Impact of Obstructive Sleep Apnea on

**Orthognathic Surgery Perioperative Outcomes** 

BY

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# THESIS

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Defense Committee:

Veerasathpurush Allareddy, Chair and Advisor Min Kyeong Lee, Orthodontics Flavio Sanchez, Orthodontics Maysaa Oubaidin, Orthodontics Praveen Gajendrareddy, Periodontics This thesis is dedicated to Dr. Arshad Mohammed who taught me to never take life for granted, the value of orthodontic research, the importance of a good laugh, and the necessity to prioritize our patients' needs above all.

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CHA	ER	<u>PAGE</u>
I.	INTRODUCTION	1
	A. Background	1
	B. Purpose of the Study	3
	C. Significance of the Study	3
	D. Null Hypotheses	3
II.	REVIEW OF THE LITERATURE	4
	A. Adult Obstructive Sleep Apnea Background	4
	B. Adult Obstructive Sleep Apnea Epidemiology	5
	C. Adult Obstructive Sleep Apnea Treatment	9
	D. Pediatric Obstructive Sleep Apnea	
	Epidemiology	13
	E. Pediatric Obstructive Sleep Apnea	
	Treatment	14
	F. Orthognathic Surgery Background	16
	G. Orthognathic Surgery Demographics	19
	H. Orthognathic Surgery: Patient Motivation & Satisfaction	21
	I. Orthognathic Surgery: Complications	22
	1. Nerve Complications	23
	a. Mandibular Nerve Complications	23
	b. Maxillary Nerve Complications	23
	2. Temporomandibular Joint Disorders	25
	3. Hemorrhage	26
	4. Hearing Problems	26
	5. Post-operative Infection	27
III.	MATERIALS AND METHODS	28
	A. Database	28
	B. Data User Agreement and Institutional Review Board Approval	29
	C. Case Selection	29
	D. Dependent Variables	30
	E. Independent Variables	31
	F. Data Analysis	31
IV.	RESULTS	32
	A. Descriptive Statistics	32
	1. Patient-Level Characteristics	32
	2. Hospital-Level Characteristics	40
	B. Linear Regression Model	41
V.	DISCUSSION	44

# TABLE OF CONTENTS

A. Compar	ison with the Literature	44
1.	Demographics	44
2.	Hospital-Level Characteristics	47
3.	Surgical Procedures	47
4.	Surgical Outcomes	48
B. Patient	Characteristics Affecting Length of Stay	50
	tive Sleep Apnea Characteristics in the NIS Database	52
D. Limitati	ons	54
VI. CONCLUSION		55
CITED LITERATURE		56
VITA		71

# LIST OF TABLES

<u>TABLE</u>		<u>PAGE</u>
I.	PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN SUBJECTS UNDERGOING ORTHOGNATHIC SUGERY IN USA, FROM 2006 TO 2014	32
II.	NUMBER OF ORTHOGNATHIC SURGERIES IN USA, FROM 2006 TO 2014	33
III.	AGE OF SUBJECTS UNDEROING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	34
IV.	RACE OF SUBJECTS UNDEROING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	34
V.	SKELETAL CHARACTERISTICS OF SUBJECTS UNDEROING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	35
VI.	PERCENT OF SUBJECTS WITH OBSTRUCTIVE SLEEP APNEA, CATEGORIZED BY SKELETAL DIAGNOSIS, UNDEROING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	35
VII.	NUMBER OF OSTEOTOMIES PERFORMED PER ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	35
VIII.	NUMBER OF COMORBIDITIES ASSOCIATED WITH SUBJECTS UNDERGOING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	36
IX.	BREAKDOWN OF AHRQ COMORBIDITY MEASURES ASSOCIATED WITH SUBJECTS UNDERGOING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	37
X.	COMPLICATIONS THAT OCCURRED POST- ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	38
XI.	PRIMARY EXPECTED PAYER (UNIFORM) OF SUBJECTS UNDERGOING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	38
XII.	MEDIAN HOUSEHOLD INCOME NATIONAL QUARTILE FOR PATIENT ZIP CODE	39
XIII.	DISPOSITION OF PATIENT (UNIFORM) UNDERGOING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	39
XIV.	LENGTH OF STAY OF SUJECTS UNDERGOING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014	40
XV.	TYPE OF HOSPITAL ORTHOGNATHIC SURGERY WAS COMPLETED	40

# LIST OF TABLES (continued)

TA	BLE		<u>PAGE</u>
	XVI.	SIZE OF HOSPITAL, BY BED QUANTITY, WHERE ORTHOGNATHIC SURGERY WAS COMPLETED.	40
	XVII.	REGION OF HOSPITAL WHERE ORTHOGNATHIC SURGERY WAS COMPLETED	41
	XVIII.	FACTORS ASSOCIATED WITH LENGTH OF STAY IN HOSPITAL (MULTIVARIABLE LINEAR REGRESSION ANALYSIS)	42

# LIST OF FIGURES

<u>FIGURE</u>		
I.	SEX OF SUBJECTS UNDERGOING ORTHOGNATHIC SURGERY IN USA,	
	FROM 2006 TO 2014)	33

# LIST OF ABBREVIATIONS

AAP	American Academy of Pediatrics
AHI	Apnea-Hypopnea Index
AHRQ	Agency for Healthcare Research and Quality
BSSO	Bilateral Sagittal Split Osteotomy
CPAP	Continuous Positive Airway Pressure
DS	Data Suppressed
EDS	Excessive Daytime Sleepiness
HCUP	Healthcare Cost and Utilization Project
ННС	Home Health Care
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICF	Intermediate Care Facility
KID	Kids Inpatient Database
MARPE	Mini-Implant Assisted Rapid Palatal Expansion
MMA	Maxillomandibular Advancement
NHANES	National Health and Nutritional Examination Survey
NIS	Nationwide Inpatient Sample
ODI	Oxygen Desaturation Index
OSA	Obstructive Sleep Apnea
PSG	Polysomnography
RDI	Respiratory Disturbance Index
RME	Rapid Maxillary Expansion
SARPE	Surgically Assisted Rapid Palatal Expansion
SEM	Standard Error of Mean
SNF	Skilled Nursing Facility

#### SUMMARY

In this study, the Nationwide Inpatient Sample (NIS), a database representing all hospitalizations in the United States, was evaluated from 2006 to 2014 in order to create a profile of orthognathic surgery patients in the United States. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) medical diagnosis and procedure codes, which are logged in the NIS, were used to identify patient characteristics, procedures done, and patient outcomes. Patient characteristics were consistent with previous studies, indicating a majority of orthognathic surgery patients presented with the following characteristics: white, mid-20-year-old, female, Class III maxillary retrognathic skeletal profile, and private insurance coverage. Orthognathic surgery is a treatment option for patients with moderate to severe OSA. We also evaluated how the presence of how obstructive sleep apnea (OSA) affected patient profile. Patients with OSA were more likely to present with bimaxillary hypoplasia and increased age. Nearly 7% of the patients who underwent orthognathic surgery in the United States from 2006 to 2014 were diagnosed with OSA; this is close to Jonas et al.'s (2017) identification of the presence of moderate to severe OSA in middle aged Americans (3.8-6.5%).

While a vast majority of patients, nearly 99%, were discharged routinely, 20 patients died prior to discharge and many had complications that led to an increased length of hospital stay. The most common complication was general infection (1.2%) followed by bacterial infection (0.4%), pneumonia (0.4%), mycoses (0.2%), viral infection (0.2%), and septicemia (0.1%). Other literature has identified pneumonia and septicemia as complications that significantly increase hospital costs (96% and 37%, respectively) and patient length of hospital stay (310% and 228%, respectively) (Allareddy, 2014).

A linear regression model, adjusting for patient and hospital level confounders, was used to identify risk factors associated with an increased patient length of hospital stay, identifying an increased burden on our healthcare system and increased patient morbidity. Presenting for elective, compared to non-elective, orthognathic surgery was the greatest risk for increased hospital length of stay, increasing length of stay by 56%. This study was the first to evaluate the effect OSA plays on length of hospital stay, showing an increased length of stay by 46% or 3.2 days on average. Other factors that were shown to

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present an increased burden on our healthcare system were: increased comorbidities, Medicaid coverage compared to private insurance, increased number of osteotomies, amongst others. Two of the three most commonly identified comorbidities, hypertension and obesity, are associated with OSA. The presence of maxillary hypoplasia, the most common skeletal characteristic, reduced average length of hospital stay by 15%.

#### I. INTRODUCTION

#### A. Background

Obstructive sleep apnea (OSA) is a dangerous and prevalent disorder that affects up to 22% and 17% of adult male and female populations, respectively, and one to three percent of the pediatric population (Redline et al., 1999). These are likely underestimates of OSA prevalence as Young et al. (1997) estimate that 80 to 90% of OSA remains undiagnosed. OSA is characterized by "recurrent events or partial or complete airway obstruction during sleep" (Chang et al., 2019). Adult OSA leads to excessive daytime sleepiness and is associated with systemic health disorders such as cardiovascular disease, diabetes, cerebrovascular events, memory impairment (Chang et al., 2019), and even increased mortality risk (Yaggi et al., 2005). Pediatric OSA may lead to learning and behavior problems, ranging from ADHD and anger to developmental and neurological delays, and cardiovascular disease (Isono et al., 1998; Brouillette et al., 1982; Lipton and Gozal, 2003).

OSA treatment aims to prevent airway obstruction during sleep. OSA treatment varies based on severity of OSA and location of airway obstruction. The most common OSA treatments are continuous positive airway pressure (CPAP), oral appliances, and surgical procedures (Chang et al., 2019). CPAP, the gold standard treatment for moderate to severe OSA, is shown to improve signs and symptoms associated with OSA (Antic et al., 2011). CPAP provides positive pressure orally and nasally to improve patency of the upper airway during sleep (Chang et al., 2019). Lack of patient compliance is reported as the main drawback of CPAP treatment. Oral appliances are less effective at improving OSA signs than CPAP but are preferred, compared to CPAP or orthognathic surgery, by most patients (Chang et al., 2019; Kushida et al., 2006). Oral appliances, which aim to improve upper airway patency by changing the position of the tongue and affiliated structures, are recommended by the "American Association of Sleep Medicine for patients with mild to moderate OSA or patients with severe OSA who cannot tolerate CPAP or refuse orthognathic surgery" (Kushida et al., 2006).

Maxillomandibular advancement is an orthognathic surgery procedure that requires alteration of the position of both maxilla and mandible. The skeletal advancement, which subsequently advances the base of the tongue and soft palate while elevating the hyoid bone position, aims to increase the anteroposterior upper airway volume, thus decreasing airway obstruction during sleep (John et al., 2018; Hsieh and Liao, 2013). MMA has been shown to be very effective at improving OSA with extensive literature reviews observing 65 to 95% success rate (Hsieh and Liao, 2013) while John et al. (2018) observed 100% success rate and greater success in patients with more severe OSA signs. Walte and Shetar (1996) even consider MMA the gold standard treatment for patients with OSA.

Orthognathic surgeries are a relatively common procedure in the United States; Information from the Nationwide Inpatient Sample (NIS) indicate that nearly 5,500 patients undergo orthognathic surgery per year in the United States. That being said, estimates indicate that over one million persons in the United States are candidates for orthognathic surgery. Orthognathic surgery includes procedures that alter the position of the maxilla and/or mandible with osteotomies and, most commonly, rigid internal fixation. These surgeries aim to correct dentofacial deformities while improving dentofacial function and/ or esthetics (Mutaz and Habal, 2013). Orthognathic surgery provides an opportunity improve anteroposterior, vertical, or transverse skeletal discrepancies that are too severe for treatment with orthodontics alone or that esthetically require underlying skeletal alteration (Cunningham and Johal, 2015). Improvement in oral function and facial esthetics are reported as the primary patient motives for undergoing orthognathic surgery, and a vast majority (87-88%) of patients are satisfied with their surgical results (Oland et al., 2011; Posnick et al., 2016).

Despite high levels of patient satisfaction, orthognathic surgery involves patient morbidity, even mortality at a very low rate, and post-surgical complications that may burden the health field. Published data on post-surgical complications focus on local complications, such as nerve injury, temporomandibular joint disorders, irregular fractures during surgery, and post-surgical infections, but fail to commonly identify systemic complications, such as specific types of infection, that are associated with increased hospital resource utilization and increased burden on our health care system.

## B. **Purpose of the Study**

**Aim #1**- To provide a profile of patients in the United States that underwent orthognathic surgery for maxillary and/or mandibular hypoplasia from 2006 to 2014.

**Aim #2-** To evaluate and identify which patient-level and hospital-level characteristics are associated with altered hospital length of stay in patients undergoing orthognathic surgery.

## C. <u>Significance of the Study</u>

OSA negatively impacts a vast number of Americans annually, leading to behavioral problems, development issues, systemic disease, decreased quality of life, and increased mortality. One treatment option for OSA is orthognathic surgery. A large number, around 5,500, orthognathic surgeries are completed annually in the United States. The association between OSA and orthognathic surgery outcomes has not been evaluated on a large-scale, long-term, national level. The NIS database provides information on all orthognathic surgery patients that require a hospital stay in the United States, thus providing an extensive overview of orthognathic surgery related factors. An improved understanding of which factors lead to increased length of hospital stay post-orthognathic surgery may improve hospital efficiency and minimize healthcare burden.

## D. Null Hypotheses

1. The presence of obstructive sleep apnea is not associated with increased length of hospital stay after orthognathic surgery.

2. Additional patient-level and hospital-level characteristics are not associated with increased length of hospital stay after orthognathic surgery.

#### **II. REVIEW OF THE LITERATURE**

#### A. Adult Obstructive Sleep Apnea Background

Recurrent episodes of partial or complete airway obstruction during sleep characterizes OSA such episodes result in apnea, the "cessation of breathing", or hypopnea, "abnormally slow or shallow breathing", during sleep (Chang et al., 2019). OSA, a dangerous and prevalent disorder, leads to excessive daytime sleepiness and is associated with systemic health disorders such as cardiovascular disease, diabetes, cerebrovascular events, and memory impairment (Chang et al., 2019). Increased severity of OSA is associated with increased mortality risk (Yaggi et al., 2005). Further, OSA prevalence is associated with decreased quality of life and increased risk of motor vehicle accidents (Jonas et al., 2017).

Overnight polysomnography (PSG), conducted in a laboratory (level 1 sleep study) or at home (level 2 sleep study) setting, is the gold standard for diagnosis of OSA (Garg et al., 2017). While sleeping, PSG evaluates respiratory and neurologic parameters (Chang et al., 2019). Air flow changes, measured by respiratory sensors, are classified as apneas (complete flow cessation for 10 seconds), hypopneas (partial flow cessation for 10 seconds), or respiratory-effort-related arousals (minor flow changes that leads to arousal) (Chang et al., 2019). OSA diagnosis is based on the apnea-hypopnea index (AHI), a measure of the average number of apnea or hypopnea events per hour of sleep (Chang et al., 2019). According to the American Academy of Sleep Medicine guidelines for adult OSA, 5-15, >15-30, and >30 AHI indicate mild, moderate, and severe OSA, respectively (Epstein et al., 2009). The threshold for OSA is lower in children according to the American Academy of Sleep Medicine; in children, AHI >1 is considered abnormal, while in infants, 1-5, 5-10, and >10 AHI indicates mild, moderate, and severe OSA, respectively (Hilmisson et al., 2020).

Despite the fact that overnight PSG is the gold standard for OSA diagnosis, several studies have observed inconsistent AHI results when comparing results from different nights (Dean and Chaudhary, 1992; Le Bon et al., 2000; Sforza et al., 2020). The cause of variability is unclear, but may be due to patient discomfort during initial testing affecting their sleep position and sleep structure (Sforza et al., 2020). Simpler methods of diagnosis are needed in order to better identify OSA. Questionnaires are commonly used by physicians and dentists to screen patients that are at high risk for OSA; at risk patients are subsequently referred to their physician for OSA diagnosis by PSG (Abrishami et al., 2010). Chang et al. (2019), among others, argue that additional metrics, such as blood oxygen desaturation extent and severity, arousal extent and duration, and sympathetic activation extent, may improve our understanding and diagnosis of OSA severity. While simpler diagnostic techniques require further validation, level 3 or 4 sleep studies (evaluating respiratory effort, nasal airflow, and/or blood oxygen desaturation) have shown promising and effective diagnostic accuracy and may increase our ability to effectively diagnose OSA (Eastwood et al., 2010).

Upon confirmation of OSA presence, identification of the etiology of airway obstruction may improve treatment results. One technique, drug-induced sleep endoscopy, evaluates anatomical obstructions in the upper airway while the patient is under unconscious sedation (Chang et al., 2019).

## B. Adult Obstructive Sleep Apnea Epidemiology

The drastic variance of OSA prevalence is likely due to lack of OSA awareness in the general population; Young et al. (1997) estimates that 80 to 90% of subjects with OSA remain undiagnosed.

Franklin and Lindberg's (2015) review of the literature from 2008 to 2013 estimates that OSA (AHI≥5) affects 22% (9-37% range) of the male and 17% (4-50% range) of the female population. A study evaluating middle aged adults in the United States reported "mild" and "moderate to severe" OSA prevalence as 10% and 3.8-6.5%, respectively (Jonas et al., 2017). Prevalence of OSA in Taiwan is reported to affect 2.6% of adults, affecting males (3.4%) more than females (1.9%) (Chuang et al., 2008).

Increased age, obesity, and male gender are risk factors for OSA (Franklin and Lindberg, 2014). Independent of confounding risk factors, increasing age is associated with increased prevalence of OSA (Franklin et al., 2013; Bixler et al., 1998; Lindberg et al., 1999; Peppard et al., 2000). While it is commonly thought that snoring is a sign of OSA, OSA prevalence continues to increase with age while snoring increases up to ages 50 to 60 prior to declining. Obesity, measured by BMI, is a major risk factor for OSA (Franklin et al., 2013). Low calorie diet or bariatric surgery has been shown to decrease OSA severity (Peppard et al., 2000; Barvaux et al., 2000; Young et al., 2005; Grunstein et al., 2007; Greenburg et al., 2009). Over half (58%) of moderate to severe OSA subjects are considered obese (BMI  $\geq$ 25 kg/mg<sup>2</sup>), and while 39% of normal weighted women have OSA, 99.9% of these women do not have severe OSA (Young et al., 2005; Franklin et al., 2013). It is believed that increased upper airway mass is the pathologic cause for the association between increased BMI and OSA prevalence (Shelton et al., 1993). OSA is associated with systemic disease, such as stoke, hypertension, and coronary artery disease, and cross-sectional studies indicate OSA is associated with increased risk for diabetes mellitus (Franklin and Lindberg, 2014). In the population under 70 years old, OSA diagnosis increases risk of death (Franklin and Lindberg, 2014; Yaggi et al., 2005). The male predilection for OSA is not well understood but could be explained by gender differences in body fat distribution, upper airway anatomy, or hormonal effects on airway muscle (Franklin and Lindberg, 2014).

Other potential OSA risk factors include cigarette smoking and alcohol consumption (Franklin and Lindberg, 2014). While cigarette smoking is not an established risk factor for OSA, an association between smoking is shown in several cross-sectional epidemiological studies (Schmidt-Nowara et al., 1990; Lindberg et al., 1997; Franklin et al., 2004; Wetter et al., 1994). Some studies show a relationship between consistent "secondhand smoking" and OSA prevalence. (Franklin et al., 2004). Contradictory and inconclusive evidence exists regarding this association, and studies have not proven that smoking increases incidence or that smoking cessation decreases OSA incidence (Franklin et al., 2004; Newman et al., 2001). Krol et al. (1984) showed that alcohol consumption decreases the function of upper airway and oropharyngeal muscles but results from epidemiological studies vary whether chronic alcohol consumption increases prevalence of OSA (Udwadia et al., 2004; Lindberg et al., 1998; Bearpark et al., 1995; Peppard et al., 2007; Worsnop et al., 1998).

The most prevalent and most serious symptom of OSA is commonly regarded as excessive daytime sleepiness (EDS), but only a fraction of OSA patients exhibit EDS (Stradling et al., 2000; Kapur et al., 2005). Continuous positive airway pressure (CPAP), the gold standard for OSA treatment, shows improvement in EDS compared to sham CPAP and oral placebos (Engleman et al., 1999; Faccenda et al.,

2001; McDaid et al., 2009). There is uncertainty whether OSA or snoring induces EDS. EDS is more prevalent in male and female snorers, 16% and 23%, compared to non-snorers, 10% and 3%, respectively (Young et al., 1993). Further, patients with chronic diseases, such as congestive heart failure or end-stage renal disease, show a weaker association between OSA and EDS than healthy patients (Arzt et al., 2006; Walsleben et al., 2004; Hanly, 2008).

Several cross-sectional studies indicate a relationship between OSA and hypertension, two diseases that are prevalent in the adult population (Bixler et al., 2000; Durán et al., 2001; Franklin et al., 2013; Nieto et al., 2000). Peppard et al. (2000) conducted a study of 709 participants comparing AHI scores from polysomnography tests and hypertension prevalence at baseline and four years later. Subjects with OSA showed an increased risk for hypertension of two to three times, depending on severity of OSA (mild OSA, OR=2.03; moderate to severe OSA, OR=2.89) (Peppard et al., 2000). Further follow up showed a dose response relationship between OSA severity and development of systolic non-dipping blood pressure while sleeping (HIa et al., 2008). When considering age of patients with severe OSA (AHI  $\geq$ 15), a 2.38 increased odds ratio (95% CI, 1.30-4.38) for hypertension exists in subjects under 60 years old, while no relationship exists for elderly subjects (Haas et al., 2005). Despite the apparent relationship between OSA and hypertension, it has not been shown that OSA treatment with CPAP improves hypertension (Haentjens et al., 2007).

Cross-sectional studies show a significant association between OSA and coronary artery disease, specifically angina pectoris and/or myocardial infarction (Franklin et al., 1995; Mooe et al., 1996). Shahar et al. showed increased risk (odds ratio 1.27) of developing coronary artery disease in subjects in the top 25% of OSA (AHI>11) (Shahar et al., 2001). Prospective studies evaluating whether OSA is a primary etiology for coronary artery disease have not been conducted, but it has been shown that CPAP treatment of OSA showed improved cardiovascular outcomes (Buchner et al., 2007; Milleron et al., 2004; Peker et al., 2006).

Stroke is another complication of OSA. Independent of other factors, OSA with EDS significantly increases risk for stroke (Yaggi et al., 2005). A 10-year follow up showed a dose response

relationship between OSA, diagnosed as AHI from polysomnography, and stroke incidence (Valham et al., 2008). A cross-sectional study supports these findings, showing increased risk of developing stroke (hazards ratio 2.52; 95% CI, 1.04-6.01) in subjects 70-100 years of age (Munoz et al., 2006).

Cross-sectional studies show a strong association between diabetes mellitus and OSA, independent of confounders (Ip et al., 2002; Punjabi et al., 2004; Punjabi and Beamer, 2009; Reichmuth et al., 2005). However, contradictory results have been published whether OSA is a risk factor for diabetes mellitus; Reichmuth et al. showed an increased risk (OR 1.62; 95% CI, 0.7-3.6) for diabetes development over four years in subjects with severe versus mild OSA, but lacked statistical significance (Reichmuth et al., 2005) while Botros et al. (2009) observed a positive, independent association between baseline OSA and diabetes incidence. Independent of risk factors for OSA and diabetes, such as BMI, age, and hypertension, and OSA treatment with CPAP, an association (OR 4.4; 95% CI, 1.1-18.1) was observed between oxygen desaturation index >5 and diabetes mellitus incidence at an 11-year follow up (Lindberg et al., 2012).

The effect of OSA on clinical mortality has not been well established, but indicates an age-related association (Bliwise et al., 1988; Lavie et al., 1995; Lindberg et al., 1998; Mant et al., 1995; Punjabi et al., 2009; Young et al., 2008). AHI significantly predicted increased mortality risk in men in 30-49 years of age, but not in elderly men, in a prospective study (Lavie et al., 1995); another study showed no association between OSA and increased mortality in elderly men (Bliwise et al., 1988; Mant et al., 1995). A cross-sectional questionnaire study on a large population in Sweden reflected similar results, indicating a significantly increased mortality rate up to, but not beyond, the age of 50 in men with OSA who snore (Lindberg et al., 1998). Results from cohort studies, such as the Wisconsin study (Young et al., 2008) and the Sleep Heart Health Study (Punjabi et al., 2009), indicate increased mortality rates with increasing AHI, thus increasing OSA severity. In subjects with AHI  $\geq$ 30 compared to those with AHI <5, increased adjusted hazard ratio, thus all-cause mortality, was 3.0 (CI 95%, 1.4-6.3) and 1.46 (CI 95%, 1.14-1.86), in two separate studies (Punjabi et al., 2009; Young et al., 2008). While results are neither from the highest

level of studies nor consistent across studies, it appears that increased mortality risk is associated with more severe OSA in non-elderly populations.

## C. Adult Obstructive Sleep Apnea Treatment

From least to most invasive, common treatments for adult OSA include behavioral and lifestyle modifications, medication, continuous positive airway pressure (CPAP), oral appliances, and surgical procedures (Chang et al., 2019).

Behavioral modifications aim to reduce the risk of airway obstruction during sleep. Avoidance of sedatives and alcohol, in order to avoid upper airway muscle relaxation, is recommended for all subjects with OSA while weight loss, in order to reduce the size of soft palate and/or tongue, has been shown to improve OSA symptoms in certain populations (Chang et al., 2019). The avoidance of supine sleep position, preventing the tongue and mandible from obstructing the airway by moving posterior, also has been shown to decrease AHI (Chang et al, 2019).

Pharmacotherapy has been proposed as a technique to improve OSA, but the efficacy has yet to be effectively established (Chang et al., 2019). A variety of pharmacological agents have been evaluated including "ventilatory stimulants, serotoninergic and REM sleep suppressant agents, acetylcholinesterase inhibitors, medications for predisposing endocrine disorders, stimulants..." (Lin et al., 2012). In a review of the literature, Lin et al., (2012) found that no single pharmacological agent has been shown to be effective for OSA treatment, but that medications can be used to supplement therapy. One medication that has shown promise in OSA treatment is Donepezil, an acetylcholinesterase inhibitor, which was shown in two studies to improve AHI, oxygen saturation, and decrease daytime sleepiness (Moraes et al., 2008; Susky et al., 2012). Ventilatory stimulants have shown mild clinical and minimal therapeutic effect in OSA treatment (Lin et al., 2012; Hedner et al., 1996); often, the negative side effects outweigh the benefits (Orth et al., 2005; Nussbaumer-Ochsner et al., 2012). Finnimore et al. (1995) found that low-dose baclofen, a GABA agonist, may improve sleep continuity and improve OSA symptoms in subjects with mild OSA. Adjunctive medications are also used. Stimulants, such as modafinil and armodafinil, have

been shown to improve OSA side effects such as daytime sleepiness and memory impairment, but 10% of subjects exhibit negative side effects (Hirshkowitz et al., 2007; Roth et al., 2006). Further research is needed in this area.

CPAP, the first line treatment for OSA, provides positive pressure orally and nasally to improve patency of the upper airway during sleep (Chang et al., 2019). In moderate to severe OSA subjects, CPAP is the gold standard for treatment and effectively improves signs (decreased AHI; improved cardiovascular parameters) and symptoms (improved quality of life; decreased daytime sleepiness) associated with OSA (Antic et al., 2011). Handan (2019) observed a 75% success rate, defined as 50% improvement in AHI score, in treatment of subjects with moderate to severe OSA with CPAP. However, noncompliance rates, due to machine noise, xerostomia, discomfort, risk of claustrophobia, and upper airway infection, range from 46 to 83% (Chang et al., 2019; Weaver and Grunstein, 2008).

While oral appliances are less effective than CPAP at reducing AHI, most patients prefer oral appliance therapy over CPAP or surgical treatment (Chang et al., 2019; Kushida et al., 2006). Oral appliances aim to improve upper airway patency by changing the position of the tongue and affiliated structures (Chang et al., 2019). While many designs exist, mandibular advancement appliances and tongue retaining devices are the two most common types of oral appliances (Chang et al., 2019). Oral appliances should be custom, tooth borne, and titratable and overseen by a qualified dentist (Ramar et al., 2015).

The American Association of Sleep Medicine "recommends the use of oral appliances in patients with mild to moderate OSA and patients with severe OSA who cannot tolerate CPAP or refuse orthognathic surgery" (Chang et al., 2019). Comparing oral appliances and CPAP, Ramar et al. (2015) reported no statistical difference in achieving desired AHI for patients with mild OSA. Compared to controls, oral appliance usage showed a mean reduction of 13.60 AHI (95% CI; range -15.25 to -11.95) (Ramar et al., 2015). However, when comparing AHI reduction in oral appliances compared to CPAP treatment, CPAP reduced AHI by a greater magnitude (6.24 events per hour) (Ramar et al., 2015). When used in the correct patient population, oral appliances can

effectively improve OSA signs and symptoms. The following craniofacial characteristics are associated with more favorable outcomes with oral appliance therapy: with retrusive mandibles, short anterior facial heights, and narrow retroglossal airways (Hoekema et al., 2007; Shen et al., 2012). Dentoalveolar changes, specifically lower incisor proclination, decreased overjet, and decreased overbite, are negative side effects of long-term oral appliance therapy (Araie et al., 2018). Skeletal side effects, such as mandibular rotation or mandibular length, do not appear to be consistent based upon Araie and coworkers' (2018) analysis of the literature and meta-analysis. The negative side effects require consistent monitoring of patients with oral appliances, but do not outweigh the benefits of oral appliance therapy and do not contraindicate their use (Chang et al., 2019).

In pre-pubertal children, dentally anchored rapid maxillary expansion (RME) has been shown to effectively increase oral cavity size allowing a more anterior position of the tongue during sleep and increase nasal airway volume reducing nasal airway resistance (Yoon et al., 2020). RME has been recommended as a non-invasive option to improve OSA symptoms and has been shown to improve pediatric OSA in children with narrow maxillary dimensions (Camacho et al., 2017). RME is not feasible in adults due to increased resistance from increased interdigitation of midpalatal and circummaxillary sutures (Proffit et al., 2019). Predictable maxillary distraction osteogenesis is achieved in young adults with a skeletally anchored expander, termed mini-implant assisted rapid palatal expansion (MARPE); the addition of minimally invasive osteotomies increases predictability in the adult population (Yoon et al., 2020). Yoon et al. (2020) observed an improvement in all OSA descriptors, including a 53% reduction (from 17.65 to 8.17, p <0.0001) in AHI score in adult subjects with narrow maxilla and high vaulted palates.

Surgical treatments for OSA include uvulopalatopharyngoplasty, tracheostomy, and maxillomandibular advancement (MMA) surgery (Chang et al., 2019). Uvulopalatopharyngoplasty is a surgical procedure that aims to remove the tonsils, uvula, and posterior velum; several surgical variations exist (Chang et al., 2019). It has been shown to improve OSA symptoms in adults with excessive tonsillar

tissue and relatively normal palatal position but has not been shown to consistently normalize AHI (Choi et al., 2016). Thus, the use of uvulopalatopharyngoplasty as a primary method to treat moderate to severe OSA is not recommended (Auroa et al., 2010). Considered the last-resort method for OSA treatment, tracheostomy is a surgical procedure placing a cannula into the trachea, thus allowing patients to breathe by bypassing an upper airway obstruction (Chang et al., 2019). It has been shown to be effective for patients who do not tolerate CPAP or who have refused or are not candidates for MMA or other soft tissue surgeries (Chang et al., 2019; Haapaniemi et al., 2001).

MMA is an orthognathic surgical procedure involving LeFort 1 maxillary surgery and bilateral sagittal split osteotomy (BSSO) surgery of the mandible (Hsieh and Liao, 2013). The skeletal advancement, which subsequently advances the base of the tongue and soft palate while elevating the hyoid bone position, aims to increase the anteroposterior upper airway volume, thus decreasing airway obstruction during sleep (John et al., 2018; Hsieh and Liao, 2013). Hsieh and Liao's (2013) evaluation of the literature observed an association between MMA and successful OSA treatment in 65 to 95% of subjects and reduction of AHI by 61 to 92%. John et al. (2018) identified a 100% success rate treating OSA patients with MMA and observed a greater improvement in patients whose pre-surgical AHI was greater. Walte and Shetar (1996) even consider MMA the gold standard treatment for patients with OSA. Subsequent sections will delve into negative side effects of such orthognathic surgeries.

In 2014, the United States Food and Drug Administration approved hypoglossal nerve stimulation as a technique to treat obstructive sleep apnea (Chang et al., 2019). Hypoglossal nerve stimulation, first described in 1993, aims to activate the genioglossus muscle, protruding the base of the tongue, to minimize retro-lingual airway collapse during sleep (Schwartz et al., 1993). Strollo et al. (2014) evaluated the effect of hypoglossal nerve stimulation on adults with moderate to severe OSA, "low BMI" (<32), with anteroposterior airway collapse in the retro-lingual region who did not respond to CPAP therapy. Results showed a significant improvement in objective (68% AHI reduction; 70% oxygen desaturation index (ODI) reduction) and subjective (daytime sleepiness; quality of life) measurements of OSA 12 months after surgical placement of hypoglossal nerve stimulator (Strollo et al., 2014). Subjective improvements with hypoglossal nerve stimulation were comparable to those found by Weaver et al. (2007) when evaluating patients with moderate to severe OSA with CPAP. Only 2% of subjects evaluated complained of discomfort requiring surgical repositioning of the device (Strollo et al., 2014). Chang et al. (2019) referred to hypoglossal nerve stimulation as a "less invasive and more effective option for selected patients".

## D. Pediatric Obstructive Sleep Apnea Epidemiology

Childhood OSA has been reported to occur from 1 to 3% of the pediatric population (Redline et al., 1999), but a significantly higher prevalence is reported in pediatric patients with craniofacial anomalies: "22 to 65% in children with cleft lip and/or palate (MacLean et al., 2009), 40 to 68% of children with Apert, Crouzon, and Pfeiffer craniosynostosis syndromes (Hoeve et al., 2003; Driessen et al., 2013), and 85% of infants with Pierre Robin sequence (Anderson et al., 2011)" (Garg et al., 2017). Other studies have identified the prevalence of pediatric OSA as 3 to 27% in children and 1 to 10% in adolescents (Huynh et al., 2016). Side effects of pediatric OSA range from problems with learning and behavior, such as ADHD, anger, and aggression, (Isono et al., 1998) to serious systemic consequences such as developmental and neurological delays, failure to thrive, and cardiovascular disease (Brouillette et al., 1982; Lipton and Gozal, 2003).

The threshold for OSA is lower in children than adults, according to the American Academy of Sleep Medicine; in children, AHI >1 is considered abnormal, while in infants, 1-5, 5-10, and >10 AHI indicates mild, moderate, and severe OSA, respectively (Hilmisson et al., 2020). Upon diagnosis of OSA with overnight polysomnography, anatomical evaluation should be done to identify the location of obstruction. Endoscopy of the airway and imaging (lateral cephalograms and computed tomography) can help identify anatomical obstructions and craniofacial skeletal relationships that may contribute to OSA (Myatt and Beckenham, 2000; Guilleminault et al., 2004). It is believed that soft tissue hypertrophy is the most frequent etiology of pediatric OSA, but upper airway obstruction may also occur from abnormality in the relationship between craniofacial skeletal and soft tissue anatomy (Garg et al., 2017).

## E. <u>Pediatric Obstructive Sleep Apnea Treatment</u>

The American Academy of Pediatrics' (AAP) guidelines for treatment of childhood OSA, which are not based upon strong scientific evidence, focuses on (1) reduction of hypertrophic lymphoid tissue in subjects with OSA and hypertrophic lymphoid tissue or (2) CPAP in patients with refractory OSA after tonsillectomy or with OSA but no hypertrophic lymphoid tissue (Marcus et al., 2013). These guidelines are indicated for children who are otherwise healthy, without craniofacial anomalies or systemic illnesses (Marcus et al., 2013). About 80% of patients with OSA and adenotonsillar hypertrophy benefit from adenotonsillectomy (Marcus et al., 2013), the AAP's first-line treatment (Marcus et al., 2012), showing improved OSA and decreased secondary symptoms such as behavior problems (Ali et al., 1996), learning impairment (Gozal, 1998), and cardiovascular problems (Laurikainen et al., 1992). Post-adenotonsillectomy, 20% of patients have persistent OSA symptoms whom the AAP recommends CPAP therapy (Marcus et al., 2013; Lipton and Gozal, 2003; Tang et al., 2016). Marcus et al. (1995) observed CPAP effectiveness in 86% of patients. A major limitation of CPAP, the second-line treatment for pediatric OSA recommended by the American Association of Pediatrics, is noncompliance in infants (25 to 75%) (Katz et al., 2012) and children (50%) (Adeleye et al., 2016).

Alternative treatment options include, but are not limited to, orthodontics (rapid maxillary expansion or oral appliance therapy), medical treatment (intranasal corticosteroids), and/or craniofacial surgery (Garg et al., 2017). RME, distraction of the midpalatal suture, increases the transverse dimension of the maxilla which causes subsequent increased nasal airway volume and potentially anterior tongue positioning (Pirelli et al., 2004; Monini et al., 2009). Pirelli et al. (2004) evaluated the effect of RME in children, mean age of 8.7 years old, with OSA (mean AHI 12.2), maxillary constriction, but without adenotonsillar hypertrophy. Results showed a significant decrease in AHI (AHI<1) in all of the children after four months (Pirelli et al., 2004). A 12-year follow up showed stable maxillary expansion in these patients (Pirelli et al., 2015). A review of the literature supports Pirelli's findings, showing that RME improves, not worsens, OSA by decreasing AHI by 70% (Camacho et al., 2017). Interestingly,

Guilleminault et al. (2011) observed similar improvements in OSA in patients indicated for both adenotonsillectomy and RME, regardless of the order of treatments; Guilleminault et al. (2011) concluded a greater sample size was needed to provide adequate power.

In patients with OSA who have a retrognathic mandible, orthodontic oral appliances that posture the mandible forward, aiming to redirect mandibular growth anterior, are believed to improve pediatric OSA by increasing oropharyngeal volume (Huynh et al., 2016). A significant reduction in AHI with mandibular advancement oral appliances was observed in 64.2% (Villa et al., 2002) of treated subjects while Cozza et al. (2004) observed an average 54% reduction in AHI. Interestingly, a significant reduction in tonsillar hypertrophy was noted in 66.7% of patients treated with oral appliances compared to only 14.3% of controls (Villa et al., 2002). Larger studies are needed to validate the effectiveness of oral appliances in treatment of pediatric OSA.

Anti-allergy medications and leukotriene antagonists were shown to improve OSA symptoms post-adenotonsillectomy (Kheirandish et al., 2006). Fluticasone, an intranasal spray, was shown to decrease AHI, (Alexopouloset al., 2004) and improve quality of life (Mansfield et al., 2004) in children with allergic rhinitis and pediatric OSA. Leukotriene antagonists, aiming to prevent lymphoid proliferation, were shown to effectively improve sleep, measured by respiratory disturbance index (RDI), and reduce adenoid size (Goldbart et al., 2005; Kheirandish et al., 2006).

Craniofacial surgery, such as mandibular or midfacial distraction osteogenesis, is often performed after conservative therapy is deemed ineffective for patients with craniofacial anomalies and airway obstruction (Perkins et al., 1997; Tapia et al., 2008; Denny et al., 2004; Abel et al., 2012; Ahmed et al., 2000). Mandibular distraction osteogenesis prevented 91.3% of infants from undergoing post-surgical tracheotomy or intubation and is significantly associated with decreased AHI (Ow and Cheung, 2008). Midfacial distraction osteogenesis is often performed to improve midface hypoplasia in skeletally immature patients. Xu et al. (2009) and Flores et al. (2009) observed significant increase in airway volume and improvement in OSA subsequent to midfacial distraction osteogenesis. Ettinger et al. (2011) identified that the vector, not magnitude, of distraction is more strongly associated with improvement in respiratory status; post-LeFort 3 distraction osteogenesis in syndromic patients, AHI improvement was observed when sella-nasion-subspinale increased by 22.8 degrees while no AHI improvement was observed with a 7.6 degree increase.

## F. Orthognathic Surgery Background

With advances in surgical technique, stability, and technology, vast progress in orthognathic surgeries has occurred over the past 70 years. The modern era of orthognathic surgery began in 1957 with the development of the bilateral sagittal split osteotomy (BSSO), a surgical procedure allowing anteroposterior movement of the mandible (Trauner and Onwegeser, 1957). The most common maxillary orthognathic surgery, the LeFort 1 osteotomy, underwent significant advances in the 1960s allowing surgeons to manipulate the position of the maxilla in all three spatial planes (Bell, 1975; Epker and Wolford, 1975). The repositioning of one or both jaws, the chin, or dentoalveolar segments was surgically plausible by the 1980s (Proffit et al., 2019). Surgical predictability and post-surgical patient comfort improved due to improved understanding of postsurgical relapse and rigid internal fixation, respectively, in the 1990s (Proffit et al., 2019).

Orthognathic surgery is a procedure that is done in conjunction with orthodontic treatment to treat dentofacial deformities while improving dentofacial function and esthetics (Mutaz and Habal, 2013). Treating such individuals with orthodontics alone, referred to as compensating orthodontics or orthodontic camouflage, has been shown to lead to periodontal damage, root resorption, and potentially dental relapse (Boyd et al., 1989). Orthognathic surgery may be used to treat subjects with anteroposterior, vertical, or transverse skeletal discrepancies that are too severe for treatment with orthodontics alone or that esthetically require underlying skeletal alteration (Cunningham and Johal, 2015). Orthognathic surgery candidates often present with Class II or III malocclusion, anterior open bite or severe deep bite, or facial asymmetries (Cunningham and Johal, 2015). Surgeries include maxillary, mandibular osteotomies, or bimaxillary (maxillary and mandibular) osteotomies. In contemporary orthognathic surgery, the LeFort 1 osteotomy is by far the most prevalent maxillary surgical technique (Proffit et al., 2019). Repositioning of the maxilla up and/or forward is reported to be very predictable with LeFort 1 osteotomies; vital structures prevent surgically moving the maxilla backwards (Proffit et al., 2019). Maxillary LeFort 1 surgeries can include segmental osteotomies in order to treat skeletal arch form discrepancies, whether in the transverse or vertical dimension (Posnick et al., 2018). Increased resistance of midpalatal and circummaxillary sutures prevents common orthopedic expansion, RME, in adults; surgically assisted rapid palatal expansion (SARPE) provides an alternative treatment option for adult expansion while mini-implant assisted rapid palatal expansion (MARPE) provides an alternative that is more predictable in younger adults than older adults (Proffit et al., 2019). SARPE includes, most commonly, midpalatal and LeFort 1 osteotomies followed by distraction with a conventional tooth-borne expander (Proffit et al., 2019). Similar stability is observed in SARPE and surgical expansion with LeFort 1 segmental osteotomies (Chamberland and Proffit, 2011).

Subjects with maxillary anterior-posterior deficiency, which represent as a class III malocclusion, are almost always treated with LeFort 1 osteotomy for maxillary advancement (Posnick et al., 2018). Often, these patients benefit from mandibular ramus osteotomies in order to improve asymmetry, cant, occlusal plane pitch, and/or the horizontal position of the mandible (Proffit, 1991). In 92% of the patients evaluated, LeFort 1 and BSSO's improved all facial characteristics associated with primary maxillary deficiency (Posnick et al., 2018).

The BSSO is the most common mandibular orthognathic surgical procedure (Proffit et al., 2019). The main benefits of BSSO include: ability to adjust both the horizontal position and angulation of the distal (tooth-bearing) segment, compatibility with internal rigid fixation (preventing need for maxillomandibular fixation), and improved healing and stability due to increased bone-to-bone contact (Proffit et al., 2019). While mandibular constriction is surgically feasible, it is rarely done; mandibular transverse expansion requires distraction osteogenesis (Proffit et al., 2019). Genioplasty, a repositioning of the inferior border of the mandible or chin point, is done in about 30% of maxillary and mandibular surgeries (Proffit et al., 2019). Distraction osteogenesis is a procedure to lengthen bone by using a device, an internal or external distractor, to stretch hard and soft tissues at a surgical osteotomy site (Proffit et al., 2019). The distraction is done at a rate that allows both hard and soft tissues to adapt to their new position with minimal relapse (Proffit et al., 2019). Distraction osteogenesis provides two major benefits over orthognathic surgery with rigid fixation: (1) increased magnitude of skeletal movements and (2) earlier intervention, as young as infants (Proffit et al., 2019). This provides a major advantage for patients with craniofacial syndromes who may have significant mandibular, midface, or maxillary deficiency (Proffit et al., 2019). Moderate to severe hemifacial microsomia often requires mandibular distraction osteogenesis while Crouzon and Apert syndrome often require maxillary distraction osteogenesis (Proffit et al., 2019). Inability to precisely control the vector of movement is the major disadvantage (Proffit et al., 2019).

Epidemiological studies in the United States and the United Kingdom have estimated that 5% of the population are affected by dentofacial deformities (Baume et al., 1974; Foster and Walpole Day, 1974; Salzmann, 1968). Foster and Walpole Day (1974) estimated that 20% of subjects seeking orthodontic treatment will have a skeletal deformity, and thus are candidates for orthognathic surgery. Proffit and White (1990) estimated that over one million persons in the United States were candidates for orthognathic surgery while over 250,000 orthognathic surgery candidates exist in the United Kingdom (Sandy et al., 2001). While low rates of surgery-related complication and high patient satisfaction are frequently reported, decreasing insurance coverage and decreased surgeon compensation were reported as the primary reasons for the decrease in total number of orthognathic surgeries per year (Murphy et al., 2011; Kim and Park, 2007; Teltzrow et al., 2005; Farrell and Tucker, 2009; Zins et al., 2008).

Reported cost for correction of dentofacial deformities with orthognathic surgery and orthodontics range from \$6,206 at community-based hospitals in the late 1990's (Panula et al., 2002) to  $\in$ 3,924.90 for LeFort 1,  $\in$ 4,334.50 for BSSO, and  $\in$ 7,388.10 for bimaxillary surgery in an Italian hospital (Tewfik et al., 2019). Cunningham et al., (2003) compared orthognathic surgery cost with change in quality of life and determined that orthognathic surgeries are cost effective, providing positive results with relatively low cost. Panula et al. (2002) confirmed such findings that orthognathic surgeries are cost effective, despite the significant cost. Gupta et al. (2017) identified that patients treated by high volume surgeons, performing the top quartile of surgeries annually, have 40% lower odds of extended length of hospital stay and lower hospital costs, by \$1,484.74 on average.

## G. Orthognathic Surgery Demographics

International epidemiological studies indicate that orthognathic surgery patients are most commonly women ranging from 24 to 28 years old (Mutaz and Habal, 2013; Marques et al., 2010; Chew, 2006; Gupta et al, 2017). The female predilection for orthognathic surgery ranges from 61.4% to 63.4% (Gupta et al, 2017; Mutaz and Habal, 2013). Gupta et al. (2017) identified demographic data of orthognathic surgery patients from the NIS from 2001 to 2009. Sex and age matched previously mentioned averages, noting 61.4% female prevalence and a mean age of 26 years old with 68.3% being under the age of 30 (Gupta et al., 2017). A majority of the patients were white (80.6%), privately insured (84.6%), with no comorbidities (91%) (Gupta et al., 2017). Evaluating the Kids Inpatient Database (KID) from 2000-2012, orthognathic surgeries to resolve skeletal malocclusion were completed most commonly on white (77.8%) patients while Hispanic / Latino (10%), black (4.6%) and Asian/ Pacific Islander (3.3%) subjects accounted for less than 20% of surgeries (Peck et al., 2020).

Reported craniofacial phenotype also varies in the literature, but most report a greater prevalence of class III surgery than class II surgery (Boeck et al., 2011; Espeland et al., 2008; Mutaz and Habal, 2013; Proffit et al., 2013; Venugoplan et al., 2012). Mutaz and Habal (2013) reported Class III skeletal patients underwent surgery most commonly followed by class II skeletal patients, reporting 41.3% and 37.1% prevalence, respectively, while only 2.5% of surgeries were completed on subjects with short vertical facial height. Proffit et al. (2013), evaluating patients at University of North Carolina Chapel Hill (UNC) from 2006-2010, also observed a greater prevalence of Class III (54%) than Class II (41%) surgical patients. A similar trend was observed in Osland, Norway (Class III: 64% of males and 48% of females; Class II: 23% of males and 36% of females) (Espeland et al., 2008), Sao Paulo, Brazil (Class III: 47%; Class II: 46%) (Boeck et al., 2011), and in the 2008 United States National Inpatient Sample (NIS)

(Class III: 47%; Class II: 30%) (Venugoplan et al., 2012). On the contrary, an unpublished survey completed by and mentioned by Proffit et al., (2013), orthognathic surgeries were more commonly done for class II phenotype than class III phenotype in a US Medical Center (52% Class II; 48% Class III) and one private practice in Alabama (40% Class II; 34% Class III; 26% Class I).

Proffit et al. (2013) evaluated the change in characteristic of orthognathic surgery patients at UNC from 1996-2000 to 2006-2010 and found increasing Class III prevalence (25% to 54%), decreasing class II prevalence (59% to 41%), and minimal change in subjects with asymmetries (around 35%) or vertical excess (around 30%). This trend was also observed in the Alabama private practice orthognathic surgery population (Proffit et al., 2013).

Brunelle et al. (1996) observed racial differences in extreme malocclusions using data from the National Health and Nutritional Examination Survey (NHANES) III; severe class III pattern was three times more prevalent in Asians and two times more prevalent in Hispanics than white or African Americans; severe class II pattern prevalence was greater in African Americans and Hispanics than whites; extreme long face, or open bite, prevalence was seven times greater in African Americans than whites and is nearly never observed in Hispanics. Proffit et al. (1998), using the same NHANES data, observed that severe malocclusion, increasing likelihood of orthognathic surgery, was observed most in African Americans.

Gupta et al. (2017) observed more maxillary than mandibular surgeries, occurring 52.4% and 47.6% of the time, respectively. Of patients undergoing bimaxillary surgeries, 30% presented with excessive vertical growth, 25% with maxillary deficiency, 19% with mandibular asymmetries, 15% with mandibular deficiency, 6% with deficient vertical growth, 2% with bimaxillary dental protrusion, and 3% with uncategorized deformity (Posnick et al., 2016). 67% of these subjects had maxillary skeletal arch form discrepancies requiring segmental LeFort 1 osteotomies, half being two-piece and half being three-piece procedures (Posnick et al., 2016). 84% of bimaxillary surgery patients who underwent segmental LeFort 1 osteotomy had maxillary transverse deficiency (Posnick et al., 2016) and stability of maxillary transverse expansion with segmental LeFort 1 osteotomy is statistically similar to surgically assisted rapid

palatal expansion (SARPE) (Chamberland and Proffit, 2008; Phillips et al., 1992). Risk of LeFort 1 osteotomy varies; Posnick et al. (2016) reported no increased risk (dental, periodontal, infectious, etc.) with segmental LeFort1 osteotomies while Thygesen et al. (2009) observed a significant risk for postsurgical neurosensory alteration in segmental, compared to non-segmental, maxillary osteotomies.

### H. Orthognathic Surgery: Patient Motivation & Satisfaction

Orthognathic surgery in combination with orthodontic treatment is completed in order to improve functional and esthetic dentofacial deformities. It is generally accepted that surgical-orthodontic treatment is associated with improvement in psychosocial well-being (Cunningham et al, 1995; Flanary et al., 1990; Oland et al., 2011). In retrospective studies, it has been shown that the most frequent motivation for patients to opt for a surgical-orthodontic treatment is to improve esthetics and oral function (Cunningham et al., 1995; Oland et al., 2011). Oland et al. (2011) underwent a prospective evaluation of 118 orthognathic surgery-orthodontic candidates and how patient satisfaction was affected by treatmentmotivation, type of surgery, psychosocial well-being, and fulfillment of pre-treatment motives. Questionnaire results confirmed results from retrospective studies that primary motivations for orthognathic surgery, in descending order, were oral function (#1) and esthetics followed by social motives and disease prevention (Oland et al., 2011).

Motives were separated into self-concept, such as appearance and function, and social interaction, such as work performance and being in public. Subjects ranked satisfaction in improvement in oral function and esthetics, self-concept motives, significantly greater than improvement in social determinants, such as work performance and talking with others. That being said, satisfaction with selfconcept motives correlated with satisfaction with social determinants.

Greater improvement was noted in self-concept than social interaction motives; while a majority of subjects underwent an increase in self-concept (88.1%) and social interaction (57.6%), some expressed no change (5.9% and 20.3%, respectively) and some felt self-concept and social interaction decreased (5.9% and 22%, respectively) (Oland et al., 2011). The most satisfied patients were those whose primary motive

was improvement in facial appearance (rho 0.20; P=0.03), while those prioritizing improvement in oral function (rho -0.20; P=0.03) or social motives (rho -0.21; P=0.02) negatively correlated with post-treatment satisfaction (Oland et al., 2011). Post-treatment satisfaction was correlated with the number of fulfilled pre-surgical motives (Oland et al., 2011). Thus, setting patient expectations and understanding patient's motivations prior to surgery is essential. It appears more predictable to improve self-image motives than social determinant motives.

Compared to controls, subjects rated self-image significantly lower pre-surgery, but significantly higher post-surgery (Oland et al., 2011). Surgical motivation and satisfaction were not affected by age or gender. Type of surgery only affected surgical healing; subjects undergoing bimaxillary surgery were more satisfied with healing. Overall patient satisfaction in orthognathic surgery, which ranged from 87-88%, was similar between Oland et al. (2011) and Posnick and Wallace's (2008) results.

From the orthodontist's perspective, Posnick et al. (2016) observed 91% and 97% satisfaction with occlusal results and facial esthetics, respectively, after bimaxillary jaw surgery. Recurrent malocclusion occurred in 100% and 80% of the subjects voted as worse occlusal and facial esthetic results post-surgery (Posnick et al., 2016). Orthodontists reported that surgical treatment improved treatment efficiency for patients undergoing segmental, compared to non-segmental, LeFort 1 osteotomies (Posnick et al., 2016).

## I. Orthognathic Surgery: Complications

Despite reported satisfaction with orthognathic surgery, perioperative and postoperative complications occur at a low rate (Jędrzejewski, et al., 2015). According to a systematic review by Jędrzejewski, et al. (2015), the most frequently reported complications are nerve injury or alteration in sensation (50%) followed by temporomandibular joint disorders (TMD) (13.64%), hemorrhage (9.09%), hearing problems (6.82%), post-operative infection (6.82%), and irregular or unfavorable fracture of the mandibular osteotomy, termed "bad split" (incidence 1 to 23%).

## 1. Nerve Complications

The most common post-surgical complication is neurosensory injury or alteration, which is cited in literature up to 50% of the time (Jędrzejewski, et al., 2015). Immediately post-surgery, "almost all patients reported altered sensation" (Phillips et al., 2007) and Henzelka et al. (2011) reported that only 3% experienced paresthesia one-year post-surgery.

## a. Mandibular Nerve Complications

Damage to the inferior alveolar nerve may occur during mandibular surgeries. Per Jędrzejewski, et al.'s (2015) review, risk factors for neurosensory damage include, "patient's age... length of procedure... experience of the surgeon... type of procedure (... inverted L ramus osteotomy seems to be a better choice than the BSSO method) ... mandibular advancement >10 mm.... type of fixation (bicortical fixation seems to be a risk factor) ... surgical space on the medial side of the mandibular ramus and the subsequent manipulation of the IAN in that region... tactile sensory threshold before surgery (patients with low sensory thresholds before BSSO experienced a higher degree of impairment after surgery...)". Complications associated with inferior alveolar nerve damage included sensory deficit and issues with facial function such as drooling, speech difficulties, dysesthesia touching the gingiva, kissing difficulties, and eating difficulties (Phillips et al., 2007). Ow et al. (2009) observed similar neurosensory damage, both exhibiting some neurosensory damage one-year post-surgery, in mandibular retrognathic patients undergoing BSSO and mandibular distraction osteogenesis.

#### b. Maxillary Nerve Complications

LeFort 1 osteotomies, the most common maxillary orthognathic surgery, are associated with somatosensory, not motor, changes in 7 to 60%, depending on the location evaluated, of patients 12 months post-surgery (Thygesen et al., 2009). Thygesen et al. (2009) found that objective and subjective sensory alteration was found in the cutaneous infraorbital region, facial and palatal gingiva and mucosa, and pulp tissues of canines post-surgery. At 12 months post-surgery, decreased tactile sensitivity (p < 0.01) and thermal hypersensitivity (heat, p<0.01; cold, p<0.001) occurred extra-orally; intraorally, decreased tactile sensitivity gingivally and palatally was noted with no change in pain perception; pulpal thresholds initially increased, but decreased lower than baseline at 12 months. Subjectively, patients complained of altered sensation cutaneously (upper lip, 14% of patients at 6 and 24% at 12 months; and below the eyes, 0% at 6 and 19% at 12 months), mucosally (upper lip, 14% of patients at 6 and 7% at 12 months; palate, 18% at 6 and 29% at 12 months; and gingivally,64% at 6 and 60% at 12 months), and dentally (41% of patients at 6 and 31% at 12 months) throughout the observation period(Thygesen et al., 2009). Patients perceived the greatest change in gingiva (60% of patients at 12 months), teeth (31% of patients at 12 months) and the palate (29% at 12 months) (Thygesen et al., 2009). Despite observed and perceived somatosensory changes, somatosensory improvement was generally observed over 12 months of observation and "all subjects reported satisfaction with the surgical result and would recommend the procedure to others" (Thygesen et al., 2009).

Amongst the literature, results vary about the percentage, but not the presence, of neurosensory alteration due to LeFort 1 surgeries. Nardi et al. (2002) observed trigeminal alteration in 17% and 43% of patients at 2 and 8 years postoperatively, respectively, while Gent et al. (2003) observed irreversible alteration in palatal gustation, which was not evaluated by Thygesen et al. Al-Din et al. (1996) observed permanent alteration in intraoral sensation, but only temporary alteration in extraoral sensation. Vedtofte (1989), who reported 2.3% prevalence of pulp canal obliteration, and Ellingsen and Artun (1993) report significant pulpal pathology after LeFort 1 procedures.

Risk factors for neurosensory damage associated with LeFort 1 osteotomies include: segmented maxillary osteotomies and increased palatal and gingival tactile thresholds both objectively, p<0.05, and subjectively, p<0.001; vertical maxillary movements-- negative movement, "impaction", was associated with decreased pulpal pain thresholds, p<0.01, while positive movement, "down-fracture", was associated with increased pulpal thresholds and increased palatal sensory change, p<0.05); decreased osteotomy proximity to infraorbital foramen, thus a more superior osteotomy, and decreased spatial sensitivity in the

palate and gingiva (r =-0.25, p<0.05) (Thygesen et al., 2009). The magnitude of anterior-posterior maxillary advancement was not associated with somatosensory changes postoperatively (Thygesen et al., 2009).

### 2. <u>Temporomandibular Joint Disorders</u>

TMD is the second most common post-surgical complication (Jędrzejewski, et al., 2015). Common TMJ complications include: "TMJ dysfunction, derangement of the condylar surface, condylar resorption, or malocclusion due to condylar sag" (Jędrzejewski, et al., 2015). The etiology of postsurgical temporomandibular dysfunction is not well understood, but Hu et al. (2000) observed increased post-surgical TMD, particularly in patients with pre-surgical TMD symptoms, in patients who underwent BSSO compared to intraoral oblique ramus osteotomy. TMJ dysfunction symptoms may present as pain, clicking, or crepitus (Hwang et al., 2000).

Condylar resorption occurs most frequently in females undergoing mandibular advancement presenting with high mandibular plane angle, skeletal class II malocclusion, and abnormal condyles (condylar neck that is posteriorly inclined based upon cephalometric radiographs and smaller based upon panoramic radiographs) (Hwang et al., 2000; Kobayashi et al., 2012). Condylar resorption may begin around six months after surgery and can continue for up to two years (Kobayashi et al., 2012). Condylar sag, a differing post-surgical position of the condyle in the glenoid fossa observed clinically compared to the pre-surgical plan, can lead to altered post-surgical occlusion (Politi et al., 2007; Reyneke and Ferretti, 2002). Potential risk factors for condylar sag include incorrect condylar positioning during surgery, tissue interferences preventing condylar seating (bony due to incomplete or green-stick fracture, ligamentous, muscular, or periosteal), or intra-articular swelling, hemorrhage, or edema during fixation (Reyneke and Ferretti, 2002). Accurate positioning of the condyle is essential to prevent condylar sag; methods to minimize condylar sag occurrence have been identified by Reyneke and Ferrette (2002) using a technique to specifically position the condyle and to accurately diagnose its position intraoperatively and by Politi et al. (2007) by awakening the patient intraoperatively, mid-conscious analgosedation, in order to examine passive and active mandibular movements to ensure an accurate occlusal relationship.

## 3. Hemorrhage

In maxillary LeFort 1 surgeries, Kramer et al. (2004) identify hemorrhage, excessive blood loss requiring intraoperative erythrocyte transfusion in addition to autogenous blood supply, as the most common complication while Jędrzejewski, et al. (2015) observed hemorrhage occurring in 9.09% of articles reviewing LeFort 1 complications. Such hemorrhage is associated with pterygomaxillary separation affecting the descending palatine artery most commonly, but also the pterygoid venous plexus (O'Regan and Bharadwaj, 2007). Most hemorrhaging is successfully managed intraoperatively by local compression and ligation or coagulation, but postoperative hemorrhage, while rare (0 to 0.7% incidence) can be fatal and is managed conservatively to maintain blood pressure or surgically (Politis, 2012). Surgical interventions include nasal packing, osteotomy revisions, and arterial ligation (Politis, 2012).

#### 4. Hearing problems

Hearing issues are associated with excess middle ear pressure (surgical edema, lymphoedema, or hematoma) or altered muscle tension preventing normal auditory tube function (Yaghmaei et al., 2009; Wong et al., 2002). Nasal intubation may increase risk for edema, lymphoedema, or hematoma leading to middle ear effusion causing symptoms such as tinnitus, fullness, otalgia (Wong et al., 2002). Post-surgical muscular compromise or scarring of the auditory tube muscles may prevent normal ventilation of the middle ear (Yaghmaei et al., 2009). Despite presence of auditory dysfunction, Yaghmaei et al. (2009) observed only transient, mild issues which were primarily associated with maxillary or bimaxillary surgeries.

## 5. **Post-operative infection**

In a review of articles, Jędrzejewski, et al. (2015) observed post-surgical infection in 6.82% of articles. Kramer et al. (2004) observed post-surgical infection in 1.1% of patients post-LeFort 1 surgery. Of infections in patients undergoing LeFort 1 procedure, 0.5% developed abscess and 0.6% developed sinusitis (Kramer et al., 2004). Obstruction of the osteomeatal complex leads to sinusitis which may be due to anatomical abnormalities or long-term intubation (Pereira-Filho et al., 2011). Alpha et al. (2006) reported infection in 26% of patients post-BSSO surgery, but only 6.5% required hardware removal. Increased infection rates occurred in patients who were smokers, diabetics, and patients with retained third molars (Alpha et al., 2006). Distance from the screw to the osteotomy site was not associated with increased infection while decreased distance from the screw to the inferior border of the mandible was significantly associated with decreased infection rates (Alpha et al., 2006).

#### **III. MATERIALS AND METHODS**

#### A. Database

The Nationwide Inpatient Sample (NIS) was evaluated to evaluate orthognathic surgeries in the United States from years 2006 to 2014. The NIS is part of a group of public databases that were developed for the Healthcare Cost and Utilization Project (HCUP) in order to better understand longitudinal healthcare trends, improve national and regional healthcare delivery and decision making (HCUP-US NIS Overview, 2021). Information from the NIS is frequently utilized for research projects and for the development and refinement of healthcare software. The Agency for Healthcare Research and Quality (AHRQ) sponsors HCUP (HCUP-US NIS Overview, 2021). Datasets within HCUP compromise the largest set of longitudinal, descriptive hospital data in the United States (HCUP-US Overview, 2021). More than 7 million hospital stays per year are included in the NIS (HCUP-US NIS Overview, 2021). In order to best understand national trends, NIS data is weighted, providing an understanding of over 35 million hospitalizations per year (HCUP-US NIS Overview, 2021).

The NIS includes a wide variety of patient-level and hospital-level characteristics. Patient-level characteristics include patient age, race, sex, comorbidities, diagnosis, procedure types, post-operative infections, discharge status, insurance coverage, and median household income. An annual database by Claritas provides annual income by quartiles; using these annual statistics, patients are stratified into quartiles based on the estimated median annual income of residents in their zip code (HCUP-US NIS Overview, 2021).

Hospitals are characterized based on size (small, medium, or large), hospital type (rural, urban nonteaching, or urban teaching), and geographic region (Northeast, Midwest/ North Central, South, or West) (HCUP-US NIS Overview, 2021). Size is based on the number of hospital beds but varies between regions and hospital type. In all regions, to be considered a "large" hospital, urban, teaching hospitals require a greater number of hospital beds than urban, nonteaching hospitals while rural hospitals require the fewest number of hospital beds to be considered "large". In the Northeast region: rural hospitals are identified as small, medium, or large with 1-49, 50-99, or 100+ beds, respectively; urban, nonteaching

hospitals are identified as small, medium, or large with 1-124, 125-199, or 200+ beds, respectively; and urban, teaching hospitals are identified as small, medium, or large with 1-249, 250-424, or 425+ beds, respectively. In the Midwest region: rural hospitals are identified as small, medium, or large with 1-29, 30-49, or 50+ beds, respectively; urban, nonteaching hospitals are identified as small, medium, or large with 1-74, 75-174, or 175+ beds, respectively; and urban, teaching hospitals are identified as small, medium, or large with 1-249, 250-374, or 375+ beds, respectively. In the Southern region: rural hospitals are identified as small, medium, or large with 1-249, 250-374, or 375+ beds, respectively. In the Southern region: rural hospitals are identified as small, medium, or large with 1-39, 40-74, or 75+ beds, respectively; urban, nonteaching hospitals are identified as small, medium, or large with 1-99, 100-199, or 200+ beds, respectively; and urban, teaching hospitals are identified as small, medium, or large with 1-249, 250-449, or 450+ beds, respectively. In the Western region: rural hospitals are identified as small, medium, or large with 1-249, 250-449, or 450+ beds, respectively. In the Western region: rural hospitals are identified as small, medium, or large with 1-249, 250-449, or 450+ beds, respectively. In the Western region: rural hospitals are identified as small, medium, or large with 1-249, 250-449, or 450+ beds, respectively. In the Western region: rural hospitals are identified as small, medium, or large with 1-99, 100-174, or 175+ beds, respectively; and urban, teaching hospitals are identified as small, medium, or large with 1-99, 100-174, or 175+ beds, respectively; and urban, teaching hospitals are identified as small, medium, or large with 1-199, 200-324, or 325+ beds, respectively.

#### B. Data User Agreement and Institutional Review Board Approval

Prior to initiating the study, the data user agreement was signed and submitted to AHRQ. Any discharge information cell count less than or equal to 10 persons was suppressed, marked "DS" (data suppressed), in order to minimize risk of patient identification and maintain patient confidentiality. The University of Illinois at Chicago College of Dentistry exempted this study from the institutional review board.

## C. Case Selection

Patients within the NIS database were identified using procedure codes, as identified by the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), related to orthognathic surgery. All subjects, regardless of age, with orthognathic surgery procedure code and diagnosis code for maxillary/mandibular hypoplasia were included for analysis.

The description of various codes used for identifying maxillary/mandibular hypoplasia are as follows:

524.03 = Maxillary hypoplasia

524.04 = Mandibular hypoplasia

The procedure codes for orthognathic surgery include:

76.61 = Closed osteoplasty [osteotomy] of mandibular ramus

76.62 = Open osteoplasty [osteotomy] of mandibular ramus

76.63 = Osteoplasty [osteotomy] of body of mandible

76.64 = Other orthognathic surgery on mandible (Mandibular osteoplasty/Segmental or subapical osteotomy)

76.65 = Segmental osteoplasty [osteotomy] of maxilla (Maxillary osteoplasty)

76.66 = Total osteoplasty [osteotomy] of maxilla

76.67 = Reduction genioplasty

76.68 = Augmentation genioplasty

76.69 = Other facial bone repair (Osteoplasty of facial bone)

## D. Dependent Variables

Length of hospital stay is the primary outcome variable of interest. Since length of stay was highly skewed, it was log transformed and used as the dependent variable in the regression model.

## E. Independent Variables

Several patient-level and hospital-level characteristics were used as independent variables. Patientlevel characteristics include: patient age, race, sex, comorbidities, diagnosis, procedure types, postoperative infections, discharge status, insurance coverage, and median household income. Hospital level characteristics include: size (small, medium, or large), hospital type (rural, urban nonteaching, or urban teaching), and geographic region (Northeast, Midwest/ North Central, South, or West). The primary predictor variable of interest was presence of obstructive sleep apnea.

## F. Data Analysis

Descriptive statistics were used to summarize the data. Using the SAS callable SUDAAN Software (Version 11.0.3, Research Triangle Institute) for the Statistical Analysis of Correlated Data software, a linear regression model was used to identify associations between independent variables and the dependent variable, length of hospital stay. The Taylor Linearization Method, Assuming a With Replacement (WR) design was used for the multivariable linear regression model. Clustering of effects within hospitals was adjusted. All statistical tests were two-sided and a p-value of <0.05 was deemed to be statistically significant.

#### **IV. RESULTS**

### A. **Descriptive Statistics**

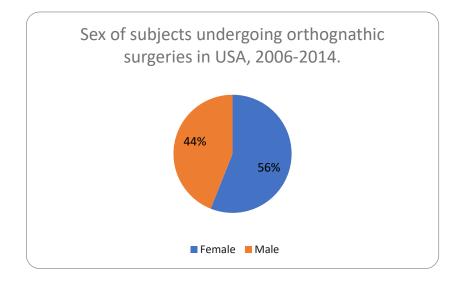
#### 1. **Patient-level Characteristics**

A total of 49,336 orthognathic surgeries were completed in the United States reported by the NIS from 2006 to 2014. 93.2% of the patients were not diagnosed with obstructive sleep apnea, while 6.8% were, as displayed in **Table I. Table II** displays the number of surgeries conducted each year. On average there were 5,482 surgeries annually; the greatest number of surgeries, 6,392, were done in 2011 and the least, 4,615, were done in 2009. 56% of the patients were female while 44% were male, as indicated in **Figure I**. The mean patient age at admission was 23.6 years (standard error of mean [SEM] = 0.2 years) and the median age at admission was 19.1 years. Patients with obstructive sleep apnea (mean and median age at admission 23.1 and 18.9 years, respectively) (**Table III**). With respect to race or ethnicity, a majority were White (71.9%); the remaining patients were Hispanic (12.2%), Black (5.3%), Asian or Pacific Islander (5.3%), Native American (0.3%), and other (4.95%) (**Table IV**).

TABLE I
PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN SUBJECTS UNDERGOING
ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014

OSA Diagnosis	Weighted Frequency	Percent
No	46000	93.2
Yes	3336	6.8
Total	49336	100

	I ADLE II				
NUMBER OF ORTHOGNATHIC SURGERIES IN USA, PER YEAR, FROM 2006 TO 2014					
Year	Weighted Frequency	Percent			
2006	5115	10.4			
2007	5070	10.3			
2008	5201	10.5			
2009	4615	9.4			
2010	5878	11.9			
2011	6392	13.0			
2012	5580	11.			
2013	5905	12.0			
2014	5580	11.3			
Total	49336	100			



**TABLE II** 

Figure 1. Sex of subjects undergoing orthognathic surgery in USA, from 2006 to 2014

# TABLE III

Age of subjects undergoing orthognathic surgeries in USA based on presence of obstructive sleep apnea, from 2006 to 2014

OSA Diagnosis	Mean	Std Error of Mean	Median	Std Error of Median
With OSA	30.3	1	32	2
Without OSA	23.1	0.2	18.9	0.1
All Subjects	23.6	0.2	19.1	0.1

#### **TABLE IV** RACE OF SUBJECTS UNDERGOING UNDERGOING ORTHOGNATHIC SURGERY IN USA, FROM 2006 TO 2014 Race Weighted Frequency Percent White 71.9 28536 2114 5.3 Black Hispanic 4827 12.2 Asian or Pacific Islander 2101 5.3 Native American 128 0.3

1963

4.9

Other

Total39670100Table V shows the distribution of anterior-posterior skeletal diagnosis; 24.7% of the patients werediagnosed with hypoplasia of both maxilla and mandible, 19.7% with isolated mandibular hypoplasia,44.4% with isolated maxillary hypoplasia, and 11.3% with neither hypoplastic maxilla nor mandible.Amongst the patients diagnosed with aforementioned skeletal diagnoses, 16.8% of subjects withbimaxillary hypoplasia were diagnosed with OSA, 9.7% of patients with mandibular hypoplasia werediagnosed with OSA, and 2.7% of patients with maxillary hypoplasia were diagnosed with OSA. (TableVI).

 TABLE V

 Skeletal characteristics of subjects undergoing orthognathic surgery in USA, from 2006 to 2014

Diagnosis	Weighted Frequency	Percent
Maxillary Hypoplasia	34077	69.1
Mandibular Hypoplasia	21889	44.4
Maxillary & Mandibular		
Hypoplasia	12188	24.7

### TABLE VI

Percent of subjects with obstructive sleep apnea, categorized by skeletal diagnosis, undergoing orthognathic surgery in USA, from 2006 to 2014

Diagnosis	Weighted Frequency	OSA Prevalence, Percent
Maxillary Hypoplasia	736	2.7
Mandibular Hypoplasia	1487	9.7
Maxillary & Mandibular Hypoplasia	1113	16.8

The number of surgical osteotomies per orthognathic procedure is displayed in Table VII. Nearly

90% of the surgeries were performed with two or fewer osteotomies. About 43.6% underwent one

surgical osteotomy, 44.8% underwent two surgical osteotomies, 10.7% underwent three surgical

osteotomies, and less than one percent of patients had more than three surgical osteotomies.

# **TABLE VII**

Number of osteotomies performed per orthognathic surgery in USA, from 2006 to 2014

Number of Osteotomies		Weighted Frequency	Percent
	1	21539	43.7
	2	22082	44.8
	3	5273	10.7
	4	422.38169	0.9
	5	19.15576	0.03
Total		49336	100

Most patients presented with no comorbid conditions (79.4%) while, 15.5% had one comorbidity,

4.0% two comorbidities, 0.8% three comorbidities, and about 0.3% of the patient population presented with

more than three comorbidities (**Table VIII**). In terms of types of comorbidities, the ten most common conditions were chronic pulmonary disease (7.24%), hypertension (3.60%), obesity (2.64%), depression (2.62%), hypothyroidism (1.81%), deficiency anemias (1.47%), fluid and electrolyte disorders (1.37%), other neurological disorders (1.26%), uncomplicated diabetes (0.92%), and psychoses (0.82%) (**Table IX**). Six types of complications were noted post-surgically, and the rate of these complications ranged from 0.1% to 1.2%: 1.2% developed general infection, 0.5% developed bacterial infection, 0.4% developed pneumonia, 0.2% developed mycoses, 0.2% developed viral infection (0.2%), and 0.1% developed septicemia (0.1%) (**Table X**).

**TABLE VIII** 

Number of comorbidities associated with subjects undergoing orthognathic surgery in USA, from 2006 to 2014

2014	
Weighted Frequency	Percent
39171	79.4
7656	15.5
1960	4.0
395	0.8
104	0.2
40	0.1
DS	-
49336	100
	Weighted Frequency           39171           7656           1960           395           104           40           DS

\*DS = data suppressed. Per the NIS data user agreement, for any given cell of count  $\leq 10$  discharge information was suppressed.

# TABLE IX

Breakdown of AHRQ comorbidity measures associated with subjects undergoing orthognathic surgery in USA, from 2006 to 2014

Comorbidity Type	Weighted Frequency	Percent
Acquired immune deficiency syndrome	0	0
Alcohol abuse	52	0.1
Deficiency anemias	725	1.5
Rheumatoid arthritis/ collagen vascular diseases	199	0.4
Chronic blood loss anemia	40	0.1
Congestive heart failure	29	0.1
Chronic pulmonary disease	3574	7.2
Coagulopathy	240	0.5
Depression	1291	2.6
Diabetes, uncomplicated	451	0.9
Diabetes with chronic complications	26	0.1
Drug abuse	237	0.5
Hypertension (combine uncomplicated and complicated)	1775	3.6
Hypothyroidism	893	1.8
Liver disease	56	0.1
Lymphoma	DS	-
Fluid and electrolyte disorders	675	1.4
Metastatic cancer	0	0
Other neurological disorders	621	1.3
Obesity	1303	2.6
Paralysis	198	0.4
Peripheral vascular disorders	12	0.02
Psychoses	404	0.8
Pulmonary circulation disorders	70	0.1
Renal failure	36	0.1
Solid tumor without metastasis	DS	-
Peptic ulcer disease excluding bleeding	0	0
Valvular disease	379	0.8
Weight loss	135	0.3

\*DS = data suppressed. Per the NIS data user agreement, for any given cell of count  $\leq 10$  discharge information was suppressed.

Complication Type	Weighted Frequency	Percent
Septicemia	71	0.1
Bacterial Infection	222	0.4
Viral Infection	93	0.2
Mycoses	114	0.2
Pneumonia	177	0.4
General Infection	579	1.2

 TABLE X

 Complications that occurred post-orthognathic surgery in USA, from 2006 to 2014

Primary payer of orthognathic surgery is displayed in **Table XI**. Of the 49,336 patients, 78.5% paid with private insurance, 12.6% paid with Medicaid, 2.9% self-payed, 1.0% paid with Medicare, and 0.3% had the surgery completed at no charge. The remaining 4.7% identified payment type as "other".

In terms of patient median annual income quartiles, 41.42% of the patients resided in top quartile zip codes, 23.35% resided in the second highest quartile, 18.62% resided in the second lowest quartile, and 13.61% resided in the lowest quartile (**Table XII**).

## TABLE XI

Primary expected payer (uniform) of subjects undergoing orthognathic surgery in USA, from 2006 to 2014

	2014	
Primary Payer	Weighted Frequency	Percent
Medicare	485.36844	1.0
Medicaid	6220	13
Private insurance	38645	78
Self-Pay	1444	2.9
No charge	144.39172	0.3
Other	2299	4.7
Total	49238	100

Median Household Income	Weighted Frequency	Percent
0 to 25th Percentile	6590	13.6
26th to 50th Percentile	9019	18.6
51st to 75th Percentile	12764	26.4
76th to 100th Percentile	20062	41.4
Total	48435	100

 TABLE XII

 Median household income national quartile for patient ZIP code.

Discharge status is summarized in **Table XIII**. Almost all of the patients were routinely discharged (98.6%), while 1.1% were transferred to home health care, 0.2% were transferred to short-term hospital, 0.1% were transferred to other facilities (including skilled nursing facility (SNF), intermediate care facility (ICF), and another type of facility), 0.04% or 20 patients died during hospitalization.

	Weighted	
Disposition at Discharge	Frequency	Percent
Routine	48640	98.6
Transfer to Short-term Hospital	74	0.2
Transfer Other: Includes Skilled Nursing Facility (SNF), Intermediate Care		
Facility (ICF), Another Type of Facility	65	0.2
Home Health Care (HHC)	526	1.1
Against Medical Advice (AMA)	DS*	DS*
Died	20	0.04
Total	49336	100

 TABLE XIII

 Disposition of patient (uniform) undergoing orthognathic surgery in USA, 2006-2014.

\*DS = data suppressed

The mean length of stay was 2.6 days (SEM = 0.1 days) and the median length of stay was 1.0 days; 75% of patients spent under 1.74 days in the hospital. The length of stay was 3.2 days longer in subjects with OSA (mean LOS 5.6 days, SEM 0.6 days; median LOS 1.6 days) than those without OSA (mean LOS 2.4 days, SEM 0.1 days; median LOS 1.0 days) (**Table XIV**).

### TABLE XIV

Length of stay of subjects undergoing orthognathic surgery based upon presence of obstructive sleep apnea in USA, from 2006 to 2014

OSA Diagnosis	Mean	Std Error of Mean	Median	Std Error of Median
With OSA	5.6	0.6	1.6	0.1
Without OSA	2.4	0.1	1	0.001
All Subjects	2.6	0.1	1	0.04

### 2. Hospital-level Characteristics

A majority of orthognathic surgeries from 2006 to 2014 were conducted in urban teaching (72.3% c.f. 2.6% rural and 25.1% urban non-teaching hospitals) (**Table XV**). Over two thirds of surgeries were performed in large bed size hospitals (68.3%); medium (20.7%) and small (11%) bed size hospitals made up less than one third of all surgeries (**Table XVI**). Distribution of hospital regions was the following: 31.5% in the South, 27.3% in the West, 21.6% in the Northeast, and 19.6% in the Midwest or North Central (**Table XVII**).

Hospital Type	Weighted Frequency	Percent
Rural	1275	2.6
Urban Nonteaching	12369	25.1
Urban Teaching	35621	72.3
Total	49266	100

 TABLE XV

 Type of hospital orthognathic surgery was completed

TABLE XVI
Size of hospital, by bed quantity, where orthognathic surgery was completed

Hospital Size	Weighted Frequency	Percent
Small	5426	11.0
Medium	10178	20.7
Large	33661	68.3
Total	49266	100

Region	Weighted Frequency	Percent
Northeast	10676	21.6
Midwest or North Central	9643	19.5
South	15560	31.5
West	13457	27.3
Total	49336	100

 TABLE XVII

 Region of hospital where orthognathic surgery was completed.

## B. Linear Regression Model

Results of multivariable linear regression of length of hospital stay is shown in **Table XVIII**. Of significant findings (p<0.05), the strongest indicators of increased length of stay were elective versus nonelective admission (B=0.5629; p<0.0001; compared to patients presenting with non-elective admission) followed by presence of sleep apnea (B=0.4603; p<0.0001; compared to subjects without sleep apnea). Comparing primary payers of surgery, compared to self-pay patients, Medicaid patients had a significant increase in length of hospital stay (B=0.1542; p<0.0001) while Medicare had a non-significant increase (B=0.1262; p=0.0534). Per comorbidity, length of stay significantly increased (B=0.1434; p<0.0001). Compared to the west region, only the Midwest had a significant increase in length of stay (B=0.1128; p=0.0081). Evaluating calendar year of surgical procedure, a significant increase in length of stay was observed in 2009 (B=0.1056; p=0.0482). Compared to white subjects, only Blacks showed a significant increase in length of stay (B=0.0745; p=0.0449). Per increase in number of osteotomies, a significant increase in length of stay was observed (B=0.0716; p<0.0001). The strongest indicator of deceased length of stay was diagnosis of maxillary hypoplasia (B=-0.1478; p<0.0001) followed by age, per year, in years at admission (B=-0.0164; p<0.0001).

# TABLE XVIII

Factors Associated with Length of Stay in Hospital (Multivariable linear regression analysis)

Characteristic Bate Coefficient n value			
Characteristic (Independent	Beta Coefficient	p-value	
(Independent			
Variables)	0.4602	0.0001	
Presence of Sleep	0.4603	<0.0001	
Apnea	0.01.61	0.0001	
1 year increase in age	-0.0164	< 0.0001	
in years at admission			
Male	Reference	Reference	
Female	0.0032	0.7925	
White	Reference	Reference	
Black	0.0745	0.0449	
Hispanic	0.0401	0.1678	
Asian/Pacific Islander	-0.0036	0.9048	
Native American			
Other races	0.2422	0.810	
Missing race	0.0737	0.1384	
information	-0.0172	0.6206	
Elective versus non-	0.5629	< 0.0001	
elective admission			
Presence of comorbid	0.1434	< 0.0001	
conditions, increase			
per comorbidity			
Private insurance	Reference	Reference	
Medicare	0.1262	0.0534	
Medicaid	0.1542	0.0000	
Uninsured	-0.0159	0.6942	
Other insurance	0.0130	0.7186	
West	Reference	Reference	
Northeast	-0.0200	0.6626	
Midwest	0.1128	0.0081	
South	0.0651	0.0923	
Small/medium bed size	Reference	Reference	
Large bed size			
	-0.0442	0.1318	
Median household			
income for patient's			
ZIP Code			
0-25 <sup>th</sup> Percentile	Reference	Reference	
26-50 <sup>th</sup> Percentile	-0.0096	0.7264	
51 <sup>st</sup> -75 <sup>th</sup> Percentile	-0.0005	0.9832	
76 <sup>th</sup> -100 <sup>th</sup> Percentile	-0.0251	0.3567	

Characteristic	Beta Coefficient	p-value
(Independent		
Variables)		
Non-teaching Hospital	Reference	Reference
Urban Teaching		
Hospital	0.0398	0.1508
Maxillary &	Reference	Reference
Mandibular		
Hypoplasia		
Maxillary hypoplasia	-0.1478	< 0.0001
Mandibular hypoplasia	0.0166	0.5521
Number of	0.0716	0.0000
osteotomies, increase		
per osteotomy		
Y2010	Reference	Reference
Y2006	0.0690	0.1767
Y2007	0.0590	0.3345
Y2008	0.0504	0.3510
Y2009	0.1056	0.0482
Y2011	-0.0259	-0.5163
Y2012	-0.0000	< 0.0001
Y2013	0.0333	0.5272
Y2014	0.0482	0.3592

#### V. DISCUSSION

#### A. Comparison with the Literature

#### 1. **Demographics**

According to our evaluation of the NIS database from 2006 to 2014, the most frequently observed patients undergoing orthognathic surgery were 23.6 years old, white (71.9%), females (56.0%) with isolated maxillary hypoplasia (44.4%) zero comorbidities (79.4%). Such demographics are relatively consistent with previous literature, as discussed below (Mutaz and Habal, 2013; Marques et al., 2010; Chew, 2006; Gupta et al, 2017; Peck et al., 2020).

In our study, the median patient age was 19.1 years old while the mean age was 23.6 years old, which was younger than other cited means. The 4.5-year difference between mean and median indicates outliers, much older patients, skewed the mean resulting in a higher average. Other literature indicates a slightly older average patient age at time of orthognathic surgery, ranging from 24 to 28 years old (Chew, 2006; Gupta et al, 2017; Marques et al., 2010; Mutaz and Habal, 2013). Using the NIS from 2001 to 2009, Gupta et al. (2017) observed an average age of 26 years old.

No previous study has examined the effect of OSA on patient age at time of surgery, but we observed that patients with OSA were significantly older (mean and median age at admission 30.3 and 32.0 years, respectively) than patients without OSA at time of surgery (mean and median age at admission 23.1 and 18.9 years, respectively). While indication for surgery was not noted in the NIS database, it is possible that subjects with OSA were treated with orthognathic surgery at an older age after other treatment techniques were ineffective. Alternatively, the younger age of the patients without OSA may be a result of orthodontic treatment and surgery around the time of facial growth cessation (Proffit et al., 2019).

The female predilection for orthognathic surgery, compared to males, in our study (56.0%) is consistent, but slightly less strong, than previous studies which indicate females undergoing between 61.4% and 63.4% of all orthognathic surgeries (Gupta et al, 2017; Mutaz and Habal, 2013). Consistent with literature evaluating NIS and KID samples from earlier in the 21<sup>st</sup> century, over 70% of orthognathic surgery patients in the United States are white, followed Hispanics, Blacks, and Asians (Gupta et al., 2017; Peck et al., 2020). This is contradictory to Proffit et al.'s. (1998) observation that African Americans present with the most severe malocclusion, indicating greater necessity for orthognathic surgery.

Maxillary hypoplasia, indicating a Class III skeletal relationship, was the most common skeletal diagnosis for patients in our study. This is consistent with several other studies published over the past 13 years (Boeck et al., 2011; Espeland et al., 2008; Mutaz and Habal, 2013; Proffit et al., 2013; Venugoplan et al., 2012). No published study from the 21<sup>st</sup> century indicated a greater percentage of Class II orthognathic surgeries, but two surgical locations, a US Medical Center (52% Class II; 42% Class III) and a private practice in Alabama (40% Class II; 34% Class III; 26% Class I), showed an increased prevalence of Class II orthognathic surgeries.

No previous study has examined the effect of OSA on skeletal characteristics of patients undergoing orthognathic surgery. We defined patient's skeletal characteristic as bimaxillary hypoplasia, mandibular hypoplasia, and maxillary hypoplasia. Amongst these groups, the bimaxillary hypoplasia group contained the greatest percent of patients with OSA. OSA was diagnosed in nearly 17% of our bimaxillary hypoplasia patients, in less than 10% of our mandibular hypoplasia patients, and in less than 3% of our maxillary hypoplasia patients. The large percentage of bimaxillary hypoplasia patients with OSA may be explained by the orthognathic procedure used to treat OSA, MMA, requiring both maxillary and mandibular surgery. It is possible that insurance companies require a diagnosis of bimaxillary hypoplasia to cover bimaxillary surgery. MMA, a procedure that aims to increase the anteroposterior dimension of the airway in subjects with moderate to severe OSA, has shown astounding success rates, ranging from 100% (John et al., 2018) to 65 to 95% (Hsieh and Liao, 2013) and is even considered the gold standard treatment for patients with OSA by Walte and Shetar (1996).

That being said, mandibular deficiency is indicated as a risk factor for pediatric OSA. Several techniques of improving pediatric OSA, including oral appliances, maxillary expansion, and myofunctional therapy, aim to redirect mandibular growth in an anterior, instead of inferior, direction to

improve the oropharyngeal volume (Huynh et al., 2016). This may explain why more patients with OSA were diagnosed with mandibular hypoplasia (9.7%) compared to maxillary hypoplasia (2.7%).

Past literature estimated a significantly greater need for orthognathic surgery than seen in the NIS database. Two studies indicate that about 0.4% of a country's population are candidates for orthognathic surgery; Proffit and White (1990) estimated over one million orthognathic surgery candidates exist in the United States while more recent estimates in the United Kingdom estimated over 250,000 orthognathic surgery candidates (Sandy et al., 2001). Foster and Walpole Day (1974) estimated that 20% of subjects seeking orthodontic treatment will have a skeletal deformity, and thus are candidates for orthognathic surgery. The NIS database, which was weighted to effectively represent the total number of orthognathic surgeries requiring hospitalization in the United States from 2006 to 2014, indicates a total of 49,336 surgeries were done over the nine-year span with an average of 5,482 surgeries per year. The total number of surgeries per year consistently ranged between 5,000 and 6,000 surgeries, which occurred in seven of the nine years. 2011 and 2009 were the only years with a greater or fewer number of surgeries, respectively. The consistency in surgical volume over the nine-year span is contradictory to reports that indicate orthognathic surgery volume is decreasing due to lessened insurance coverage and surgeon compensation despite high patient satisfaction and low surgery-related complication rates (Murphy et al., 2011; Kim and Park, 2007; Teltzrow et al., 2005; Farrell and Tucker, 2009; Zins et al., 2008).

It has not been previously reported, but we identified that about 7% of subjects undergoing orthognathic surgery were diagnosed with OSA. Estimates of OSA prevalence are quite variable, which may be due to healthcare providers failing to identify and diagnose OSA and/ or the general population lacking awareness of OSA. Young et al. (1997) estimates that 80 to 90% of subjects with OSA remain undiagnosed. The estimated prevalence of OSA in the American population varies drastically between studies from 3.8 to 6.5% in subjects with moderate to severe OSA and 10% in subjects with mild OSA (Jonas et al., 2017) to around 20%, reported by Franklin and Lindberg's (2015) review of the literature. The effectiveness of orthognathic surgery, as a means of OSA treatment, increases with increasing severity of OSA (John et al., 2018). This may explain why we observed a similar prevalence of OSA in

orthognathic surgery patients, 7%, to Jonas et al.'s (2017) observation of moderate to severe OSA in middle aged Americans, 3.8 to 6.5%.

## 2. <u>Hospital level-characteristics</u>

Most orthognathic surgeries were completed in Large (68.3%), urban teaching (72.3%) hospitals while very few were completed at small (11.0%), rural (2.6%) hospitals. This is consistent with an evaluation of the NIS database from 2001 to 2009 (Gupta et al., 2017). Regionally, most of the surgeries occurred in the South (31.5%) and the West (27.3%). Gupta et al. (2017) identified patients treated by high volume surgeons, performing the top quartile of surgeries annually, have 40% lower odds of extended length of hospital stay and lower hospital costs, by \$1,484.74 on average. It is assumed that the highest volume surgeons are working in large, urban-teaching hospitals.

A vast majority of the subjects treated were covered by private insurance (78.5%) compared to Medicaid (12.6%), self-pay (2.9%) and other means; only 0.3% of procedures were done at no charge. Gupta et al. (2017) observed a slightly higher percentage (84.6%) of orthognathic surgery patients with private insurance. A majority of subjects (67.8%) were residents in neighborhoods in the lower 50<sup>th</sup> percentile of household income while 41.2% of them resided in neighborhoods earning incomes in the lowest quartile. While statistically insignificant, the lowest quartile of socioeconomic status was associated with an increased length of hospital stay compared to the top quartile ( $\beta$ =-0.0251; p<0.3567).

#### 3. Surgical Procedures

Literature indicates that the most common maxillary and mandibular orthognathic surgical procedures are the LeFort 1 osteotomy and the BSSO, respectively (Proffit et al., 2019). While the NIS database does not identify which surgical technique is used, the number of osteotomies per procedure are noted in Table IV. A maxillary surgery using a LeFort 1 osteotomy varies from one to three, depending on the surgical goals. Disharmony in the transverse dimension between the mandible and maxilla often requires two or more maxillary osteotomies in order to increase, or significantly less commonly to

decrease, the width of the maxilla. A third maxillary osteotomy may be performed in order to differentially alter the vertical position of the anterior and the posterior maxilla; this procedure is often done most commonly in anterior open bite patients. The BSSO mandibular surgery technique requires one osteotomy per ramus. The NIS database does not indicate whether a BSSO is considered one or two osteotomies. An additional osteotomy at the inferior border of the mandible, or chin point, is done in about 30% of orthognathic surgeries (Proffit et al., 2019). Bimaxillary surgeries, combining both maxillary and mandibular osteotomies and fixations, may be done to improve asymmetry, cant, occlusal plane pitch, and/or the horizontal position of the mandible (Proffit, 1991) and are shown to improve over 90% of facial characteristics in patients with primary maxillary deficiencies (Posnick et al., 2018).

Nearly 90% of the surgeries were performed with two or fewer osteotomies. About 43.6% underwent one surgical osteotomy, 44.8% underwent two surgical osteotomies, 10.7% underwent three surgical osteotomies, and less than one percent of patients had more than three surgical osteotomies. While our database does not specifically indicate which jaw was operated on, it appears consistent with a previous study by Gupta et al. (2017) that maxillary surgeries occur more than mandibular surgeries considering the greater prevalence of maxillary deficient subjects in our study. We found that each additional osteotomy, beyond one, is associated with an increased length of hospital stay (B=0.0716; p<0.0001). This corresponds with findings that segmental maxillary osteotomies, thus maxillary surgeries with more osteotomies, present a significant risk for post-surgical neurosensory alteration (Thygesen et al., 2009). Addressing a maxillary transverse deficiency with maxillary skeletal expansion, either RME in adolescence or MARPE in early adulthood, may improve surgical outcomes.

#### 4. Surgical Outcomes

Our study aimed to evaluate infectious complications in order to identify the type of quality of care that our healthcare system and specific hospital types are providing. While such complications have not been previously evaluated in the literature, understanding how to predict and avoid these complications will likely improve our ability to decrease patient length of stay, hospital cost, patient

mortality, and in total, an extra burden on our healthcare system. Previous literature, on the other hand, primarily evaluates local complications.

Our analysis identified six post-surgical complications in descending order of frequency: general infection (1.2%), bacterial infection (0.4%), pneumonia (0.4%), mycoses (0.2%), viral infection (0.2%), and septicemia (0.1%). Infection rates may remain relatively low because antibiotic prophylaxis and postsurgical antibiotics are routinely prescribed (Khechoyan, 2013). Overall, we observed that 2.5% of patients experienced some sort of post-surgical infectious complication. Jędrzejewski, et al. (2015) observed infection in 6.8% of reviewed papers while Kramer et al. (2004) observed post-surgical infection in 1.1% of patients post-LeFort 1 surgery, of which 0.5% developed abscess and 0.6% developed sinusitis. Post-BSSO surgery, Alpha et al. (2006) identified a much greater prevalence of infection, with infection occurring in 26% of patients; only 6.5% required hardware removal which likely significantly increased surgical costs. Alpha et al., (2006) identified patient risk factors (smoking, diabetes, and retained mandibular third molars) and surgery risk factors (decreased distance from the fixation screw to the inferior border of the mandible) for post-BSSO infections. Development of postsurgical septicemia or pneumonia has been shown to increase hospital fee by 96% and 37%, respectively, and increase patient's length of hospital stay by 310% and 228%, respectively (Allareddy, 2014). While our study does not identify individual comorbidities associated with increased infection risk or hospital stay, we observe a positive association between increased length of stay and number of comorbidities.

A majority of the previously published literature has identified local complications that affect patient morbidity, such as nerve complications, temporomandibular joint disorders, hearing problems, and "bad split" during surgery. Jędrzejewski, et al. (2015), in a review of the literature, identified nerve complications as the most common complication, occurring in up to 50% of patients, followed by temporomandibular joint disorder, occurring in 13.6% of patients. Maxillary nerve complications are associated with only somatosensory dysfunction, while mandibular nerve complications may also affect motor function, affecting a patient's ability to speak, eat, and even kiss (Thygesen et al., 2009; Phillips et al., 2007). Thygesen et al. (2009) identified an increase in number of osteotomies, thus performing

segmental maxillary osteotomies, as the primary risk factor for neurosensory damage in patients undergoing maxillary surgeries. Similarly, we observed a positive association between increased length of stay and number of osteotomies.

One complication that is not identified in the NIS database is hemorrhaging, excessive blood loss requiring intraoperative erythrocyte transfusion in addition to autogenous blood supply; Jędrzejewski, et al. (2015) observed this in 9.1% of patients while Kramer et al. (2004) identified hemorrhaging as the most common complication in LeFort 1 procedures. Hemorrhaging is most commonly an iatrogenic complication due to severing, or damaging, the descending palatine artery and is generally managed intraoperatively by local compression and ligation or coagulation (O'Regan and Bharadwaj, 2007).

No previous studies have identified discharge status of patients post orthognathic surgery. We found that 98.6% of our patients were discharged routinely. While the indicators are not equals, there may be overlap between routine discharge and patient satisfaction. Overall patient satisfaction in orthognathic surgery ranged from 87-88%, (Oland et al., 2011; Posnick and Wallace, 2008). 1.1% of patients were discharged to home health care (HHC). Despite a low statistical value at 0.04%, 20 patients died prior to discharge. No further information was noted on these patients.

#### B. Patient Characteristics Affecting Length of Stay

Outliers with increased lengths of stay drastically increased the means compared to the most common results, the median. Amongst all patients, the median length of hospital stay, 1.0 days, was 1.6 days shorter than the mean.

Identifying patient characteristics associated with increased length of hospital stay, thus increased cost and greater burden on our hospitals and health care system, was a primary aim of our study. A statistical evaluation on such a grand scale has not been done before. We found that the patients presenting for elective orthognathic surgery and patients with obstructive sleep apnea presented the greatest risk for increased length of hospital stay, thus burdening our hospitals and healthcare system the greatest amount. Patients presenting for elective surgery, likely for esthetic improvements, spent greater

time in the hospital post-surgically (B=0.5629; p<0.0001). Such patients should be informed of greater post-surgical risk compared to the non-elective patient. Patients with OSA showed the second greatest increase in length of hospital stay (B=0.4603; p<0.0001). Patients with OSA (mean LoS 5.6 days; median LoS 1.6 days) spent an additional 3.2 days in the hospital compared to those without OSA (mean LoS 2.4 days; median LoS 1.0 days). Further evaluation of why these patients experienced an increased hospital stay should be completed and patients with OSA should understand that greater risk for post-surgical complications, but there are potential explanations. For one, MMA procedures, an effective OSA treatment, require at least three surgical osteotomies (1 maxillary LF1, 2 mandibular for BSSO); we observed an increased LOS per additional osteotomy(B=0.0716; p<0.0001). Additionally, OSA is associated with several other systemic diseases, indicating these patients may present with an increased number of comorbidities, which increases their risk for LOS per comorbidity (B=0.1434; p<0.0001). That being said, OSA is a condition that is reported to be under-diagnosed; Young et al. (1997) estimates that 80 to 90% of subjects with OSA remain undiagnosed. Thus, improvement in our identification of patient's with OSA may improve our ability to improve their post-surgical outcomes and decrease the burden placed on our healthcare system.

Compared to patients with bimaxillary hypoplasia, patients with maxillary hypoplasia showed the greatest decrease in post-surgical hospital stay. Coincidentally, amongst the skeletal characteristics, OSA was diagnosed three to six times less commonly in patients with maxillary hypoplasia. An increase in age was associated with decreased length of hospital stay. This is interesting, considering patients in our study with OSA were, on average, 6 years older than patients without OSA and Franklin and Lindberg (2014) indicated increased age as a risk factor for OSA.

As stated, OSA prevalence is underreported, and several of our evaluated comorbidities overlap as OSA risk factors or show positive associations with OSA. Thus, it is not surprising that an increase in length of stay was observed per comorbidity ( $\beta$ =0.1434; p<0.0001).

Per osteotomy, an increase in length of hospital stay was observed. Thus, a patient undergoing a bimaxillary surgery with a three-piece segmented maxilla is at risk for an increased length of stay, on

average, compared to a patient undergoing a surgery with one osteotomy such as a one-piece LeFort 1 maxillary osteotomy. It may be beneficial to minimize number of surgical osteotomies in pre-surgical orthodontic treatment; for example, MARPE may effectively correct a maxillary skeletal transverse deficiency instead of a segmental LeFort osteotomy. While patients are unlikely to remain in the hospital due to neurosensory damages associated with surgery (because this is very common immediately post-surgery), segmental osteotomies, thus additional osteotomies, in LeFort 1 surgeries have been identified as the primary risk factor for post-surgical neurosensory damage (Thygesen et al., 2009).

Medicaid coverage showed a significant increase in length of stay ( $\beta$ =0.1542; p<0.0001), compared to privately insured patients, but, oddly, the lowest income quartile zip codes showed a non-significant, but decrease, in length of stay ( $\beta$ =-0.0251; p=0.3567). Patients with Medicare also showed an increase in length of stay, compared to privately insured patients, close to statistical significance ( $\beta$ =0.1262; p=0.0534). Compared to white patients, black patients observed an increase in length of hospital stay ( $\beta$ =0.0745; p=0.0449).

Other factors shown to be significantly associated with increased length of stay were Midwest region ( $\beta$ =0.1128; p=0.0081) compared to the West and year 2009 ( $\beta$ =0.1056; p=0.0482) compared to year 2010.

As shown by our statistical models, the following factors were associated with increased length of stay: Medicaid coverage, decreased age, black race, bimaxillary hypoplasia, obstructive sleep apnea, increased number of comorbidities, presentation for an elective orthognathic surgery, and increased number of surgical osteotomies.

## C. Obstructive Sleep Apnea Characteristics in the NIS Database

The prevalence of adult OSA ranges in the literature depending on several factors such as severity, race, and region. A review of the literature by Franklin and Lindberg (2015) estimated that OSA (AHI<sub>25</sub>) affects 22% of adult males and 17% of adult females while Jonas et al. (2017) observed 10% and 3.8-6.5% prevalence of mild and moderate to severe OSA in middle aged Americans, respectively. A

lower prevalence, 2.6%, was observed in an adult Taiwanese population (Chuang et al., 2008). The information retrieved from the NIS database does not indicate severity of sleep apnea, but the prevalence of orthognathic surgery patients with OSA (7%) is similar to Jonas et al.'s (2017) observation of moderate to severe OSA in middle aged Americans, 3.8 to 6.5%. We can infer that a majority of our OSA patients had moderate to severe OSA.

While our data analysis did not identify which comorbidities increase risk for longer hospital stays, an increase in length of stay was observed per comorbidity (B=0.1434; p<0.0001) and an increase in length of stay was observed in orthognathic surgery patients with sleep apnea (B=0.4603; p<0.0001). Several OSA risk factors, according to the literature, are amongst the comorbidities that subjects in the NIS database present with, as depicted in TABLE VI. The five most common comorbidities that orthognathic surgery patients presented with were chronic pulmonary disease (7.2%), hypertension (3.6%), obesity (2.6%), depression (2.6%), and hypothyroidism (1.8%). Two of the three most common comorbidities, hypertension (3.6% of patients) and obesity (2.6% of patients), are also associated with increased OSA risk (Peppard et al., 2000; Young et al., 2005). Peppard et al. (2000) observed an increased risk for hypertension development in patients with obstructive sleep apnea. As OSA severity worsened, as measured by AHI, the risk for hypertension increases (Peppard et al., 2000). Obesity is considered a major risk factor for OSA; according to Young et al. (2005), over half of the population with moderate to severe OSA are obese. The OSA risk factors that present as common comorbidities in orthognathic surgery patients may indicate that the percent of patients with OSA is underestimated in our study, as is previously indicated in the literature (Young et al., 1997)

Diabetes (uncomplicated, 0.9%, and with chronic complications, 0.05%) and alcohol abuse (0.1%) are other less common comorbidities that patients presented with that may show associations with OSA. Several cross-sectional studies have shown a strong association between diabetes mellitus and OSA, independent of confounders (Ip et al., 2002; Punjabi et al., 2004; Punjabi and Beamer, 2009; Reichmuth et al., 2005). Botros et al. (2009) observed an independent association between baseline OSA and diabetes incidence while Reichmuth et al. (2005), in a 4-year prospective study, observed an

increased risk of OSA development in subjects with diabetes mellitus, although results lacked statistical significance.

Alcohol abuse is not specifically identified as a risk factor for OSA, and the literature is contradictory whether alcohol consumption is associated with OSA (Udwadia et al., 2004; Lindberg et al., 1998; Bearpark et al., 1995; Peppard et al., 2007; Worsnop et al., 1998), but alcohol consumption is shown to decrease the function of upper airway and oropharyngeal muscles (Krol et al., 1984) increasing risk for upper airway collapse during sleep.

#### D. Limitations

The use of a secondary data set introduces the primary limitations of our study. While we were able to identify associations between variables and outcomes, evaluating a retrospective cohort prevents the identification of cause-and-effect relationships. Ideally, future studies will prospectively observe a cohort to identify patient-level and hospital-level characteristics that affect the burden placed on the hospital and healthcare system. Further, the NIS data set used does not provide information to adequately control for all confounding variables. The linear regression model aimed to control for confounding variables, but it is possible that additional comorbidities, outside of the 22 included in our data set, may have influenced outcomes. In addition, potential confounding variables such as comorbidity severity, surgical technique, or surgeon training are not identified in the NIS database which is based upon the ICD-9-CM system. It would be useful to understand if, and to what extent, the severity of OSA, or other comorbidities, affects surgical outcomes. For educational purposes and to improve our medical services, it would be ideal to gain an improved understanding of which surgical techniques and which surgeons (between medical specialties or demographic differences) provide the best surgical outcomes. The NIS database is also missing some patient information, such as race and insurance type in nearly 5% of the population, which may have affected results. While other studies generally focus on long-term, local complications, the NIS database is limited to a particular hospital stay and does not provide any postdischarge outcomes, thus we were not able to evaluate long-term health effects.

#### **VI. CONCLUSION**

Despite the aforementioned limitations, this study has several strengths. The evaluation of neither post-surgical, pre-discharge outcomes nor the relationship between OSA and orthognathic surgical outcomes have not been evaluated in current literature. The use of a nationally representative data set, evaluating novel associations, provides the opportunity to address trends that may minimize burden on our national health care system and improve patient outcomes.

OSA, a dangerous and prevalent disorder, is shown to significantly increase hospitalization length of stay in orthognathic surgery patients. This is significant because orthognathic surgery is an effective means of improving OSA, particularly in those with severe OSA. While it is not uncommon, we recommend that OSA screening is done for all orthognathic surgery candidates. Further, patients presenting for elective, compared to non-elective, surgery had increased hospitalizations. Identification and improved management of high-risk patients, such as patients with presence of sleep apnea, increased number of comorbidities, and presentation for elective surgery, may allow hospitals to improve treatment outcomes and decrease the associated burden placed on the healthcare system in the United States.

In addition, we provided an updated profile of patients undergoing orthognathic surgery in the United States, which showed consistency from studies from the early 21<sup>st</sup> century. Our findings included presence of OSA and found that nearly 7% of all orthognathic surgery patients, which is similar to the prevalence of moderate to severe OSA (Jonas et al., 2017), are diagnosed with OSA and nearly 17% of orthognathic surgery patients bimaxillary hypoplasia are diagnosed with OSA. While nearly 99% of patients undergoing orthognathic surgery experienced routine discharge, 20 patients (0.04%) died prior to discharge.

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