model was also assessed by the likelihood ratio test. Independent predictors included OSA severity (with no OSA as the reference category), age, sex, BMI and co-morbidities. Non-significant interaction terms were deleted for the final adjusted models. We included co-morbidities in the final adjusted models, even though there was no change in the likelihood ratio test when compared to a model that adjusted for age, sex

and BMI only. This final adjusted model is similar to those developed by Smith et al., which showed the model that best fit measures of health resource use included only age, gender, BMI and co-morbidity (55).

Both age and BMI were initially treated as continuous variables. After identifying significant non-linearity as defined by the likelihood ratio test of their squared and cubic terms, age has categorized into quartiles and BMI into normal weight ($< 25 \text{ kg/m}^2$), overweight ($25\text{-}29.9 \text{ kg/m}^2$) and obese ($\geq 30 \text{ kg/m}^2$). For all statistical tests, p values < 0.05 were considered statistically significant.

Some of the main features of Poisson regression are that the variance is equal to the mean and that the distribution tends to be skewed to the right when the mean value is very small. We determined if the assumptions of Poisson regression were upheld prior to modeling the data. Initially, we determined if there was a log-linear relationship between OSA severity and each specific measure of health care utilization by plotting them against one another. If the data approximated a straight line, then this assumption has not been violated. We also assessed for over-dispersion (extra-Poisson regression). This occurs when the residual variance is greater than the mean. This may be due to the presence of outliers or because an important explanatory variable has not been included in the model. The deviance goodness-of-fit test was also used to determine if over-dispersion was present. If over-dispersion was present, a negative binomial regression model was used to determine rates. This regression model is a more conservative measure that corrects for the over-dispersion and results in larger confidence intervals around the point estimate.

Not all subjects were present in Alberta for the 18 months prior to sleep testing. Therefore, we needed to account for person time spent in the study. When study subjects are followed for different lengths of time, it is common to annualize the utilization rates; in other words calculate the health care use based on person time, within one year intervals (12). Person time for each patient was determined using immigration and emigration dates provided within the Alberta Health Insurance Plan (AHCIP) Registry. A patient was assumed to be present for the 18-month period if they were was no emigration date within the two-year period prior to sleep testing. We calculated rates and rate ratios (RR) for each measure of health care utilization using patients with no OSA as the reference group (this was the denominator in the ratio).

2.6.3. Secondary Objectives:

We defined “increased health care use” based on the distribution of the count data for each dependent variable using the entire cohort of patients referred for sleep testing to determine this cut-point. In all cases, the dependent variable of increased health care utilization was defined as the upper quartile of use. Once this binary variable had been created, univariate predictors of increased health care utilization were identified by simple logistic regression. Predictive variables were those found to be statistically significant within the univariate analysis and were fit into a full model. At this point the model was reduced using a backwards selection technique. Similar models were created for outpatient physician visits and emergency room visits based on the distribution of the counts for each variable. Independent predictors included OSA severity, ESS (score of ≥ 10), age (≥ 65 years), sex, BMI (≥ 30 kg/m²), co-morbidities (present or absent) and

nocturnal oxygen saturation profile ($\geq 12\%$ of the total sleep time spent below 90% oxygen saturation). This cut-point is based on previous findings from the Sleep Heart Health study. They concluded that oxygen saturations below this level were associated with increased risk of hypertension amongst patients with OSA (6).

OSA was modeled as both a binary variable (presence or absence) and a categorical variable (levels of severity) with no OSA as the reference group. As logistic regression does not have any distributional assumptions, we did not log transform the data if it was highly skewed. One assumption for logistic regression is that continuous variables are linear on the log scale. As we had determined early, this assumption did not hold for age and BMI. For this reason, they were modelled as binary variables (Age ≥ 65 years to represent older patients vs. younger patients) and (BMI $\geq 30 \text{ kg/m}^2$ to compare obese vs. non-obese patients).

To assess the agreement between self-reported co-morbidity and administrative databases among patients referred for sleep diagnostic testing, we calculated proportions of subjects with each co-morbid condition based on: self-report only, administrative data sources only, and self-reported and administrative data combined. We evaluated consistency between self-reported co-morbidity and administrative data (physician claims and inpatient discharge abstracts) without assigning either of the sources as a 'gold standard'. For all binary variables, the Kappa (κ) statistic and 95% confidence intervals were calculated. The Kappa statistic is an index of the degree of agreement between two raters classifying the same set of items. Kappa can be thought of as the chance-corrected proportional agreement, and possible values range from +1 (perfect agreement) to 0 (no agreement above that expected by chance). Kappa values were defined as follows: <0.40

as poor or fair agreement, 0.40-0.60 as moderate agreement, 0.61-0.80 as substantial agreement, and 0.81-1.00 as almost perfect agreement (101).

In addition, the McNemar's test of paired proportions was determined. This is a statistical procedure used to compare two proportions, which are dependent or correlated. It is a test of marginal homogeneity that compares the agreement between discordant pairs.

A sub group analysis was also performed in which patients were stratified by severity of OSA to determine trends in co-morbidity measure. Presence of co-morbidities was tabulated for each stratum using self-report only, administrative sources only, and a combination of self-report and administrative data.

2.6.4. Statistical Software Used for Analysis:

All statistical analysis was conducted using STATA 10.0 software (Statacorp, College Station, Texas).

RESULTS

3.1. Study Participants:

From July 2005 to August 2007, 2295 patients were referred for sleep diagnostic testing in the city of Calgary (Figure 1). 78 (3.4%) patients refused to participate and 42 (1.8%) patients were from out of province and therefore were excluded. Of the remaining 2175 patients, 26 (1.2%) were excluded because they were not present in the Alberta Health and Wellness registry file. These patients included RCMP ($n = 2$), and un-linkable provincial health care numbers ($n = 24$). The result was a final study population size of 2149. Within this study population, 367 patients underwent full overnight polysomnography and the remainder ($n = 1782$) had ambulatory monitoring either through a private home care facility ($n = 388$) or through the Alberta Lung Association Sleep Clinic ($n = 1394$). Sleep specialists accounted for 84.6% of referrals for sleep testing whereas general practitioners accounted for 15.4%.

From the study cohort, 432 (20.1%) patients were identified as having no OSA, 738 (34.3%) with mild OSA, 443 (20.6%) with moderate OSA and 536 (24.9%) with severe OSA. Data analysis was performed on these sub-cohorts.

3.2. Full Study Population:

Descriptive characteristics of all patients included in the study are presented in Table 3, stratified by OSA severity. 1717 (79.9%) referred patients had OSA as defined by an $RDI \geq 5$ events/hr⁻¹. There were a larger proportion of males (62.6%) who completed an assessment for OSA compared to women, reflecting the gender difference in the prevalence of this condition (1). RDI values ranged from 0 to 167 events/hr⁻¹ with a

median value (IQR) of 13.2 events/hr⁻¹ (6.0, 29.9). Age of the cohort ranged from 18 to 87 years with a mean value (standard deviation) of 50.1 years (12.9). It was noted that proportion of male subjects, age, body mass index, Epworth Sleepiness Score, neck circumference and total sleep time spent below 90% oxygen saturation all increased as OSA severity increased ($p < 0.001$).

3.3. Comparison of Co-Morbidity Determined by Self-Report and Administrative Data Algorithms:

Table 4 presents the proportions for all co-morbidities determined by self-report, as well as validated administrative data algorithms. The most prevalent co-morbidity in both self-report and administrative data was hypertension and depression, with 35% and 27% of subjects referred for sleep testing self-reporting the presence of these conditions respectively. The proportions based on self-report and administrative algorithms differed significantly (McNemar's p value < 0.05) for all conditions except depression and COPD. Diabetes had substantial agreement between self-report and administrative algorithms with a $\kappa = 0.79$. There was good agreement for hypertension ($\kappa = 0.60$), depression ($\kappa = 0.50$) and asthma ($\kappa = 0.49$). Poor agreement was seen for COPD ($\kappa = 0.31$), heart failure ($\kappa = 0.28$), myocardial infarction ($\kappa = 0.27$), stroke ($\kappa = 0.22$) and cardiac arrhythmia ($\kappa = 0.14$). There was a large discrepancy between self-report and administrative data for the presence of cardiac arrhythmia (5.7% vs. 30.4%).

When “both” self-reported and administrative measures of co-morbidity were required to define each condition, proportions for all nine conditions were much lower when compared to a definition that required “either” self-report or administrative

measure. For example, the proportion of patients with hypertension was 25.1% when “both” were used and 43.2% when “either” was used.

3.3.1. Co-Morbidity Measurement by OSA Severity:

Proportions for each co-morbidity determined by self-report and administrative algorithms were calculated and stratified by OSA severity (Table 5). Looking at self-report of co-morbidity alone, the proportions of patients presenting with hypertension, diabetes, myocardial infarction and stroke increased as OSA severity increased. When using the administrative algorithms, this trend was only observed for hypertension, diabetes and stroke. Table 6 depicts a combination of either self-report or administrative data to determine the co-morbidities. This enhanced measure of co-morbidity was based on the presence of a co-morbid condition in either data source. The prevalence of hypertension, diabetes and myocardial infarction tended to increase as OSA severity increased ($p < 0.001$, chi squared test), while the prevalence of depression tended to decrease with increasing severity of OSA, although the trend was not statistically significant ($p = 0.12$). This enhanced method to determine the presence of the co-morbidities was used for the purposes of this study.

3.4. Outpatient Physician Visits

The association between OSA severity and all outpatient physician visits, (regardless of physician specialty) were examined within the cohort of patients referred for sleep diagnostic testing. In addition, outpatient GP (general practitioner) visits and

outpatient specialist visits (including respirologists, general internists and psychiatrists) were examined separately.

3.4.1. Total Outpatient Physician Visits

Total outpatient physician visits stratified by OSA severity are presented in Table 7. Amongst the 2149 patients, the majority (98.7%) had a least one outpatient visit within the 18-month period prior to sleep diagnostic testing. The total number of outpatient visits within this timeframe ranged from 0 to 132 with a median value (IQR) of 16 visits (9, 27) (Figure 2). After accounting for duration of follow-up and calculating the median number of visits, outpatient physician visits did not increase as OSA severity increased (no OSA: 9.34 visits/yr, mild OSA: 10.67 visits/yr, moderate OSA: 11.34 visits/yr, severe OSA: 10.67 visits/yr) (Table 7). There was no evidence that mean outpatient physician visits increased with OSA severity ($p = 0.62$). This test for trend was assessed using the mean values from the negative binomial distribution and conducting a likelihood ratio test with 3 degrees of freedom.

To determine the association between OSA severity and likelihood of outpatient physician visits, rate ratios were then calculated using mean number of visits and no OSA as the reference group. Initially, a crude Poisson regression model comparing mild, moderate and severe OSA to patients with no OSA was developed. Significant over-dispersion was identified within this model as determined by the deviance goodness-of-fit test ($p < 0.001$). As a result, a negative binomial regression model was developed to account for this over-dispersion. This unadjusted model showed that the likelihood of outpatient visits did not increase as OSA severity increased (RR (95% CI) mild OSA:

1.00 (0.92, 1.09), moderate OSA: 1.08 (0.97, 1.19), severe OSA: 1.05 (0.95, 1.15)). After adjusting for age quartiles, BMI categories, sex, co-morbidity and significant interaction terms (OSA x sex), there was no evidence to suggest that the likelihood of outpatient visits increased with increase severity of OSA. To assess the effect of these outlying values on the results, a sensitivity analysis was performed in which patients with an extreme number of outpatient physician visits were removed. There was no difference in the findings with these values removed, and therefore these values were retained in the analysis.

There was a significant interaction between sex and patients with severe OSA ($p = 0.004$). Males with severe OSA had an increased likelihood of physician visits compared to males with no OSA, while females with severe OSA had a decreased likelihood compared to females with no OSA. Neither of these results were statistically significant. Non-significant interaction terms were not included in the final reported model.

3.4.2. Outpatient GP Visits

Outpatient GP visits stratified by OSA severity are presented in Table 8. The majority of subjects (98.7%) had a least one outpatient GP visit within the 18-month period prior to sleep diagnostic testing, with the number of visits ranging from 0 to 112 and a median of 9 visits (IQR: 5, 14). After adjusting for follow-up time, the median number of visits per year was 6.00 (IQR: 3.33, 9.33). When stratified by OSA severity, the median number of GP visits increased with increasing OSA severity, however, this

trend was not statistically significant ($p = 0.26$) based on an assessment of mean visits per year.

Rate ratios, to determine the association between OSA severity and likelihood of outpatient GP visits, were then calculated using no OSA as the reference group. As outlined above, a crude negative binomial regression model was developed to account for over-dispersion observed within the initial Poisson regression model (deviance goodness-of-fit test: $p < 0.001$). This unadjusted model showed that the likelihood of outpatient GP visits increased as OSA severity increased, although none of the results were statistically significant. Again, a significant interaction between sex and patients with severe OSA was observed in the adjusted model ($p = 0.001$). Males with severe OSA had an increased likelihood of physician visits compared to males with no OSA (RR 1.05; 95% CI: 0.93, 1.19) whereas females with severe OSA had a lower likelihood compared to females with no OSA (RR 0.91; 95% CI: 0.78, 1.07). Both of these results were not statistically significant.

3.4.3. Outpatient Specialist Visits

Outpatient specialist visits stratified by OSA severity are presented in Table 9. Amongst the 2149 patients, 935 (43.5%) had at least one visit to a respirologist, psychiatrist or general internist within the 18-month period prior to sleep testing. Within the cohort of patients that had at least one specialist visit, 355 patients (38%) had a visit to a respirologist. Only 210 patients (22.5%) had a psychiatric visit and 572 (61.2%) had at least one visit to a general internist. Within the defined timeframe, the number of specialist visits ranged from 1 to 73 with a median (IQR) of 2 visits (1, 4). The median

number of specialist visits per year did not increase with OSA severity after accounting for person-time.

The initial Poisson regression model developed to calculate rate ratios was determined to have significant over-dispersion ($p < 0.001$). As a result, an unadjusted negative binomial regression model was generated. This model showed that the likelihood of an outpatient specialist visit did not increase as OSA severity increased. In fact, prior to adjustment, patients with mild and severe OSA were significantly less likely to have a specialist visit compared to patients with no OSA (RR (95% CI) mild OSA: 0.79 (0.66, 0.95), severe OSA: 0.66 (0.54, 0.80)). After adjusting for age quartiles, BMI categories, sex, and co-morbidity, the likelihood of an outpatient specialist visit was still significantly lower amongst patients with severe OSA compared to those with no OSA (RR: 0.75; 95% CI: 0.61, 0.92).

3.5. All-cause Hospitalizations

The results for all-cause hospitalizations, stratified by OSA severity, are presented in Table 10. Only 296 (13.8%) patients had at least one hospitalization within the 18-month period prior to sleep testing. Amongst those patients with at least one hospitalization, the number of hospitalizations ranged from 1 to 11 with a median (IQR) of 1 hospitalization (1, 2) (Figure 2). All strata had similar median rates for hospitalizations and there was no trend of increasing utilization with increasing OSA severity based on the assessment of mean number of hospitalization within each strata ($p = 0.63$). Compared to patients with no OSA, the likelihood of hospitalization did not increase with increasing severity of OSA in the crude or adjusted models. No significant

interactions were identified in the model and were therefore eliminated before reporting the adjusted rate ratios.

3.6. Length of Stay

Table 11 presents data on total length of stay (in days) amongst the 296 patients with at least one hospitalization during the study period. Hospital length of stay ranged from 1 to 154 days with a median (IQR) of 5 days (2, 10). When person time was accounted for, the median number of hospital days per year increased with increasing OSA severity (mild OSA: 1.67 days/yr, moderate OSA: 3.34 days/yr, severe OSA: 4.67 days/yr). This trend was not significant when assessed using the mean number of days per year based on the negative binomial distribution (log likelihood test: $p = 0.10$). A crude negative binomial regression model was generated after significant over-dispersion was observed within the initial Poisson model ($p < 0.001$). Compared to patients with no OSA, patients with increased severity of OSA were significantly more likely to have a longer length of stay. After adjustment for age, BMI, sex, and co-morbidity, there was no longer a statistically significant increase in the likelihood of longer length of stay with increasing OSA severity. Compared to patients with no OSA, the Rate Ratio (95% CI) for mild, moderate and severe OSA were (1.30 (0.86, 1.97), 1.39 (0.92, 2.11) and 1.51 (0.99, 2.30) respectively. No significant interaction terms were identified and were therefore eliminated from the adjusted model.

3.7. Emergency Room Visits

Results for emergency room visits, stratified by OSA severity, are presented in Table 12. Within this cohort, 768 (35.7%) had at least one emergency room visit within the 18-month period prior to sleep testing. The number of visits amongst patients with at least one visit ranged from 1 to 49 with a median (IQR) of 1 visit (1, 3) (Figure 2). After accounting for person-time and calculating the median number of emergency room visits per year, the rate of emergency room visits was similar across all categories of OSA severity. An unadjusted negative binomial regression model showed no trend of increasing likelihood of an emergency room visit with increasing severity of OSA. After adjusting for age quartiles, BMI categories, sex, and co-morbidity, rate ratios for total emergency room visits did not increase with increasing OSA severity. In fact, patients with moderate and severe OSA were significantly less likely to have an emergency room visit than controls (Moderate OSA: RR 0.70; 95% CI: 0.58, 0.86, $p = 0.001$, Severe OSA: RR 0.80; 95% CI: 0.65, 0.98, $p = 0.029$). No interaction terms were found to be significant and were therefore removed from the final reported model.

3.8 Predictors of Increased Health Care Utilization

3.8.1. Outpatient Physician Visits

Multiple logistic regression models were used to identify determinants of increased outpatient physician visits. To determine the cut-point used for “increased health care use” we used the distribution of the count data for outpatient physician visits. The dependent variable of increased health care utilization was defined as the upper quartile of use. OSA was modeled as both a dichotomous variable (present or absent) and

a categorical variable (mild, moderate and severe OSA) using no OSA as a reference group. The adjusted odds ratios (OR) and 95% CI's are presented in Table 13. In the adjusted model, OSA was not a predictor of increased outpatient physician visits when examined as either a dichotomous variable (OR: 1.01; 95% CI: 0.71, 1.44) or categorical variable (OR mild OSA: 1.08; 95% CI: 0.81, 1.45, moderate OSA: 1.05; 95% CI: 0.75, 1.47, severe OSA: 0.94; 95% CI: 0.66, 1.34).

A number of significant predictors of increased outpatient physician visits were identified including older age, female sex, increased daytime sleepiness, greater percent sleep time spent below 90% oxygen saturation and the co-morbidities of hypertension, diabetes and depression.

3.8.2. All-cause Hospitalizations

Determinant of all-cause hospitalization were assessed in a similar manner to that undertaken for outpatient physician visits. In this analysis increased use for hospitalizations was defined as the upper quartile of hospitalizations amongst patients that had at least one hospitalization within the 18-month period prior to sleep testing. In the adjusted model, OSA was not a predictor of increased all-cause hospitalizations when examined as either a dichotomous variable (OR: 5.68; 95% CI: 0.68, 47.47) or categorical variable (OR mild OSA: 3.75; 95% CI: 0.39, 36.60, moderate OSA: 7.77; 95% CI: 0.86, 70.25, severe OSA: 7.13; 95% CI: 0.64, 78.78) (Table 14).

Within both the dichotomous and categorical models, age and increased daytime sleepiness were identified as significant predictors of increased all-cause hospitalizations.

No underlying co-morbidities amongst OSA patients were determinants of increased hospital utilization.

3.8.3. Length of Stay

Determinant of increased length of stay were assessed in a similar manner to that undertaken for outpatient physician visits and all-cause hospitalizations. In this analysis increased length of stay was defined as the upper quartile of hospital days amongst patients that had at least one hospitalization within the 18-month period prior to sleep testing. Odds ratios and 95% confidence intervals for predictors of increased length are presented in Table 15. When analysed as either a binary or categorical variable, OSA was not a predictor of increased length of stay.

Within both models, elderly patients, female sex, and greater percent sleep time spent below 90% oxygen saturation were significant predictors of increased length of stay in hospital. No underlying co-morbidities amongst OSA patients were determinants of increased length of stay.

3.8.4. Emergency Room Visits

Determinants of increased emergency room visits, amongst patients that had at least one emergency room visit with the 18-month timeframe, were determined using multiple logistic regression models. Increased emergency room visits were defined as the upper quartile of visits. Calculated odds ratios and 95% confidence intervals are presented in Table 16. OSA was not a predictor of increase emergency room use when analyzed as a dichotomous variable (OR: 0.68; 95% CI: 0.37, 1.27) or categorical

variable (OR mild OSA: 0.77; 95% CI: 0.39, 1.49, moderate OSA: 0.44; 95% CI: 0.20, 0.98, severe OSA: 0.87; 95% CI: 0.40, 1.90).

Within the dichotomous and categorical model, OSA patients that had a previous myocardial infarction were more likely to have increased emergency room visits. No other significant predictors were identified within this model or the categorical model.

DISCUSSION

This study found that health care resource use is high amongst patients referred for sleep diagnostic testing. However, there was no evidence that suggested health care use (as defined by total outpatient physician visits, total hospitalizations, length of stay, and emergency room visits) increased with OSA severity. Although presence of OSA, or OSA of increasing severity was not a predictor of increased health care use, a number of significant predictors were identified. These included increasing age, female sex, and patients with significant daytime sleepiness and percent sleep time spent below 90% oxygen saturation. Underlying hypertension, depression, diabetes and previous myocardial infarction were also significant predictors of increased health care use. In addition, we found varying degrees of agreement between self-reported co-morbidity and validated administrative algorithms.

4.1. Outpatient Physician Visits

In this study we found that patients referred for sleep diagnostic testing are heavy users of health resources, but there was no association between total outpatient physician visits and OSA severity. It was observed that as OSA severity increased, the rate of physician visits did not increase, but remained high within each category (no OSA: 9.34 visits/yr, mild OSA: 10.67 visits/yr, moderate OSA: 11.34 visits/yr, severe OSA: 10.67 visits/yr). These rates are similar to those reported in the literature. Albarrak et al. calculated the mean (SE) number of physician visits one year prior to sleep testing, within a small cohort of patient in Manitoba, to be 9.21 (0.44) (57). A study by Ronald et al., also based on a Manitoba cohort, found the average number of physician claims prior

to OSA diagnosis, to be 10.9 claims/yr (55). Although the rates are similar, the small discrepancies may be due to minor differences in cohort characteristics or differences in access to care between the two provinces. It may also be explained by the general trend of increasing health service use over time. Annual health indicator documents, provided by Statistics Canada, have shown that physician visit rates have increased each year (38). As the Albarrak study looked at patients diagnosed with OSA prior to 2003, this may explain the slightly lower rates reported.

After adjustments for age, body mass index, sex, co-morbidity, and relevant interactions, the likelihood of a physician visit was also similar amongst all OSA severities, when compared to no OSA. The finding of a significant interaction between gender and severe OSA in this analysis may have been a chance finding or due to residual confounding. It is also possible that the highly skewed distribution of health resource use may have resulted in this finding. The calculated range for all outpatient physician visits was 0 to 132. As rate ratios are based on the comparison of two means from the negative binomial distribution, patients with extreme use will have a significant impact on these mean values. A closer look at the data found some female patients within the control category that had greater than 100 visits per year. This likely drove the mean number of visits up in the control group, resulting in a rate ratio that shows patients with no OSA had a higher likelihood of a physician visit than those with severe OSA.

4.1.1. Total Outpatient GP visits

When analyzing outpatient GP visits separately, all patients referred for sleep testing had high visit rates, yet there was still no association between these rates and OSA

severity. It was found that GP visits remained high, regardless of their underlying OSA severity. The values determined amongst this cohort are significantly higher than the average GP visit rates calculated for Alberta and the Calgary Health Region within a similar period of time. Between 2005 and 2006, the Canadian Institute for Health Information (CIHI) calculated the average GP visit rate to be 103/100,000 person years for all of Alberta and 109/100,000 person years for the Calgary Health Region (38). These values are significantly lower than those calculated within this cohort of patients.

It was observed that the crude rate ratio of GP visits increased with OSA severity. However, after adjusting for age, sex, BMI, co-morbidity, and interactions, the likelihood of a GP visit was similar amongst all OSA severities, when compared to patients with no OSA. A similar interaction between OSA severity and gender was observed. Males with severe OSA were more likely to have a GP visit than males without OSA, whereas females with severe OSA were less likely to have a GP visit compared to females with no OSA. Again, this significant interaction between sex and severe OSA may have been a chance finding or a result of residual confounding.

4.1.2. Total Outpatient Specialist Visits

We found no association between outpatient specialist visits and OSA severity. Rates were similar across all strata with a median value (IQR) of 1.33 visits/year (0.67-2.67 visits/year). These values are much higher than the average rates determined for the province of Alberta. The average rate for outpatient specialist visits for 2005-2006 as calculated by CIHI was 88/100,000 person years for the entire province of Alberta and 110/100,000 person years for the Calgary Health Region specifically (38). This is likely a

reflection of the large number of underlying co-morbidities that these patients present with. Research has shown that specialist visits increase as the number of co-morbid conditions increases (102). Specifically, a study by Starfield et al. demonstrated this trend and showed that GP visits also increased with co-morbidity.

After calculating crude rate ratios for specialist visits, we found that the likelihood of an outpatient specialist visit did not increase as OSA severity increased. In fact, patients with mild and severe OSA were significantly less likely to have a specialist visit compared to patients with no OSA. Though this result was statistically significant, it must be interpreted with caution. As mentioned previously, rate ratios are based on the comparison of mean values within the negative binomial distribution and are affected by extreme values. In this instance, patients with higher health resource use, identified within the control group, may have resulted in a statistically significant difference in the rates between patients with mild or severe OSA and those with no OSA.

4.2. Total Hospitalizations

We observed no association between OSA severity and all-cause hospitalizations amongst this cohort. Rates of hospitalizations were high within all OSA categories with a median value of 0.67 hospitalizations/year. This value is similar to those reported in the current sleep literature. A case-control study by Tarasiuk et al. calculated a mean annual hospitalization rate (SE) of 0.95 (0.16) within a two-year period prior to sleep testing amongst a cohort of patients from southern Israel (61). These values are also significantly higher than those observed in the general population. Between 2005 and 2006, the Canadian Institute for Health Information (CIHI) calculated the average rate of all-cause

hospitalizations to be 426/100,000 person years within Alberta and 315/100,000 person years in the Calgary Health Region (37)

It was observed that both the crude and adjusted rate ratios did not increase with increasing OSA severity. This is not surprising, as we had limited statistical power due to the relatively small number of patients with at least one hospitalization ($n = 296$) and the further stratification of these small numbers into three severity categories.

4.3. Length of Stay

We found that duration of stay (in days) in hospital was high in patients referred for sleep diagnostic testing. It was observed that the calculated length of stay increased with OSA severity (mild OSA: 1.67 days/yr, moderate OSA: 3.34 days/yr, severe OSA: 4.67 days/yr). The median value (IQR) amongst patients with OSA was 3.34 (1.33-7.67 days/year). This value is similar to those observed in current literature. Smith et al. found that the mean number of days (SE) spent in hospital amongst a cohort of 773 OSA patients in Manitoba was 2.98 (0.24) within a 5-year period prior to sleep testing (55). Again, this small discrepancy may be due to differences in access to care between the two provinces (37).

After adjusting for age, sex, BMI, and co-morbidity, we found that the likelihood of a longer length of stay in hospital increased with OSA severity. Though these values were not statistically significant, this trend may be due to increasing numbers of complications amongst OSA patients that result in greater lengths of stay. Though we have adjusted for a number of co-morbid conditions, there is always the possibility of residual confounding.

Research has shown that specific co-morbid conditions are associated with increased length of stay; one of which is depression. Bourgeois et al. found that depressed patients had mean length of stays that were 2.5 days longer than non-depressed patients (46). We observed that 36.8% of the patients referred for sleep testing had prevalent depression as defined by our enhanced measure of co-morbidity, which may contribute to this high rate that is observed within this cohort. A further study by Kapur et al. also showed that scores on the Chronic Disease Score (a measure of total co-morbidity) are associated with increased health care use (59).

4.4. Total Emergency Room Visits

We found that rates of emergency room visits were not associated with OSA severity. The median (IQR) amongst OSA patients was 0.67 visits/yr (0.67, 2.00). This value is similar to that found by Tarasiuk et al. within a cohort of patients in Israel. They found that the median number of emergency room visits amongst OSA patients was 1.3 visits per year (56). A more recent case-control study by the same research group found similar median rates (IQR) amongst OSA patients (1 visit/yr (0, 13 visits/yr)). These values are significantly larger than the average provincial values determined by the Canadian Institute for Health Information. The 2005-2006 rates for emergency department visits was 417/100,000 person years in Alberta and 313/100,000 person years in the Calgary Health Region (37).

It was observed that the crude or adjusted rate ratio of emergency department visits did not increase with OSA severity. The likelihood of an emergency room visit was similar amongst all OSA severities, when compared to patients with no OSA. The fact

that patients with moderate and severe OSA were less likely to have an emergency room visit compared to patients with no OSA may have been a chance finding or the result of underpowered calculations due to the small number of patients that had emergency room visits ($n = 768$).

4.5. Predictors of Increased Health Care Utilization

In the present study, OSA was not a predictor of any measure of health care utilizations when analyzed as either a dichotomous variable or categorical variable. However, a number of significant predictors of increased health care utilization were identified.

4.5.1. Sex

It was determined that women were more likely to be in the upper quartile of total outpatient physician visits. The odds of increased physician visits were two times greater for women than for men (OR: 2.25; 95% CI: 1.82, 2.78). These results are similar to other sleep cohorts that have compared health resource use prior to OSA diagnosis. A recent study by Greenberg-Dotan et al., explored gender differences in morbidity and total health care utilization five years prior to OSA diagnosis. They found that women had 1.3 times higher health expenditures as defined by total physician visits (62).

We also found that the odds of increased length of hospital stay was also two-times greater for females compared to men. Again, these findings are similar to those observed in the Greenberg-Dotan study. They found females with OSA had longer

lengths of stay compared to males with OSA (2.7 days/year vs. 2.3 days/year), though this difference was not statistically significant (62).

Sex-based differences in health care utilization have been reported with other medical conditions (103-107). It has been demonstrated that, compared to men, women in general have greater awareness of physical symptoms that will trigger them to seek more medical help (104). A number of studies have reported that prior to OSA diagnosis, women are being treated for secondary manifestations and non-specific symptoms (105-107).

4.5.2. Increasing Age

Health care utilization amongst the elderly population is a growing concern amongst health care planners. Over the past 30 years, health resource use has increased the fastest in this age group (108). We found that elderly patients (≥ 65 years) were more likely to be in the upper quartile of total outpatient physician visits. The odds of increased physician visits were two times greater for elderly patients compared to younger patients. This finding is similar to those observed by Tarasiuk et al. in which elderly patients with OSA used approximately twice the number of health care resources than younger patients. Specifically, they found that the mean rate of physician visits, two-years prior to sleep testing, was significantly higher in elderly OSA patients compared to middle-aged OSA patients (4.2 visits/year vs. 2.7 visits/year; $p < 0.01$). They also determined that elderly patients had significantly higher duration of stay when hospitalized compared to middle-aged OSA patients (0.6 days/person vs. 1.3 days/person; $p = 0.007$). Again, these findings are similar to our own. The odds of increased length of stay and total

hospitalizations was approximately 3 times higher for elderly patients compared to younger patients.

There are a number of factors that may contribute to this finding. The main difference between elderly and younger OSA patients was significantly higher RDI values and percentage sleep time spent below 90% oxygen saturation in elderly patients. These results are in accordance with earlier reports (109-111). This reduction in sleep quality combined with the increased morbidity observed in elderly patients may be one reason for the observed trend (112).

4.5.3. Daytime Sleepiness

This study found that increased daytime sleepiness (Epworth Sleepiness Score \geq 10) was an independent predictor of increased outpatient physician use and total hospitalizations. The odds of increased physician visits were approximately 1.3 times higher in sleepy patients compared to non-sleepy patients. The odds of increased hospitalizations were also approximately 4-times higher in sleepy patients. This is a novel finding within the sleep literature as no previous study has identified daytime sleepiness as an independent predictor of increased health care use.

Possible mechanisms for such an association require further investigation. It has been suggested that sleepiness may be a surrogate for OSA in the general population. However, this is unlikely to be the case given that OSA was not an independent predictor of health care utilization. Moreover, the correlation between RDI and ESS is relatively poor. The original Epworth Sleepiness Scale paper by Johns, calculated the correlation between RDI and ESS to be 0.55 (89).

Alternatively, sleepiness may be a better predictor of clinically significant disease in patients with OSA than RDI alone. In one of the few randomized control trials evaluating CPAP and hypertension, Barbe et al. failed to find a significant effect from CPAP in non-sleepy patients (113). Though the physiologic mechanisms underpinning these findings remain unclear, this suggests that sleepiness may be an important determinant of which OSA patients benefit from treatment.

Finally, it is possible that excessive daytime sleepiness is either associated with underlying co-morbidities or is a prognostic indicator in patients with these co-morbidities. For example, co-morbid conditions such as hypothyroidism are common in patients with OSA (1.6-11%) and may contribute to this subjective measure of daytime sleepiness obtain by the ESS (114, 115). Unfortunately, no technique for assessing subjective sleepiness has been consistently validated as the reference standard. In addition, the best objective evaluation of sleepiness – the Multiple Sleep Latency Test – is not routinely included in epidemiologic research settings.

4.5.4. Nocturnal Oxygen Saturation

The oxygen desaturation profile as defined by the total sleep time spent < 90% oxygen saturation was also found to be a significant predictor of increased health care utilization. The odds of increased physician visits was approximately 1.5 times greater in patients with more time spent below 90% oxygen saturation. The log odds of increased length of stay were also 3 times higher in patients with a greater degree of hypoxemia.

Significant nocturnal oxygen desaturations have been associated with a number of physiological conditions such as diabetes mellitus, myocardial infarction and

hypertension amongst patients with OSA (4-9, 20). However, the results of this study must be interpreted with caution. The cut-point used in this study ($\geq 12\%$ of the total sleep time spent $< 90\%$ oxygen saturation) is based on findings for the Sleep Heart Health Study (6). They determined this value to be a significant predictor of hypertension amongst a large community-based cohort. A recent paper by Punjabi et al. supports the claim that nocturnal oxygen desaturation is an important contributor to adverse health outcomes associated with OSA, including coronary heart disease (116). They also state that oxygen saturation profile should be an important factor used in defining OSA severity. Unfortunately, there is little research that has assessed the amount of oxygen desaturation required before these health outcomes are observed in cohorts of patients referred for sleep testing.

4.5.5. Co-morbidity

The presence of underlying hypertension, depression and diabetes amongst OSA patients were all independent predictors of increased outpatient physician visits. These co-morbid conditions have been shown to be associated with increased health care resource use in previous literature (117-119). A study by Carriere et al. showed that hypertension was associated with increased outpatient physician visits within an Albertan population (117). They found that physician visit rates were significantly higher amongst patients with hypertension when compared to patients without hypertension. Similar studies have shown health care use, as defined by total hospitalizations and outpatient physician visits, to be significantly higher in patients with diabetes compared to patients without this condition. This is likely due to both conditions requiring continued follow-up

upon diagnosis (75). Furthermore, underlying depression has been shown to further increase health resource use in patients with other co-morbidities (119). This use is even higher amongst patients with multiple co-morbidities (120). Natarajan et al. concluded that emergency room visits, hospitalizations and physician visits were higher in patients with combinations of co-morbidity when compared to patients with just one condition.

Previous myocardial infarction amongst patients with OSA was also found to be a determinant of increased emergency room visits. Myocardial infarction is the leading cause of morbidity and is deemed to be the most expensive medical condition, in terms of total resource costs (37). The observation of increased emergency visits may be related to premature discharge following a myocardial infarction or increased morbidity and complications associated with the initial event (121-123).

4.5.6. Obstructive Sleep Apnea

We found no association between OSA severity and health care utilization. Furthermore, OSA was not a predictor of increased health care use. However, the high number of patients with co-morbidity and obesity may have been key factors in high resource use in this cohort; thus reducing the relative contribution from OSA.

This lack of association may best be explained using the signal-to-noise ratio analogy commonly used in epidemiology (124). In this analogy, the “signal” is the measure of the association the researcher is hoping to hear. The variation in observations may be considered the “noise”. These are the aggregate influences of true biological variation, random events, and measurement errors through which the signal must pierce to be heard. A very loud signal will be heard even amidst considerable background noise.

A soft signal may still be heard if the background noise is minimal. However, a loud signal may go undetected if the background noise is deafening.

A ratio of these two is required to find clear evidence of an association. When the ratio exceeds a conventional threshold, the apparent signal may be considered significantly robust to overcome the background noise. Yet, when the ratio falls below the threshold, no matter how loud the signal, the data cannot be considered to provide evidence of an association.

In the case of OSA severity and health care utilization, it may be that the signal (OSA severity) was too weak to be heard. For example, it may be that the current definition of OSA severity is not ideal and that the respiratory disturbance index (RDI) is an imperfect linear measure of severity. Given that OSA severity as assessed by the RDI is a crude measure, we may not have been able to identify patients with severe enough disease to exhibit increased health care utilization.

It is likely that no single measure adequately defines OSA severity and predicts health care utilization. A number of other factors must also be assessed in the definition of OSA severity, including oxygen desaturation and daytime sleepiness. Punjabi et al. demonstrated that oxygen desaturation is a significant predictor of health outcomes among patients with OSA (116). Hypopneas with desaturations of less than 4% were not associated with cardiovascular disease, while those accompanied by at least a 4% oxygen desaturation were independently associated with cardiovascular disease. Adjustment of the diagnostic threshold based on oxygen saturation can have significant effects on previously accepted associations between OSA and cardiovascular disease.

However, the lack of association between OSA and health care utilization is most likely attributable to the background noise (underlying co-morbidity amongst the patients). Previous literature has shown that the average OSA patient is symptomatic and likely to have hypertension for 5 to 10 years prior to OSA evaluation (55). Patients with OSA have also been reported to be heavy users of antihypertensive medications prior to OSA diagnosis (125). Thus, an obesity-related co-morbidity like hypertension may be driving the increased health care utilization observed in OSA patients.

Kenneth Rothman discussed the idea of multi-causality (126). In his causal pie model, a number of “component causes” each play a role in the occurrence of the defined outcome. In this study, we have seen that there are a number of predictors of increased health care utilization. No individual predictor (component) is responsible for the heavy use of health care resources amongst patients referred for sleep testing. Instead they each play an important role in the development of a profile that results in this outcome. Rothman also described a “necessary cause”; that is to say that one or more components must be present, or is necessary for an outcome to occur. In our study, it could be inferred that this necessary cause is obesity or age. Both appear to be driving the number of co-morbidities. Furthermore, obesity has been well established as a risk factor for OSA in population-based studies (1, 15, 16). It is estimated that more than half of the prevalence of OSA is attributable to excess body weight (15,16). In contrast to other studies, we did not find obesity to be an independent predictor of health care utilization. However, this is almost certainly related to the high number of obese patients distributed in all OSA severity categories, including the reference group (no OSA).

Unfortunately, to truly assess the role of OSA on health care utilization, we would need to identify OSA patients within the general population that do not have co-morbidity or obesity. This may be an impossible task considering that more than half of the prevalence of OSA is attributable to excess body weight (15,16). The rising levels of obesity in North America further compound this task.

A further question is whether health care use would decrease if OSA patients were treated with CPAP. This is less likely given the lack of association between OSA and increased health care utilization to begin with. However, a few studies have reported an association between CPAP use and health care utilization. In a small study of 88 OSA patients with severe cardiovascular and pulmonary disease, a significant decrease in hospitalization for these illnesses was found after the initiation of nasal CPAP among 19 who reported regular use (127).

A larger prospective cohort study looked at 344 OSA patients before and after initiation of CPAP (128). The difference in physician claims between the OSA patients and a group of randomly selected age, gender and socio-economic matched controls was significantly less than the difference in the year prior to diagnosis. However, patients were not matched based on co-morbidities or BMI. In addition, duration of hospital stays for sleep apnea patients decreased from 1.27 days \pm 0.25 (SE) per patient per year one year before diagnosis to 0.54 \pm 0.13 per patient per year ($p = 0.01$). A post-hoc analysis revealed that the differences were only significant in the group of patients who reported to be compliant with CPAP therapy.

In relation to changes in health outcomes associated with OSA, a recent meta-analysis of several randomized, placebo-controlled trials demonstrated a small but

significant decrease in mean 24-hour blood pressure (1.69 mm Hg; 95% CI: -2.69, -0.69 mm Hg) when compared to placebo (129). It was also observed that this reduction was greater in patients with more severe OSA, sleep fragmentation, and who had greater adherence to nightly CPAP therapy. However, many of these studies have been limited by small sample size and limited to patients with severe OSA.

4.6. Comparison of Co-Morbidity Determined by Self-Report and Validated Administrative Algorithms

In this study we found that patient self-report of specific co-morbid conditions had varying levels of agreement with validated administrative algorithms within an 18-month period prior to the sleep diagnostic testing. Diabetes and hypertension were two conditions with the highest agreement ($\kappa = 0.79$ and $\kappa = 0.60$ respectively). These findings are very similar to those in current literature. Robinson et al. (95) compared Manitoba administrative data (hospital and physician records) to survey data from the Manitoba Heart Health Project for diabetes, hypertension, stroke, acute myocardial infarction, and non-specific forms of heart disease. Agreement between the two sources, as measured by the kappa statistic, was highest for diabetes ($\kappa > 0.70$) and hypertension ($\kappa > 0.50$), and lowest for non-specific heart disease ($\kappa = 0.38$). A study by Cricelli et al. also found good agreement between diabetes and hypertension (75). The authors suggested that the consistency of self-reported and administrative data for these two conditions occurs because they are diseases that have a “clear-cut diagnosis” and require ongoing medical treatment.

We found very poor agreement between self-report and administrative data for the presence of cardiac arrhythmia ($\kappa = 0.14$). Under reporting of this condition likely occurred because respondents are not aware of the diagnoses, or lack of familiarity with this medical term found on the self-report questionnaire (79). Though cardiac arrhythmia is very common in patients with OSA (1), accurate self-reporting is more likely to occur for conditions that require frequent contacts with a health professional; cardiac arrhythmia is not one of these conditions. The enhanced definition of cardiac arrhythmia is likely to be an accurate reflection of the prevalence of this co-morbidity within the cohort (32.2%). Previous studies have found slightly higher prevalence values for cardiac arrhythmia amongst patients referred for sleep testing (130, 131). Guilleminault et al. conducted a study on 400 patients referred for PSG and found that 48% of patients with OSA had an arrhythmia. This increased value may be due to cohort differences including the fact that this study was comprised of 96% male subjects. Sleep physicians should be aware of the high prevalence of cardiac arrhythmia in patients referred for sleep testing and the potential under-recognition of this co-morbidity if they rely on patient self-report to determine the presence of this condition.

4.7. Co-Morbidity Measurement by OSA Severity

The measure of co-morbidity using the enhanced combination of data sources found that as OSA severity increased, the proportion of patients with hypertension, diabetes, and myocardial infarction also increased. This dose-response relationship for these specific conditions has been documented in previous studies. The Sleep Heart Health Study prospectively evaluated 6132 randomly selected subjects across the United

States, and demonstrated that OSA was an independent risk factor for hypertension, and that the odds of hypertension increased as OSA severity increased (6). Kapur et al. (59) conducted a chart review of 238 OSA patients and found that 39% of patients had hypertension. This is very similar to the proportion of hypertension identified in this study using the enhanced measure (43.2%) suggesting that this cohort of patients is similar to those referred to other sleep centers throughout North America. A recent cohort study has also shown that severe OSA is associated with an increased risk of cardiac events, such as myocardial infarction (4) and that this risk increases with OSA severity. This supports the dose-response relationship we observed between OSA severity and prevalent myocardial infarction using the enhanced measure of co-morbidity within this cohort.

Interestingly we found that the prevalence of diabetes increased with increasing OSA severity. There is increasing evidence suggesting that OSA is independently associated with insulin resistance and glucose intolerance (20, 30-33). Previous studies have also shown a dose-response relationship between prevalent diabetes and OSA severity (20, 33). Despite these findings, definitive evidence supporting the direction of causality is still needed from population-based longitudinal studies that have carefully selected OSA patients and have adequately controlled for potential confounders, including visceral adiposity (132, 133).

Somewhat surprisingly we found that the prevalence of depression decreased as OSA severity increased. This is consistent with some of the literature that suggests depression and OSA are not associated (26). The fact that self-reported proportions decreased with increasing OSA severity may be due to higher numbers of patients being

actively treated with antidepressant or hypnotic medications with increasing OSA severity. In many cases, patients that are being actively treated will be less likely to report the presence of this condition (55, 76). The result will be an under-reporting of the true proportion. In terms of this similar trend seen in the administrative data, depression is a difficult diagnosis to make due to its varied presentation. It may be under diagnosed in patients with more severe OSA, as physicians may be unable to differentiate between fatigue associated with the sleep disorder and true depressive symptoms (26).

LIMITATIONS

The results of our study should be interpreted in context of the study limitations. The major limitations of this study are a result of its observational design and the data sources used. Although a large number of demographic, clinical, and procedural variables were collected through administrative data sources and within the Alberta Lung Association Sleep Centre, the possibility of residual confounding still exists as there are a number of predictors, such as alcohol intake and physical activity level that are likely associated with health resource use.

Another limitation is the use of self-reported information to characterize the patients past medical history, which may result in an under-report of many medical conditions. However, our use of administrative data and validated algorithms enabled us to more accurately determine the presence of co-morbid conditions.

The use of administrative data to obtain the outcome measures has a number of limitations itself. Physician visits were determined based on claims submitted by physicians. An increasing proportion of specialists are remunerated by salary, thus there may be an under-reporting of claims for this group of physicians. Although they are required to “shadow bill”, the extent to which salaried physicians complete their claims has not been assessed in Alberta. There is also the possibility of misclassification of physician specialty within the claims database. The majority of specialist visits within this study were coded as “internal medicine” (61.2%). This may have resulted in an underestimate of claims by specialist groups such as respirology or psychiatry. However, we have no reason to believe that these misclassifications would occur differentially for a specific OSA category.

In three of the conditions of interest (depression, cardiac arrhythmia, and COPD), validated administrative algorithms were unavailable to compare proportions with self-report. Using an algorithm of at least one physician claim or hospitalization in an 18-month period likely resulted in an under-reporting of these conditions. In addition, the algorithms that were available to establish disease diagnosis only spanned a three-year period prior to sleep testing. Previous work by Robinson et al. (95) considered the effect of both the number of years of administrative data required to establish disease diagnosis, and the number of times a diagnosis code was required to appear in the administrative data to confirm the presence of a disease. As expected, there was a positive relationship between kappa values and the number of years of data and a negative relationship between kappa values and the number of required contacts. Due to the large age range seen in this cohort (18 to 87 years), it is very possible that an elderly patient may have had heart failure or a myocardial infarction a number of years prior to sleep testing. In this case, these conditions may be an underestimate of the true proportions. This may explain the self-report values for these two conditions being higher than the administrative data values.

Finally, our study was limited to a single geographic region (Calgary Health Region) and included only subjects referred for sleep diagnostic testing, which may limit the generalizability of the results. However our results regarding the rates of physician visits and hospitalizations are similar to those reported in the literature, suggesting that our cohort is similar to other sleep cohorts, and the results may be generalizable to other referred populations.

SIGNIFICANCE AND FUTURE RESEARCH

This is one of the largest observational studies to assess the association between OSA severity and health care utilization amongst patients referred for sleep diagnostic testing. Overall, our results suggest that patients referred for sleep testing are heavy users of health care resources. However, there was no evidence that health care use (as defined by total outpatient physician visits, total hospitalizations, length of stay, and emergency room visits) increased with increasing OSA severity. Although presence of OSA, or OSA of increasing severity was not a predictor of increased health care use, a number of significant predictors were identified. These included increasing age, female sex, and patients with significant daytime sleepiness and percent sleep time spent below 90% oxygen saturation.

Although these findings may not be generalizable to the population at large, the results do provide key information to other sleep centers; which form the bulk of sleep diagnostic testing and management. It will also be of particular interest to health care decision-makers responsible for the rational use and distribution of our health care budget. Given the number of co-morbidities present in this population, and in particular the prevalence of hypertension and diabetes, multidisciplinary care clinics directed at treating patients with multiple medical conditions may be an effective strategy to provide comprehensive care to this population.

In a time of limited health resources, and given the high prevalence of OSA, treatment of all patients referred for sleep diagnostic testing would be costly, and likely not feasible. Therefore, determining predictors of increased health care utilization and associated morbidity would allow more effective allocation of health care resources by

focusing on a group of patients at highest risk. This study has been effective in assessing the burden OSA imposes on the health care system. Our large study size allowed us to stratify our cohort into four categories of OSA severity. We were also able to adjust for obesity and underlying co-morbidities within this population; a major limitation of the studies conducted to date.

Further research includes targeting the “at risk” population and the assessment of healthcare utilization after treatment of OSA with CPAP. However, as mentioned previously, CPAP only treats one aspect of the obesity-related diseases that the majority of these patients present with. It would therefore be difficult to determine if CPAP therapy would have a significant reduction on total health resource use amongst patients with OSA. This does not mean that health care utilization is the most relevant clinical endpoint. Quality of life and health benefit are two important endpoints that must also be considered when assessing effectiveness of CPAP therapy.

Finally, this study identified a number of significant predictors of increased health resource use, including excessive daytime sleepiness and nocturnal oxygen saturation. As mentioned previously, the current method of defining OSA severity, through a single polysomnographically defined threshold, is not ideal and it is unlikely such a measure will adequately predict important outcomes including health care utilization. The development of a more prognostic definition of OSA severity, which relies on more than one quantitative measure observed in overnight sleep testing, will help target the “at risk” population in both the clinical and research setting. This may be achieved through cross-collaboration with other disciplines such as cardiology, nephrology and psychiatry.

Table 1. ICD-9-CM and ICD-10 Codes to Define Co-morbidity Among Patients Referred for Sleep Diagnostic Testing

Co-morbidities	ICD-10 diagnostic codes	ICD-9-CM diagnostic codes
Hypertension (with and without complication)	I10.x, I11.x-I13.x, I15.x	401.x, 402.x-405.x
Depression	F20.4, F31.3-F31.5, F32.x, F33.x, F34.1, F41.2, F43.2	296.2, 296.3, 296.5, 300.4, 309.x, 311
Diabetes (with and without complication)	E10.0-E10.9, E11.0-E11.9, E12.0-E12.9, E13.0-E13.9, E14.0-E14.9	250.0-250.9
Asthma	J45.0, J45.1, J45.8, J45.9	493.0, 493.1, 493.8, 493.9
COPD	J44	491.21, 493.2, 496
Myocardial Infarction	I21.x, I22.x, I25.2	410.x, 412.x
Congestive Heart Failure	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5-42.9, I43.x, I50.x, P29.0	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4-425.9, 428.x
Cerebrovascular Accident (CVA)/Transient Ischemic Attack (TIA)	H34.1, I63.x, I64.x, I61.x, I60.x, G45.x	362.3, 430-438
Cardiac Arrhythmia	I44.1-I44.3, I45.6, I45.9, I47.x-I49.x, R00.0, R00.1, R00.8, T82.1, Z45.0, Z95.0	426.0, 426.13, 426.7, 426.9, 426.10, 426.12, 427.0-427.4, 427.6-427.9, 785.0, 996.01, 996.04, V45.0, V53.3

Table 2. Validated Administrative Data Algorithms for Chronic Diseases

Co-morbidities	Authors	Algorithm	Sensitivity	Specificity
Hypertension	Tu et al. ⁹²	2 physician claims in 3 years	73%	95%
Diabetes	Hux et al. ⁹³	1 hospitalization or 2 physician claims in 2 years	86%	97%
Asthma	Huzel et al. ⁹⁴	1 or more physician claims in 1 year	70.1%	99.8%
Myocardial Infarction	Robinson et al. ⁹⁵	At least 1 physician claim or hospitalization in 3 years	69%	97%
Congestive Heart Failure	Austin et al. ⁹⁶	Primary or secondary discharge diagnosis of CHF in CIHI discharge abstracts (in 1 year)	96.8%	85.4%
Cerebrovascular Accident (CVA)/Transient Ischemic Attack (TIA)	Kokotailo and Hill ⁹⁷	Primary discharge diagnosis of stroke in hospitalization discharge abstracts (in 1 year)	67%	97%
Depression, COPD, Cardiac arrhythmia	N/A	No Validated Algorithm	N/A	N/A

Table 3. Patient Characteristics (n=2149)

	All (n=2149)	No OSA (AHI <5) (n=432)	Mild OSA (AHI 5-14.9) (n=738)	Moderate OSA (AHI 15-29.9) (n=443)	Severe OSA (AHI >30) (n=536)	p-value*
Male n (%)	1346 (62.6)	197 (45.6)	463 (62.7)	281 (63.4)	405 (75.6)	<0.001
Age, yrs mean (SD)	50.1 (12.9)	44.0 (12.9)	50.0 (12.5)	52.8 (12.5)	53.0 (11.9)	<0.001
BMI, kg/m ² median (IQR)	31.3 (27.3, 36.6)	27.8 (24.9, 32.2)	30.6 (27.2, 35.4)	32.0 (28.1, 36.8)	34.5 (30.4, 39.8)	<0.001
Neck Circumference, inches mean (SD)	16.0 (1.9)	14.9 (1.5)	15.8 (1.7)	16.3 (1.7)	17.1 (1.8)	<0.001
Epworth Sleepiness Score, mean (SD)	11.3 (5.4)	10.9 (5.1)	10.7 (5.3)	11.4 (5.4)	12.4 (5.5)	<0.001
% TST spent <90% O ₂ Saturation, median (IQR)	6.1 (0.9-29.0)	0.3 (0.1-2.1)	2.7 (0.8-10.1)	10.5 (4.0-34.7)	33.2 (12.9-61.0)	<0.001
Current Smoker, n (%)	354 (16.5)	89 (20.6)	116 (15.7)	60 (13.5)	89 (16.6)	0.111

Abbreviations: AHI = apnea-hypopnea index; BMI = body mass index; TST = total sleep time; IQR = inter-quartile range; SD = standard deviation

* Chi-squared test, analysis of variance (3 degrees of freedom)

Table 4. Agreement between Self-reported Co-Morbidity and Administrative Measure of Co-Morbidity (n=2149)

Validated Algorithm	Self-Report	Administrative Algorithms (claims+hosp)	Both	Either	Kappa [†] (95% CI)	McNemar's ^{††} p-value
Hypertension n (%)	754 (35.1)	714 (33.2)	539 (25.1)	929 (43.2)	0.60 (0.52, 0.63)	0.0428
Diabetes n (%)	289 (13.4)	238 (11.1)	214 (10.0)	313 (14.6)	0.79 (0.75, 0.83)	<0.001
Asthma n (%)	358 (16.7)	247 (11.5)	168 (7.8)	437 (20.3)	0.49 (0.43, 0.54)	<0.001
Myocardial Infarction n (%)	194 (9.0)	53 (2.5)	37 (1.7)	210 (9.8)	0.27 (0.20, 0.35)	<0.001
Heart Failure n (%)	72 (3.4)	29 (1.3)	15 (0.7)	86 (4.0)	0.28 (0.17, 0.40)	<0.001
Stroke n (%)	62 (2.9)	9 (0.4)	8 (0.4)	63 (2.9)	0.22 (0.09, 0.35)	<0.001
No defined Algorithm	Self-Report	No defined Algorithm*	Both	Either	Kappa (95% CI)	McNemar's p value
Depression n (%)	581 (27.0)	573 (26.7)	364 (16.9)	790 (36.8)	0.50 (0.45, 0.54)	0.6983
Cardiac Arrhythmia n (%)	123 (5.7)	654 (30.4)	86 (4.0)	691 (32.2)	0.14 (0.10, 0.17)	<0.001
COPD n (%)	67 (3.1)	77 (3.6)	24 (1.1)	120 (5.6)	0.31 (0.21, 0.41)	0.3074

* At least one physician claim or hospitalization diagnosis in 18 months.

[†] The Kappa statistic is an index of the degree of agreement between two raters.

^{††} McNemar's test of paired proportions is a test of marginal homogeneity that compares the agreement between discordant pairs.

Table 5. Self-reported Co-Morbidity and Administrative Measure of Co-Morbidity Stratified by OSA Severity

	Self-Report				Administrative Algorithms			
	No OSA	Mild OSA	Moderate OSA	Severe OSA	No OSA	Mild OSA	Moderate OSA	Severe OSA
Hypertension	22.7%	29.1%	42.2%	47.4%	19.2%	27.8%	41.3%	45.3%
Depression	30.1%	28.0%	28.4%	22.0%	29.4%	27.2%	27.8%	22.3%
Diabetes	7.6%	10.6%	11.5%	23.7%	6.7%	8.3%	9.5%	19.8%
Asthma	19.7%	17.1%	17.8%	12.7%	12.3%	10.6%	14.2%	9.9%
COPD	3.2%	2.7%	4.3%	2.6%	3.5%	3.3%	3.4%	4.3%
Myocardial Infarction	4.2%	8.5%	11.1%	11.9%	0.9%	2.0%	1.8%	4.9%
Heart Failure	1.4%	3.1%	2.9%	5.6%	0.5%	1.2%	1.1%	2.4%
Stroke	2.3%	2.2%	2.9%	4.3%	0%	0.1%	0.7%	0.9%
Cardiac Arrhythmia	4.2%	6.0%	6.5%	6.0%	23.4%	28.7%	35.0%	34.7%

Table 6. Enhanced Measure of Co-Morbidity using Either Self-Report or Administrative Databases Stratified by OSA Severity

Either Self-Report or Administrative Database (Enhanced)					
Co-morbidity	No OSA (n=432)	Mild OSA (n=738)	Moderate OSA (n=443)	Severe OSA (n=536)	p-value*
Hypertension	28.0%	36.3%	51.0%	58.6%	<0.001
Depression	40.3%	37.5%	38.1%	31.7%	0.12
Diabetes	9.3%	11.9%	12.6%	24.1%	<0.001
Asthma	20.8%	21.3%	21.7%	17.5%	0.41
COPD	5.6%	4.7%	6.8%	5.8%	0.56
Myocardial Infarction	4.6%	8.9%	11.5%	13.6%	<0.001
Heart Failure	1.6%	3.5%	3.4%	7.1%	0.09
Stroke	2.3%	2.2%	3.2%	4.3%	0.15
Cardiac Arrhythmia	24.8%	31.0%	36.6%	36.0%	0.08

* Chi-squared test (3 degrees of freedom)

Table 7. Crude Rates and Crude and Adjusted Rate Ratios for Outpatient Physician Visits, by OSA Severity

OSA Severity	Crude Rate Visits/yr, median (IQR)	Crude Rate Ratio (95% CI's)	Adjusted Rate Ratio*	
No OSA	9.34 (5.34,17.35)	Reference	Reference	
Mild OSA	10.67 (5.34,17.34)	1.00 (0.92, 1.09)	0.98 (0.90, 1.06)	
Moderate OSA	11.34 (6.00,18.68)	1.08 (0.97, 1.19)	1.00 (0.91, 1.10)	
Severe OSA	10.67 (6.67,18.68)	1.05 (0.95, 1.15)	Male: 1.01 (0.89, 1.15)	Female: 0.89 (0.77,1.04)

*Adjusted for sex, age, BMI, co-morbidity and interaction between OSA severity and sex (for severe OSA).

Table 8. Crude Rates and Crude and Adjusted Rate Ratios for Outpatient GP Visits, by OSA severity

OSA Severity	Crude Rate Visits/yr, median (IQR)	Crude Rate Ratio (95% CI's)	Adjusted Rate Ratio*	
No OSA	5.34 (3.34, 8.67)	Reference	Reference	
Mild OSA	5.34 (2.67, 9.34)	1.01 (0.92, 1.10)	0.99 (0.91, 1.07)	
Moderate OSA	6.00 (4.00, 10.01)	1.05 (0.95, 1.16)	0.96 (0.87, 1.06)	
Severe OSA	6.00 (4.00, 9.34)	1.08 (0.98, 1.20)	Male: 1.05 (0.93, 1.19)	Female: 0.91 (0.78,1.07)

* Adjusted for sex, age, BMI, co-morbidity, and interaction between OSA severity and sex (for severe OSA).

Table 9. Crude Rates and Crude and Adjusted Rate Ratios for Outpatient Specialist[†] Visits, by OSA severity

OSA Severity	Crude Rate Visits/yr, median (IQR)	Crude Rate Ratio (95% CI's)	Adjusted Rate Ratio*
No OSA	1.33 (0.67, 2.67)	Reference	Reference
Mild OSA	1.13 (0.67, 2.00)	0.79 (0.66, 0.95)	0.84 (0.70, 1.01)
Moderate OSA	1.33 (0.67, 2.67)	0.84 (0.69, 1.03)	0.88 (0.72, 1.08)
Severe OSA	1.33 (0.67, 2.00)	0.66 (0.54, 0.80)	0.75 (0.61, 0.92)

* Adjusted for sex, age, BMI, and co-morbidity

† Specialists include general internists, respirologists and psychiatrists.

Table 10. Crude Rates and Crude and Adjusted Rate Ratios for All-cause Hospitalizations, by OSA Severity

OSA Severity	Crude Rate Hospitalizations/yr, median (IQR)	Crude Rate Ratio (95% CI's)	Adjusted Rate Ratio*
No OSA	0.67 (0.67, 1.33)	Reference	Reference
Mild OSA	0.67 (0.67, 0.67)	0.83 (0.62, 1.11)	0.83 (0.61, 1.11)
Moderate OSA	0.67 (0.67, 1.33)	0.94 (0.72, 1.24)	0.92 (0.68, 1.23)
Severe OSA	0.67 (0.67, 1.33)	0.94 (0.71, 1.23)	0.94 (0.70, 1.26)

* Adjusted for sex, age, BMI, and co-morbidity

Table 11. Crude Rates and Crude and Adjusted Rate Ratios for Length of Stay (in days), by OSA Severity

OSA Severity	Crude Rate Days/yr, median (IQR)	Crude Rate Ratio (95% CI's)	Adjusted Rate Ratio*
No OSA	3.34 (1.00, 5.67)	Reference	Reference
Mild OSA	1.67 (1.33, 4.00)	1.54 (1.03, 2.30)	1.30 (0.86, 1.97)
Moderate OSA	3.34 (2.00, 6.67)	1.61 (1.08, 2.40)	1.39 (0.92, 2.11)
Severe OSA	4.67 (2.00, 11.34)	1.56 (1.05, 2.31)	1.51 (0.99, 2.30)

* Adjusted for sex, age, BMI, and co-morbidity

Table 12. Crude Rates and Crude and Adjusted Rate Ratios for Emergency Room Visits, by OSA Severity

OSA Severity	Crude Rate Visits/yr, median (IQR)	Crude Rate Ratio (95% CI's)	Adjusted Rate Ratio*
No OSA	0.67 (0.67, 2.00)	Reference	Reference
Mild OSA	0.67 (0.67, 1.33)	0.99 (0.83, 1.18)	0.93 (0.78, 1.12)
Moderate OSA	0.67 (0.67, 1.33)	0.75 (0.62, 0.92)	0.70 (0.58, 0.86)
Severe OSA	0.67 (0.67, 2.00)	0.90 (0.75, 1.08)	0.80 (0.65, 0.98)

* Adjusted for sex, age, BMI, and co-morbidity

Table 13. Determinants of Increased Health Care Utilization – Outpatient Physician Visits

Dichotomous OSA variable model		
Predictors	Odds Ratio (95% CI)	p-value
OSA	1.01 (0.71, 1.44)	0.95
Age	1.82 (1.36, 2.43)	<0.001
BMI	0.96 (0.76, 1.21)	0.74
Female sex	2.25 (1.82, 2.78)	<0.001
ESS	1.25 (1.00, 1.57)	0.048
% TST spent <90%	1.33 (1.06, 1.67)	0.014
Hypertension	1.58 (1.24, 2.02)	<0.001
Diabetes	2.14 (1.57, 2.93)	<0.001
Depression	2.75 (2.17, 3.48)	<0.001
Categorical OSA variable model		
No OSA	Reference	Reference
Mild OSA	1.08 (0.81, 1.45)	0.60
Moderate OSA	1.05 (0.75, 1.47)	0.79
Severe OSA	0.94 (0.66, 1.34)	0.72
Age	2.48 (1.88, 3.26)	< 0.001
BMI	1.14 (0.91, 1.42)	0.25
Female sex	2.11 (1.71, 2.59)	< 0.001
ESS	1.30 (1.04, 1.61)	0.021
% TST spent <90%	1.50 (1.18, 1.91)	0.001
Hypertension	1.61 (1.26, 2.05)	<0.001
Diabetes	2.20 (1.60, 3.00)	<0.001
Depression	2.72 (2.15, 3.44)	<0.001

Table 14. Determinants of Increased Health Care Utilization – Total Hospitalizations

Dichotomous OSA variable model		
Predictors	Odds Ratio (95% CI)	p-value
OSA	5.68 (0.68, 47.47)	0.11
Age	3.49 (1.18, 10.28)	0.023
BMI	0.66 (0.22, 2.02)	0.47
Female sex	1.40 (0.50, 3.92)	0.53
ESS	3.94 (1.03, 15.04)	0.045
% TST spent <90%	0.64 (0.21, 1.97)	0.44
Categorical OSA variable model		
No OSA	Reference	Reference
Mild OSA	3.75 (0.39, 36.60)	0.26
Moderate OSA	7.77 (0.86, 70.25)	0.068
Severe OSA	7.13 (0.64, 78.78)	0.11
Age	3.19 (1.06, 9.58)	0.039
BMI	0.67 (0.22, 2.07)	0.49
Female sex	1.40 (0.49, 3.97)	0.53
ESS	3.93 (1.03, 15.06)	0.046
% TST spent <90%	0.54 (0.16, 1.87)	0.33

Table 15. Determinants of Increased Health Care Utilization – Length of Stay

Dichotomous OSA variable model		
Predictors	Odds Ratio (95% CI)	p-value
OSA	1.08 (0.42, 2.81)	0.87
Age	2.73 (1.32, 5.65)	0.007
BMI	0.61 (0.29, 1.32)	0.21
Female sex	2.12 (1.05, 4.30)	0.036
ESS	1.65 (0.81, 3.37)	0.17
% TST spent <90%	2.93 (1.34, 6.41)	0.007
Categorical OSA variable model		
No OSA	Reference	Reference
Mild OSA	0.97 (0.33, 2.87)	0.96
Moderate OSA	1.04 (0.35, 3.07)	0.94
Severe OSA	2.03 (0.64, 6.43)	0.23
Age	3.19 (1.53, 6.66)	0.002
BMI	0.64 (0.30, 1.37)	0.25
Female sex	2.06 (1.02, 4.16)	0.044
ESS	1.63 (0.80, 3.33)	0.18
% TST spent <90%	2.36 (1.02, 5.43)	0.044

Table 16. Determinants of Increased Health Care Utilization – Total Emergency Room Visits

Dichotomous OSA variable model		
Predictors	Odds Ratio (95% CI)	p-value
OSA	0.68 (0.37, 1.27)	0.22
Age	1.43 (0.75, 2.73)	0.28
BMI	1.57 (0.92, 2.68)	0.098
Female sex	1.12 (0.69, 1.82)	0.64
ESS	0.83 (0.52, 1.34)	0.45
% TST spent <90%	1.21 (0.73, 2.01)	0.46
Myocardial Infarction	2.63 (1.46, 4.76)	0.001
Categorical OSA variable model		
No OSA	Reference	Reference
Mild OSA	0.77 (0.39, 1.49)	0.43
Moderate OSA	0.44 (0.20, 0.98)	0.046
Severe OSA	0.87 (0.40, 1.90)	0.72
Age	1.48 (0.77, 2.82)	0.24
BMI	1.54 (0.90, 2.64)	0.11
Female sex	1.14 (0.70, 1.85)	0.61
ESS	0.83 (0.51, 1.33)	0.43
% TST spent <90%	1.17 (0.67, 2.03)	0.58
Myocardial Infarction	2.56 (1.41, 4.64)	0.002

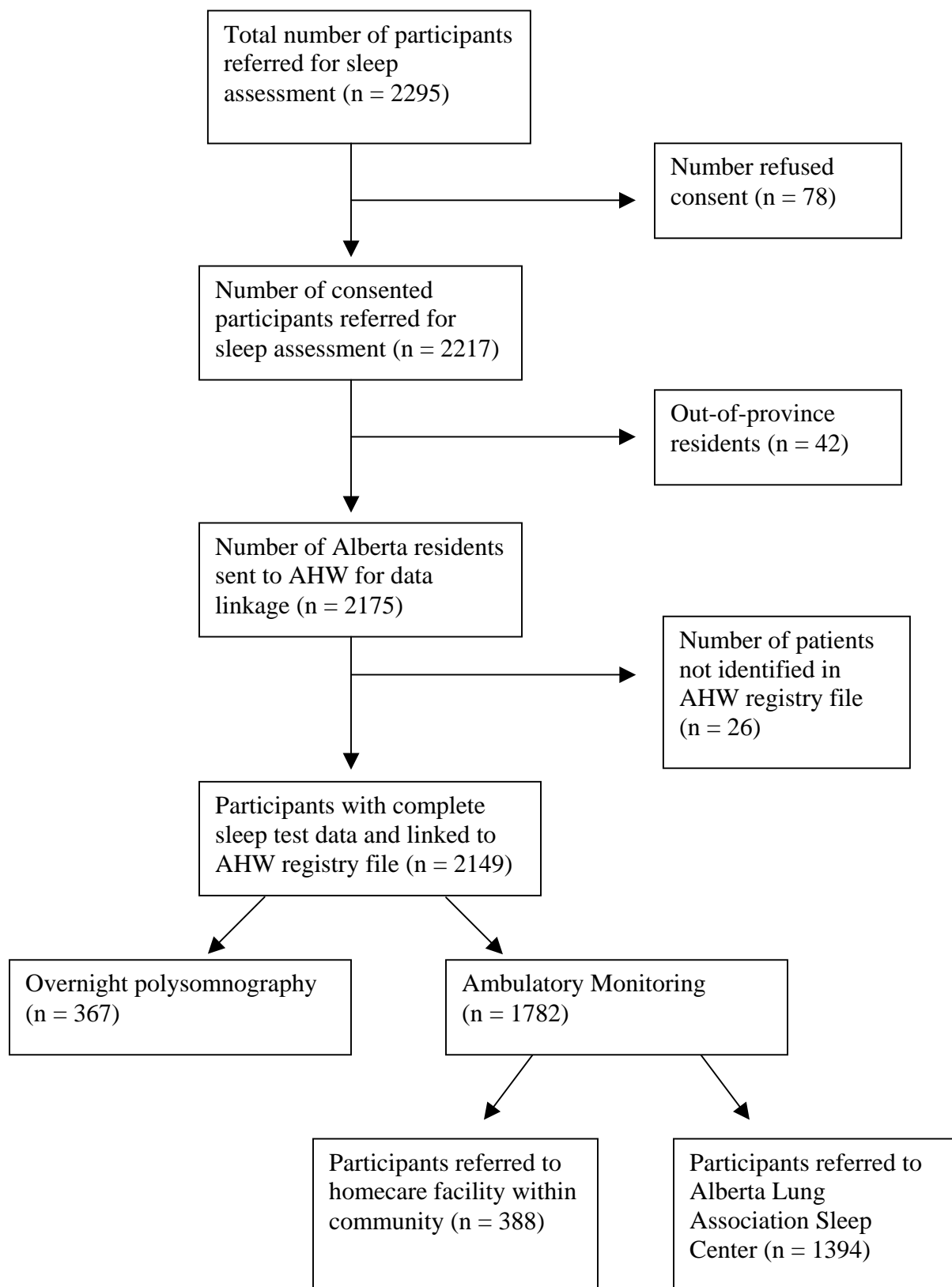
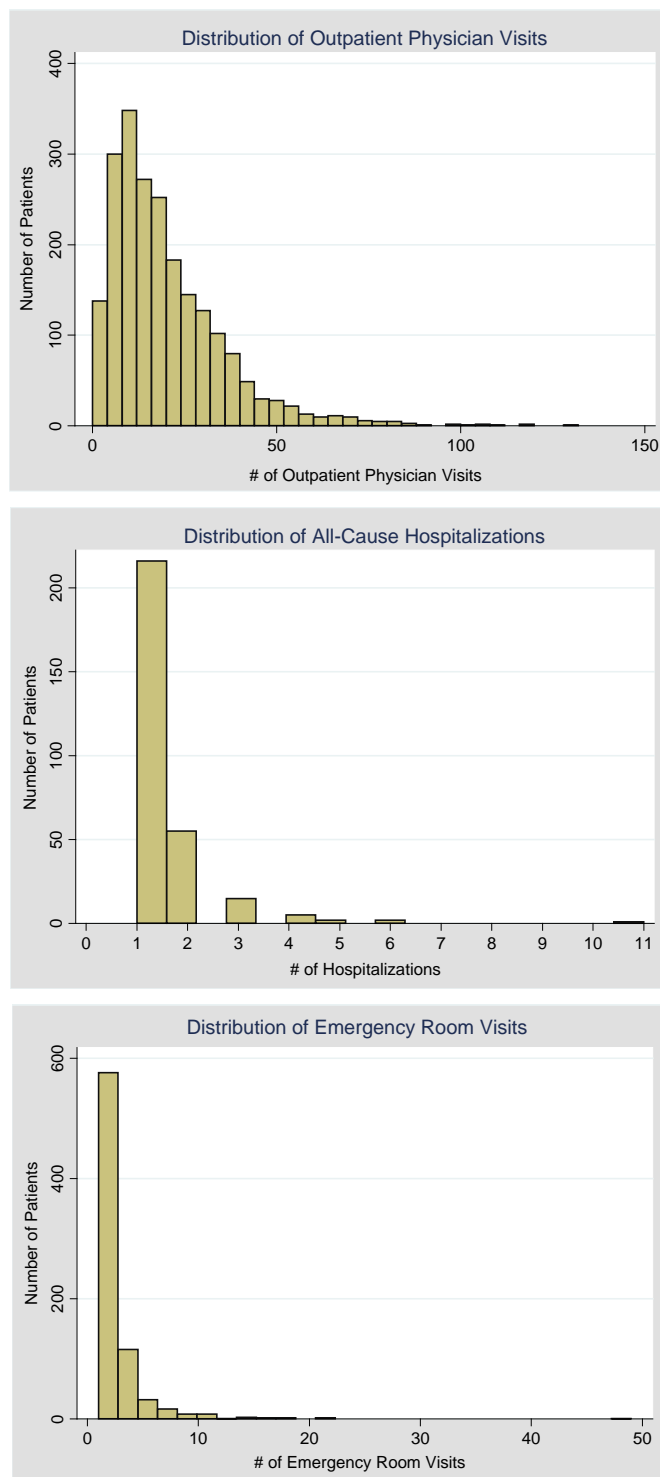
Figure 1. Patient Flow Diagram.

Figure 2. Distributions of Health Care Utilization – Outpatient Physician Visits (all subjects), All-Cause Hospitalizations and Emergency Room Visits (among subjects with at least one hospitalization or visit)



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Appendix 1. Patient Demographic and Clinical Questionnaire.

Date _____

Ht (in) _____

Wt (lb) _____

BMI _____

Neck Circumference (in) _____

Stamp Patient Blue
Card Here☐ Not on Prescription Medication☐ Medication List Unavailable☐ Medication List**List medications (if known):****Current Smoker: yes / no****Entered into Database** ☐**Medical history:**☐ High blood pressure☐ Heart Attack☐ Heart Failure☐ Asthma☐ COPD☐ Other Lung Disease☐ Other Heart Disease☐ Diabetes☐ Kidney Disease☐ Depression☐ Psychiatric condition☐ Stroke☐ Fibromyalgia☐ Dialysis☐ Other*☐ Atrial Fibrillation/ Arrhythmia

*If Other, please list:

Appendix 2. Copy of Ethical Approval



FACULTY OF MEDICINE | UNIVERSITY OF CALGARY

June 19, 2007

OFFICE OF MEDICAL BIOETHICS

Room 93, Heritage Medical Research Bldg
3330 Hospital Drive NW
Calgary, AB, Canada T2N 4N1
Telephone: (403) 220-7990
Fax: (403) 283-8524
Email: omb@ucalgary.ca

Dr. W. Tsai
Department of Medicine
Rockyview General Hospital
Calgary, Alberta

Dear Dr. Murphy:

RE: The Effect of Continuous Positive Airway Pressure on Health Care Utilization and Costs Among Patients with Obstructive Sleep Apnea - Ethics ID: 16344

Thank you very much for the progress report and the annual renewal request, which you have provided on the above-named protocol on June 14, 2007. Please be advised that this report has been reviewed and approved.

The research protocol's ethical approval has been continued by the Conjoint Health Research Ethics Board of the Faculties of Medicine, Nursing and Kinesiology, University of Calgary, and the Affiliated Teaching Institutions. The Board conforms to the Tri-Council Guidelines, ICH Guidelines and amendments to regulations of the Food and Drugs Act re clinical trials, including membership and requirements for a quorum.

The study continues to meet the requirements of the Health Information Act.

You and your co-investigators are not members of the CHREB and did not participate in review or voting on this study.

As Chair of the Conjoint Health Research Ethics Board of the Faculty of Medicine, University of Calgary, and the Affiliated Teaching Institutions, I am pleased to advise you that ethical approval for this proposal has been extended to **2008-04-04**.

Please note that this approval is contingent upon strict adherence to the original protocol. Prior permission must be obtained from the Board for any contemplated modification(s) of the original protocol.

A progress report and annual renewal request concerning this study will be required by **2008-04-04**. This report should contain information concerning:

- (i) the number of subjects recruited;
- (ii) a description of any protocol modification;
- (iii) any unusual and/or severe complications, adverse events or unanticipated problems involving risks to subjects or others, withdrawal of subjects from the research, or complaints about the research;
- (iv) a summary of any recent literature, finding, or other relevant information, especially information about risks associated with the research;
- (v) a copy of the current informed consent form;
- (vi) the expected date of termination of this project;

Please accept the Board's best wishes for continued success in your research.

Yours sincerely,

Margaret Chu
for Glenys Godlovitch, BA(Hons), LLB, PhD
Chair, Conjoint Health Research Ethics Board

c.c. Adult Research Committee

Dr. J. Conly (information)

Research Services