

**TRACKING PULSE OXIMETER FINDINGS BEFORE, DURING AND AFTER
TITRATION OF MANDIBULAR ADVANCEMENT DEVICES FOR PATIENTS
WITH MODERATE AND SEVERE OBSTRUCTIVE SLEEP APNEA**

by

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A thesis submitted to the Faculty of the
Orofacial Pain Graduate Program
Naval Postgraduate Dental School
Uniformed Services University of the Health Sciences
in fulfillment of the requirements for the degree of
Master of Science in Oral Biology

June 2018

Naval Postgraduate Dental School
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Bethesda, Maryland

CERTIFICATE OF APPROVAL

MASTER'S THESIS

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2018

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ABSTRACT

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Introduction: Obstructive Sleep Apnea (OSA) is a sleep-related breathing disorder that impacts quality of life and operational readiness and increases the risk of long term health consequences. Military veterans are four times more likely to be diagnosed with OSA compared to the general population. Treatment typically includes the use of a continuous positive airway pressure (CPAP) machine which requires patient tolerability and compliance. An option for OSA management is oral appliance therapy. The Mandibular Advancement Device (MAD) maintains an open upper airway by moving the lower jaw and tongue forward to prevent tissue collapse and airway obstruction. Currently, MAD treatment is guided by patient reported symptom improvement but little objective data is available to determine success. This pilot study evaluated 1) the association of objective oxygenation levels with perceived sleep quality and stress, 2) the feasibility of home pulse oximetry nightly with MAD titration, and 3) the efficacy of pulse oximetry to guide MAD titration.

Methods: Participants were active duty personnel newly diagnosed with OSA. Prior to consent, potential participants were evaluated at the Orofacial Pain Center for eligibility.

A custom-made MAD was titrated over a period of 4-8 weeks. Before, during, and after titration, a portable pulse oximeter was worn nightly to capture continuous oxygenation levels. Jaw comfort, stress, sleep quality, and MAD adherence were assessed daily. Once maximum tolerable MAD titration was achieved, participants completed a second sleep study to assess MAD efficacy. **Results:** By the end of the study, all subjects showed a significant decrease in oxygen desaturation index (ODI). Comparing pre and post treatment polysomnography, 75% of subjects had a reduced apnea-hypopnea index (AHI) and 100% of subjects showed improved sleep efficiency. **Discussion:** There has been no previous study to track real time, nightly pulse oximetry and explore associations with AHI, subjective measures of sleep quality, stress, oral appliance adherence and jaw discomfort levels during MAD titration. Currently, there is no objective data set that captures continuous oxygenation during home MAD titration. Sleep medicine center laboratory technicians may adjust the MAD during the follow up sleep study if oxygenation levels are not optimum. This sleep center MAD adjustment causes sleep fragmentation, waking the patient during the sleep study, and potentially advances the mandible too quickly, causing MAD tolerability and/or adherence issues due to jaw pain. **Conclusion:** The results of this pilot study will provide the foundation for future research using subjective and objective information to address OSA severity. This approach for MAD titration may lead to improved care, reduced health care cost, and better resource utilization by decreasing expensive clinic-based sleep studies. Additionally, maintaining good sleep quality plays a significant role in patient well-being and has a tremendous impact on military healthcare and mission readiness.

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LIST OF ABBREVIATIONS

AASM	American Academy of Sleep Medicine
AHI	Apnea-Hypopnea Index
APAP	Automatically Self-adjusted Positive Airway Pressure
ArTH	Arousal Threshold
BiPAP	Bi-level Positive Airway Pressure
CNS	Central Nervous System
CO ₂	Carbon Dioxide
CPAP	Continuous Positive Airway Pressure
CT	Computed Tomography
ESS	Epworth Sleepiness Scale
FOSQ	Functional Outcomes of Sleep Questionnaire
ICSD	International Classification of Sleep Disorders
IRB	Institutional Review Board
MAD	Mandibular Advancement Device
MRI	Magnetic Resonance Imaging
NPDS	Naval Postgraduate Dental School
OA	Oral Appliance
OCST	Out of Center Sleep Test
ODI	Oxygen Desaturation Index
OPC	Orofacial Pain Center
OSA	Obstructive Sleep Apnea
OSAHS	Obstructive Sleep Apnea-Hypopnea Syndrome
PAP	Positive Airway Pressure

PO	Pulse Oximeter
POB	Posterior Open Bite
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
PTSD	Post Traumatic Stress Disorder
RERA	Respiratory Effort-Related Arousals
RDI	Respiratory Disturbance Index
SaO ₂	Arterial Oxygen Saturation
SAHS	Sleep Apnea-Hypopnea Syndrome
SDB	Sleep Disordered Breathing
SNS	Sympathetic Nervous System
SpO ₂	Peripheral Oxygen in the Blood
TMD	Temporomandibular Disorder
TMJ	Temporomandibular Joint
TRD	Tongue Retained Device
UPPP	Uvulopalatopharyngoplasty
VAS	Visual Analogue Scale
WRNMMC	Walter Reed National Military Medical Center

CHAPTER I: REVIEW OF THE LITERATURE

Types of Sleep Apnea

Sleep-disordered breathing (SDB) is a general term used to classify disorders characterized by abnormal respiratory patterns; more specifically, pauses in breathing. These disorders range from basic snoring to sleep apnea-hypopnea syndrome (SAHS) (Dieltjens et al., 2012). While snoring may not always have adverse physiological effects, SAHS is associated with daytime sleepiness and cognitive issues and increases the risk of developing health problems such as hypertension, arrhythmias, diabetes, stroke and premature death from cardiovascular disease (Ross et al., 1998; Young et al., 2009).

The American Academy of Sleep Medicine (AASM) classifies sleep apnea as central, mixed or obstructive. Central and mixed sleep apnea involve respiratory center dysfunction in the central nervous system (CNS) resulting in inadequate or complete cessation of breathing effort during sleep. Obstructive sleep apnea (OSA), on the other hand, is due to recurrent episodes of complete or partial blockage of the upper airway despite respiratory effort. Apnea is a cessation of breathing attributed to complete airway obstruction during sleep. Hypopnea involves episodes of shallow breathing or a low respiratory rate that does not meet metabolic needs and is attributed to partial airway blockage (Dempsey et al., 2010). These apneic and/or hypopneic episodes reduce oxygen saturation (hypoxemia), increase carbon dioxide levels (hypercapnia), induce arousals from sleep, and cause abnormal pauses in breathing. Episodes that last longer than 10 seconds are used in the diagnosis of OSA (AASM Task Force, 1999; Malhotra & White, 2002; ICSD-3, 2014). Apneas and hypopneas share similar pathophysiology and are categorized as part of obstructive sleep apnea-hypopnea syndrome (OSAHS) when daytime interference occurs due to this SDB (AASM Task Force, 1999). Although OSAHS is the most accurate acronym, many authors simply use OSA, which will be implemented in this document.

OSA represents 85% of all sleep apnea cases, 80% of which are often undiagnosed (Kapur et al., 1999). In a 2009 publication, Young et al. reported that 15% of the U. S. population has untreated sleep apnea. OSA also plays a major role in the health of military service members. Military personnel are at a high risk to sustain blunt evoked traumatic brain injury; such injuries have been reported to be associated with sleep issues to include OSA (Collen et al., 2011). Additionally, Veterans are 4 times more likely to suffer from OSA than the general population (Teng & Won, 2012). Mysliwiec et al. found that 62.7% of the military personnel in their study met diagnostic criteria for OSA. Veterans with OSA have significantly more anxiety, post-traumatic stress disorder (PTSD), and mental disorder symptoms compared to veterans without OSA (Sharafkhaneh et al., 2005).

OSA: Pathophysiology and Risk Factors

The complex pathophysiology involved in OSA patients is most influenced by major factors like airway anatomy, depressed upper airway muscle activity, and genetic predisposition (Deegan &

McNicholas, 1995). Airway collapse resulting in obstruction is the most common anatomical finding associated with sleep disorders; these mechanical issues are secondary to enlarged pharyngeal tissues and relaxed tongue, both of which occur when sleeping in the supine position.

Adequate upper airway patency for breathing, speech, or swallowing is coordinated by areas of the CNS that control motor activity of the peripheral respiratory and oral musculature. More than 20 pharyngeal skeletal dilatory muscles help maintain upper airway patency. These muscles help reduce upper airway collapse due to negative intraluminal pressure caused by the diaphragm, pressure from surrounding extraluminal tissues and potential nasal obstruction (Malhotra & White, 2002). Individuals more vulnerable to collapse of the upper airway while sleeping are those who have compromised airway anatomy due to factors like facial skeletal abnormality or severe obesity (Malhotra & White, 2002). In OSA patients, reduced reflexive dilatory muscle activity during sleep results in greater reduction of airway patency than occurs in healthy individuals (Dempsey et al., 2010). Sleep-induced restriction of air flow initiates a weak reflexive response to increase dilatory muscle activity, and in OSA patients, this weak increase is generally insufficient to re-establish upper airway patency (Berry & Gleeson, 1997; Gleeson et al., 1990).

In OSA patients, dilatory muscle activity of the upper airway is greater during daytime inspiration compared to healthy individuals (Mezzanotte et al., 1992). Fogel et al reported that during wakefulness, OSA patients experience increased pharyngeal dilatory muscle activity to compensate for greater negative intraluminal pressure. This increased effort enabled OSA patients to achieve the same air flow rate (filling the lungs with the same amount of air) as healthy subjects (Fogel et al., 2001), but it is diminished when sleeping.

Using computed tomography (CT) and magnetic resonance imaging (MRI), upper airway size in the OSA patient is reduced compared to age and weight matched controls during wakefulness. OSA patients have smaller retropalatal areas with fat deposits around the upper airway (Horner et al., 1989; Schwab et al., 1993). A 1997 study that compared 17 healthy patients to 40 OSA patients found smaller pharyngeal airways and increased airway collapsibility in OSA patients (Isono et al., 1997).

Apneas and hypopneas, as discussed in the previous section, are associated with increased arterial carbon dioxide (CO₂) levels as well as increased sympathetic nervous system (SNS), brain, muscle and heart activity. This sleep arousal (Berry & Gleeson, 1997; Dempsey et al., 2010) induces pharyngeal dilatory muscle activity which improves airflow and decreases arterial CO₂ levels. Ongoing apneic events allow for persistent SNS activity which may lead to hypocapnia, decreased central respiratory drive, and less effective pharyngeal dilatory muscle activity which may compromise upper airway patency (Deegan & McNicholas, 1995). OSA patients are aroused from sleep repeatedly throughout the night to resolve the apnea/hypopnea-induced hypoxemia. When apneas occur with sufficient frequency, the patient cannot progress through a full sleep cycle during the night (AASM Task Force, 1999). This sleep fragmentation coupled by surges in SNS activity

builds the foundation for long term negative health outcomes and decreased quality of life (Vanden Brook, 2010).

Snoring, a possible precursor of OSA, is the most prevalent sleep breathing disorder and afflicts 40% to 60% of all adults (Ohayon et al., 1997). Hallmark signs of OSA include loud snoring, sleep arousal due to gasping for breath, and poor sleep quality. It has also been suggested that a low respiratory arousal threshold (ArTH) is a prominent physiologic trait in patients with mild or moderate OSA. A decrease in the apnea hypopnea index (AHI), a measure of OSA severity, and oxygen saturation as well as a greater number of hypopneas compared to apneas were found to be significant independent predictors of a low ArTH. These findings from a 2014 study may help characterize why healthy, non-obese and/or non-cardiac compromised patients, which comprise the majority of active duty military personnel, may be diagnosed with mild to moderate OSA (Edwards et al., 2014).

OSA, like sleep apnea-hypopnea syndrome (SAHS), has been implicated as a risk factor for various medical conditions to include cardiovascular disease and diabetes (AASM Task Force, 1999; ICSD-3, 2014). Undiagnosed OSA can result in health consequences like excessive daytime sleepiness, impaired cognitive performance and reduced quality of life. These symptoms can result in neuropsychological changes like decreased concentration, memory loss and an elevated risk for motor vehicle accidents (Teng & Won, 2012). Periods of inattention, decreased productivity and safety related hazards in the work place can be a direct result of OSA-associated daytime sleepiness and fatigue.

Risk factors for OSA include increased age, male gender and obesity (Eckert & Malhotra, 2008). Particular risk factors that increase the probability for the onset of OSA include: (1) a neck circumference greater than 17 inches for men and greater than 16 inches for women, (2) a body mass index greater than 35, (3) a Modified Mallampati score of 3 or 4, (4) craniofacial variation, (5) nasal obstruction, (6) pharyngeal crowding, (7) daytime tiredness (8) snoring history (9) hypertension, and (10) sedative medication use (Epstein et al., 2009; Chung et al., 2008; Culpepper & Roth, 2009). The Modified Mallampati score (1-4) is determined by assessing the visibility of structures in the oral cavity (Nuckton et al., 2006).

- Class 1: Full visibility of tonsils, uvula and soft palate
- Class 2: Visibility of hard and soft palate, upper portion of tonsils and uvula
- Class 3: Only the soft and hard palate and base of the uvula are visible
- Class 4: Only hard palate visible

Individuals with scores of 3 or 4 and who have accompanying daytime symptoms should be evaluated for OSA.

Diagnosis and Assessment of OSA

Although general physicians and dentists may recognize signs of OSA and make a referral for further evaluation, the definitive diagnosis of OSA is made by a sleep physician. A full night sleep

study or polysomnography (PSG) is considered the gold standard for OSA diagnosis as it provides objective measures of neurological, chemical, and physical parameters directly related to SDB (Dieljtens et al., 2012); however, four types of instrumentation can assess physiological aspects of sleep apnea.

- Type 1: The full night PSG conducted by a sleep lab attendant in a formal sleep lab uses 8 or more channels (7-12 leads) to record data. This PSG includes the following: electroencephalogram, electrocardiogram, electro-oculogram, electromyogram, nasal/oral airflow, chest/abdominal respiratory effort, AHI, blood oxygen saturation, oxygen desaturation index (ODI), respiratory disturbance index (RDI) and respiratory event related arousal (RERA) experienced per hour of sleep (AASM Task Force, 1999; Epstein et al., 2009).
- Type 2: Instrumentation gathers the same parameters as a Type 1 PSG but does not use a sleep lab attendant.
- Type 3: These monitoring devices record at least 4 parameters, including 2 pulmonary functions, heart rate and blood oxygen saturation via pulse oximetry. While not as definitive as Type 1 or Type 2 instrumentation, Type 3 monitoring can be used in an out of center or home sleep environment and still provide the sleep physician sufficient data to make a OSA diagnosis (Collop et al., 2012; ICSD-3, 2014).
- Type 4: These devices typically measure less than 4 parameters, but always include a pulse oximeter. Type 4 devices are inexpensive and easy to use by patients at home. These devices measure pulse rate and blood O₂ saturation levels (Dawson et al., 2015). However, they may not provide sufficient objective data to positively diagnose OSA (Collop et al., 2012).

The diagnosis of OSA is confirmed if PSG, or similar data recording instrumentation, shows an AHI of 5 or more apnea/hypopnea events per hour of sleep and there is no neurological evidence of CNS dysfunction.

The severity of OSA is measured by the AHI; the International Classification of Sleep Disorders 3rd Edition (ICSD-3) in 2014 defined this as the number of obstructive apnea and/or hypopnea events per hour of sleep. As PSG measures multiple physiological parameters; it is viewed as the ideal method for determining AHI. The AHI parameters described in the ICSD-3 are listed below.

- Mild 5 to 15 events per hour
- Moderate > 15 to 30 events per hour
- Severe > 30 events per hour

Respiratory disturbance index (RDI) is also used in sleep medicine to categorize the severity of OSA but has varied in definition throughout the year (Epstein et al., 2009). RDI uses the same numeric range as AHI to define mild, moderate, and severe OSA; but, in addition to measuring apnea and hypopnea events per hour, RDI also includes less severe respiratory effort-related arousals (RERA) as part of its scoring. These events consist of reduced airflow that does not

meet oxygen desaturation criteria for hypopnea. AHI and RDI can be derived from PSG data and can also be assessed by an out-of-center sleep test (OCST) using portable, at home monitoring devices. Unfortunately, these home monitors cannot differentiate when the patient is sleeping which allows for inaccurate AHI or RDI data often resulting in an underestimated OSA severity (Park et al., 2011). RDI measured from oximetry during PSG may slightly overestimate AHI, but it may correlate closely with AHI for OSA patients (Vasquez et al., 2000).

OSA Treatment Options

Patient education is vital when executing treatment for all forms of OSA. Information includes the benefit of lifestyle changes such as weight loss and/or smoking cessation, maintenance of nasal patency, avoidance of respiratory depressants such as alcohol intake close to bedtime, and adjustments to sleep habits. For some patients, OSA severity is dictated by their sleep posture. Positional OSA, defined as an AHI 2 times higher in the supine position compared to lying on one's side, could be addressed with a simple, non-invasive treatment by having the patient sleep more on their side (Malhotra & White, 2002).

Positive Airway Pressure (PAP) has long been considered the gold standard medical therapy for all forms of OSA (Young et al., 1993; Qaseem et al., 2013). PAP can improve the patency of an obstructed upper airway and is usually delivered through a face mask device (both nose and mouth or nasal only) to prevent upper airway collapse during sleep (Sullivan et al, 1981; AASM Task Force, 1999; Qaseem et al., 2013). PAP therapy improves sleep quality because the positive pressure it delivers can be adjusted to reduce the frequency of apneas, hypopneas, and snoring as well as improve oxygen saturation. Successful PAP therapy can enhance patient quality of life and decrease excessive daytime sleepiness or depressive symptoms while improving cognitive function and blood pressure (Bazzano et al., 2007; Qaseem et al., 2013). The traditional continuous positive airway pressure (CPAP) has expanded to include therapies like bi-level positive airway pressure (BiPAP) and automatically self-adjusting positive airway pressure (APAP). BiPAP mimics normal breathing more closely than CPAP; APAP devices detect the variability of airway resistance on a breath to breath basis and vary the air pressure to provide the lowest and most comfortable positive pressure needed to keep the upper airway patent. Culpepper & Roth suggested these alternative PAP devices may be better tolerated than CPAP (2009).

Patients diagnosed with OSA who fail or cannot tolerate PAP therapy can consider an oral appliance (OA) as an alternative treatment modality. The OA functions to pull the mandible and tongue position forward, thus maintaining upper airway patency. In many cases, the intolerable effects of PAP are a result of incorrect pressure settings, inadequate device fit, or inconvenience and the claustrophobic feeling of the mask on the face. While OA therapy is more effective in less severe forms of OSA, it can be advocated in the severe if PAP adherence is poor (Ramar et al., 2015). Low compliance to PAP therapy warrants referral from the sleep physician to a

dentist for fabrication of OA to help manage OSA symptoms.

For severe OSA cases or for patients who cannot tolerate PAP or OAs, surgical intervention may be a viable treatment option. The various surgical options aim to reduce upper airway collapse by increasing its size via tissue removal, permanent advancement of the tongue and/or mandible, or stabilizing the pharyngeal tissues with implants. Tonsillectomy and/or uvulopalatopharyngoplasty (UPPP) are popular procedures to remove excess tissue to facilitate a more patent airway. Unfortunately, positive results from these irreversible procedures have been inconsistent, ranging from 16% to 83% (Khan et al., 2009). A review by Sutherland et al reported a comparison study of OA treatment to UPPP surgery noting greater AHI reduction in the OA group after 12 months and at 4 year follow up (Sutherland et al., 2014).

With the growing challenge of PAP adherence, OA therapy has emerged as a viable first-line treatment (George, 2001; Hoekema et al., 2004; Hoffstein, 2007). The AASM has revised its guidelines to recommend OA use as a first-line therapy not only in patients with mild to moderate OSA or more severe OSA in patients who cannot tolerate PAP but also for patients who prefer OA therapy in the absence of previous treatment failure (Sutherland et al., 2014). In a 2013 crossover study of 108 OSA patients, the mandibular advancement device (MAD), which is a form of OA therapy, was not inferior to CPAP in the treatment of moderate to severe OSA because the OA adherence was better than that of CPAP (Phillips et al., 2013). Although CPAP continues to be superior to OA therapy in reducing AHI, arousal index, and ODI scores for OSA, evidence suggests that OA adherence is greater than that observed with CPAP (Ramar et al., 2015).

Titration refers to adjustment of a particular device or therapy and the subsequent evaluation of clinical parameters that assess treatment efficacy. During a PSG, PAP and MAD position can be titrated; some of the objective clinical parameters that can be assessed for optimum therapeutic effect during this titration include AHI (Epstein et al., 2009), oxygen saturation, and ODI (Dieltsjens et al., 2012). Symptoms as reported by the patient that may indicate treatment acceptance and/or efficacy include improved sleep quality, decreased or eliminated daytime sleepiness, or improved concentration at work. Various questionnaires are available to assess before and after treatment changes of various subjective measures.

Oral Appliance Therapy and the Mandibular Advancement Device

Oral appliances are available in both titratable and non-titratable designs. With titratable OAs, the mandible can be moved in an anterior or posterior direction. Non-titratable OAs protrude the mandible but are set in a fixed position (Lettieri et al., 2011). Another type of OA used in OSA management is a tongue retained device (TRD) that acts like a suction cup on the tongue and pulls it forward to help open the upper airway. The TRD is the best option in an individual who is edentulous or lacks the dental support for a more traditional appliance.

A MAD is custom fitted to the maxillary and mandibular dentition, worn at night, and can be incrementally titrated to move the mandible forward thus advancing the base of the tongue. Such forward repositioning increases pharyngeal airway space and reduces airway instability (Chan et al., 2007; Culpepper & Roth, 2009; Dieltjens et al., 2012). Kato et al. reported that the MAD-induced mandibular protrusion is also associated with AHI reduction (2000). While patient anatomy and tolerance/comfort are limiting factors of total protrusion, greater mandibular position does not always correspond with more favorable AHI reduction even if subjective findings like patient-reported improved sleep quality or reduced daytime sleepiness continue to improve (Dieltjens et al 2012). This may be due to the fact that the cross sectional area of the upper airway in OSA patients is suggested to be more elliptic than round in shape (Leiter, 1996, Ogawa et al., 2007). An over-advanced mandible during MAD titration may actually narrow this unique upper airway morphology making it less patent, thus increasing AHI.

Ideal treatment for OSA management with oral appliance is provided by a multidisciplinary team that includes a sleep physician and a dentist with training in the management of sleep disorders. The specific roles of physicians and dentists in the treatment of snoring and OSA with MADs have been defined by the AASM Task Force as well as the American Academy of Dental Sleep Medicine. Once the diagnosis of OSA is made by a sleep physician using subjective and objective assessments and if the patient is a candidate for OA therapy, the sleep physician will make a referral to a qualified dentist for further evaluation (Kushida et al., 2005). The referral to the dentist should include a copy of the PSG result, the Epworth Sleepiness Scale (ESS) score and pertinent medical information (Ferguson et al., 2006).

Upon referral, the dentist assesses the suitability of the patient's dentition for customized MAD treatment (Chan et al., 2007). It's suggested that patients have a minimum of six healthy, non-mobile teeth per arch and at least one posterior tooth per quadrant. They must also be able to protrude the mandible at least 6 millimeters (Ferguson et al., 2006; Campbell et al., 2009). Further assessment includes a complete dental/medical history and examination of extra- and intra-oral tissues. Soft tissue anatomy, periodontal status, dental caries, the temporomandibular joints (TMJ), muscles of mastication, and nocturnal bruxism are also evaluated. Major restorative dental needs must be completed prior to MAD fabrication to avoid OA fit issues.

A variety of MAD designs are commercially available for OSA treatment (Aherns et al., 2011). Clinicians are encouraged to select FDA approved MADs which can be found at the following website: http://www.ihatecpap.com/oral_appliance.html. MAD design has expanded from the non-adjustable mono-bloc device in which the maxillary and mandibular parts are rigidly fixed together to the current duo-bloc design which enables titration/adjustment of the mandibular protrusive position. If the patient is a suitable dental candidate for the MAD, it is fabricated in accordance with the manufacturer's instructions. The patient is given written and oral instructions on OA care, use, and how to titrate the MAD. A suggested titration starting point for the MAD is 50-75% of the patient's maximum mandibular protrusion; this starting position can be reduced if initially not

tolerated (Ferguson et al., 2006). The patient may be encouraged to acclimate to the initial protrusive setting (Doff et al., 2011) before active MAD advancement commences. A built-in advancement mechanism enables the patient to adjust the MAD before going to sleep each night. This allows a patient to gradually protrude or retrude the mandible based on symptoms until positive subjective OSA effect is achieved to include reduced snoring or daytime tiredness prior to a follow up sleep physician assessment which often includes a second PSG (Aarab et al., 2011).

Mild and transient side effects are common with the use of a MAD and generally decrease with continued use and/or appliance adjustment (Doff et al., 2011; Perez et al., 2012; Bailey, 2005; Ferguson et al., 1997). Adverse effects may include excessive or reduced salivation, odontogenic pain, gingival irritation, headache, masticatory myalgia, and TMJ noises or discomfort. These symptoms usually last several days to months, but may persist even if the MAD is discontinued (Sutherland et al., 2014). Transient signs and symptoms of temporomandibular disorder (TMD) may occur in patients who were pain-free before starting MAD treatment for OSA, however these symptoms usually decrease over time. In a 13 month study by Perez et al, MAD use did not significantly increase pre-existing TMD signs and symptoms in OSA patients (Perez et al., 2012).

Long term use of a MAD can cause occlusal changes (Almeida et al., 2006). One of the most prevalent long term side effects with MAD use is a dental posterior open bite (POB). An average incidence of POB occurred in 17.9 % of patients who used a MAD for 13 months. However, many patients were unaware of these dental changes and the majority concurred that the positive effects of their OSA symptoms when using the MAD outweighed any adverse effects related to dental changes (Perez et al., 2012). Another study reported that after an average of 11 years of MAD therapy, there was a noted decrease in overbite and overjet. These occlusal changes were progressive and the decrease in overbite and overjet continued for as long as the OA was used (Pliska et al., 2014). Morning jaw exercises to relax the muscles of mastication and help reduce the risk for potential occlusal changes may be offered to patients who use OAs. (Perez et al, 2012).

Titration of the MAD to achieve an optimal protrusive setting involves slowly advancing the mandible over time to a comfortable position that opens the airway and maximally reduces AHI. This technique reduces risk to develop TMD symptoms by allowing patients to slowly accommodate to a more forward mandibular position over several nights in the patient's home environment. A review of MAD titration protocols by Dieltjens et al summarized numerous studies in which MADs were titrated to optimal mandibular protrusion positions during a single night PSG study before the patient used the MAD at home. In most cases, the patients had to be woken to adjust the MAD (Dieltjens et al., 2012; Almeida et al., 2009; Kuna et al., 2006), yet some studies employed experimental motorized devices which allow sleep medicine lab technicians to remotely titrate the MAD and minimize patient waking (Dort et al., 2006; Tsai et al., 2004; Petelle et al., 2002). Attempting to negotiate optimal mandibular protrusion in a single night's PSG to maximize objective measures, may not allow adequate time for the muscles of mastication and or the TMJ to adapt/accommodate to an increased mandibular protruded position. Single night MAD titration during a PSG, may interfere with the patient's already compromised normal sleep cycle and can alter the ratio of the various sleep stages. Since the

severity of OSA may change during the sleep stages throughout the night, the results of MAD titration by a sleep medicine lab technician during a PSG can bias mandibular protrusion settings (Almeida et al., 2009). At present, MAD titration to decrease the AHI is considered an inconsistent trial and error process (Dieljtens et al., 2012).

Subjective and objective sleep measures to assess sleep quality can be used during home MAD titration. Subjective measures include daytime sleepiness, snoring, and mandibular comfort; these can be used to assess how or when to adjust the MAD. Objective measures may comprise the following: Portable Type 2 instruments, a type of OCST equipment, collect similar data to that of a PSG, but these devices are expensive. Portable Type 3 instruments are less expensive but are not simple to use. They typically have four channels of recorded data to assess pulse oximetry, air flow from which an AHI is derived, snoring by sound and head movement. The OCST equipment must meet AASM practice parameters and have been shown to be comparable in diagnostic ability to PSG (ICSD-3, 2014). A Type 4 pulse oximeter can be used to derive an ODI which could serve as a monitoring parameter for MAD titration at home (Chung et al., 2012).

Using objective or subjective measures during MAD titration does not always achieve optimal therapeutic endpoints (AHI reduction) (Levendowski et al., 2007; Fleury et al., 2004). Patients may subjectively over-titrate the MAD based on the assumption that more is better. Others may under-titrate the MAD based on perceived improvement in subjective sleepiness outcomes, regardless of the objectively measured ODI levels (Almeida et al., 2009; Fleury et al., 2004). Optimal mandibular titration for a MAD should be guided by a combination of both subjective symptom improvement and objective monitoring of overnight oximetry to achieve the most effective mandibular protrusion position that normalizes AHI (Sutherland et al., 2014).

Pulse Oximetry

A pulse oximeter (PO) uses a non-invasive probe and a microprocessor to continuously measure the saturation level of peripheral oxygen in the blood (SpO₂). The probe is typically worn on the finger, though a toe, ear lobe or the nose can be used. The microprocessor is worn on the wrist or may lay by the patient's side. The PO assesses the percentage of available hemoglobin saturated with oxygen. Although it is an indirect measurement of arterial oxygen saturation (SaO₂), SpO₂ closely correlates with actual oxygen saturation (Gries & Brooks, 1996). The probe has two light emitting diodes that emit red and infrared light (respective wavelengths of 660 nm and 940 nm) and photo detectors that receive the light as it passes through a pulsatile tissue bed. The microprocessor receives data from the photo detectors, detects the pulse of arterial flow, and analyzes the changes in light absorption in the tissue to yield SpO₂ (Clark et al., 2006; Valdez-Lowe et al., 2009). Blood highly saturated with oxygen allows more red light and less infrared light to be detected by the probe. As saturation decreases, less red light and a greater amount of infrared light passes through the blood. The photo detectors measure the amount of light at each wavelength transmitted through the blood and sends this data to the microprocessor. Awake, healthy individuals typically have SpO₂ in the range of 97- 99% when breathing room air (Schutz, 2001). Pulse oximeter readings with a SpO₂ of 95% or greater are

considered clinically acceptable (Clark et al., 2006). With increased age, oxygen saturation rate tends to decrease. An average SpO₂ below 90% indicates hypoxemia, a red flag for clinicians (Schutz, 2001).

Oxygen Desaturation Index (ODI)

ODI is the average number of oxygen desaturation events per hour that persist for greater than 10 seconds. One event is defined as a decrease in SpO₂ by 3-4% below the baseline level during the preceding 2 minutes (Chung et al., 2012). ODI obtained from a pulse oximeter has a strong positive correlation with the AHI obtained from a PSG (Chung et al., 2012). For most OSA patients, ODI diagnostic accuracy is not affected by its night-to-night variability (Fietze et al., 2004). In a study by Chung et al., ODI slightly underestimated AHI by 1.6 events per hour (plus or minus 10) over the range of 5 to 30 events per hour; this closely predicted the AHI at 5, 15 or 30 events per hour which characterize mild, moderate and severe OSA.

- An ODI > 5 was 87% accurate in predicting AHI > 5
- An ODI > 15 was 84% accurate in predicting AHI > 15
- An ODI > 30 was 93% accurate in predicting AHI > 30

The authors concluded that ODI from a high-resolution nocturnal oximeter is a sensitive and specific tool to detect undiagnosed SDB. Their findings reinforced conclusions from earlier studies (Tsai et al., 1999; Magalang et al., 2003; Vazquez et al., 2000) indicating that ODI derived from a finger mounted pulse oximeter has excellent correlation with AHI derived from PSG.

Type 3 or 4 PSG instrumentation, with the addition of a pulse oximeter, have high sampling frequency and resolution and require little training. They detect fluctuations in oxygen saturation caused by episodes of apnea and hypopnea that can be analyzed by commercially available computer programs (Chung et al., 2012). In portable multichannel sleep screening devices that lack electroencephalographic or thoracic muscle activity monitoring capability, pulse oximetry is considered the most important parameter for identifying SDB (Netzer et al., 2001). Even though pulse oximetry can be an effective preliminary screening instrument for SDB, it cannot be used to definitively diagnose OSA since oxygen desaturation cannot be discerned if it is due to OSA or some other cause (Nijima et al., 2007; Chung et al., 2012). Further, if a diagnosis of OSA using Type 1, 2 or 3 PSG instrumentation is confirmed by a sleep physician, an increased ODI derived from pulse oximetry data can be attributed to OSA (Collop et al., 2012).

Practice guidelines, published in 1992 by the American Association for Respiratory Care, recommend 2 uses for pulse oximetry:

1. As a warning signal for patients at risk for arterial desaturation.
2. For evaluating response to a therapeutic intervention or a diagnostic procedure.

This Walter Reed National Military Medical Center (WRNMMC) protocol will employ the second recommended use for pulse oximetry to monitor home MAD titration. Pulse Oximeters

provide a noninvasive, objective measurement of oxygen saturation levels. They are inexpensive, easy to use, and may enhance the clinical ability to determine what mandibular protrusion setting during MAD titration offers optimum oxygen saturation while minimizing jaw discomfort.

Despite convenience and cost, high resolution pulse oximetry has its limitations. Pulse oximetry only measures the oxygen saturation change and does not monitor nasal flow and respiratory effort so it is not able to distinguish OSA from central sleep apnea (Chung et al., 2012). It is also vulnerable to the effects of poor peripheral arterial blood flow because it relies on pulsatile blood flow for its measurements. Bodily movements, vasoconstriction, and hypotension can cause artifacts through an interruption of the pulse signal. Since pulse oximeters do not always detect movement, artifacts due to motion would overestimate the number of desaturations (Netzer et al., 2001).

This study is a first of its kind to assess correlations with AHI and subjective / objective measures during MAD home titration by tracking continuous pulse oximetry on a nightly basis. Pulse oximetry data may influence and guide MAD titration for optimum jaw protrusion and improved sleep quality. Maintaining good sleep quality plays a significant role in patient wellbeing and has a tremendous impact on military healthcare and mission readiness.

CHAPTER II: MATERIALS AND METHODS

This purpose of this pilot study was to evaluate if the nightly use of home pulse oximetry during MAD titration is feasible and acceptable to patients who have been diagnosed with moderate or severe OSA. It also explored the association of home pulse oximetry, objective data, and subjective recall of sleep quality, stress, MAD adherence, and pain levels with pre and post treatment AHI measures.

Prospective study subjects had to be diagnosed with moderate to severe OSA by a sleep provider at the WRNMMC Sleep Disorders Center and be able to meet the inclusion and exclusion criteria as determined by a qualified orofacial pain provider from the Naval Postgraduate Dental School (NPDS) Orofacial Pain Center (OPC).

Study participants had to be 18 years of age or older, available for 6 months and have greater than 5 healthy teeth per dental arch. Patients with previous treatment for OSA were excluded from participation. Other exclusion criteria included a mouth opening of less than 24 mm, symptoms of temporomandibular disorder (TMD) that would prevent MAD use, and active

dental disease (Table 1). Prospective participants not meeting specific criteria were treated for their OSA by the WRNMMC Sleep Disorders Center. Power analysis projected that a total of 20 participants would be needed for this study protocol.

Subjective measures in this study included daily diaries for stress, sleep quality and jaw pain utilizing a 0-10 visual analog scale. Additionally, the following inventories were used to assess patient-reported symptoms:

- Epworth Sleepiness Scale (ESS): this is a subjective measure of the participant's sleepiness level.
- Functional Outcome of Sleep Questionnaire (FOSQ): this determines if participants have difficulty performing activities due to being too sleepy or tired.
- The Perceived Stress Scale (PSS): this measures a participant's subjective appraisal of the stressfulness of situations within the past 30 days.
- The Pittsburgh Sleep Quality Index (PSQI): this assesses a participant's usual sleep habits during the past month.

Objective measures included night-to-night ODI captured by the VirtuOx pulse oximeter. The VirtuOx Pulse Oximeter Device, or VPOD, is FDA approved to track respiratory data. The wireless VPOD uploads oxygen saturation data to the secure internet cloud owned by Virtuox Inc. This technology allows real time monitoring of ODI during home MAD titration.

All participants wore a portable pulse oximeter to monitor ODI during home MAD titration. The ODI data automatically uploaded to a secure internet cloud every 5 minutes or when the device was powered off. Any data that did not transmit due to poor cellular reception was stored on the device hard drive for up to 72 hours. To protect personal information, all subjects were identified by a 7-digit "patient ID" provided by the secure cloud when preparing the subject's personal VirtuOx pulse oximeter; the patient ID and respective subject identifying information was stored in a locked cabinet within a locked office to which only the lead research clinician in the NPDS OPC had access.

The FDA approved MAD utilized in this study is the Thornton Adjustable Positioner (TAP)-3 Elite. This MAD can be titrated slowly to move the mandible forward. It incrementally increases upper airway opening with a 180 degree clockwise turn of the adjustment key which equates to 0.25 mm anterior mandibular advancement. Refer to Figure 1 for the description of the study protocol.

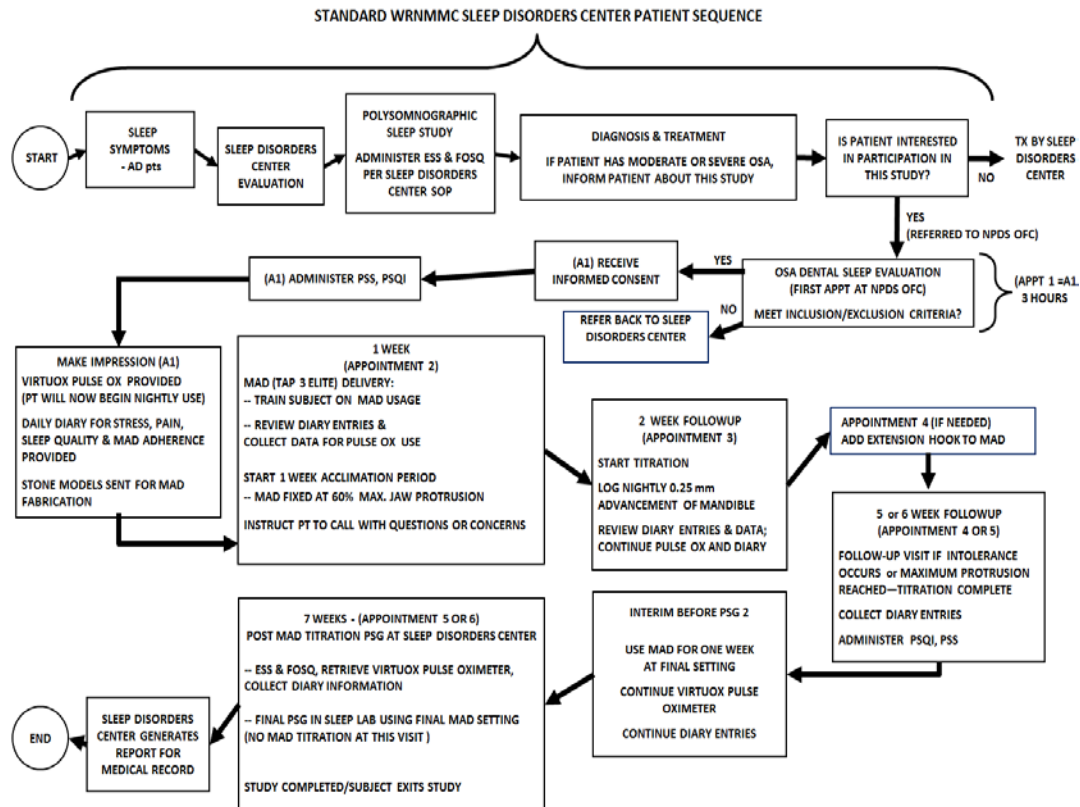


Figure 1: Study Participant Protocol. Eligible participants will be identified by a WRNMMC Sleep Disorders Center physician after receiving a diagnosis of moderate or severe OSA (Visit 3 at Sleep Disorders Center). If the participant is interested in the study, an appointment will be scheduled at the Naval Postgraduate Dental School (NPDS) Orofacial Pain Center (OPC) (Visit 4). If prospective subjects meet inclusion/exclusion criteria and agree to participate, written informed consent will be received. If the participant does not meet study criteria (Table 1 and 2 below) or chooses not to participate, follow-up at the WRNMMC Sleep Disorders Center will be arranged for standard OSA treatment options.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria

1. Diagnosed in WRNMMC Sleep Center with moderate or severe OSA (AHI < 45) and referred to Orofacial Pain Center
2. Age 18 or older
3. Non smoker
4. Available for 6 months
5. Agrees to participate by informed consent
6. ≥ 6 healthy teeth per dental arch
7. ≥ 1 posterior tooth per dental quadrant
8. Protrude the jaw ≥ 5 mm
9. Restorative dental treatment completed

Exclusion Criteria

1. AHI < 15
2. Under 18 years of age
3. Smoker
4. ≤ 6 healthy teeth per arch
5. A dental quadrant without posterior teeth
6. Restricted jaw opening ≤ 25 mm
7. TMD symptoms that prevent MAD use
8. Dental caries, periodontal disease, oral pathosis
9. Previous upper airway

- intervention for OSA: CPAP,
MAD, Surgery
- 10.** Periodic limb movement
 - 11.** Nighttime supplemental oxygen therapy
 - 12.** Cannot tolerate 50% mandibular advancement
 - 13.** Maximum mandibular protrusion ≥ 14 mm

Table 2: Reason for the “NO” path in the block diagram

- 1. Sleep disorders other than OSA (central or mixed sleep apnea)**
- 2. Candidates must have an AHI ≥ 15 but < 45 .**
- 3. Candidates who cannot adhere with the protocol are returned to the WRNMMC Sleep Disorders Center for conventional treatment.**
- 4. Candidates must meet the inclusion / exclusion criteria of the study. Those failing to qualify, who drop out of the study or for whom the MAD was not effective are referred to the appropriate clinic for conventional treatment:**
 - WRNMMC Readiness Dental Clinic for dental issues not quickly correctable
 - Orofacial Pain Center for temporomandibular disorder issues
 - WRNMMC Sleep Disorders Center for those who are edentulous, at high risk for dental caries, restricted mouth opening, previously treated for sleep apnea

The following section summarizes step-by-step appointments required for each prospective subject prior to and following informed consent.

- Visit 1 at the Sleep Disorders Center (standard care for all patients): Active duty patients referred with sleep disturbance are evaluated by a sleep medicine physician. If a PSG is recommended, then the patient continues to visit 2.
- Visit 2 at the Sleep Disorders Center (standard care for all patients): The patient completes the ESS and FOSQ and receives an in-lab PSG.
- Visit 3 at the Sleep Disorders Center (standard care for all patients): The sleep medicine physician offers, when appropriate, the patient PAP vs. OA therapy if positive for OSA. They inform all patients that if the first treatment chosen is not effective, the other treatment option is provided. All patients are counseled on their choices regarding PAP and OA therapy for OSA. After this counseling, if the diagnosis of moderate or severe OSA is made, then the patient is informed about the study and invited to participate.
 - If the patient is interested in this study, they are referred to the OPC located at the NPDS, Navy Medicine Professional Development Center (NMPDC).

- If the patient declines study participation, they are provided other treatment options by the WRNMMC Sleep Disorders Center.
- Visit 4 at the OPC (standard care for all patients): This will be the first appointment for the potential study participant at the NPDS OPC. They will be evaluated for MAD use. If they are candidates for a MAD and meet study inclusion/exclusion criteria they will be provided further study detail and written informed consent will be reviewed and received.
 - If they do not meet study criteria or are not interested in participation, they will be referred back to the WRNMMC Sleep Disorders Center for standard care.
 - If consent is signed, the following will be received.
 - The study participant will complete the PSS and the PSQI.
 - OPC providers will make maxillary and mandibular alginate impressions. Stone dental models will be made from the molds and sent to the NPDS Maxillofacial Prosthodontic Lab for MAD fabrication.
 - The VirtuOx pulse oximeter will be provided to the participant with instructions on nightly device use.
 - Daily diaries will be reviewed and provided regarding stress, pain, sleep quality and MAD adherence measures.
- Visit 5 at the OPC: 1 week after visit 4, the participant will return to the OPC for the following:
 - MAD delivery and instruction of how to use the TAP-3 Elite.
 - Review and collect the participant's diary entries for stress, pain, sleep quality and MAD adherence levels.
 - Begin the one week MAD acclimation period at the fixed position of 60% of the participant's maximum jaw protrusion.
 - Inform the participant to call the OPC if any questions or concerns arise.
- Visit 6 at the OPC: 1 week after visit 5.
 - Review mechanics of the TAP-3 Elite and begin nightly MAD titration (0.25 mm mandibular advancement each night).
 - Review and collect daily diary entries; continue pulse oximeter use and recording daily diary entries.
- Visit 7 at the OPC:
 - This appointment is only needed if an extension hook is necessary to be added to the MAD to continue mandibular advancement.
- Visit 7 or 8 at the OPC:
 - This will be a follow-up visit if MAD intolerance occurs.
 - If maximum protrusion is achieved, then MAD titration is complete.
 - Administer the PSQI and PSS.
 - Between this visit and the next, the subject will continue to use the MAD at the final mandibular protrusion setting with the VirtuOx pulse oximeter and continue to make daily dairy entries.

- Visit 8 or 9 at the WRNMMC Sleep Disorders Center: One week after the previous visit, the participant will return to the Sleep Disorders Center for the following:
 - Second PSG using the final MAD setting (no additional titration made).
 - Complete ESS & FOSQ
 - Retrieve the VirtuOx pulse oximeter (figure 2) and collect diaries.

After the second and final PSG, the subject participation in the study is complete and they will continue follow up care by WRNMMC Sleep Disorders Center regarding their OSA condition (standard of care).



Fig 2. VirtuOx pulse oximeter and components retrieved by sleep lab after second PSG.

The analysis of the data will be exploratory. AHI will be used to assess the efficacy of the MAD home titration protocol by evaluating pre and post PSG AHI. PSG AHI data will also be utilized to measure the accuracy of pulse oximetry measurements. The association between MAD titration and home pulse oximetry data will be analyzed using a mixed model with subject level random effect. Covariates may include subjective sleep quality, stress, MAD adherence and pain levels as these may influence sleep quality and pulse oximetry.

CHAPTER III: RESULTS

Preliminary results suggest that use of a pulse oximetry device to track nightly oxygenation is feasible and acceptable to OSA patients while titrating a MAD. With any human study, there will be individual protocol compliance issues, but overall the practice is tolerable. Furthermore, all subjects for which oxygenation data was collected, whether the entire protocol was finished or not, showed significant decrease in ODI (figures 3-4). Finally, for the subjects with a follow up, post titration PSG, 75% of subjects showed a reduced AHI; and 100% showed increased sleep efficiency. Both these parameters suggest that improvements in ODI, as detected by pulse

oximetry, correlate to objective data collected during PSG (figures 5-6). Due to the significant amount of objective and subjective data collected for each subject on a nightly basis, further analysis is required and will continue in the future months.

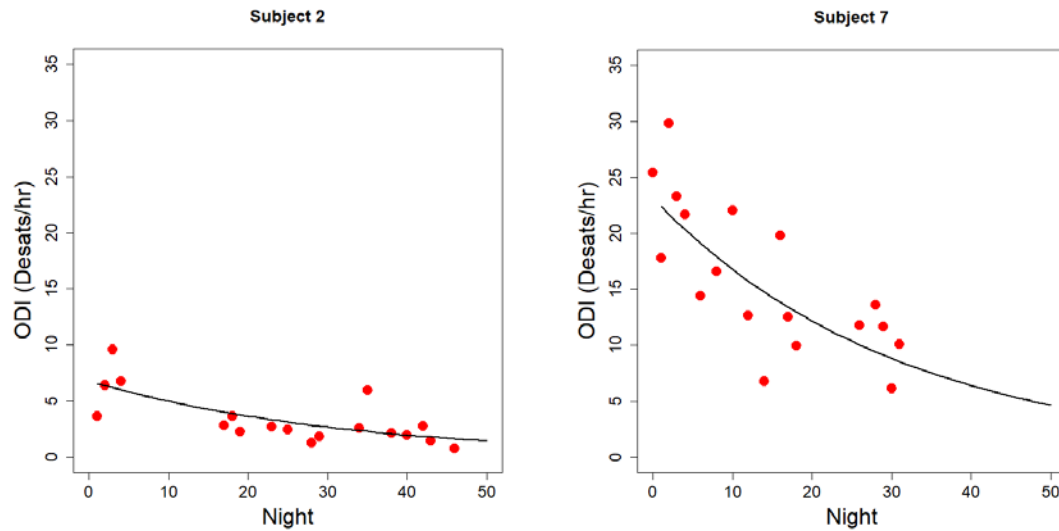


Fig 3. This scatter plot data from 2 individual subjects depict a model fit line of the ODI trends for all subjects. The Y axis shows ODI as calculated by the VirtuOx ODI algorithm per night that the pulse oximeter was worn. The X axis depicts the number of nights beginning with delivery of the MAD.

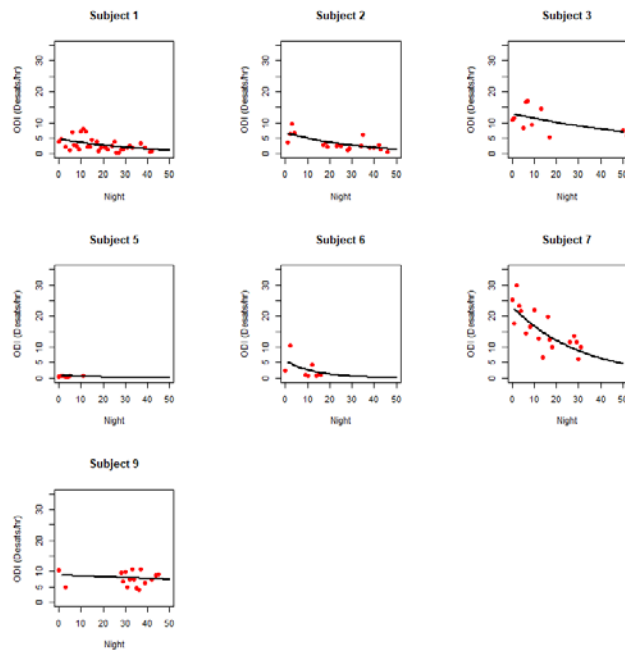


Fig 4. Scatter plot with model fit from 7 of 9 subjects depicts individual variability with overall decreased ODI trends. 2 subjects missing data due to technology malfunction.

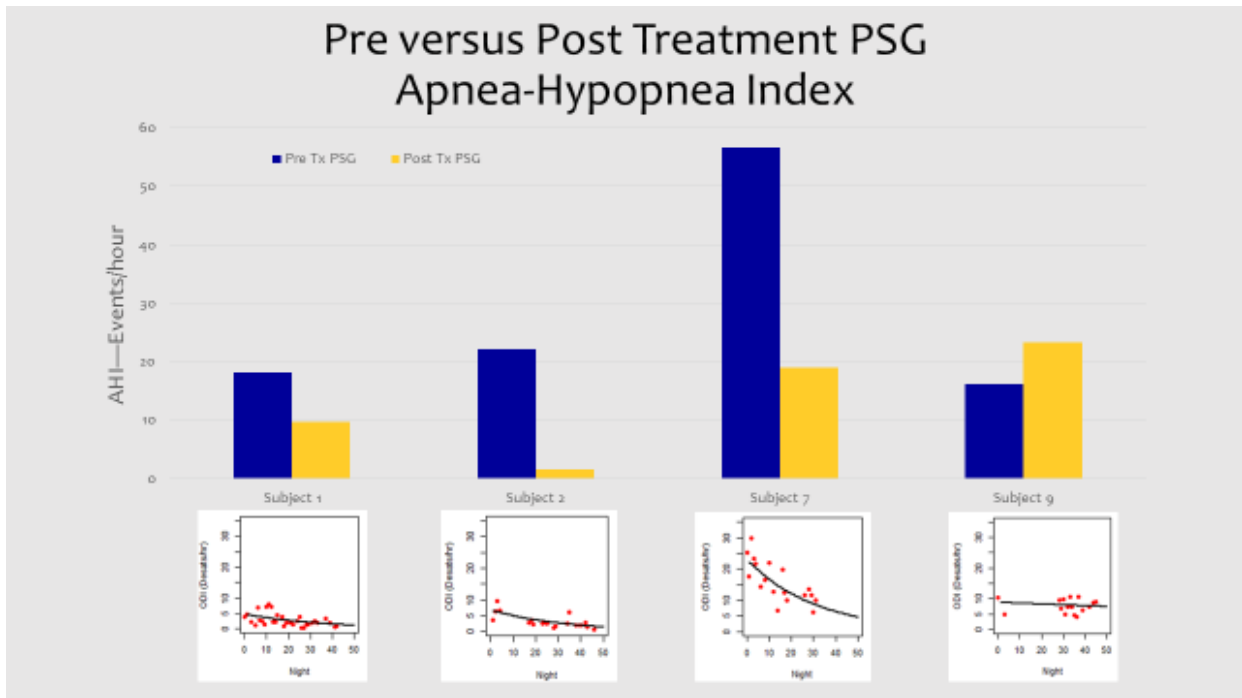


Fig 5. AHI trends for all subjects that completed the entire protocol to include post titration PSG. The increased AHI in subject 9 could be explained by diagnosis of other sleep disorders.

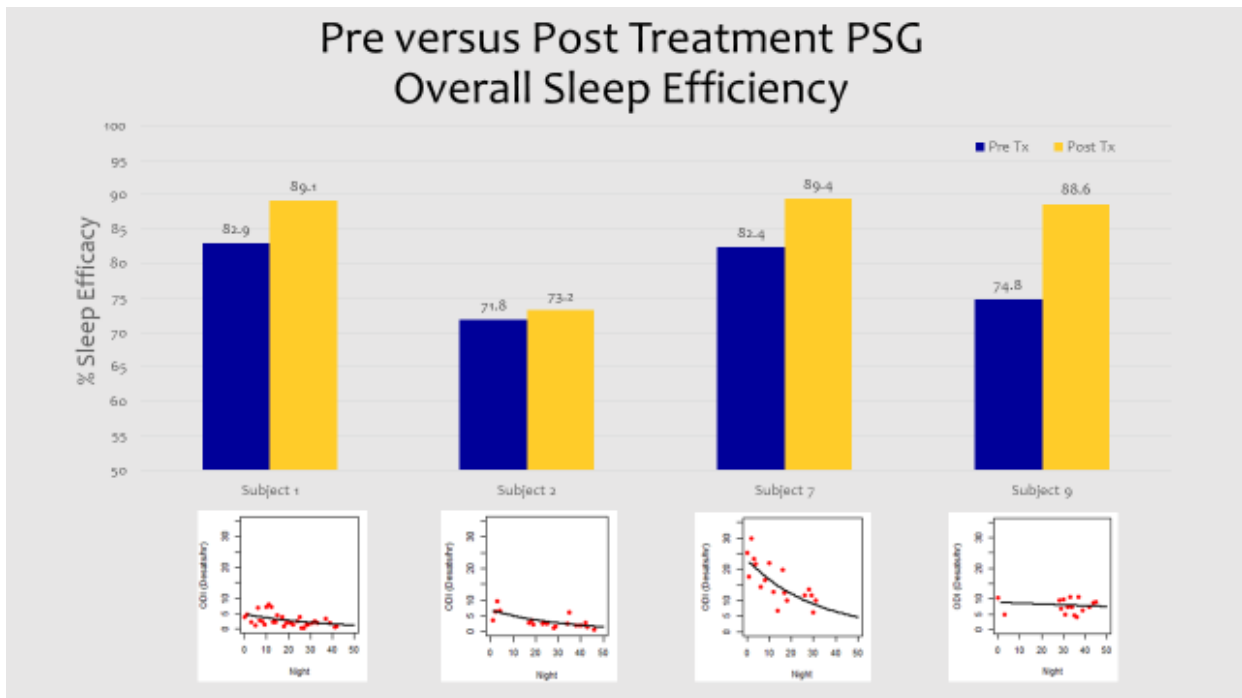


Fig 6. Overall sleep efficiency improvement for all subjects that completed the entire protocol to include post titration PSG.

With further data analysis, the following are anticipated results:

- Findings may establish an objective and subjective data set providing a foundation for future research which could be used to more accurately guide MAD titration for OSA patients.

- Study results may influence future standards of care for home MAD titration protocols for OSA patients ideally by reducing or eliminating the need for a post-MAD titration PSG. Factors dictating improved titration protocols could maximize MAD adherence, influence AHI reduction, and minimize treatment side effects, especially pain of the masticatory muscles or temporomandibular joints, related to oral appliance therapy.

CHAPTER IV: DISCUSSION

Preliminary results suggest that use of a pulse oximetry device to track nightly oxygenation is feasible and acceptable to OSA patients while titrating a MAD. All subjects for which oxygenation data was collected showed significant decrease in ODI. For the subjects with a follow up, post titration PSG, 75% showed reduced AHI and 100% showed increased sleep efficiency both of which suggest that improvements in ODI as detected by pulse oximetry correlate to objective data collected during PSG. Despite these findings, further data analysis is required. The partial data to include oxygen desaturation collected from the VirtuOx pulse oximeter, initial objective PSG findings, subjective assessments, and all collected VAS logs will be utilized as possible to determine overall trends in treatment.

At the post titration PSG, the sleep medicine laboratory technician was instructed not to adjust the MAD. With further data analysis, pre and post MAD titration ODI will be correlated to the mandibular protrusive settings, with ESS, FOSQ, PSQI, PSS, visual analogue scale for stress, discomfort and sleep quality as well as the diagnostic and post titration PSG AHIs. Preliminary results showed trends for decreased ODI as seen in Figures 3 and 4. Despite variability of individual ODI over time, improvements can be appreciated in both AHI and sleep efficiency as seen in figures 5 and 6. Both AHI and sleep efficiency are objective data points collected during a PSG. The one subject that did not show reduced AHI did, in fact, have reduced ODI and improved sleep efficiency. The unexpected AHI increase for this subject could be explained by concurrent diagnosis of both periodic limb movement and positional OSA. While our results suggest improved objective PSG data indicated by reduced ODI collected by pulse oximetry at home during treatment, further research is needed to determine how the nightly changes to ODI translate to treatment effectiveness which is currently determined with a costly post-titration PSG. Analysis of the subjective data along with night-by-night changes in oxygenation may help identify if ODI can accurately predict when optimal MAD titration has been objectively achieved. Currently, AHI is the gold standard parameter used to classify OSA severity and MAD treatment efficacy so future research questions could include 1) what degree of improvement needs to occur in nightly ODI to predict a sufficiently reduced AHI or 2) is there a particular percentage of ODI improvement that correlates to AHI reflecting optimal MAD titration and overall treatment efficacy?

This research investigation was approved by the institutional review board (IRB) in March 2017 with continuing review approved as of March 2018. This was a feasibility pilot study for 20 participants. Initial subject enrollment started in May 2017. To date, 9 of 20 subjects have been enrolled, participated in preliminary data collection, and received a custom-fit MAD. Five subjects have completed the entire protocol and 4 have undergone the required post-titration PSG. Three subjects withdrew from study participation due to difficulty wearing the MAD. All 3 subjects denied dental or jaw pain secondary to the oral appliance but reported pretreatment difficulty with nasal breathing which contributed to feelings of claustrophobia secondary to intraoral bulk when wearing the appliance. One subject was discontinued due to failed follow up appointments as required by the study protocol. Average length of treatment was 7.5 weeks (range 5-10 weeks); most often dictated by subject availability for clinical appointments. As with any human study, limitations existed with subject compliance. As mentioned, only 1 subject failed multiple follow up appointments, but several others reported forgetfulness with recording daily VAS or completing the titration log to track nightly MAD adjustment. One subject misunderstood instruction and did not wear the pulse oximeter until MAD delivery which prevented capture of baseline oxygenation.

Active duty participants with moderate and severe OSA incrementally and maximally advanced the mandible to a protrusive setting that did not cause discomfort and improved sleep quality based on subjective measures. One limitation of this study was development of intolerable jaw pain upon waking in the morning. Only 1 of 9 subjects reached maximum protrusion while all other subjects terminated titration due to development of discomfort at which time they were advised to step titration back to the furthest setting before symptom onset which relieved discomfort.

A pulse oximeter provides an easy, non-invasive capture of quantifiable oxygenation data that can be utilized in combination with subjective information to more accurately improve home MAD titration for OSA. This pilot study has attempted to fill the gap in knowledge due to lack of an objective and subjective data set that shows how a home mandibular titration protocol could optimize clinical outcomes achieved by MADs. VirtuOx device reliability created limitations in this particular protocol in the form of missing nights of oxygenation data secondary to device malfunction and data transmission issues. Newer device models with improved cellular connectivity would likely reduce or eliminate such issues. There were also problems with specific devices disconnecting from the pre set patient ID forcing subjects to make extra trips to the OPC for replacement units. It is unclear at this time how these missing nights of data will impact correlations yet to be made between reduced ODI and improved AHI. Finally, inaccuracy was discovered with the ODI algorithm that had to be corrected prior to patient enrollment in order to ensure that collected oxygenation data could be analyzed appropriately.

No previous study has tracked real time, nightly pulse oximetry and explored associations with AHI, subjective measures of sleep quality, stress and jaw protrusion during MAD treatment. To date, there is no objective data set to evaluate for the feasibility and adequate oxygenation during home MAD titration prior to the patient's follow up sleep medicine center study. Because of this, sleep laboratory technicians often adjust the MAD during the follow up sleep study if oxygenation levels have not been optimally reached with subjective measures while titrating the MAD at home. This onsite MAD adjustment not only causes sleep fragmentation when waking the patient during the sleep study, but potentially advances the mandible too quickly, leading to future MAD tolerability and/or adherence issues secondary to jaw pain.

A low respiratory ArTH is a physiologic trait involved in OSA pathogenesis. A significant predictor of low respiratory ArTH includes a decrease in oxygen saturation (Edwards et al., 2014). This may help characterize why healthy, non-obese and/or non-cardiac compromised patients, which comprise the majority of military personnel, may receive OSA as a diagnosis. No study has assessed the subjective recall of stress as a possible variable that may affect night to night variation of oxygenation levels during MAD home titration.

CHAPTER V: CONCLUSION

Conclusions from this preliminary data analysis include the following:

- 1) Using pulse oximetry device to track nightly oxygenation is feasible and acceptable to OSA patients during MAD titration
- 2) Trends in decreased ODI as detected with at home pulse oximetry positively correlate to improved objective PSG measurements to include AHI, the current gold standard parameter in diagnosis of OSA.
- 3) Further analysis of the objective oxygenation and PSG data along with the subjective symptom assessments and daily VAS for stress, discomfort, and sleep quality is needed to better understand if ODI can accurately predict when optimal MAD titration has been objectively achieved.

Directions for this research and future projects include better understanding of how the nightly changes in ODI translate to treatment effectiveness as indicated by objective PSG data and/or the percentage of individual nightly ODI improvement that correlates to a reduced AHI reflecting sufficient MAD titration. If objective pulse oximetry data collected at home during MAD titration can be used to guide oral appliance treatment protocols for OSA, there could be significant healthcare savings regarding costly post-treatment PSG and resource utilization. For military service members, reducing risk for OSA-related long term health consequences and

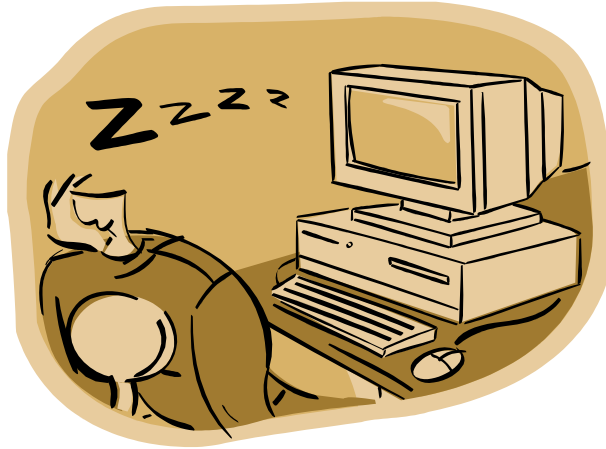
maintaining good sleep quality plays a significant role in patient well-being and has a tremendous impact on military healthcare and mission readiness.

Due to the length of this project and retirement of key committee members,
patient recruitment will end with subject 9.

APPENDIX A

DENTAL SLEEP MEDICINE EXAM FORM

Orofacial Pain Center
Naval Postgraduate Dental School
8955 Wood Road
Bethesda, MD 20889
(301) 295-1495
FAX (301) 295-2070



Dental Sleep Medicine Exam Form (MAY 2016)

Please complete pages 1 through 8 & circle choices whenever available.

Name _____ Date _____

Sponsor SSN _____ DOB _____

Gender: M _____ F _____

Active Duty / Retired / Family member _____ Age _____

Ethnicity _____

Branch of Service _____ Rank / Rate _____

Phone (H) (____) _____ (W) (____) _____

(Cell) (____) _____

Address _____

City _____ State _____ Zip _____

Email _____

Are you enrolled in? TRICARE Prime TRICARE Extra TRICARE Standard Medicare

Do you have other Insurance? Y N Insurance Company _____

Who referred you for this evaluation? _____

Name _____

BP ____/____

Pulse _____

O₂ Sat _____%

Height _____

SLEEP HISTORY:

Why are you here? Describe your sleep problem(s):

When did your problem(s) start? _____

Who have you seen for this problem? _____

What position do you fall asleep? Back Side Stomach

Do you have a consistent sleep schedule? Y N Are you a shift worker? Y N

How many hours do you sleep? Average night ____ Good night ____ Bad night ____

How long does it take to fall asleep? Average night ____ Good night ____ Bad night ____

Do you have difficulty falling asleep? Y N _____

Do you have difficulty staying asleep? Y N _____

* What may interrupt your sleep? _____

Do you snore? Y N _____

Do you hold your breath or gasp for air while sleeping? Y N _____

Is your sleep? sound light restless _____

Do you have nightmares? Y N How often & are they recurrent? _____

Is your sleep restorative/restful? Y N _____

Have you had a sleep study in the past 12 months? Y N _____

To be completed by staff

Date of PSG:

AHI:

O₂ Sat:

Sleep latency:

Other:

RDI:

Sleep Efficiency (%)

Time in stage N3:

How have you managed your sleep issues in the past? _____

Have you used an air mask to manage your sleep apnea before? Y N N/A

* What was your experience with this/side effects?

Have you used an oral appliance to manage your sleep apnea before? Y N N/A

* What was your experience with this/side effects? _____

Do you use any of the following sleep aids? (Circle all that apply)

Ambien Sonata Lunesta Trazodone Belsomra Benadryl Tylenol PM Melatonin

Alcohol Other _____

* What is the dose? _____ How soon before bed do you take this? _____

* How many days per week do you use this? _____

* How long have you been using this? _____

* How well does this work? Good Fair Poor

What sleep issue(s) has any provider diagnosed you with? (Circle all that apply)

Sleep apnea Insomnia Snoring Restless legs syndrome Tooth grinding

Narcolepsy Sleepwalking Sleep talking Sleep eating Night terrors

Other: _____

Other sleep information: (Circle all that apply)

With the lights out, is your bedroom... Too bright Too dark Just right

The temperature of your bedroom is... Too warm Too cold Just right

The environment around your bedroom is... Too noisy Too quiet Just right

How sleepy are you?

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = no chance of dozing

1 = slight chance of dozing

2 = moderate chance of dozing

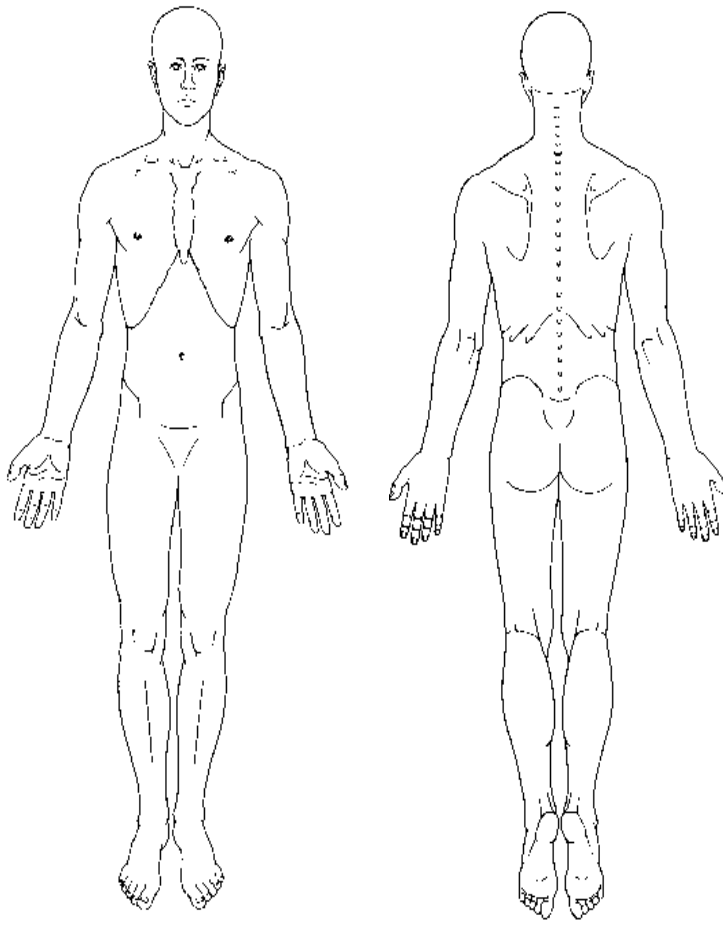
3 = high chance of dozing

SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

TOTAL SCORE _____

PAIN HISTORY:

Draw the location(s) of **ANY & ALL** pain area that you experience.



**List your pain problems.
Prioritize (worst pain first)**

1. _____
2. _____
3. _____
4. _____
5. _____

Which pain occurred first?

**Does movement initiate or aggravate
your pain? Y N**

Circle which word(s) characterize your pain(s)?

Sharp Burning Electric-like Aching Throbbing Dull Pulsing Pressing
Stabbing

What is the level of your overall body pain/tension? (Mark the levels on the lines
below

No discomfort

Worst pain imaginable

Today 0 _____ 10

At its Worst 0 _____ 10

On Average 0 _____ 10

Pain on Best day 0 _____ 10

Any pain free days? Y N How many pain free days per month? _____

* When were you last completely pain free? _____

Please rate your overall levels of:

	None	Worst possible
Stress	0	10
Anxiety	0	10
Depression	0	10
Anger	0	10

Have you ever thought of harming yourself? Y N _____

Estimate in hours, for any reason, how long your teeth are together or touching in a 24 hour period? _____ hours

Circle the feeling(s) that let you know when your teeth are touching?

pain tightness fatigue motion touch

Do you clench or grind your teeth? Y N Don't know

* If yes, how do you know?

self-aware told by dentist told by others

Do you have any of the following habits? Y N

* Circle all habits that apply.

bite nails	bite the inner aspect of the cheeks
chew gum	hold phone between the head & shoulder
protrude the tongue forward	hold the tongue to the roof of the mouth
move the jaw forward or side to side	bite the lower or upper lip

Describe any other habit(s): _____

MEDICAL & DENTAL HISTORY:

Medical Conditions:

Allergies: _____

Current prescription medications: _____

Herbal/dietary supplements: _____

Current non-prescription medications: _____

When was your last dental check up? _____

Do you have any dental care required that has not yet been completed? Y N

* If yes, please explain _____

Do you have a history of headaches? Y N

* Location of headache (s): _____

* Do you wake up with headache(s)? Y N

Do you experience any of the following?

Jaw pain/stiffness? Y N

* Is this worse in the morning mid day evening varies

Tooth pain? Y N _____

A changed or different bite? Y N _____

* If yes, location and how is it changed? _____

Altered jaw movement(s)? Y N _____

Jaw (joint) sounds? Y N _____

* When were you first aware of the jaw sound(s)? _____

* Have there been any changes to the jaw sound(s)? _____

* Does the jaw sound/pain affect your ability to eat? Y N _____

Ear symptoms? Y N pain ringing fullness muffled hearing

What is your consumption of the following?

Nicotine: Y N cigarettes ____/day cigars ____ pipe ____ snuff ____

Alcohol: Y N beer ____/day wine ____ glasses/day liquor ____ drinks/day

Caffeine: Y N cups(cans)day ____ coffee tea soda chocolate

Is your diet? balanced high sugar high carbohydrate high fat

Do you skip any meals? Y N Which? Breakfast Lunch Dinner

* Any recent weight gain/loss? _____

Personal/Family History

Occupation: _____

Do you have a history of the following or other similar threatening, stressful or frightening life events?
Abuse, at any age (physical, emotional or sexual), childhood neglect, physical or sexual assault, near
drowning, panic attacks, post-traumatic stress disorder, deployment to a conflict zone, a significant
motor vehicle accident? Y N

Other: _____

Exercise level: None Slight Moderate Active

* Activity limitations: _____

Thank you.

EXAMINATION

CN SCREENING EXAM:

(I-XII): WNL Finding(s): _____
Not assessed

CERVICAL EXAM:

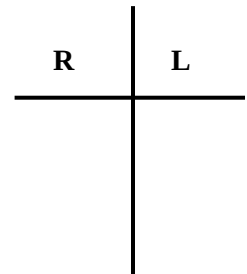
Head/ Neck Position _____ WNL Forward head/body _____
Head tilt _____ R _____ L Head turned _____ R _____ L
Rounded shoulders _____
Neck circumference: _____ inches
Cervical ROM with or without pain: _____

MANDIBULAR RANGE OF MOTION:

Incisal opening: without increasing pain _____ mm	Pain level _____
maximum unassisted _____ mm	Pain level _____
maximum assisted _____ mm	Pain level _____
Location of pain _____	

Is there pain on?

Right Lateral Movement _____ No _____ Yes _____ R _____ L _____ mm
Left Lateral Movement _____ No _____ Yes _____ R _____ L _____ mm
Protrusive Movement _____ No _____ Yes _____ R _____ L _____ mm
Deflection / Deviation _____ No _____ Yes _____ R _____ L _____ mm
End Feel (with restriction) Hard _____ Soft _____
Overbite: _____ mm Overjet: _____ mm



TMJ SOUNDS:

Crepitus: None Right Left Mild Moderate Severe

Click/pop: None Right Opening Reciprocal Intermittent Painful
 None Left Opening Reciprocal Intermittent Painful

Is sound eliminated with protrusion? _____ No _____ Yes

CLENCHING TEST:

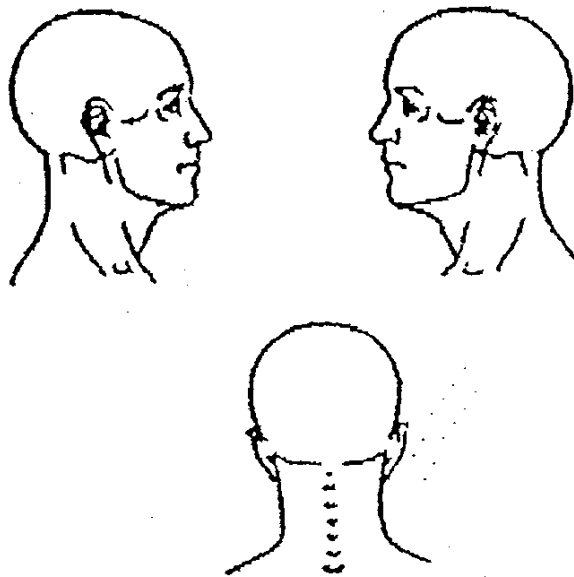
Is there pain when clenching on posterior teeth? _____ No _____ Yes R L
 Clenching on tongue blades is?

Bilateral:	Better	Same	Worse	R	or	L
Right:	Better	Same	Worse	R	or	L
Left:	Better	Same	Worse	R	or	L

PALPATION:

Codes: 0 = Non Painful, 1 = Tenderness, 2 = Painful, 3 = Pain with withdrawal
 T = Trigger Point (draw arrow to depict pattern of referral, if present)
 A = allodynia, H = hyperalgesia ↑ = hypertrophy ↓ = atrophy

	Right	Left
Rhomboids	_____	_____
Lev Scap	_____	_____
Trapezius	_____	_____
SCM	_____	_____
Splenius	_____	_____
Occipital	_____	_____
Paracervical	_____	_____
C Spine	_____	_____
Masseter	_____	_____
Temporalis	_____	_____
Frontalis	_____	_____
TMJ (static)	_____	_____
TMJ (dynamic)	_____	_____
TMJ (EAC)	_____	_____
Lat Ptery	_____	_____
Joint Loading	_____	_____
Temp Tend	_____	_____
Med Ptery	_____	_____
Digastric	_____	_____



ORAL EXAM:

Acute malocclusions? _____ No _____ Yes Location/when? _____

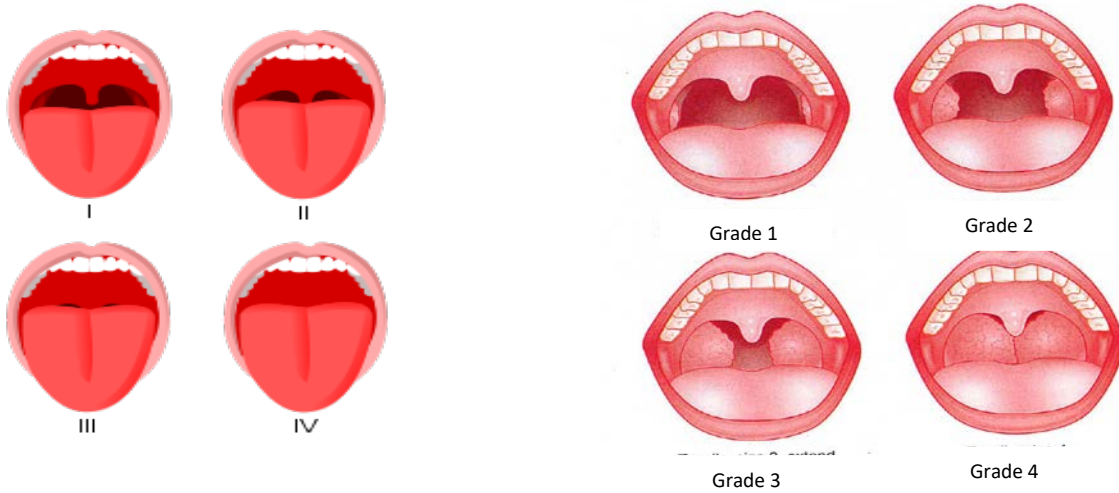
Soft Tissue _____ WNL: _____

Periodontal Health: _____ WNL: _____

Tooth sensitivity/percussion: _____

General description of the dentition: _____

Tooth Wear: Physiologic _____ Moderate _____ Severe _____



Mallampati Classification: _____

Tonsil size grading: _____

Is the occlusion stable? No Yes _____

Class I _____ Class II _____ Div 1 2 Class III _____

Open Bite? No Yes _____

Guidance/interferences? No Yes _____

Splint History: No Yes _____

Mandibular posturing/tongue thrusting? No Yes _____

Dental criteria for MAD? No Yes

- At least 6 teeth per arch
- One posterior tooth per quadrant
- Able to protrude at least 5 or more mm

IMAGING:

Radiographs/ Imaging: _____ Not Indicated

_____	Panoramic	_____
_____	TMJ Series	_____
_____	Intraoral	_____
_____	CT Scan	_____
_____	MRI	_____
_____	Other	_____

MANAGEMENT PLAN:

_____ Sleep hygiene

_____ Sleep diary

_____ Nutritional counseling/weight mgmt

_____ MAD (mandibular advancement device) therapy

_____ Appliance of choice: _____

_____ Sleep Medicine referral

_____ Rx Hypnotic

_____ Other: _____

Procedure	CPT Code	Cost	
New pt, expanded (20)	99202	\$184	
New pt, moderate complexity (45)	99204	\$400	
New pt, high complexity (60)	99205	\$501	
Established pt, expanded (15)	99213	\$179	
Established pt, detailed (25)	99214	\$265	
Established pt, comprehensive (40)	99215	\$355	
Observation/inpt hospital care (25)	99232	\$176	
Observation/inpt hospital care (45)	99234	\$323	
Prolonged service w/o contact	99358	\$258	
Prolonged service w/o contact (ADD)	99359	\$124	
Injection, tendon sheath ligament	20550	\$138	
Trigger point injection (1 or 2)	20552	\$130	
Trigger point injection (3 or 4)	20553	\$152	
Muscle testing, extremity or trunk	95831	\$65	
Range of motion measurements	95851	\$43	
Biofeedback training	90901	\$97	
Application of hot or cold packs	97010	\$14	
Application of electric stimulation	97032	\$39	
Ultrasound one or more areas	97035	\$31	
Manual therapy, myofascial release	97140	\$73	
Prevent. med ind. counseling (15)	99401	\$87	
Exercises, develop range of motion	97110	\$78	
Neuromuscular reeducation	97112	\$81	
Acupuncture, w/o stim, 15 min	97810	\$86	
Acupuncture, w/o stim, (ADD 15 min)	97811	\$65	
Acupuncture w stim, 15 min	97813	\$93	

Procedure	Code	Cost	
Detailed, extensive evaluation	D0160	\$95	
Pall (Emerg) tx: dental pain	D9110	\$87	
Local anes injection (GON)	64405	\$234	
Local anesth not conj w opr/surg	D9210	\$33	
Regional block anesthesia	D9211	\$36	
Trigeminal div block anesthesia	D9212	\$58	
Therapeutic drug injection	D9610	\$47	
Pulp vitality tests	D0460	\$47	
Behavior management (1/15min)	D9920	\$85	
Nutrition counseling	D1310	\$39	
Tobacco counseling	D1320	\$43	
Individual OHI	D1330	\$41	
Other drugs/ meds	D9630	\$26	
Occlusal orthotic device	D7880	\$592	
Sleep apnea device	A7881	\$1,197	
Athletic mouth guard	D9941	\$144	
Repair/ reline occlusal guard	D9942	\$127	
Occlusal adjustment, limited	D9951	\$85	
Diagnostic casts	D0470	\$80	
Oral/ facial photography	D0350	\$47	
Patient seating	A9999	\$0	
Botox injection (per 10 units)	A9875	\$91	
Imaging			
Panoramic image	D0330	\$99	
Intraoral, first image	D0220	\$25	

Acupuncture, w stim (ADD 15 min)	97814	\$74		Intraoral, each additional image	D0230	\$21	
Disability eval by treating doctor	99455	\$263		Occlusal Image	D0240	\$38	

Patient Name: _____

Last 4 SSN: _____

Provider: _____

Status: _____

Date: _____

Jan 2016

Wounded warrior: Yes No

Co-morbidities:

Combat TBI PTSD IBS GERD Anxiety

Abuse/Assault IC FM CFS OSA Panic Depression

Diagnosis: (Number 1 – 5 as applicable, where 1 is the primary diagnosis)

Atypical facial pain
Burning mouth syndrome
Trigeminal nerve disorder
Disorders of other cranial nerves

Cluster headache
Hemicrania
Chronic daily headache
Migraine with aura
Migraine without aura
Tension type headache

Myalgia (masticatory, cervical)
Cervical MFP
Masticatory MFP
Non-neutral head and neck posture
Protective co-contraction

TMJ arthralgia
Disc displacement with reduction
Disc displacement without reduction
Osteoarthritis
Subluxation

Sleep apnea
Sleep disturbance
Sleep disorder
Insomnia

Bruxism
Fibromyalgia
Otagia (specify)
Reaction to chronic stress

APPENDIX B

EPWORTH SLEEPINESS SCALE

How sleepy are you? How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = no chance of dozing

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting inactive in a public place (e.g a theater or a meeting)	_____

As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____

TOTAL SCORE _____

APPENDIX C

SCORING INSTRUCTIONS FOR EPWORTH SLEEPINESS SCALE

The Epworth Sleepiness Scale

The Epworth Sleepiness Scale is widely used in the field of sleep medicine as a subjective measure of a patient's sleepiness. The test is a list of eight situations in which you rate your tendency to become sleepy on a scale of 0, no chance of dozing, to 3, high chance of dozing

When you finish the test, add up the values of your responses. Your total score is based on a scale of 0 to 24. The scale estimates whether you are experiencing excessive sleepiness that possibly requires medical attention.

How Sleepy Are You?

How likely are you to doze off or fall asleep in the following situations? You should rate your chances of dozing off, not just feeling tired. Even if you have not done some of these things recently try to determine how they would have affected you.

For each situation, decide whether or not you would have:

- ☐ ☐ No chance of dozing =0
- ☐ ☐ Slight chance of dozing =1
- ☐ ☐ Moderate chance of dozing =2
- ☐ ☐ High chance of dozing =3

Write down the number corresponding to your choice in the right hand column. Total yourscore below.

Situation Chance of Dozing

Sitting and reading

Watching TV

Sitting inactive in a public place (e.g., a theater ora meeting)

As a passenger in a car for an hour without a break

Lying down to rest in the afternoon when circumstances permit

Sitting and talking to someone

Sitting quietly after a lunch without alcohol

In a car, while stopped for a few minutes in traffic

Total Score = _____

Analyze Your Score

Interpretation:

0-7:It is unlikely that you are abnormally sleepy.

8-9:You have an average amount of daytime sleepiness.

10-15:You may be excessively sleepy depending on the situation. You may want to consider seeking medical attention.

16-24:You are excessively sleepy and should consider seeking medical attention.

Reference: Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. *Sleep* 1991; 14(6):540-5.

This printed version of the Epworth Sleepiness Scale is provided courtesy of Talk About Sleep, Inc.
www.talkaboutsleepp.com

APPENDIX D

FUNCTIONAL OUTCOME OF SLEEP QUESTIONNAIRE

Site: _____ ID #: _____
 Date of Data Entry: _____ Trial _____
 Name: _____ Date: _____

FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE (FOSQ)

Some people have difficulty performing everyday activities when they feel tired or sleepy. The purpose of this questionnaire is to find out if you generally have difficulty carrying out certain activities because you are too sleepy or tired. In this questionnaire, when the words "sleepy" or "tired" are used, it means the feeling that you can't keep your eyes open, your head is droopy, that you want to "nod off", or that you feel the urge to take a nap. These words do not refer to the tired or fatigued feeling you may have after you have exercised.

DIRECTIONS: Please put a () in the box for your answer to each question. Select only one answer for each question. Please try to be as accurate as possible. All information will be kept confidential.

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
1. Do you have difficulty concentrating on the things you do because you are sleepy or tired?		☐	☐	☐	☐
2. Do you generally have difficulty remembering things, because you are sleepy or tired?		☐	☐	☐	☐
3. Do you have difficulty finishing a meal because you become sleepy or tired?		☐	☐	☐	☐
4. Do you have difficulty working on a hobby (for example, sewing, collecting, gardening) because you are sleepy or tired?	☐	☐	☐	☐	☐

Site: _____ ID #: _____
 Date of Data Entry: _____ Trial _____
 Name: _____ Date: _____

(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
---	-------------------------	---------------------------------------	---------------------------------------	--------------------------------------

5. Do you have difficulty doing work around the house (for example, cleaning house, doing laundry, taking out the trash, repair work) because you are sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

6. Do you have difficulty operating a motor vehicle for short distances (less than 100 miles) because you become sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

7. Do you have difficulty operating a motor vehicle for long distances (greater than 100 miles) because you become sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

8. Do you have difficulty getting things done because you are too sleepy or tired to drive or take public transportation?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

9. Do you have difficulty taking care of financial affairs and doing paperwork (for example, writing checks, paying bills, keeping financial records, filling out tax forms, etc.) because you are sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

Site: _____ ID #: _____
 Date of Data Entry: _____ Trial _____
 Name: _____ Date: _____

(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
---	-------------------------	---------------------------------------	---------------------------------------	--------------------------------------

10. Do you have difficulty performing employed or volunteer work because you are sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

11. Do you have difficulty maintaining a telephone conversation, because you become sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

12. Do you have difficulty visiting with your family or friends in your home because you become sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

13. Do you have difficulty visiting with your family or friends in their home because you become sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

14. Do you have difficulty doing things for your family or friends because you are too sleepy or tired?

☐	☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

(4) No	(3) Yes, a little	(2) Yes, moderately	(1) Yes, extremely	
-----------	-------------------------	---------------------------	--------------------------	--

15. Has your relationship with family, friends or work colleagues been affected because you are sleepy or tired?

☐	☐	☐	☐
--------------------------	--------------------------	--------------------------	--------------------------

In what way has your relationship been affected? _____

Site: _____ ID #: _____
 Date of Data Entry: _____ Trial _____
 Name: _____ Date: _____

	(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
16. Do you have difficulty exercising or participating in a sporting activity because you are too sleepy or tired?	☐	☐	☐	☐	☐
17. Do you have difficulty watching a movie or videotape because you become sleepy or tired?	☐	☐	☐	☐	☐
18. Do you have difficulty enjoying the theater or a lecture because you become sleepy or tired?	☐	☐	☐	☐	☐
19. Do you have difficulty enjoying a concert because you become sleepy or tired?	☐	☐	☐	☐	☐
20. Do you have difficulty watching TV because you are sleepy or tired?	☐	☐	☐	☐	☐
21. Do you have difficulty participating in religious services, meetings or a group or club, because you are sleepy or tired?	☐	☐	☐	☐	☐

Site: _____
 Date of Data Entry: _____
 Name: _____

ID #: _____
 Trial: _____
 Date: _____

(0) I don't do this activity for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
--	-------------------------	---------------------------------------	---------------------------------------	--------------------------------------

22. Do you have difficulty being as active as you want to be in the evening because you are sleepy or tired?

☐ ☐ ☐ ☐

23. Do you have difficulty being as active as you want to be in the morning because you are sleepy or tired?

☐ ☐ ☐ ☐

(0) I don't do this for other reasons	(4) No difficulty	(3) Yes, a little difficulty	(2) Yes, moderate difficulty	(1) Yes, extreme difficulty
--	-------------------------	---------------------------------------	---------------------------------------	--------------------------------------

24. Do you have difficulty being as active as you want to be in the afternoon because you are sleepy or tired?

☐ ☐ ☐ ☐

25. Do you have difficulty keeping pace with others your own age because you are sleepy or tired?

☐ ☐ ☐ ☐

(1) Very Low	(2) Low	(3) Medium	(4) High
-----------------	------------	---------------	-------------

26. How would you rate your general level of activity?

☐ ☐ ☐ ☐

Site: _____ ID #: _____
 Date of Data Entry: _____ Trial _____
 Name: _____ Date: _____

	(0) I don't engage in sexual activity for other reasons	(4) No	(3) Yes, a little	(2) Yes, moderately	(1) Yes, extremely
27. Has your intimate or sexual relationship been affected because you are sleepy or tired?	☐	☐	☐	☐	☐
28. Has your desire for intimacy or sex been affected because you are sleepy or tired?	☐	☐	☐	☐	☐
29. Has your ability to become sexually aroused been affected because you are sleepy or tired?	☐	☐	☐	☐	☐
30. Has your ability to "come" (have an orgasm) been affected because you are sleepy or tired?	☐	☐	☐	☐	☐

Thank you for completing this questionnaire.

APPENDIX E

SCORING INSTRUCTIONS FOR FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE

FUNCTIONAL OUTCOMES OF SLEEP QUESTIONNAIRE (FOSQ)

*Scoring Instructions September 1996 Version
(Revised 7/18/00)*

<u>Subscales</u>	<u># Questions</u>	<u>Item #</u>
General Productivity	8 questions	1 - 4, 8 - 11
Social Outcome	2 questions	12, 13
Activity Level	9 questions	5, 14 - 16, 22 - 26
Vigilance	7 questions	6, 7, 17 - 21
Intimate Relationships and Sexual Activity	4 questions	27 - 30

Subscale Scores: A response score of 0 for an item should be coded as a N/A or missing response. Thus, the potential range of scores for any item is 1 - 4. Calculate the mean of the answered items with responses equal to or greater than 1 for each subscale. This is the weighted mean item total or subscale score. For example, if a subscale has six questions, and one question has a missing response and one with a N/A response, then you would not include those two questions when you added the responses and you would divide by four instead of six when calculating the mean. This prevents a score bias due to missing answers or skipped questions because an individual does not engage in a particular activity do to reasons other than disorders of excessive sleepiness. The potential range of scores for each subscale is 1 - 4.

To obtain a Total Score: Take all of the subscale scores and calculate the mean of these scores and then multiply that mean by five. Multiply by five regardless of the number of subscales scores used in the computation of the mean. For example, if you a subscale score for all subscales, then you multiply the mean of those scores by 5; if you have subscale scores for only 4 of the 5 subscales, then you would also multiply the mean by five. The potential range of scores for the Total Score is 5 - 20.

APPENDIX F

PITTSBURGH SLEEP QUALITY INDEX

Pittsburgh Sleep Quality Index (PSQI)

For staff use only:

Global PSQI Score: _____

Instructions:

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

Please answer all questions.

1. During the past month, what time have you usually gone to bed at night?
BED TIME _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
NUMBER OF MINUTES _____
3. During the past month, what time have you usually gotten up in the morning?
GETTING UP TIME _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)
HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you...

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. ...cannot get to sleep within 30 minutes	☐	☐	☐	☐
b. ...wake up in the middle of the night or early morning	☐	☐	☐	☐
c. ...have to get up to use the bathroom	☐	☐	☐	☐
d. ...cannot breathe comfortably	☐	☐	☐	☐
e. ...cough or snore loudly	☐	☐	☐	☐
f. ...feel too cold	☐	☐	☐	☐
g. ...feel too hot	☐	☐	☐	☐
h. ...have bad dreams	☐	☐	☐	☐
i. ...have pain	☐	☐	☐	☐
j. Other reason(s), please describe:				
How often during the past month have you had trouble sleeping because of this?	☐	☐	☐	☐

	Very good	Fairly good	Fairly bad	Very Bad
6. During the past month, how would you rate your sleep quality overall?	☐	☐	☐	☐

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?	☐	☐	☐	☐
8. During the past month, how often have you had trouble staying awake while driving, eating meals or engaging in social activity?	☐	☐	☐	☐

	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?	☐	☐	☐	☐

	No bed partner or roommate	Partner/room mate in other room	Partner in same room, but not same bed	Partner in same bed
10. Do you have a bed partner or roommate?	☐	☐	☐	☐

If you have a room mate or bed partner, ask him/her how often in the past month you have had:

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Loud snoring	☐	☐	☐	☐
b. Long pauses between breaths while asleep	☐	☐	☐	☐
c. Legs twitching or jerking while you sleep	☐	☐	☐	☐
d. Episodes of disorientation or confusion during sleep	☐	☐	☐	☐
e. Other restlessness while you sleep	☐	☐	☐	☐

Please describe: _____

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NPDS/OPC – PQSI (Reviewed: Sep 2013)

APPENDIX G

SCORING INSTRUCTIONS FOR PITTSBURGH SLEEP QUALITY INDEX

Pittsburgh Sleep Quality Index (PSQI)

Form Administration Instructions, References, and Scoring

Form Administration Instructions

The range of values for questions 5 through 10 are all 0 to 3.

Questions 1 through 9 are not allowed to be missing except as noted below. If these questions are missing then any scores calculated using missing questions are also missing. Thus it is important to make sure that all questions 1 through 9 have been answered.

In the event that a range is given for an answer (for example, '30 to 60' is written as the answer to Q2, minutes to fall asleep), split the difference and enter 45.

Reference

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research* 28:193-213, 1989.

Scores – reportable in publications

On May 20, 2005, on the instruction of Dr. Daniel J. Buysse, the scoring of the PSQI was changed to set the score for Q5J to 0 if either the comment or the value was missing. This may reduce the DISTB score by 1 point and the PSQI Total Score by 1 point.

PSQIDURAT

DURATION OF SLEEP

IF $Q4 \geq 7$, THEN set value to 0

IF $Q4 < 7$ and ≥ 6 , THEN set value to 1

IF $Q4 < 6$ and ≥ 5 , THEN set value to 2

IF $Q4 < 5$, THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIDISTB

SLEEP DISTURBANCE

IF $Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j$ (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) = 0, THEN set value to 0

IF $Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j$ (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) ≥ 1 and ≤ 9 , THEN set value to 1

IF $Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j$ (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 9 and ≤ 18 , THEN set value to 2

IF $Q5b + Q5c + Q5d + Q5e + Q5f + Q5g + Q5h + Q5i + Q5j$ (IF Q5JCOM is null or Q5j is null, set the value of Q5j to 0) > 18 , THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQILATEN**SLEEP LATENCY**

First, recode Q2 into Q2new thusly:

IF $Q2 \geq 0$ and ≤ 15 , THEN set value of Q2new to 0

IF $Q2 > 15$ and ≤ 30 , THEN set value of Q2new to 1

IF $Q2 > 30$ and ≤ 60 , THEN set value of Q2new to 2

IF $Q2 > 60$, THEN set value of Q2new to 3

Next

IF $Q5a + Q2new = 0$, THEN set value to 0

IF $Q5a + Q2new \geq 1$ and ≤ 2 , THEN set value to 1

IF $Q5a + Q2new \geq 3$ and ≤ 4 , THEN set value to 2

IF $Q5a + Q2new \geq 5$ and ≤ 6 , THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIDAYDYS**DAY DYSFUNCTION DUE TO SLEEPINESS**

IF $Q8 + Q9 = 0$, THEN set value to 0

IF $Q8 + Q9 \geq 1$ and ≤ 2 , THEN set value to 1

IF $Q8 + Q9 \geq 3$ and ≤ 4 , THEN set value to 2

IF $Q8 + Q9 \geq 5$ and ≤ 6 , THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIHSE**SLEEP EFFICIENCY**

Diffsec = Difference in seconds between day and time of day Q1 and day Q3

Diffhour = Absolute value of diffsec / 3600

newtib = IF diffhour > 24, then newtib = diffhour – 24

IF diffhour $\leq$ 24, THEN newtib = diffhour

(NOTE, THE ABOVE JUST CALCULATES THE HOURS BETWEEN GNT (Q1) AND GMT (Q3))

tmphse = $(Q4 / \text{newtib}) * 100$

IF tmphse $\geq$ 85, THEN set value to 0

IF tmphse < 85 and $\geq$ 75, THEN set value to 1

IF tmphse < 75 and $\geq$ 65, THEN set value to 2

IF tmphse < 65, THEN set value to 3

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQISLPQUAL**OVERALL SLEEP QUALITY**

Q6

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQIMEDS**NEED MEDS TO SLEEP**

Q7

Minimum Score = 0 (better); Maximum Score = 3 (worse)

PSQI**TOTAL**

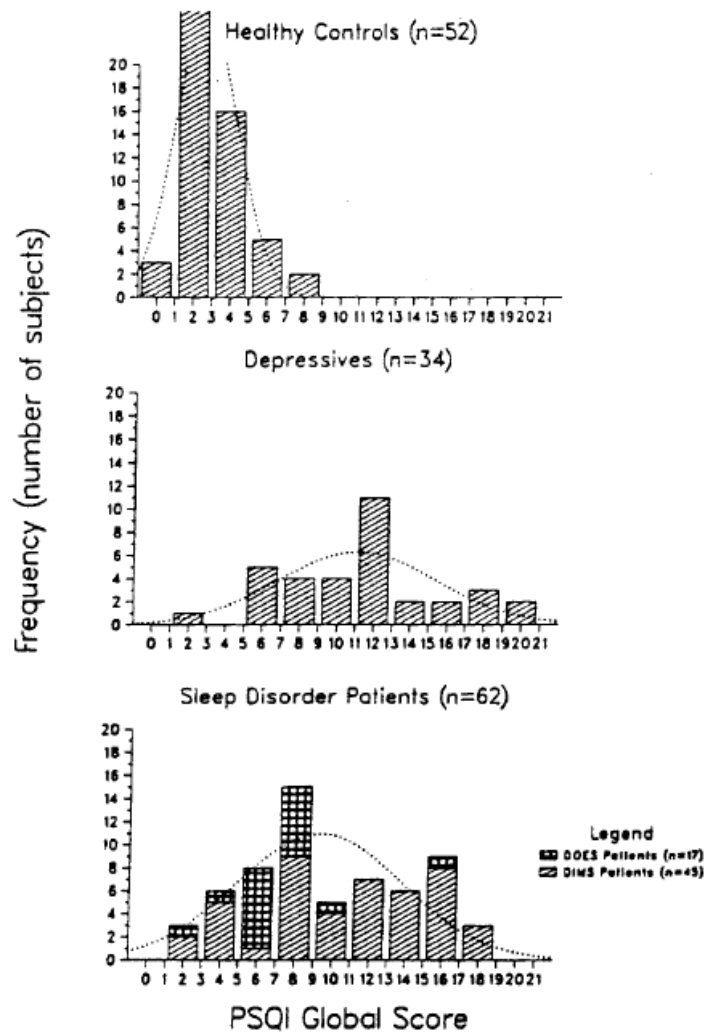
DURAT + DISTB + LATEN + DAYDYS + HSE + SLPQUAL + MEDS

Minimum Score = 0 (better); Maximum Score = 21 (worse)

Interpretation: TOTAL $\leq$ 5 associated with good sleep quality

TOTAL $>$ 5 associated with poor sleep quality

Fig. 2. Pittsburgh Sleep Quality Index (PSQI) global scores



PSQI global scores showed different distributions for control subjects, depressed patients, and sleep-disorder patients. A global score cutoff of > 5 correctly identified 88.5% of all controls and patients, yielding a sensitivity of 89.6% and a specificity of 86.5% (Kappa = 0.75, $p < 0.001$).

Reference:

Buyssse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research* 28:193-213, 1989.

APPENDIX H

PERCEIVED STRESS SCALE

Perceived Stress Scale

For staff use only:
PSS Total Score: _____

The questions in this scale ask you about your feelings and thoughts **during the last month**. In each case, you will be asked to indicate by circling *how often* you felt or thought a certain way.

0 = Never 1 = Almost Never 2 = Sometimes 3 = Fairly Often 4 = Very Often

- | | | | | | |
|--|---|---|---|---|---|
| 1. In the last month, how often have you been upset because of something that happened unexpectedly? | 0 | 1 | 2 | 3 | 4 |
| 2. In the last month, how often have you felt that you were unable to control the important things in your life? | 0 | 1 | 2 | 3 | 4 |
| 3. In the last month, how often have you felt nervous and “stressed”? | 0 | 1 | 2 | 3 | 4 |
| 4. In the last month, how often have you felt confident about your ability to handle your personal problems? | 0 | 1 | 2 | 3 | 4 |
| 5. In the last month, how often have you felt that things were going your way? | 0 | 1 | 2 | 3 | 4 |
| 6. In the last month, how often have you found that you could not cope with all the things that you had to do? | 0 | 1 | 2 | 3 | 4 |
| 7. In the last month, how often have you been able to control irritations in your life? | 0 | 1 | 2 | 3 | 4 |
| 8. In the last month, how often have you felt that you were on top of things? | 0 | 1 | 2 | 3 | 4 |
| 9. In the last month, how often have you been angered because of things that were outside of your control? | 0 | 1 | 2 | 3 | 4 |
| 10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them? | 0 | 1 | 2 | 3 | 4 |

References:

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of psychological stress. *Journal of Health and Social Behavior*, 24, 385–396.

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NPDS/OPC – PSS (Reviewed: Sep 2013)

APPENDIX I

SCORING INSTRUCTIONS FOR PERCEIVED STRESS SCALE

Perceived Stress Scale Score

The Perceived Stress Scale is a 10-item self report questionnaire that measures a persons' subjective appraisal of the stressfulness of the situations in the past 30 days.

- Each item is rated on a 5-point Likert scale ranging from *never* (0) to *almost always* (4).
- There are two subscales within the ten questions: 6 negatively worded questions and 4 positively worded questions. Question numbers 4, 5, 7, and 8 are the positively stated items. Questions 1, 2, 3, 6, 9 & 10 are the negatively stated items.
- Scores can range from 0 to 40, with higher scores indicating greater stress.

Score Calculation:

1. Reverse the scores on the four positive items (4, 5, 7 & 8): 0 = 4, 1 = 3, 2 = 2 and 3 = 1.
2. Negative item scores do not change (1, 2, 3, 6, 9 & 10): 0 = 0, 1 = 1, 2 = 2, 3 = 3 and 4 = 4
3. The overall PSS-10 score is the sum all 10 items.

Interpretation

The PSS is not a diagnostic instrument, so there are no cut-offs. There are only comparisons between people in a given sample. There are some normative data on the PSS based on a *1983 Harris Poll of a representative U.S. sample.

Higher PSS Scores are associated with:

- Higher levels of stress
- Increased stress interference with daily activity and quality of life
- Increased susceptibility to stress-induced illness
- Increased vulnerability to compromised health, especially if a significant life stressor (loss of a job, end of a relationship, death of a loved one, etc.) occurs in the near future

Question:	Score: (0-4)
1	
2	
3	
4 (reversed)	
5 (reversed)	
6	
7 (reversed)	
8 (reversed)	
9	
10	

Total Score: _____

<u>*Total Score</u>	<u>*Your Perceived Stress Level is:</u>	<u>* Health Concern Level</u>
6	Much Lower than Average	Very Low
7 - 10	Slightly Lower than Average	Low
11 - 18	Average	Average
19 - 22	Slightly Higher than Average	High
22 and over	Much Higher than Average	Very High

APPENDIX J
PERSONAL DATA LOG BOOK
Personal Data Log Book

**Titration of Mandibular Advancement Device
(MAD)**

Visual Analogue Scales

INITIAL 7-DAY ACCLIMATION PERIOD LOG

DAILY TITRATION LOG

Study ID: _____

Sleep Study Daily VAS (Visual Analog Scales)

Study ID: _____

Date _____

Before Dinner: VAS for Day's Stress

Please rate how stressful your day was by circling a number on the 0 to 10 scale below. 0 represents a completely stress-free day and 10 represents the worst stress imaginable.

^	^	^	^	^	^	^	^	^	^	^
0	1	2	3	4	5	6	7	8	9	10
No Stress					Worst Possible					

Upon waking: VAS for Sleep Quality

Please rate the quality of each night's sleep by circling a number on the 0 to 10 scale below. 0 represents the worst sleep imaginable and 10 represents the best sleep imaginable.

^	^	^	^	^	^	^	^	^	^	^
0	1	2	3	4	5	6	7	8	9	10
Terrible									Best Possible	

Upon waking: VAS for any Jaw Pain

Please rate the amount of jaw pain you are experiencing upon awakening by circling a number on the 0 to 10 scale below. 0 represents no pain and 10 represents extreme pain.

^	^	^	^	^	^	^	^	^	^	^
0	1	2	3	4	5	6	7	8	9	10
No Pain									Worst Possible	

DO NOT FORGET TO FILL OUT THE DAILY TITRATION LOG

INITIAL 7-DAY ACCLIMATION PERIOD LOG

STUDY ID: _____

DATE (DD/MM/YY)	RETIRE TIME (HH:MM)	RISE TIME (HH:MM)	APPLIA NCE WORN? (Estimate # of Hrs 0-10)	ADJUSTME NT 0=none +1= 1/2 turn clockwise (advance) -1=1/2 turn counterclockwis e (reverse)	PULSE OX WORN? (Estimate # of Hrs 0- 10)	Any Adverse effects (If yes, Please describe on the notes page)	Download Data & Charge battery (√)
				0			x
				0			
				0			x
				0			
				0			x
				0			
				0			x

DAILY TITRATION LOG

STUDY ID: _____

DATE (DD/M M/YY)	RETIRE TIME (HH:MM)	RISE TIME (HH: MM)	APPLIANCE WORN? (Estimate # of Hrs 0-10)	SCHEDULED ADJUSTMEN T (TOTAL ADVANCEME NT)	SUBJECT ACTION 0=none +1= 1/2 turn (180°) clockwise (advance) -1=1/2 turn (180°) counterclock wise (reverse)	PULSE OX WORN? (Estimate # of Hrs 0- 10)	Any Adverse effects (If yes, Please describe on the notes page)	Download Data & Charge battery (√)
				1/2 turn (0.25 mm)				
				1/2 turn (0.5mm)				
				1/2 turn (0.75 mm)				
				1/2 turn (1.0 mm)				
				1/2 turn (1.25 mm)				
				1/2 turn (1.5 mm)				
				1/2 turn (1.75 mm)				
				1/2 turn (2.0 mm)				
				1/2 turn (2.25 mm)				

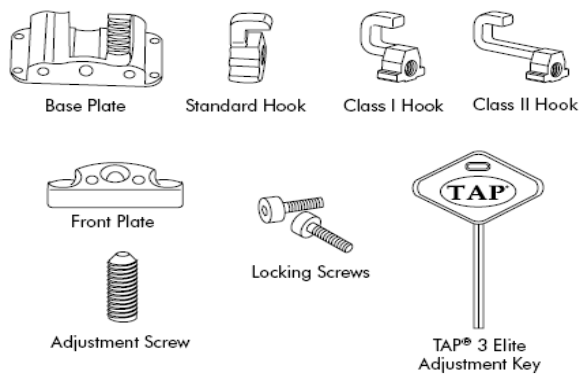
				1/2 turn (2.5 mm)				
				1/2 turn (2.75 mm)				
				1/2 turn=(3.0 mm)				
				1/2 turn (3.25 mm)				
				1/2 turn (3.5mm)				
				1/3 turn (3.75 mm)				
				1/2 turn (4.00 mm)				
				1/2 turn (4.25 mm)				
				1/2 turn (4.5 mm)				
				1/2 turn (4.75 mm)				
				1/2 turn (5.00 mm)				

Study ID No:

NOTES & COMMENTS

<u>DATE</u> (DD/MM/YYYY)	

APPENDIX K TAP 3-ELITE AND PROGAUGE



Permission to use Airway Management images smcclure@amisleep.com; www.tapintosleep.com

APPENDIX L VIRTUOX PULSE OXIMETER



Permission to use VirtuOx images kyle.miko@virtuox.net; www.virtuox.net

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