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Eastern Virginia Medical School
AT OLD DOMINION UNIVERSITY

Sleep Apnea in Pregnancy: Known and Unknown

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Objectives

Review the scientific evidence demonstrating potential maternal/fetal harm from obstructive sleep apnea (OSA)

Delineate some existing and new knowledge about OSA in pregnancy

Discuss recommendations for clinical management

Why study sleep? A Scientific Journey

Approximately 1/3 of our life spent in sleep

Sleep is not a passive state

Evidence of adverse impact of abnormal sleep

- Morbidity
- Mortality

We are not making progress in maternal morbidity and mortality

- Are we missing a risk factor?

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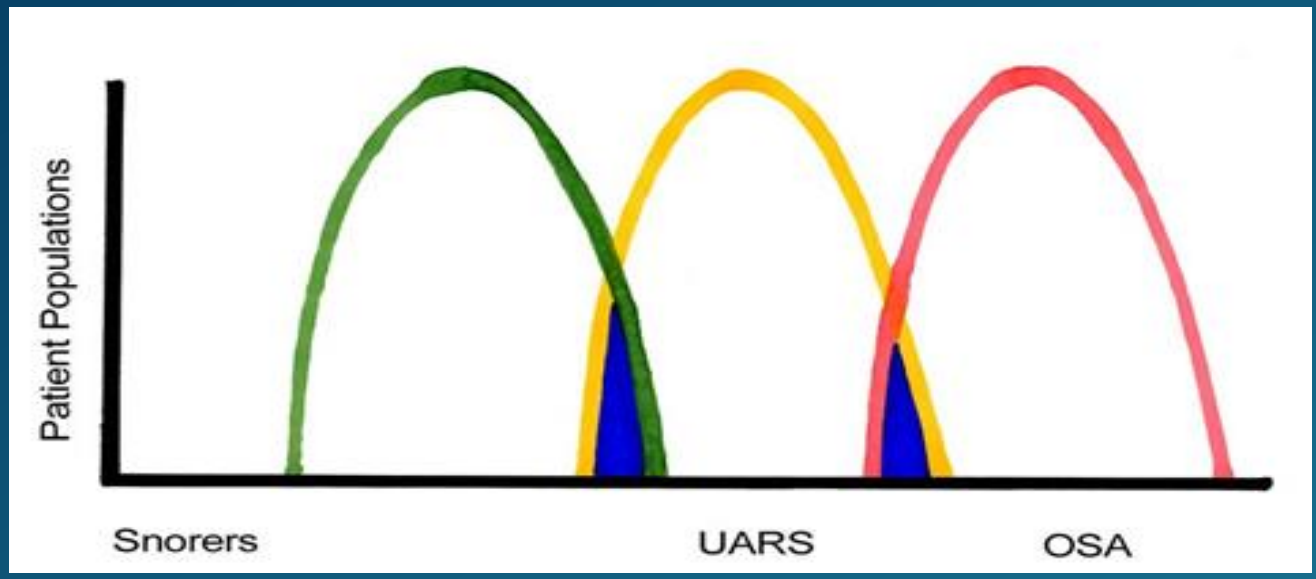
- Abnormal Sleep Behavior Disorders
- Bruxism
- Central Sleep Apnea
- Chronic Fatigue Syndrome
- Circadian Rhythm Sleep Disorders
- Excessive Sleepiness
- Hypersomnia
- Insomnia
- Narcolepsy
- Night Terrors
- Non-24-Hour Sleep Wake Disorder
- Obstructive Sleep Apnea
- Parasomnias
- Periodic Limb Movements
- Disorder Rhythmic Movement
- Disorder REM Sleep Behavior Disorder
- Restless Leg Syndrome (RLS)
- Shift Work Disorder
- Sleepwalking
- Sleep-Related Movement Disorders
- Sleep Paralysis

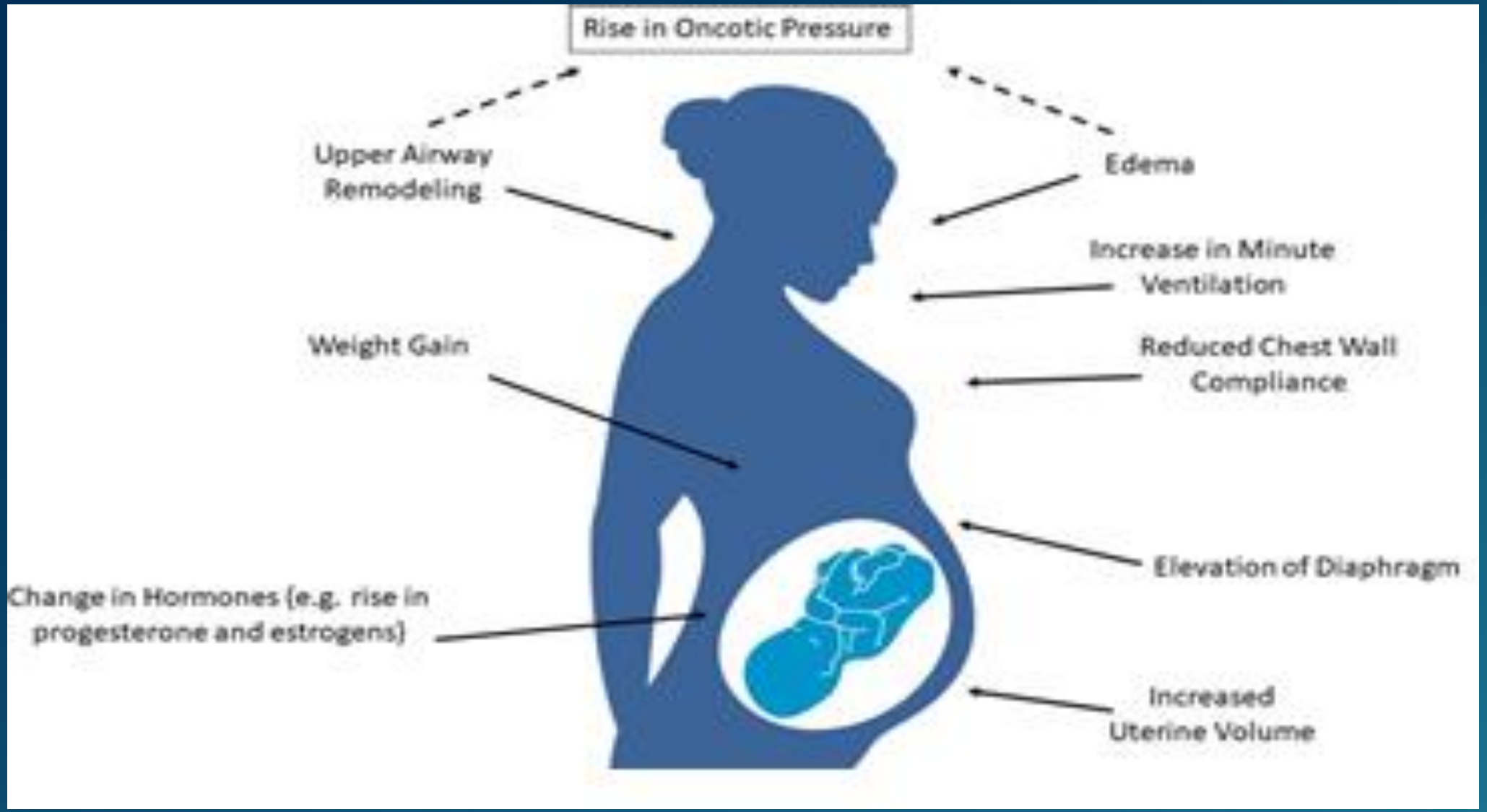
Meers JM, Nowakowski S. Sleep During Pregnancy. Curr Psychiatry Rep. 2022 Aug;24(8):353-357.

Sleep Disordered Breathing (SDB)

- Represents a continuous spectrum of disease
- Recurrent hypopnea and apnea
- OSA is most severe form
- OSA characterized by:
  - Intermittent Hypoxia
  - Arousals
  - Sleep Fragmentation

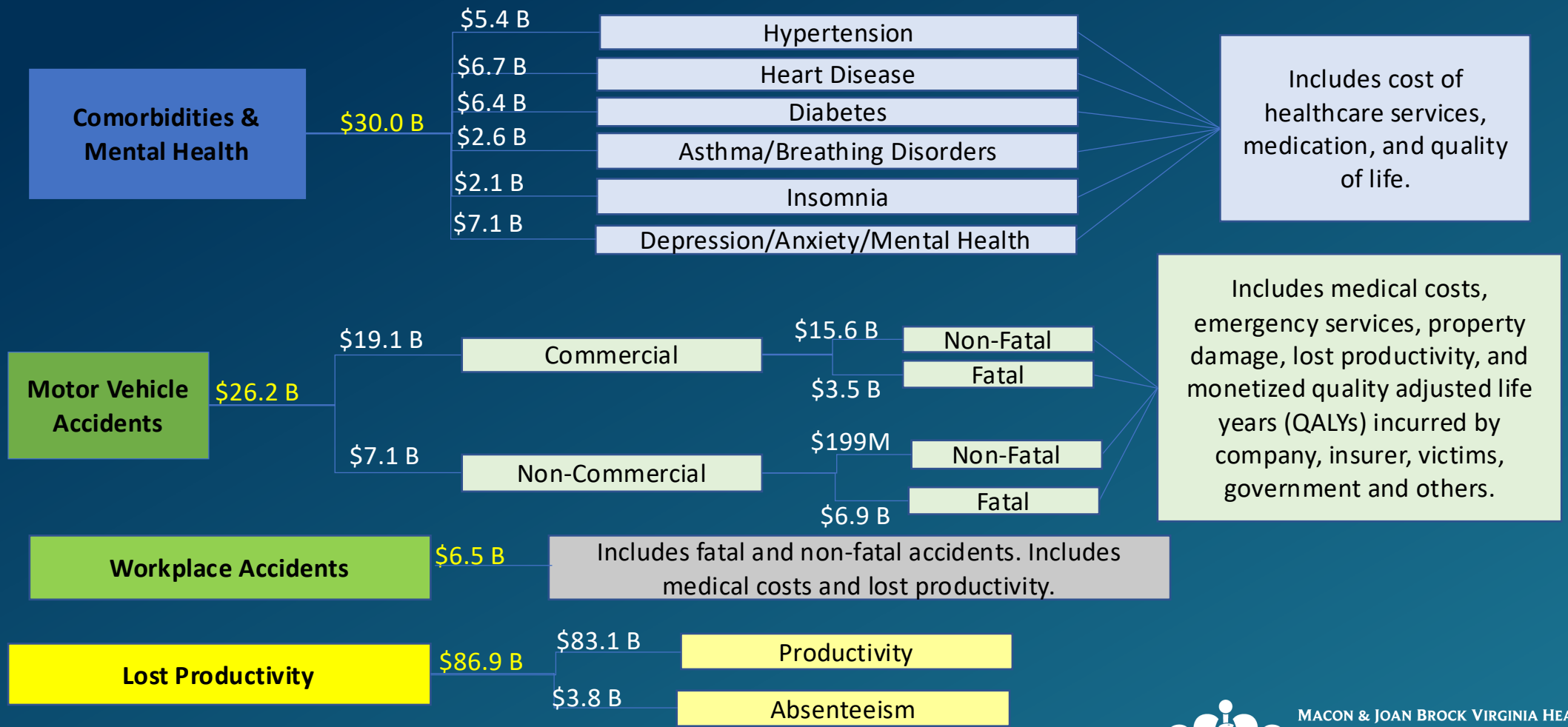


https://emedicine.medscape.com/article/295807-overview



Kryger, Roth & Goldstein. Principles and Practice of Sleep Medicine, Seventh edition. Elsevier Saunders, Philadelphia, 2022

Sources of Cost for Undiagnosed OSA



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How commonly is pregnancy affected?

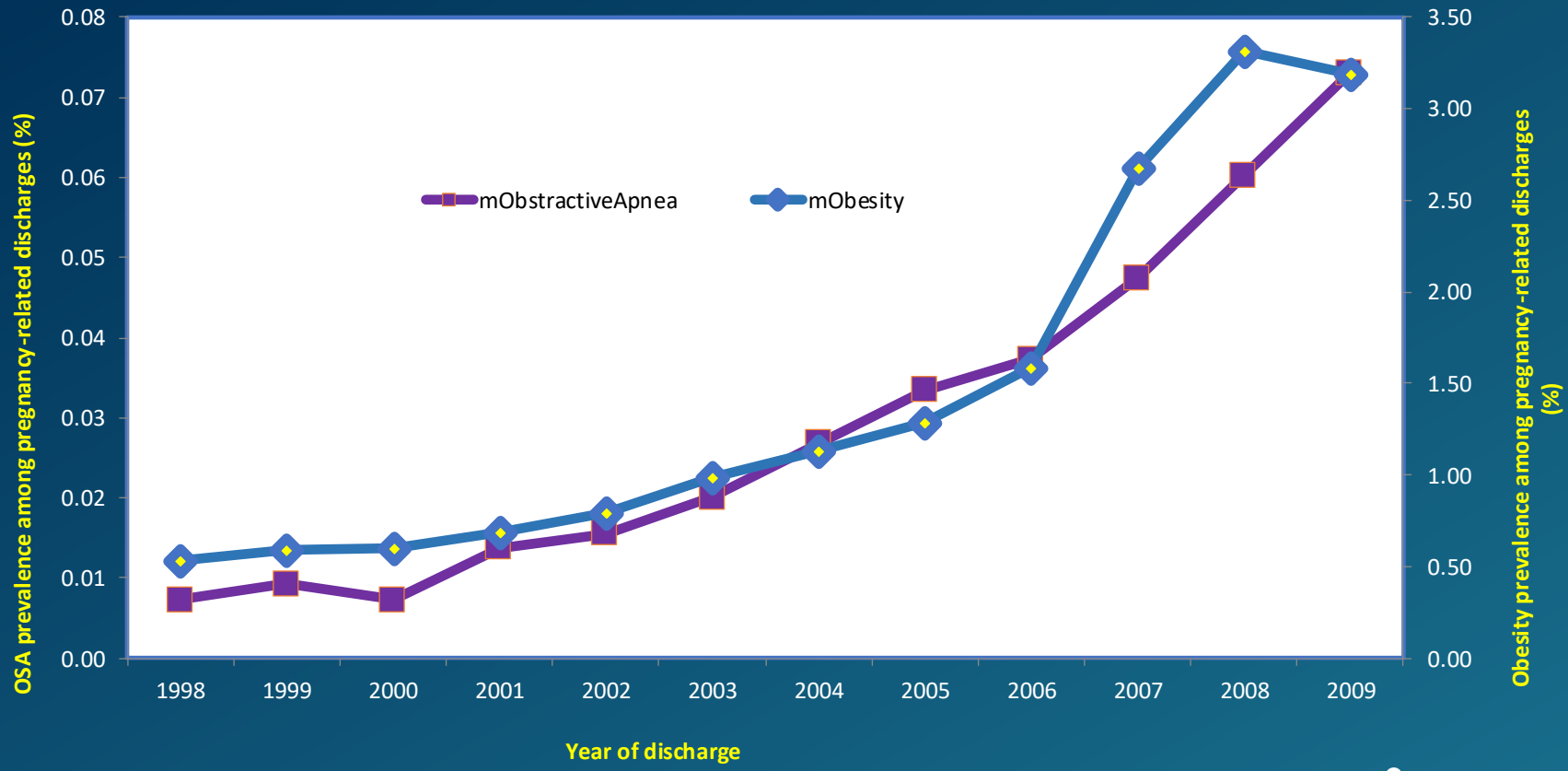
SDB-Prevalence

	Definition	N	Prevalence (%)	Site
Bourjeilly 2010	Questionnaire	1000	35	US
O' Brien 2013	Habitual snoring	1673	35	US
Ko 2013	Questionnaire	276	23	Korea
Fung 2013	Questionnaire	371	29	US
Ugur 2011	Questionnaire	465	14	Turkey
Higgins 2011	Questionnaire	4074	32	US

OSA - Pregnancy prevalence

	Setting	Number of Subjects	Prevalence (%)
Olivarez 2010	In hospital	100	20
Louis 2012	Portable	182	15
Facco 2012	Portable	114	24
Pien 2013	In laboratory	105	10-26
Facco 2017	Portable	3,600	3-8

OSA and obesity increased over time



Cain et al. Semin Perinatol. 2015 Jun;39(4):304-9

What are the perinatal outcomes?

NuMom2b Sleep Sub study N=3,132

	GDM	Preeclampsia
Early Pregnancy	3.47 (1.95-6.19)	1.94(1.07-3.51)
Mid pregnancy	2.79 (1.63-4.77)	1.95(1.18-3.23)

- Prevalence of SDB:
  - Early Pregnancy: 3.6%
  - Mid pregnancy: 8.3%
- Preeclampsia: 6%
- All Hypertensive Disorders : 13%
- GDM: 4.1%

Facco et al. Obstet Gynecol. 2017 Jan;129(1):31-41

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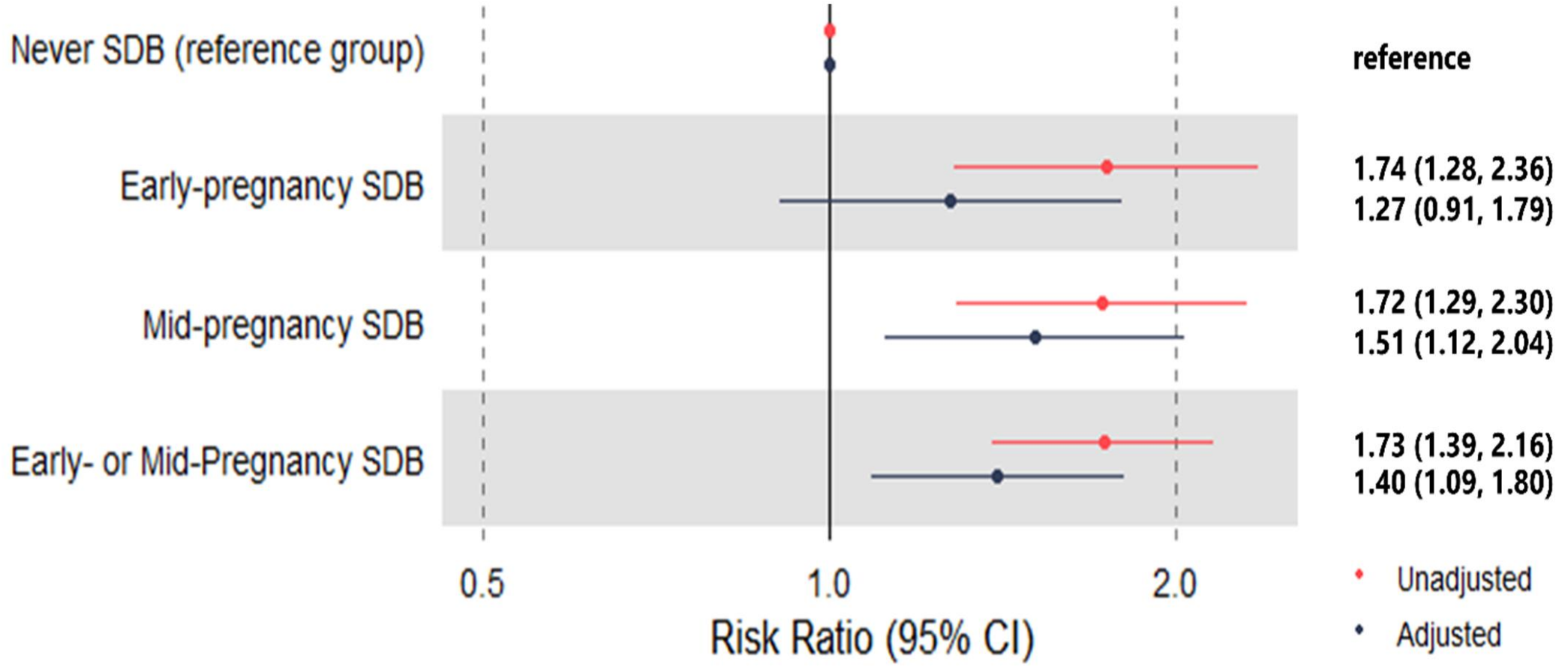
Figure: Risk ratios and 95% confidence intervals representing the association between sleep-disordered breathing (SDB) phenotype and an adverse neonatal outcome



Adverse Outcomes: respiratory distress syndrome, transient tachypnea of the newborn, or other respiratory support, treated hyperbilirubinemia, treated hypoglycemia, large-for-gestational age (LGA), seizures treated with medications or confirmed by electroencephalography, confirmed sepsis (based on culture), or neonatal death.

Delgado A et al. Am J Perinatol. 2023 Jul 29

What about severe maternal morbidity?

OSA is associated with Severe Morbidity: National Inpatient Survey Data

Outcomes	OSA	
	With obesity	Without obesity
	OR (95% CI)	OR (95% CI)
Cesarean section	2.08 (1.8 – 2.3)	2.09 (1.8 – 2.3)
Gestational diabetes	4.13 (3.54 – 4.82)	3.35 (2.90 – 3.88)
Gestational hypertension	2.83 (2.24 – 3.58)	2.01 (1.58 – 2.56)
Pre-eclampsia	5.32 (4.43 – 6.37)	3.41 (2.84 – 4.10)
Eclampsia	2.93 (0.68 – 12.66)	10.41 (6.20 – 17.50)
Pulmonary embolism	14.06 (6.10 – 32.40)	8.07 (2.61 – 24.92)
Cardiomyopathy	19.12 (15.12 – 24.18)	15.86 (12.45 – 20.19)
Hospital stay > 5 days	6.1 (5.3 – 7.2)	7.5 (6.7 – 8.4)
Death	7.8 (3.2-18.7)	5.07 (1.6-15.7)

Louis et al. Sleep. 2014 May 1;37(5):843-9

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Louis et al. Sleep. 2014 May 1;37(5):843-9

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OSA is associated with early delivery

	OSA	
	With obesity	Without obesity
	OR (95% CI)	OR (95% CI)
Early onset delivery	1.46 (1.20 – 1.77)	1.49 (1.27 – 1.76)
Poor fetal growth	1.17 (0.79 – 1.73)	1.43 (1.05 – 1.96)
Stillbirth	0.75 (0.38 – 1.51)	1.42 (0.83 – 2.40)

Louis et al. Sleep. 2014 May 1;37(5):843-9

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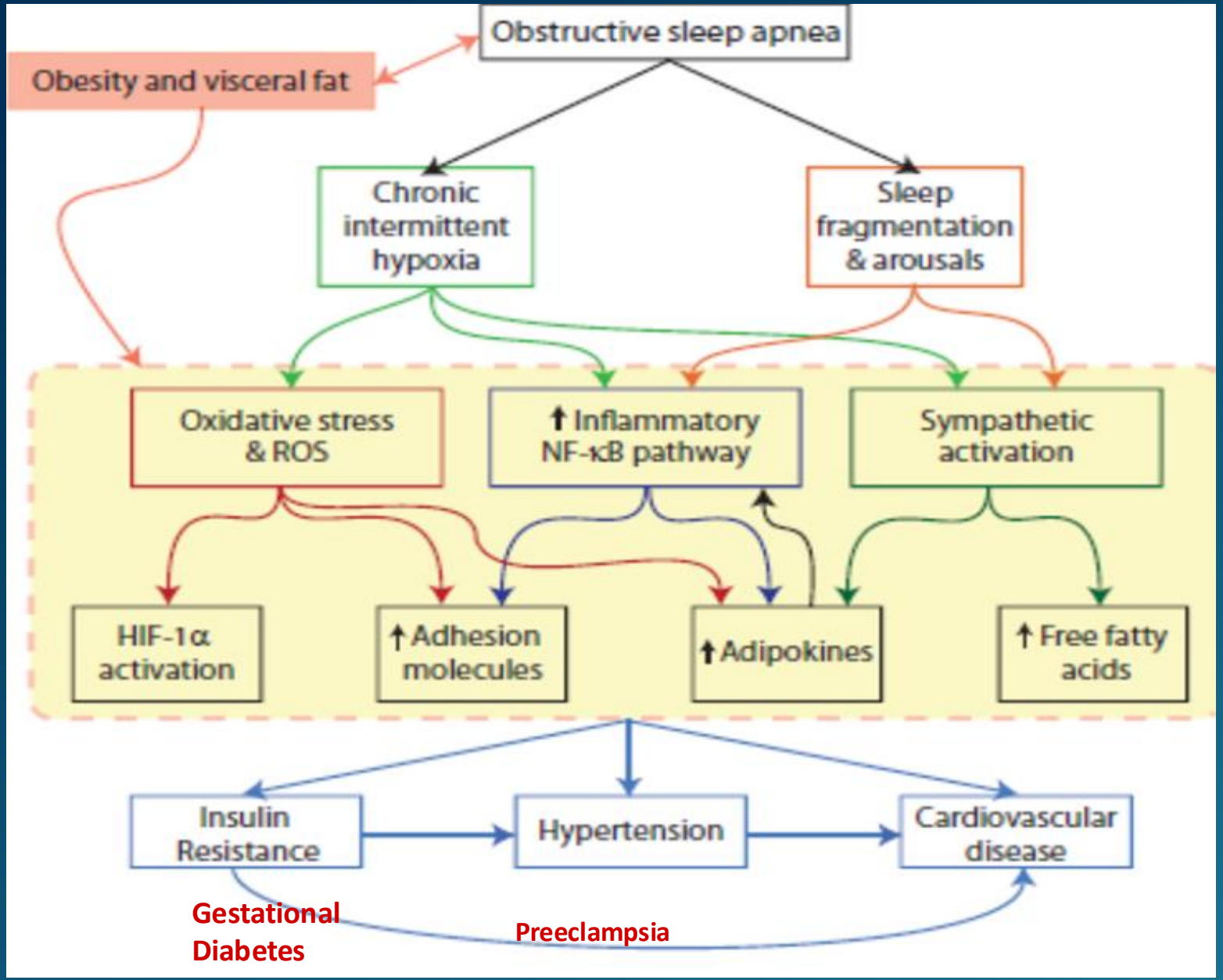
What are the mechanisms of disease?



Arnardottir ES et al. Sleep. 2009 Apr;32(4):447-70

Let’s Talk About Screening

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Screening Tools

- STOP (Snoring, Tired, Observed, Pressure)
- STOP- BANG (Snoring, Tired, Observed, Pressure- BMI, Age, Neck, Gender)
- Epworth Sleepiness Scale
- Berlin Questionnaire

All function poorly

Tantrakul et al. J Clin Sleep Med. 2015 Jan 15;11(2):157-63

Women BMI ≥ 40km/m2

Objective testing: Type III unattended home sleep apnea testing

TABLE 3

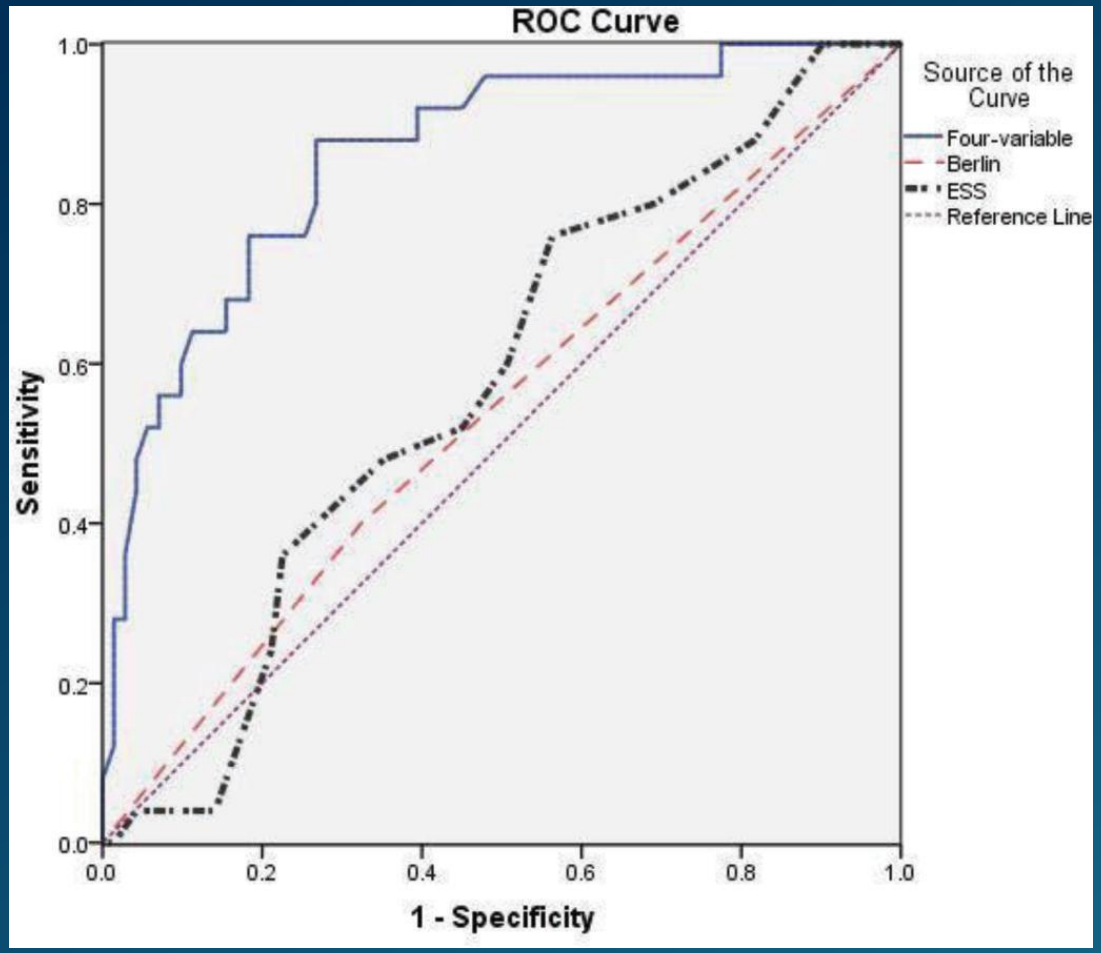
Performance of obstructive sleep apnea screening tools and sleepiness scale

Screening tool	Obstructive sleep apnea status		*P* value	Odds ratio (95% confidence interval)	Area under the receiver operating characteristic curve	High risk for obstructive sleep apnea by tool		
	No (n=61)	Yes (n=19)				High risk, n (%)	Sensitivity	Specificity
Berlin Questionnaire[a,20]	2 [2, 3]	2 [2, 3]	.567	1.20 (0.59, 2.43)	0.541 (0.394, 0.688)	64 (80.0)	0.79	0.20
STOP-BANG questionnaire[a,19,21,22,25]	3 [3, 4]	4 [2, 5]	.092	1.58 (1.00, 2.49)	0.625 (0.466, 0.784)	34 (42.5)	0.63	0.36
Epworth Sleepiness Scale[a,24]	3 [2, 5]	2 [2, 5]	.810	1.09 (0.85, 1.40)	0.519 (0.356, 0.681)	0 (0.0)	0.00	1.00
American Society of Anesthesiologists checklist,[23] n (%)	58 (95.1)	17 (89.5)	.588	0.44 (0.07, 2.85)	0.528 (0.452, 0.604)	75 (93.8)	0.23	0.05
Facco et al score[a,2]	87 [78, 93]	98 [88, 112]	.001	1.06 (1.02, 1.10)	0.752 (0.637, 0.868)	67 (83.8)	1.00	0.21

[a] Data are given as median [Q1, Q3].

Dominguez et al. OSA screening in obese parturients. Am J Obstet Gynecol 2018.

Best predictor?



- Frequent Snoring (15 points)
- Chronic hypertension (15 points)
- Age
- BMI

- Score >75 is high risk

Facco et al. J Clin Sleep Med. 2012 Aug 15;8(4):389-94

OBSTETRICS

Predictors of sleep-disordered breathing in pregnancy

Judette M. Louis, MD, MPH; Matthew A. Koch, MD, PhD; Uma M. Reddy, MD, MPH; Robert M. Silver, MD; Corette B. Parker, DrPH; Francesca L. Facco, MD, MSCI; Susan Redline, MD, MPH; Chia-Ling Nhan-Chang, MD; Judith H. Chung, MD, PhD; Grace W. Pien, MD, MSCE; Robert C. Basner, MD; William A. Grobman, MD, MBA; Deborah A. Wing, MD, MBA; Hyagriv N. Simhan, MD; David M. Haas, MD, MS; Brian M. Mercer, MD; Samuel Parry, MD; Daniel Mobley, RPSGT; Benjamin Carper, MS; George R. Saade, MD; Frank P. Schubert, MD, MS; Phyllis C. Zee, MD, PhD

Best predictors

- Age
- BMI
- Frequent snoring

Louis J et al . Am J Obstet Gynecol. 2018 May;218(5):521.e1-521.e12.

Should you screen?

Weak evidence – A lot of “expert opinion”

Individualized Risk/Benefit- Patient centric

What is the goal?

- Short term
  - Pregnancy risks
  - Perioperative risks
- Long term
  - Future health
  - Future pregnancy

Algorithms for screening

No right answer

Consider Sleep Health Equity

Some examples:

- Risk scoring: survey + comorbidity
- Morbid obesity + comorbidity
- Clinical suspicion

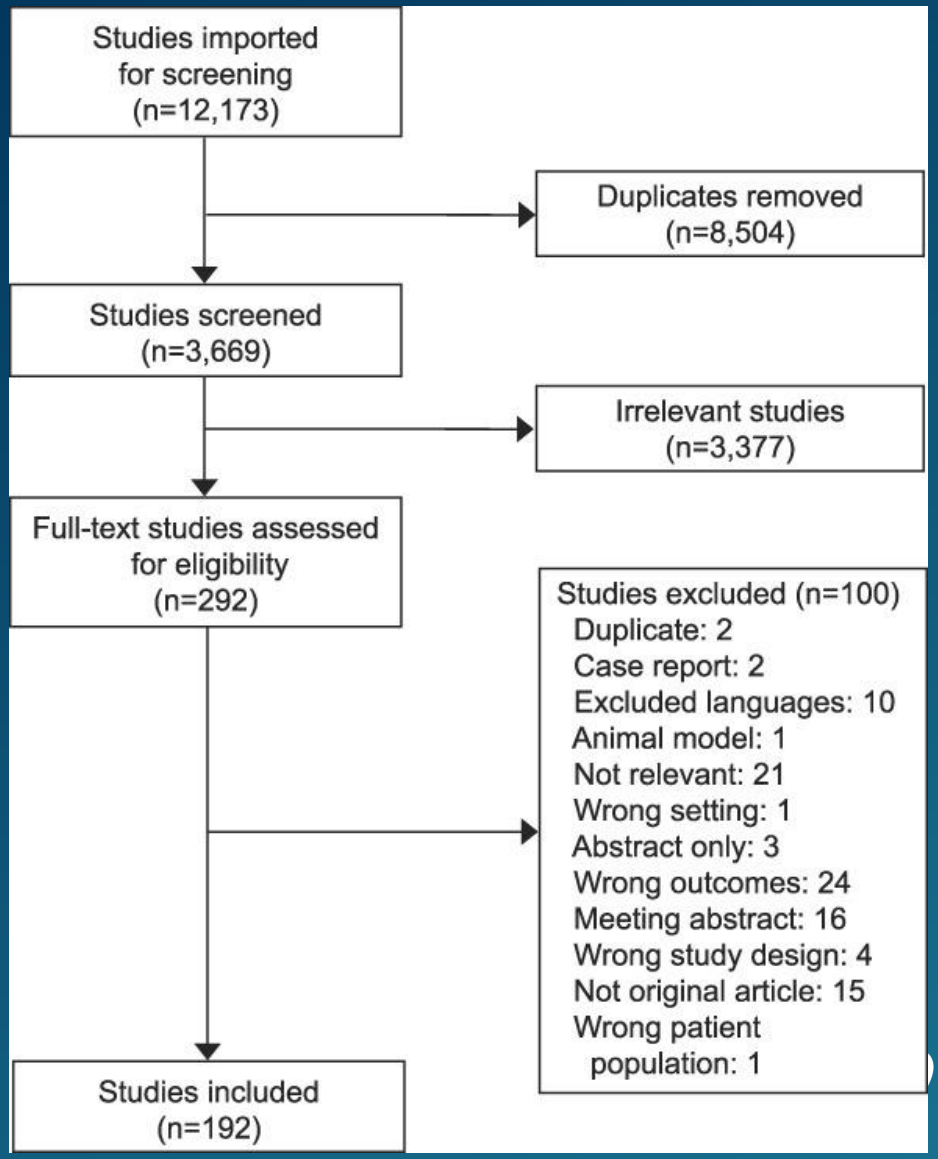
Should you manage the pregnancy differently?

Society of Anesthesia and Sleep Medicine and the Society for Obstetric Anesthesia and Perinatology Consensus Guideline on the Screening, Diagnosis, and Treatment of Obstructive Sleep Apnea in Pregnancy

Dominguez, Jennifer E. MD, MHS*; Cantrell, Sarah MLIS; Habib, Ashraf S. MBBCh; Izci-Balserak, Bilgay MS, PhD; Lockhart, Ellen MD; Louis, Judette M. MD, MPH; Miskovic, Alice MBBS, FRCA; Nadler, Jacob W. MD, PhD; Nagappa, Mahesh MD, MSc; O'Brien, Louise M. PhD, MS; Won, Christine MD, MSc; Bourjeily, Ghada MD*

Obstetrics & Gynecology 142(2):p 403-423, August 2023.

Methodology



SASM Guideline: Screening

No benefit to universal screening

Recommend screening high-risk individuals: hypertension and diabetes

Recommend screening in the first or second trimester

Which tool to use? It's complicated.

SASM Guideline: Diagnosis

Portable sleep study is reasonable

Overnight pulse oximetry is insufficient for diagnosis

Repeat testing in the postpartum period may be appropriate, but timing is unclear

SASM Guideline: Treatment

The treatment benefit outweighs the risk.

The maternal fetal benefit of treatment is unknown.

Follow the standard of care for the general population.

Use auto-titrating CPAP

Do not recommend weight loss in pregnancy; alcohol use should be avoided.

Other Aspects of Management

Prenatal

- Management and screening for comorbid conditions
- Obesity is common
- Looks for hypertension, diabetes, arrhythmia

Fetal Surveillance

- Growth ultrasounds
- Antenatal testing per ACOG guidelines

Delivery

- High risk of cesarean delivery

Higher risk of cesarean delivery

- With obesity- difficult neuraxial anesthesia
- Often difficult intubation
- Collapsibility of airway

Sudden response to opioids and anesthetics

- Hypoventilation

Doofas AG et al. PLoS. One. 2013;8(1):e54807.
Lamon AM, Habib Reg Anesth. 2016; 9():45-57

Perioperative Monitoring

Protocols vary/ Have a plan

- Who?
- Where?
- How?
- How long?

What are the local resources?

How long do you monitor?

Society of anesthesia and sleep medicine guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea: Until they are no longer high risk

What does that mean for postdelivery patients?

- Early ambulation
- “Baby friendly” = “Maternal sleep unfriendly”
- Protocols have varied 12-48 hours

Chung F, Memtsoudis SG, et al. Anesthesia and analgesia. 2016;123:452.

ASA- Preoperative evaluation

Neuraxial morphine- controversial

Components may depend on presence of hypoxemia

Multi-modal post-operative analgesia

- Non-steroidal anti-inflammatory agents and acetaminophen are recommended when possible, to decrease the risk of sedation and hypoventilation associated with opioids.
- Transversus abdominis plane block, local anesthetic wound catheters and neuraxial techniques
- Avoid standing orders: Sedating medications

American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Anesthesiology. 2014 Feb; 120(2):268-86.

How do you diagnose and treat it?

Treatment: CPAP

The “Gold Standard” in the treatment of OSA

- Works the best in the most people
- Positive pressure ventilation functions as a pneumatic splint for the collapsing upper airway

But... adherence is very poor

- 29-83%
- ? Higher with modern technology

Sunwoo et al. Respirology. 2020 Apr;25(4):363-371.

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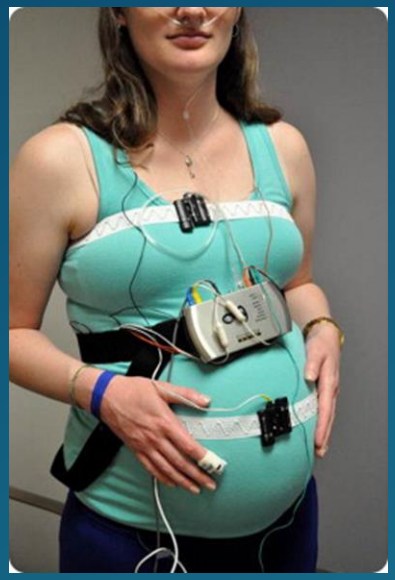
- Overnight PSG

- Portable polysomnography may underestimate AHI

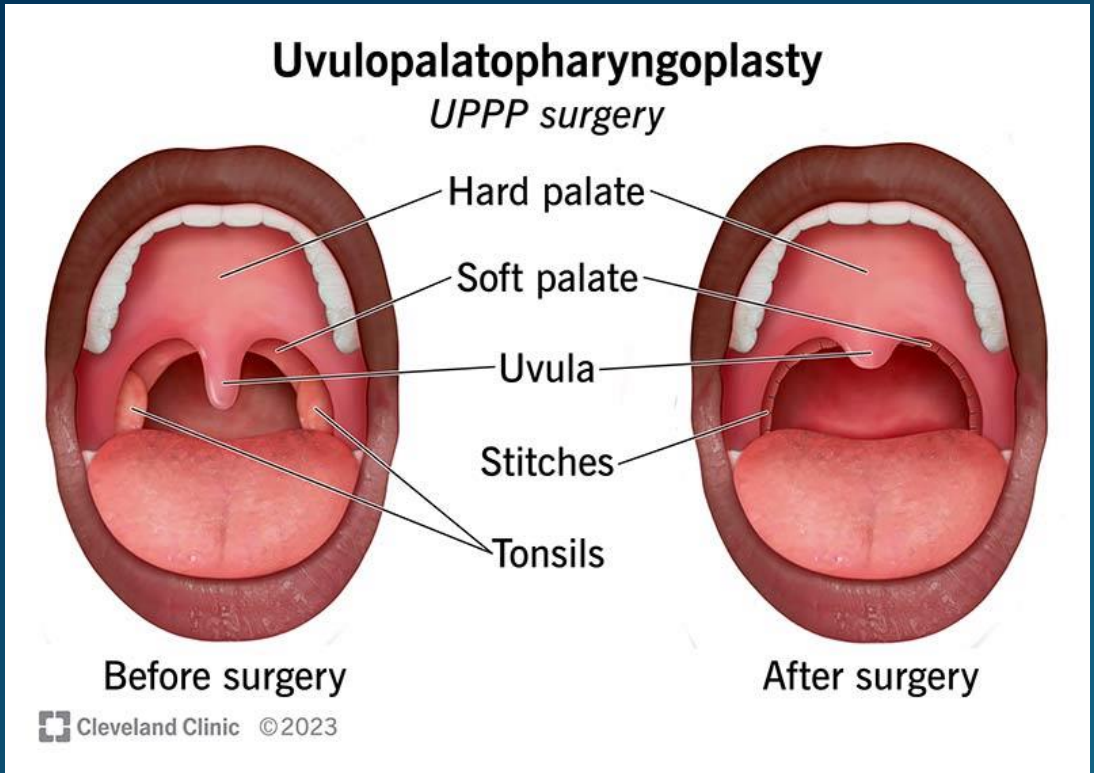


Louis et al. Obstetrics & Gynecology 2012. 119(4):864-868

Treatment

Interventional

- Surgery
  - UP3 (uvulopalatopharyngoplasty) or uvulectomy
  - Tonsillectomy /Adenoidectomy



https://my.clevelandclinic.org/health/treatments/25059-uvulopalatopharyngoplasty-uppp

Treatment: Oral appliance

- Oral Appliances
  - Variable success rates, though probably more useful for mild to moderate apnea
  - ?Adherence
- Effective
- Often considered only as second-line therapy following positive airway pressure (PAP) therapy failure.

Ng et al. Sleep Med Clin. 2020 Jun;15(2):241-250.

Is treatment effective?

RESEARCH Open Access

Treatment of obstructive sleep apnea in high risk pregnancy: a multicenter randomized controlled trial

Visasiri Tantrakul[1,2,3,4], Atiporn Ingsathit[1*], Somprasong Liamsombut[3,4], Sasivimol Rattanasiri[1], Prapun Kittivoravitkul[5], Nutthaphon Imsom-Somboon[6], Siwaporn Lertpongpiroon[7], Surasak Jantarasaengaram[8], Werapath Somchit[9], Worakot Suwansathit[4], Janejira Pengjam[4], Sukanya Siriyotha[1], Panyu Panburana[9], Christian Guilleminault[10], Aroonwan Preutthipan[4,11], John Attia[12] and Ammarin Thakkinstian[1]

Respir Res. 2023 Jun 27;24(1):171

Table 7 Secondary outcomes on preeclampsia, and hypertensive disorders in pregnancy using the per-protocol and counterfactual analyses

Endpoints	CPAP group	Usual-care group	Risk difference, % (95%CI)[a]	Number needed to treat (95%CI)[a]	*p* value
Per-protocol analysis	(*n* = *50*)	(*n* = *155*)			
Preeclampsia, no. (%)	6 (12.0)	35 (22.6)	− 11 (− 22, 6)	–	0.124
Severe preeclampsia[b]	6 (12.0)	22 (14.19)	− 2 (− 8, 13)	–	0.684
Early preeclampsia[c]	4 (8.0)	4 (2.58)	5 (− 13, 3)	–	0.180
Late preeclampsia[d]	2 (4.0)	31 (20.0)	− 16 (− 24, − 8)	7 (3, 10)	0.024
Hypertensive disorders in pregnancy[e], no. (%)	7(14.0)	39(25.2)	− 11 (− 23, 1)	–	0.120
Counterfactual analysis	(*n* = *52*)	(*n* = *258*)			
Preeclampsia, no. (%)	6 (11.5)	49 (19.0)	− 17 (− 27, − 6)	6 (2, 10)	< 0.001
Severe preeclampsia[b]	6 (11.54)	29 (11.24)	9 (− 19, 0.4)	–	0.062
Early preeclampsia[c]	4 (7.69)	4 (1.55)	2 (− 5, 5)	–	0.938
Late preeclampsia[d]	2 (3.85)	45 (17.44)	− 18 (− 27, − 10)	6 (3, 8)	< 0.001
Hypertensive disorders in pregnancy[e], no. (%)[e]	7 (13.5)	53 (20.5)	− 19 (− 30, − 9)	5 (2, 8)	< 0.001

CPAP continuous positive airway pressure; *95%CI* 95% confidence interval

[a] Binary logistic regression analysis was used to calculate the risk difference and number needed to treat of preeclampsia and hypertensive disorders in pregnancy between participants in CPAP versus usual-care groups

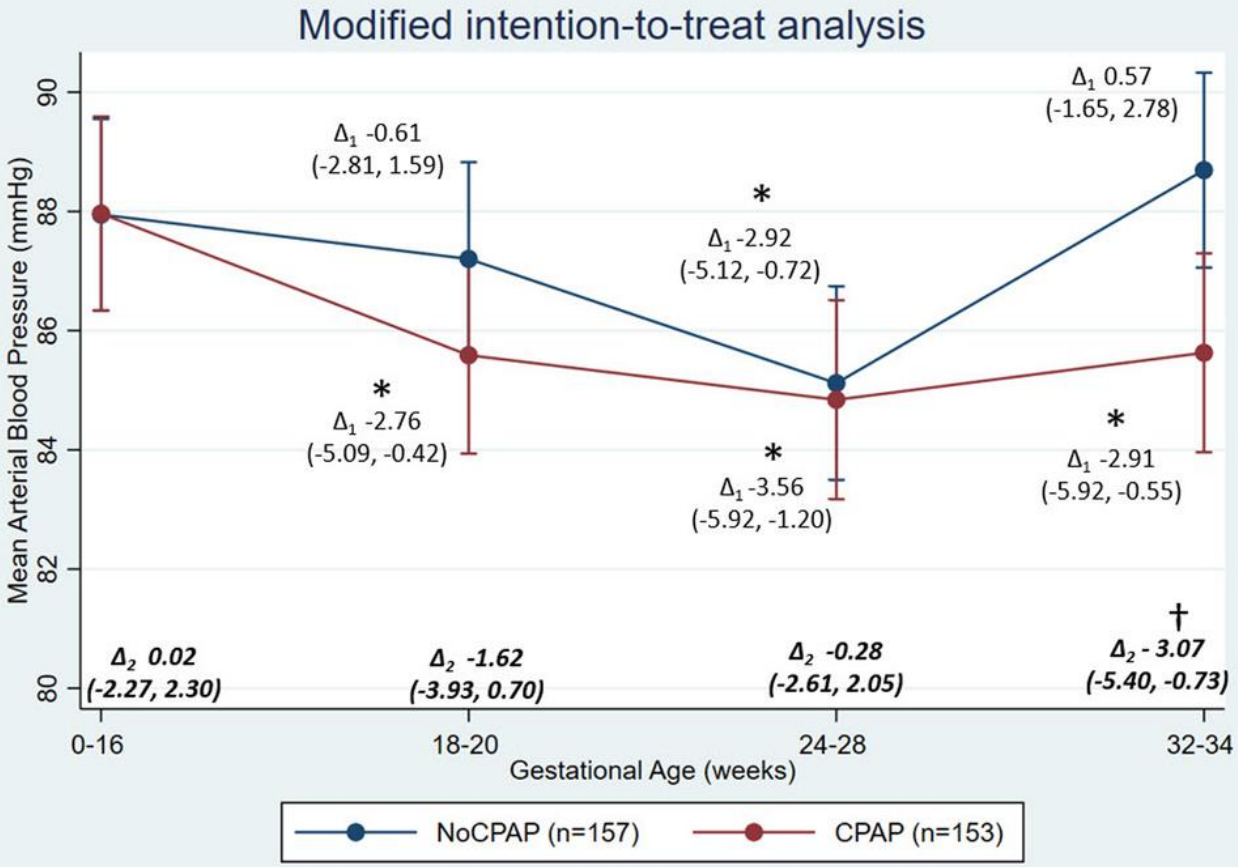
[b] Severe preeclampsia was defined according to Report of the American College of Obstetricians and Gynecologists' Task Force on hypertension in pregnancy [31, 32]

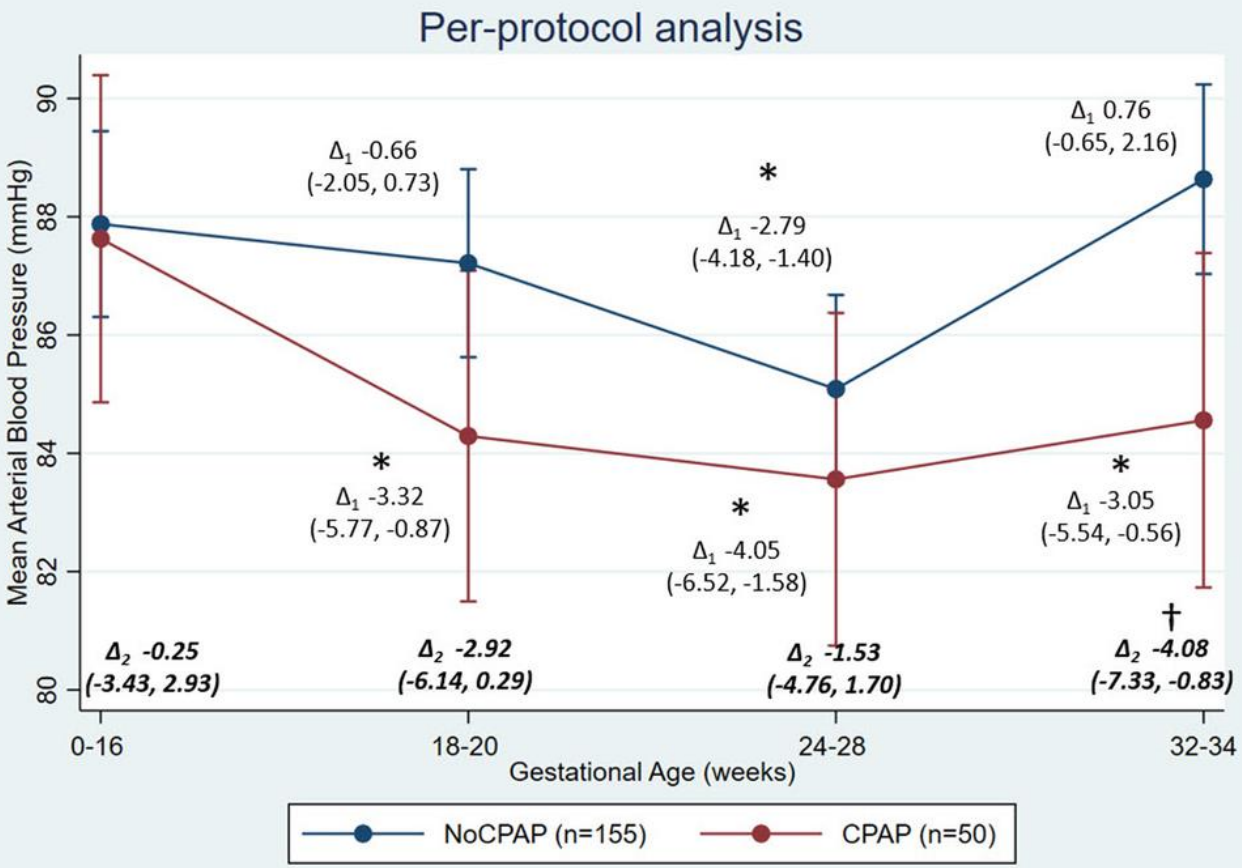
[c] Early-onset preeclampsia was defined as developing preeclampsia before 34 completed weeks' gestation;

[d] Late-onset preeclampsia was defined as developing preeclampsia a or beyond 34 weeks' gestation

[e] Hypertensive disorders in pregnancy comprised of preeclampsia and gestational hypertension

The Temporal Change of Mean Arterial Blood Pressure: The intra-and-inter Groups Differences





In Process: MFMU CPAP Trial

What happens postpartum?

Postpartum: Short-term outcomes

? Increased Postpartum Depression

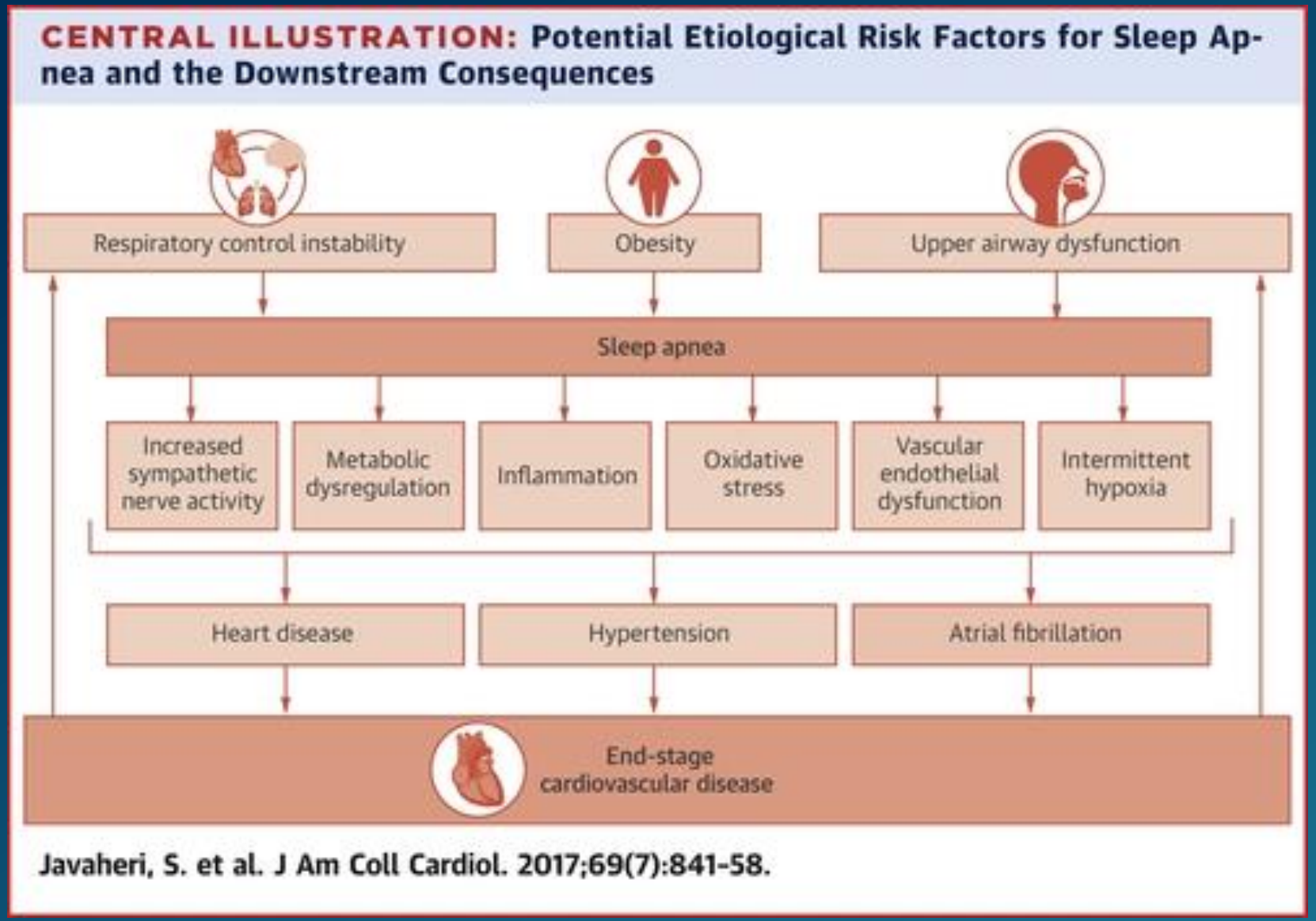
Unclear impact on lactation

“Gestational sleep apnea”- may resolve postpartum

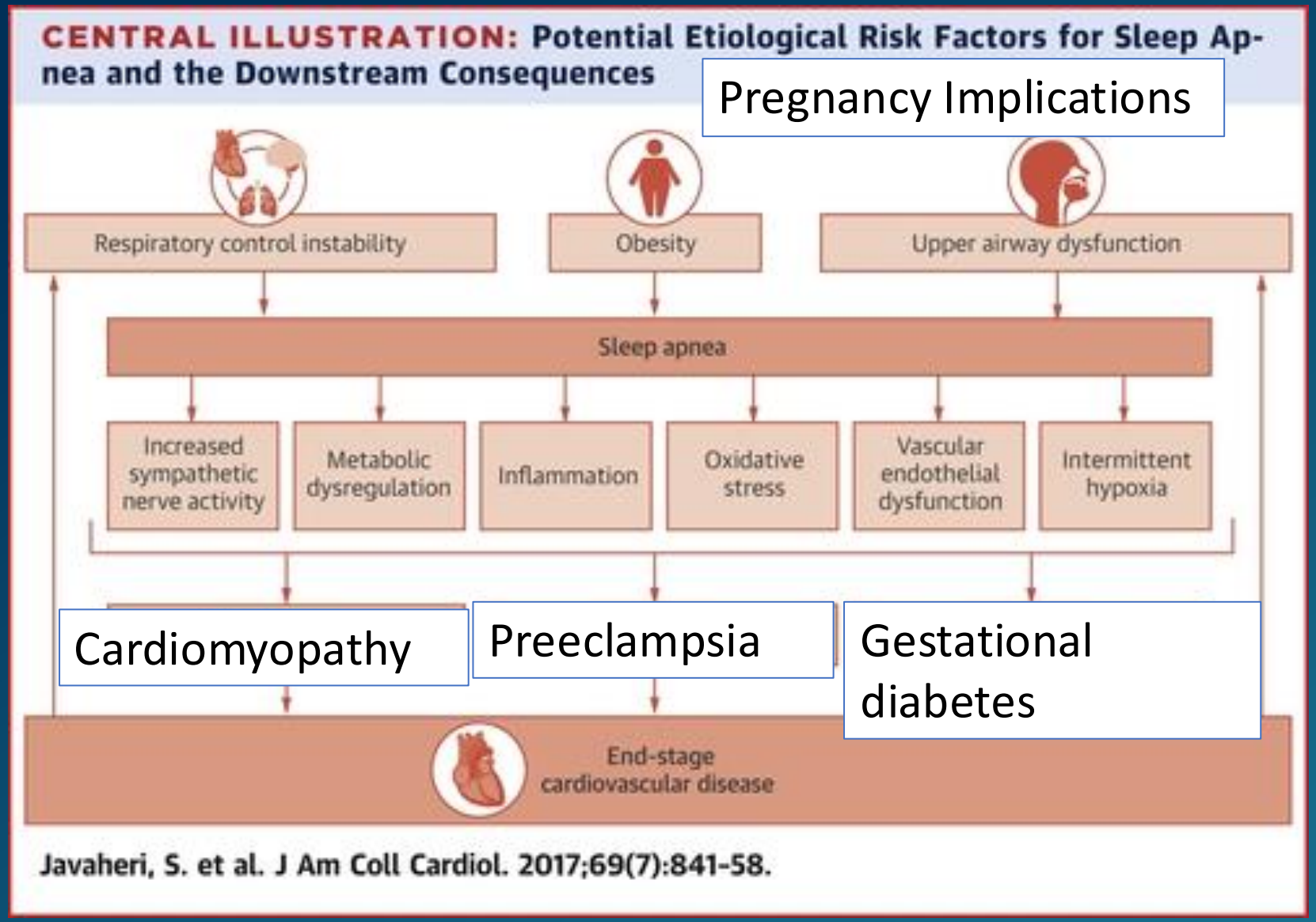
Severe sleep apnea may improve

Recommend evaluation by sleep medicine

- Timing is unclear
- Goal is optimization of health before next pregnancy



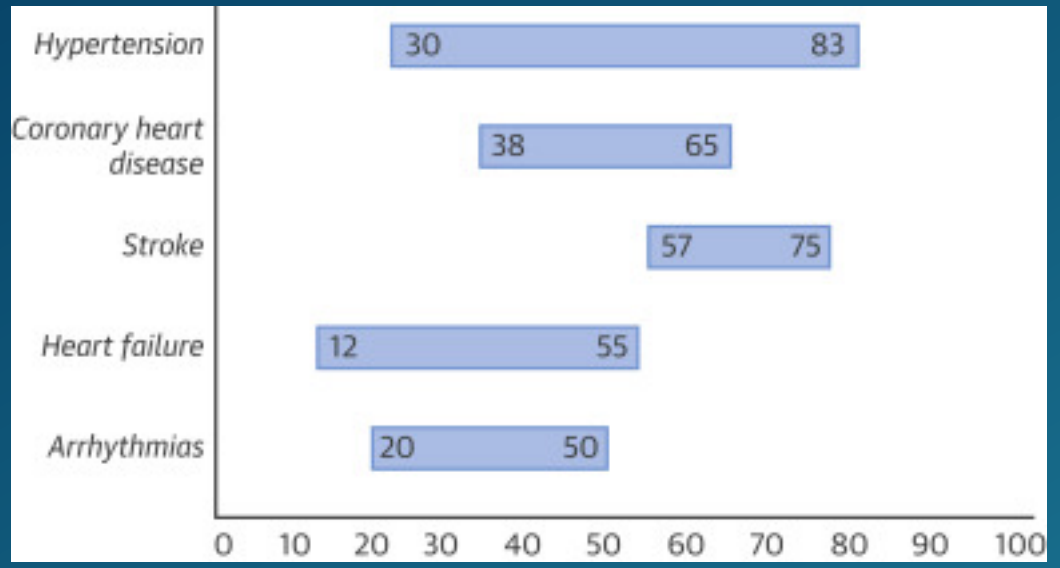
Sleep Apnea, Volume: 69, Issue: 7, Pages: 841-858, DOI: (10.1016/j.jacc.2016.11.069)



Sleep Apnea, Volume: 69, Issue: 7, Pages: 841-858, DOI: (10.1016/j.jacc.2016.11.069)

Cardiovascular disease and OSA

- Bidirectional relationship
- Dose response relationship



Prevalence (%) of OSA in CVD

Javaheri S. Volume 69, Issue 7, 21 February 2017, Pages 841-858

CPAP Treatment with ? Effectiveness?

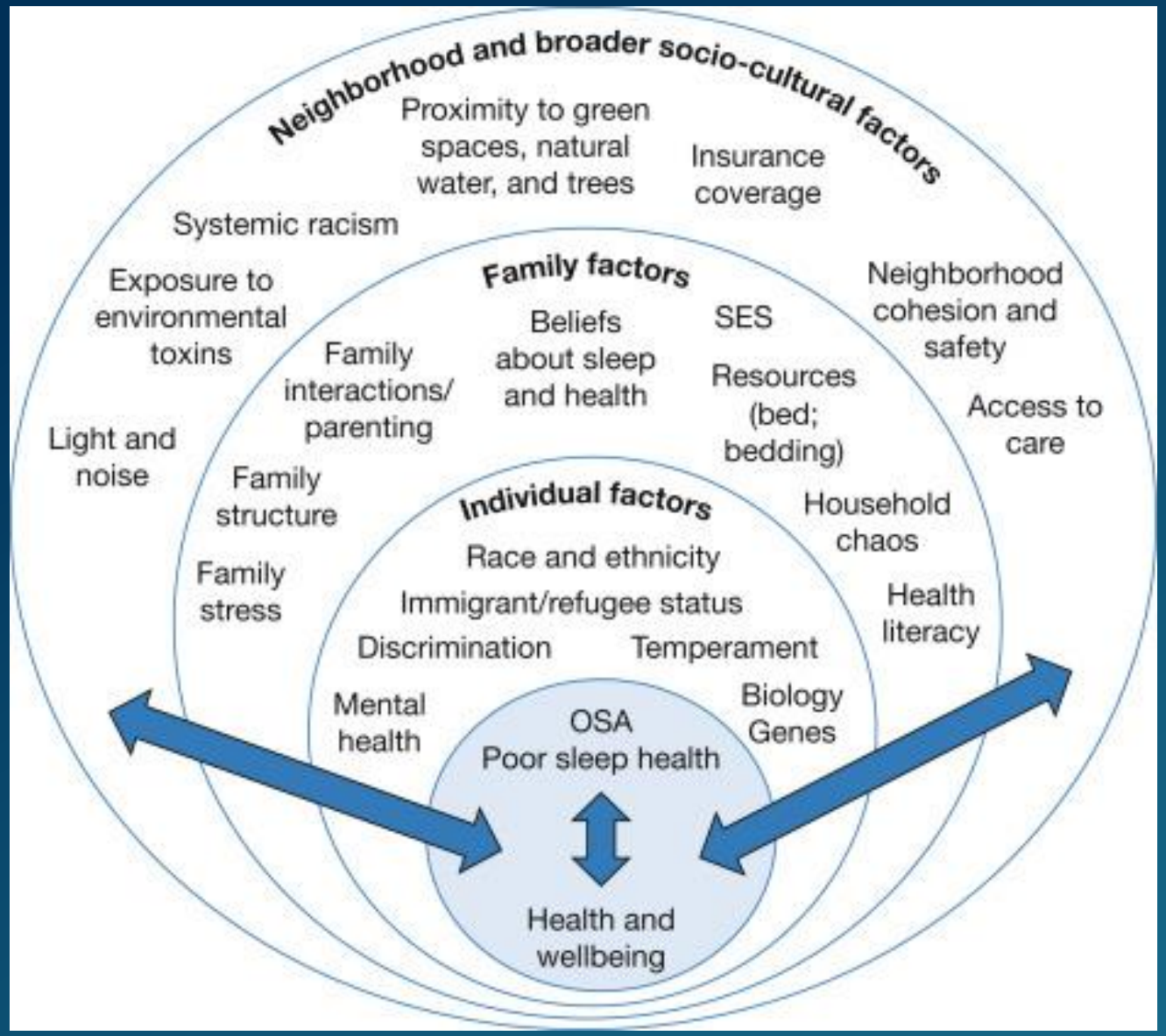
CPAP- treatment of choice

Some benefit for hypertension, especially drug resistant

Not effective for other cardiovascular disease

Limited information about impact on arrhythmias

Sleep Health Equity



Jackson CL et al. Sleep. 2020 Aug 12;43(8):zsaa037

Sleep Health Equity

Higher prevalence in persons of color

Lower diagnosis/treatment rates/ Higher severity at diagnosis

Lower rates of referral follow-up

Lower adherence to treatment

Interventions

- Screening during unrelated hospitalizations
- Use of home testing
- Peer buddies
- Improve communication
  - Race concordant care

Billings ME et al. *Chest*, *159*(3), 1232–1240

What we know

- SDB is prevalent among high risk patients
- Prevalence increased across pregnancy
- Older age, hypertension, obesity and diabetes are risk factors
- SDB is associated with GDM and hypertensive disorders in pregnancy
- Some SDB resolves after delivery
- SDB associated with future hypertension and metabolic syndrome

What we don’t know

- What is the best screening tool?
- Does treatment make a difference?
- Is there a window of susceptibility?
- What is the optimal treatment?
- Does “gestational OSA’ behave differently?
- What is the neonatal harm from OSA?

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Hi
CONNECT

Questions?
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Judettelouis

The case that changed everything

37 y.o. G3P0020 at 36 weeks – restrained driver MVA

Femur fracture-Underwent ORIF

Hypertension- preeclampsia ruled out

Tylenol 3 at 1 am – Code Blue 3 a.m.

Review of case

- Untreated sleep apnea
- Fell asleep at the wheel
- Pulse ox 84% in OR- improved with 4L O2 nasal cannula
- No oxygen monitoring

Autopsy: pulmonary hypertension consistent with severe sleep apnea and respiratory suppression

Breaches in Care

Prenatal care

- Treatment of OSA
- Sleep Medicine Consultation only addressed outpatient recommendations

Full review of her vital signs from the MVA

Lack of communication with OB regarding intraoperative events

Lack of appropriate postoperative care of a patient with OSA