

17th Annual Sleep Medicine Virtual Course

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Evaluation and conservative management of sleep disordered breathing

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Conflict of Interest Disclosures for Speakers

Meir Kryger, MD disclosed a relationship with Bodimetrics
(consultant).

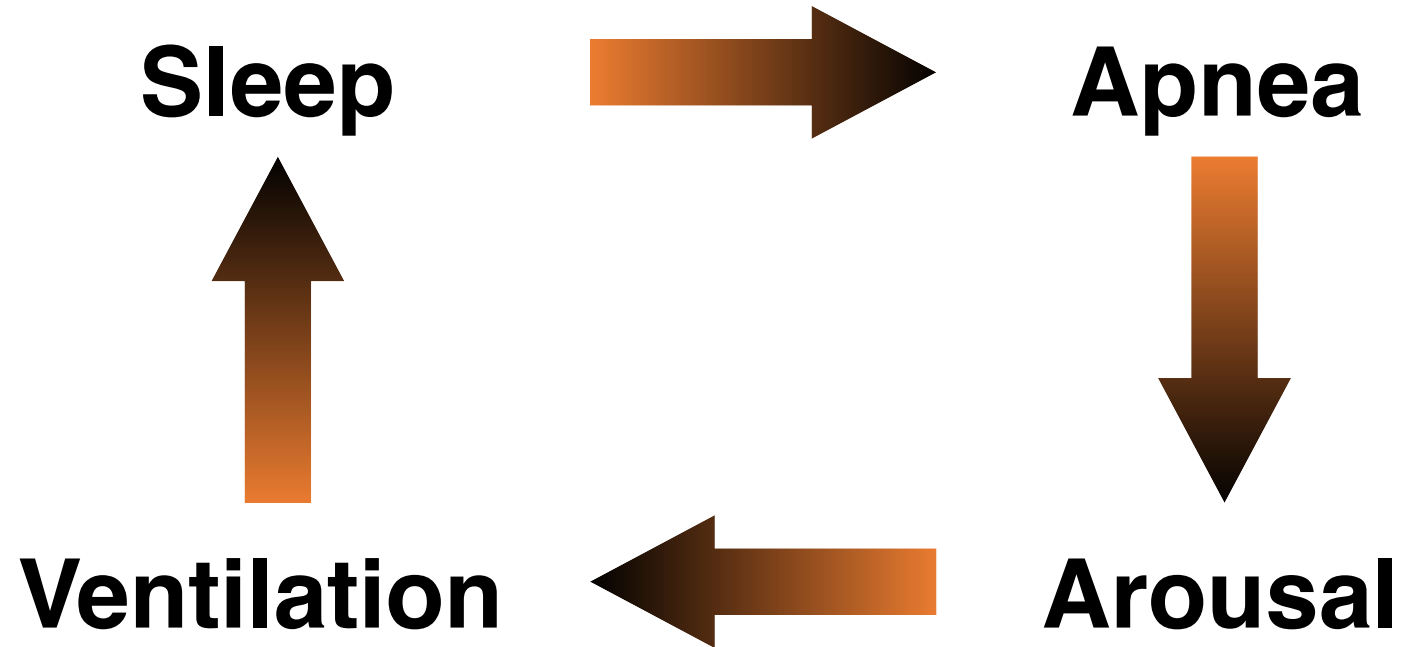
The relevant financial relationship has been mitigated.

Learning Objectives

At the conclusion of this lecture, learners will be able to:

- 1.Learners will analyze factors causing OSA
- 2.Learners will be able to apply the principles of phenotyping OSA
- 3.Learners will evaluate and appreciate that OSA is associated with many co-morbidities
- 4.Learners will be better able to identify and manage the many groups of patients with OSA

Patients with apnea can't sleep and breathe at the same time



A Brief History

- First documented use of term “sleep apnea”
 - Guilleminault C, Eldridge FL, Dement WC. Insomnia with sleep apnea: a new syndrome. *Science*. 1973 Aug 31;181(102):856-8.
- The term “obstructive sleep apnea” doesn’t appear for another 2-3 years.
- An exquisitely rare disease?
- Obviously this is not a new disease . . .

Sleep Apnea: The First Case



Back to Ancient Greece...

Dionysius, Tyrant of Heracleia

Dionysius, tyrant of Heracleia (now Crete),
born in 360 BC (the era of Alexander the Great)

“was an unusually fat man, which increased to such a degree that he could take no food which was not introduced into his stomach by artificial means. At last, however he was choked by his own fat.”

-Athenaeus: The Deipnosophists,
Harvard U Press, 1863.

More About Dionysius...

Athenaeus continues:

“When he held audiences with people who desired to see him he placed a box in front of his body in order that while hiding the other parts of his person, his face alone might project above them as he conversed with his interviewers.”

Symptoms Were...

 **The Physicians found...**

Sleepiness

Difficult to arouse

Problems breathing

 2

First Treatment of Apnea



“So the physicians prescribed that he should get some fine needles, exceedingly long that they thrust through his ribs and belly when he happened to fall into a very deep sleep. Now up to a certain point under the flesh, completely callused as it was by fat, the needle caused no sensation; but if the needle went through so as to touch the region which was free of fat, then he would be thoroughly aroused.”

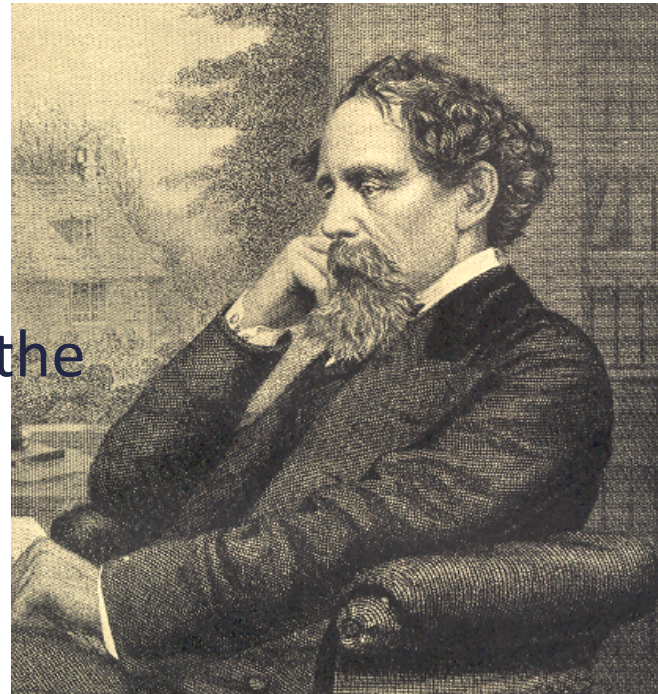
What Dionysius Looked Like



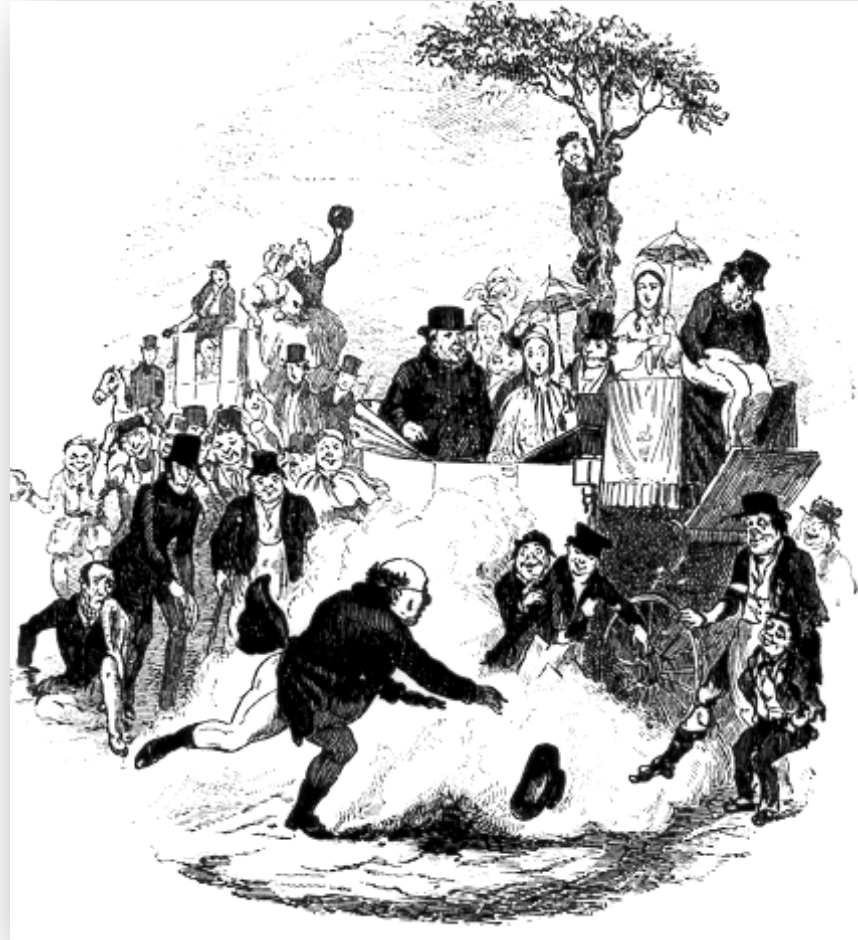
It's nice being a king, but not
if you have apnea...

To England 1836

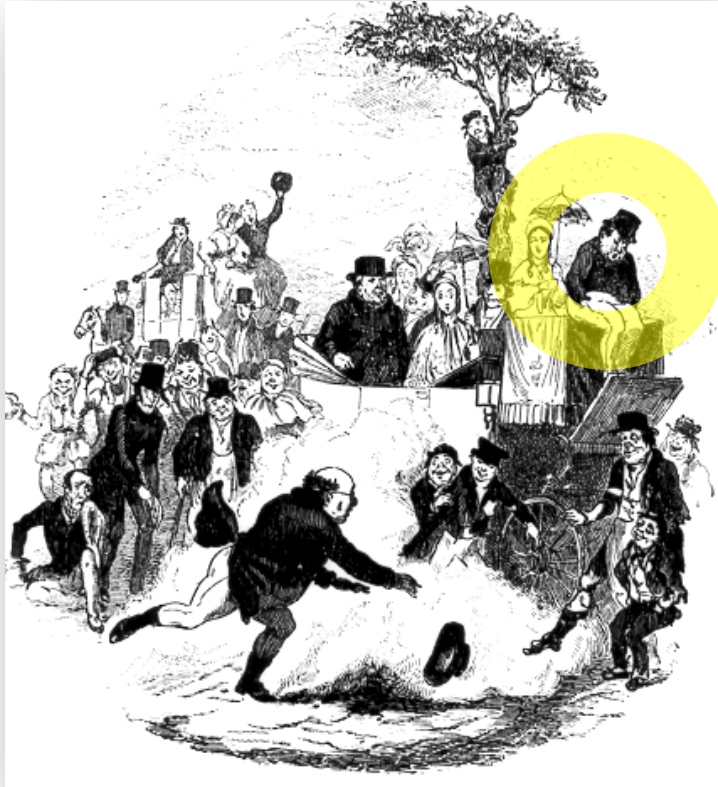
Barely 20 years old
Charles Dickens
publishes his first novel
The Posthumous Papers of the
Pickwick Club



Dickens Describes Apnea in 1836



Introduction to Joe, the Fat Boy



“...and on the box sat a fat and red-faced boy, in a state of somnolency.”

How Dickens Describes Joe



- Twenty stun
- Red-faced
- Young dropsy

Joe: Sleepy and Difficult to Arouse

- “The fat boy rose, opened his eyes, swallowed a huge piece of pie he had been in the act of masticating when he last fell asleep”
- In response to the firing of enormous guns at a military exercise “everybody was excited except the fat boy who slept as soundly as if the roaring of cannon were his ordinary lullaby”

Joe Snored

- “Joe snores as he waits on at table...”
- “The snoring of the fat boy penetrated in a low monotonous sound from the distant kitchen”

Annie Spitz: 1937



Described 3 cases who had cyanosis, sleepiness (which she called “narcolepsy”) and right sided heart failure. They also had Cheyne-Stokes respiration, snoring and apneas. Believed disorder caused by polycythemia.

1956: Famous Case Report

The patient “was accustomed to playing poker once a week and on this crucial occasion he was dealt a hand of three aces and two kings... A full house. Because he had dropped off to sleep, he failed to take advantage of the opportunity.”

Table 1: (Burwell et al. 1956) Features of the Pickwickian Syndrome

- Obesity, marked
- Somnolence
- Twitching
- Cyanosis
- Periodic respiration
- Polycythemia, secondary
- Right ventricular hypertrophy
- Right ventricular failure

Three European groups

- Report sleep studies in Pickwickian Syndrome in 1964
 - Obstructive apnea described
 - Hypoxemia
 - Hypertension

- Thought to be rare

1974



The start of my career started with a case . . .

- 42 year old obese male
- Severe daytime sleepiness last 2-3 years
- Urinary incontinence last 2-3 years
- 4-5 month history of nocturnal seizures
- He didn't fit the medical literature

First sleep study

An explanation for the seizures

The first treatment was tracheostomy

- Sleepiness resolved
- Seizures resolved
- Arrhythmias resolved
- Patient was cured

My first paper . . .

Kryger M, Quesney LF, Holder D, Gloor P, MacLeod P.

The sleep deprivation syndrome of the obese patient. A problem of periodic nocturnal upper airway obstruction.

Am J Med. 1974 Apr;56(4):530-9.

Early 1970s in North America

- Insomnia with sleep apnea (Guilleminault et al, 1973)
- The sleep deprivation syndrome of the obese patient. A problem of periodic nocturnal upper airway obstruction. (Kryger M, et al 1974)
- For the next 20 years the conventional wisdom was:
 - Apnea is rare
 - Apnea is disease of middle aged obese males

The stereotype obese apneic



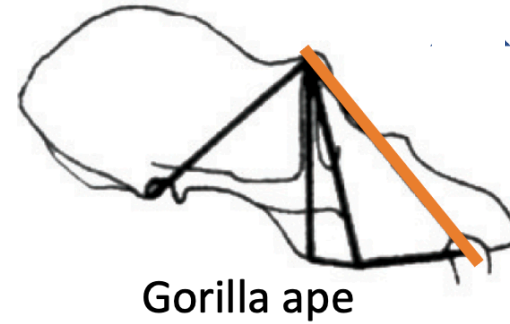
Sleep Apnea is not a disease

It is the common pathway of many disorders



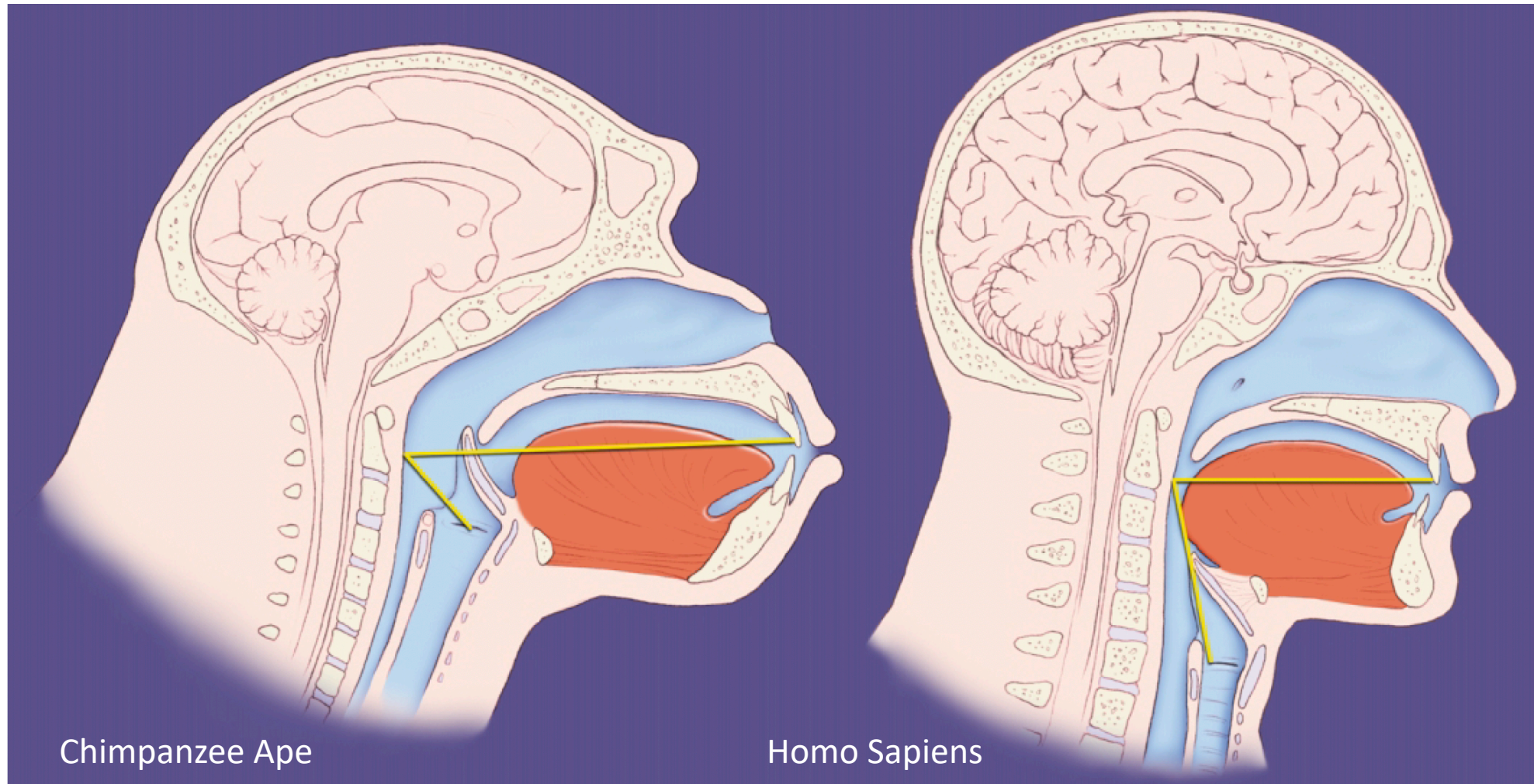
What causes apnea?

Anatomy is one factor



*Evolution
of the face*

Why the change? Speech!



What causes apnea?
Genetics, upper airway abnormality, and physiology



What caused obesity? Migration

Humans evolved in Africa

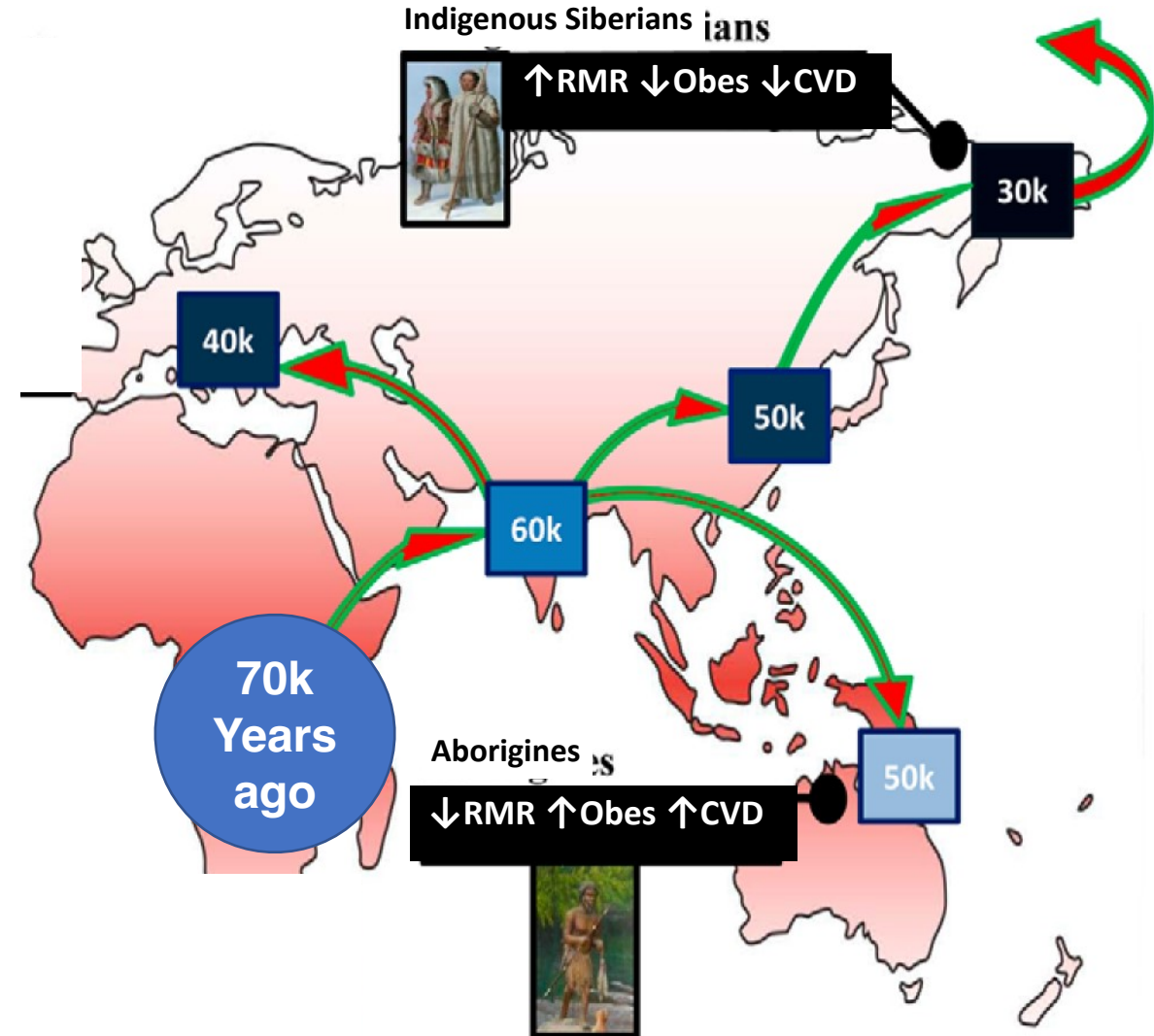
Migrations started about 70,000 years ago

Resting metabolic rate changed with climate

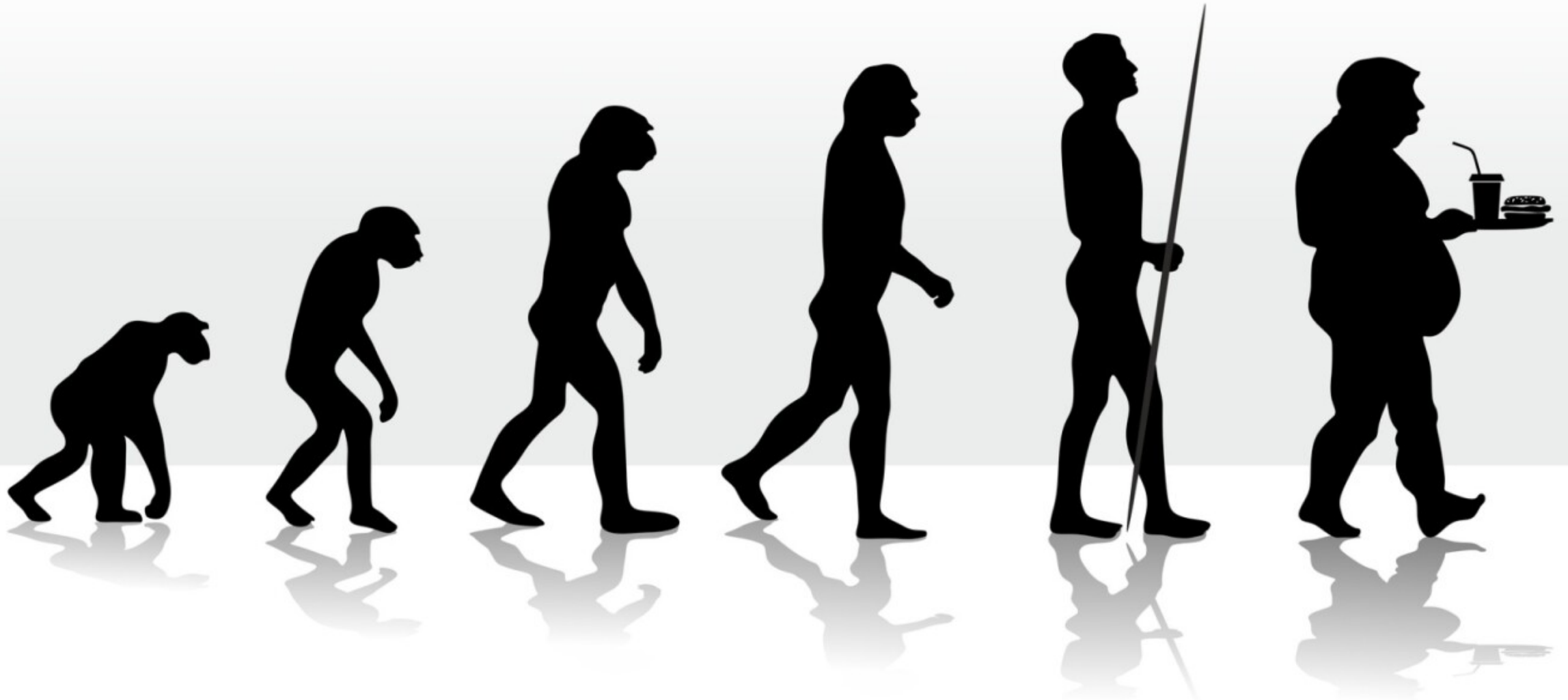
Hot climate Cold adapted



Cold climate Heat adapted



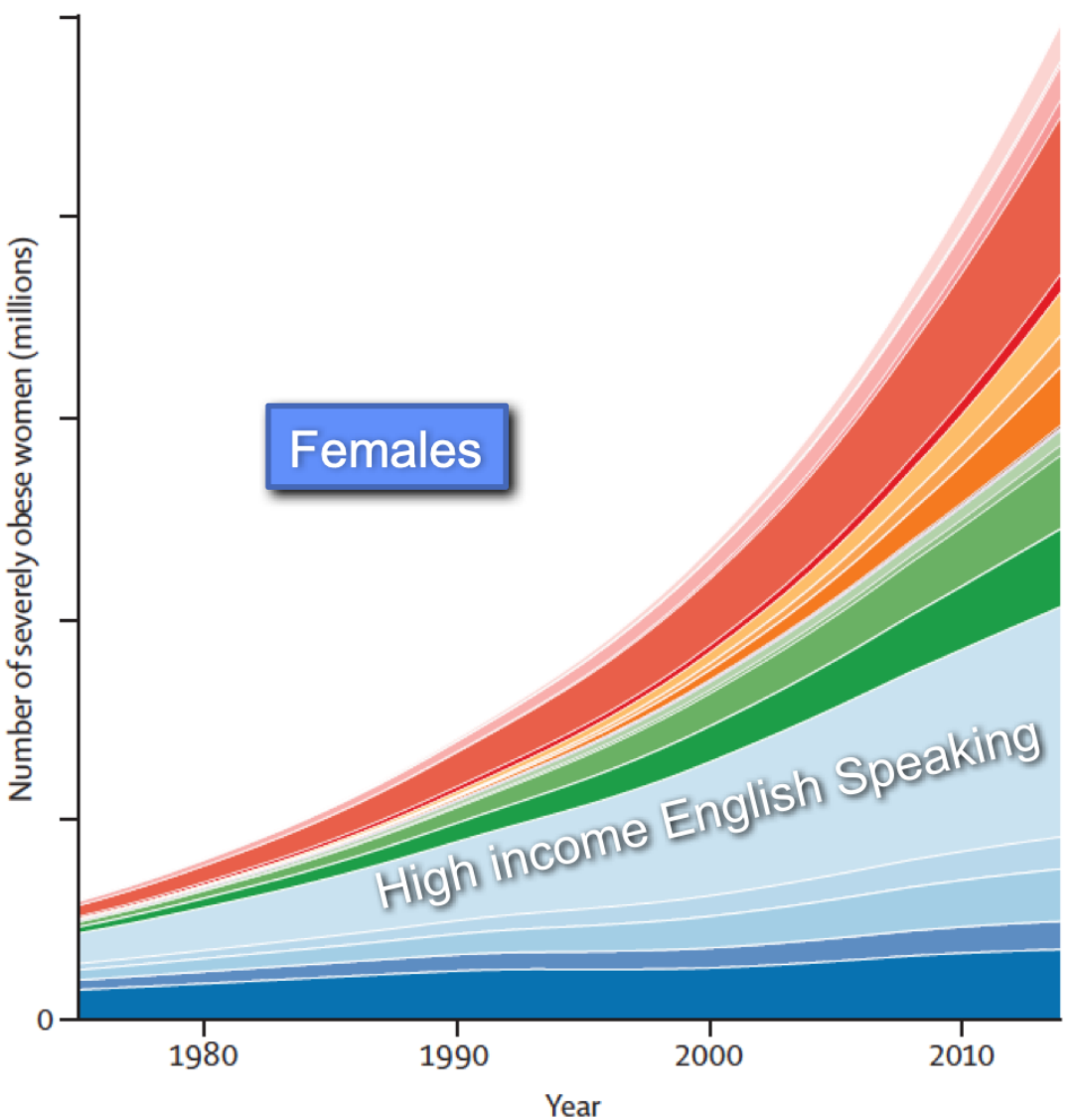
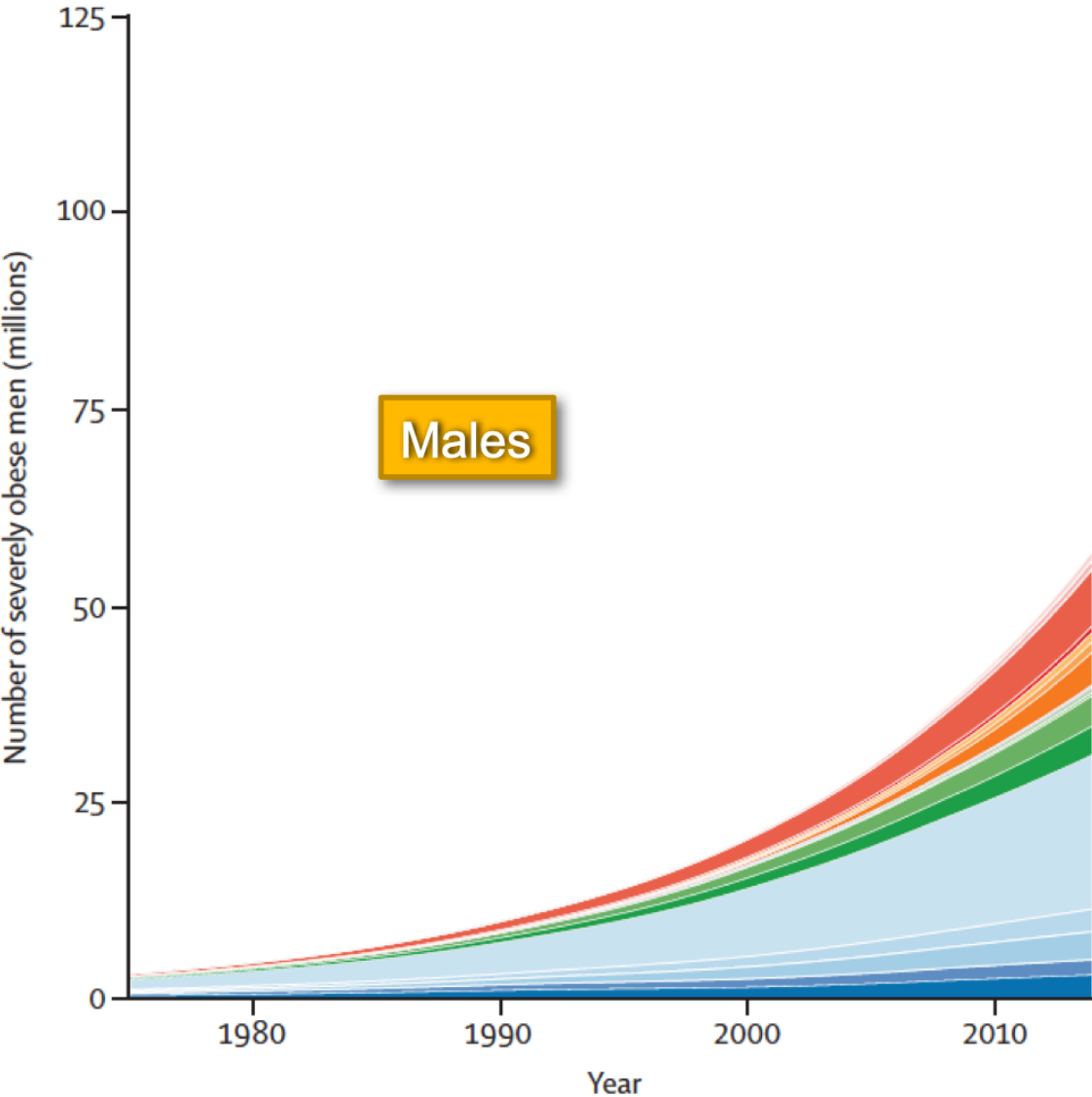
What caused obesity? Diet



We sleep less today

- Humans evolved being active during the day and sleeping when it is dark (diurnal) and slept about 2 hours more than we do today.
- Restricted sleep leads to obesity

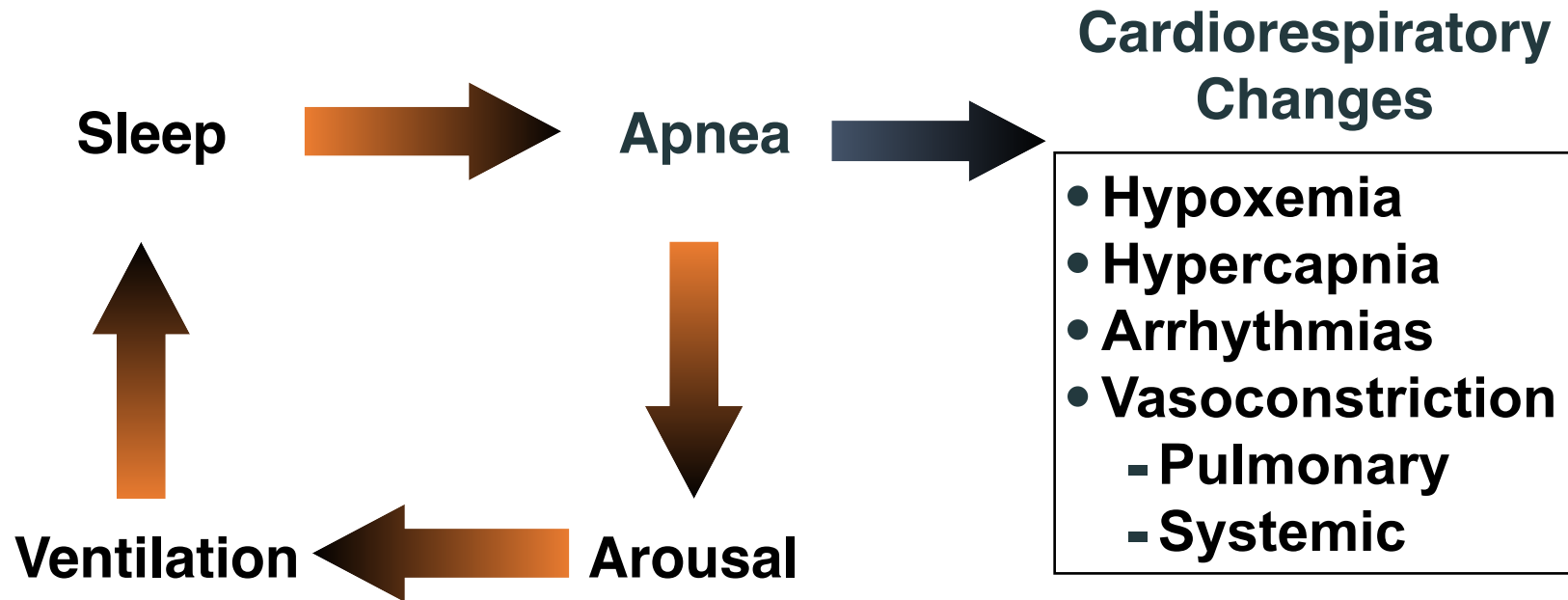
Epidemic of obesity in adults



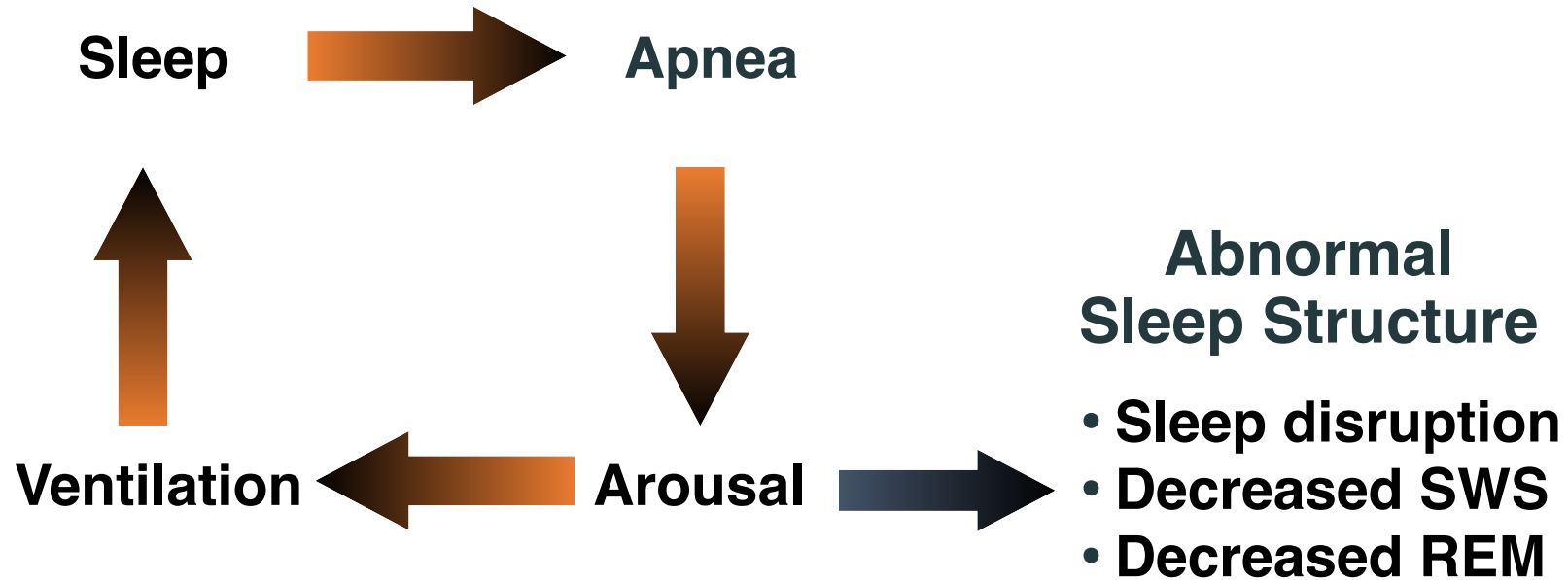
Many millions have ...



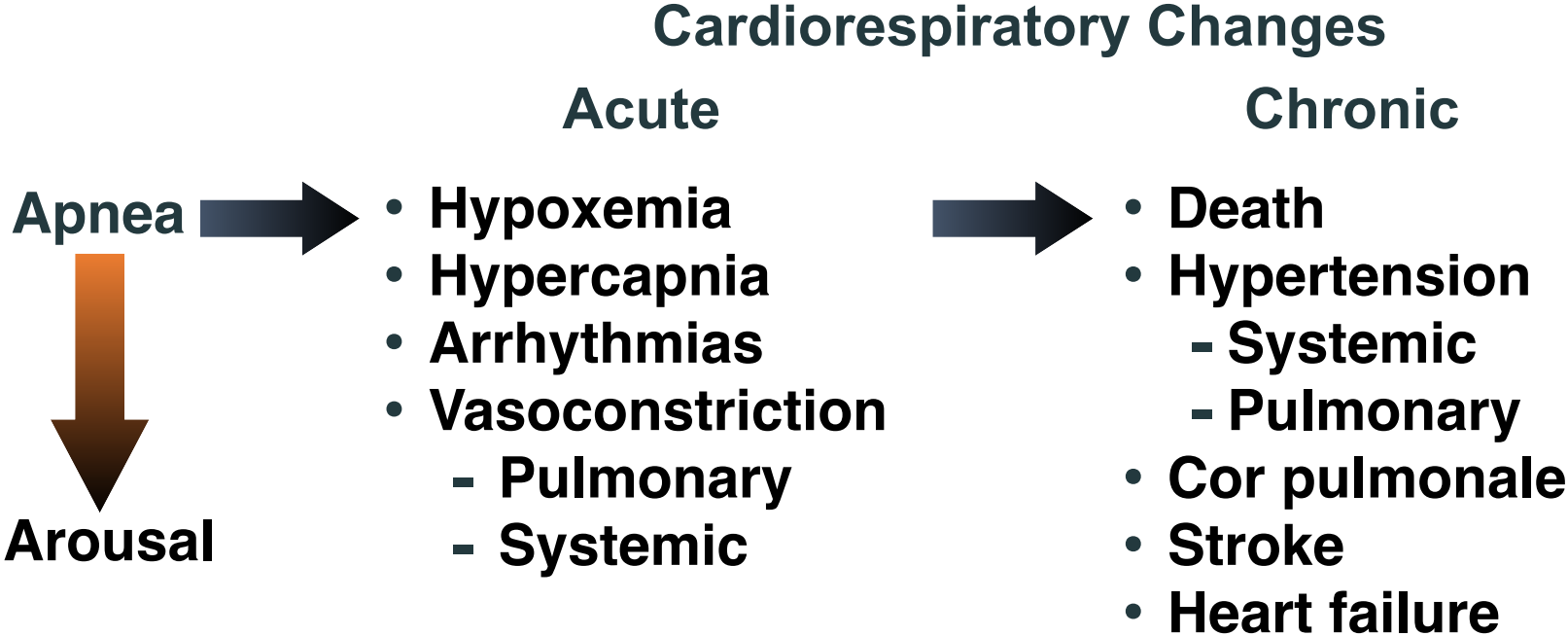
Acute Complications of Apnea



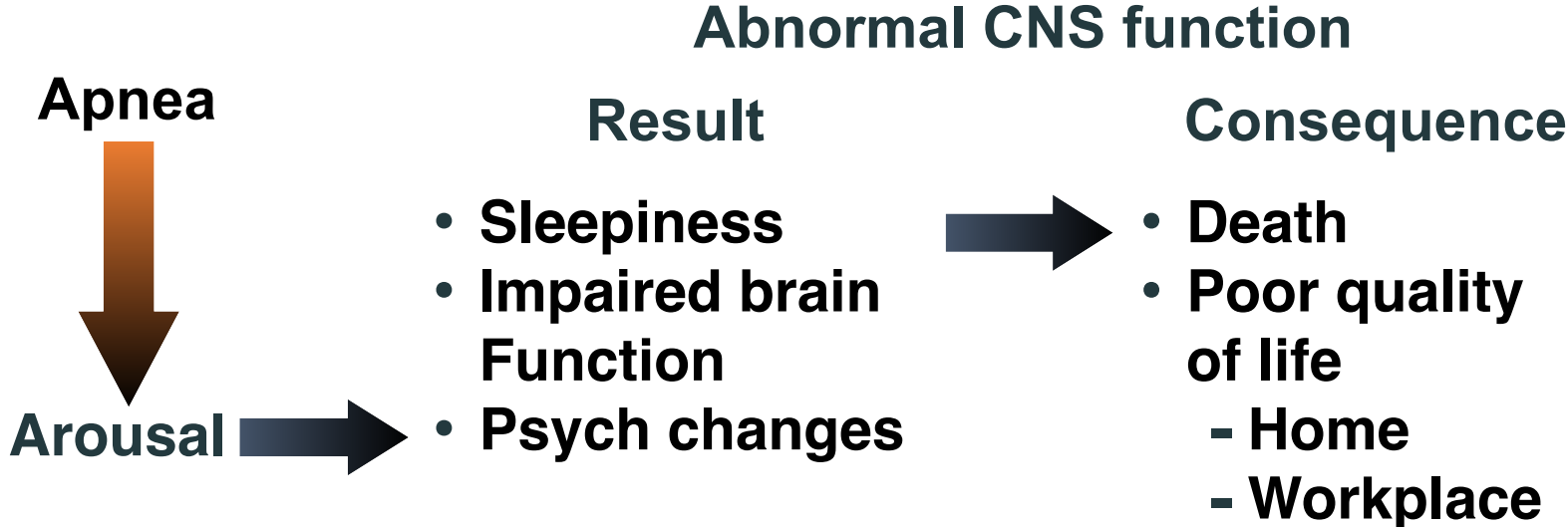
Acute Complications of Arousals



Chronic Complications of Apnea



Chronic Complications of Arousal



Understanding Consequences

Apnea

- Hypoxemia
- Hypercapnia
- Arrhythmias
- Vasoconstriction
 - Pulmonary
 - Systemic

Arousal

- Death
- Poor quality of life
 - Home
 - Workplace

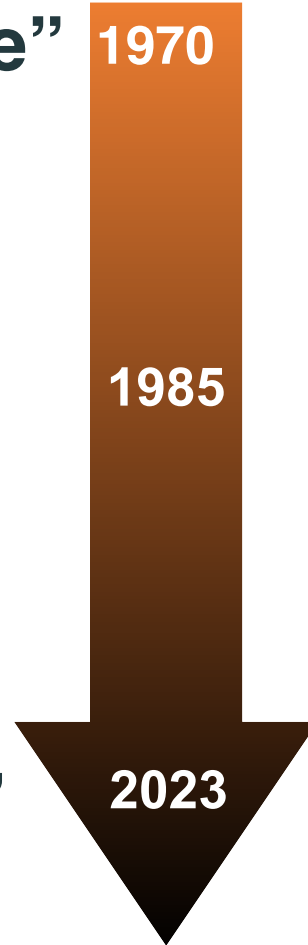
“Severe”

1970

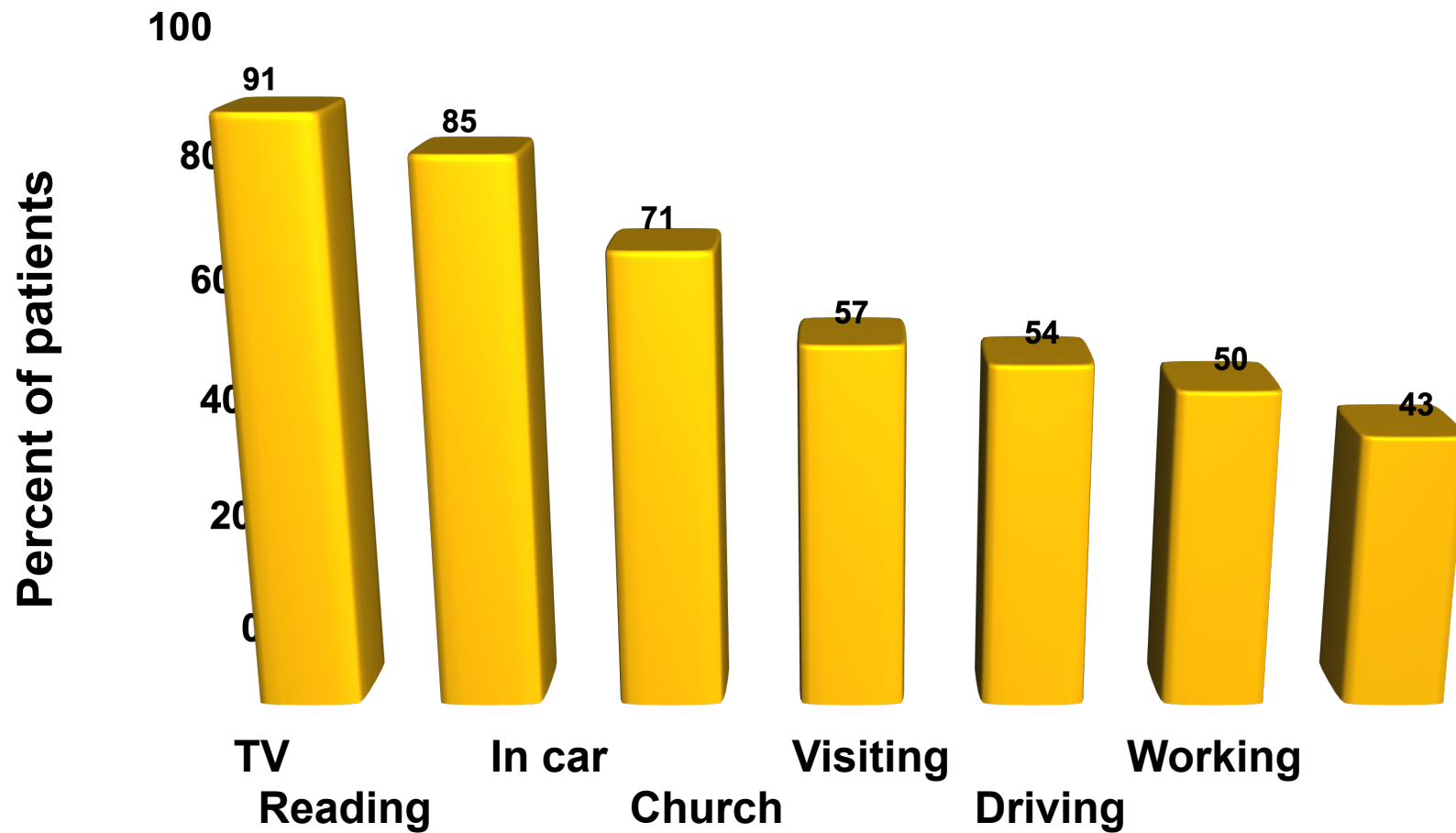
1985

“Mild”

2023



Sleepiness in Apnea

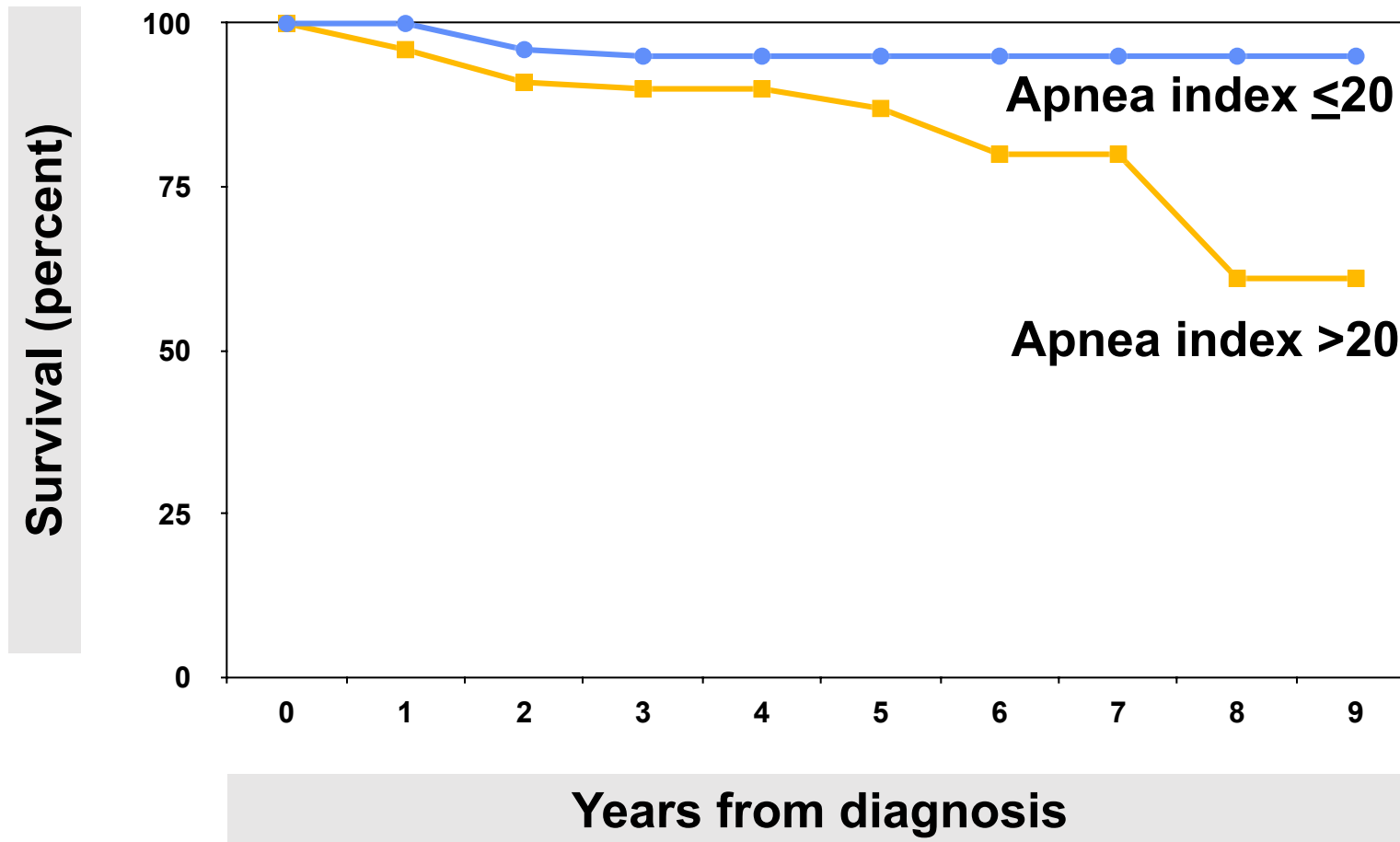


Accident Rate Twice as High In

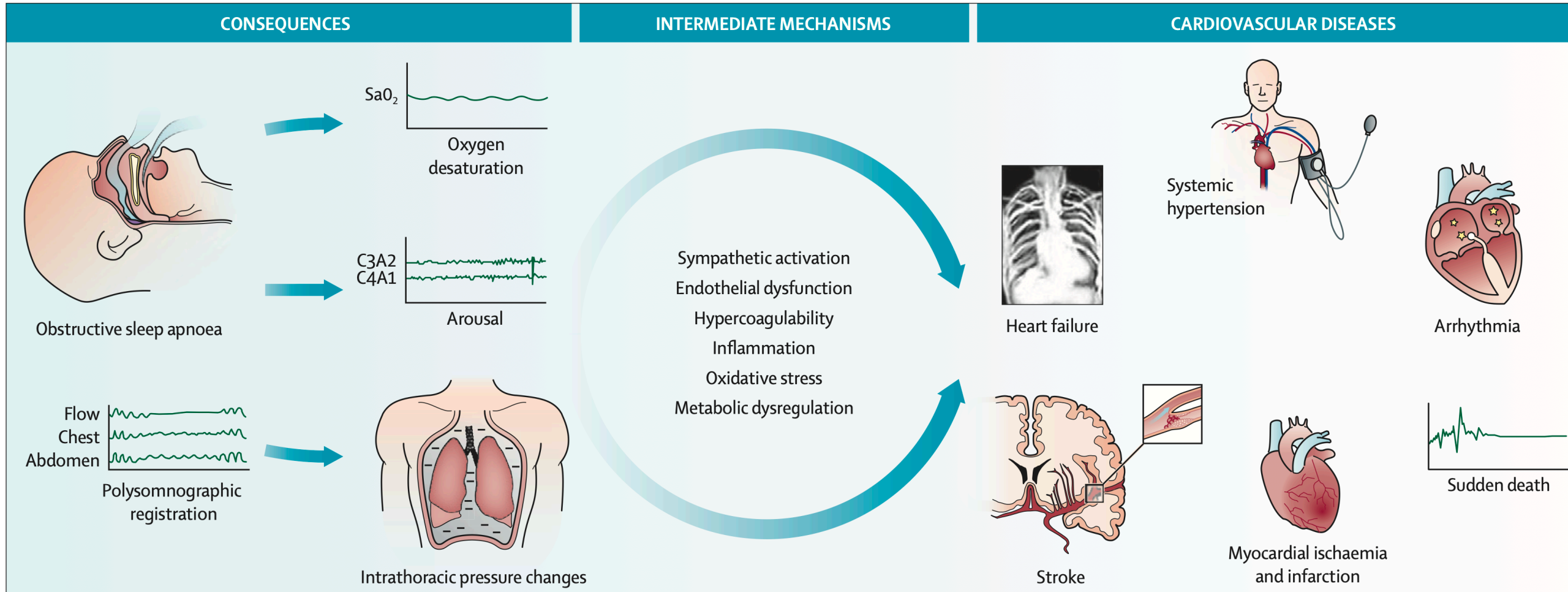
- USA
- Canada
- France
- ...



Untreated Apnea Causes Death



Causes of death . . .



Sleep Apnea: Cost to Patient

- Increases mortality
- Causes morbidity
 - Cardiovascular
 - Neuropsychiatric
- Impairs quality of life

Diagnosis today

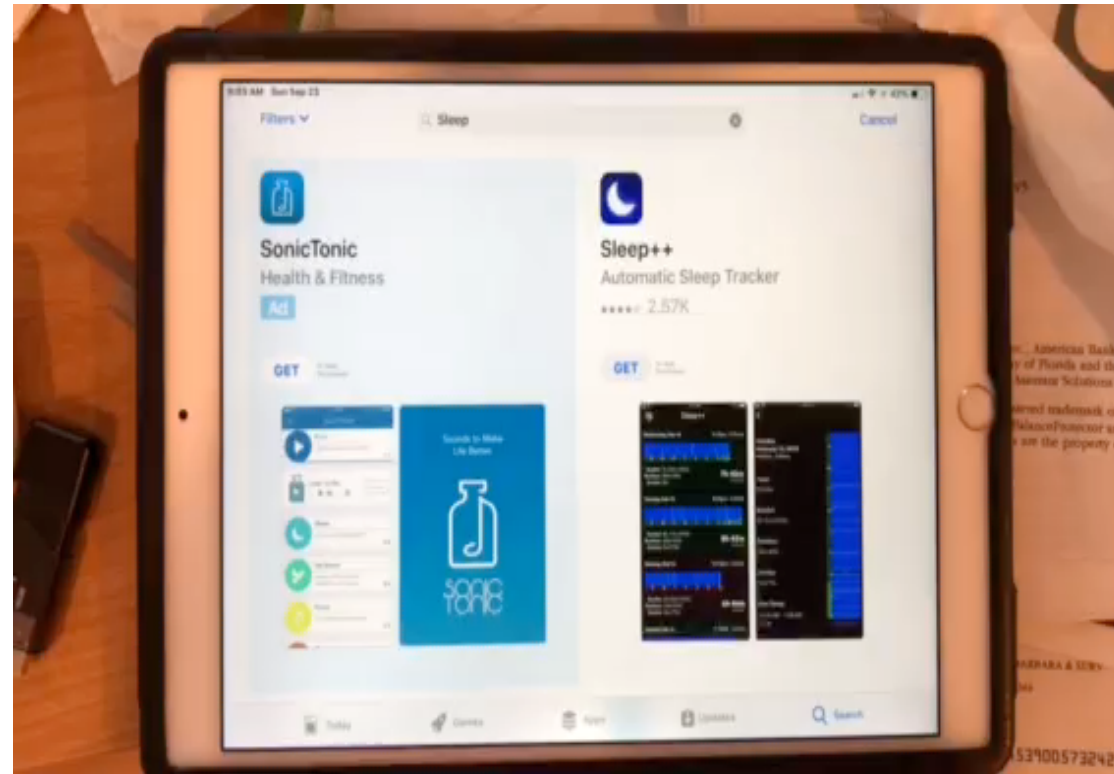


In the laboratory
Complete PSG
Diagnostic and PAP



In the home
Fewer channels
Diagnostic
? Start therapy

Hundreds of sleep apps



New Sensors

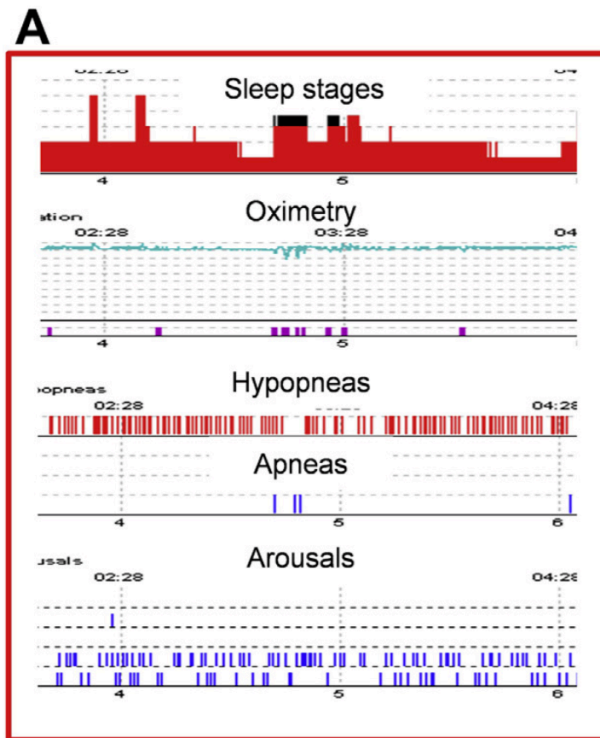


Other smart devices

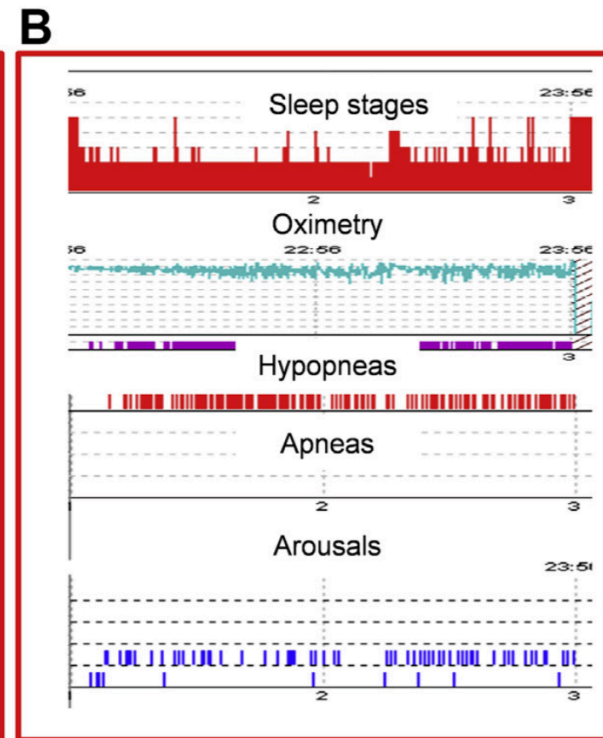


Polysomnography & AHI - different phenotypes emerge

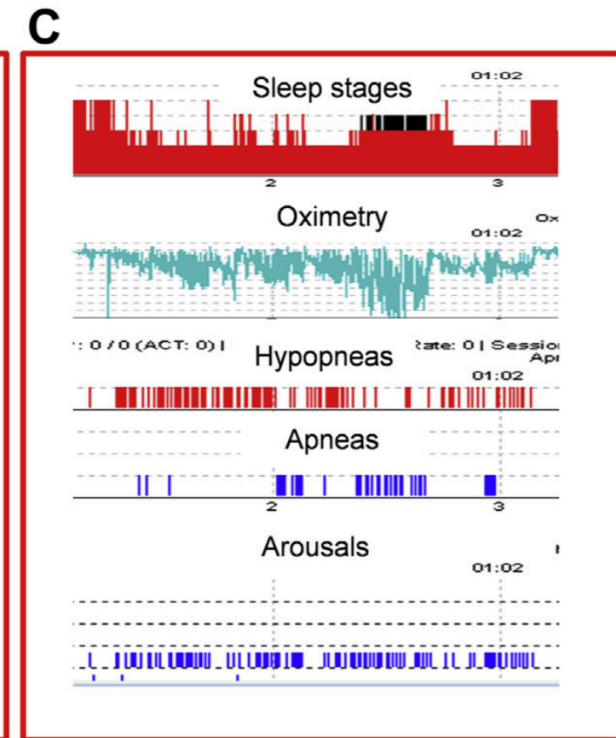
AHI = 45 / hour



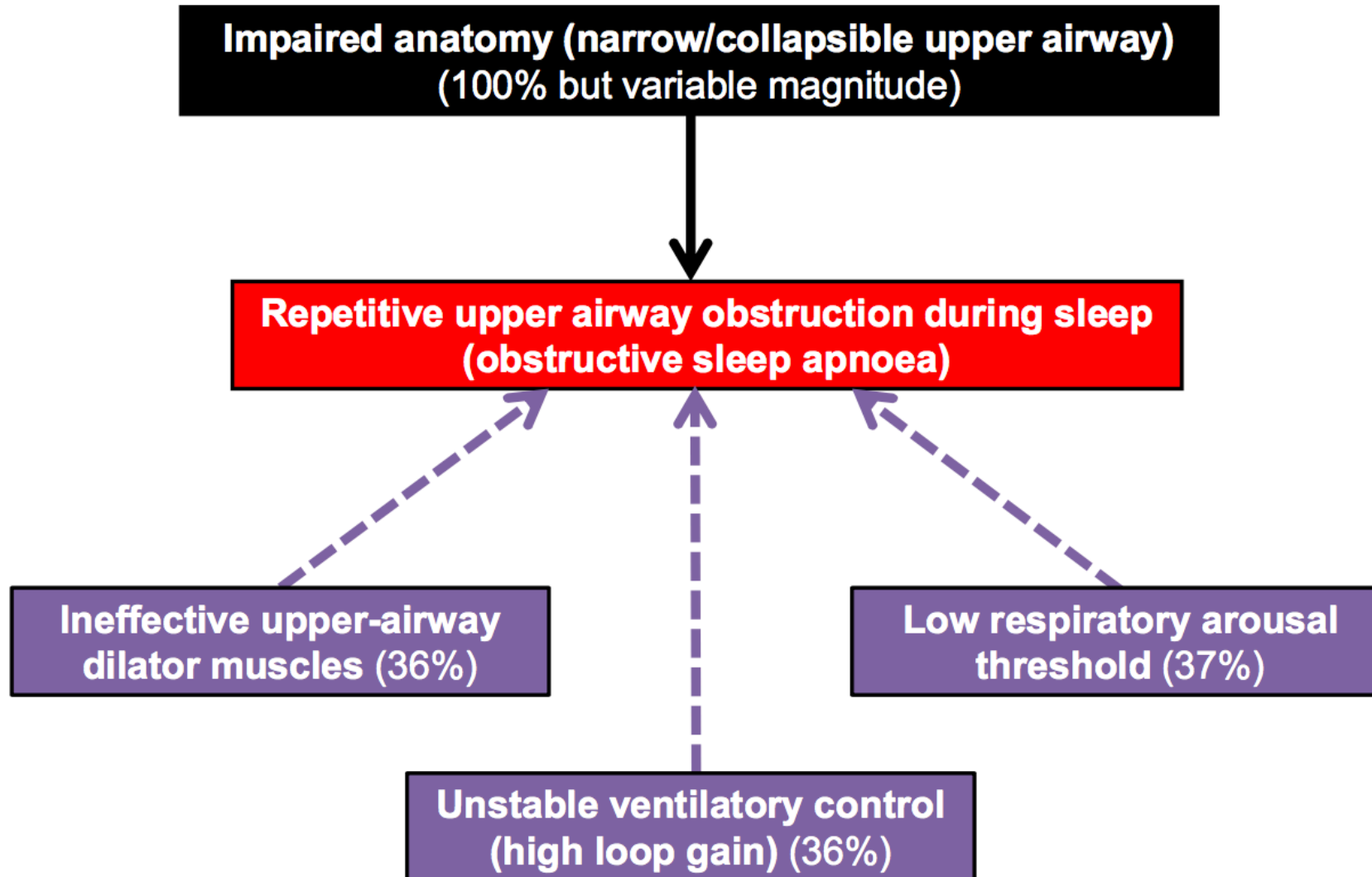
AHI = 45 / hour



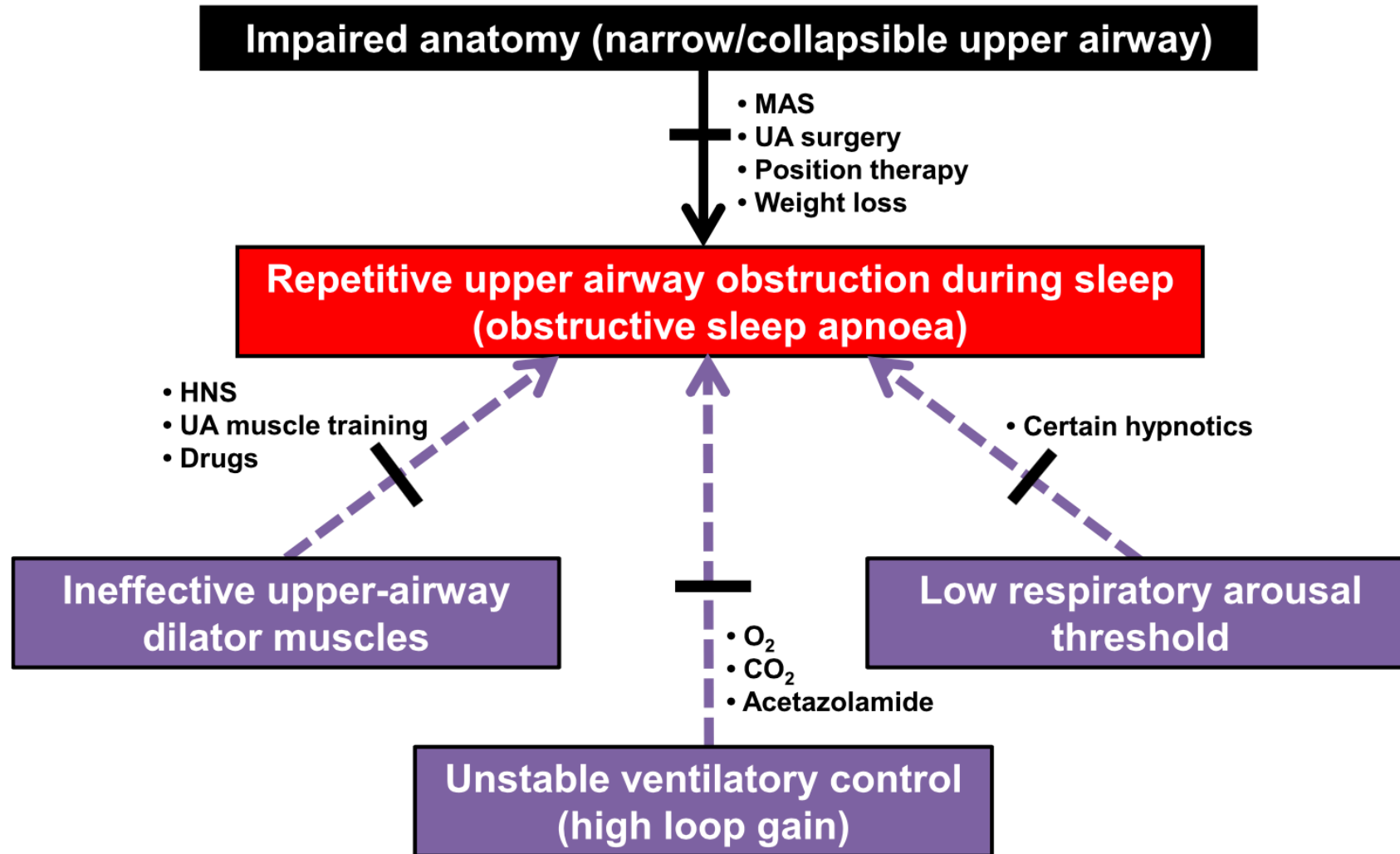
AHI = 45 / hour



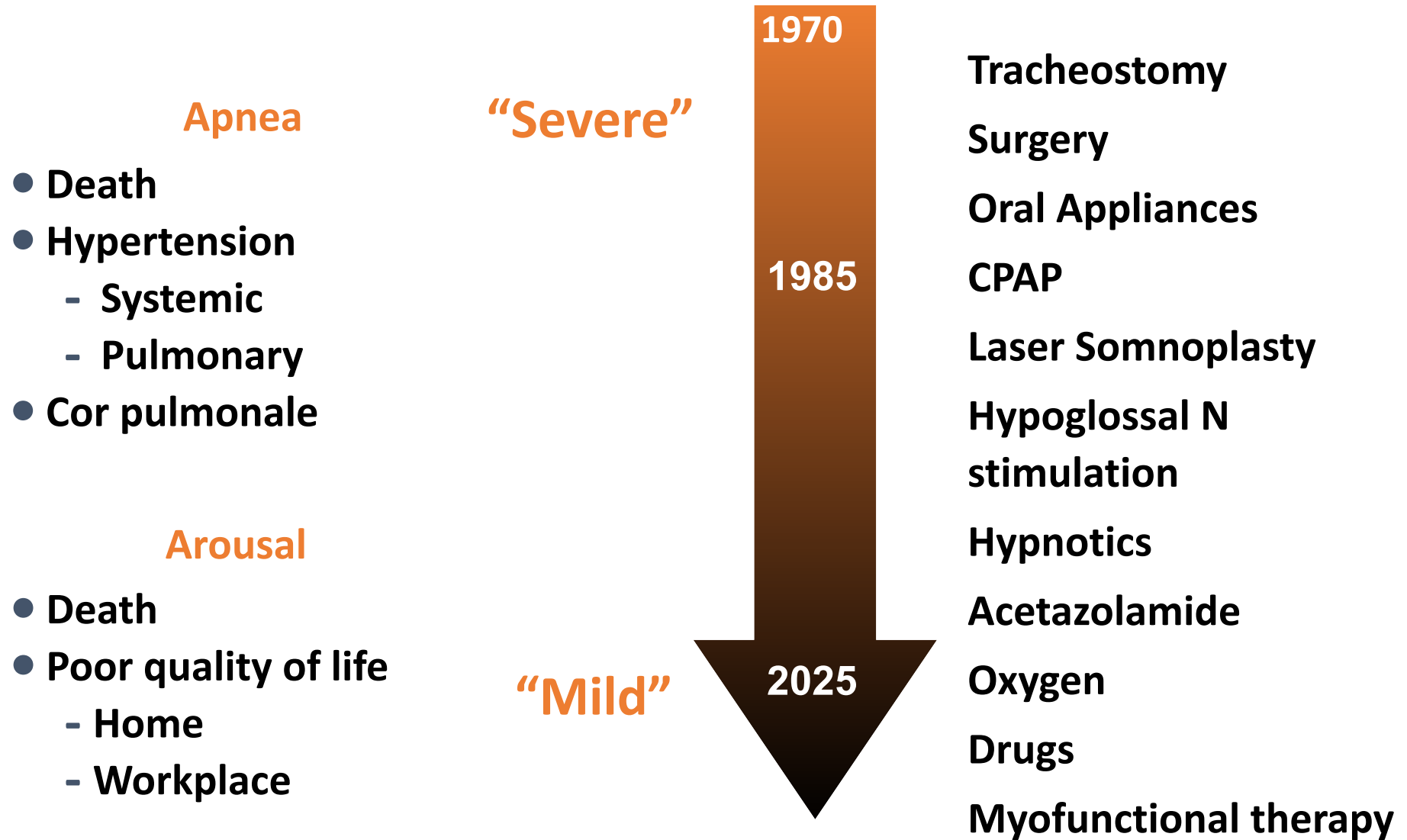
Pathophysiology of OSA



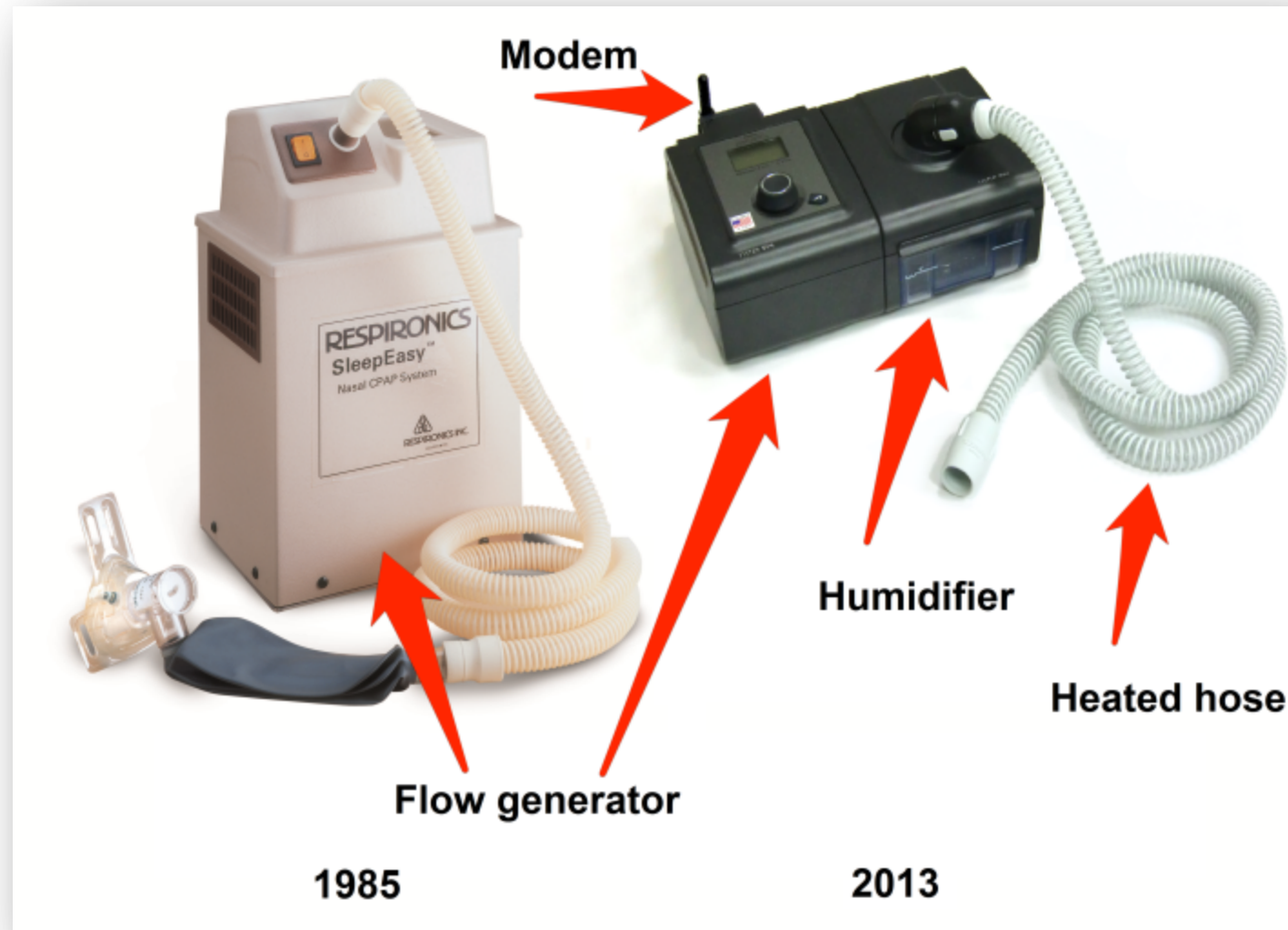
Manipulating Physiological Traits



Why Treat? To Prevent Consequences



Evolution of CPAP machines



Evolution of CPAP machines



*What if the patient won't use
CPAP?*

I can't use CPAP because . . .

- The noise is a problem
- Power is a problem
- Travel is a problem
- Job is a problem
- I hate it because ...
- It doesn't work
- "My friend told me"

I can't use CPAP because ...

Nasal Effects

Rhinorrhea
Nasal congestion
Oronasal dryness
Epistaxis

Mask Effects

Skin abrasion or rash
Conjunctivitis from air leak

Flow-Related Effects

Chest discomfort
Aerophagia
Sinus discomfort
Claustrophobia
Difficulty exhaling
Pneumothorax (very rare)
Pneumoencephaly (very rare)

Other Problems

Noise
Partner intolerance
Inconvenience

- *What can be done to treat OSA patients who can't or won't use CPAP?*

Available Treatments (Invasive)

- Hypoglossal nerve stimulation
 - Requires implantation of device
 - A very select patient anatomy
- Somnoplasty
 - Very select patient anatomy
 - Variable success
- Uvulopalatopharyngoplasty (UPPP)
 - Very select anatomy
 - Poor efficacy
 - Difficult to tolerate CPAP
- Maxillomandibular Advancement (MMA)
 - Long recovery
 - Changes facial appearance
 - Most effective surgical modality

Other Treatments (non-invasive)

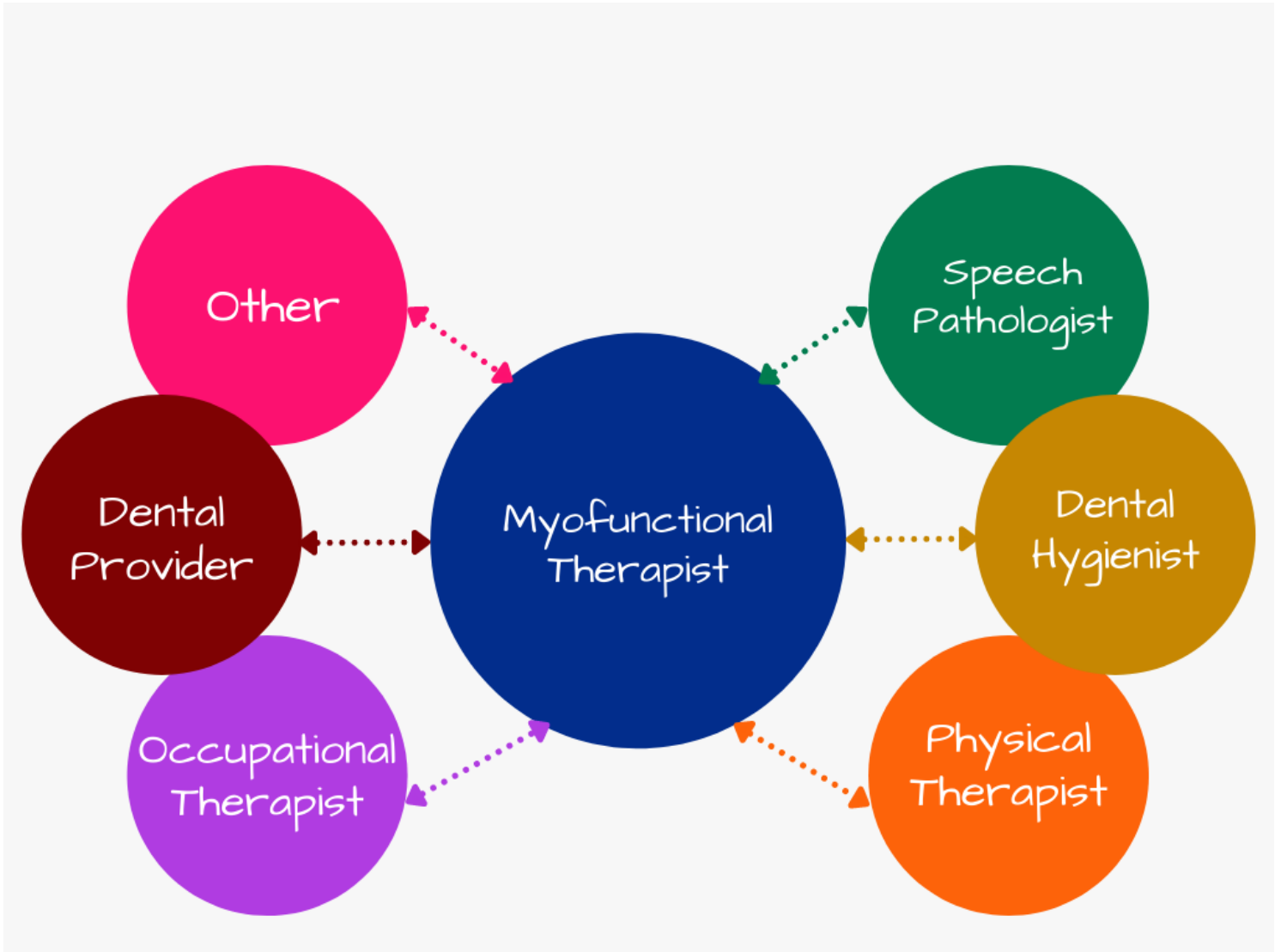
- **Nasal gadgets**
- Provent – end expiratory pressure
 - Nasal congestion
 - Not recommended for severe OSA.
 - No longer available
- Bongo – end expiratory pressure
 - Nasal congestion
 - Not recommended for severe OSA.
 - Too new
- **Oral appliances**
 - Tongue-retaining devices
 - Mandibular advancement devices (MADs)
 - **REFER TO DENTIST OR ORTHODONTIST (BOARDED)**



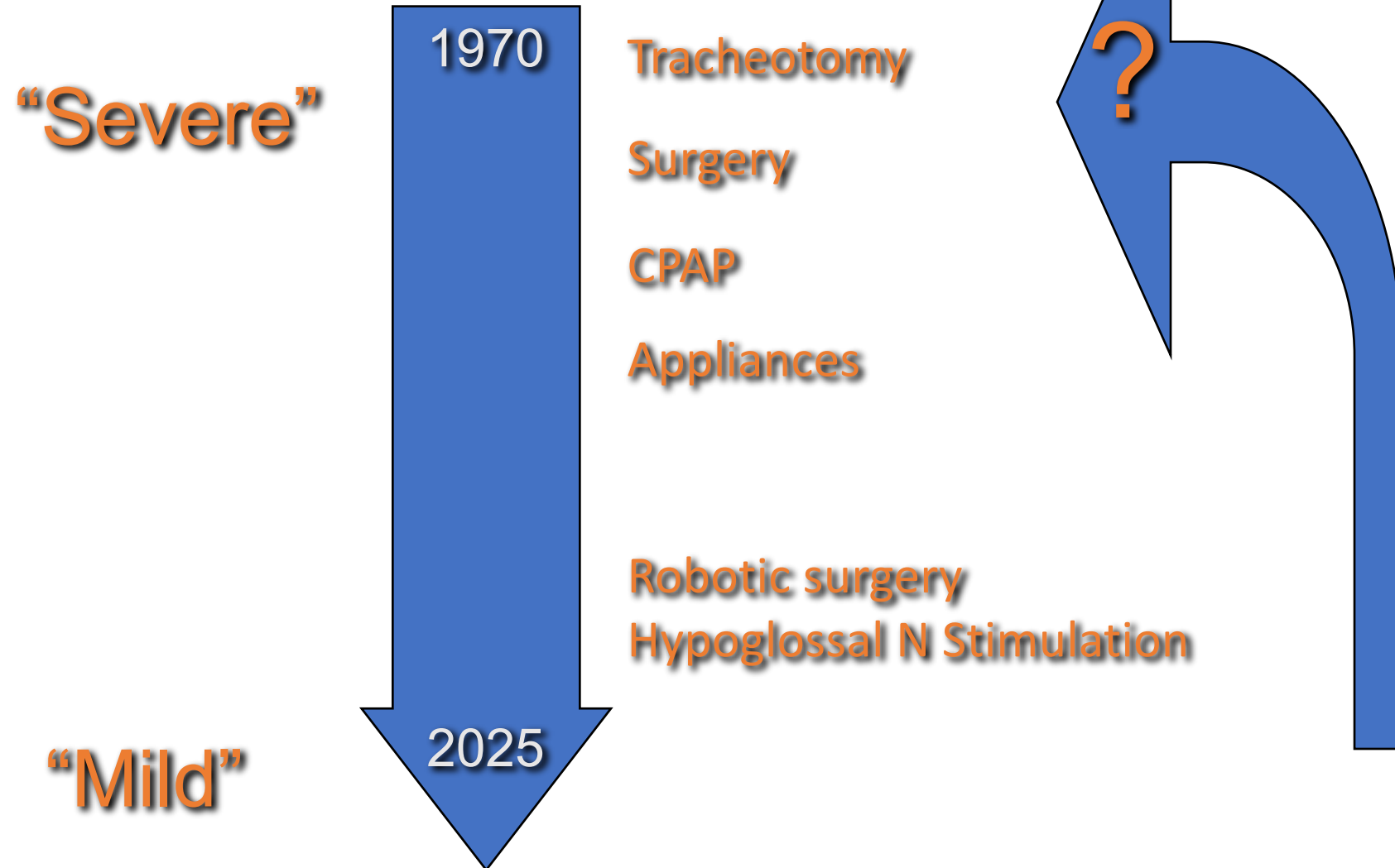
Mandibular Advancement Devices

- Advantages
 - Non-invasive
 - Not permanent
 - Easier to tolerate
- Disadvantages
 - Need to have teeth (in good condition)
 - Expensive
 - May not be covered by insurance
 - Difficult to predict efficacy

Who performs Myofunctional Therapy?



Treatments actually being used



What about medications?

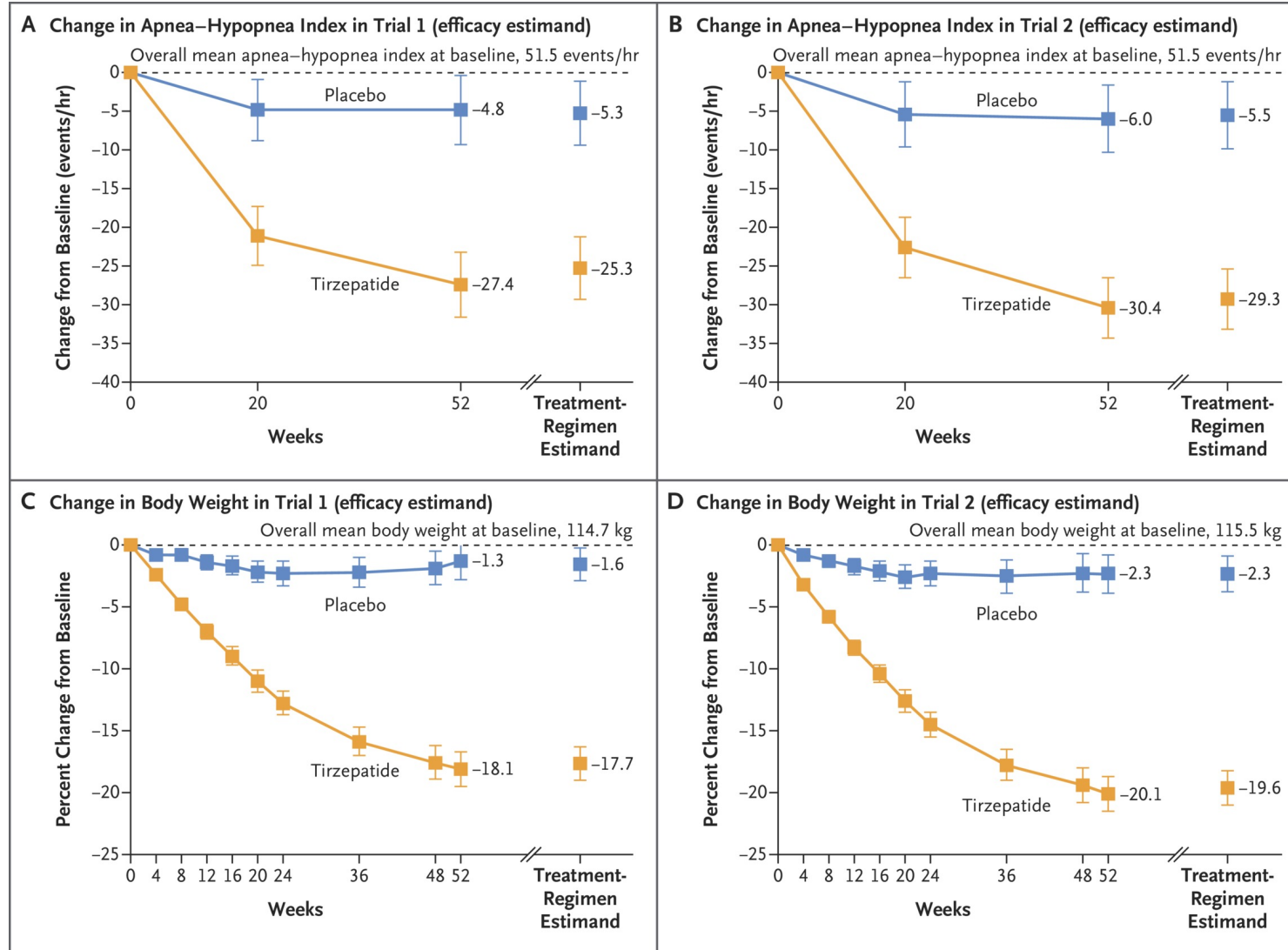
- GLP-1 agonists
- Atomoxetine-plus-oxybutynin

GLP-1 Medications can help!: Finally approved by FDA and CMS for OSA

- Tirzepatide (Mounjaro[®], Zepbound[®])
 - Mounjaro Indications
 - as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
 - Zepbound Indications
 - 30 kg/m² or greater (obesity) or
 - 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea, or cardiovascular disease).
- Semaglutide (Ozempic[®], Wegovy[®])

Medications can help! Tirzepatide

AHI



Change in body weight

Tirzepatide: SURMOUNT trial

- Trial 1 included participants who were unable or unwilling to use PAP therapy
- Trial 2 included participants who had been using PAP therapy for at least 3 consecutive months at the time of screening and who planned to continue PAP therapy during the trial

There are
side effects

Table 4. Adverse Events and Safety.*

Variable	Trial 1		Trial 2	
	Tirzepatide N=114	Placebo N=120	Tirzepatide N=119	Placebo N=114
	<i>number (percent)</i>			
≥1 Adverse event while receiving tirzepatide or placebo	91 (79.8)	92 (76.7)	99 (83.2)	83 (72.8)
Death	0	0	0	0
Serious adverse events	9 (7.9)	7 (5.8)	7 (5.9)	12 (10.5)
Adverse events leading to discontinuation of trial drug or placebo	5 (4.4)	2 (1.7)	4 (3.4)	8 (7.0)
Adverse events occurring in ≥5% of participants in any trial group				
Diarrhea	30 (26.3)	15 (12.5)	26 (21.8)	10 (8.8)
Nausea	29 (25.4)	12 (10.0)	26 (21.8)	6 (5.3)
Vomiting	20 (17.5)	5 (4.2)	11 (9.2)	1 (0.9)
Constipation	18 (15.8)	3 (2.5)	18 (15.1)	5 (4.4)
Eructation	9 (7.9)	0	10 (8.4)	1 (0.9)
Gastroesophageal reflux disease	9 (7.9)	1 (0.8)	6 (5.0)	0
Injection-site reaction	8 (7.0)	1 (0.8)	6 (5.0)	0
Abdominal pain	7 (6.1)	4 (3.3)	5 (4.2)	2 (1.8)
Upper respiratory tract infection	7 (6.1)	10 (8.3)	5 (4.2)	8 (7.0)
Coronavirus disease 2019	6 (5.3)	10 (8.3)	8 (6.7)	11 (9.6)
Nasopharyngitis	3 (2.6)	8 (6.7)	15 (12.6)	12 (10.5)
Dyspepsia	5 (4.4)	2 (1.7)	11 (9.2)	1 (0.9)
Gastroenteritis	3 (2.6)	4 (3.3)	8 (6.7)	1 (0.9)
Upper abdominal pain	4 (3.5)	2 (1.7)	7 (5.9)	2 (1.8)
Influenza	4 (3.5)	8 (6.7)	3 (2.5)	3 (2.6)
Arthralgia	3 (2.6)	6 (5.0)	4 (3.4)	5 (4.4)
Bronchitis	0	0	3 (2.5)	7 (6.1)

Atomoxetine-plus-oxybutynin

- About 40-50% reduction in AHI
- About 2-3 point reduction in ESS
- About 20% of patients had urinary hesitancy

In clinical trials

When all else fails...

“Severe”

1970

Tracheotomy

Surgery

CPAP

Appliances

Laser

Somnoplasty

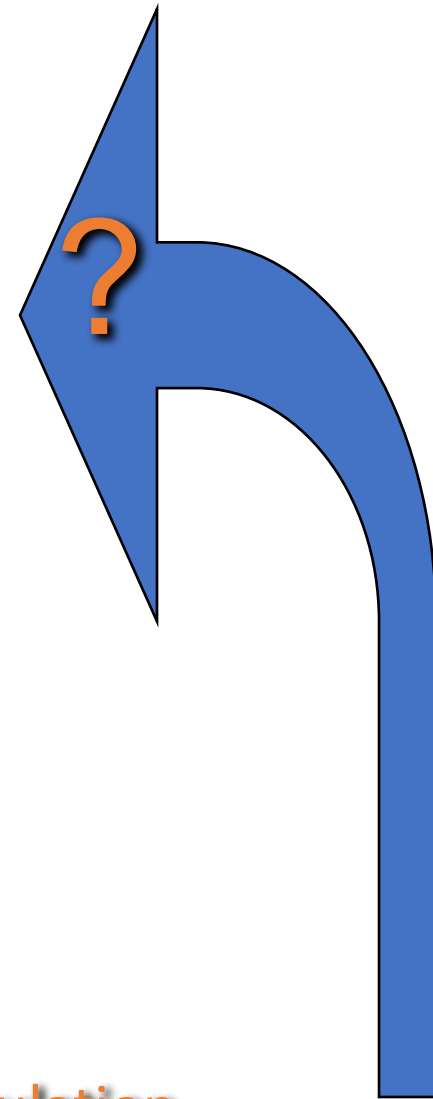
Provent

Robotic surgery

Hypoglossal N Stimulation

2025

“Mild”



Alerting medications can help!

- Modafinil (Provigil®)
 - 200 mg qam (I start at 100 qam)
- Armodafinil (Nuvigil®)
 - 150 mg qam (I start on 50 qam)
- Solriamfetol (SUNOSI®)
 - Start 37.5 mg qam (up to 150 mg)
- Pitolisant (Wakix®)
 - Not FDA or EU approved

Alerting medications can help!

Endpoint	Placebo	Modafinil 200 mg	Modafinil 400 mg	Pitolisant	Solriamfetol
Efficacy Z-score (ESS + OSLER/MWT)	0.00	<i>0.48</i>	<i>0.47</i>	<i>0.78</i>	<i>0.76</i>
Ranking	5	3	4	1	2
ESS	0.01	<i>0.57</i>	<i>0.57</i>	<i>0.63</i>	<i>0.73</i>
Ranking	5	3	3	2	1
OSLER/MWT	0.03	0.51	<i>0.62</i>	<i>0.66</i>	<i>0.69</i>
Ranking	5	4	3	2	1
Benefit-risk (efficacy/safety)	0.00	0.32	<i>0.56</i>	<i>0.81</i>	<i>0.67</i>
Ranking	5	4	3	1	2
QoL	0.27	0.25	0.69	0.73	0.66
Ranking	4	5	2	1	3

Few side effects ...

Parameter	Placebo	Modafinil 200 mg	Modafinil 400 mg	Pitolisant	Solriamfetol
Overall safety (Risk ratio)	<i>0.93</i>	0.39	0.29	0.69	0.21
Ranking	1	3	4	2	5
Overall safety (Z-score)	<i>0.91</i>	0.37	0.29	0.81	0.12
Ranking	1	3	4	2	5
Cardiovascular safety (Risk ratio)	<i>0.7</i>	0.42	0.53	0.72	0.14
Ranking	2	4	3	1	5
Cardiovascular safety (Z-score)	<i>0.67</i>	0.4	0.51	0.8	0.13
Ranking	2	4	3	1	5

What about the future and AI?

I asked ChatGPT – 4o: “Create a 3d realistic image of a doctor who is elderly and conjuring up a future in sleep medicine”



There will always be patients we can't treat

- Remember the driving issue
- Keep on working on weight loss
- Medications for weight loss?
- Give the patient option later to reconsider

Take home messages

- PAP usually works
- Another pathology may cause the symptoms
- Do the best you can solving problems
- In many patients PAP is not an acceptable treatment
- Consider EPAP, oral appliances, neurostimulation, and surgery
- Tracheostomy seldom needed
- Medications indeed may be the answer!