LONG TERM PATIENT CENTERED OUTCOMES FOLLOWING TREATMENT WITH ORAL APPLIANCE THERAPY FOR OBSTRUCTIVE SLEEP APNEA

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ABSTRACT

Carolyn Cronin: Long Term Patient Centered Outcomes Following Treatment with Oral Appliance Therapy for Obstructive Sleep Apnea
(Under the direction of Ceib Phillips)

The long-term patient-centered outcomes of oral appliance therapy (OAT) for management of obstructive sleep apnea (OSA) are not well understood. This study aims to assess the general and condition specific quality of life and perceived occlusal and functional changes of individuals with OSA who had OAT delivery two years or longer ago. 3 validated (SAQLI, SF-36, PSPOF) and 1 custom (Oral Compliance) questionnaire were mailed to 139 identified patients from the UNC School of Dentistry Sleep Clinic who had met inclusion criteria of: a PSG diagnosis of OSA, age 18-60 at time of OAT delivery and had delivery of OAT 2 years or longer ago for management of OSA. 31 patients, 58% male with mean age of 49 returned completed questionnaires. 58% of these patients continued to wear OAT for a mean 4.9 years (SD=1.77), and those who discontinued OAT reported use of CPAP, weight loss, BSSO, or nothing to manage their OSA. For quality of life, there were no statistically significant average differences between wearers and non-wearers of OAT in regards to PSPOF or SF-36 subscores. In the SAQLI, those that continued OAT reported greater perception of general health than non-wearers. Non-wearers reported significantly greater problems with side effects from current treatment for OSA than wearers did from OAT. The long-term adherence to OAT was high suggesting quality of life benefits to this type of therapy for managing OSA. Long term OAT

adherence is a function of patients' perceptions to both the conferred benefits of treatment and the unfavorable treatment induced side effects.

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LIST OF ABBREVIATIONS

AADSM	American Academy of Dental Sleep Medicine
AASM	American Academy of Sleep Medicine
AHI	Apnea-Hypopnea Index
BMI	Body Mass Index
BSSO	Bilateral Sagittal Split Osteotomy
CPAP	Continuous Positive Airway Pressure
ECG	Electrocardiography
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
FOSQ	Functional Outcomes of Sleep Questionnaire
HIPAA	Health Insurance Portability and Accountability Act
MAD	Mandibular Advancement Device
MCS	Mental Component Score
MMA	Maxillomandibular Advancement
NHANES	National Health and Nutrition Examination Survey
OAT	Oral Appliance Therapy
OSA	Obstructive Sleep Apnea
OSAS	Obstructive Sleep Apnea Syndrome
PCS	Physical Component Score
PSG	Polysomnogram
PSPOF	Problems with Occlusion and Function

PSQI	Pittsburg Sleep Quality Index
RDI	Respiratory Disturbance Index
SAQLI	Calgary Sleep Apnea Quality of Life Index
SAS	Statistical Analysis System
SDB	Sleep Disordered Breathing
SF-36	Medical Outcomes Study Short Form
TMJ	Temporomandibular Joint

A REVIEW OF THE LITERATURE

Obstructive Sleep Apnea

Epidemiology

Obstructive Sleep Apnea (OSA) is a type of sleep disordered breathing (SDB) that has gained attention in recent years due its prevalence and associated health concerns. However, this respiratory disorder has been recognized for over sixty years in the field of pulmonology. The clinical presentation of OSA was first described in the literature in the 1950s in a case report. The term Pickwickian Syndrome was coined to describe the patient who had "extreme obesity associated with alveolar hypoventilation"[1]. In the following decades, the focus was turned to sleep in an effort to understand the pathophysiology of this respiratory disorder, and how the clinical symptoms of daytime hyper-somnolence and obesity were involved[2]. It was not until population-based studies discovered a surprisingly high prevalence of OSA in adults that notable recognition of OSA outside the field of sleep medicine occurred [3].

The prevalence of OSA is remarkable. Using polysomnographic data from the Wisconsin Sleep Cohort, a sample of 602 middle-aged, working, men and women, Young et al[4] reported that 24% of men and 9% of women had an apnea hypopnea index (AHI) of 5 or greater and estimated that 4% and 2% of middle-aged North American men and women have Obstructive Sleep Apnea Syndrome (OSAS). Obstructive Sleep Apnea Syndrome is defined as having both sleep-disordered breathing, diagnosis of 5 or greater AHI, coupled with self-reported

daytime hyper-somnolence[4]. According to Young et al[4], the data may underestimate the actual prevalence of OSA in North Americans, because on average, the working population is healthier than the non-working population.

In 2013, Peppard et al[5] reported an increased prevalence of SDB and OSAS in recent decades. Extending the Wisconsin Sleep Cohort Data to 2007-2010, a sample of 1520 middle-aged men and women who underwent administration of sleep studies and the Epworth Sleepiness Scale (ESS) was used to update the prevalence of SDB and model it as a function of age, sex, and Body Mass Index (BMI) from National Health and Nutrition Examination Survey (NHANES) data. Peppard et al[5] reported an overall prevalence of 26% adults who have an AHI of 5 or greater, and 10% have AHI of 15 or greater. Estimates are that 13% of adult men and 6% of adult women have moderate to severe OSA (AHI greater than or equal to 15), and that 14% of adult men, and 5% of women have OSAS (AHI>5 and daytime sleepiness symptoms), which is more than double the estimates from 1993. The prevalence of SDB is significantly higher in older individuals, men, and individuals with higher BMIs[5]. It is estimated that 75-80% of individuals with SDB in the United States remain undiagnosed, and could benefit from treatment[6].

Diagnosis

The Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine (AASM) performed a review and developed diagnostic and practice parameters to improve the management and long-term care of individuals with OSA[7]. Diagnosis of OSA is an involved process that begins with a thorough health and sleep history and a physical examination. Thorough medical history and physical examination are critical because

individuals with obesity (a BMI greater than 30), diagnosis of congestive heart failure, Type 2 diabetes, stroke, atrial fibrillation, pulmonary hypertension, treatment refractory hypertension, and high-risk driving populations are at high risk for OSA[7]. Evaluating whether an individual has a history of snoring, gasping or apneas witnessed by others, nocturia, excessive daytime sleepiness or decreased concentration and memory not explained by other factors is part of the comprehensive sleep history[7]. A polysomnogram (PSG), or overnight sleep study administered by a sleep physician, is considered the gold standard for diagnosis of sleep disorders. A PSG records objective measures of the following parameters: oxygen saturation (oximetry), thorocoabdominal respiratory excursions, respiratory airflow and effort, electrocardiography (ECG), submental electromyography (EMG), electroencephalography (EEG), and electrooculography (EOG). Body positioning and snoring with a microphone are also recorded during a PSG[8].

The PSG indicates the severity of OSA by measuring oxygen saturation, apneic events per hour and arousals. Severity of OSA is diagnosed based on AHI which is the number of apneic and hypopneic events per hour of sleep. Apnea is defined as the cessation of airflow for 10 seconds or greater and is considered obstructive if there is presence of respiratory effort[9]. Hypopnea is defined as a reduction of airflow by at least 50% often with a coincident oxygen desaturation[8]. Mild OSA is an AHI of 5 to 14, moderate 15-29, and severe an AHI of 30 or greater[10].

Pathophysiology

OSA is a complex disorder that occurs from repeated episodes of pharyngeal collapse during sleep. To restore patency to the upper airway, individuals experience multiple arousals,

which ultimately lead to repeated activation of the sympathetic nervous system and sleep fragmentation[9]. The vasoconstricted circulation from activation of sympathetic nervous system causes an increase in systemic blood pressure. Chronically, this can lead to sustained hypertension in these individuals. Reduced oxygen saturation in the blood and hemodynamic changes are associated with hypertension and other sequela such as cardiovascular disease and cerebrovascular events[9]. Comorbid conditions associated with OSA include diabetes and metabolic syndrome, hypertension, coronary artery disease, myocardial infarction, congestive heart failure, and stroke. It is unclear whether this strong association is due to common risk factors for both OSA and diabetes and the cardiovascular diseases, or causation[6].

Disruption of sleep has been associated with cognitive and behavioral consequences including decreased quality of life, excessive daytime sleepiness, increased reaction times, decreased concentration and changes to mood and memory[9,11]. The neurocognitive consequences of OSA strongly contribute to occupational and motor vehicle accidents[12,13].

Male sex and increased age are strong risk factors for OSA. Other established risk factors for OSA include obesity, greater neck circumference, central body fat distribution, and certain craniofacial and upper airway abnormalities. Dysmorphic maxilla and mandibles in terms of proportion and position, hypertrophic tonsillar tissues, and narrowed nasal cavities may play a role in OSA development. It is suspected that there is a genetic predisposition to OSA, but risk factors related to a shared lifestyle may be causative[6].

Management

Obstructive Sleep Apnea is a chronic disorder that requires long term, multidisciplinary management. The AASM recommends the following therapies to manage the disease: behavior

therapy, Continuous Positive Airway Pressure (CPAP), Oral Appliance Therapy (OAT), and Maxillomandibular advancement surgery (MMA)[7]. Conservative management of OSA involves behavior therapy: weight loss, modifying position of body to non-supine during sleep, and avoidance of alcohol or other sedatives before bedtime. These behavior modifications are often prescribed as an adjunct to other primary treatments[7]. CPAP splints the airway with pressurized air, delivering oxygen as well as preventing collapse of the pharyngeal muscles[14]. Oral appliances advance the mandible to a titrateable protrusive position, in which the attached tongue and soft tissues follow, increasing the volume and patency of the upper airway[15]. MMA in comparison to OAT and CPAP, offers a surgical cure to the etiology, rather than a compliance dependent disease management. MMA involves surgically advancing the maxilla and mandible thus expanding the pharyngeal airway as the skeletal framework is advanced[16,17]. This prevents collapse of the pharynx upon inspiration and success, defined as AHI <20 and ≥50% reduction in AHI post surgery, is reported as 86% and cure, defined as AHI <5 reported as 43.2%[16].

Oral Appliance Therapy

The mechanism of action of mandibular advancement devices (MADs) is likely explained by increasing the upper airway size and cross-sectional area at multiple levels as recorded in lateral cephalograms, taken in both supine and upright positions, and magnetic resonance imaging (MRI) and cone beam computed tomography (CBCT) volumetric data. It has also been demonstrated that MADs increase tone of upper airway muscles thus improving airway patency[18,19]. Protrusion of the mandible is necessary for efficacy of OAT as demonstrated by Mehta et al[20]. Those patients who received the sham oral appliance that did not advance the mandible showed no improvement in AHI, when compared to patients using an MAD that protruded the mandible. The degree of protrusion typically reported is 6 to 10mm or 50 to 75%

of the patient's maximum mandibular protrusion[20]. Furthermore, higher magnitude of protrusion in MADs produces greater reduction of AHI and respiratory events[19]. Walker-Engström et al reported that advancing MAD to the 75% maximum reduced AHI <10 in 52% of the patients whereas advancing MAD to 50% only reduced AHI <10 in 31% of patients[21]. In comparison, a recent cohort study by Anitua et al reported successful reduction of AHI <50% in 30% of the sample who wore the oral appliance without mandibular advancement[22]. Anitua et al hypothesized that the two-piece splint made by a maxillary splint connected to a mandibular splint with tensors may be sufficient to obtain airway patency in some patients without advancing the mandible[22]. Both custom-made and titratable MADs consistently demonstrate higher effectiveness at reducing AHI and improving oxygen saturation over pre-fabricated and fixed MADs respectively[18]. Therefore, adjustable, custom-made MADs are recommended by the AASM and American Academy of Dental Sleep Medicine (AADSM) for management of OSA[7,10].

MADs are efficacious at significantly reducing AHI to clinically controlled levels[23]. The literature uses varying criteria to define successful OAT treatment, ranging from the most stringent-reduction of AHI <5- to the most liberal- reduction of baseline AHI by 50% or more[19]. As a result of varying criteria, reported success rates range from 21-80%[18]. Ferguson et al reported average success rates of 42% for reduction of AHI <5, 52% for reduction of AHI <10, and 65% for reduction of AHI by 50% or more[19]. The success rate of OAT is dependent on the selection of response criteria[24] Liberal criteria (reduction of baseline AHI by 50% or more) should be used with caution in severe OSA patients, as concurrent insufficient restoration of oxygen may be present and lead to adverse health outcomes[24]. The severity of OSA influences the success of MAD, with overall higher success in patients with lower AHI. In addition to the

degree of protrusion of MAD and initial severity of OSA, sleep position (supine versus non-supine) and BMI are believed to influence efficacy of OAT[19].

Randomized crossover trials have indicated that compared to CPAP, OAT is less efficacious at reduction of AHI and improvement of oxygen saturation levels for all levels of OSA severity[19,23]. Meta-analysis determined that although OAT produces a significant mean reduction in AHI, the mean reduction is 6.24 events/hour less than with CPAP [10]. However, compliance has been reported as higher with oral appliances than CPAP[25,26]. This evidence may be considered weak because the studies all compared subjective OAT adherence to objective CPAP adherence measures[10]. The discrepancy in compliance seems to offset the increased efficacy of the CPAP, and thus OAT and CPAP show similar overall effectiveness at reducing symptoms of OSA, including improvement in quality of life outcomes and excessive daytime sleepiness for patients with mild, moderate, and severe OSA[10,27].

Quality of Life

Systemic objective measurements such as AHI and oxygen saturation are important for diagnosis and evaluation of the severity of OSA, but these values correlate poorly with subjective symptomology of the disease[28]. Excessive daytime sleepiness is moderately associated with OSA as measured by Epworth Sleepiness Scale (ESS) in the Sleep Heart Health Study of middle-aged OSA patients [29]. Weaver et al. concluded that there is a weak association at best, between PSG indices and self-reported general and mental health, and daytime sleepiness. Furthermore, AHI, which defines OSA severity, correlates poorly with these quality of life measures[30]. Patient-centered outcomes of quality of life (QOL), daytime sleepiness, cognitive status, and performance in daily activities including work can be more important to

individuals suffering from OSA[11,31]. These functional outcomes are often the reason individuals with OSA seek treatment in the first place[30].

Subjective quality of life outcomes have been measured for OSA patients undergoing CPAP, MMA, and OAT. In regards to quality of life outcomes, MMA has shown to reduce excessive daytime sleepiness, the need for auxiliary CPAP, and most individuals reported satisfaction with surgical results and OSA symptomology[16,17]. Phillips et al's systematic review of the literature indicated that CPAP and MMA show similar effectiveness at reduction of ESS across all levels of OSA[25]. Furthermore, CPAP and MAD show comparable improvement of QOL as measured by disease-specific Functional Outcomes of Sleep Questionnaire (FOSQ)[25] and Calgary Sleep Apnea Quality of Life Index (SAQLI)[23]. Interestingly, a statistically significant improvement in 4 of the 8 domains of SF-36 was shown for MADs over CPAP. These general QOL domains were vitality, bodily pain, mental health and social function[25]. In comparison, Schwartz et al reported no statistically significant differences between OAT and CPAP for subscales nor mental and physical summary scores for the Medical Outcomes Study Short Form (SF-36) [26]. However, there exists limited long-term data for patient-centered outcomes for patients being treated with MAD for OSA[32].

Side Effects

OAT offers an effective treatment modality for patients suffering from OSA, but continued follow-up by the provider is necessary to manage signs and symptoms. Inevitably, with therapeutic use of MADs, come unintended side effects. These side effects can be appliance, intraoral, or TMJ related most commonly[33]. Systematic evaluation of the dental changes and perceived side effects of MADs and their prevalence is not strongly documented in

the literature. Cochrane's systematic review reported that early side effects or adverse events include jaw discomfort, excess salivation, dry mouth, gingival irritation, and dental soreness[23].

Patient Reported Outcome Measures

Understanding the patient-centered outcome of quality of life is paramount to successful management of OSA. Unfortunately, there is not a single questionnaire that encompasses all aspects of subjective outcome measures for OSA management. There are several general and condition-specific validated questionnaires used to assess perception of quality of life for patients with OSA that are used in clinical and research settings[34], including the SF-36, SAQLI, and PSPOF.

The SF-36 is a validated general health quality of life questionnaire that includes 36 questions scored on a Likert-scale[35,36]. The SF-36 is used frequently to compare diseases as well as to assess patient-centered outcome to treatment. Health is measured on a multi-item scale in the following eight dimension: 1) physical functioning, 2) role limitations because of physical health problems, 3) bodily pain, 4) social functioning, 5) general mental health, 6) role limitations because of emotional problems, 7) vitality, and 8) general health perceptions. Answered questions are scored, and these scores are summed and represent the raw scaled score. The raw scaled score for each of the eight dimensions is then transformed to a 0-100 scale. Two summary scores are calculated with special algorithms and represent the Physical Component Summary (PCS) and Mental Component Summary (MCS). The questions are positively scored; higher scores are associated with better quality of life[36]. Average completion time is 5-10 minutes.

The SAQLI is a validated condition-specific questionnaire that measures quality of life outcomes for patients with sleep apnea [11]. It was designed to be administered by a qualified personnel, but has been utilized as a self-administered questionnaire in clinical settings. The SAQLI assesses quality of life, mood, and performance for individuals who have received therapeutic treatment for sleep apnea. There are forty items that comprise 5 domains: role functioning, social interactions, emotional functioning, symptoms, and treatment-related symptoms[11].

Problems with Occlusion and Function (PSPOF) is a custom questionnaire developed for an NIH grant that was designed to assess patient perception of occlusal, functional, and temporomandibular joint (TMJ) related problems following orthognathic surgery[37]. The questionnaire consists of 14 items rated on a 5 point Likert-scale from strongly disagree to strongly agree. Six items are reversed keyed so that a higher score indicates greater negative perception. Two domain scores are calculated to reflect a patient's perception of occlusal problems and TMJ related problems. Domain scores are calculated as the average of the items in each domain. Average completion time is 3 minutes.

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Introduction

Obstructive Sleep Apnea (OSA) is a type of sleep disordered breathing (SDB) that has gained attention in recent years due its prevalence and associated health concerns. Obstructive Sleep Apnea Syndrome (OSAS) is defined as having both sleep-disordered breathing and a diagnosis of 5 or greater AHI, coupled with self-reported daytime hyper-somnolence [1]. Using polysomnographic data from the Wisconsin Sleep Cohort of 602 middle-aged, working, men and women, Young et al reported that 24% of men and 9% of women had an AHI of 5 or greater and that 4% and 2% respectively had Obstructive Sleep Apnea Syndrome (OSAS) - AHI>5 and daytime sleepiness symptoms[1]. In 2013, Peppard et al reported an increased prevalence of SDB and OSAS in recent decades using the Wisconsin Sleep Cohort 1990s and 2007-2010 data of 1520 middle-aged men and women who underwent the administration of sleep studies and completed the Epworth Sleepiness Scale (ESS)[2]. Peppard et al reported an overall prevalence of 26% adults who had an AHI of 5 or greater, and 10% with AHI of 15 or greater[2]. Estimates were that 13% of adult men and 6% of adult women had moderate to severe OSA (AHI greater than or equal to 15), and that 14% of adult men, and 5% of women had OSAS. These estimates are more than double the estimates from 1993[2].

OSA is a chronic disorder that requires long term, multidisciplinary management. The American Academy for Sleep Medicine (AASM) recommends the following therapies to manage

the disease: behavior therapy, Continuous Positive Airway Pressure (CPAP), Oral Appliance Therapy (OAT), and Maxillomandibular advancement surgery (MMA)[3]. Oral appliances, or mandibular advancement devices (MADs), advance the mandible to a titrateable protrusive position, in which the attached tongue and soft tissues follow, increasing the volume and patency of the upper airway[4]. The gold standard, CPAP, has been shown to be more efficacious at reducing AHI than OAT[5–7]. However, compliance has been reported to be higher with oral appliances than CPAP[5,7]. The discrepancy in compliance seems to offset the increased efficacy of the CPAP, and thus OAT and CPAP show similar overall effectiveness at reducing symptoms of OSA, including improvement in quality of life outcomes and excessive daytime sleepiness for patients with mild, moderate, and severe OSA[8,9]. However, the long-term compliance of MADs is not well documented in the literature.

Systemic objective measurements such as Apnea-Hypopnea Index (AHI) and oxygen saturation are important for diagnosis and evaluation of the severity of OSA, but these values correlate poorly with subjective symptomology of the disease[10]. Patient-centered outcomes of quality of life, daytime sleepiness, cognitive status, and performance in daily activities including work can be more important to individuals suffering from OSA[11,12]. Individuals with OSA often seek initial treatment due to their subjective symptoms and the disruption that their daytime sleepiness has on daily functioning[10].

Overall, there exists limited long-term data for patient-centered outcomes of quality of life and perceived functional and occlusal changes for patients being treated for OSA with OAT[6,13]. Understanding the long-term patient-perceptions of OAT will help guide clinicians to better manage OSAS patients. The objective of this study was to determine the patient-centered

outcomes of quality of life and functional and occlusal changes following long-term use of OAT (greater than 2 years) for OSAS.

Materials and Methods

This study, a survey distributed to patients who met inclusion and exclusion criteria, was approved by the the Institutional Review Board at the University of North Carolina at Chapel Hill (IRB 16-1659). Eligible participants who were treated at least two years prior to March 2017 at the University of North Carolina at Chapel Hill School of Dentistry Sleep Clinic for management of Obstructive Sleep Apnea with a titrateable mandibular advancement device were identified by a systematic search of the UNC Sleep Medicine Database. All patients were treated by Dr. Greg Essick, who was responsible for delivering and adjusting the custom mandibular advancement devices. Patients were eligible to participate if they had been diagnosed with OSA by a sleep physician and polysomnogram and referred to UNC for treatment; were age 18 to 60 at time of oral appliance delivery; and complete chart entries, with demographic and contact information, were available. Patients who had a diagnosis of Central or Complex Sleep Apnea or a congenital syndrome with or without severe retrognathia were excluded. Of the 828 potentially eligible patients from the sleep medicine database, 139 participants met the inclusion and exclusion criteria.

Demographics

Demographic data collected from the UNC Sleep Clinic database for eligible participants included: sex, age and body mass index (BMI) at the time of delivery of the oral appliance, date of delivery of the oral appliance, OSA diagnosis, polysomnogram (PSG) results, overjet, and skeletal class.

Questionnaires

Medical Outcomes Study Short Form (SF-36) is a validated general health quality of life questionnaire that includes 36 questions scored on a Likert-scale[14,15]. The SF-36 is used frequently to compare diseases as well as to assess patient response to treatment. Health is measured on a multi-item scale in the following eight dimension: 1) physical functioning, 2) role limitations because of physical health problems, 3) bodily pain, 4) social functioning, 5) general mental health, 6) role limitations because of emotional problems, 7) vitality, and 8) general health perceptions. Answered questions are scored, and these scores are summed and represent the raw scaled score. The raw scaled score for each of the eight dimensions is then transformed to a 0-100 scale. Two summary scores are calculated with special algorithms and represent the Physical Component Summary (PCS) and Mental Component Summary (MCS). The questions are positively scored; higher scores are associated with better quality of life. Average completion time is 5-10 minutes.

The Calgary Sleep Apnea Quality of Life Index (SAQLI) is a validated condition-specific questionnaire that measures quality of life outcomes for patients with sleep apnea[12]. It was designed to be administered by a qualified personnel, but the Short-Form SAQLI, as used in this study, functions as an abbreviated, self-administered questionnaire in clinical settings[16]. Questions 1-14 asses daily functioning, social interactions, and emotional functioning and are rated on a 7 point Likert-scale from "a very large amount" to "not at all." Higher scores indicate better quality of life. For questions 15-17, respondents list up to three treatment symptoms and rate them based on degree of problem on a 7 point Likert-scale with higher scores indicating a greater problem. The final question, number 18, weights treatment induced symptoms from

questions 15-17 relative to the quality of life benefits derived from questions 1-14[16]. Question 18 is answered in a 7 point Likert-scale with higher scores indicating a greater problem.

The Problems with Occlusion and Function (PSPOF) is a custom questionnaire developed for an NIH grant that was designed to assess patient perception of occlusal, functional, and temporomandibular joint (TMJ) related problems following orthognathic surgery[17]. The questionnaire consists of 14 items rated on a 5 point Likert-scale from strongly disagree to strongly agree. Six items are reversed keyed so that a higher score indicates greater negative perception. Two domain scores are calculated to reflect a patient's perception of occlusal problems and TMJ related problems. Domain scores are calculated as the average of the items in each domain. Average completion time is 3 minutes.

A custom oral appliance questionnaire was developed to address outcomes not included in the above questionnaires. Questions related to compliance of oral appliance therapy, an explanation for discontinuation of the oral appliance if applicable, and whether auxiliary sleep apnea management therapies were being used. A section of five questions adapted from the Pittsburgh Sleep Quality Index[18] were included to address sleep habits and quality from the month prior to answering the questionnaires.

Distribution of Questionnaires

Eligible participants were sent an envelope containing an information sheet explaining the study, a Health Insurance Portability and Accountability Act (HIPAA) authorization form, the 4 questionnaires, and an addressed, stamped envelope for return of completed questionnaires to the University of North Carolina School of Dentistry. The information sheet and HIPAA authorization form were for the participant to keep for their records, and described that informed

consent was affirmed upon return of the completed questionnaires. The information sheet explained that return of the questionnaires un-completed in the return postage envelope would signify the patient elected to not participate in the study and would not be contacted further. Three rounds of questionnaires were sent to eligible participants, the second and third rounds were only sent to non-respondents from previous rounds. There was a one-month grace period between subsequent rounds. Google and yellow page searches were used to identify current addresses for potential respondents for whom envelopes were returned undelivered. Questionnaires were completed between October 2017 and February 2018.

Statistical Analysis

Statistical analysis was performed using SAS version 9.3 [19]. Unpaired T-tests and chi-square tests were used to analyze differences in demographics and clinical characteristics between responders and non-responders and between OAT wearers and non-wearers. Two-sided exact Wilcoxon rank-sum tests were used to analyze average differences in the subscales for SF-36, SAQLI, and PSPOF between responders who are wearing oral appliances and those who discontinued use. Level of significance was set at 0.05. Descriptive statistics were developed to explain reasons for discontinuation of OAT, current management for OSA, and perceived side effects.

Results

Twenty-two percent (n=31) of the 139 patients identified under the inclusion and exclusion criteria returned completed questionnaires. Five declined to participate and 25 envelopes were returned as addressee unknown. There were no statistically significant differences between respondents (those who completed questionnaires N=31) and non-

respondents (N=108) when comparing age, sex, BMI, AHI at time of OAT delivery, and time since OAT delivery (p= 0.54, p= 0.9, p= 0.32, p=0.09, p= 0.59 respectively) (Table 1).

Of the 31 who completed the questionnaires, 58% were male with a mean age of 49.19 (SD=10.02) (Table 1). The mean time since delivery of the OAT was 4.9 years (SD=1.77), the mean BMI at OAT delivery was 27.38 (SD=5.61) and the mean AHI at OAT delivery was 17.15 (SD=10.59) (Table 1). In terms of OSA Severity: 58.06% were Mild and 41.94% Moderate to Severe (Table 1).

Fifty-eight percent of the respondents currently manage their OSA with OAT while 42% had discontinued use of OAT. The reasons for discontinuation of OAT included perception that it did not appear to be working, TMJ aggravation and pain, dental and gingival discomfort, and resolution of OSA through surgery or weight loss (Table 3). Of the 13 individuals who had discontinued OAT, 7 switched to CPAP, 2 used weight loss to control OSA, 1 had a Bilateral Sagittal Split Osteotomy (BSSO) advancement, and 3 currently use nothing to manage their OSA (Table 4).

There were no statistically significant average differences between those who discontinued OAT and those who continued OAT for the subscales of SF-36: physical functioning, role limitations because of physical health problems, bodily pain, social functioning, general mental health, role limitations because of emotional problems, vitality, and general health perceptions (p=0.60, p= 0.64, p=0.0.35, p=0.15, p=0.49, p=0.17, p=0.60, p=0.20 respectively) (Table 5). Although no significant differences were found in the subscales, of interest were responses to “In general, would you say your health is?” and “How TRUE or FALSE is the following statement for you: I am as healthy as anybody I know.” Of those who

have discontinued use of OAT 7.69% report their general health as excellent, 38.46% as very good, 46.15% as good, and 7.69% as poor. Of those who continue to use OAT, 22.22% report their general health as excellent, 66.67% as very good, 5.56% as good, and 5.56% as fair (Table 6). Of those who have discontinued use of OAT, 38.46% find the statement "I am as healthy as anybody I know" as "definitely to mostly true" while those who continue to use OAT, 77.78% find the statement "I am as healthy as anybody I know" as "definitely to mostly true". (Table 6).

The average differences between those who discontinued OAT and those who continue OAT for the TMJ and Functional/Occlusal summary scores on PSPOF were not statistically significantly different ($p=0.86$, $p=0.26$ respectively) (Table 5).

In the Short-form SAQLI, the average difference between those who discontinued OAT and those who continue OAT for questions 1-14 summary score was marginally statistically significant ($p=0.052$). OAT wearers had higher median scores than non-wearers, corresponding to fewer problems with daily and emotional functioning and social interactions (Table 5). There were statistically significant average differences between those who discontinued OAT and those who continue OAT for questions 15-17 summary score and for the weighted question 18 ($p=0.009$, $p=0.02$ respectively) (Table 5). Those who discontinued OAT reported having a greater problem with side effects in the past 4 weeks from their current OSA management than those who currently use OAT to manage OSA (Table 5). Considering the side effects and comparing those to the benefits of current treatment in Question 18, those who discontinued OAT reported having a larger problem with side effects (Table 5). Reported side effects for OAT and other OSA treatment modalities are listed in Table 7.

Discussion

Individuals with sleep apnea often seek initial treatment due to their subjective symptoms, which include daytime sleepiness and impaired quality of life. Health related quality of life has become an important and recognized outcome measure of OSA treatment as well as an influence on the type of management chosen for the patient[16,20]. Furthermore, patient perception of the corresponding side effects of treatment plays an important role in patient adherence to therapy.

Understanding the quality of life outcomes and perceived side effects from treatment are paramount to successful management of OSA. Unfortunately, there is not a single questionnaire that encompasses all aspects of subjective outcome measures for OSA management. For this reason, our study used both general and condition-specific questionnaires, SF-36, SAQLI, and PSPOF, to assess perception of quality of life and side effects of OAT for OSA patients.

After a mean 4.4 years, 58% of our respondents continued to use OAT to manage their OSA. This adherence rate is similar to other long-term studies that showed. 76% adherence after 1 year[21] and 62% adherence after 4 years of OAT[22]. The reasons reported for discontinuation of OAT were also consistent with other studies: perceived lack of effect, temporomandibular joint discomfort, dental and gingival discomfort, and no longer needing it due to resolution of OSA by weight loss or orthognathic surgery[8,21].

General QOL was compared between wearers and non-wearers through the SF-36 and no statistically significant differences were observed between the two groups. The mean scores in the eight individual domains of the SF-36 ranged from 75 to 100 indicating positive QOL for OAT wearers in regards to their physical and social functioning, role limitations because of

physical health and emotional problems, bodily pain, vitality, and general and mental health perceptions. The literature supports these results by reporting OAT is effective at improving QOL for OSA patients, and that both OAT and CPAP show comparable improvements in QOL as measured by the SF-36 [6–8,13].

The short-form SAQLI compared the condition-specific QOL between wearers and non-wearers. Wearers reported less of a problem with side effects from OAT than non-wearers did with non-OAT therapeutic side effects and also perceived a better QOL benefits from OAT relative to the experienced side effects than non-wearers. Literature is sparse in regards to the self-administrated short-form SAQLI and therefore this study provides novel evidence to the risk-weighted QOL benefits of OAT.

OAT related side effects on the SAQLI included TMJ related discomfort and jaw displacement as well as changes in bite and dental and gingival sensitivity. Reports of similar adverse effects of OAT have been documented in the literature with frequency and duration of effects varying[7,9]. Studies have indicated that OAT wear causes objective dental and occlusal changes in individuals, most notably decrease in overbite, overjet, and number of posterior contacts [23–27], with duration correlating to dental changes of decreased overbite[26]. Perez et al determined that after a year of OAT, 17.9% of patients developed a posterior open bite, but that only 28.6% of these patients were aware of a change in bite[27]. Perception of and actual dental changes are discordant. Furthermore, despite evidence that OAT leads to development of TMJ related signs or symptoms in a small percentage of patients, it is usually transient in nature[27].

A main limitation of our study was the inability to compare the oral appliance wearers to a control group of patients with untreated OSA. Our comparison of OAT wearers to those who

had discontinued OAT was sub-optimal because the group of non-wearers was using a blend of therapeutic treatments for their OSA, which included CPAP, BSSO, weight-loss, as well as some who were using nothing to manage the disease. Secondly, the subjective nature of survey research is limiting, as respondents may experience recall or social desirability bias. Finally, in regards to adherence, omission of inquiry to the date of discontinuation of OAT prohibited investigation of whether discontinuation was a reflection of either short or long-term side effects of treatment.

Because OAT is considered a viable treatment for individuals with OSA who cannot tolerate CPAP or do not prefer an alternate therapy[8] more individuals are using OAT to manage their OSA. As a result, the recognition of treatment related side effects is increasing through self-report in the literature. The relationship between these dental and functional side effects and long-term adherence is still unknown. Prospective, systematic, future studies are needed to clarify the effects of ongoing OAT treatment in efforts to improve adherence and manage or mitigate these untoward effects. Studies comparing objective dental and functional side effects to perception of dental problems would provide insight to the actual impact these changes have on the individual.

OAT is reported to be as effective as CPAP in improving health related QOL[9], but long-term studies are needed to follow up on the perceived improvements in QOL. Future studies are needed to help understand the long-term subjective symptoms so that patients' quality of life is continually managed.

Conclusions

1. Long term OAT adherence is a function of patients' perceptions to both the conferred benefits of treatment and the unfavorable treatment induced side effects.
2. The Long term OAT adherence was high suggesting quality of life benefits from this type of therapy to manage OSA.

Table 1: Demographic Comparison of Survey Respondents Versus Non-Respondents							
	Respondents			Non Respondents			
Demographic	N	Mean	SD	N	Mean	SD	p-value
Age	31	49.19	10.02	108	47.98	8.77	0.54
Years Since Delivery	31	4.9	1.77	108	5.09	1.6	0.59
BMI	26	27.38	5.61	96	28.69	6.73	0.32
AHI	31	17.15	10.59	105	21.84	20.35	0.09
	N	%		N	%		
Sex	31			108			0.9
Female	13	41.94%		44	40.74%		
Male	18	58.06%		64	59.26%		
OSA Severity	31			108			0.65
Mild	18	58.06%		54	50%		
Moderate/Severe	13	41.94%		54	50%		

Table 1: Demographic and clinical characteristics of survey respondents and non-respondents. Age, BMI, AHI, and OSA Severity reflect time of oral appliance delivery. Statistical significance was set at $p<0.05$

Table 2: Demographic Comparison of OAT Wearers Versus Non-Wearers							
	Wearers			Non-Wearers			
Demographic	N	Mean	SD	N	Mean	SD	p-value
Age	18	49.61	9.5	13	48.62	11.08	0.8
Years Since Delivery	18	4.44	1.73	13	1.69	1.6	0.089
BMI	14	26.57	4.021	12	28.32	7.12	0.46
AHI	18	16.72	11.39	13	17.74	9.81	0.8
	N	%		N	%		
Sex	18			13			0.74
Female	8	44.44%		5	38.46%		
Male	10	55.56%		8	61.54%		
OSA Severity	18			13			0.69
Mild	11	61.11%		7	53.85%		
Moderate/Severe	7	38.89%		6	54.87%		

Table 2: Demographic and clinical characteristics of those who currently wear Oral Appliance Therapy (OAT), and those who have discontinued use. Age, BMI, AHI, and OSA Severity reflect time of oral appliance delivery. Statistical significance was set at $p<0.05$

Table 3: Reasons for Discontinuing OAT
Did not appear to be working
TMJ Aggravation/Pain
Dental/Gingival Discomfort
Resolution of OSA (Surgery or Weight Loss)

Table 3: Reported reasons why individuals discontinued their oral appliance therapy (OAT)

Table 4: Current Method of OSA Management	
	N
CPAP	7
Weight Loss	2
BSSO	1
Nothing	3

Table 4: Current method of Obstructive Sleep Apnea (OSA) management significance set at $p<0.05$.

Table 5: Comparison of OAT Wearers and Non-Wearers Questionnaire Responses							
	Wear (N=18)			No Wear (N=13)			
SF 36	Median	p25	p75	Median	p25	p75	p-value
General Health	77	67	87	62	42	87	0.20
Mental Health	85	70	95	85	55	95	0.49
Role-Physical	100	81.25	100	100	68.75	100	0.64
Role-Emotional	100	75	100	83.33	58.33	100	0.17
Vitality	75	62.5	87.5	68.75	37.5	87.5	0.60
Bodily Pain	84	72	84	73	67	84	0.35
Social Functioning	93.75	75	100	87.5	50	100	0.15
Physical Functioning	95	95	100	95	90	100	0.60
PSPOF	Median	p25	p75	Median	p25	p75	p-value
TMJ	1.7	1	2.2	1.6	1.2	2.6	0.86
Function/Occlusion	2.44	1.5	3.25	2	1.75	2.88	0.26
SAQLI	Median	p25	p75	Median	p25	p75	p-value
Questions 1-14	6.04	5.21	6.43	5.14	4	6.07	0.052
Questions 15-17	2	2	5	9	6	11	0.0093
Question 18	0.5	0.5	0.75	0.75	0.5	1	0.14
Weighted Question 18	1.5	0.5	3.75	6.5	3	10	0.019

Table 5: Comparison of SF-36, PSPOF, and SAQLI responses between OAT wearers and non-wearers. Statistical significance was set at $p<0.05$.

Table 6: Statistically Significant Findings (SF-36 Questionnaire)

Question 1: In general, would you say your health is? p= 0.025

	Excellent	Very Good	Good	Fair	Poor
Wearers	22.22%	66.67%	5.56%	5.56%	0%
Non-Wearers	7.69%	38.46%	46.15%	0%	7.69%

Question 11.b: How true or false is the following statement for you:
I am as healthy as anybody I know? p= 0.041

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
Wearers	16.67%	61.11%	16.67%	0%	5.56%
Non-Wearers	23.08%	15.38%	30.77%	23.08%	7.69%

Table 6: Statistically significant questions 1 and 11b of the SF-36 with distribution of answer responses between wearers and non-wearers of oral appliance therapy (OAT). Statistical significance set at $p<0.05$.

Table 7: Reported Side Effects from OAT and CPAP

OAT	N	CPAP	N
TMJ		Wake up frequently	4
Pain Inflammation	6	Poor fit of mask (slipping, dislodging)	4
Jaw Displacement/Moving Forward	5	Dry Mouth	2
Bite Change	3	Dry Throat	1
Difficulty Breathing/Nasal Stuffiness	3	Dry eyes	1
Dental Pain	2	Mark on face from mask	1
Sensitive Gums	2	Awkward using	1
Dry Mouth	2	Claustrophobia	1
Dry Throat	2	Stomach bloating	1
Headache	2	Noise of air	1
Waking Up	1	Sore joints	1
Snoring	1		
Increased Space Between Teeth	1		
Soreness in Interior Cheek	1		

Table 7: Reported side effects from Oral Appliance Therapy (OAT) and Continuous Positive Airway Pressure (CPAP).

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