# International Classification of Sleep Disorders 3: the 2023 Text Revision Update (ICSD-3-TR)

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UPMC
LIFE CHANGING MEDICINE

# Disclosures:

I have received grant funding in the past through the University of Pittsburgh from Bayer Pharmaceuticals, Philips Respironics, Respicardia, and Sommetrics.

I have received consulting fees in the past from Bayer Pharmaceuticals, NovaResp Technologies, Philips Respironics, and Powell Mansfield.

I am currently consulting for Apnimed Inc.

I served as the chair of the ICSD-3-TR Sleep Related Breathing Disorders Working Group

# History of the ICSD

- The first nosology of sleep disorders was developed by the Association of Sleep Disorders Centers and the Association for the Psychophysiological Study of Sleep and published in SLEEP in 1979.

- This Diagnostic Classification of Sleep and Arousal Disorders (DCSAD) classified disorders based on symptoms.

- The American Academy of Sleep Medicine with the European, Japanese, and Latin American sleep societies, created a new nosology, the International Classification of Sleep Disorders in 1990.

- The ICSD classified disorders by known or presumed pathology and described:
  - Diagnostic, duration, and severity criteria
  - Epidemiology and risk factors
  - Pathology and pathophysiology
  - Life course
  - Laboratory test findings
  - Differential diagnosis

# The original ICSD classification

1. Dyssomnias
   A. Intrinsic sleep disorders (Insomnia, Narcolepsy, OSA, RLS, etc)
   B. Extrinsic sleep disorders (Environmental sleep disorder, Inadequate Sleep Time, etc)
   C. Circadian rhythm sleep disorders
2. Parasomnias
   A. Arousal disorders
   B. Sleep-wake transition disorders
   C. REM related parasomnias
   D. Other parasomnias
3. Sleep disorders secondary to mental, neurologic or medical disorders
   A. Associated with mental disorders
   B. Associated with neurologic disorders
   C. Associated with medical disorders
4. Proposed sleep disorders

# Updating ICSD

- Every 5-10 years, the AASM puts together a Task Force to update the ICSD.
- The process has slowly moved from an expert panel to evidence-based literature review.
- Slow move to increase prominence of PSG findings for diagnosis.
- In 2020, the AASM put together a panel to update the ICSD-3.

| Year | Update |
|---|---|
| 1990 | ICSD |
| 1997 | ICSD-R (Revised) |
| 2005 | ICSD-2 |
| 2014 | ICSD-3 |
| 2023 | ICSD-3-TR (Text Revision) |

# ICSD-3-TR goals

- Perform literature reviews since those used for ICSD-3 and update disease descriptions where new knowledge of epidemiology, pathophysiology, risk factors was available.
- Provide more consistent information across diseases on things like life course, sex/racial differences, differential diagnosis.
- Update diagnostic criteria only where there was strong evidence to justify making a change.
- **NOT to confirm prior diagnostic criteria or disease descriptions.**

# What about clinical management?

- The ICSD provides a description of how diseases are defined.
- Recommendations for how to treat each disorder are made by the AASM (or others) in clinical practice guidelines.
- Nevertheless, how you define what is a disease to some extent depends on whether treatment improves outcomes.

# Practical use of the ICSD-3-TR

- Relatively brief summary (400 pages) of the definitions of all sleep disorders.
- It is an easy resource for trainees to review an unfamiliar disorder. Each entry is ~5 pages.
- It is expected that all board-certified sleep physicians are familiar with the content.

# Type 1 Narcolepsy – ICSD3

A+B+C

A. Daily irrepressible need to sleep or daytime lapses into drowsiness.

B. The presence of one or both of the following:

   1. Cataplexy and mean sleep latency ≤ 8 mins and ≥ 2 SOREMPs on MSLT. A SOREMP within 15 mins on preceding PSG may replace one SOREMP on MSLT.

   2. CSF hypocretin-1 ≤ 110 pg/mL

C. Not better explained by another disorder.

# Type 1 Narcolepsy – ICSD3-TR

A+B+C

A. Daily irrepressible need to sleep or daytime lapses into drowsiness.

B. The presence of one or both of the following:

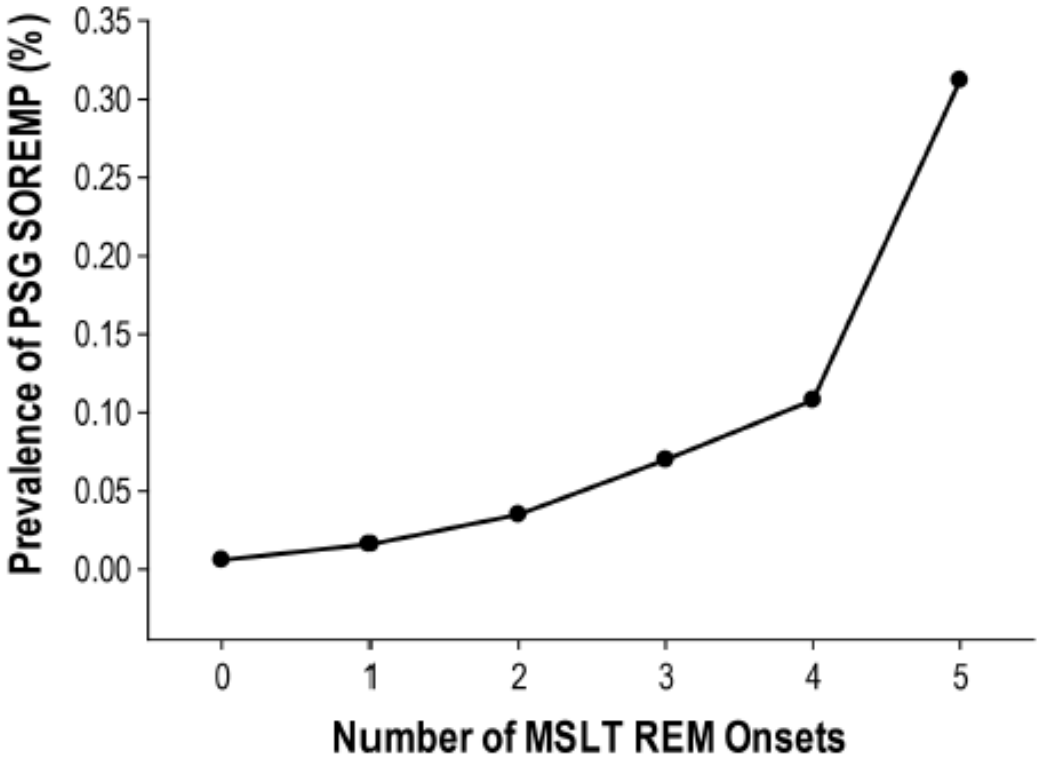
   1. Cataplexy and either: ~~mean sleep latency ≤ 8 mins and ≥ 2 SOREMPs on MSLT. A SOREMP within 15 mins on preceding PSG may replace one SOREMP on MSLT.~~
      a. Mean sleep latency ≤ 8 mins and ≥ 2 SOREMPs on MSLT.
      b. A SOREMP within 15 mins on nocturnal PSG.

   2. CSF hypocretin-1 ≤ 110 pg/mL

C. Not better explained by another disorder.

# Predictive value of nocturnal SOREMP

- Analysis of 3,059 patients undergoing PSG/MSLT and 79,651 undergoing PSG




- Positive predictive value of nocturnal SOREMP in those getting MSLT (using ICSD-2): 99.5%
- Prevalence in general population: 0.8%

- Predictors of false positive nocturnal SOREMP:
  - Shiftwork
  - PAP titration

Cairns A et al. SLEEP 2015; 38:1575-81

# Rationale for change:

- A SOREMP on PSG is highly specific for narcolepsy and would avoid the burden of MSLT in patients who have this finding.
- Limiting use of this to patients who have cataplexy (which is also highly specific) prevents misdiagnosis in the setting of shiftwork, acute medication changes, etc.
- Note: may want to still pursue MSLT if cataplexy is atypical.

# Chronic Insomnia Disorder – ICSD3

A+B+C+D+E+F

A. One or more of the following nocturnal symptoms:
   1. Difficulty initiating sleep.
   2. Difficulty maintaining sleep.
   3. Final awakening earlier than desired.
   4. Resistance to going to bed on appropriate schedule.
   5. Difficulty sleeping without caregiver present.

B. One or more of the following daytime symptoms due to nighttime issues:
   1. Fatigue/malaise.
   2. Impaired attention, concentration, memory.
   3. Impaired social, family, occupational, or academic performance.
   4. Mood disturbance/irritability.
   5. Subjective daytime sleepiness.
   6. Hyperactivity, impulsivity, aggression.
   7. Proneness for errors/accidents.
   8. Concerns about or dissatisfaction with sleep.

C. Problems not explained by inadequate sleep opportunity.

D. Symptoms occur ≥ 3 times/wk.

E. Symptoms present ≥ 3 months.

F. The sleep/wake difficulties are not better explained by another disorder.

# Chronic Insomnia Disorder – ICSD3-TR

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   7. Proneness for errors/accidents.
   8. Concerns about or dissatisfaction with sleep.

C. Problems not explained by inadequate sleep opportunity.

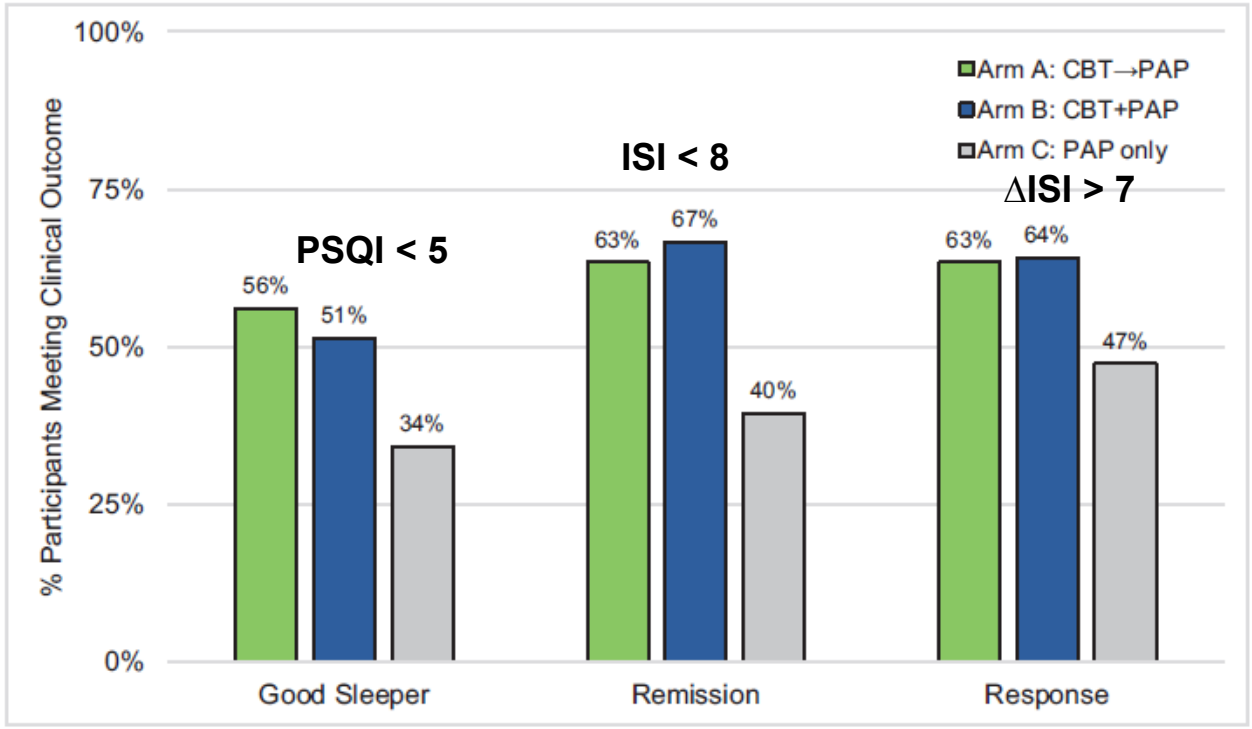
D. Symptoms occur ≥ 3 times/wk.

E. Symptoms present ≥ 3 months.

F. The sleep/wake difficulties are not ~~better explained by another disorder~~ solely due to another disorder.

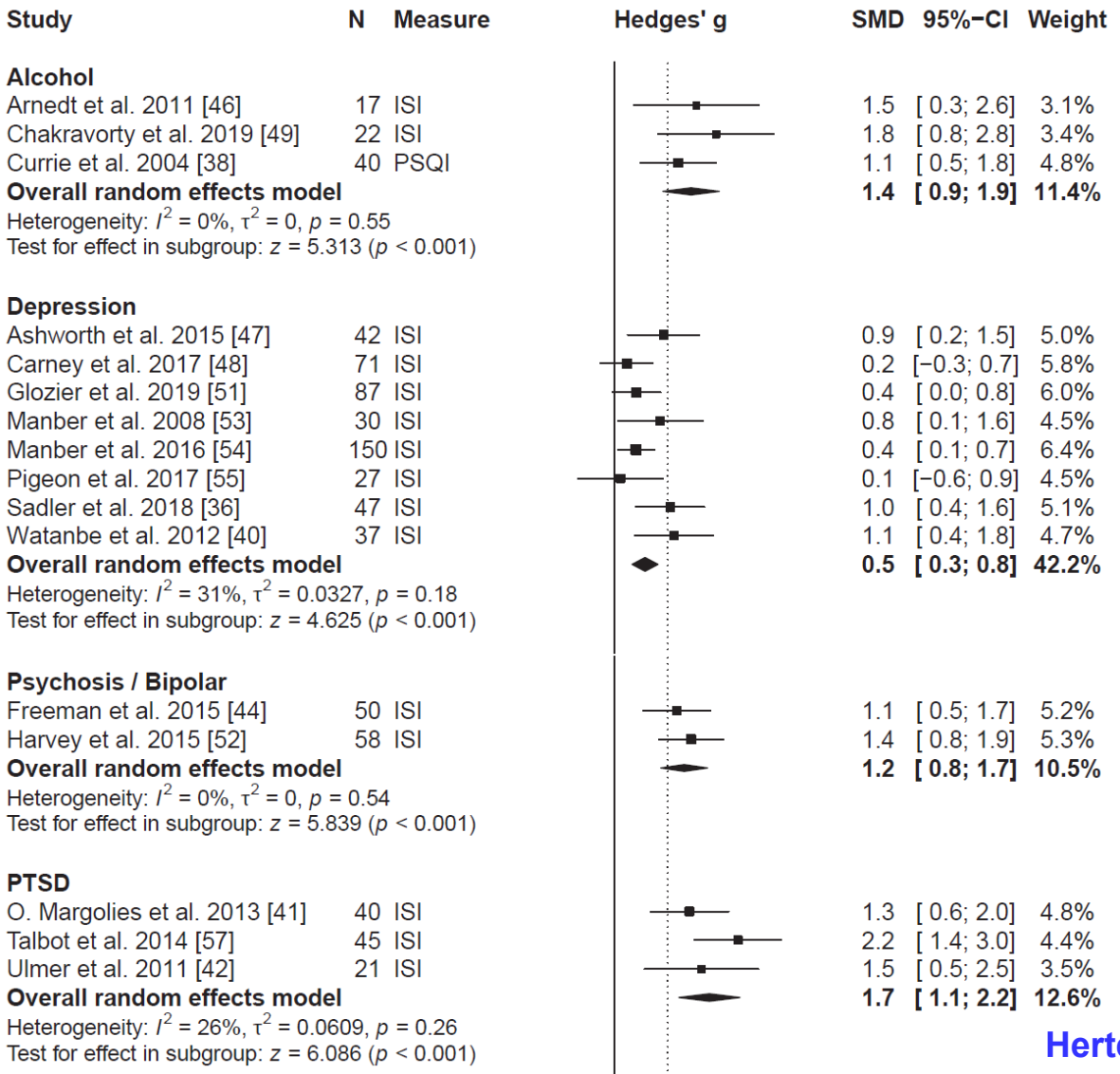
# Treating comorbid insomnia in OSA

- 121 patients with OSA and comorbid insomnia randomized to:
  - CBT-I and simultaneous PAP
  - CBT-I and subsequent PAP
  - PAP alone




Ong JC et al. SLEEP 2020; 43:zsaa41

# Treating insomnia in psychiatric diseases




Hertenstein E et al. Sleep Med Rev 2022; 62:101597

# Rationale for change:

- Sleep difficulties due to an underlying disorder may over time become a source of stress and lead to development of a comorbid insomnia.
- Intervention studies have repeatedly demonstrated that treating comorbid insomnia improves outcomes in patients with two (or more) disorders affecting sleep.

# Adult OSA – ICSD3

((A and B) or C

A. The presence of one or more of the following:
    1. Sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms.
    2. Wakes with breath-holding, gasping, or choking.
    3. Bed partner reports habitual snoring or breathing interruptions during sleep.
    4. Hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes.
B. PSG or HSAT demonstrates AHI ≥ 5 events/hr.
C. PSG or HSAT demonstrates AHI ≥ 15 events/hr.

# Adult OSA – ICSD3-TR

(((A and B) or C) and D

A. The presence of one or more of the following:
   1. Sleepiness, ~~nonrestorative sleep,~~ fatigue, insomnia, or other symptoms leading to impaired sleep-related quality of life.
   2. Wakes with breath-holding, gasping, or choking.
   3. Bed partner reports habitual snoring or breathing interruptions during sleep.
   4. ~~Hypertension, mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes.~~

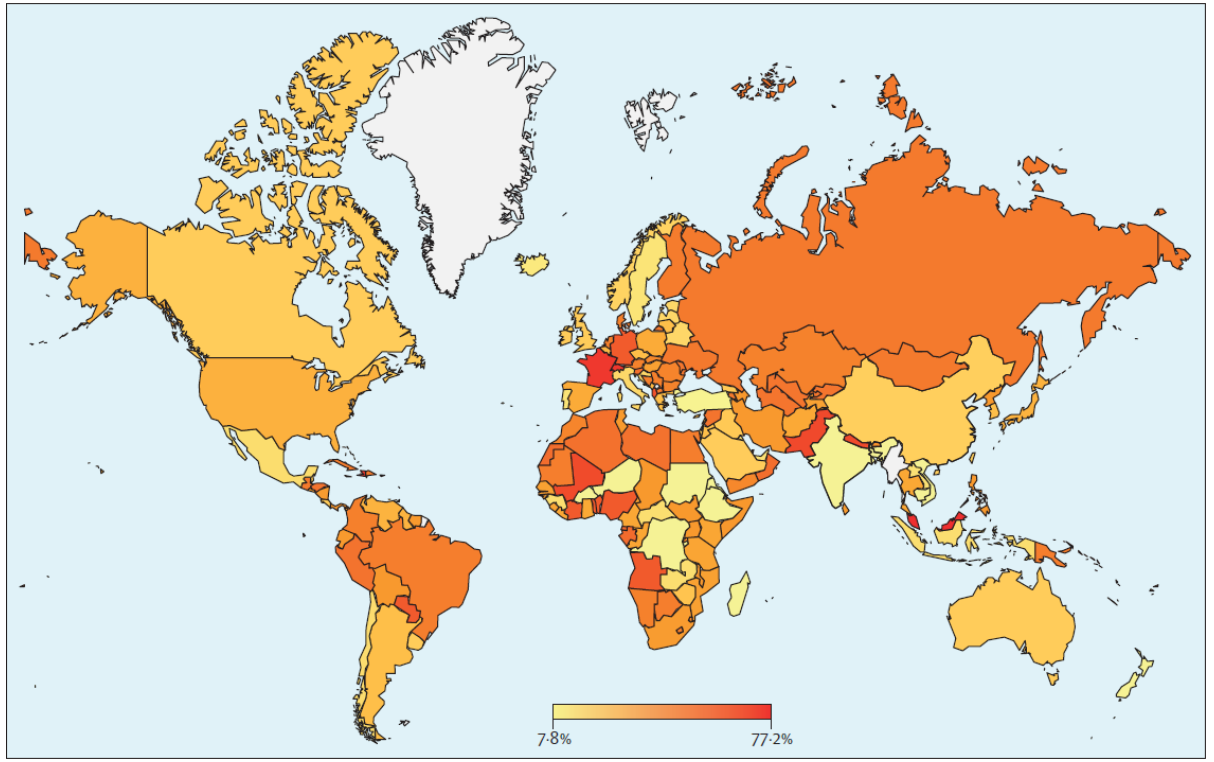
B. PSG or HSAT demonstrates AHI ≥ 5 events/hr.

C. PSG or HSAT demonstrates AHI ≥ 15 events/hr.

D. Not better explained by another disorder.

# Worldwide prevalence of AHI ≥ 5

936,360,689 adults globally




Benjafield AV et al, Lancet Respir Med 2019; 7:687-98

# Prevalence of elevated AHI in Hypnolaus

Prevalence in Adults aged 35-75 in 2009-2013

| | Chicago Criteria | CMS Criteria | AASM 2012 Criteria |
|---|---|---|---|
| Men | | | |
| AHI ≥ 5 | 85.4% | 59.2% | 84.0% |
| Women | | | |
| AHI ≥ 5 | 64.1% | 35.3% | 60.8% |

Hirotsu C et al, JCSM 2019; 15:183-94

# Cross-sectional association of OSA and CVD

**ADJUSTED* RELATIVE ODDS (95% CONFIDENCE INTERVAL) OF PREVALENT CORONARY HEART DISEASE, HEART FAILURE, OR STROKE, ACCORDING TO QUARTILE OF THE APNEA–HYPOPNEA INDEX**

| | Quartile | | | | |
|---|---|---|---|---|---|
| | I | II | III | IV | p Value† |
| Coronary heart disease | | | | | |
| Full model | 1.0 | 1.01 (0.77–1.32) | 1.20 (0.92–1.57) | 1.22 (0.93–1.59) | 0.08 |
| Parsimonious model | 1.0 | 0.92 (0.71–1.20) | 1.20 (0.93–1.54) | 1.27 (0.99–1.62) | 0.004 |
| Heart failure | | | | | |
| Full model | 1.0 | 1.19 (0.56–2.53) | 1.96 (0.99–3.90) | 2.20 (1.11–4.37) | 0.008 |
| Parsimonious model | 1.0 | 1.13 (0.54–2.39) | 1.95 (0.99–3.83) | 2.38 (1.22–4.62) | 0.002 |
| Stroke | | | | | |
| Full model | 1.0 | 1.24 (0.76–2.01) | 1.38 (0.86–2.83) | 1.55 (0.96–2.50) | 0.06 |
| Parsimonious model | 1.0 | 1.15 (0.72–1.83) | 1.42 (0.91–2.21) | 1.58 (1.02–2.46) | 0.03 |

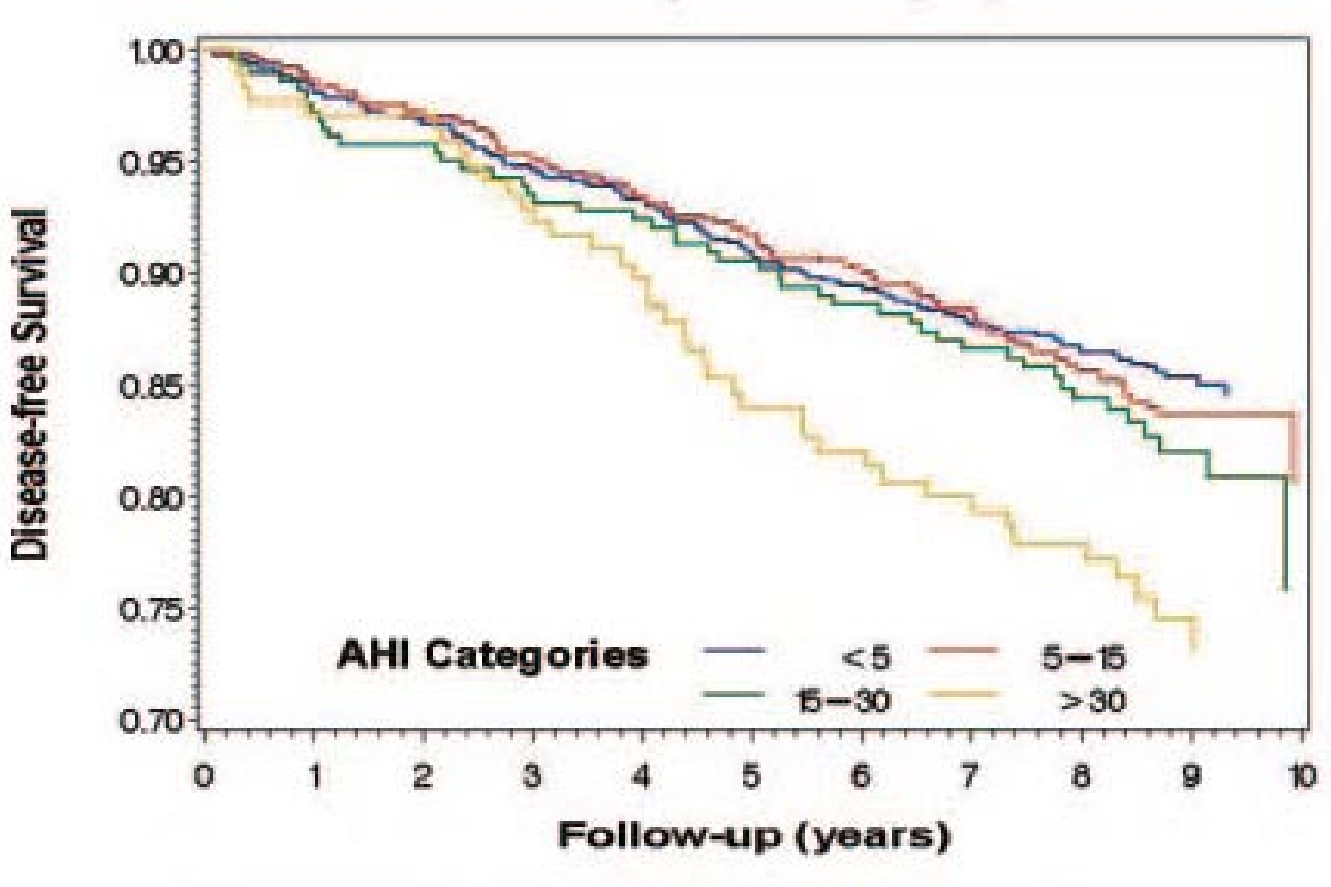
Q1: AHI < 1.3
Q2: AHI 1.3-4.4
Q3: AHI 4.4-11.0
Q4: AHI > 11.0

Full model includes age, race, sex, BMI, smoking, total chol, HDL, DM, HTN, SBP, anti-HTN meds.
Parsimonious model includes age, race, sex, total chol, HDL, DM.

Shahar E et al. AJRCCM 2001; 163:19-25

# OSA and incident coronary artery disease in men

Incident CAD defined as revascularization, MI, or cardiac death

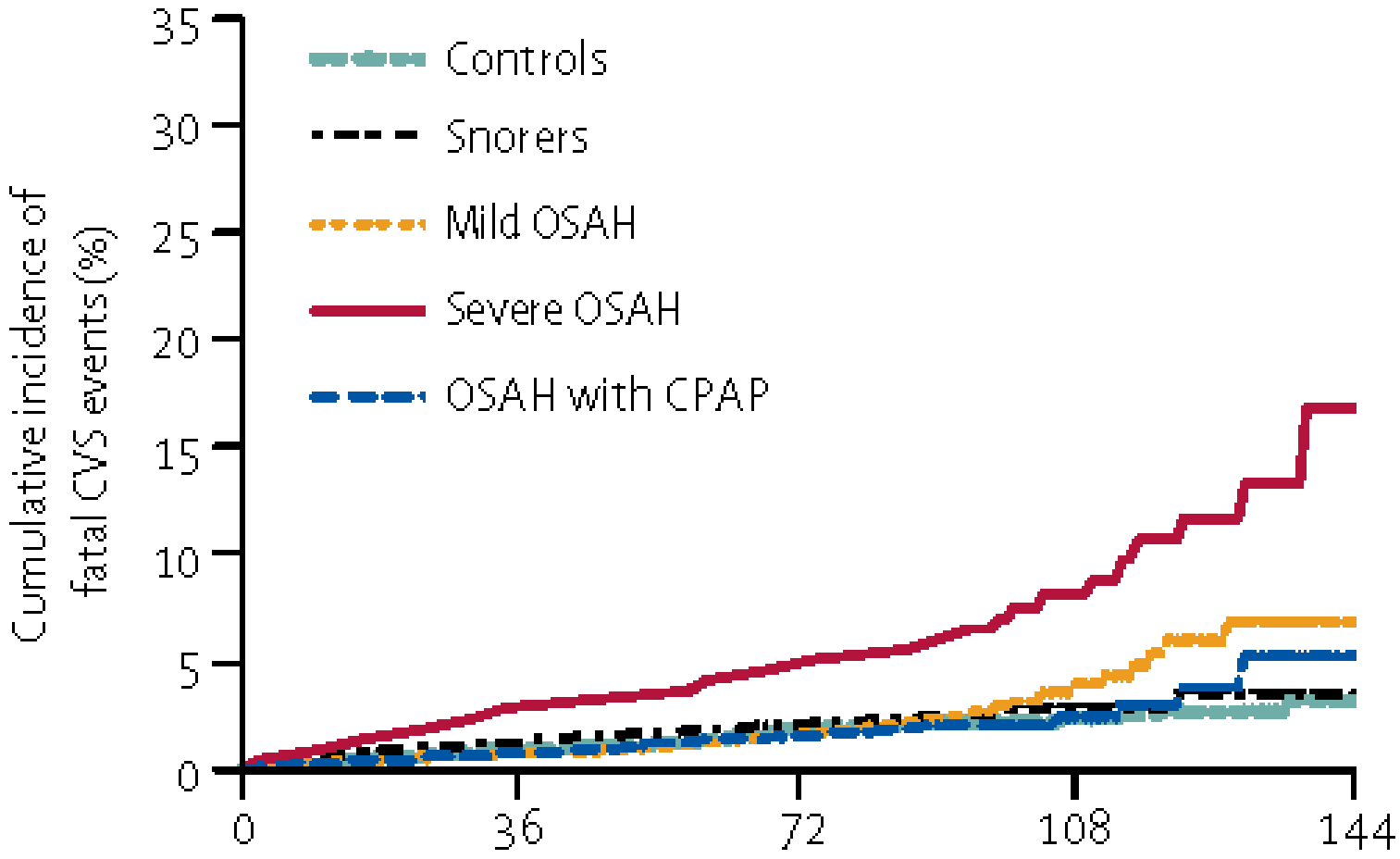



| | AHI < 5 | AHI 5-15 | AHI 15-30 | AHI > 30 |
|---|---|---|---|---|
| HR* | 1.00 | 0.94 (0.71-1.24) | 1.07 (0.75-1.52) | 1.45 (0.99-2.13) |

*Adjusted for age, race, BMI, smoking.

Gottlieb D et al. Circulation 2010; 122:352-60

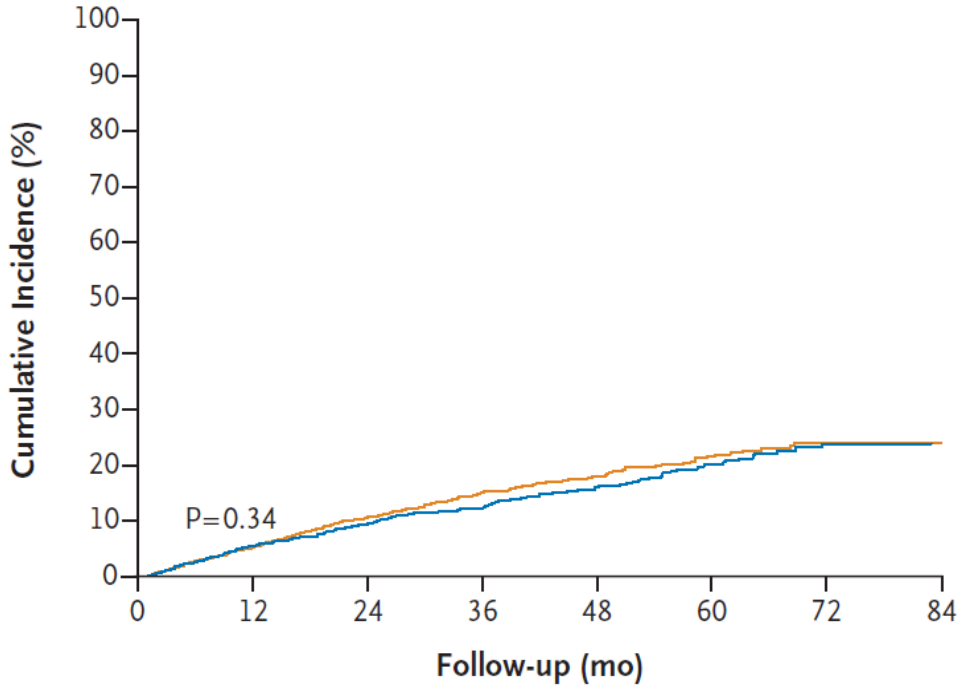
# OSA and fatal cardiovascular events




Marin J et al, Lancet 2005; 365: 1046-53

# RCT of treatment of non-sleepy OSA

RCT of 2,717 non-sleepy moderate-severe OSA and CVD patients randomized to CPAP or usual care for 3.7 years

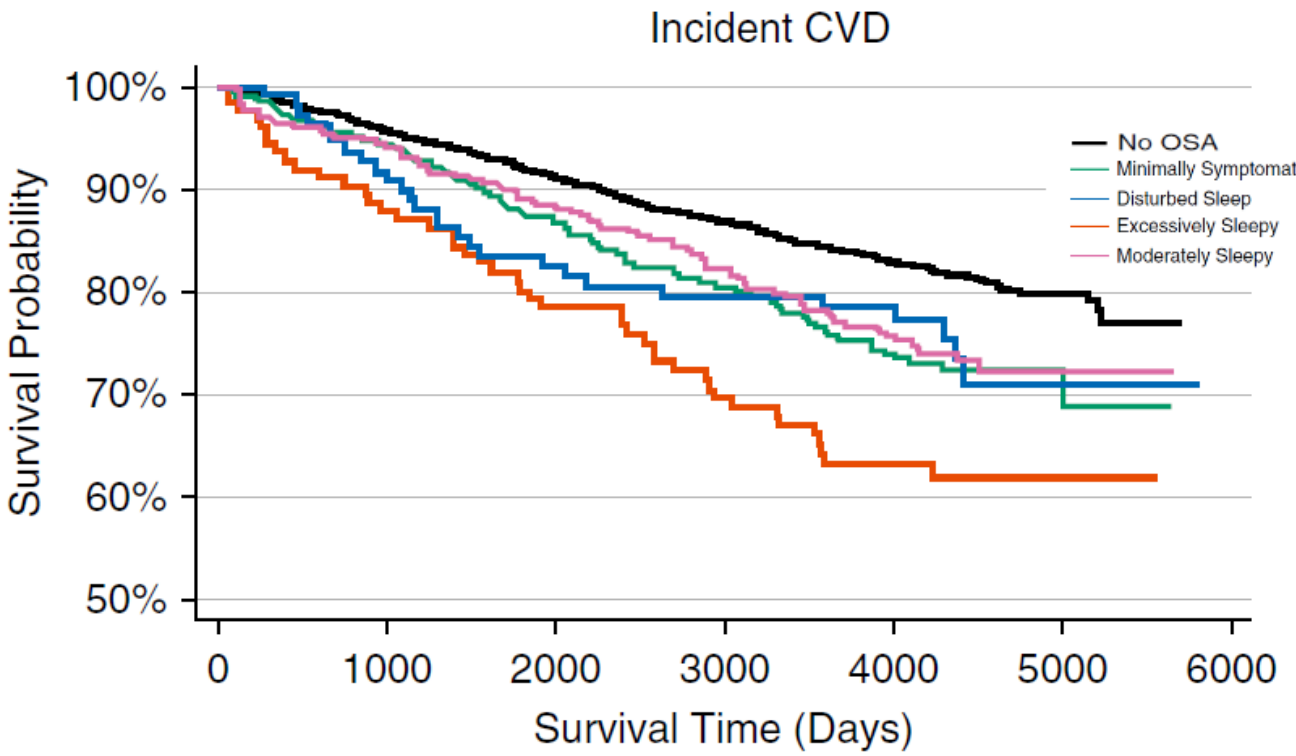



| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CPAP | 1346 | 1222 | 1118 | 754 | 482 | 278 | 146 | 146 |
| Usual care | 1341 | 1211 | 1108 | 727 | 499 | 290 | 103 | 103 |

No effect on CVD endpoints.

McEvoy RD et al, NEJM 2016; 375: 919-31

# OSA subgroups and incident CVD



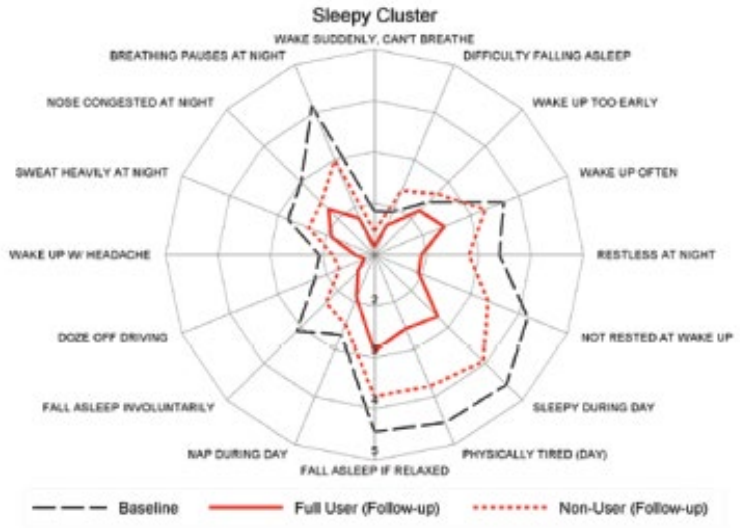

| | Adjusted HR* |
|---|---|
| Min Symptoms | 0.80 |
| Disturbed Sleep | 0.72 |
| Mod Sleepy | 0.79 |
| Excess Sleepy | **2.01** |

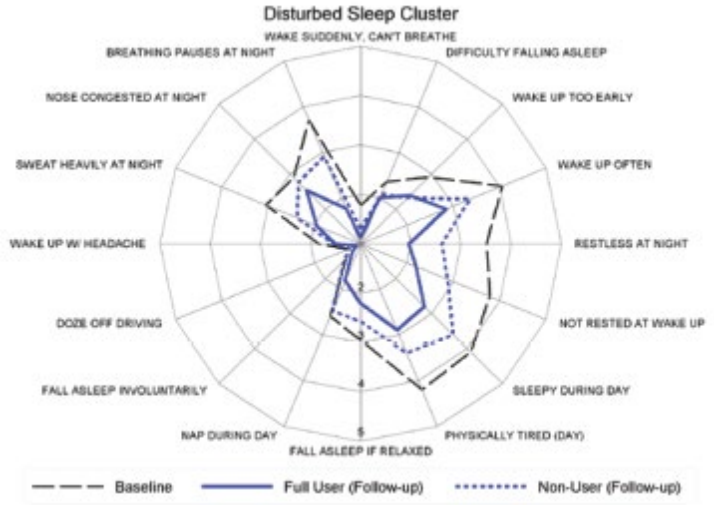
*Adjusted for age, sex, BMI, T2DM, HTN, HDL, TChol, TG, EtOH, Smoking, Race, Ethnicity, Statin Use

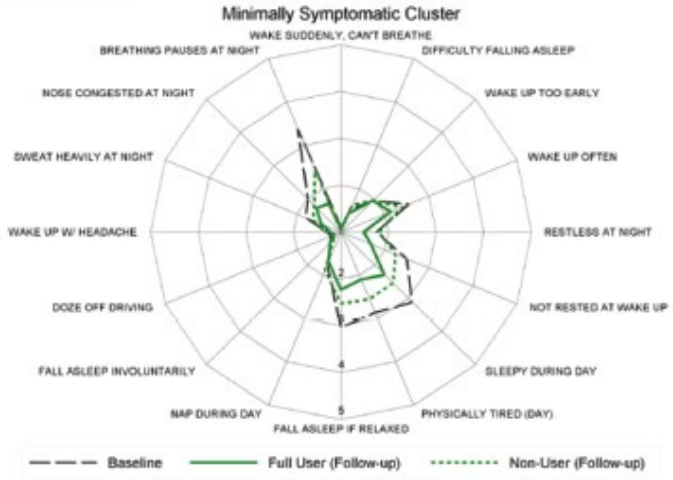
Only excessively sleepy moderate – severe OSA patients are at elevated CVD risk.

Mazzotti DR et al. AJRCCM 2019; 200: 493-506

# Who benefits from treatment?




Pien GW et al, Sleep 2018; 41:zsx201

# Impact of OSA over-diagnosis

- Decrease access to care for those who would benefit
  - Reduced access to testing and specialists
  - Reduced access to PAP or other treatments
- Reduce enthusiasm by PCPs and health system
  - Nihilistic view of treatment acceptance / benefits
- Unnecessary burden on patients
  - Treatment costs and discomfort
  - Psychologic distress and distraction

# Rationale for change:

- The prevalence of AHI>5 is 70% in community studies and approaches 90% in many of the listed comorbidities – is this a disease or normal variant?
- Observational data do not convincingly demonstrate increased risk of these comorbidities among those with AHI 5-15.
- Interventional data (both RCT and non-randomized) do not demonstrate benefit of OSA treatment in those with AHI 5-15 with these comorbidities.
- Evidence suggests the risk of OSA on these comorbidities is greatest in those with sleepiness and evidence demonstrates improvement in these symptoms with treatment in those with AHI 5-15, raising importance of symptoms for making diagnosis in mild OSA.

# Treatment Emergent CSA – ICSD3

A+B

A. Diagnostic PSG/HSAT reveals AHI ≥ 5 events/hr that is predominantly obstructive.
B. PSG during use of PAP without back-up rate reveals resolution of obstructive events and emergence or persistence of central event with:
    1. CAHI ≥ 5 events/hr.
    2. Central events are ≥ 50% of total events.

# Treatment Emergent CSA – ICSD3-TR

A+B+C+D

A. Diagnostic PSG/HSAT reveals AHI ≥ 5 events/hr that is predominantly obstructive.

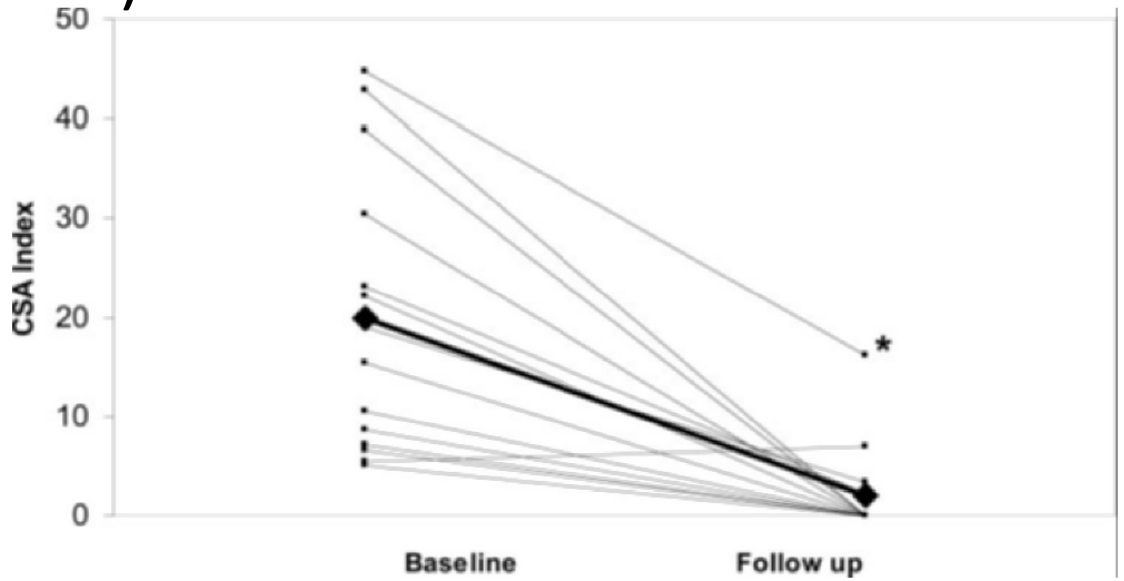
B. PSG during use of ~~PAP without back-up rate~~ CPAP reveals resolution of obstructive events and emergence or persistence of central event with:
   1. CAHI ≥ 5 events/hr.
   2. Central events are ≥ 50% of total events.

C. Symptoms or signs thought attributable to central events:
   1. Sleepiness.
   2. Difficulty initiating/maintaining sleep, frequent awakenings, or nonrestorative sleep.
   3. Awakening short of breath.
   4. Witnessed apneas.

D. Not better explained by another disorder.

# Time course of CPAP-induced CSA

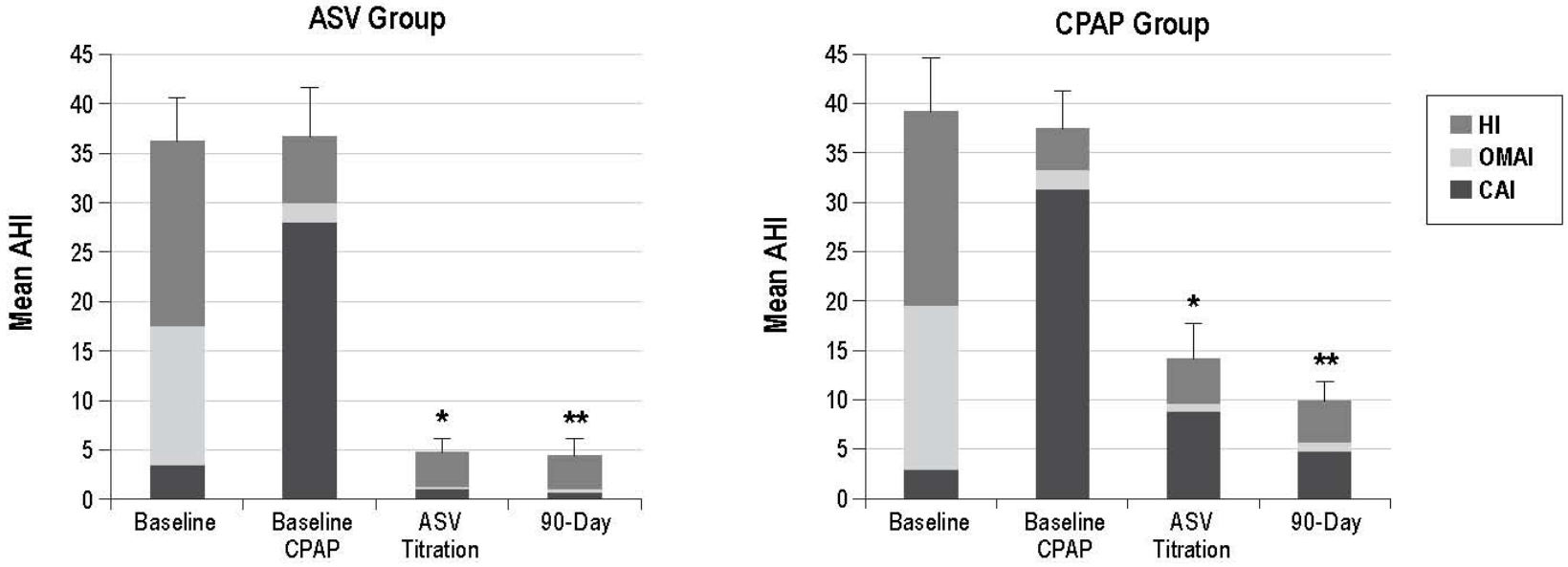
- Patients with OSA (AHI≥20) without central events on diagnostic portion of split-night study, 20% demonstrated elevated CAHI at optimal CPAP pressure.
- Of those returning for follow-up PSG on CPAP 8-12 weeks later, CSA resolved in 12/14 patients (92%).




Dernaika T et al, Chest 2007; 132: 81-7

# Effect of treatment of acute CPAP-induced CSA

- 3 month RCT in 66 patients.
  - Initial AHI 38 (CAI 3) and CPAP AHI 37 (CAI 30)
  - AHI improved more with ASV (4.4 vs. 9.6)
  - No difference in usage (4.7 hrs vs. 4.5 hrs).
  - No difference in sleepiness or quality of life measures.




Morgenthaler TI et al, Sleep 2014; 37: 927-34

# Rationale for change:

- Treatment emergent events are frequent initially, often asymptomatic and self-resolve over time.
- There is currently a lack of evidence that aggressive treatment of asymptomatic events improves clinical outcomes.

# Sleep-Related Hypoxemia – ICSD3

A+B

A. PSG, HSAT, or overnight oximetry reveals SpO2 ≤ 88% in adults or ≤ 90% in children for ≥ 5 minutes.

B. Sleep-related hypoventilation is not documented.

# Sleep-Related Hypoxemia – ICSD3-TR

A+B

A. PSG, HSAT, or overnight oximetry reveals SpO2 ≤ 88% in adults or ≤ 90% in children for ≥ 5 minutes.

B. ~~Sleep-related hypoventilation is not documented.~~ The desaturation is not fully explained by sleep-related hypoventilation, obstructive sleep apnea, or other sleep-related breathing disorders.

(Note: If diagnostic testing reveals hypoxemia during sleep but clinical evaluation has not been conducted to rule out other etiologies, this should be noted as a test result but not as a diagnosis until clinical evaluation has been completed.)

# Rationale for change:

- The clinician should make a correct diagnosis, not a convenient diagnosis.
- Old criteria made diagnosis based on non-patient factors (availability of $CO_2$ monitoring) rather than based on the patient's physiology.
- Correct distinction between sleep-related hypoxemia and sleep-related hypoventilation is important because it impacts therapeutic decisions.
- Abnormal oximetry readings are a laboratory finding not a diagnosis in themselves. A clinical evaluation is necessary to interpret this finding and place in the proper diagnostic context.

# Primary Central Sleep Apnea – ICSD3

A+B+C+D

A. The presence of at least one of:
    1. Sleepiness.
    2. Difficulty initiating/maintaining sleep, frequent awakenings, or nonrestorative sleep.
    3. Awakening short of breath.
    4. Snoring.
    5. Witnessed apneas.
B. PSG reveals all of the following:
    1. CAHI ≥ 5 events/hr.
    2. Central events are ≥ 50% of total events.
    3. No CSR.
C. No evidence of hypoventilation.
D. Not better explained by another disorder.

# Primary Central Sleep Apnea – ICSD3-TR

A+B+C+D

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B. PSG reveals all of the following:
   1. CAHI ≥ 5 events/hr.
   2. Central events are ≥ 50% of total events.
   3. No CSR.

C. No evidence of hypoventilation.

D. Not better explained by another disorder.

# Rationale for change:

- Snoring is indicative of obstructive physiology.

- NOTE: this change made for all of the CSA diagnoses.

# Central Sleep Apnea due to Medication or Substance – ICSD3

A+B+C+D+E

A. The patient is taking an opioid or other respiratory depressant.
B. The presence of at least one of:
    1. Sleepiness.
    2. Difficulty initiating/maintaining sleep, frequent awakenings, or nonrestorative sleep.
    3. Awakening short of breath.
    4. Snoring.
    5. Witnessed apneas.
C. PSG reveals all of the following:
    1. CAHI ≥ 5 events/hr.
    2. Central events are ≥ 50% of total events.
    3. No CSR.
D. The disorder occurs as a consequence of an opioid or other respiratory depressant.
E. Not better explained by another disorder.

# Central Sleep Apnea due to Medication or Substance – ICSD3-TR

A+B+C+D~~+E~~

A. The patient is taking an opioid~~ or other respiratory depressant~~, ticagrelor or other medication known to impact respiratory control.

B. The presence of at least one of:
   1. Sleepiness.
   2. Difficulty initiating/maintaining sleep, frequent awakenings, or nonrestorative sleep.
   3. Awakening short of breath.
   ~~4. Snoring.~~
   5. Witnessed apneas.

C. PSG reveals all of the following:
   1. CAHI ≥ 5 events/hr.
   2. Central events are ≥ 50% of total events.
   ~~3. No CSR.~~

~~D. The disorder occurs as a consequence of an opioid or other respiratory depressant.~~

D. Not better explained by another disorder.

# Ticagrelor

- P2Y12 antagonist known to increase chemosensitivity and so known to cause dyspnea.
- Specific to ticagrelor (not seen with clopidogrel or prasugrel).

| | On Ticagrelor | On Prasugrel | Ticagrelor Reintroduction |
|---|---|---|---|
| Fatigue score | 14 | 4 | 11 |
| Borg dyspnea score | 8 | 3 | 8 |
| TST | 5h 44 min | 6h 35 min | 7h 42 min |
| CAI | 16 | 4 | 14 |

Puel V et al, Br J Clin Pharm 2019; 85: 1855-8

# Rationale for change:

- Ticagrelor can clearly cause CSA by increasing ventilatory drive.
- Snoring indicates obstructive physiology.
- Cheyne-Stokes pattern can be seen in opiate and ticagrelor induced CSA.

# Sleep Related Hypoventilation due to Medical Disorder – ICSD3

A+B+C

A. Sleep-related hypoventilation is present.

B. A lung parenchymal or airway disease, pulmonary vascular pathology, chest wall disorder, neurologic disorder, or muscle weakness is believed to be the primary cause of hypoventilation.

C. Hypoventilation is not primarily due to obesity hypoventilation syndrome, medication use, or a known congenital central alveolar hypoventilation syndrome.

# Sleep Related Hypoventilation due to Medical Disorder – ICSD3-TR

A+B+C

A. Sleep-related hypoventilation is present.

B. A lung parenchymal or airway disease, ~~pulmonary vascular pathology,~~ chest wall disorder, neurologic disorder, or muscle weakness is believed to be the primary cause of hypoventilation.

C. Hypoventilation is not primarily due to obesity hypoventilation syndrome, medication use, or a known congenital central alveolar hypoventilation syndrome.

# Rationale for change:

- Pulmonary vascular disorders produce sleep-related hypoxemia not hypoventilation.
- Chronic hypoventilation can cause secondary pulmonary hypertension.
- The presence of pulmonary hypertension in the setting of hypoventilation is likely secondary to the hypoventilation or a comorbid disorder causing both (e.g., COPD). The underlying cause of the hypoventilation should be further investigated.

# Conclusions

- The ICSD-3-TR provides updated criteria for diagnosing sleep disorders, incorporating scientific evidence from the past 10 years.

- In general, there has been a re-calibration away from the excesses of ICSD-2 and -3 to better balance patient experience with objective sleep findings.

- Understanding ICSD-3-TR is important to take optimal care of patients with sleep disorders and is definitely important to pass the sleep medicine boards.