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Docket Services (m-30)
U.S. Department of Transportation
West Building, Ground Floor, Room W12-140
1200 New Jersey Avenue SE
Washington D.C. 20590-0001

Attention: Docket No. FMCSA-2015-0419 & FRA-2015-0111

To Whom It May Concern:

The American Academy of Sleep Medicine (AASM), a professional society representing a membership of 11,000 physicians, scientists, allied health professionals, and accredited sleep centers, is the leader in setting standards and promoting excellence in sleep medicine health care. We have reviewed the Advance Notice of Proposed Rulemaking regarding the Evaluation of Safety Sensitive Personnel for Moderate-to-Severe Obstructive Sleep Apnea. We are pleased to submit our comments.

The Academy has long standing experience and expertise in the diagnosis and management of sleep disorders, which includes Obstructive Sleep Apnea (OSA). Our interest, as specialist health care professionals, is not only for the health and safety of our patients but to the population as a whole.

Question 1. What is the prevalence of moderate-to-severe OSA among the general adult U.S. population? How does this prevalence vary by age?

Young et al. estimated the prevalence of OSA in middle-aged, working adults in 1994 in what is known as the Wisconsin Cohort Study. They found that in women, moderate-to-severe OSA was found at rates ranging from 3.7 to 4.4%. Among men, rates were two to three times higher than those found in women, and ranged from 6.2 to 11%.[1] The strongest risk factor for sleep apnea was not age, but obesity. An increase in weight by one standard deviation from average of any measure of body habitus was associated with a three-fold increase in the risk of having any sleep apnea.

Given this strong association with weight, and because the prevalence of obesity in the U.S. is rising, more recent investigations have sought to provide updated estimates of the prevalence of OSA. At 4-year intervals, participants in the Wisconsin Sleep Cohort were invited to have repeat sleep studies, and the prevalence of OSA was estimated as a function of age, sex and body mass index (BMI, one way to estimate the degree of obesity). These estimates were extrapolated to the distribution of BMI scores from a large sample of adults in the United States obtained by National Health and Nutrition Examination Surveys (NHANES). Estimates of OSA prevalence based on BMI data from the 1988-1994 NHANES survey were compared against combined data from NHANES 2007-2008 and 2009-2010. These investigations revealed that the prevalence of at least moderate sleep apnea is 10% and 17% among men aged 30-49 years and 50-70 years, respectively; among women in the same age groups, the respective rates are 3% and 9%. *These estimates are substantially higher than they were two decades ago, and reflect an increase of 14-55% in prevalence, depending on the subgroup evaluated.*

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Even these newer estimates of the prevalence of sleep apnea likely underestimate the true prevalence of the full spectrum of breathing abnormalities during sleep which can also contribute to downstream medical consequences, including not only daytime sleepiness but also cardiovascular disease and cognitive dysfunction[2]. These milder forms of breathing abnormalities not only include milder OSA, but also arousals from sleep due to a number of different phenomena, including snoring, smaller reductions in airflow, or simply from the muscles of breathing struggling harder to pull air through a partially obstructed airway, even when the airflow is normal.

Question 2. What is prevalence of moderate-to-severe OSA among individuals occupying safety sensitive transportation positions? If it differs from that among the general population, why does it appear to do so? If no existing estimates exist, what methods and information sources can the agencies use to reliably estimate this prevalence?

Several studies have evaluated the prevalence of sleep apnea in commercial truck drivers. These estimates range from 28 to 78%.[3,4,5,6] In one study, 4,280 commercial driver's license holders in the Philadelphia area were surveyed, and 1,392 responses were obtained; a subgroup of 407 responders were then tested in a laboratory for OSA using polysomnography (PSG). This study, commissioned by the Federal Motor Carrier Safety Administration (FMCSA), estimated the prevalence of OSA to be 28%. In a separate study of 3,268 commercial truck drivers in Australia, which had a higher proportion of men and a higher proportion of those studied in the laboratory, 60% had confirmed OSA, and 24% had excessive sleepiness, which was related to increased accident risk.[4] In a third study, which was done in California, 78% of truck drivers employed by a single company had OSA based on sleep testing.[6] This group had a higher prevalence of obesity than the group in Australia. In a large study of over 19,371 drivers at Schneider International,[3] an online screening tool characterized a total of 5,908 (30%) as being at higher risk for OSA; after testing 2,103 drivers with PSG, 80% had OSA. A more recent study of 104 self-identified commercial drivers' license holders in the Philadelphia area[7] found that nearly one third had severe OSA and 61% had at least moderate OSA, and commercial drivers in this study also had a higher prevalence of obesity than in the other studies.

The higher prevalence of OSA in commercial truck drivers compared to general populations has been attributed to a high prevalence of risk factors for OSA in this group; the majority of commercial drivers are male, obese and middle-aged, three common risk factors for OSA.

A screening program was instituted for OSA for Metro-North rail operators in New York. This program was instituted after a serious crash of a Metro-North train in Bronx, New York on December 1, 2013. The crash resulted in 4 deaths and injuries to 59 other individuals. The National Transportation Safety Board determined that the train's engineer had fallen asleep while operating the train due to untreated, severe OSA.[8] The program tested all 438 Metro-North engineers and engineers-in-training. Since that pilot program was initiated, due to the initial findings, the program has since expanded to include conductors and other safety sensitive personnel. Subsequently, the Human Factors Research Division of the FRA published data based solely on surveys. Their data indicated an overall prevalence of 7.27% of rail employees in safety sensitive positions having the diagnosis of OSA.[9] They recognize this number is likely to be low, as it is based on self-report. While no studies based on objective findings have been done on U.S. rail workers, there is data from other countries. In Brazil, 35.03% of rail workers were found to have OSA based on polysomnography.[10]

In any specific group of individuals, the agencies may use the methodology described by Peppard et al. to extrapolate the prevalence of moderate-to-severe sleep apnea using the distribution of BMI, age, and gender in that particular group.

Question 3. Is there information (studies, data, etc.) available for estimating the future consequences resulting from individuals with OSA occupying safety sensitive transportation positions in the absence of new restrictions? For example, does any organization track the number of historical motor carrier or train accidents caused by OSA? With respect to rail, how would any OSA regulations and the current PTC requirements interrelate?

One meta-analysis, commissioned by the FMCSA,[11] pooled the data from 10 studies to estimate an overall crash risk in drivers with untreated OSA. Overall, the odds that a driver with OSA will have a crash is 243% higher than a driver without OSA. The meta-analysis estimated that 95% of drivers with untreated OSA have a crash risk that ranges from 21% to as high as 489% higher than those without OSA. Furthermore, the same, FMCSA-commissioned group found that treatment of OSA with continuous positive airway pressure (CPAP)[12] 1) lowers crash risk to the same levels as that seen in individuals without OSA; 2) improves sleepiness in as little as 2 days, and 3) improves performance on a driving simulator in as little as 2 to 7 days.

More recently, Schneider Trucking compared 1,603 commercial truck drivers with OSA confirmed by polysomnography, 403 without OSA based on polysomnography, and 2,016 matched control drivers who were unlikely to have OSA. They offered Positive Airway Pressure (PAP) therapy to drivers confirmed to have OSA, and monitored adherence rates objectively using built-in monitoring systems (rather than through self-reporting). They also tracked preventable, Department-of-Transportation-reportable crashes per 100,000 miles driven. Those who did not use PAP had a crash rate that was five-fold higher than that of those without OSA (the control group); those who used PAP had crash rates similar to the control group.[13]

Taken together, these data suggest a relationship between OSA and crashes; the evidence that PAP treatment for OSA lowers crash risk to rates similar to those in drivers without OSA provides compelling evidence that OSA plays a causal role in crashes.

Question 4. Which categories of transportation workers with safety sensitive duties should be required to undergo screening for OSA? On what basis did you identify those workers?

It is our opinion that screening should be performed on employees who work in safety-sensitive positions, in which the danger to the public is significant if the operator were to become suddenly impaired or incapacitated. At present, both agencies have existing definitions of who should be screened. Federal Railroad Administration (FRA) includes anyone involved in train movement, dispatching, signal, and maintenance personnel.[14] Federal Motor Carrier Safety Administration (FMCSA) defines drivers as safety sensitive employees.[15] The American Academy of Sleep Medicine does not recommend expanding screening beyond those already defined.

Question 5. What alternative forms and degrees of restriction could FMCSA and FRA place on the performance of safety-sensitive duties by transportation workers with moderate-to-severe OSA, and how effective would these restrictions be in improving transportation safety? Should any regulations differentiate requirements for patients with moderate, as opposed to severe, OSA?

Accidents and distractions are not only dangerous, but extremely expensive. A commercial trucking accident can cost anywhere from $304,500 to $7 million depending on the size of the truck and parties who may have been injured.[16] These costs result from property and vehicular damage, lost wages from absenteeism, insurance and related medical expenses. Rail accidents can cost much more. Significant research indicates that treatment for commercial drivers can have a major impact on reducing the risk of crashes.

General Recommendations Regarding OSA for Transportation Workers with Safety-Sensitive Duties

If a transportation worker with safety-sensitive duties is diagnosed with OSA, restrictions may be appropriate. We recommend the following:

No restrictions

A worker with an OSA diagnosis would NOT receive restrictions if the following conditions are met:

1. The worker has untreated OSA with an apnea-hypopnea index (AHI) of less than or equal to 20 (i.e., mild-to-moderate OSA), and
    a. The worker does not report experiencing excess sleepiness during the major wake period, or
2. The worker's OSA is being effectively treated.
    a. Minimally acceptable compliance with treatment would be defined as at least 4 hours per day of use on 70 percent of days.
    b. Workers should be made aware that optimal benefits occur with 7 or more hours of daily use.
    c. The worker does not report experiencing excess sleepiness during the major wake period

Immediate Disqualification

Workers should be disqualified immediately or denied working with safety-sensitive duties if any of the following conditions are met:

1. The worker admits to experiencing excessive sleepiness during the major wake period while operating safety-sensitive duties, or
2. The worker experienced an accident associated with falling asleep, or
3. The worker fell asleep while performing a safety-sensitive duty, or
4. The worker has been found to be non-compliant with treatment recommendations or follow-up.

Conditional Restrictions

1. Workers may be granted conditional restrictions if they do not meet conditions for immediate disqualification, and any of the following conditions are met:
    a. The worker has screened positive for possible OSA and is waiting to have a sleep study.
    b. The worker has an AHI of greater than 20 until compliant with PAP, or
    c. The worker has undergone surgery and is pending post-op evaluation.
2. Conditional restrictions should include the following elements:
    a. A worker who has screened positive for possible OSA may continue in their safety sensitive work for 60 days pending sleep study and treatment (if the worker is diagnosed with OSA).
    b. Once the worker is diagnosed with OSA and has started PAP therapy, they may return to safety-sensitive work after a minimum of one week of demonstrated compliance. This conditional period should be limited to 30 days.
        I. The worker should return to the certifying clinician once 30 days have elapsed and, if continued compliance is demonstrated, a further 60-day extension to this conditional period should be granted.
        II. At the end of the 60-day extension, if the worker has showed compliance, unrestricted duty may be restored with re-evaluation at least yearly.

3. The worker who has undergone surgical treatment should remain out of service until they have completed at least a 90-day recovery period and then be re-evaluated. We recommend that this include a post-operative sleep study. Further restrictions, if any, would be based on the criteria given above.

Sleep apnea is characterized not only by apneas (cessation in airflow), but also by reductions in airflow (hypopneas) which result in a drop in blood oxygen levels and a subsequent arousal from sleep. The apneas and hyopneas are summed together and divided by total sleep time (if an in-lab sleep study is done) or by monitoring time (if a home sleep apnea test is done), and the number is called the Apnea-Hypopnea Index, or AHI for in-lab tests and Respiratory Event Index (REI) for home sleep apnea tests (HSAT). The REI from HSATs is often lower than the AHI as determined by polysomnography in part due to the use of a larger denominator (monitoring time, rather than total sleep time) than that obtained using traditional sleep staging (requiring EEG, EMG and EOG). The AHI/REI threshold has been used as a surrogate measure of the severity of sleep apnea.

The AHI/REI threshold may be used to prioritize workers with OSA who need prompt, effective therapy. At this time, the first-line therapy for this group remains positive airway pressure. The AHI threshold advised for prompt PAP therapy is 20 per hour. Data linking crash risk for those with AHI≥20/hour is consistent, whereas data linking crashes to AHI values in the 5-15 range is less consistent.[44] Workers with mild OSA (AHI levels 5 to 15) can still benefit from OSA treatment, and should be encouraged to explore treatment options. Moreover, workers with an AHI between 5 and 20 should be required to seek treatment if they have experienced a fatigue-related crash or if they report sleepiness while engaging in safety-sensitive duties.

When considering the AHI thresholds given above and throughout this document, recognize these are based on data generated from Type 1 in-lab polysomnography. As mentioned above, when home sleep apnea tests are performed, these generate a Respiratory Event Index (REI). While at present there is no good data establishing specific cut-offs based on REI, insurance payers recognize an REI greater than 10 represents treatable OSA.

Recent data, specifically evaluating commercial drivers, suggests that close follow-up of recently diagnosed patients improves long term compliance. Data in non-commercial drivers shows similar results. Therefore we recommend the stepped conditional certification approach.[17] Disturbingly, the Schneider study cited earlier showed that nearly 60% of drivers with OSA that were non-compliant with treatment simply quit to avoid any potential impact on their driving career. One assumption is that they will simply drive for another carrier and not disclose their diagnosis to the medical examiner. This reinforces the benefits of close follow-up just after diagnosis.

Question 6. What are the potential costs of alternative FMCSA/FRA regulatory actions that would restrict the safety sensitive activities of transportation workers diagnosed with moderate-to-severe OSA? Who would incur those costs? What are the benefits of such actions and who would realize them?

Frost & Sullivan, a research and economic consulting company, estimates that undiagnosed OSA cost the United States approximately $149.6 billion in 2015. When calculating the respective costs for leaving OSA undiagnosed versus diagnosing and treating it, financial modeling indicates that treatment costs are only approximately 33% of non-treatment costs resulting in a significant net cost savings to healthcare and transportation stakeholders across the nation.

Frost & Sullivan estimates that the cost to diagnose and treat OSA in the United States in 2015 was approximately $12.4 billion. Given that 5.9 million U.S. residents have been diagnosed with the

condition, costs per OSA patient average $2,105 per person per year. Most OSA patients do not require surgery, so when removing surgical treatment costs, the average drops to $1,190. In context, this is less than the average cost of a single emergency department visit for a "moderate" problem ($1,200) according to the Healthcare Bluebook.

The cost savings of OSA diagnosis and treatment are particularly salient to the transportation industry. Among employees being actively treated with CPAP, a large CMV company saw a 73% reduction in preventable driving accidents. Potential annual cost savings for a hypothetical trucking company with 1,000 employees would be approximately $19.1 million and for a company with 11,000 employees up to $1.2 billion. Table 1 provides a summary of this data.

The benefits to this program are many. Third party payers (private as well as Medicare and Medicaid), employers, and patients would benefit financially from a comprehensive OSA screening, diagnosis, and treatment program as proposed in this formal rulemaking announcement. Patients would experience reductions in the prevalence and severity of co-morbidities such as hypertension, diabetes, heart disease, stroke, and mental illness, and see improvements in quality of life and well-being. Employers would see improvements in employee performance, reduced absenteeism, and reductions in occupational accidents. Self-insured employers would also see health care cost savings. Although diagnosis and treatment costs would be borne by these entities, they would be recaptured by savings due to reduced healthcare utilization related to co-morbidities. Indeed, one study showed that diagnosing OSA and treating with CPAP resulted in an average savings of $550 per driver per month.[18] Hospital admissions were reduced by nearly 25% and overall healthcare dollars spent were cut in half.

Table 1 – Cost Burden of OSA in Undiagnosed Versus Diagnosis and Treatment Costs in the United States (2015)

	Undiagnosed	**Diagnosed**
# People with OSA	23,500,000	5,900,000

Cost of Undiagnosed OSA ($US Mil)		**Cost of Diagnosed OSA** ($US Mil)	
Comorbidities & Mental Health	$30.0	Diagnosis, Testing and Follow-Up	$0.8
Motor Vehicle Accidents	$26.2	Non-Surgical Treatment (PAP and Oral Appliances)	$6.2
Workplace Accidents	$6.5	Surgical Treatment	$5.4
Lost Productivity	$86.9	---	---
Total Costs	**$149.6** ($US Mil)	**Total Costs**	**$12.4** ($US Mil)
Cost per Person	$6,366 ($US dollars)	**Cost per Person**	$2,105 ($US dollars)

Question 7: What are the potential improved health outcomes for individuals occupying safety-sensitive transportation positions and would receive OSA treatment due to regulations?

Several health outcomes may potentially be improved through the diagnosis and treatment of OSA among individuals occupying safety-sensitive transportation positions. These include a reduction in all-cause mortality, improved health-related quality of life, improved control of hypertension and its attendant benefits, and decreased risk of cardiovascular and cerebrovascular disease with its inherent impacts on health, safety, and productivity.

When looking at populations of individuals with OSA, sleep apnea is associated with increases in all-cause mortality.[19,20] A meta-analysis of over 25,000 individuals in 12 studies showed relative risks of 1.79 for cardiovascular disease (CVD), 2.15 for fatal and non-fatal stroke, and 1.92 for death from all causes.[21]

The current evidence for an association between OSA and hypertension, independent of obesity and other potentially contributing factors, is robust. Evidence from the Sleep Health Heart Study (SHHS) is illustrative. This study began in 1997 and included 6,642 men and women. All went through full, in-home polysomnography. In those with OSA, Nieto and colleagues (2000) found that, compared to individuals who had an AHI of <1.5 per hour, the odds of hypertension were 20%, 30%, and 40% higher for individuals in mild (5 to 15/hour), moderate (15 to 30/hour), and severe (>30/hour) AHI categories, respectively.[22]

The American Heart Association lists OSA first among causes of reversible hypertension.[23] OSA has been cited as a cause of so-called "resistant" hypertension, in which blood pressure fails to improve despite the use of at least two blood pressure lowering medications. For these individuals, screening for and treating OSA is an important and essential step in achieving blood pressure control.

Evidence shows that PAP treatment reverses daytime hypertension in the first few weeks after starting treatment.[24,25,26] However, long term benefits are less well-defined. One explanation for the failure to reverse chronic hypertension is that such elevations in blood pressure over long periods may incur permanent, irreversible damage to the vascular system in ways that render it unresponsive to the beneficial, blood pressure-lowering effects of PAP therapy. Early identification and treatment of OSA is thus recommended, and longitudinal studies of improvements in hypertension following long-term OSA treatment are needed.

Diabetes and sleep apnea are closely linked. Many of the risk factors for diabetes and OSA overlap. Diabetes is a well-known, significant risk factor for coronary artery disease, cardiovascular disease and other complications all on its own. Sleep apnea is also an independent risk for subsequent development of diabetes.[27] Individuals with untreated OSA and diabetes have been shown to have poorer control of blood sugar, thus increasing risk of morbidity and mortality.

Cerebrovascular Disease is strongly associated with OSA.[28,29] This is seen in both mild to moderate OSA as well as moderate to severe. This association has been observed to be independent of other risk factors such as hypertension, hyperlipidemia, diabetes and others.[30] Those who have had a stroke and have their OSA successfully treated, have significantly reduced mortality.[31]

Even quality of life (QOL) is significantly impacted. Patients with OSA ranging from mild to severe have been shown in several studies to have decreased quality of life based on a number of measures including physical function, vitality, and health perception.[32] There is good evidence OSA is associated with depression,[33] with some limited evidence of association with other mental health disorders. There is also some evidence that successful treatment improves QOL,[34] though admittedly further research is needed for a definitive conclusion.

Question 8. What models or empirical evidence is available to use to estimate potential costs and benefits of alternative restrictions?

Cost Burden of Undiagnosed OSA

Frost & Sullivan cost estimates referenced in question 6 above were generated in the following manner. The total cost impact of OSA in the United States was assumed to be made up of four components, each calculated with their own method. A confidence level was assigned to each component reflecting Frost &

Sullivan's assessment of what the low and high-end estimates of costs are likely to be based on unknown quantities related to epidemiology, cost and access to care.

1) Comorbidities & Mental Health (±30%)

The total cost impact of comorbidities and mental health were assumed to consist of the following six conditions which clinical literature has shown to have a strong connection to OSA.

I. Hypertension
II. Heart Disease
III. Diabetes
IV. Asthma and Other Breathing Disorders
V. Insomnia
VI. Depression, Anxiety and Other Mental Health Problems

Cost for each comorbidity was calculated in the following way (Table 2):

Table 2 - Comorbidities

Comorbidity Cost Factors	
Prevalence of Comorbidity	A
Total National Cost Burden for Comorbidity	B
Total Cost of Comorbidity Per Person	C = B / A
Number of Individuals with Undiagnosed OSA	D
Prevalence Percentage of Comorbidity in Individuals with OSA	E
Total Number of Individuals with Undiagnosed OSA and the Comorbidity	F = D x E
Percentage of Individuals with the Comorbidity Who Show Improvement with OSA Treatment	G = E x F
Total Cost of Comorbidity Directly Related to Undiagnosed OSA	**H = C x F**

Note: This applies to the United States only

2) Motor Vehicle Accidents (±20%)

The total cost impact of motor vehicle accidents was assumed to consist of the following two categories which literature and government data sources have shown to have a strong connection to drowsiness and OSA (Table 3).

I. Commercial Accidents
II. Non-Commercial Accidents

Table 3 - Motor Vehicle Accidents

Motor Vehicle Accident Cost Factors	
Cost of Commercial Small to Medium-Sized Trucks with 2-3 Trailers Accidents	A
Cost of Commercial Fatal Semi-Truck Accidents	B
Total Cost of Commercial Accidents	C = A + B
Percentage of Motor Vehicle Accidents Where Undiagnosed OSA a Factor	D
Total Cost of Commercial Accidents Due to Individuals with Undiagnosed OSA	E = C X D
Cost of Reported Non-Commercial Non-Fatal Accidents	F
Cost of Reported Non-Commercial Fatal Accidents	G
Total Cost of Reported Non-Commercial Accidents Due to Individuals with Undiagnosed OSA	H = (F+G) x D
Total Cost of Non-Reported Non-Commercial Accidents Due to Individuals with Undiagnosed OSA	I = 10% x H
Total Cost of Motor Vehicle Accidents Where Undiagnosed OSA a Contributing Factor	**J = E + H + I**

Note: This applies to the United States only. All commercial accidents reported. Accidents where OSA is contributing assumed to only occur with undiagnosed OSA assuming that diagnosed OSA is well-managed to the point of not being a contributing factor.

3) Workplace Accidents (±30%)

The total cost impact of workplace accidents was assumed to consist of non-motor vehicle related workplace injuries which literature and government sources has shown to have a strong connection to OSA (Table 4).

Table 4 - Workplace Accidents

Workplace Accident Cost Factors	
Number of Workplace Injuries	A
Cost of Single Workplace Injury	B
Total Cost of Workplace Injuries	C = A x B
Prevalence of OSA in Employed Population	D
Incidence Rate of Workplace Injury Among Fatigued Workers	E
Number of Workplace Injuries Due to Undiagnosed OSA	F = A x D x E
Total Cost of Workplace Accidents for Individuals with Undiagnosed OSA	**G = B x F**

Note: This applies to the United States only. Accidents where OSA is contributing assumed to only occur with undiagnosed OSA assuming that diagnosed OSA is well-managed to the point of not being a contributing factor.

4) Productivity (±30%)

The total cost impact of lost productivity due to undiagnosed OSA was assumed to include the cost of increased absences as well as decreased productivity while employees were on the job. Data from the Bureau of Labor Statistics and Social Security Administration were used to determine average wages for both hourly and salaried workers (Table 5).

Table 5 - Productivity

Productivity Cost Factors	
Percent of Individuals with OSA Employed	A
Number of Individuals with Undiagnosed OSA	B
Total Number of Individuals with Undiagnosed OSA Employed	C = A x B
Percentage of U.S. Workers Who are Hourly	D
Percentage of U.S. Workers Who are Salaried	E
Total Number of Individuals with Undiagnosed OSA Employed as Hourly Workers	F = D x C
Total Number of Individuals with Undiagnosed OSA Employed as Salaried Workers	G = E x C
Average Number of Absences from Work per Year Due to OSA	H
Average Hourly Pay for Hourly Workers	I
Average Annual Salary for Salaried Workers	J
Costs Due to Undiagnosed OSA Related Absences Among Hourly Workers	K = ((8 x I) x H) x F
Costs Due to Undiagnosed OSA Related Absences Among Salaried Workers	L = ((J/246) x H) x G
Total Costs Due to Undiagnosed OSA Related Absences Among All Workers	M = K + L
Percentage of Workday Considered Unproductive by OSA Patients Due to OSA Symptoms	N
Costs Due to Unproductive Work Time Among Hourly Workers with Undiagnosed OSA	O = ((N x I) x 35 hrs p/wk x 50 wks p/yr) x F
Costs Due to Unproductive Work Time Among Salaried Workers with Undiagnosed OSA	P = (N x J) x G
Total Costs Due to Unproductive Work Time Among All Workers with Undiagnosed OSA	Q = O + P
Total Cost of Lost Productivity Due to Undiagnosed OSA	**R = M + Q**

Total diagnosis and treatment costs calculated as the sum of the following:

1) Diagnosis

A) Number of OSA patients initially diagnosed in 2015 estimated based on survey of 506 OSA patients receiving treatment.

B) Diagnostic care pathway mapped out based on what percentage of patients receive in-lab PSG testing (standard vs. split night) versus home sleep apnea testing (HSAT), which requires confirmatory in-lab PSG for patients with indeterminate HSAT results. Conservative and aggressive scenarios were developed which applied different assumptions on the utilization rates of different testing types. The following procedures and related HCPCS codes were mapped:

- Home Sleep Apnea Testing (95806)
- In-Laboratory PSG (95810)
- In-Laboratory PSG (Split Night) (No HST) 95811
- Clinic Visit (1 Diagnosis Appointment and 2 Follow-Up in First Year) (Average of 99201-99205)

C) To determine pricing, Frost & Sullivan used the HCPCS 2015B fee schedule for diagnostic services at the “Facility” price and the global value for both professional and technical components. Researchers designated MAC locality "0" for a national average. They applied Medicare costs to the 24.1% of the diagnosed OSA population Medicare/Medicaid eligible then added a 25% premium to Medicare fees to develop private insurance fee rates based on 2014

research by the Commonwealth Fund. Finally, the researchers applied those costs to the remaining 75.9% of patients.

D) For patients already diagnosed with OSA before 2015, only costs for a single annual clinic visit was applied using an average fee of HCPCS 99211-99215. The same assumptions applied as for those initially diagnosed in 2015. No testing beyond the patient's initial test was considered in cost assumptions.

2) Non-Surgical Treatment Costs (PAP and Oral Appliances)

A) All patients diagnosed with OSA were assumed to initiate and maintain treatment. Based on Frost & Sullivan survey findings, 69% of diagnosed OSA patients were assumed to be using a CPAP/AutoPAP machine (E0601) and 23% using a Bilevel PAP machine (Average of E0470/ E0471/ E0472). Patients were assumed to receive one machine the same year of diagnosis and a new machine every 7.5 years afterward. These assumptions were applied to the number of diagnosed OSA patients to calculate the number of PAP machines sold each year. Pricing for Medicare patients was calculated by multiplying the national average as of January 2015 for the corresponding DMEPOS code for a monthly rental by 13 months, after which the device is assumed to be sold per CMS policy. To calculate prices paid by private insurers, Frost & Sullivan added a 25% premium to Medicare fees to develop private insurance fee rates based on 2014 research by the Commonwealth Fund. These PAP machine prices were multiplied by the number of patients with the respective insurance type by the corresponding price to calculate PAP machine costs.

B) Recognizing that the accessories used with PAP machines are highly variable, each patient with a PAP machine was conservatively assumed to use the following accessories every 6 months: 1 Mask: A7030 / A7034/ A7044/ A7027 (Averaged) + 1 Headgear Set (A7035) + 1 Tubing Set (A7037) + 1 Filter (A7038). Prices and costs for accessories were calculated in the same way as for PAP machines themselves.

C) Frost & Sullivan results indicated 6% of the diagnosed OSA population used a custom oral appliance (E0486). The products may be used as an alternative or an adjunct to PAP therapy. Costs for the products are highly variable with a significant portion of them paid in cash or with high deductibles. Frost & Sullivan developed an estimated price for the Medicare and non-Medicare populations based on research done in the oral appliance market in 2015. The products were assumed to have a lifespan of 7 years. The number of oral appliances was calculated by multiplying the percentage penetration of the devices and product lifespan value by the number of diagnosed OSA patients. This number was then multiplied by the number of diagnosed OSA patients split by insurance type and corresponding price to calculate total cost.

3) Surgical Treatment Costs

Sum of costs calculated for each of the following surgeries using the following formula:

(Total number of procedures performed in 2015) X (% Patients receiving procedure estimated to be suffering from OSA) X (Average total cost of procedure assuming a weighted payer mix)

- Nasal Reconstruction or Polyp Removal
- UPPP (Standard or Laser-Assisted)
- Maxillomandibular/ Genioglossus/ Hyoid Advancement

- Temperature-controlled RF Tongue Base Reduction/ Palatoplasty (Somnoplasty, Coblation)
- Pillar Procedure
- Sclerotherapy
- Tracheotomy for OSA
- Bariatric Surgery
- Tonsillectomy/ Adenoidectomy
- Hypoglossal Nerve Stimulation

Note that in some procedures, treatment of OSA may not have been the primary indication, but the percentage used still reflects the prevalence of the condition in that population.

Question 9. What costs would be imposed on transportation workers with safety sensitive duties by requiring screening, evaluation, and treatment of OSA?

Initial screening should be done by the medical examiner at the time of the operator's certification exam, therefore, we are of the opinion that no extra cost would be incurred since this should be part of that examination.

Testing for sleep apnea has become more widely available and in many markets, more affordable over time. Costs to workers include those associated with the medical exam (which may be covered in the general fitness for duty exam; or may also include an additional examination depending upon the determination of the ME) and sleep study. Both out-of-pocket costs may be reduced or eliminated by health insurance coverage. Using published weighted Medicare reimbursements as a proxy for payer cost (2016 Medicare price weights and coverage policies), a specialty clinic new patient visit may cost $166.13, and follow-up visit may cost $108.13. In-lab testing is typically more expensive; again using weighted 2011 Medicare reimbursements as a proxy, an in-lab test is $631.23. If clinically significant OSA is diagnosed, this would be followed by a PAP titration which would be $663.45. A split night in-lab test (typically, diagnostic testing followed by PAP treatment) has a payer cost of $663.45. In contrast home sleep apnea testing payer cost is reported at $170.43. It should be emphasized that health insurance may cover the cost of these visits and tests in appropriate clinical situations. It should also be emphasized that there exists substantial degrees of regional and payer specific variability in costs.

Costs for treatment of sleep apnea involve procurement and use of a PAP device and supplies, or oral appliance. The cost of CPAP is typically covered by health insurances, but cash prices range from $229-$400+ for a new device with compliance monitoring, plus recurring costs for supplies (mask, tubing, filters) every 3-6 months (also covered by insurance, cash price starting at about $120 for filters, mask/ headgear, and tubing). Many health insurances also cover the cost of oral appliance therapy. PAP therapy requires an energy source or battery to operate, however, oral appliances do not. After treatment with oral appliance, a follow-up sleep study may be recommended by the health provider which may add to the cost of this treatment approach.

As mentioned previously, it must be noted that treatment of OSA can positively impact comorbid medical conditions including cardiovascular and metabolic disease (e.g. hypertension, arrhythmia, diabetes, etc.) – and potentially act to counterbalance the cost of OSA detection and treatment since these medical conditions are costly to manage. In fact, patients with unidentified and/or untreated OSA accrue two-fold higher medical expenses, largely associated with cardiovascular disease.[35] In a study of commercial drivers undergoing a corporate-driven sleep apnea detection and treatment program, CPAP intervention in 348 drivers with sleep-disordered breathing resulted in a 47.8% reduction in per member per month health care spending.[18] Also, a recent study conducted with the Union Pacific Railroad Employees Health Systems found that a focused educational campaign on sleep-disordered breathing improved health

outcomes and lead to a measureable reduction in medical expenses – a differential cost savings of $4.9 million for the 2-year study period.[36]

Question 10. Are there any private or governmental sources of financial assistance? Would health insurance cover costs for screening and/or treatment of OSA?

Sleep testing is typically covered by both private and governmental health insurers when considered medically necessary. Current medical commercial insurance policy states that sleep apnea testing is considered medically necessary[37] with any or the following: 1) observed apneas during sleep; OR 2) at least two of the following: a) Epworth Sleepiness Scale (ESS) score > 10, or inappropriate daytime napping, or sleepiness that interferes with daily activities and is not explained by another medical condition, b) habitual snoring, or gasping/choking episodes during sleep associated with awakenings, c) treatment-resistant hypertension, d) BMI > 30 kg/m^2 or neck circumference greater than 17 inches (men) or 16 inches (women); or e) craniofacial or upper airway soft tissue abnormalities; OR 3) coexistence of certain high-risk medical conditions such a history of stroke, coronary artery disease, arrhythmias, etc. Sleep testing is also considered medically necessary when sleep disorders other than OSA are suspected. Even covered services, however, may involve cost-sharing with the covered individual in the form of a copay or deductible, depending on the specifics of the health plan. Equally, sleep treatment (e.g. PAP and recurring supplies) is typically covered by health insurance for a diagnosis of mild sleep apnea plus symptoms or moderate to severe sleep apnea. Follow-up studies to assess treatment efficacy are often covered as well.

In addition, private sources of assistance are available for procuring CPAP if financial hardship exists. A few are: the Reggie White Foundation (http://www.reggiewhitefoundation.org/support/default.asp), Breathe California of the Bay Area (https://www.lungsrus.org/BreatheCA/index.php/services/sleep-apnea-cpap), and the American Sleep Apnea Association (http://www.sleepapnea.org/resources/cpap-assistance-program.html). These offer free or low-cost PAP assistance programs. Multiple commercial entities also offer significantly discounted pre-owned PAP devices.

Question 11. What medical guidelines other than the AASM FAA currently uses are suitable for screening transportation workers with safety sensitive duties that are regulated by FMCSA/FRA for OSA? What level of effectiveness are you seeing with these guidelines?

Guidelines available for screening for OSA in commercial vehicle operators have been proposed by several entities, including: 1) a Joint Task Force comprised of the National Sleep Foundation, American College of Chest Physicians, and the American College of Occupational and Environmental Medicine;[38] and by groups convened by the FMCSA: 2) a Medical Expert Panel (MEP),[39] a Medical Review Board,[40] and jointly by the MRB and Motor Carrier Safety Advisory Committee (MCSAC)[41,42] of the Federal Motor Carrier Safety Administration (FMCSA). They have been summarized recently.[43]

All of them offer ways to keep drivers in service while undergoing evaluation and treatment for OSA. All suggest the use of objective measures, such as BMI, neck size or the presence of hypertension to identify high-risk individuals who should undergo sleep studies to evaluate for OSA. All of these guidelines encourage the use of objective measures because self-reporting of OSA has been shown in multiple research studies to be unreliable.[44,45,46] In one study, even though 78% of those screened had confirmed OSA, none admitted to the common symptoms of snoring and sleepiness;[19] in another, 187 were deemed to be at high-risk based on physical examination criteria, but none had marked “yes” to the question on the CDME form regarding snoring, sleep disorders, pauses in breathing while asleep, or daytime sleepiness. In another study,[45] all but one of the individuals with severe OSA, (defined as an hourly rate of breath flow reduction or complete stop in airflow at a rate of at least 30 times per hour) denied sleepiness when asked using a validated questionnaire called the Epworth Sleepiness Scale. Finally,

Schneider trucking used their own version of an online questionnaire to screen drivers for risk for OSA. They, too, found that self-reported symptoms were not useful, and cited a specific instance of a driver with very severe apnea, with breathing stops or reductions in airflow happening 164 times per hour, whose Epworth score was well within the normal range.[3]

To date, we know of no specific recommendations for screening of rail workers in the United States, though studies of foreign rail workers suggests a prevalence of OSA similar to that of commercial drivers.[10] Australia requires operators with a BMI greater than or equal to 40 or with a BMI of 35 AND diabetic OR hypertensive needing 2+ medications for control to undergo a sleep study. They also require anyone with evidence of a sleep disorder, such as admitted sleepiness or involvement in a sleep-related incident, to be evaluated.[47]

Data show that, by using existing guidelines, healthcare providers are only capturing the "tip of the iceberg" in terms of the actual numbers of potential OSA cases.[45,46,48] By using guidelines provided by the Joint Task Force (which rely on the same BMI threshold of $\geq$35 kg/m^2, which was recommended the MCSAC-MRB), only 10-13% of commercial truck drivers screen positive, despite the fact that the estimated prevalence of OSA in this group is much higher (as stated under Question 1). Furthermore, none of those identified as high-risk then marked "yes" to the question about sleep disorders on the CDME form;[49] of those identified as high-risk who completed the recommended PSG testing, 79-100% had confirmed OSA; only one individual returned on PAP therapy;[47] and 34-81% did not return to the medical examiner for follow-up evaluation.

Therefore, a recommendation for PSG using existing guidelines yields high rates of positive diagnoses, suggesting that the BMI threshold of $\geq$35 kg/m^2 leaves high numbers of at-risk drivers untested. The failure of individuals to accept PAP therapy or return for follow-up evaluation suggests that doctor-shopping was an issue, in the absence of a mandate for universal screening and treatment of identified cases.

Question 12. What were the safety performance histories of transportation workers with safety sensitive duties who were diagnosed with moderate-to-severe OSA, who are now successfully compliant with treatment before and after their diagnosis?

Neglecting OSA leads to individual health burden – including increased risk of mortality – but also the possibility of increased risk of accidents, fatalities, destruction or damage of equipment, vehicles, and roadways, permanent injury and lost time from work, to name a few.

Berger, et al. studied a corporate-driven sleep apnea detection and treatment program at Schneider National, Inc.[18] In this study, analysis of 255 drivers found to have a sleep-disordered breathing (SDB) diagnosis and treated with CPAP, 75% incurred a preventable accident during the study period (pre or post CPAP). Of the drivers with accidents, 93% had an accident before treatment for SDB, and 25% incurred an accident after CPAP treatment. Only 7% incurred an accident after treatment for SDB, but not before. Overall the accident rate was reduced 73%, from 93% pre-CPAP to 25% post-CPAP, among commercial drivers with SDB. In this study, 91% of drivers assessed for CPAP compliance were using CPAP 6-7 nights per week. Of note, the report does not fully detail AHI statistics among those given the SDB diagnosis, but does indicate that 44% of drivers with SDB diagnosed at the one testing site analyzed had severe SDB (AHIs from 34-112 events per hour of sleep).

Question 13. When and how frequently should transportation workers with safety sensitive duties be screened for OSA? What methods (laboratory, at-home, split, etc.) of diagnosing OSA are appropriate and why?

Routine screening should be conducted as part of the pre-existing required fitness-for-duty medical evaluation. If the screening yields positive results, suggesting the presence of OSA, we believe a comprehensive sleep evaluation should result.[49] We recommend this evaluation be performed by a board-certified sleep physician.

We recommend the following criteria at a minimum:

1. OSA Screening (i.e., identifying individuals with undiagnosed OSA). Individuals with the following should be referred for diagnostic sleep evaluations
    a. Individuals with a BMI $\geq$40 mg/kg^2
    b. Individuals who have admitted fatigue or sleepiness during the duty period OR who have been involved in a sleep-related crash or accident
    c. Individuals with a BMI $\geq$33 mg/kg^2 and either
        i. Hypertension requiring two or more medications for control; or
        ii. Type 2 diabetes

Based on published data, using these criteria would result in a positive predictive value exceeding 90%.

1. However, there are other risk factors that are associated with OSA. In addition to a BMI of 33 or above, the following information may help a clinician screen an operator for the possible presence of sleep apnea:
    a. Symptoms may include loud snoring, witnessed apneas, or sleepiness during the major wake period;
    b. Risk factors of OSA may include the following factors. However, a single risk factor alone may not infer risk, but a combination of multiple factors should be examined.
        i. Factors associated with high-risk*:*
            1. Small or recessed jaw
            2. Small airway (Mallampati Scale score of Class 3 or 4)
            3. Neck size > 17 inches (male), 15.5 inches (female)
            4. Hypertension (refractory)
            5. Type 2 diabetes (treated or untreated)
            6. Hypothyroidism (untreated)
        ii. Other factors:
            1. BMI greater than or equal to 28 kg/m^2
            2. Age 42 and above
            3. Family history
            4. Male or post-menopausal female
            5. Experienced a single-vehicle crash, off-road deviation, or rear-ended another vehicle

We therefore recommend that operators with BMI $\geq$33 mg/kg^2 and 2 or more of the other risk factors also be strongly considered for a comprehensive evaluation.

The FMCSA MEP recommends that an in-lab polysomnogram(PSG) is the preferred method of diagnosis. This has the advantage of comprehensive evaluation for other sleep disorders as a possible cause of excessive daytime sleepiness (EDS) and is considered the most accurate test available. The disadvantages are cost, time, access and the requirement to sleep in a laboratory. The in-lab PSG is expensive due to the infrastructure required and access is limited particularly in underserved areas which may result in a delay in diagnosis of up to 3 months. The Academy echoes this recommendation in that an in-lab PSG is the most optimal test, particularly when there is concern for another sleep disorder or when the pre-test likelihood of OSA is low.

The advent of home sleep apnea testing brings advantages of more rapid evaluation and lower cost. This method of diagnosis would be most helpful "ruling in" OSA. The typical device is a Type 3 monitor, which includes four channels: these assess respiratory effort, airflow, oxygen saturation, and heart rate. For those with a high pre-test likelihood of OSA, the Type 3 multichannel home sleep apnea test would facilitate rapid diagnosis, treatment, and return to duty. In the absence of suspicion for another sleep disorder *and* a high suspicion of OSA, this method of testing would be most appropriate. Unfortunately, there are some limitations that proscribe using this technology.

Type 3, multichannel home sleep apnea test tends to underestimate AHI. It should not be used if the risk of OSA is low (since the device can miss the diagnosis entirely), if the operator has multiple comorbid medical conditions, or if the clinician suspects another sleep disorder. In addition, there are technical limitations. Ten to fifteen percent of home sleep apnea tests will require an in-lab study due to inconclusive or corrupt data. We recommend HSAT only be performed in conjunction with a comprehensive sleep evaluation by a sleep health professional and not be used for rapid screening. Custody and control should also be considered to ensure that the individual wearing the device is the intended worker who is being evaluated. We do not recommend the Type 4 test, which uses only 1-2 channels, as there is limited data that these devices are adequate for diagnosis of OSA.

One frequently raised issue is "how long is a sleep study good for?" This is not a question that has an absolute answer. The examining clinician will need to make a decision based on their clinical judgment. However, there is some information available for consideration. When the Wisconsin Cohort population was evaluated, the researchers noted that a 10% weight gain was associated with a 32% increase in AHI. This translated to a 6-fold increase in the odds of developing moderate to severe OSA.[50] In addition, age is associated with an increase in OSA prevalence peaking in the middle decades of 45-65 years. Therefore, we would recommend if a clinician notes a significant change in an individual's health such as development of diabetes or refractory hypertension, particularly if coupled with significant change in weight or age, that consideration may be given to re-evaluating that individual with a sleep study.

Question 14. What if any, restrictions or prohibitions should there be on a transportation worker's safety sensitive duties while they are being evaluated for moderate-to-severe OSA?

When the question arises as to what should be done with an operator who has been screened and referred on for definitive evaluation but does not yet carry a diagnosis, we feel this must be determined on a case by case basis. Clinicians should be encouraged to inquire about symptoms that would suggest an imminent threat to public safety such as falling asleep while working in their safety-sensitive position or having a sleep-related accident.

However, we also emphasize that in an employment setting, (see Question 11, final paragraph) self-reporting of symptoms such as sleepiness or prior accidents tends to be unreliable. More work is needed in this area to identify prompt, easily-accessible tests that assess driving capability not only prior to treatment, but in the course of therapy.

Absent an imminent threat, it is unrealistic for most safety-sensitive operators to be stood down. The Academy refers to the Department of Transportation's (DOT) drug testing regulations which prohibit those in safety-sensitive positions to be pulled from those positions prior to receipt of the final result from the Medical Review Officer[51] suggesting this might be a similar situation.

Question 15. What methods are currently employed for providing training or other informational materials about OSA to transportation workers with safety sensitive duties? How effective are these methods at identifying workers with OSA?

There are many resources available to the safety-sensitive worker regarding OSA. The FAA has developed educational materials.[52] FMCSA has one web page devoted to OSA.[53] We were unable to locate any educational material regarding OSA on the FRA website. The American Academy of Sleep Medicine hosts www.sleepeducation.org which contains a wealth of information regarding OSA. There are a multitude of other on-line resources such as WebMD, Mayo Clinic, and AAFP. Transportation companies have their own resources as well. Schneider National has a comprehensive program that is well known in the industry as do other larger truck carriers. Patient education programs for management of chronic disease are widely accepted as effective.[54]

Despite these resources there are numerous barriers to the information having the desired effect. There is near universal resistance to evaluation and treatment of OSA in the commercial driving community. Most drivers are either independent owner/operators or belong to smaller companies without the resources to have a comprehensive in-house program. Educational programs, outside of those mandated by corporate or insurance programs, are entirely voluntary. Most of the educational material is neither user friendly nor written at a level comprehensible by the general public.[55] We are unaware of any data that shows that educational programs, in and of themselves, have any success identifying individuals with OSA. Indeed, there is a multitude of data showing that reliance on self-reporting in the commercial driving community results in very few cases of OSA being identified. We do not recommend the use of subjective symptoms alone as an effective identification method (see Question 11 above). Education should be offered as part of screening and evaluation, and not relied on as an independent method of identifying OSA patients.

We have the following specific recommendations:

1. We recommend that the FMCSA put educational material about sleep apnea back on the internet targeted toward drivers and motor carriers. We recommend FRA deploy similar material. We refer to the FAA's information developed for pilots and recommend that this material be developed with the input of sleep health professionals and designed to be read by the general public.

2. We recommend that FMCSA require specific instruction to MEs as part of the required NRCME training program. This may require training providers to revise their material but would ensure that examiners are educated in the pathophysiology, screening, diagnosis, and treatment of OSA.

3. We recommend FRA require similar instruction for their examiners.

4. We recommend specific educational material and guidance be returned to the FMCSA's Medical Examiner's Handbook and that similar content be available to FRA examiners.

5. We recommend that examiners educate operators at risk for OSA about the reasons for this risk. We also feel the examiner should provide the operator an outline of the process he/she will need to go through to evaluate them for OSA.

6. Sleep apnea and symptoms of excessive daytime sleepiness are not readily provided to medical examiners or even to treating clinicians in the context of fitness for duty. It is well-understood that individuals faced with perceived possible loss of their livelihood, loss of income, or increased expenses for the diagnostic process will not disclose symptoms.

In fact, this lack of disclosure may even lead to insurance carriers declining to cover recommended testing as the individual being tested reports being asymptomatic. A study done on commercial drivers published in 2011 showed that in an anonymous, non-punitive environment, drivers had a positive Berlin

Questionnaire 56% of the time and nearly 21% admitted they fell asleep at stoplights.[56] The fitness for duty process in and of itself may be perceived as "punitive" as failing to be considered fit leads to adverse consequences. Public safety necessitates this process but better education and information may help ameliorate this. We recommend that education material and both screening and treating clinicians emphasize that this is a treatable disorder. Once diagnosed and treated, the overwhelming majority return to a normal life. In fact, most will be healthier and have a better quality of life.

Question 16. What qualifications or credentials are necessary for medical practitioner who performs OSA screening? What qualifications or credentials are necessary for a medical practitioner who performs the diagnosis and treatment of OSA?

We recommend that clinicians that are screening employees are, at a minimum, appropriately licensed and certified as appropriate to their credentials. We feel that allopathic and osteopathic physicians, nurse practitioners and physician assistants would be most appropriate. We do not feel that chiropractors have the necessary training in physiology or pharmacology to serve in this role and would recommend that they not be utilized. We note that at least 4 states (Rhode Island, Utah, Washington, and Wyoming) already list DOT examinations as outside the chiropractic scope of care.

Medical examiners (ME) should have training with regards to signs and symptoms of OSA to be able to accurately screen and refer those who screen positive for confirmatory testing. Emphasis should be placed on physical features rather than subjective reports. While commercial drivers are penalized for making false or misleading information to a NRCME examiner,[57] OSA symptoms may be downplayed or not appreciated by affected individuals.[56] Screening assessments should not exclude at-risk individuals based on subjective report of symptoms.

Drivers identified by MEs should be referred for diagnosis and treatment to board-certified sleep medicine physicians and accredited sleep centers. We emphasize that OSA is a medical disorder and therefore should be managed by medical clinicians. Several studies have shown improved treatment compliance, greater patient satisfaction and greater timeliness in patients treated at accredited sleep centers or Sleep Medicine board-certified physicians.[58,59]

Question 17. With respect to FRA should it use Railroad MEs to perform OSA screening, diagnosis and treatment?

The Academy recommends that MEs are trained to appropriately screen and identify those employees with a high likelihood of OSA. Diagnosis and treatment should be done by clinicians with appropriate board certification as discussed in Question 16.

Question 18. Should MEs or other Agencies' designated medical practitioners impose restrictions on a transportation worker with safety sensitive duties who self-reports experiencing excessive sleepiness while performing safety sensitive duties?

A policy that restricts transportation workers from occupational duties after self-reported daytime sleepiness could pose a significant impediment to symptom disclosure. However, the recent report by Berger et al. showed a 73% reduction in accident rate after treatment of OSA in a program that required mandatory screening of all employees and treatment of those confirmed to have OSA on subsequent PSG testing.[18] Given the significant consequences of sleep related accidents, MEs or treating physicians should be able to restrict hazardous work duties in high-risk individuals. Consideration should be given to specific features of an individual's work duties. Transportation workers admitting to excessive sleepiness require a thorough evaluation to identify the cause and institute effective treatment.

Question 19. What should be the acceptable criteria for evaluating the effectiveness of prescribed treatments for moderate to severe OSA?

Sleep apnea is a medical disorder and should be managed by a clinician with appropriate experience and/or board certification in sleep medicine. We strongly recommend at least annual follow-up with a sleep specialist. As such, the physician should direct treatment and may include several options. The primary goal of any treatment for obstructive sleep apnea, whether it is positive airway pressure, oral appliance therapy (OA), upper airway surgery, positional therapy, or weight loss, is to demonstrate improvement of sleep apnea severity, adherence to therapy, and improved patient symptoms.[60] Therefore, the AASM would recommend that acceptable criteria for evaluating effectiveness of prescribed OSA treatments include these three elements.

Improvement in OSA severity with a therapeutic intervention has traditionally been performed through a sleep study assessment and could be performed as a home sleep apnea test or in-lab sleep study. With interventions such as PAP, OA, or positional therapy, a sleep study is performed while the patient uses the intervention. In contrast, with other therapies including upper airway surgeries or weight loss, improvements in sleep apnea severity are determined after the intervention. In the specific instance of PAP therapy, improvements in OSA severity can, in most instances, be determined through analyses of data recorded by many PAP devices. PAP devices contain algorithms which can determine the residual OSA severity, which have been generally useful.[61] This technology is not available to non-PAP therapies at present, thus require formal sleep testing to assess the efficacy of therapy.

Adherence to therapy OSA is another element that should be used as criteria for evaluation effectiveness of treatment for moderate-severe OSA. Adherence to treatment has been shown to be an important determinant in the resolution of patient symptoms. Specifically, progressive improvements in adherence are associated with greater normalization in subjective (e.g. Epworth Sleepiness Scale; ESS) and objective (e.g. multiple sleep latency test; MSLT) measures of sleepiness as well as sleep-related quality of life (E.g. Functional Outcomes in Sleep Questionnaire; FOSQ).[60,62] Furthermore, individuals adherent to treatment for OSA demonstrate reduced incident hypertension[63] and improved survival[64] compared to non-adherent individuals. The importance of tracking adherence to therapy has been recognized by previously proposed recommendations announced by the FMCSA in conjunction with an evaluation performed by its Medical Review Board.[65] Adherence to OSA treatment is primarily available to PAP therapies where currently accepted standards for adherence are defined as use for at least 4 hours per night for 70% of nights. This definition is currently utilized by the Center for Medicare and Medicaid Services (CMS) in providing payment for PAP devices and related supplies. Technology has only recently been developed for OA therapy with one FDA-approved monitoring system currently available. Adherence tracking for positional therapy has not been well-developed and validated at this time although this may become available in the very near future. Given the concerns of minimizing sleepiness and reducing risks of transportation-related accidents in safety sensitive personnel, the AASM advocates that monitoring adherence to treatment is an important criterion to demonstrated effectiveness of therapy. We recommend using the minimum adherence standard of 4 hours per night for 70% of nights when an examiner is monitoring compliance.

Improvements in OSA symptoms, particularly sleepiness, are a primary goal of OSA treatment in safety-sensitive personnel in the transportation industry. Assessment of sleepiness over time can generally be done using standardized questionnaires such as the Epworth Sleepiness Scale or a clinical provider evaluation. However, transportation workers are often known to underreport symptoms, making it difficult to fully rely on a subjective assessment. As a result, current guidelines for the assessment and treatment of OSA in transportation workers have focused on monitoring objective data such as improvements in OSA severity, adherence to treatment, and improvements in clinical outcomes such as blood pressure. Nevertheless, given that OSA is a chronic disease that requires long-term,

multidisciplinary management, clinical providers should closely assess patients to develop a global impression of improvements in sleepiness and other patient-reported outcomes. This assessment could be performed by a sleep medicine or primary care clinician to help inform the medical examiner decision making process for fitness for duty. The AASM, therefore, advocates that clinical assessment of improvement in OSA-related symptoms should be included as a criterion to monitor the effectiveness of therapy.

We recommend PAP treatment for most patients diagnosed with OSA. It is the most established, effective, and studied mode of treatment. There is data showing that treatment with PAP reduces crash risk, improves health, and decreases mortality as discussed previously. We recognize that OAs are an effective treatment for OSA.[66] However, at present there is not enough data to make recommendations regarding the impact of OA use on transportation safety. In particular, there is no data showing decreased risk of crash or improvements in health over the long term. The response is unpredictable and concerns remain about airway remodeling with subsequent return of clinically significant OSA with long term use. Nevertheless, OAs may be better tolerated, certainly more portable, and may show increased compliance. Certainly these other therapies should be prescribed by a sleep physician as part of a comprehensive treatment program. We await further data to make a definitive recommendation.

Question 20. What measures should be used to evaluate whether transportation employees with safety sensitive duties are receiving effective OSA treatment?

The primary goal of any treatment for obstructive sleep apnea (OSA), whether it is positive airway pressure (PAP), oral appliance therapy (OA), upper airway surgery, positional therapy, or weight loss, is to demonstrate improvement of sleep apnea severity, adherence to therapy, and improved patient symptoms.[49] Specific measures or approaches are available to assess these criteria and were discussed in the response for comments for question 19. We recognize that the interventions discussed in Question 19 are optimal but not necessarily universally achievable. Employees in safety-sensitive positions pose some unique challenges. Their time may be more limited and therefore access to care more limited, the population has inherit resistance to the diagnosis and treatment of sleep disorders, and the treatment must be compatible with their job duties.

Improvements in OSA severity: OSA severity is determined by a home sleep apnea test or in-lab sleep study. The measure of OSA severity used by clinicians is the apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) for the in-lab testing and REI for home sleep apnea testing. We discuss the differences in these indexes in Question 5 above. Although there are slight differences in these measures, current clinical guidelines advocate that OSA-related therapies target a reduction to an AHI/RDI < 5 events/h. In the specific instance of PAP therapy, PAP devices have monitoring systems capable of determining the residual severity of OSA and provide an analogous AHI/RDI that has been validated. This technology, however, is not available in non-PAP therapies. The AASM, therefore, would recommend that the AHI or RDI as ascertained by a sleep study on therapy (e.g. oral appliance) or post therapy (e.g. upper airway corrective surgery or bariatric surgery) be used as a measure to monitor improvements in OSA severity.

Adherence to Treatment: Adherence to treatment is readily monitored by PAP-based therapies. Current guidelines recommend that adherence to PAP therapies be defined as use of PAP for at least 4 hours of more for at least 70% of nights. This definition has been adopted by CMS and some 3rd party insurers for reimbursement for PAP devices and PAP-related supplies. Monitoring of adherence with OA therapy has only recently become possible with currently one FDA-approved system available on the market. If an OA is accepted as an effective treatment for moderate-severe OSA, similar criteria as used for PAP based therapies should be used to determine adherence. Measures for adherence are not possible with upper airway corrective surgeries and medical or surgical weight loss, thus it would not be appropriate to use

time-based measures of treatment use in these patients. Rather demonstration of resolution of moderate-severe OSA should be demonstrated. The AASM, therefore, recommends that a time-based measure of adherence using currently accepted clinical criteria described above, be used to assess adherence with the exception of treatments such as upper airway corrective surgery or weight loss, where this would not be possible.

Improved patient symptoms: Although measures are available to assess improvements in patient symptoms, these measures should be considered in the context of a comprehensive assessment performed by a clinician. Sleepiness is the cardinal OSA-related symptom that is the most concerning in transportation personnel in safety sensitive positions. Measures of sleepiness that are utilized in clinical practice include the Epworth sleepiness scale, with an ESS of ≥ 11 taken to define sleepiness. Objective measures of sleepiness, such as the multiple sleep latency test (MSLT) or of alertness, such as the maintenance of wakefulness test (MWT), can help a clinician assess improvements in sleepiness or alertness. However, these tests have large ranges for normative data and normal results can result in false negatives in assessing the risk for a transportation-related accident. Given these concerns, the AASM would advocate that no specific measure be used alone to assess the criteria of improved patient symptoms. Rather, a comprehensive clinical evaluation by a clinician with experience in sleep medicine should be used that may include the measures discussed above if considered appropriate by the evaluating clinician.

We thank you for considering our response, and we welcome any questions or feedback you may have. To discuss this issue in more detail, please contact AASM Executive Director Jerome Barrett at (630) 737-9700.

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References

[1] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. New England Journal of Medicine 1993;328:1230-5.

[2] Quan S, Gillin JC, Littner M, Shepard J. Sleep-related breathing disorders in adults: Recommendations for syndrome definition and measurement techniques in clinical research. editorials. Sleep 1999;22:662-89.

[3] Berger M, Varvarigou V, Rielly A, Czeisler CA, Malhotra A, Kales SN. Employer-Mandated Sleep Apnea Screening and Diagnosis in Commercial Drivers. J Occup Environ Med 2012;54:1017-25.

[4] Howard, Mark E., et al. "Sleepiness, sleep-disordered breathing, and accident risk factors in commercial vehicle drivers." *American Journal of Respiratory and Critical Care Medicine* 170.9 (2004): 1014-1021.

[5] Pack AI, Dinges DF, Maislin G. A Study of Prevalence of Sleep Apnea Among Commercial Truck Drivers. In: Administration FMCS, ed. Washington, D.C.; 2002.

[6] Stoohs RA, Bingham LA, Itoi A, Guilleminault C, Dement WC. Sleep and sleep-disordered breathing in commercial long-haul truck drivers. Chest 1995;107:1275-82.

[7] Platt AB, Wick LC, Hurley S, et al. Hits and misses: screening commercial drivers for obstructive sleep apnea using guidelines recommended by a joint task force. Journal of Occupational and Environmental Medicine 2013;55:1035-40.

[8] McKay MP. Fatal consequences: obstructive sleep apnea in a train engineer. The Annals of Family Medicine 2015;13:583-6.

[9] Raslear TG (2014) Prevalence and Treatment of Sleep Apnea in Safety-Critical Railroad Employees. J Sleep Disord Ther 3:179. doi:10.4172/2167-0277.1000179

[10] Koyama, Renata G. et al. (2012) Prevalence of and risk factors for obstructive sleep apnea syndrome in Brazilian railroad workers. Sleep Medicine 13:8. 1028-1032.

[11] Tregear S, Reston J, Schoelles K, Phillips B. Obstructive Sleep Apnea and Risk of Motor Vehicle Crash: Systematic Review and Meta-Analysis. J Clin Sleep Med 2009;5:573-81.

[12] Tregear S, Resto J, Schoelles K, Phillips B. Continuous positive airway pressure reduces risk of motor vehicle crash among drivers with obstructive sleep apnea: Systematic review and meta-analysis. Sleep 2010;33:1373-80.

[13] Burks SV, Anderson JE, Bombyk M, et al. Nonadherence with Employer-Mandated Sleep Apnea Treatment and Increased Risk of Serious Truck Crashes

[14] 49 CFR Part 219

[15] 49 CFR Part 382

[16] 2015 Pocket Guide to Large Truck and Bus Statistics." Federal Motor Carrier Safety Administration U.S. Department of Transportation. National Transportation Library, April 2015.

[17] Colvin LJ, Dace GA, Colvin, RM, Ojile J, Collop, N. Commercial motor vehicle driver positive airway pressure therapy adherence in a sleep center. J Clin Sleep Med 2016;12(4):4777-485

[18] Berger, MD FCCP, Mark B., Wendy Sullivan, RN, Ross Owen, MPA, Charlotte Wu, MS, Precision Pulmonary Diagnostics, Inc., Schneider National, Inc., and Definity Health Corp. "A Corporate Driven Sleep Apnea Detection and Treatment Program: Results and Challenges." Sleep Apnea Detection and Disordered Breathing Treatment Program. CHEST Journal, 2006.

[19] Marshall NS; Wong KK; Cullen SR; Knuiman MW; Grunstein RR. Sleep apnea and 20-year follow-up for all-cause mortality, stroke, and cancer incidence and mortality in the Busselton health study cohort. J Clin Sleep Med 2014;10(4):355-362.

[20] Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, Stubbs R, Hla KM. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep. 2008 Aug 1;31(8):1071-8.

[21] Obstructive sleep apnea and risk of cardiovascular disease and all-cause mortality: A meta-analysis of prospective cohort studies Wang, Xia et al. International Journal of Cardiology , Volume 169 , Issue 3 , 207 - 214

[22] Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, D'Agostino RB, Newman AB, Lebowitz MD, Pickering TG. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. JAMA 2000;283:1829–1836.

[23] Calhoun, David A., Daniel Jones, Stephen Textor, David C. Goff, Timothy P. Murphy, Robert D. Toto, Anthony White et al. "Resistant hypertension: diagnosis, evaluation, and treatment a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research." *Hypertension* 51, no. 6 (2008): 1403-1419.

[24] Young, Terry, Paul E. Peppard, and Daniel J. Gottlieb. "Epidemiology of obstructive sleep apnea: a population health perspective." American journal of respiratory and critical care medicine 165.9 (2002): 1217-1239.

[25] Martínez-García M, Capote F, Campos-Rodríguez F, et al. Effect of CPAP on Blood Pressure in Patients With Obstructive Sleep Apnea and Resistant Hypertension: The HIPARCO Randomized Clinical Trial. JAMA. 2013;310(22):2407-2415. doi:10.1001/jama.2013.281250

[26] Durán-Cantolla Joaquín, Aizpuru Felipe, Montserrat Jose María, Ballester Eugeni, Terán-Santos Joaquín, Aguirregomoscorta Jose Ignacio et al. Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial BMJ 2010; 341 :c5991

[27] Botros, Nader et al. Obstructive sleep apnea as a risk factor for type 2 diabetes. The American Journal of Medicine , Volume 122 , Issue 12 , 1122 - 1127

[28] Michael Arzt, Terry Young, Laurel Finn, James B. Skatrud, and T. Douglas Bradley "Association of Sleep-disordered Breathing and the Occurrence of Stroke", American Journal of Respiratory and Critical Care Medicine, Vol. 172, No. 11 (2005), pp. 1447-1451.

[29] Susan Redline, Gayane Yenokyan, Daniel J. Gottlieb, Eyal Shahar, George T. O'Connor, Helaine E. Resnick, Marie Diener-West, Mark H. Sanders, Philip A. Wolf, Estella M. Geraghty, Tauqeer Ali, Michael Lebowitz, and Naresh M. Punjabi "Obstructive Sleep Apnea–Hypopnea and Incident Stroke", American Journal of Respiratory and Critical Care Medicine, Vol. 182, No. 2 (2010), pp. 269-277

[30] H. Klar Yaggi, M.D., M.P.H., John Concato, M.D., M.P.H., Walter N. Kernan, M.D., Judith H. Lichtman, Ph.D., M.P.H., Lawrence M. Brass, M.D., and Vahid Mohsenin, M.D.N Engl J Med 2005; 353:2034-2041

[31] Miguel Ángel Martínez-García, Juan José Soler-Cataluña, Laura Ejarque-Martínez, Youssef Soriano, Pilar Román-Sánchez, Ferrán Barbé Illa, Josep María Montserrat Canal, and Joaquín Durán-Cantolla "Continuous Positive Airway Pressure Treatment Reduces Mortality in Patients with Ischemic Stroke and Obstructive Sleep Apnea", American Journal of Respiratory and Critical Care Medicine, Vol. 180, No. 1 (2009), pp. 36-41

[32] Yang EH, Hla KM, McHorney CA, Havighurst T, Badr MS, Weber S. Sleep apnea and quality of life. Sleep. 2000 Jun;23(4):535-41.

[33] Akashiba T, Kawahara S, Akahoshi T, Omori C, Saito O, Majima T, Horie T. Relationship between quality of life and mood or depression in patients with severe obstructive sleep apnea syndrome. CHEST Journal. 2002 Sep 1;122(3):861-5.

[34] Bolitschek J, Schmeiser-Rieder A, Schobersberger R, Rosenberger A, Kunze M, Aigner K. Impact of nasal continuous positive airway pressure treatment on quality of life in patients with obstructive sleep apnoea. European Respiratory Journal. 1998 Apr 1;11(4):890-4.

[35] Tarasiuk A, Reuveni H. The economic impact of obstructive sleep apnea. Curr Opin Pulm Med. 2013 Nov;19(6):639-44.

[36] Potts KJ, Butterfield DT, Sims P, Henderson M, Shames CB. Cost savings associated with an education campaign on the diagnosis and management of sleep-disordered breathing: a retrospective, claims-based US study. Popul Health Manag. 2013 Feb;16(1):7-13.

[37] "Polysomnography and Home Sleep Testing", Medical Policy number 525, Blue Cross Blue Shield of Massachusetts. http://www.bluecrossma.com/common/en_US/medical_policies/525%20Polysomnography%20and%20Home%20Sleep%20Testing%20prn.pdf accessed April 11, 2016.

[38] Hartenbaum N, Collop N, Rosen IM, et al. Sleep Apnea and Commercial Motor Vehicle Operators: Statement From the Joint Task Force of the American College of Chest Physicians, American College of Occupational and Environmental Medicine, and the National Sleep Foundation. Journal of Occupational and Environmental Medicine 2006;48:S4-37.

[39] Ancoli-Israel S, Czeisler CA, George CF, Guilleminault C, Pack AI. Expert Panel Recommendations: Obstructive Sleep Apnea and Commercial Motor Vehicle Driver Safety In; 2008.

[40] FMCSA MRB. Meeting Summary, United States Department of Transportation [released 2008 Jan 14; access date 2016 Apr 15]. In http://mcsacfmcsadotgov/Documents/Jan2012/MEP%20and%20MRB%20Recommendations%20for%20OSAdocx; August 13–14, 2007.

[41] Final Report: Obstructive sleep apnea (Task 11-05) (MCSAC/MRB February 2012 meeting) [released 2011 Dec 13; access date 2016 Apr 15] http://mcsac.fmcsa.dot.gov/documents/DEC2011/Final_Report_Task_11-05.docx. In; 2012.

[42] U.S. Department of Transportation FMCSA. U.S. Federal Register 77 FR 23794. Proposed recommendations on obstructive sleep apnea [Internet]. [released 2012 Apr 20; access date 2016 Apr 15]. Available from: https://www.federalregister.gov/articles/2012/04/20/2012-9555/proposed-recommendations-on-obstructivesleep-apnea.

[43] Colvin LJ, Collop N. Commercial Motor Vehicle Driver Obstructive Sleep Apnea Screening and Treatment in the United States: An Update and Recommendation Overview. Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine 2015.

[44] Dagan Y, Doljansky JT, Green A, Weiner A. Body Mass Index (BMI) as a first-line screening criterion for detection of excessive daytime sleepiness among professional drivers. Traffic injury prevention 2006;7:44-8.

[45] Parks P, Durand G, Tsismenakis A, Vela-Bueno A, Kales S. Screening for Obstructive Sleep Apnea During Commercial Driver Medical Examinations. Journal of Occupational and Environmental Medicine 2009;51:275–82.

[46] Talmage JB, Hudson TB, Hegmann KT, Thiese MS. Consensus Criteria for Screening Commercial Drivers for Obstructive Sleep Apnea: Evidence of Efficacy. Journal of Occupational and Environmental Medicine 2008;50:324-9.

[47] National Standard for Health Assessment of Rail Safety Workers. October 2012. National Transport Commission. www.ntc.gov.au.

[48] Xie, Wen, Sangita Chakrabarty, Robert Levine, Roy Johnson, and James B. Talmage. "Factors associated with obstructive sleep apnea among commercial motor vehicle drivers." *Journal of Occupational and Environmental Medicine* 53, no. 2 (2011): 169-173.

[49] Epstein LJ et al. Clinical guideline for the evaluation, management, and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 2009; 5: 263-276.
[50] Peppard, Paul E., Terry Young, Mari Palta, Jerome Dempsey, and James Skatrud. "Longitudinal study of moderate weight change and sleep-disordered breathing." *Jama* 284, no. 23 (2000): 3015-3021.
[51] 49 CFR Part 40, Section 40.21
[52] http://www.faa.gov/pilots/safety/pilotsafetybrochures/media/Sleep_Apnea.pdf
[53] https://www.fmcsa.dot.gov/driver-safety/sleep-apnea/driving-when-you-have-sleep-apnea
[54] Warsi A, Wang PS, LaValley MP, Avorn J, Solomon DH. Self-management Education Programs in Chronic Disease: A Systematic Review and Methodological Critique of the Literature. Arch Intern Med. 2004;164(15):1641-1649. doi:10.1001/archinte.164.15.1641.
[55] Graber, M., Roller, C, Kaeble, B. Readability Levels of Patient Education Material on the World Wide Web. Journal of Family Practice Jan 1999: 58.
[56] Smith B; Phillips BA. Truckers drive their own assessment for obstructive sleep apnea: a collaborative approach to online self-assessment for obstructive sleep apnea. J Clin Sleep Med 2011;7(3):241-245.
[57] 49.U.S.C. 521(b)(2)(b), either for making a false statement of or concealing a disqualifying condition.
[58] Parthasarathy S, Haynes PL, Budhirafa R, et.al. A national survey of the effect of sleep medicine specialists and American Academy of Sleep Medicine Accreditation on management of obstructive sleep apnea. J Clin Sleep Med 2006;2:133-42.
[59] Parthasarathy S, Subramanian S, Quan SF. A multicenter prospective comparative effectiveness study of the effect of physician certification and center accreditation on patient-centered outcomes in obstructive sleep apnea. J Clin Sleep Med 2014;10(3):243-49.
[60] Weaver TE, Chasens ER. Continuous positive airway pressure treatment for sleep apnea in older adults. Sleep Med Rev. 2007 Apr;11(2):99-111. Epub 2007 Feb 1.
[61] Berry RB, Kushida CA, Kryger MH, Soto-Calderon H, Staley B, Kuna ST. Respiratory event detection by a positive airway pressure device. Sleep. 2012 Mar 1;35(3):361-7.
[62] Antic NA, Catcheside P, Buchan C, Hensley M, Naughton MT, Rowland S, Williamson B, Windler S, McEvoy RD. The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. Sleep. 2011 Jan 1;34(1):111-9.
[63] Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, Chiner E, Masa JF, Gonzalez M, Marín JM, Garcia-Rio F, Diaz de Atauri J, Terán J, Mayos M, de la Peña M, Monasterio C, del Campo F, Montserrat JM; Spanish Sleep And Breathing Network. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. JAMA. 2012 May 23;307(20):2161-8.
[64] Campos-Rodriguez F, Peña-Griñan N, Reyes-Nuñez N, De la Cruz-Moron I, Perez-Ronchel J, De la Vega-Gallardo F, Fernandez-Palacin A. Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. Chest. 2005 Aug;128(2):624-33.
[65] Proposed Recommendations on Obstructive Sleep Apnea. Fed. Reg;77(77): April 20, 2012; Docket # FMCSA-2012-0102
[66] Ramar, K., Dort, L. C., Katz, S. G., Lettieri, C. J., Harrod, C. G., Thomas, S. M., & Chervin, R. D. (2014). Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015. *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine*, *11*(7), 773-827.