



# Maternal and Fetal Implications of Sleep Disturbances in Pregnancy

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## Conflicts of Interest

1. I do not have any potential conflicts of interest to disclose, **OR**

2. I wish to disclose the following potential conflicts of interest:

Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	NIH funding (NHLBI, NICHD, NIMH) ; American Sleep Medicine Foundation; Star Legacy Foundation; ResMed; Smart Human Dynamics
Consultant	Star Legacy Foundation, Smart Human Dynamics
Speakers' Bureaus	
Financial support	
Other	

3. The material presented in this lecture has no relationship with any of these potential conflicts, **OR**

4. This talk presents material that is related to one or more of these potential conflicts, and the following objective references are provided as support for this lecture:

Edwards et al. Nasal continuous positive airway pressure reduces sleep-induced blood pressure increments in preeclampsia. *Am J Resp Crit Care Med* 2000; 162(1):252-257.  
Heazell et al. Association between maternal sleep practices and late stillbirth - findings from a stillbirth case-control study. *BJOG* 2018; 125(2): 254-262

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## Healthcare Burden of Obstetric Conditions

	Frequency (US)	Annual Extra Cost (per person)	US Annual Burden
<b>Hypertensive Disorders</b> - Chronic hypertension - Gestational hypertension - Preeclampsia	8-10%	~\$14,000	~\$3 billion
<b>Gestational Diabetes</b>	5-9%	~\$7,000	~\$2 billion
<b>Perinatal Depression</b>	10-20%	~\$35,000	~\$15 billion
<b>Preterm Birth</b>	8-15%	~\$150,000 - \$500,000	~\$25 billion
<b>Pregnancy Loss / Miscarriage</b>	10-25%	\$500	~\$140 million
<b>Stillbirth</b>	0.6-1%	\$10,000	~\$240 million

All of these conditions are approximately 2-fold higher in Minority women

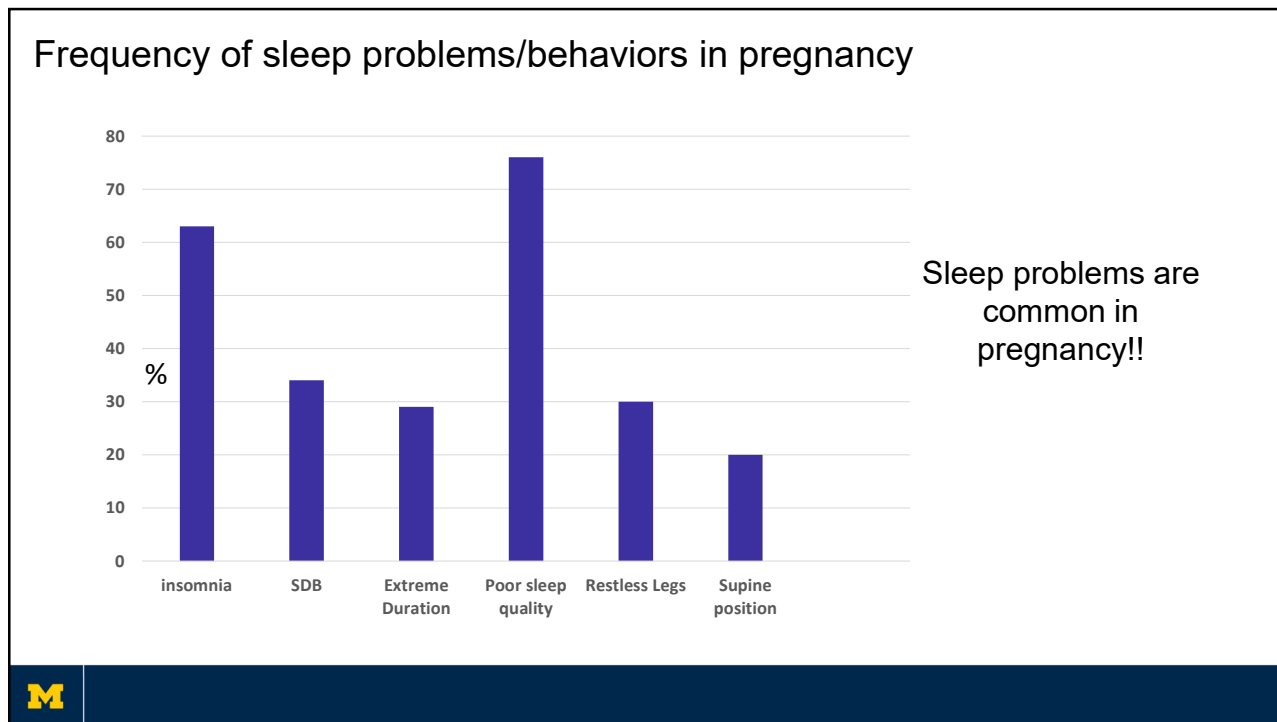


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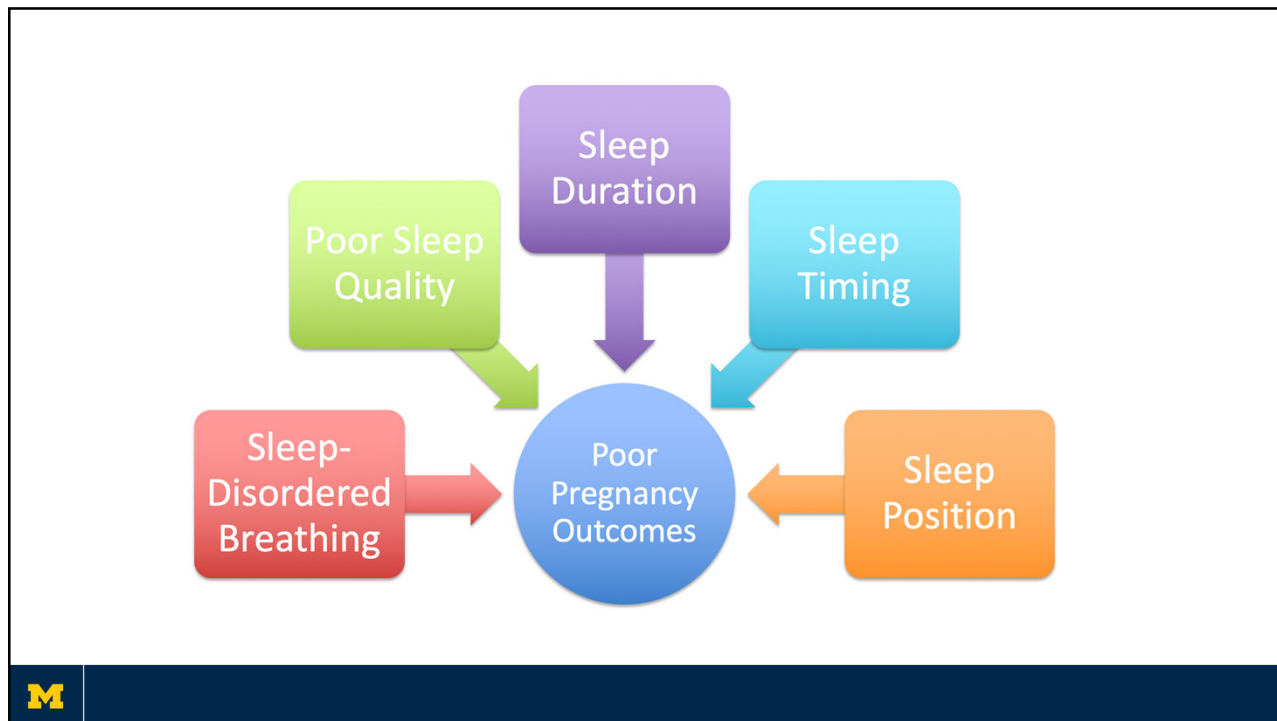
What does maternal sleep have to do with it?



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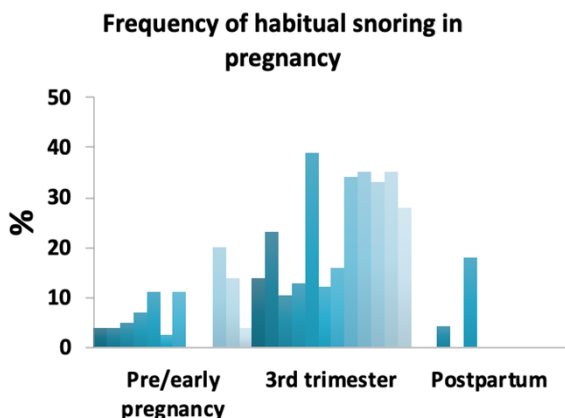
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## Sleep-Disordered Breathing (habitual snoring)

**Habitual snoring** affects ~ 35% of pregnant women by the 3<sup>rd</sup> trimester and up to 85% of those with preeclampsia



~65% of women with SDB during pregnancy had persistent sleep-disordered breathing following delivery

Unclear if or when SDB resolves



Izci 2006, Bourjeily 2010, O'Brien 2012, Louis 2012, Lui 2022

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## Sleep-Disordered Breathing (OSA)

By mid-to-late pregnancy **OSA** affects about;

- 8-10% of pregnant women
- 15-25% of obese pregnant women (BMI $\geq$ 30)
- approximately 60% of pregnant women with BMI $\geq$ 40
- 50% of women with pre-eclampsia

**How many clinicians ask patients with pre-eclampsia about their sleep?**



Reid 2011, O'Brien 2014, Facco 2017, Pitts, Treadwell, O'Brien (unpublished)

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## OSA in Hypertensive Pregnancies



- N=51 pregnant women with hypertension *unselected for sleep problems*
- Mean gestation 27±7 weeks
- 41% African American
- 78% obese
- 61% habitual snoring

**Table 3.** Comparison of hypertensive women with and without snoring

	Hypertension and snoring (n = 30)	Hypertension without snoring (n = 21)
AHI ≥5	16 (53%)*	5 (24%)
AHI ≥15	8 (27%)**	0%
AHI ≥30	6 (20%)*	0%
SpO <sub>2</sub> nadir ≤80%	6 (20%)*	0%

AHI, apnoea/hypopnoea index; SpO<sub>2</sub>, oxygen saturation.  
\*P = 0.05; \*\*P = 0.01.

### Baseline sleep study results:

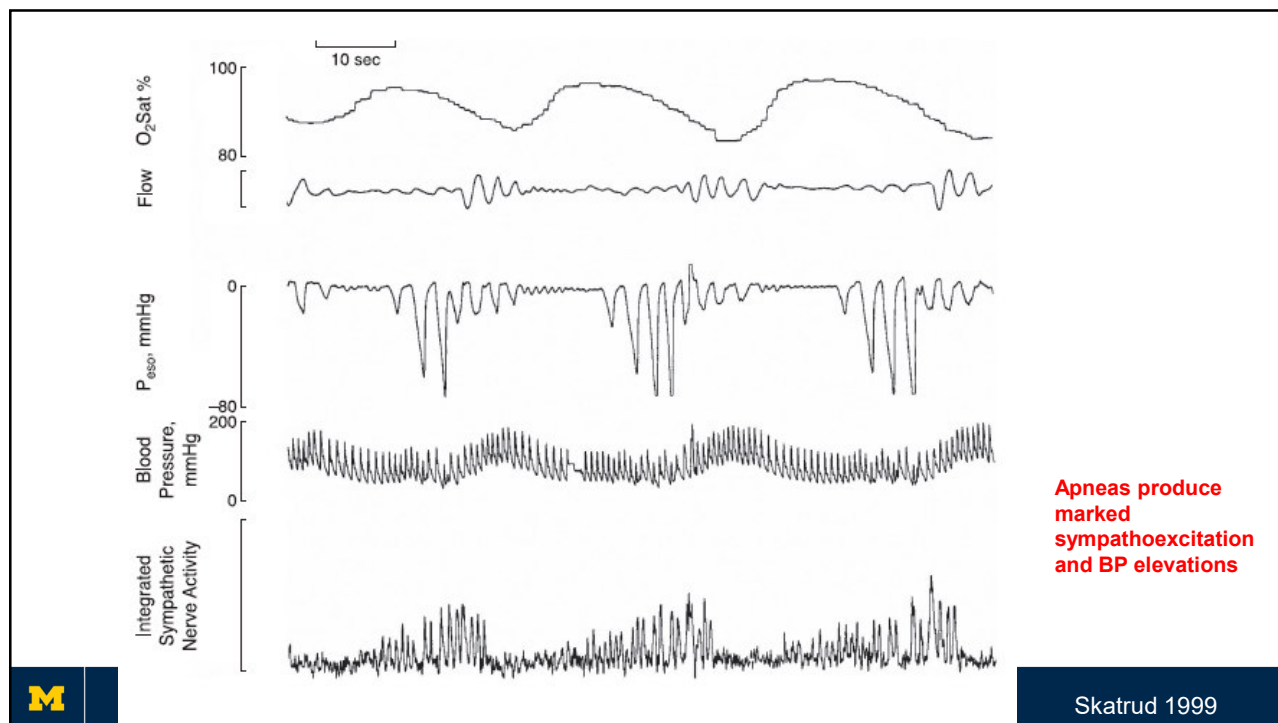
- Mean AHI=13.5 (range 0.1-117.2)
- 80% of women had AHI≥1
- 41% had AHI≥5
- 16% had AHI≥15
- 12% had AHI≥30

Pooled relative risk for OSA in hypertensive women who snored, vs. non-snoring hypertensives, was 2.0 (1.4-2.8)



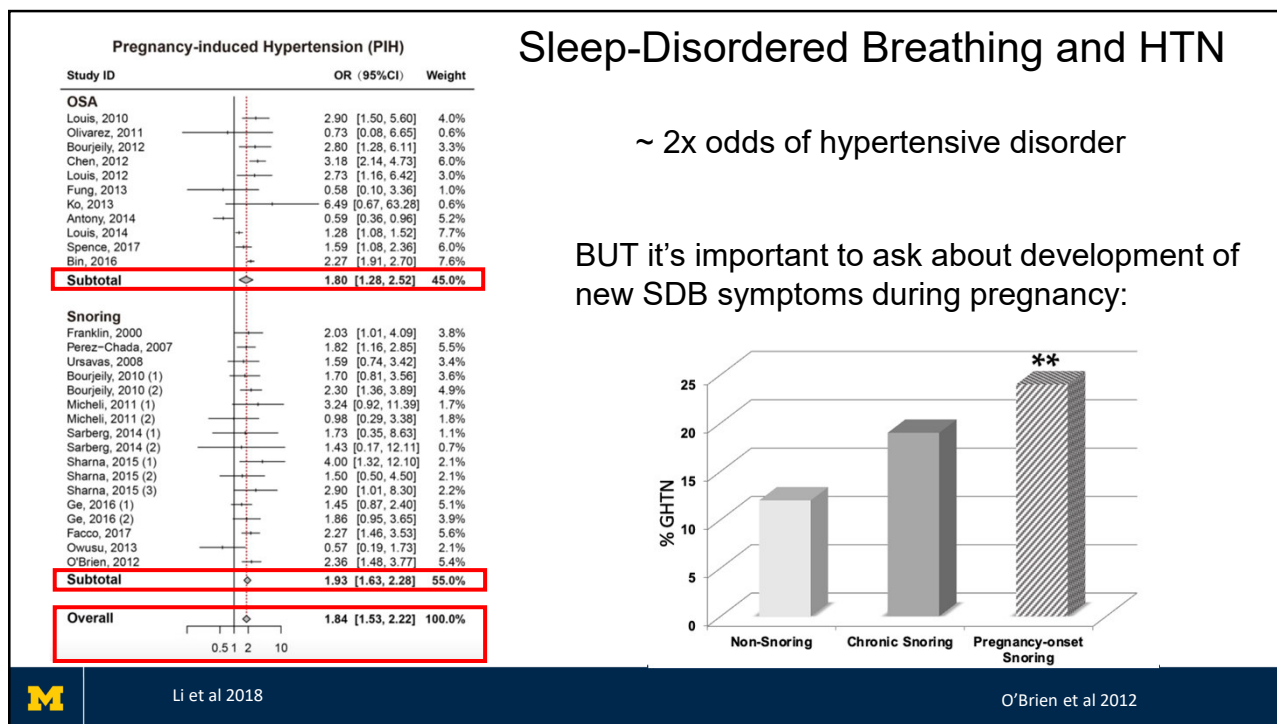
O'Brien et al 2014

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Skatrud 1999

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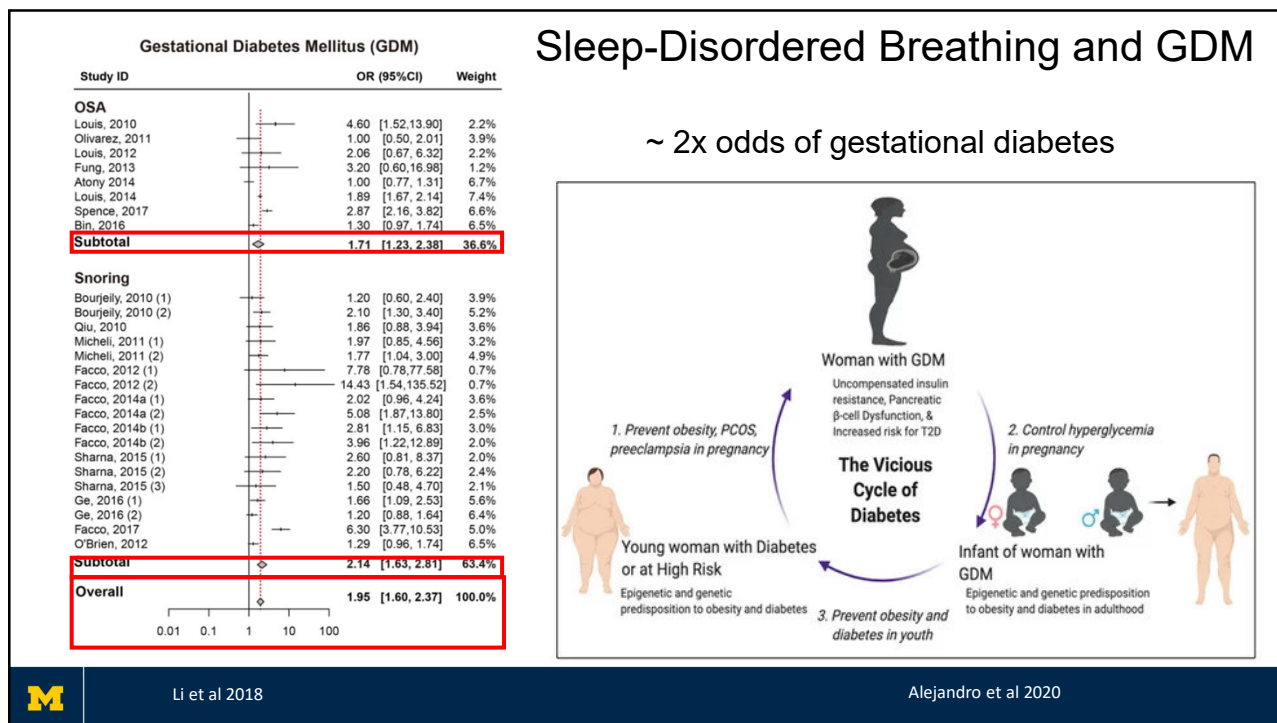


## Sleep-Disordered Breathing and HTN

~ 2x odds of hypertensive disorder

BUT it's important to ask about development of new SDB symptoms during pregnancy:

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## Sleep-Disordered Breathing and GDM

~ 2x odds of gestational diabetes

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## Sleep Duration and HTN

Trimester	<=6 hrs	7 to 8 hrs	9 hrs	10+ hrs
1st Trimester	~81.5	~80.8	~80.2	~81.0
2nd Trimester	~80.0	~79.5	~80.2	~80.2
3rd Trimester	~85.8	~84.8	~82.8	~86.2

Shorter sleep duration associated with higher uterine artery resistance

- Higher resistance assoc. with PreE and FGR
- More than doubles odds of HTN years after delivery

Williams et al 2010

Tang et al 2021, Miller et al 2021

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## Sleep Duration and GDM

Hours of Sleep	Adjusted Mean Glucose (mg/dl)
≤4	~112
5	~107
6	~104
7	~102
8	~102
9	~100
≥10	~107

aRR for GDM in those sleeping <4hrs:  
5.6 (95%CI 1.3-23.7)

Short sleep duration is inversely correlated with 1-hr 50g load OGTT:

- Each hour of reduced sleep associated with 4% increase in glucose levels in pregnancy

Facco et al 2017

Qiu et al 2010, Reutrakul et al 2011

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## Sleep timing matters!

Midpoint of sleep:

- half-way between sleep onset and wake
- Marker of circadian alignment

**Normal midpoint between 02:00am – 04:00am**

Emerging data suggest that later sleep midpoint is associated with:

- Increase in GDM
- Increase in preterm birth
- Increase in depressive symptoms

**Even if sleep duration is optimal!**

**M** Facco et al 2017, 2019

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## Disparities in sleep across pregnancy

Mean age White 31.7±4.8 : Black 28.7±6.5 years  
Mean BMI White 27.3±6.7 : Black 36.1±9.7 kg/m<sup>2</sup> early pregnancy  
Mean BMI White 31.2±6.9 : Black 42.7±9.5 kg/m<sup>2</sup> late pregnancy

Legend:

- White women early pregnancy
- White women late pregnancy
- Black women early pregnancy
- Black women late pregnancy

Not only do Black pregnant women have poorer sleep than White women, sleep appears to get even worse as pregnancy progresses

Do these changes play a role in worse perinatal outcomes in Black women?

**M** O'Brien et al (unpublished)

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## Fetal Impact of Maternal Sleep Disruption



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**Fetal size is important!** Fetal growth restriction (FGR), small for gestational age (SGA) and large for gestational age (LGA) have increased risk of perinatal morbidity and mortality.

Immediate consequences of FGR include:

- Preterm birth
- Intrauterine fetal demise (stillbirth)



**Fetal Programming**



**Increased risk for cardiovascular disease, diabetes and obesity**

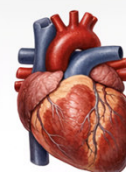
### Long-Term Effects of Intrauterine Growth Restriction



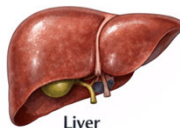
Brain



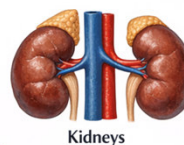
Lungs



Heart



Liver



Kidneys

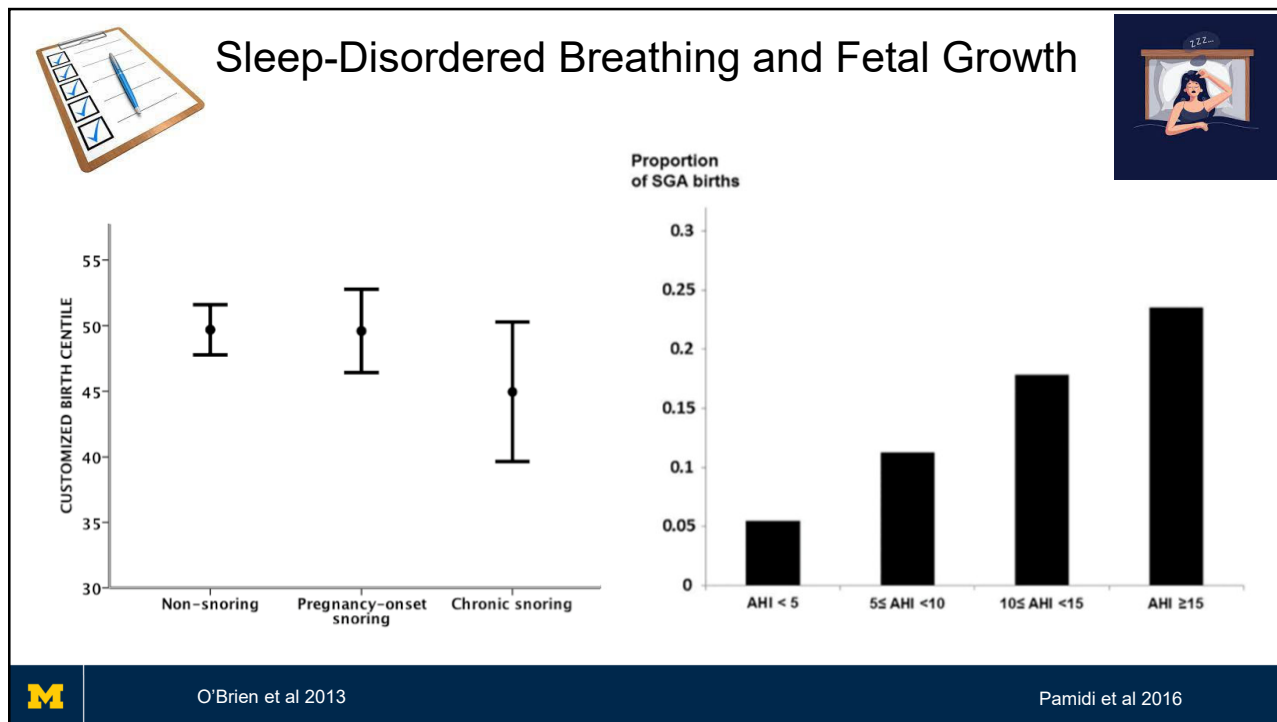


Bones

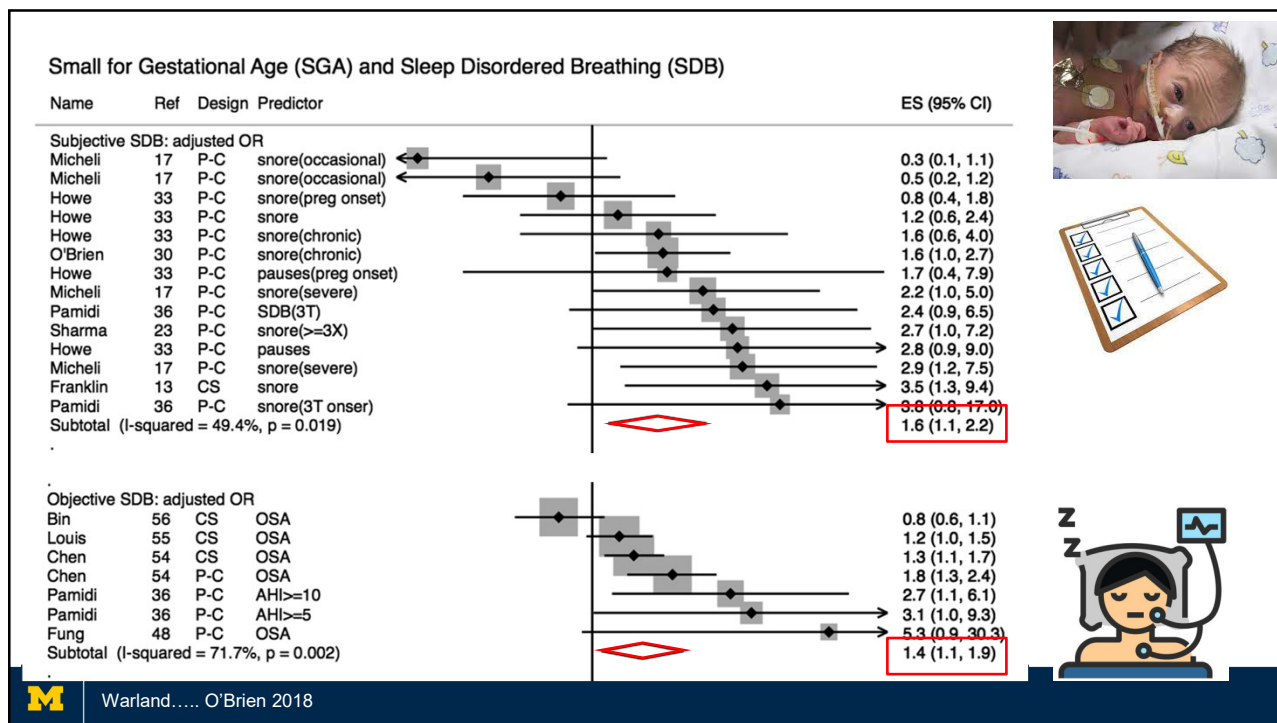


Metabolic System

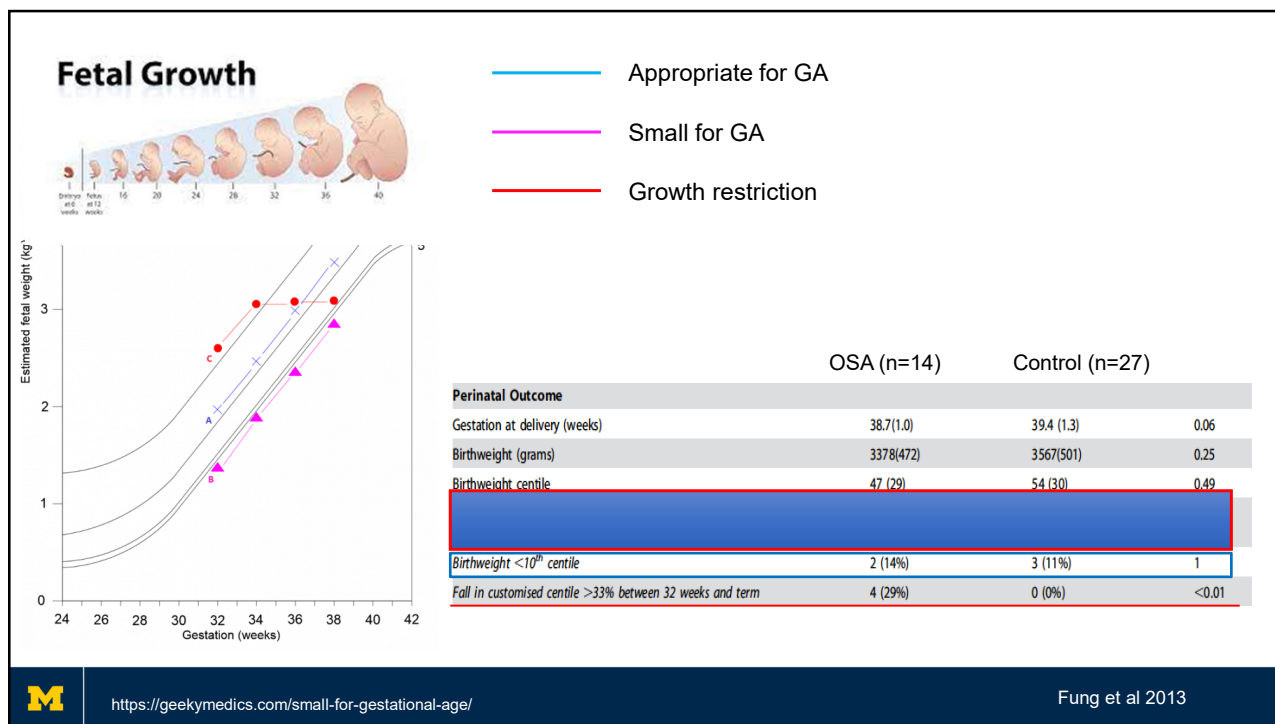
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## SDB and Fetal Heart Rate

Are maternal respiratory events temporally related to FHR?

Study of n=41 3<sup>rd</sup> trimester women  
- 23 (56%) found to have SDB

18 women had n=37 late decelerations → 84% late decels temporally related to maternal respiratory event

*\* Note that late decels are often a sign of fetal distress and can be caused by hypoxia*

6 women had n=10 prolonged decelerations (mean 4.7 min, range 3-6 min)  
*\* Prolonged decels can lead to clinical intervention*

All 6 women had SDB (mean RDI 13.3, range 10.1-18.3)

90% of prolonged decels temporally related to a maternal respiratory event

Pitts, Treadwell & O'Brien 2021

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## Stillbirth



Stillbirth is the death or loss of a baby before or during delivery.

In the US stillbirth is loss of a baby after 20 weeks of pregnancy:

- An early stillbirth is a fetal death between 20-27 weeks of pregnancy.
- A late stillbirth occurs after 28 completed weeks of pregnancy.

Isn't this a rare event?



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# NO!



US stillbirth rate: 6 per 1,000 babies (24,000 babies/year)

Approximately half of stillbirths are late ( $\geq 28$  weeks)

➔ 1 in 336 deliveries

## 10 times more common than SIDS

Equivalent to a 747  
crashing every 5  
days for a year

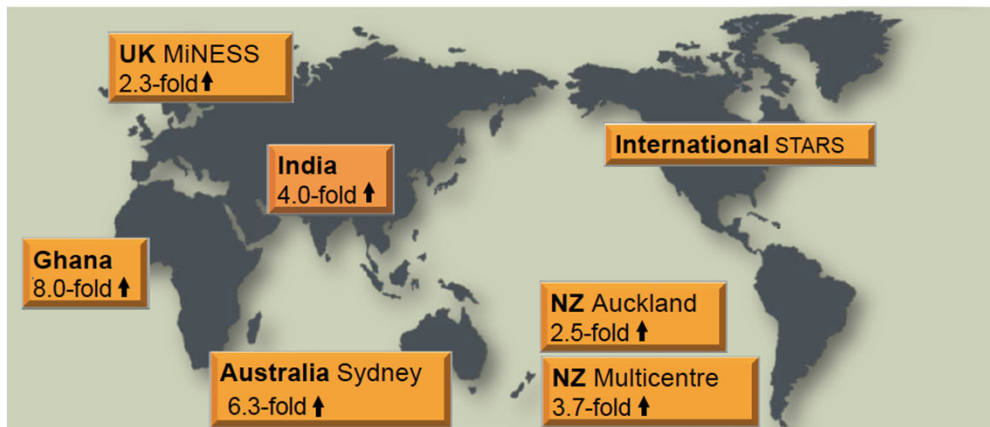


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## Sleep Position and Stillbirth

Several case-control studies and a cross-sectional study all demonstrate an association between **maternal self-report** of supine sleep and late stillbirth



Stacey 2011, Owusu & O'Brien 2013, Gordon 2015, Heazell 2017, McCowan 2017

Image Courtesy: R. Cronin

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INDIVIDUAL PARTICIPANT DATA META-ANALYSIS

Auckland
Sydney
NZ
UK
STARS

**IPD**  
851 stillbirth cases & 2257 pregnant controls


	Stillbirth Case N=851	Pregnant Control N=2257	OR (95% CI)	aOR (95%)
Going-to-sleep position last 2 weeks				Cases 826 Controls 1953
Left side	359 (42.19)	1074 (47.59)	1	1
Supine/Back	67 (7.87)	73 (3.23)	2.89 (2.01 to 4.14)	2.63 (1.72 to 4.04)
Right side	221 (25.97)	624 (27.65)	1.1 (0.9 to 1.34)	1.04 (0.83 to 1.31)
Tummy	3 (0.35)	8 (0.35)	1.15 (0.3 to 4.45)	0.63 (0.12 to 3.25)
Variable side	102 (11.99)	265 (11.74)	0.92 (0.69 to 1.23)	0.97 (0.7 to 1.35)
Propped up	20 (2.35)	46 (2.04)	1.28 (0.74 to 2.23)	1.3 (0.68 to 2.49)
No recall	79 (9.28)	167 (7.40)	1.4 (1.03 to 1.91)	2.26 (1.48 to 3.46)

Cronin et al 2019

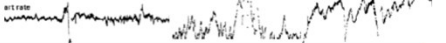


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### Fetal behavioural states in maternal positions –% time




Quiet Sleep    Active Sleep    Active Awake



**In the supine position:**

- fetal heart rate variability reduced
- Fetal behavior change from active to quiescence (low oxygen consuming state)


	1F	2F	4F
Left	11.3	79.1	9.6
Right	22.0	71.7	6.3
Semi-recumbent	16.7	81.9	1.5
Supine	34.4	63.4	2.3
Chi-Sq: 32.2 (p<0.0001)			



46% of all 4F occurred in left-lateral  
41% of all 1F occurred in supine position


In the presence of a stressor (uteroplacental perfusion or hypoxia), shift to a low oxygen consuming state would be a protective reaction.

Maternal supine position may be disadvantageous for fetal wellbeing and in compromised pregnancies may be a sufficient stressor to contribute to fetal demise


Stone et al 2016

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Gravid uterus compresses the inferior vena cava resulting in:

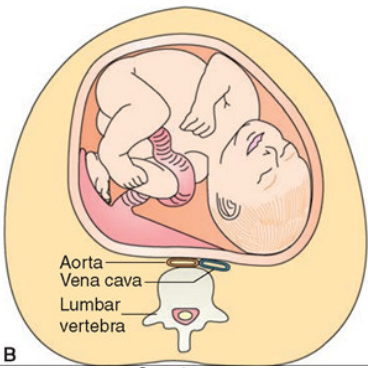


venous return  
ejection fraction  
cardiac output

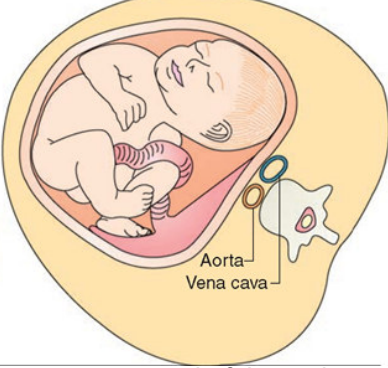
}

impaired uterine perfusion


“Maternal supine hypotensive syndrome”



**B**  
Supine

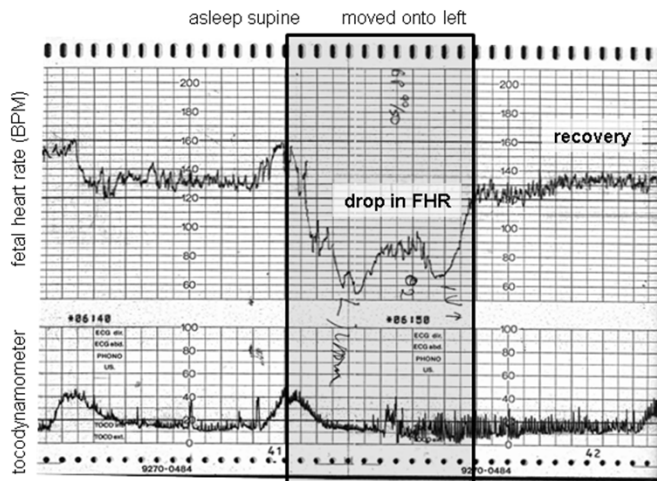


Left Lateral


<http://what-when-how.com/nursing/normal-pregnancy-maternal-and-newborn-nursing-part-4/>

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Clinical experience



Left lateral as a form of intrauterine resuscitation



(Thurlow & Kinsella (2002) Simpson & Dotti (2005)

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Summary of maternal-fetal interaction and the effect of position

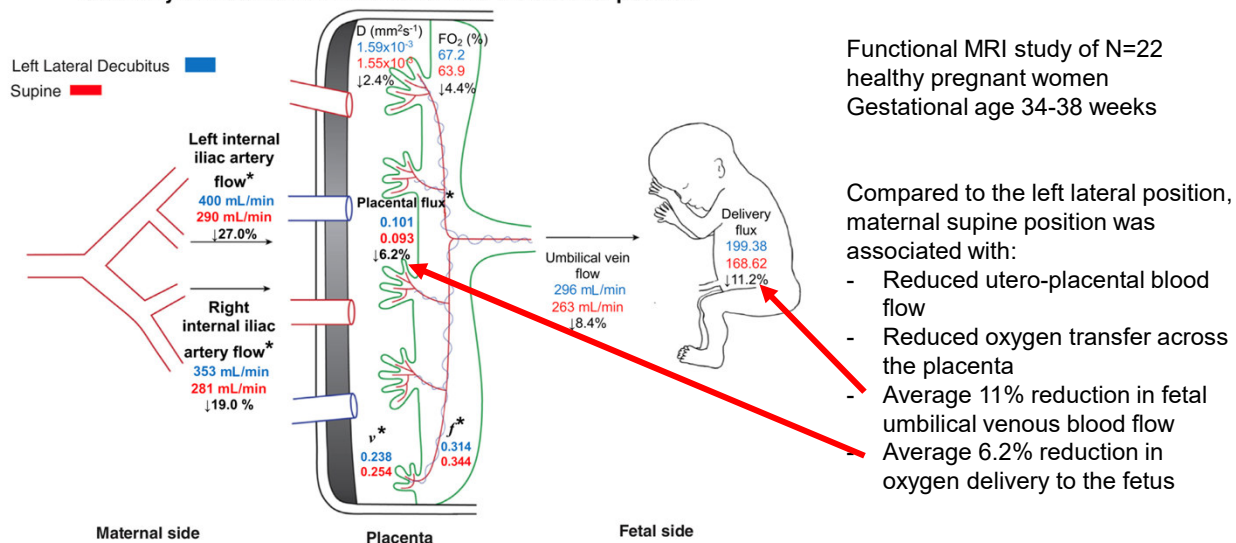


Figure 3. The summary effect of maternal position on utero-placental blood flow and oxygen delivery. Results which reached statistical significance are shown with an asterisk. [Colour figure can be viewed at wileyonlinelibrary.com]

Couper et al 2021

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## Sleep Position

No data on **objective** measures of sleep position **across** pregnancy.

Data lacking on how objective measures of sleep change as pregnancy progresses.



<19 weeks' gestation; home sleep test



Home sleep testing repeated in 3<sup>rd</sup> trimester

N=174 women; Mean age 31.3±5.0 years; 78% White  
Mean gestational age 15.3±3.0 weeks at enrollment and 35.5±1.9 weeks at follow up

Proportion of women who spent some time on their back during the night was  
36% in early pregnancy and 50% in late pregnancy

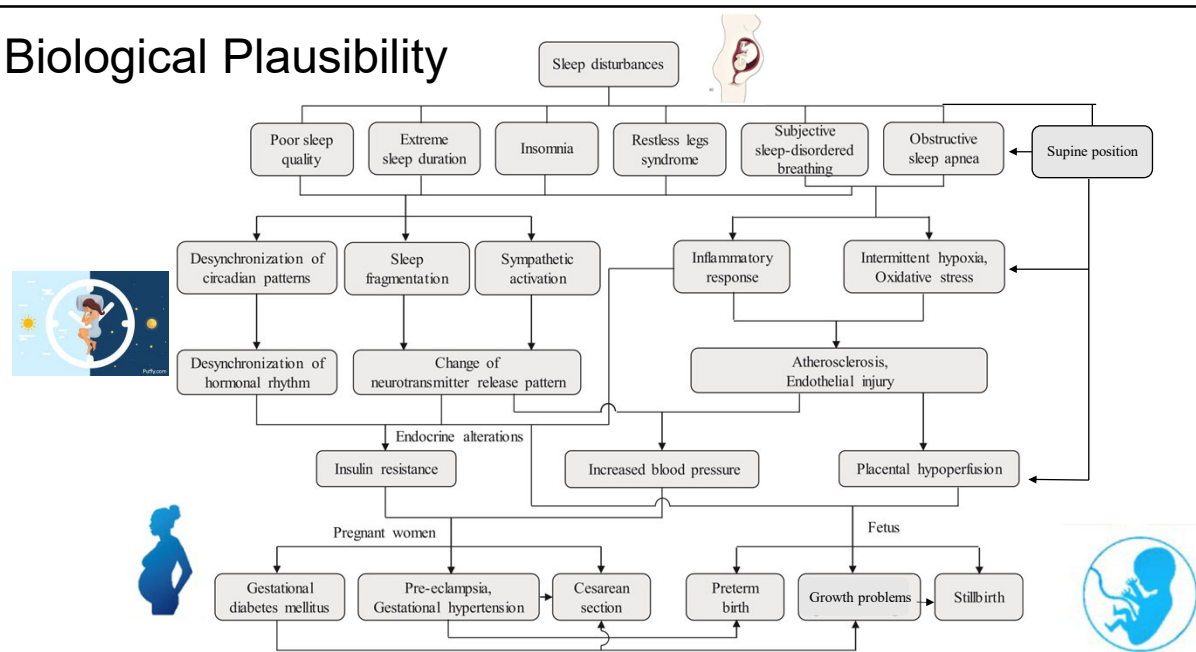
Average supine sleep time: 17% → 23% of the night



O'Brien et al (unpublished)

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## Biological Plausibility



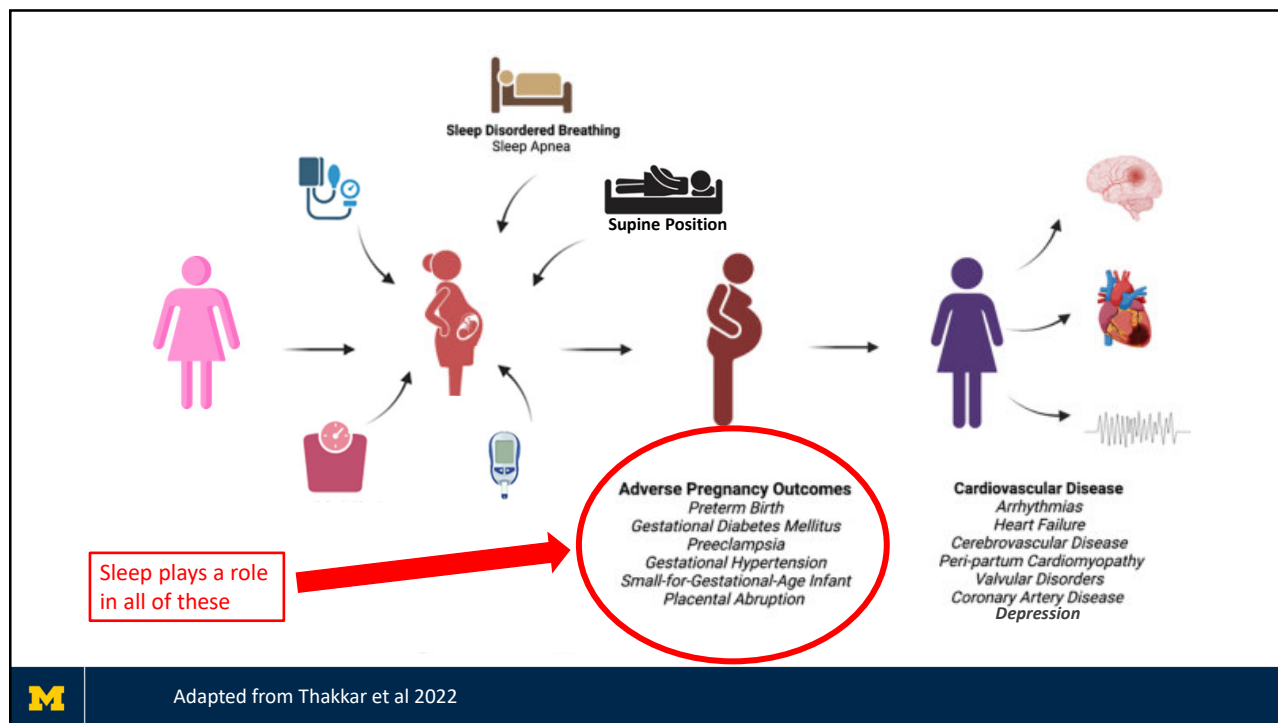
Lu 2021 (edited)

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## Is Pregnancy a Window to Intervene?

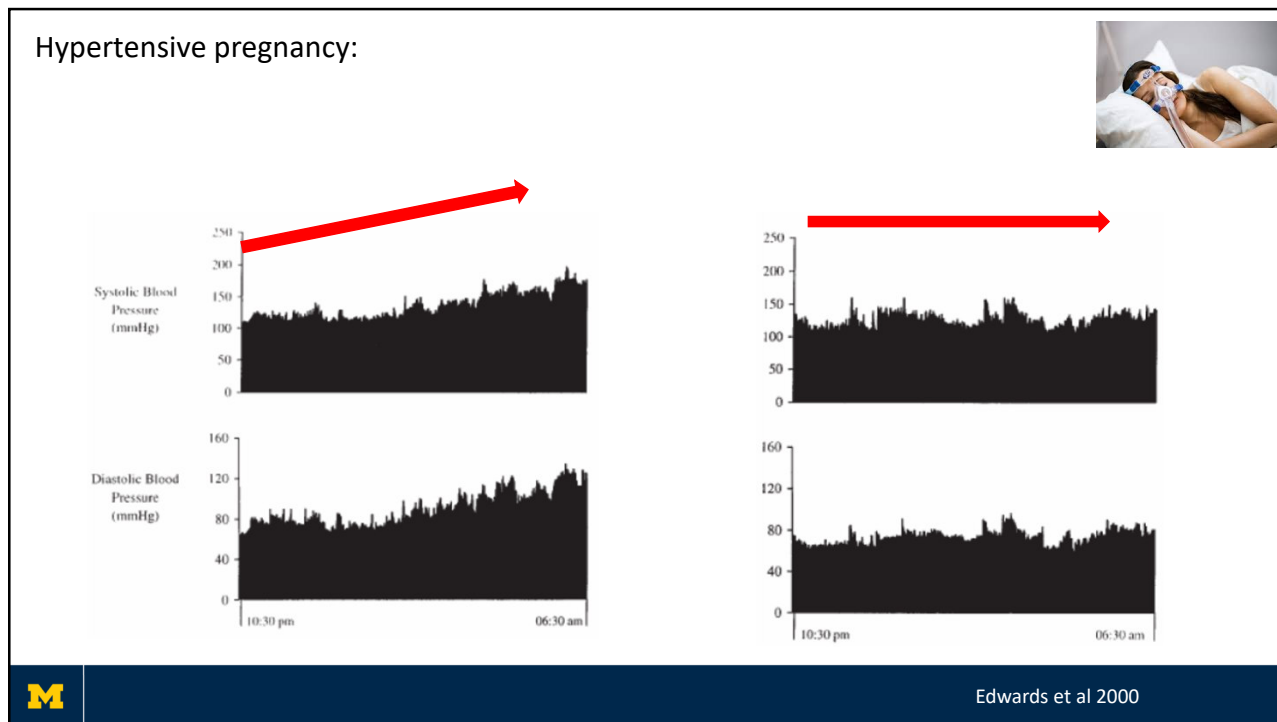


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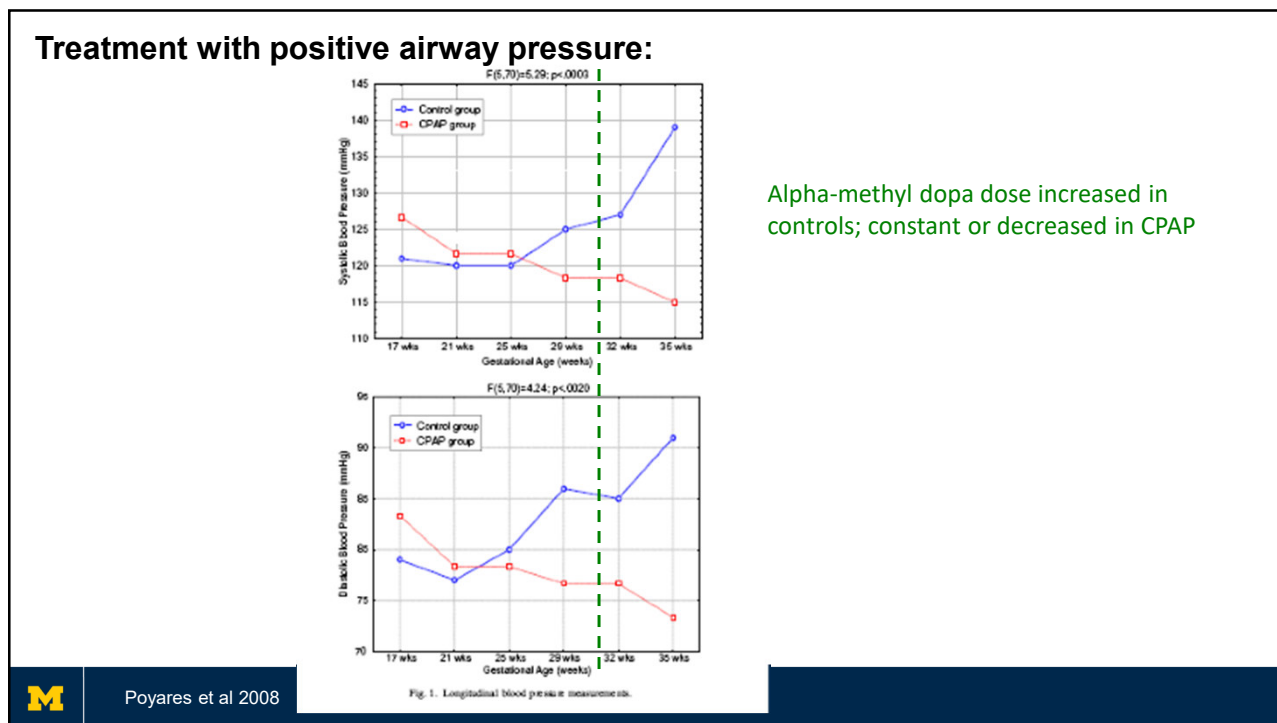


Adapted from Thakkar et al 2022

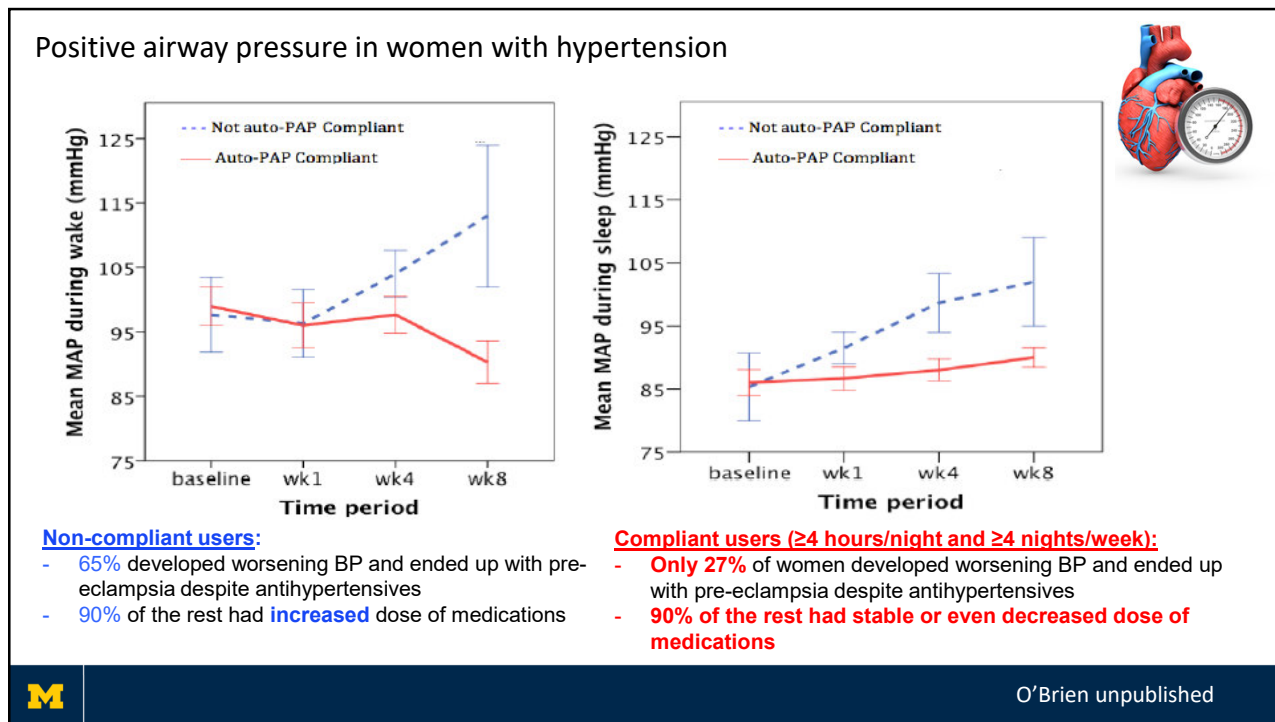
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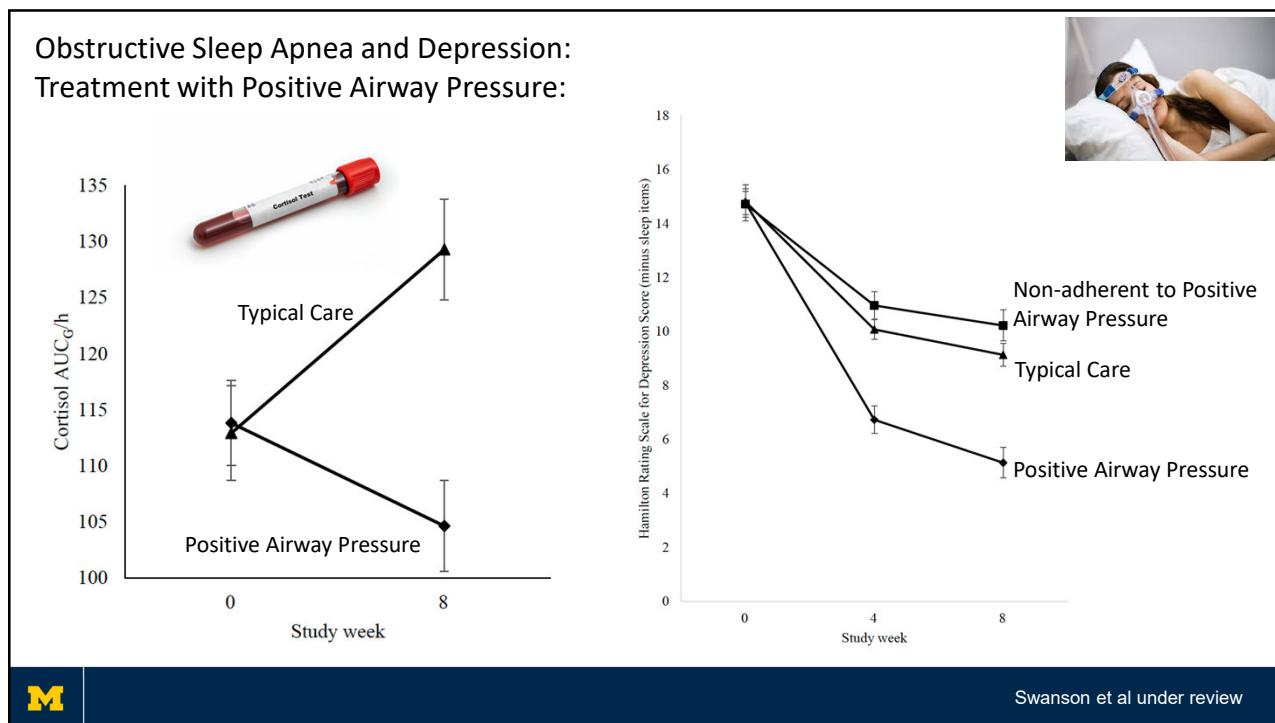
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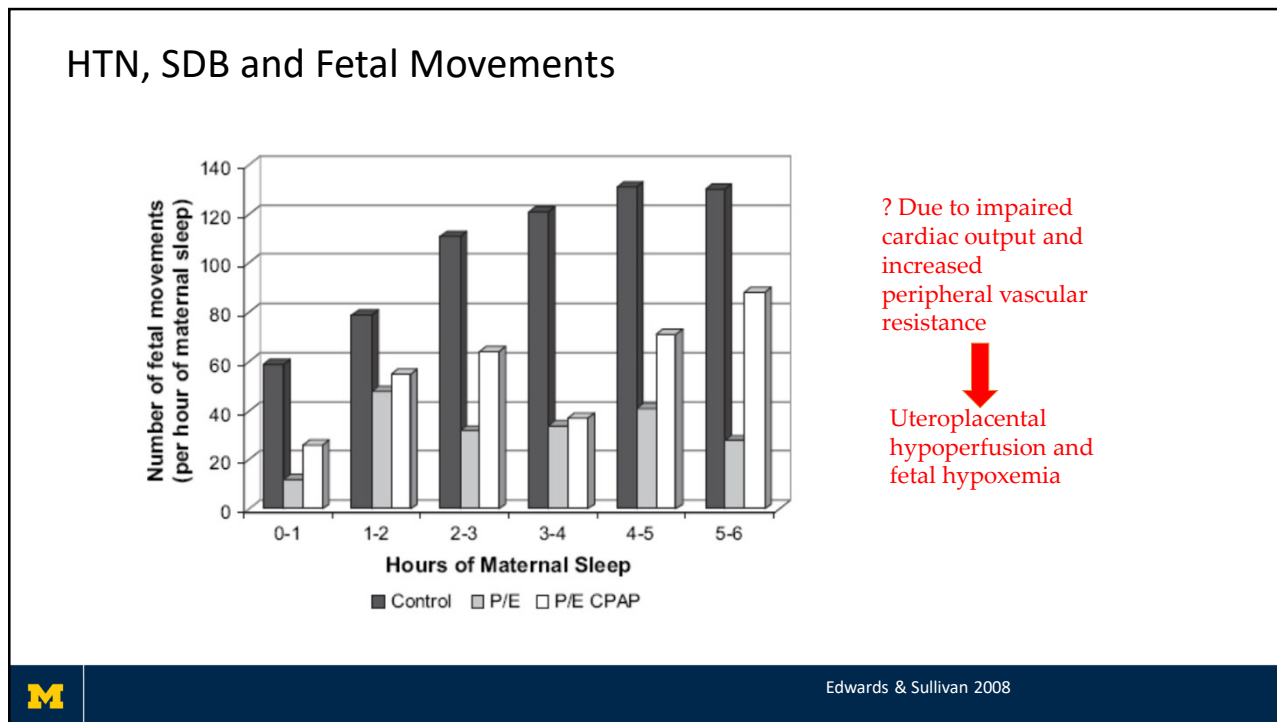
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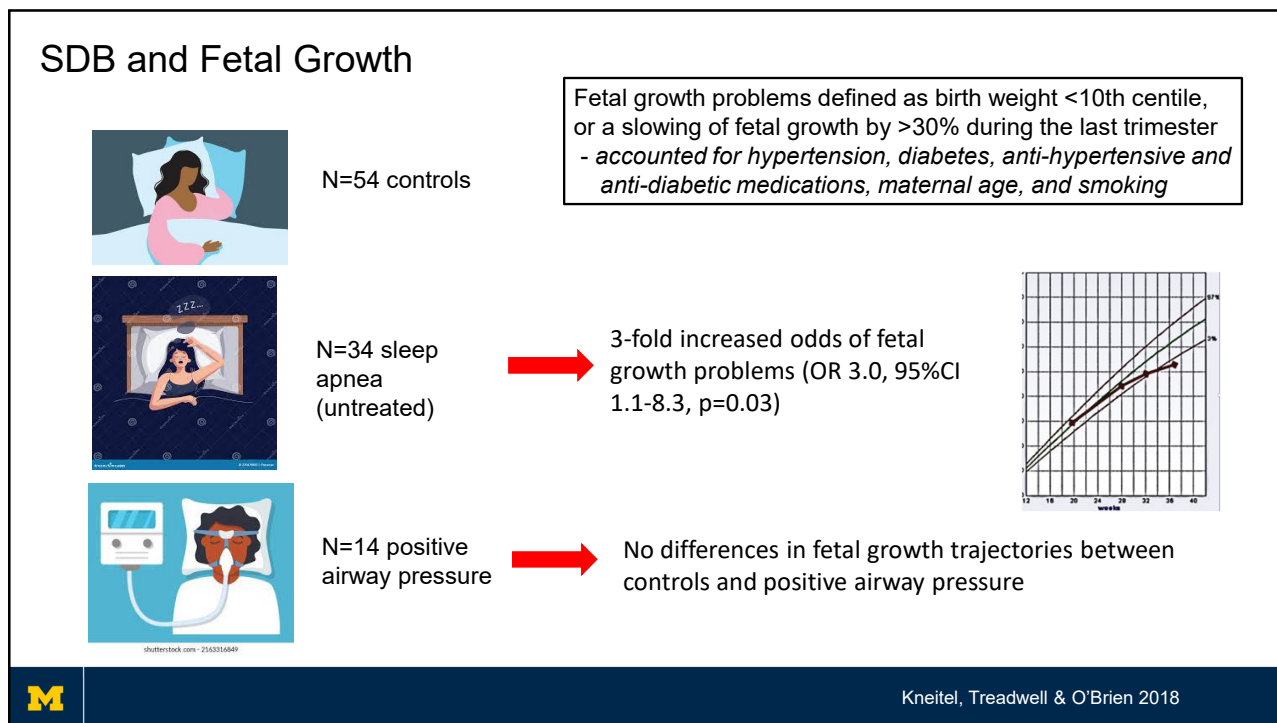
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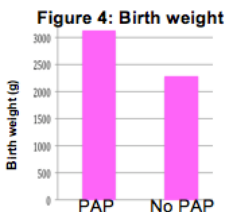


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## Positive Airway Pressure and Fetal Outcomes



APAP in high-risk pregnancies is associated with improved infant birth weight: Infants born to women who used APAP during pregnancy, compared to infants born to women who did not use APAP, have larger birth weight (**3036±833g vs. 2485±1050g, p=0.08**) even after accounting for duration of APAP use

APAP is associated with longer gestation. Women who used APAP continued their pregnancies for a mean of 2.5 weeks longer than non-users (**37.7±2.8 weeks vs. 35.1±4.1 weeks, p=0.03**)

*This is a clinically significant duration that may have long-term impact on infant health.*

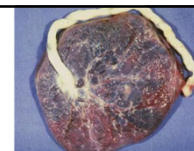
- Anecdotally women on APAP report;
- improved BP control
  - feeling better
  - increased fetal movement



O'Brien (unpublished)

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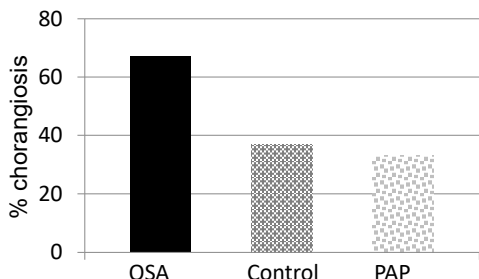
## OSA and the Placenta



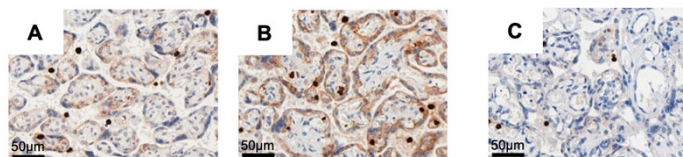
Markers of tissue hypoxia as well as markers of angiogenesis more common in OSA

Feto-placental weight ratio, balance between fetal and placental growth, is reduced as OSA severity increases:

	AHI<5 (n=23)	AHI>5 (n=14)	AHI>15 (n=6)	AHI>30 (n=4)
Feto-placental weight ratio	6.3±1.5	6.1±1.3	5.8±1.0	5.3±0.3



Chorangiogenesis, (increase in number of vessels in chorionic villi), likely a result of a hypoxic stimulus as nRBC's also elevated



Compared to controls (A), HIF-1α levels increased in OSA (B) but not in PAP-treated women (C)



Ravishankar 2015, Bourjeily 2015

O'Brien et al (unpublished); Hancock et al (unpublished)

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## Case 1

32yr Caucasian, BMI 24 G4 P1

Fetal demise #1 at 20/40

Fetal demise #2 at 19/40

Premature delivery at 27/40 - NICU

} All due to preeclampsia

Enrolled on trial at 21/40 AHI=1 and adhered to PAP

Did not develop preeclampsia

Delivered healthy male infant at 36+2/40 weighing 6lb 1oz

Interestingly, the placenta was normal except for one small infarct, unlike her previous placenta which showed typical histological changes. Was this due to PAP?



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## Case 2

34yr African American, GHTN, BMI 42 G1 P0

BPs at enrollment >150/80mmHg

- Morning after baseline sleep study, subject in triage with non-reactive FHR, reduced FM, and severe maternal desats
- OBGYN plan to deliver that day (37/40)
- Study team paged by OBGYN; decision made to start PAP immediately

Subsequently found to have severe OSA on sleep study (AHI=117)

On PAP:

- FHR became reactive
- Maternal SpO2 normal
- BPs 110-120/64-84mmHg (still on meds)
- Discharged and continued pregnancy for another week
- Delivered healthy 6lb 3oz female infant



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## Case 2 continued

### Two years later.....

- Second pregnancy
- Now known to have obstructive sleep apnea
- Instructed to use her positive airway pressure device

But she has a toddler at home and has her hands full

- Positive airway pressure device is “in a cupboard”
- Therapy is not used

At 28 weeks she presents to triage with reduced fetal movements

Baby was stillborn



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Treatment of sleep disorders in pregnancy could reduce the healthcare burden of obstetric conditions!

	Frequency (US)	Annual Extra Cost (per person)	US Annual Burden
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<b>Pregnancy Loss / Miscarriage</b>	10-25%	\$500	~ \$140 million
<b>Stillbirth</b>	0.6-1%	\$10,000	~\$240 million



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## Summary

Maternal sleep is a significant contributor to maternal and fetal health.

- Gestational hypertension/preeclampsia
- Gestational diabetes
- Fetal growth problems
- Stillbirth

Interventions to optimize sleep in pregnancy may offer significant benefit to mothers and babies and may ultimately decrease healthcare costs



Thank you!



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REFLECT NOW

<https://champions.learner.plus/sec/>

Sleep disorders causing adverse pregnancy outcomes.

### What inspired you to reflect?

Pick the context and a clinically relevant concept or phrase that inspired you to reflect.

Reflective Learning Moment

Step 1 of 4



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