Emerging Challenges in Primary Care: 2017

Recent Advances in Management of Obstructive Sleep Apnea
Faculty

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  Head of Alpha-1 Foundation Clinical Resource Center
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  Weston, FL

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  Hempstead, NY
Disclosures

- Franck Rahaghi, MD, MHS, FCCP has no relationships to disclose.

- Arunabh Talwar, MD, FCCP serves as a speaker for Boehringer Ingleheim.
Learning Objectives

1. Understand the pathophysiology of Obstructive Sleep Apnea
2. Recognize the clinical features and presentation of Sleep Apnea
3. Describe comorbidities associated with Sleep Apnea
4. Perform an appropriate evaluation to accurately diagnose Sleep Apnea
5. Discuss recent advances in management of Obstructive Sleep Apnea
PRE-TEST QUESTIONS
Pre-Test ARS Question 1

On a scale of 1 to 5, please rate how confident you would be in the diagnosis and management of a patient with Obstructive Sleep Apnea:

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident
You are evaluating a 35 year old gentleman for his yearly physical examination. You suspect he has Sleep Apnea. The most common presenting symptom of Obstructive Sleep Apnea is:

1. Excessive Daytime Sleepiness
2. Snoring
3. Morning Headache
4. Irritable Bowel Syndrome
5. Nocturnal Enuresis
Pre-Test ARS Question 3

What percentage of Patient Population with BMI >40 kg/m2 has Sleep Apnea:

1. 15
2. 30
3. 50
4. 75
A 65 year old obese male with hypertension and daytime somnolence is found to have severe obstructive sleep apnea, with an apnea-hypopnea index of 42 on an overnight polysomnogram. Which is considered to be first-line therapy for this patient’s condition?

1. An oral dental appliance
2. Continuous positive airway pressure (CPAP)
3. Uvulopalatopharyngoplasty
4. Sleep positioning therapy
5. Tracheostomy
Obstructive Sleep Apnea

- Definition

- A disease of the upper airway
  - Cessation of airflow during sleep
  - Periodic soft tissue obstruction of the airway during sleep
  - Episodes of apnea and hypopnea
  - Multiple arousals from sleep
OSA Definitions

- **Apnea**: Decrease in the peak thermal sensor amplitude by > 90% of baseline for > 10 seconds. Can be central obstructive or mixed.

- **Hypopnea**: Decrease in the nasal pressures by >30% of baseline for a duration of > 10 sec accompanied by >4% O2 desaturation.

- **Complex Sleep Apnea**: Central apneas that develop or become more frequent during CPAP titration for OSA.
OSA Demographics

- 24% of adult men and 9% of adult women. (if OSA is defined as AHI of > 5)
- 4% of adult men and 2% of adult women (if OSA is defined as AHI >5 plus EDS)
- Gender M>F
- Prevalence in women increases with menopause.
OSA: Pathophysiology

- Repetitive UA obstruction is associated with
- Fall in SaO2
- Snoring (Alternating with periods of silence)
- Arrhythmias
  - Decreased HR during UA obstruction
  - Increased HR during apnea termination
- Arousal at apnea termination
- Increased BP in immediate post apneic period.
Pathophysiology of Upper Airway Obstruction in OSA

- OSA results from collapse of the pharyngeal airway during sleep.

Obstruction at level of soft palate and base of tongue

Genioglossal EMG

Genioglossal activation necessary to open airway after obstructive apnea

no flow - apnea

SpO₂ = 95

SpO₂ = 84
Upper Airway Abnormalities in OSA

- Increased BMI, but only ~60% are overweight
- Large neck circumference: 17” m; 16” f
- UA soft tissue enlargement
  - Large tongue base, low lying soft palate/uvula
  - Adenotonsillar hypertrophy
- Skeletal morphology-retrognathia micrognathia
- Nasopharyngeal obstruction
Grading Severity of OSA

- Severity Criteria (Adults)
  - AHI = apneas (≥90% flow reduction) hypopneas (50% flow reduction with 3% ↓ in SaO₂) per hour of sleep
  - Mild: 5-14 /hr of sleep
  - Moderate: 15-30 /hr of sleep
  - Severe: > 30 /hr of sleep

- Judging severity also depends upon:
  - Degree of sleep disturbance
  - Degree of oxygen desaturation
  - Associated cardiac arrhythmias
  - Duration of respiratory events
OSA Risk Factors

- Family history of OSA
- Male gender (for adults)
- Menopausal state in women
- Aging
- Race (African-Americans, Mexican-Americans, Asians and Pacific Islanders)
- Excess body weight – major risk factors
- Central obesity (waist-hip) ratio is more important than general obesity
OSA Risk Factors

Specific craniofacial and oropharyngeal features

- Increasing neck circumference
  - 17 inches in men
  - >16 inches in women
- Nasal narrowing or congestion
- Macroglossia
- Low-lying soft palate
- Enlarged tonsils and adenoid, especially in children
- Mid-face hypoplasia, Retrognathia, Micrognathia or Mandibular hypoplasia
OSA Risk Factors

- Smoking or alcohol use
- Medications (Muscle relaxants)
- Primary disorders
  1. Untreated hypothyroidism (inconsistent data)
  2. Acromegaly
  3. Androgen therapy
  4. Neuromuscular disorders
  5. Stroke
OSA: Common clinical features

- Daytime Sleepiness (Most common complaint)
- Severity of EDS does not correlate closely with AHI
- Repeated awakenings with gasping or choking.
- Snoring
- Witnessed apneas
- Attention deficit disorder and/or hyperactivity (in children)
- Changes in mood (Treatment resistant depression)
OSA: Common clinical features

- Morning headaches
- Night time diaphoresis
- Nocturia
- Excess body weight: BMI>25
- Large neck circumference
- Nasal septal deviation or turbinate hypertrophy
- Crowded posterior pharyngeal space
OSA: Common physical findings

- Enlarged tonsils and adenoids
- High, narrow hard palate
- Large uvula, low soft lying palate
- Macroglossia
- Retro or Micrognathia

Note: Physical exam may be normal
OSA compromises the vital functions of respiration, circulation and sleep

<table>
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<tr>
<th>CONSEQUENCES</th>
<th>INTERMEDIATE MECHANISMS</th>
<th>DISEASES</th>
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<tbody>
<tr>
<td>Obstructive sleep apnoea</td>
<td>Sleep fragmentation</td>
<td>DM 2</td>
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<tr>
<td>Flow Chest Abdomen</td>
<td>Sympathetic activation</td>
<td>Metabolic syndrome</td>
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<td>Polysomnographic registration</td>
<td>Oxidative stress</td>
<td>? Cancer</td>
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<td>Intrathoracic pressure changes</td>
<td>Systemic inflammation</td>
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<td>Arousal</td>
<td>Endothelial dysfunction</td>
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<td>SaO₂</td>
<td>Insulin resistance</td>
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<tr>
<td>Oxygen desaturation</td>
<td>β-cell dysfunction</td>
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<tr>
<td>C3A2 C4A1</td>
<td>Neuronal dysfunction/apoptosis</td>
<td></td>
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</tbody>
</table>

OSA: Consequences

- Increase mortality
- Insulin resistance
- Heart Disease
- Parasomnias (Sleep related eating disorders)
- Driving and work related accidents
- Impaired school and work performance
Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study- Sleep Heart Health Study

- Prospective study examined whether sleep-disordered breathing was associated with an increased risk of death
- 6,441 men and women
- Average follow-up 8.2 yrs

![Kaplan-Meier survival curves across categories of the apnea-hypopnea index (AHI).](image)

<table>
<thead>
<tr>
<th>Apnea-Hypopnea Index (Events/h)</th>
<th>N</th>
<th>Person-Years</th>
<th>Deaths</th>
<th>Mortality Rate</th>
<th>Model 1[^b]</th>
<th>Model 2[^c]</th>
<th>Model 3[^d]</th>
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<td>Men ≤70 y</td>
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<tr>
<td>&lt;5.0</td>
<td>985</td>
<td>8,220</td>
<td>91</td>
<td>11.1</td>
<td>1.00</td>
<td>1.00</td>
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<tr>
<td>5.0-14.9</td>
<td>694</td>
<td>5,697</td>
<td>82</td>
<td>14.4</td>
<td>1.16 (0.85-1.58)</td>
<td>1.16 (0.85-1.58)</td>
<td>1.24 (0.90-1.71)</td>
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<tr>
<td>15.0-29.9</td>
<td>322</td>
<td>2,623</td>
<td>47</td>
<td>17.9</td>
<td>1.44 (1.00-2.08)</td>
<td>1.44 (1.00-2.08)</td>
<td>1.45 (0.98-2.14)</td>
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<tr>
<td>≥30.0</td>
<td>168</td>
<td>1,355</td>
<td>28</td>
<td>20.7</td>
<td>1.88 (1.19-2.95)</td>
<td>1.88 (1.19-2.95)</td>
<td>2.09 (1.31-3.33)</td>
</tr>
</tbody>
</table>

[^b]: Model 1: Adjusted for age (continuous) and race.
[^c]: Model 2: Adjusted for covariates of model 1 and body mass index (continuous).
[^d]: Model 3: Adjusted for covariates of model 2, smoking status (never, former, current), systolic and diastolic blood pressure, prevalent hypertension, diabetes, and cardiovascular disease.

*PLoS Medicine, August 2009*
OSA: Consequences

- Ischemic Heart Disease
- Cardiac Arrhythmias

1. Sinus arrhythmia – most common
   - Relative bradycardia at the onset of apneic episode
   - Relative tachycardia after the termination of the event.

2. Increased likelihood of recurrence of atrial fibrillation
Suspicion for OSA should be high in any hypertensive patient whose BMI is above 27 kg/m2.

- These individuals should be questioned thoroughly for symptoms of OSA.

- Causal association between OSA and hypertension involves both the obesity-hypertension link and an independent role of OSA in chronic BP elevation.
OSA: Consequences

Pulmonary HTN and cor pulmonale (in severe OSA)

- Greater likelihood in persons with:
  - Daytime hypoxemia and hypercapnea
  - Morbid obesity
  - Underlying COPD

- Degree of Pulm HTN is generally mild
Although there was an increased risk of incident CHD in clinic-derived samples, those who were treated with CPAP had the same risk.

Marin, Lancet 2005

12 year follow-up
All Men
N=1651
OSA: Consequences

- Worsens heart function in CHF
- Systemic HTN – independent of obesity
  (failure of systemic BP to drop during sleep: “non-dipping”)
- Stroke
OSA: Consequences

- Depression and Anxiety

- Impaired cognition
  - Alertness
  - Executive function
  - Learning
  - Memory
OSA: Consequences

- Erectile Dysfunction
- Gastroesophageal reflux
- Nocturia
- Greater healthcare utilization
Impact of Untreated Obstructive Sleep Apnea on Glucose Control in Type 2 Diabetes

- Patients with type 2 diabetes, n=60

- Increasing severity of OSA was associated with poorer glucose control after controlling for age, sex, race, BMI, number of diabetes medications, level of exercise, years of diabetes, and total sleep time on PSG (P< 0.0001 for linear trend)
OSA: Evaluation

- Clinical history
- Physical Examination
- Laboratory testing:
  - Routine screening for hypothyroidism is not indicated
  - PSG is required for the diagnosis of OSA
OSA: Polysomnography

- Current standard of practice is an attended laboratory study
  - Full Night: with separate diagnostic and PAP titrations
  - Split-night – an initial diagnostic portion and a subsequent PAP titration on the same night

- Respiratory events are more frequent, last longer and are associated with more profound o2 desaturation during REM sleep

- Paradoxical breathing
5 min segment of a polysomnographic recording showing recurrent apneas & intermittent episodes of oxygen desaturation in severe OSA.
Who Should be treated?

- Moderate to Severe OSA  AHI.15 -29 events/hours
- Severe OSA  AHI > 30 events/hours
- Mild OSA with symptoms or comorbidities
  - Mild OSA  5 - 14 events/hours
  - Symptoms—EDS, Depression, Memory Loss
  - Co morbidities –HTN, CV disease
OSA Therapy

- General measures
- Positive airway pressures
- Oral devices
- UA surgery
OSA: General Measures

- Avoidance of alcohol, smoking and muscle relaxants
- Sleep hygiene
- Safety counseling
- Optimal weight management
- Topical Nasal Corticosteroids: Adjunct therapy for concurrent rhinitis
OSA: General Measures

- Positional Therapy:

Avoidance of supine sleep position if

1. Respiratory effects occur exclusively or predominantly during supine sleep

2. PSG demonstrates normal AHI in the lateral or prone sleep position
OSA: Positive Pressure Airway Therapy

- Treatment of choice for most persons with OSA
  - Functions as a pneumatic splint that maintains the UA patency
  - Increases nasal pressure above $P_{crit}$
  - Higher pressures may be required for REM sleep or supine sleep
Positive Airway Pressure
Before CPAP

With CPAP
OSA: Indications for PAP Therapy

- AHI of > 15 events per hour or
- AHI of >5 and <14 events per hour and
  - Complaints of EDS, mood disorder, impaired cognition or insomnia, or
  - Documented HTN or CAD
  - History of Stroke
OSA: Positive airway pressure modalities

- CPAP with expiratory pressure relief technology (Cflex)
  - A single pressure is provided throughout the respiratory cycle

1. Transient reduction in pressure during expiration
2. Subsequent return of pressure to baseline setting before next inspiration
OSA: Positive airway pressure modalities

Auto-titrating positive airway pressure (APAP) – Variable pressures are provided.

- Uses device specific diagnostic and therapeutic algorithms
- Automatically and continuously adjusts delivered PAP to maintain UA patency
OSA: Beneficiary effects of PAP therapy

- Decreased mortality
- Decreased sleepiness (subjective and objective)
- Decreased Snoring
- Decreased AHI
- Increased SaO2
OSA: Beneficiary effects of PAP therapy

- Improved BP control
- Improved LVEF in patients with CHF
- Decreased healthcare utilization
OSA: Adverse consequences of PAP therapy

- Nasal congestions, epistaxis, dryness or rhinorrhea
- Sinus discomfort or pain
- Facial Skin irritation, rash or abrasion
- Eye irritation
- Gastric distension due to aerophagia
- Chest discomfort and tightness
OSA: Adherence to PAP therapy

▪ PAP use should be monitored objectively

▪ Objective compliance (Use for >4 hours/night for >70% nights) – 50 to 80%

▪ Average nightly use: 5 hours
Effective approaches to improve PAP adherence

- Patient educations
- Heated humidification
- CPAP usage should be objectively monitored
- Careful follow up first in few weeks and then yearly or as needed
- Know the home care company that supplied the machine to your patient
OSA: Factors predicting need for heated humidification

- Age > 60 years
- Use of drying medications
- Presence of chronic mucosal disease
- Prior UPPP
OSA: Approaches to improving PAP adherence

- Inconsistent Benefits:
  - Bilevel Positive Pressure Airway
  - CPAP with expiratory pressure relief technology (Cflex)
  - Ramping mechanism
  - Changing a poorly fitted nasal mask after therapy has started
<table>
<thead>
<tr>
<th>Problem</th>
<th>Solution</th>
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</thead>
<tbody>
<tr>
<td>Unable to tolerate pressure</td>
<td>Set machine to gradually ramp up pressure or auto-adjust CPAP</td>
</tr>
<tr>
<td>Difficulty falling asleep with mask on</td>
<td>Avoid daytime naps, use ramp function</td>
</tr>
<tr>
<td>Dry nose or mouth</td>
<td>Use humidification, if mouth leak try full face mask or chin strap</td>
</tr>
<tr>
<td>Mask removal in sleep</td>
<td>Exclude mouth leak (sore throat), mask leak (rush of air from side of mask). Adjustment of pressure may be required</td>
</tr>
<tr>
<td>Aerophagy (air swallowing)</td>
<td>Reduce pressure or tell patient to sleep propped up</td>
</tr>
<tr>
<td>Dry eyes or excess lacrimation</td>
<td>Adjust mask</td>
</tr>
<tr>
<td>Skin irritation</td>
<td>Recommend mask care (hot water and dilute washing-up liquid, well rinsed) or liners</td>
</tr>
<tr>
<td>Mask claustrophobia</td>
<td>Use nasal cushions, and gradually acclimatise patient during day with machine switched off</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>Prescribe topical steroid or ephedrine, if severe consider surgery</td>
</tr>
</tbody>
</table>

Greenstone.M, Hack.M; Obstructive sleep apnoea; BMJ 2014;348:g3745
OSA: Indications for BPAP

- Excessively high pressure
- Complaints of difficulty breathing out against pressure
- Gastric distension due to aerophagia
OSA: Indications for BPAP

- Comorbid lung disease:
  1. Obstructive or restrictive
  2. Hypoventilation syndrome

- Persistent O2 desaturation despite CPAP therapy
OSA: Indications for APAP

- APAP Titration: To identify a single fixed pressure for subsequent treatment with a conventional CPAP device. (Not recommended for spilt night PAP titration)

- APAP treatment: Used in self adjusting mode for nightly therapy of OSA
Oral Appliances for OSA

Oral Appliance Mechanisms of Action

- Mandibular advancement
  
  and/or

- Maintains tongue in a more anterior position
OSA: Indication for oral devices

- Snoring
- Mild to Moderate OSA
- Severe OSA (in some)
OSA: Types of oral devices

- Mandibular repositioners
  - Displace the mandible and the tongue anteriorly
  - The most commonly used oral devices

- Tongue-retaining devices
  - Secure the tongue in a soft bulb located anterior to the teeth
  - Hold the tongue in an anterior position
  - Preferred for edentulous persons or for people with compromised dentition
OSA: Benefits of Oral devices

- Efficacy: 40-80%
- Compliance: 50-80%
- Follow-up PSG after optimal fit
- Periodic assessments by dentist and sleep physician
OSA: Contraindications to oral devices

- Inability to breath nasally
- Sleep apnea that is primarily central in nature
- In growing children
- For mandibular repositioners:
  1. Inadequate or compromised dentition
  2. Significant TMJ dysfunction
OSA: Upper Airway Surgery

- Indicated primarily for definitive craniofacial or UA abnormalities
- PSG following UA surgery is indicated to determine efficiency
- Requires long term follow up
OSA: Types of upper airway surgery

- Tonsillectomy and adenoidectomy
- To increase dimensions of nasal airway:
  - Nasal septoplasty, polyp removal and turbinectomy.
- To increase dimensions of retropalatal space
  - Uvulopalatopharyngoplasty
OSA: Types of upper airway surgery

- Most effective Surgical techniques:
  - **Tracheotomy**: Only surgical procedure that is consistently effective as a sole procedure for OSA
  - Bariatric surgery for weight management
  - Maxillo – Mandibular advancement
Weight Loss Improves OSA: Best Data Based on Bariatric Surgery

### Surgical Weight Loss and Measures of OSA Severity

<table>
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<tr>
<th>Author</th>
<th>Baseline AHI (95% CI)</th>
<th>Weight</th>
</tr>
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<tbody>
<tr>
<td>Cherud</td>
<td>60.80 (50.65, 70.95)</td>
<td>9.77</td>
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<tr>
<td>Superman</td>
<td>64.00 (51.91, 76.09)</td>
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<td>Pfister</td>
<td>40.00 (24.49, 55.59)</td>
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<td>Guardiana</td>
<td>55.00 (39.62, 70.36)</td>
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<tr>
<td>Dixon</td>
<td>61.00 (49.19, 74.10)</td>
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<td>50.00 (47.08, 53.92)</td>
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<tr>
<td>Lefler</td>
<td>47.80 (34.38, 61.33)</td>
<td>7.86</td>
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<tr>
<td><strong>Overall</strong></td>
<td>54.99 (49.04, 60.94)</td>
<td>100.00</td>
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<tr>
<th>Author</th>
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<td>Dixon</td>
<td>13.40 (8.30, 18.50)</td>
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<td>Fritscher</td>
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<td>Lefler</td>
<td>24.50 (17.26, 31.74)</td>
<td>7.78</td>
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<tr>
<td><strong>Overall</strong></td>
<td>15.78 (12.58, 18.97)</td>
<td>100.00</td>
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- **BMI improves**
  - 55.3 to 37.7 Kg/m²
- **AHI improves**
  - 54.7 to 15.8
- **Residual disease in majority**
  - AHI < 10 in 44%  
  - AHI < 5 in 25%
- **Objective testing recommended after weight loss to determine ongoing need for treatment**

Weight Management Medications (FDA approved)

- Qsymia (phentermine+topiramate)
- Belviq (lorcaserine)
- Contrave (naltraxone+bupropion)
- Saxenda (liraglutide)
- Phentermine only for short term use of 3 months
Hypoglossal Nerve Stimulation Devices

During each breath, the system delivers a signal to the hypoglossal nerve.

The hypoglossal nerve activates the key muscles of the upper airway to ensure the airway remains open during sleep.

During sleep, the system monitors breathing using the respiration sensing lead.

Kezirian E et al. J Sleep Res 2014;23:77-83

Strollo P et al. NEJM 2014;370:139-149
Sleep is important!!!
They knew this 400 years ago!!!

“Sleep is that golden chain that ties health and our bodies together."

Thomas Dekker (1572-1632)
English Playwright
POST-TEST QUESTIONS
Post-Test ARS Question 1

On a scale of 1 to 5, please rate how confident you would be in the diagnosis and management of a patient with Obstructive Sleep Apnea:

1. Not at all confident
2. Slightly confident
3. Moderately confident
4. Pretty much confident
5. Very confident
Post-Test ARS Question 2

You are evaluating a 35 year old gentleman for his yearly physical examination. You suspect he has Sleep Apnea. The most common presenting symptom of Obstructive Sleep Apnea is:

1. Excessive Daytime Sleepiness
2. Snoring
3. Morning Headache
4. Irritable Bowel Syndrome
5. Nocturnal Enuresis
Post-Test ARS Question 3

What percentage of Patient Population with BMI >40 kg/m2 has Sleep Apnea:

1. 15
2. 30
3. 50
4. 75
A 65 year old obese male with hypertension and daytime somnolence is found to have severe obstructive sleep apnea, with an apnea-hypopnea index of 42 on an overnight polysomnogram. Which is considered to be first-line therapy for this patient’s condition?

1. An oral dental appliance
2. Continuous positive airway pressure (CPAP)
3. Uvulopalatopharyngoplasty
4. Sleep positioning therapy
5. Tracheostomy