The Rational Clinical Examination

# Does This Patient Have Obstructive Sleep Apnea?
## The Rational Clinical Examination Systematic Review

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**IMPORTANCE** Obstructive sleep apnea is a common disease, responsible for daytime sleepiness. Prior to referring patients for definitive testing, the likelihood of obstructive sleep apnea should be established in the clinical examination.

**OBJECTIVE** To systematically review the clinical examination accuracy in diagnosing obstructive sleep apnea.

**DATA SOURCES** MEDLINE and reference lists from articles were searched from 1966 to June 2013. Titles and abstracts (n = 4449) were reviewed for eligibility and appraised for evidence levels.

**STUDY SELECTION** For inclusion, studies must have used full, attended nocturnal polysomnography for the reference standard (n = 42).

**MAIN OUTCOMES AND MEASURES** Community and referral-based prevalence of obstructive sleep apnea; accuracy of symptoms and signs for the diagnosis of obstructive sleep apnea.

**RESULTS** The prevalence of sleep apnea in community-screened patients is 2% to 14% (sample sizes 360-1741) and 21% to 90% (sample sizes 42-2677) for patients referred for sleep evaluation. The prevalence varies based on the apnea-hypopnea index (AHI) threshold used for the evaluation (≥5 events/h, prevalence 14%; ≥15/h, prevalence 6%) and whether the disease definition requires symptoms in addition to an abnormal AHI (≥5/h with symptoms, prevalence 2%-4%). Among patients referred for sleep evaluation, those with sleep apnea weighed more (summary body mass index, 31.4; 95% CI, 30.5-32.2) than those without sleep apnea (summary BMI, 28.3; 95% CI, 27.6-29.0; $P < .001$ for the comparison). The most useful observation for identifying patients with obstructive sleep apnea was nocturnal choking or gasping (summary likelihood ratio [LR], 3.3; 95% CI, 2.1-4.6) when the diagnosis was established by AHI ≥10/h). Snoring is common in sleep apnea patients but is not useful for establishing the diagnosis (summary LR, 1.1; 95% CI, 1.0-1.1). Patients with mild snoring and body mass index lower than 26 are unlikely to have moderate or severe obstructive sleep apnea (LR, 0.07; 95% CI, 0.03-0.19 at threshold of AHI ≥15/h).

**CONCLUSIONS AND RELEVANCE** Nocturnal gasping or choking is the most reliable indicator of obstructive sleep apnea, whereas snoring is not very specific. The clinical examination of patients with suspected obstructive sleep apnea is useful for selecting patients for more definitive testing.

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## Clinical Scenarios

### Case 1

A 40-year old married woman presents with concerns about progressive daytime fatigue. She does not sleep well, awakening several times each night for no reason, and then frequently gets out of bed with a morning headache. While at work, she has difficulty concentrating and drifts asleep. While at home on weekends, she takes daytime naps. Except for these problems, she is in good physical and mental health. Her body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) is 25.

### Case 2

A 50-year old male commercial truck driver is accompanied by his wife to see you. She is awakened by her husband's snoring. Although he has snored for years, she now sees him gasp and occasionally choke while he sleeps. He feels well and he is not concerned. He has longstanding hypertension, and he has slowly gained weight over the past 10 years. He does not report feeling sleepy during the day. His BMI is 35.

## Why Is This Question Important?

The obstructive sleep apnea-hypopnea syndrome (OSAS) is characterized by excessive daytime sleepiness and nighttime breathing cessation (apnea) or reduction of airflow (hypopnea). OSAS is associated with significant morbidity and mortality[1-3] but once identified, it can be treated effectively with weight loss, nocturnal continuous positive airway pressure (CPAP), and some surgical procedures. CPAP treatment of OSAS improves hypertension control and quality of life and reduces depression and motor vehicle crashes.[4-7]

**AHI** *apnea-hypopnea index*

**BMI** *body mass index*

**CPAP** *continuous positive airway pressure*

**OSA** *obstructive sleep apnea*

**OSAS** *obstructive sleep apnea syndrome*

Obstructive sleep apnea (OSA) is associated with hypertension, heart failure, arrhythmia, and diabetes. As OSA increases in severity, there is an association with multimorbidity (the co-occurrence of 2 or more diseases).[8]

Establishing a diagnosis of OSA requires evidence of apnea, hypopnea, or both, and cessation of airflow despite the chest wall showing ventilatory effort on overnight polysomnography (**Box 1**). Although an apnea-hypopnea index (AHI) greater than 5 events per hour is now considered abnormal, AHI thresholds were higher in the past, resulting in difficulties comparing older with more recent literature. The determination of OSAS requires evidence of excessive daytime sleepiness.[9,10] Daytime sleepiness may be assessed with sleep questionnaires or by using laboratory measures of sleep propensity, such as the multiple sleep latency test (MSLT), which measures how quickly an individual falls asleep.[11,12]

### Symptoms

Fatigue is one of the most common symptoms reported by patients presenting to their primary care physicians, and it should be distinguished from sleepiness (**Box 2**). Daytime sleepiness in OSAS may develop gradually, resulting in patient unawareness of the change. Specific questions regarding daytime sleepiness should be elicited. The Epworth Sleepiness Scale (ESS) quantifies sleepiness in everyday activities, using an 8-item scale with each item scored from 0 through 3. The ESS score ranges from 0 to 24, with higher scores indicating more sleepiness.[14] Various sleep apnea screening instruments include daytime sleepiness.[15-17]

Two large community studies of unselected adults reported a 35% prevalence of snoring.[18,19] A 9-point snoring severity scale quantified snoring by its frequency, nightly duration, and intensity.[20,21] Sleeping positions affect snoring. Supine positions are associated with more snoring and apnea than the lateral sleeping position.[22,23]

Compared with the general population, individuals with OSA are more likely to be involved in motor vehicle collisions. It is important to solicit a history of drowsiness or falling asleep while driving when evaluating patients for sleep apnea.[24] A family history of sleep apnea is a risk factor for OSA and may be related to craniofacial structure[25,26] or lifestyle factors leading to obesity. Tobacco, alcohol, and sedative use and being postmenopausal may also be related to OSA.

**Box 1. Clinical Definitions of Obstructive Sleep Apnea (OSA)**

**Apnea:** breathing cessation for >10 seconds

**Hypopnea:** reduced respiratory airflow by 30% with a 4% decrease in oxygen saturation

**Apnea-hypopnea index (AHI):** number of apnea and hypopnea events recorded per hour of sleep

- Mild OSA: AHI ≥5-15/h
- Moderate OSA: AHI ≥15-30/h
- Severe OSA: AHI ≥30/h

**OSA syndrome:** AHI ≥5 with evidence of daytime sleepiness

**Box 2. Symptoms of Obstructive Sleep Apnea**

Witnesses report habitual, loud, disruptive snoring, nocturnal gasping or choking, and apnea during the patient's sleep

Snoring

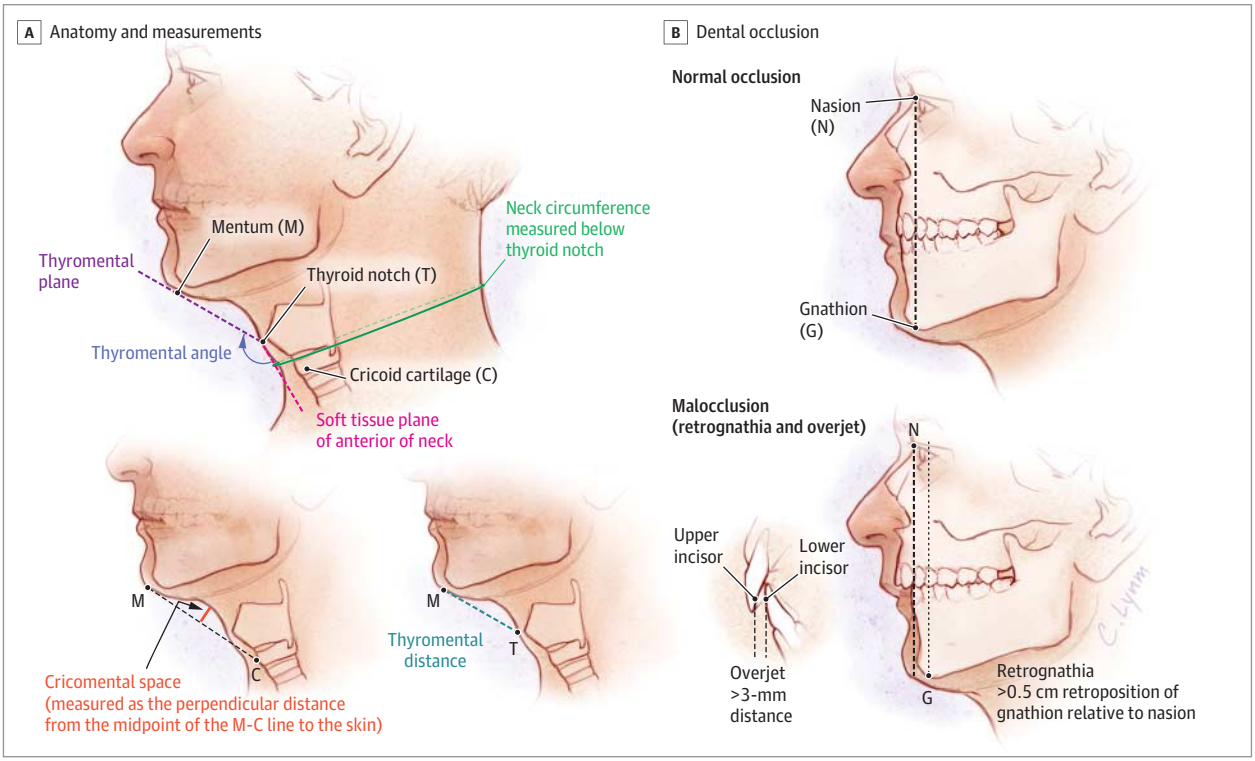
- Primary: occurs without sleep apnea or significant excessive daytime sleepiness
- Habitual: snoring that occurs most nights of the week
- Severe: occurs all night, every night, and is audible down the hall from the sleeping individual
- Apnea: breathing cessation after which a patient may awaken with a gasping or choking sensation

Daytime sleepiness: sleepiness that occurs in a situation when an individual would be expected to be alert

Fatigue: a subjective sense of weariness

Morning headache: possibly related to increased $CO_2$ during apneic episodes[13]

Figure 1. Craniofacial Anatomy and Surface Measurements




## Signs

Numerous physical signs are associated with OSAS. Some require complex measurements of pharyngeal anatomy from fiber optic observations or radiographs, while others measure changes in response to maneuvers. The most commonly used signs are static, anthropometric measurements from simple examination of oropharyngeal and craniofacial structure.

### Anthropometric Measurements

Obesity is associated with OSA and is assessed by measurement of BMI. Neck circumference at the superior border of the cricothyroid membrane can be measured to evaluate excessive adiposity in the upper body. This measurement is performed with the patient in the upright position (**Figure 1**A).

### Craniofacial Structure

Generalist physicians can measure the cricomental space and the thyromental angle and distance (Figure 1A).[26] As the neck enlarges due to adiposity, the cricomental space and thyromental distance shorten (normal cricomental space should be ≥1.5 cm).[27,28]

Relative to patients without sleep apnea, patients with OSA have a more obtuse thyromental angle. Malocclusions are associated with *retrognathia*, which is defined as greater than 0.5 cm retroposition of the most inferior contour of the chin (the "gnathion") relative to the plane of the deepest point of the superior aspect of the nasal bone (the "nasion"). *Overjet* is defined by greater than 3-mm anterior-posterior distance between the upper and lower incisors (Figure 1B).[29]

### Oropharyngeal Examination

The oropharynx (**Figure 2**) is inspected to determine whether soft tissue enlargement decreases the airway volume. Enlargement of the tonsils, tongue, and uvula along with the Mallampati airway class are all associated with OSA.[29-31] The Mallampati class (**Figure 3**) is assessed with the tongue protruded, or in a modified form with the tongue remaining on the floor of the mouth. Both the Mallampati class and tonsillar enlargement are classified into 4 categories, with increasing class indicating greater loss of airway volume.

## Methods

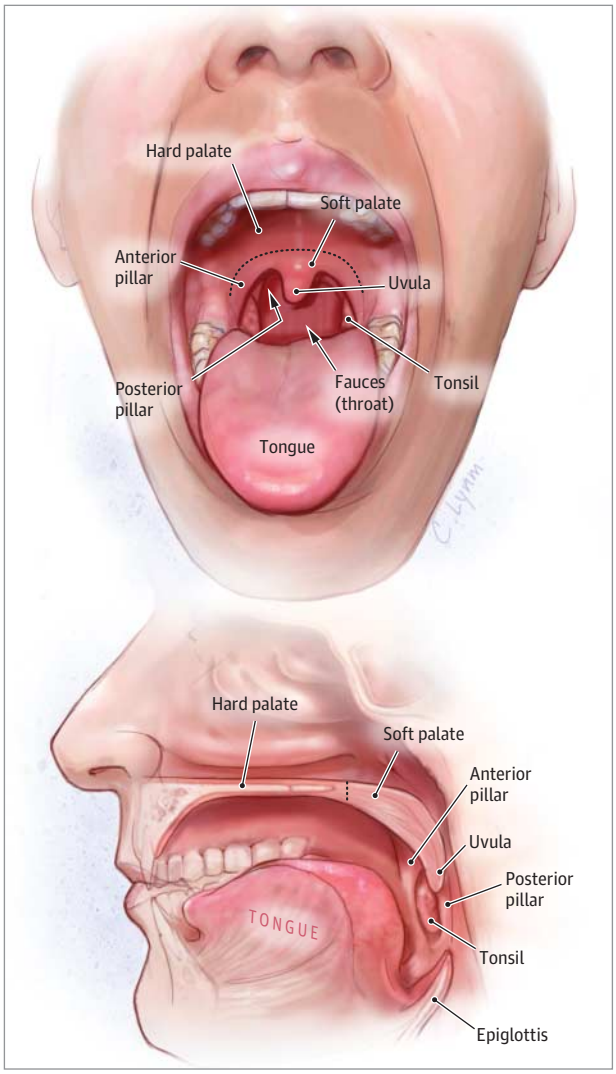
### Search Strategy

We used the MEDLINE database to search for English-language articles related to the clinical evaluation of OSAS that were published between 1966 and June 2013. The MeSH headings *sleep apnea syndromes*, *airway obstruction*, *apnea*, or *polysomnography* followed by the text words *sleep apnea* were used in the following search strategy: *physical examination/or physical exam$; medical history taking; sensitivity and specificity, reproducibility of results, observer variation; diagnostic tests, routine; decision support techniques;* and *Bayes theorem*. In addition, bibliographies from texts of clinical examination and review articles on sleep apnea syndrome were reviewed for additional material.

### Study Selection

Most experts consider full, attended, nocturnal polysomnography to be the reference standard for diagnosis of OSA. Full polysomnography includes electroencephalographic, electromyographic, and electro-oculographic measurements to monitor sleep, as well as measures of thoracoabdominal effort and oxygen saturation. Due to the limited availability and expense of nocturnal polysomnography, home screening technologies and unattended polysomnography have be-

Figure 2. Oropharyngeal Anatomy




come more prevalent for screening purposes. These technologies do not have the same reproducibility of findings as full, attended, nocturnal polysomnography, but have been used in many studies, especially those based in the community.[32,33] In one community-based study that screened patients for OSA using a portable device, subsequent full, attended polysomnography demonstrated that the portable monitoring had misclassified a significant number of patients, with false positives occurring in 45% of the men and 65% of the women. False negatives were less common but still significant (5.8% men; 11% women).[18] For this reason, and because confirming the technical standards of the many portable devices in use was beyond the scope of this article, we limited our analysis to studies that used full, attended nocturnal polysomnography as the reference standard of diagnosis. Studies were excluded if the selected diagnostic threshold for OSA was an AHI above 15/h. We excluded referral-based studies that enrolled many individuals who were referred with a wide range of suspected disorders other than sleep apnea (eg, insomnia, restless legs syndrome). One author (K.A.M.) reviewed the titles and abstracts to identify relevant articles and 2 authors assigned and reviewed quality scores (see the Supplement).[34] Studies of quality levels 1 through 3 were used to create summary measures.

### Data Analysis

We described the patient characteristics and prevalence of OSA and OSAS separately for the community and referral-based studies. The summary prevalence was estimated only for community-based studies because this would represent the prevalence closest to that in unscreened patients. We describe risk factors with odds ratios (ORs). Studies that evaluated the precision of findings were reported using the kappa (κ) results. For symptoms and signs, we calculated the likelihood ratios (LRs) and diagnostic odds ratios (DORs, **Box 3**). We reported the DOR because the studies evaluated different AHI thresholds for diagnosing sleep apnea and the DOR is a measure of overall accuracy, allowing comparisons among the different AHI thresholds. Although most patients at AHI thresholds of 15/h or higher would be both diagnosed and treated for sleep apnea, we first assessed stratum-specific LRs. For findings from a single study, we report the point estimate and confidence interval; findings reported in 2 studies are summarized as a range; findings reported in 3 studies are summarized with univariate random-effects estimates (Comprehensive MetaAnalysis, version 2.2.057, Biostat)[35]; findings evaluated in 4 or more studies are summarized with bivariate random-effects estimates (SAS version 9.2 TS Level 2M3, SAS Institute Inc). Univariate measures were used when the model did not converge on a solution. We explored heterogeneity ($I^2$) to describe the variation across studies using different AHI thresholds; for all findings, the confidence intervals for the LR were narrow even when the $I^2$ suggested heterogeneity, so we provide a single summary LR by combining results at AHI thresholds of 10/h or higher or 15/h or higher.

## Results

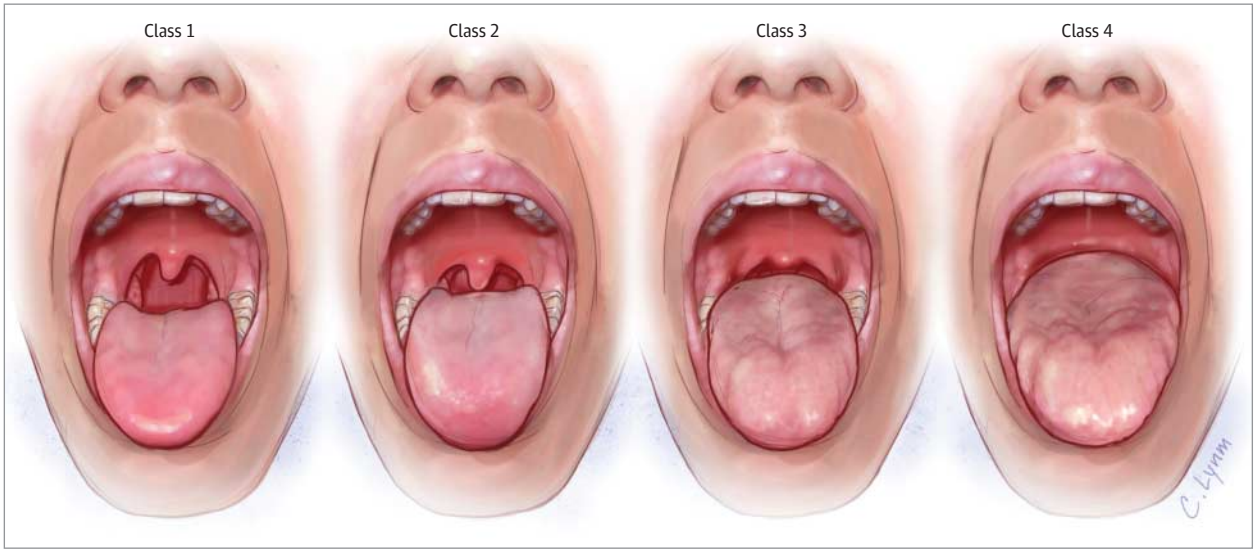
After screening abstracts, 318 articles were retrieved and reviewed in detail to assess the adequacy of the reference standard, quality of evidence, and extractability of data for use in this study (eFigure 1 in the Supplement). The most common reason for exclusion was the use of unattended polysomnography or portable devices for diagnosis. We retained 4 original population-based studies of quality level 1 (sample sizes 360-1741), 6 quality level 1 studies that reanalyzed data from these original studies (sample sizes 589-1741), and 32 quality level 3 studies conducted in referral populations (sample sizes 42-2677).

### Prevalence

#### Community-Based Studies

In community-based studies, individuals with high-risk features of OSA were oversampled (based on the results of screening questionnaires) for polysomnography.[1,36-44] After excluding the prevalence of studies from the same population, we retained 4 studies for estimating the prevalence in a community population.[1,36-38] The population prevalence was estimated by applying the results from the individuals who underwent polysomnography to the original random sample (eTable 1 in the Supplement).[1,36-38] At an AHI threshold of 5/h or higher, the prevalence of OSA ranged from 9% to 17% with higher rates in men. When OSA was defined solely by an AHI of 15/h

Figure 3. Mallampati Classification System




Mallampati classification is assessed with the tongue protruded and without phonation, or in a modified form with the tongue remaining on the floor of the mouth. Class 1 is characterized by visualization of the soft palate, uvula, palatine tonsils, and pillars. As Mallampati class increases, these structures become obscured until only the hard palate is visible (class 4).

or higher, the prevalence was 6% (eTable 1). This value is similar to the prevalence of OSAS in patients who have an AHI threshold of 5/h or higher in combination with excessive daytime sleepiness.

### Referral Populations

There were many referral-based studies, and most of these studies reported a prevalence of sleep apnea of around 50% at an AHI threshold of 10/h or higher or 15/h or higher.[21,26,29,31,45-72] Unlike the community studies, most studies of clinical predictors of sleep apnea used only the AHI as the diagnostic standard rather than the AHI plus objective measures of excessive daytime sleepiness. Due to changes in the recommendations for diagnostic thresholds over time, more recently published studies used a diagnostic threshold of AHI 5/h or higher, whereas older studies reported prevalence based on higher thresholds.

## Risk Factors Associated With OSA

At an AHI threshold of 10 or higher, patients with OSA tended to be men (OR, 3.1; 95% CI, 2.5-3.8) who were older (summary mean age 50 y, 95% CI, 49-51) than those without OSA (summary mean age 46.5 y, 95% CI, 45-48; $P < .001$ for the difference in age; eTable 2 in the Supplement). Affected patients in the referral studies had a summary BMI of 31.4 (95% CI, 30.5-32.2) that was larger than those who did not have OSA (summary BMI, 28.3; 95% CI, 27.6-29.0, $P < .001$ for the comparison; results from individual studies in eTable 2). Smoking status was not studied at consistent levels of AHI thresholds and was reported at various levels of exposure, but in most studies the OR for smoking status had broad confidence intervals that included 1.[41,51,54] Among women, postmenopausal status was associated with OSA after adjusting for other risk factors (OR, 3.5-4.3; AHI ≥15/h).[39,44] Hypertension may be a risk factor for OSA, as well as a consequence of sleep apnea.[73] However, as a screening test for OSA, hypertension alone has minimal impact on its likelihood at AHI thresholds of 10/h or higher or 15/h or higher (LR+ 1.3; 95% CI, 1.2-1.5) (**Table 1**, eTable 3 in the Supplement). Normotensive patients have a lower likelihood of sleep apnea (LR, 0.60; 95% CI, 0.51-0.72). One community study reported the relationship between AHI (threshold of ≥15/h) and multiple motor vehicle collisions controlled for age, sex, and miles driven.[42] Patients who had multiple motor vehicle crashes within the prior 5 years had an OR of 3.1 (95%

**Box 3. Statistical Definitions**

Pretest probability: The probability of disease (typically taken from the prevalence) before factoring in items from the history, physical examination, or other tests. To use Bayes theorem, this is converted to odds, where odds = prevalence/(1−prevalence).

Posttest probability: The probability of disease after factoring in the results of a clinical finding or other tests. The posttest probability of disease = posttest odds/(1 + posttest odds), where posttest odds = pretest odds × LR.

Sensitivity: The proportion of people with a positive test result among those with the target condition

Specificity: The proportion of people with a negative test result among those without the target condition

Likelihood ratio (LR): The relative likelihood that a given test result would be expected in a patient with, as opposed to one without, a disorder of interest. As LRs increase above 1, the test result is better at identifying affected patients. As LRs decrease below 1, the test result is better at identifying unaffected patients. An LR+ is the LR for a positive test result, while an LR− is the LR for a negative test result. The LR+ = sensitivity/(1−specificity) while the LR− = (1−sensitivity)/specificity.

Diagnostic odds ratio (DOR): A single measure of accuracy that tells whether a positive result correctly classifies a patient as having disease and a negative result correctly classifies a patient as unaffected. As the DOR increases beyond 1, the test is more accurate. The DOR = LR+/LR−.

Table 1. Accuracy of Symptoms, Signs, Overall Clinical Impression, and Combination of Findings for Sleep Apnea[a]

| Finding | AHI Threshold (Events/Hour) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | LR+ (95% CI) $I^2$, %, $R^2$,% | LR− (95% CI) $I^2$, %, $R^2$,% | Probability of Sleep Apnea, % (95% CI) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Positive Predictive Value (Baseline Prevalence)[b] | Negative Predictive Value (Baseline Prevalence)[b] |
| | | | | | | 6 | 6 |
| | | | | | | 14 | 14 |
| **Risk Factors** | | | | | | | |
| Hypertension[c] | ≥10[49,51,58,61,66,67] or ≥15[46,63] | 74 (65-81) | 45 (34-55) | 1.3 (1.2-1.5 ) $I^2$=86, $R^2$=0 | 0.60 (0.51-0.72) $I^2$=64, $R^2$=0 | 7.7 (7.1-8.7) | 3.7 (3.2-4.4) |
| | | | | | | 18 (16-20) | 8.9 (7.7-11) |
| **Symptoms** | | | | | | | |
| Nocturnal choking/gasping | ≥10[49,55,58,72] or ≥15[45] | 52 (34-70) | 84 (77-92) | 3.3 (2.1-4.6) $I^2$=76 | 0.57 (0.38-0.76) $I^2$=95 | 17 (12-23) | 3.5 (2.4-4.6) |
| | | | | | | 35 (26-43) | 8.5 (5.8-11) |
| Morning headache | ≥5[50,60,d] | 12-34 | 91-95 | 2.6-3.8 | 0.73-0.93 | 14-20 | 4.5-5.6 |
| | | | | | | 30-38 | 11-13 |
| | ≥10[55,72] or ≥15[50,63] | 22 (12-32) | 85 (82-88) | 1.5 (0.98-2.0) $I^2$=72 | 0.92 (0.82-1.0) $I^2$=88 | 8.7 (5.9-11) | 5.5 (5.0-6.0) |
| | | | | | | 20 (14-25) | 13 (12-14) |
| Reported apnea | ≥10[47,55,58,67,68,72] or ≥15[45,46,54] | 80 (73-87) | 42 (33-51) | 1.4 (1.2-1.5) $I^2$=79, $R^2$=73 | 0.47 (0.38-0.56) $I^2$=59, $R^2$=0 | 8.2 (7.1-9.3) | 2.9 (2.4-3.5) |
| | | | | | | 19 (16-21) | 7.1 (5.8-8.4) |
| Excessive daytime sleepiness | ≥5[59,60,62,69,71] | 46 (38-53) | 68 (59-78) | 1.4 (1.0-1.9) $I^2$=81 | 0.80 (0.67-0.92) $I^2$=89 | 8.2 (6.0-11) | 4.9 (4.1-5.5) |
| | | | | | | 19 (14-24) | 12 (9.8-13) |
| | ≥10[47,55,58,68,72] or ≥15[45,46,54,69,71] | 50 (41-60) | 61 (52-71) | 1.3 (1.1-1.4) $I^2$=50, $R^2$=0 | 0.81 (0.74-0.88) $I^2$=47, $R^2$=30 | 7.7 (6.6-8.2) | 4.9 (4.5-5.3) |
| | | | | | | 18 (15-19) | 12 (11-13) |
| Snoring | ≥5[1,38,d] | 79-97 | 27-46 | 1.3-1.5 | 0.12-0.45 | 7.7-8.7 | 0.8-2.8 |
| | | | | | | 18-20 | 1.9-6.8 |
| | ≥10[55,67,68,72] or ≥15[45,46] | 90 (77-96) | 19 (9.7-35) | 1.1 (1.0-1.1) $I^2$=26 | 0.60 (0.49-0.73) $I^2$=0 | 6.6 (6.0-6.6) | 3.7 (3.0-4.5) |
| | | | | | | 15 (14-15) | 8.9 (7.4-11) |
| **Signs** | | | | | | | |
| Mallampati class[e] | ≥5[64] | 65 (54-75) | 60 (47-72) | 1.6 (1.1-2.3) | 0.60 (0.41-0.85) | 9.3 (6.6-13) | 3.7 (2.6-5.1) |
| | | | | | | 21 (15-27) | 8.9 (6.3-12) |
| | ≥15[31] | 55 (40-69) | 65 (57-72) | 1.6 (1.1-2.2) | 0.68 (0.47-0.98) | 9.3 (6.6-12) | 4.2 (2.9-5.9) |
| | | | | | | 21 (15-26) | 10 (7.1-14) |
| Pharnygeal narrowing[f] | ≥10[58,72] or ≥15[29,46] | 67 (38-95) | 53 (25-80) | 1.4 (1.1-1.7) $I^2$=70 | 0.63 (0.39-0.87) $I^2$=96 | 8.2 (6.6-9.8) | 3.9 (2.4-5.3) |
| | | | | | | 19 (15-22) | 9.3 (6.0-12) |
| **Combinations of Findings** | | | | | | | |
| Overall clinical impression[c] | ≥10[49,55,72] or ≥15[52] | 58 (49-67) | 67 (60-73) | 1.7 (1.5-2.0) $I^2$=0 | 0.67 (0.60-0.74) $I^2$=10 | 9.8 (8.7-11) | 4.1 (3.7-4.5) |
| | | | | | | 22 (20-25) | 9.8 (8.9-11) |

(continued)

CI, 0.8-12.7) for sleep apnea with an AHI between 5/h and 15/h. A history of motor vehicle crashes had a greater association with moderate or severe OSA (AHI ≥15/h; OR, 7.3, 95% CI, 1.8-25).

## Precision of the Clinical Examination

Interrater reliability has been assessed for several of the craniofacial and pharyngeal measurements. Tsai and coauthors[28] reported

Table 1. Accuracy of Symptoms, Signs, Overall Clinical Impression, and Combination of Findings for Sleep Apnea[a] (continued)

| Finding | AHI Threshold (Events/Hour) | Sensitivity, % (95% CI) | Specificity, % (95% CI) | LR+ (95% CI) $I^2$, %, $R^2$,% | LR− (95% CI) $I^2$, %, $R^2$,% | Probability of Sleep Apnea, % (95% CI) | |
|---|---|---|---|---|---|---|---|
| | | | | | | Positive Predictive Value (Baseline Prevalence)[b] | Negative Predictive Value (Baseline Prevalence)[b] |
| STOP-Bang Questionnaire[75,g] | ≥5[48,65,71] | 88 (83-92) | 53 (43-62) | 1.8 (1.5-2.3) $I^2$=54 | 0.23 (0.15-0.35) $I^2$=66 | 6<br>10 (8.7-13) | 6<br>1.4 (0.9-2.2) |
| | | | | | | 14<br>23 (20-27) | 14<br>3.6 (2.4-5.4) |
| | ≥15[48,65,71] | 93 (91-94) | 35 (27-44) | 1.4 (1.2-1.6) $I^2$=59 | 0.20 (0.16-0.25) $I^2$=0 | 8.2 (7.1-9.3) | 1.3 (1.0-1.6) |
| | | | | | | 19 (16-21) | 3.2 (2.5-3.9) |
| Snoring Severity Scale[h] ≥4 and body mass index >26 | ≥15[21] | 97 (92-99) | 38 (27-51) | 1.6 (1.3-2.0) | 0.07 (0.03-0.19) | 9.3 (7.7-11) | 0.4 (0.2-1.2) |
| | | | | | | 21 (18-25) | 1.1 (0.5-3.0) |
| Berlin Questionnaire[77,i] | ≥5[37,56,69] | 80 (68-88) | 46 (20-75) | 1.4 (1.0-2.0) $I^2$=89 | 0.43 (0.33-0.55) $I^2$=0 | 8.2 (6.0-11) | 2.7 (2.1-3.4) |
| | | | | | | 19 (14-25) | 6.5 (5.1-8.2) |
| | ≥15[37,56,69,70] | 91 (85-95) | 37 (20-59) | 1.5 (1.1-2.0) $I^2$=90 | 0.28 (0.13-0.59) $I^2$=72 | 8.7 (6.6-11) | 1.8 (0.8-3.6) |
| | | | | | | 20 (15-25) | 4.4 (2.1-8.8) |
| Names-2[69] | ≥5[69] | 85 (81-88) | 42 (31-53) | 1.5 (1.2-1.8) | 0.36 (0.26-0.51) | 8.7 (7.1-10) | 2.2 (1.6-3.2) |
| | | | | | | 20 (16-23) | 5.5 (4.1-7.7) |
| | ≥15[69] | 92 (88-95) | 34 (28-41) | 1.4 (1.3-1.6) | 0.24 (0.16-0.36) | 8.2 (7.7-9.3) | 1.5 (1.0-2.2) |
| | | | | | | 19 (18-21) | 3.8 (2.5-5.5) |

Abbreviations: AHI, apnea-hypopnea index; LR, likelihood ratio.

[a]See eTables 3-11 for results from individual studies. Heterogeneity ($I^2$) assessed when there were at least 3 studies in the summary measure. By convention, $I^2$ = 50%-74% is considerate moderate heterogeneity and ≥75% is considered high heterogeneity. $R^2$ is a random-effect measure that expresses the percent of heterogeneity between studies attributable to the AHI threshold. This was assessed for summary measures when there were at least 3 studies at each threshold.

[b]A prevalence of 6% is the summary prevalence at AHI ≥15/h from population-based studies. A prevalence of 14% is the summary prevalence at AHI ≥5/h from population-based studies. For each finding, the top number in this column represents the probability of sleep apnea when the finding is present or absent at a prevalence of 6%; the number below represents the probability of sleep apnea at a prevalence of 14%.

[c]Univariate random-effects estimate because bivariate random effects did not converge adequately on a solution.

[d]Range used because the finding was evaluated in only 2 studies.

[e]Mallampati class 3 or 4 is considered positive.

[f]Studies used varying definitions of pharyngeal narrowing.

[g]Univariate random effects used because the finding was evaluated in only 3 studies. Questionnaire available online.[76]

[h]Snoring Severity Scale evaluated in only 1 study. The Snoring Severity Scale assigns 0-3 points each to (1) the frequency of nights with snoring, (2) duration of snoring during the night, and (3) loudness of snoring.[21]

[i]Berlin questionnaire available online.[77]

excellent interrater reliability between 2 specialist raters for measurement of cricomental space of less than 1.5 cm (κ = 1.0), moderate to excellent agreement for tonsillar enlargement and grading of pharynx (κ = 0.73; κ = 0.78 respectively), moderate agreement for overbite (κ = 0.61), and only slight agreement for retrognathia (κ = 0.22). When measurements were obtained by sleep specialists, high intra-rater reliability was demonstrated for assessment of Mallampati class, thyromental distance and angle, and neck circumference. Inter-rater reliability for thyromental angle measurement was 0.83 (95% CI, 0.71-0.90).[26]

## Accuracy of the Clinical Examination

Forty-two studies that met our criteria examined the accuracy of at least one component of the clinical examination for predicting the presence of OSA in patients referred to a sleep laboratory with suspected OSA. Only 10 of the community studies used full, attended, nocturnal polysomnography to examine the accuracy of the clinical examination.[1,36-44]

### Symptoms

At AHI thresholds of 10/h or higher or 15/h or higher, the presence of nocturnal choking or gasping was the most useful individual finding for identifying patients with OSA (summary LR, 3.3; 95% CI ,2.1-4.6, Table 1, eTable 4 in the Supplement), though the results showed heterogeneity. The presence of other individual findings, including snoring, excessive daytime sleepiness, or headache, each had an LR of less than 2.0 at thresholds of 10/h or higher or 15/h or higher (eTables 5-7 in the Supplement). Snoring is a frequent complaint, but

Table 2. Sleep Apnea Clinical Score Results for Probability of Sleep Apnea[a]

| Sleep Apnea Clinical Score | Serial LR (95% CI) | Probability of Sleep Apnea, % (95% CI)[b] | |
|---|---|---|---|
| | | Baseline Prevalence 6% | Baseline Prevalence 14% |
| >15 | 5.2 (2.5-10) | 25 (14-39) | 46 (29-62) |
| 10.01-15 | 2.0 (0.94-4.4) | 11 (5.7-22) | 25 (13-42) |
| 5.01-10 | 1.1 (0.62-1.9) | 6.6 (3.8-11) | 15 (9.2-24) |
| ≤5 | 0.25 (0.15-0.42) | 1.6 (0.9-2.6) | 3.9 (2.4-6.4) |

Abbreviation: LR, likelihood ratio.

[a]Sleep Apnea Clinical Score evaluated in only 1 study, with an apnea-hypopnea index of >10 events/hour.[49] The Sleep Apnea Clinical Score includes snoring, nocturnal gasping or choking, hypertension, and neck circumference.

[b]Prevalence varies based on the apnea-hypopnea index threshold used for the evaluation (≥5 events/h, prevalence 14%; ≥15/h, prevalence 6%).

as a single finding to suggest OSA it has no value (summary LR, 1.1; 95% CI, 1.0-1.1) with remarkable consistency across 6 studies at AHI levels of 10/h or higher or 15/h or higher ($I^2$ = 26%, $P$ = .24).

The absence of reported apneas had the lowest LR and narrowest confidence interval for sleep apnea with AHI thresholds of 10/h or higher or 15/h or higher (summary LR, 0.47; 95% CI, 0.38-0.56; Table 1, eTable 8 in the Supplement). The absence of snoring made OSA (at AHI ≥10/h) less likely (summary LR, 0.60; 95% CI, 0.49-0.73). At a threshold of AHI 5/h or higher, the absence of snoring made OSA even less likely (LR range, 0.12-0.45). Although the presence of excessive daytime sleepiness is used to define OSAS, its absence is unhelpful in discriminating among those with and without OSA at varying diagnostic thresholds (summary LR, 0.81; 95% CI, 0.74-0.88 at AHI ≥10/h or ≥15/h, Table 1, eTable 6 in the Supplement).

### Signs

**Oropharyngeal Examinations and Craniofacial Structure** | Whether the volume of the oropharynx is quantified with the Mallampati class or described by qualitatively assessing oropharyngeal volume, the presence of a narrow oropharynx (LR range, 1.4-1.6) or a more normal oropharyngeal volume (LR range, 0.60-0.68) provided similar limited information for the diagnosis of OSA at thresholds from 5/h or higher to 15/h or higher (Table 1, eTable 9).

**Craniofacial Structure** | Although the distance between the maxillary anterior teeth and the mandibular anterior teeth (overjet) is more pronounced in patients with sleep apnea, data from one study showed that both the positive and negative LR for an overjet of at least 3 mm had confidence intervals that included 1.[29] The assessment of retrognathia had LR confidence intervals that included 1.0 both for its presence and absence.[29]

**Neck Circumference** | Patients with OSA have a larger neck circumference than those without sleep apnea (summary mean [SD] difference, 2.7 [0.53] cm, $I^2$ = 94%) at AHI thresholds of 5/h or higher to 15/h or higher. No studies evaluated a diagnostic threshold for determining the LR for large neck circumference as an independent finding. The neck-height ratio, proposed by Dancey and coauthors[74] to account for variation in neck circumference due to an individual's height, can be calculated by dividing the neck circumference by height, but we found no data to support its use.

## Combinations of Findings

### Overall Impression

Four high-quality studies assessed sleep physicians' ability to diagnose OSA based on the history and physical examination (Table 1, eTable 10).[51,54,57,74] The results from the 4 trials were fairly consistent, but not dramatically different from the individual symptoms and signs despite each study using sleep medicine specialists to establish the clinical impression (summary positive LR, 1.7; 95% CI, 1.5-2.0; $I^2$ = 0%; summary negative LR, 0.67; 95% CI, 0.60-0.74; $I^2$ = 10%; sensitivity, 58%; specificity, 67%).

### Clinical Prediction Rules and Scores

We assessed only those studies that reported composites of symptoms and signs or clinical prediction rules that can be easily obtained and interpreted by primary care physicians. With one exception, all of the studies reporting composites of signs and symptoms were referral-based. We did not perform a meta-analysis of the composites of signs and symptoms because of the variation in definitions of symptoms and signs among studies. Our findings regarding heterogeneity (Table 1, eTable 11 in the Supplement) are consistent with a recently published meta-analysis that assessed 10 different screening questionnaires designed to diagnose OSA, in which the authors reported marked heterogeneity in the selected studies ($I^2$ >75%).[75]

A score below 4 on the Snoring Severity Scale and a BMI lower than 26 makes OSA much less likely (LR, 0.07; 95% CI, 0.03-0.19; sensitivity, 97%; specificity, 38%; Table 1; eTable 11 in the Supplement) at a diagnostic threshold of AHI 15/h or higher.[21] Similarly, results below the diagnostic threshold on the STOP-Bang questionnaire (8 items),[76] Berlin Questionnaire (10 items), [77] and Names-2 (7 items; a composite of historical items, ESS, measures of oropharynx, neck circumference, and BMI [eTable 11]) make sleep apnea less likely. None of these combinations of findings at the selected diagnostic thresholds makes the diagnosis of sleep apnea more likely, with summary LR less than 2 at AHI thresholds of 5/h and 15/h or higher.

Many of the large referral-based studies that developed prediction rules for sleep apnea are not practical for use in primary care. To facilitate use by clinicians, Flemons and coauthors[49] converted their original regression equation into a score, the Sleep Apnea Clinical Score (SACS) (**Table 2**, eTable 11). The 4 model variables are easily obtained by history and physical examination (neck circumference, hypertension, habitual snoring, and noctur-

nal gasping or choking). As neck circumference increases, fewer of the other 3 variables are required to increase the likelihood of OSA. On its own, neck circumference of 50 cm or higher is associated with a SACS above 15, and so even without any other features of OSA this confers modestly increased risk. At a diagnostic threshold of AHI 10/h or higher, SACS above 15 increase the likelihood of OSA (LR, 5.2; 95% CI, 2.5-10). Scores of 5 or lower made OSA less likely in this referral-based population (LR, 0.25; 95% CI, 0.15-0.42).

## Discussion

Our results are limited by diagnostic standards for clinically relevant OSA, which greatly varied in the studies we assessed. Most of the studies did not require objective evidence of excessive sleepiness to establish the diagnosis of OSAS. Although an AHI of 5/h or higher is recommended for the diagnosis of OSA, controversy exists regarding treatment of asymptomatic patients, especially those with mild sleep apnea. Most of the studies analyzed in this review were referral-based, in which the prevalence of OSA is high, and for most of the composites of signs and symptoms there was significant study heterogeneity. This limits the generalizability of these findings.

The definition of a positive sleep study has changed over time. Before we began the formal meta-analysis, we noticed that the studies with an AHI threshold of 10/h or higher had similar results to those with a threshold of 15/h or higher, and that both diagnosed patients with OSA of similar severity. This range was distinct from higher values (AHI ≥20/h) that would have diagnosed more severe sleep apnea, or lower values (≥5/h) that would have diagnosed "mild" sleep apnea. Thus, we combined studies for which the threshold was AHI 10/h or higher with those that had an AHI 15/h or higher. Because our decision to combine these studies with different thresholds might introduce uncertainty, we evaluated confidence intervals around the LRs, the $I^2$ as a measure of whether heterogeneity is real or spurious, and conducted a meta-regression to find a threshold effect when there were at least 3 studies at each threshold.[35] The $I^2$ values provide estimates that suggest whether the variance between studies is "real" or results from sampling error. By convention, an $I^2$ of 25% is considered low, 50% moderate, and 75% a high probability of the variance being real.[35] Whether the $I^2$ for the findings of OSA were low, moderate, or high, the confidence interval for almost all the LRs were in a range where the variance would not create a big impact on the probability of disease.

In a meta-regression for hypertension as a risk factor, reported apneas, and excessive data sleepiness, the $R^2$ was 0% for all but 2 summary measures. This means that the threshold effect of AHI 10/h vs 15/h did not account for the variance between studies and provides justification for combining the results. For the positive LR for reported apneas, 73% of the variance between studies was attributable to the threshold effect. However, the summary positive LR of 1.4 (95% CI, 1.2-1.5) makes the threshold effect clinically unimportant.

While we believed there was suitable justification for combining the results from studies using either an AHI threshold of 10/h or higher or 15/h or higher, this decision does create a classification problem for those patients with the mildest sleep apnea (AHI ≥5 to <10). Therefore, we chose to display the sensitivity, specificity, and LRs for studies using an AHI 5/h or higher separately from those using AHI 10/h or higher or 15/h or higher. For the 3 findings in which there were enough studies to evaluate the impact of AHI thresholds (excessive daytime sleepiness, STOP-Bang questionnaire, Berlin questionnaire), a random-effects meta-regression showed that the AHI threshold of 5/h or higher vs 10/h or higher or 15/h or higher created no difference for the positive LR ($P$ = .42 for the effect of AHI threshold) or on the negative LR ($P$ = .88). If additional studies confirm this for other findings, the choice of AHI threshold directly affects the prevalence of disease, but the value of symptoms and signs might be similar across all thresholds.

## Scenario Resolution

### Case 1

The patient's partner notes that she does not snore and she does not have nocturnal choking, gasping, or apnea. Examination shows normal craniofacial structure, neck circumference of 30 cm, a normal blood pressure, and a BMI of 25. The ESS score is 9. Based on community studies, her pretest probability of having OSA defined by an AHI 5/h or higher with evidence of objective evidence of excessive daytime sleepiness is approximately 2%. With a snoring severity scale score of 0 plus normal BMI, the LR is 0.07. There is thus a very low posttest probability of OSA (<1%) and other medical causes of fatigue require evaluation

### Case 2

The patient has had 2 minor motor vehicle collisions over the past 5 years. He has a neck circumference of 42 cm and a Mallampati airway grade of 3. Based on his symptoms of habitual snoring, nocturnal gasping and choking, the presence of hypertension, and his neck circumference, his SACS is 30.[49] Using a diagnostic threshold of AHI 10/h or higher, the likelihood ratio is at least 5.0. Assuming a community prevalence in men of approximately 15% for OSA (AHI ≥5/h without excessive daytime sleepiness), his posttest probability is close to 50%. Although his ESS score is only 8, objective measures of sleep propensity in the sleep laboratory demonstrate excessive daytime sleepiness. A sleep specialist recommends weight loss and nocturnal CPAP.

## Bottom Line

Most individual symptoms and signs have limited utility in determining the likelihood of OSA, and no one sign is sufficiently precise to rule in or rule out this condition. Although the absence of snoring makes a diagnosis of OSA less likely, snoring on its own is common and does not discriminate between those with and without OSA. Thus, snoring must be interpreted in the context of other symptoms and signs. Likewise, self-reported sleepiness and morning headaches do not help discriminate among patients with and without OSA. It is somewhat surprising that the overall impression of sleep medicine physicians of the likelihood of OSA in individual patients does not perform much better than the limited utility of individual findings. It is important to recognize that persons with normal body

weight who do not snore are unlikely to have OSA, and their complaints of daytime sleepiness or fatigue should prompt an evaluation for alternative diagnoses.

Although the evidence shows that a number of recently published multi-itemed questionnaires may help rule out OSA, they are not helpful in identifying patients affected by sleep apnea. Fortunately, it appears that an explicit combination of only a few findings, expressed as the SACS, has promise for identifying patients most likely to have OSA. Although the test is seemingly easy to use, validation at current diagnostic thresholds in more general populations by primary care clinicians would provide important evidence to justify its use in routine screening.

## ARTICLE INFORMATION

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