Transcript Details
This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/womens-sleep-health-addressing-gaps-in-osa-diagnosis-and-treatment-across-life-stages/36099/

Released: 10/15/2025
Valid until: 10/15/2026

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Women's Sleep Health – Addressing Gaps in OSA Diagnosis and Treatment Across Life Stages

Announcer:
Welcome to CE on ReachMD. This activity, titled Women's Sleep Health – Addressing Gaps in OSA Diagnosis and Treatment Across Life Stages, is provided by Omnia Education and supported by Eli Lilly & Company

This replay of a live broadcast discusses women's life stages–specific factors in OSA diagnosis and management to improve sleep and cardiometabolic outcomes.

Dr. Kole:
Okay, well, thank you so much for joining us. We have a lot to cover because sleep is a big topic. Hopefully, you will not fall asleep in our postprandial and circadian nadir.

Disclosures are listed here.

What we intend to go over, and I know you're probably going to have a ton of questions, and we're going to be available even after we speak to answer those, is we want to give you a sense of what you need to look for when it comes to a woman who's presenting with sleep apnea. It can be a bit atypical. We want to go over validated assessment tools that you can deploy in your clinical practice, and some of us also deploy them in our clinical practice. And then I'm going to move it over to Dr. Aurora, who is a specialist in menopause and the relationship of how OSA is impacted by menopause, followed by let's talk about pregnancy and how OSA impacts pregnancy with Dr. Bourjeily. And then we're going to have Dr. Audrey Wells take us home, talking about all of the treatment options for sleep apnea. And yes, I said options. It's not just about CPAP.

So let's get started. What I want you to leave home with in this talk is really understanding what sleep apnea is, why it is so vital and important that we recognize it in women, when we should be screening, and then how do we go from screening to action.

So let's talk about obstructive sleep apnea. We know that it is a repetitive obstruction of the upper airway. So when we talk about the upper airway, think thoracic inlet inside the chest. We're locking up here, outside of the chest. And this is where we have our genioglossus, our tongue muscle, and all sorts of pharyngeal muscles that make up our upper airway. And so when we're talking about the airway closing, what does occur in people that have obstructive sleep apnea is we go to sleep, our bodies relax, our muscles relax. And we can have an instance where our muscles relax in our upper airway to the point where we're actually trying to breathe, we're making effort, and our airway has closed. We call that an apnea. That's where that name comes from.

But we also look for times when the airway has narrowed to the point where it's almost completely closed. It's not enough for us to properly oxygenate, and we start to see significant drops in our oxygen levels and arousals from sleep. We call those hypopneas.

And what we do is we calculate something called an apnea-hypopnea index. How many times per hour are we not breathing properly? If it's less than 5 times an hour, hey, hot dog, you don't have sleep apnea as far as we can tell. If it's 5 to 14, that's mild. If it's 15 to 29, that is moderate. And then we get to 30 or more events per hour. If your AHI is greater than 30, especially for your patients, you've got to really think, oh, this is bad. This is severe sleep apnea, and we have to take it seriously.

Think about it. That's once every other minute, right? That's a lot.

So why does the upper airway close off? There are a number of reasons why the airway closes off, but we're going to focus on 2 of the biggies here. One is altered mechanical properties, meaning that we have these muscles and they are decreased in tone. The other biggie is anatomic compromise of the upper airway patency, and this can be for a number of reasons. Enlarged tonsils, yes, even adults can still have big tonsils. I catch it on occasion. Upper airway edema, I'm sure you may hear that from Dr. Bourjeily, because that happens more in pregnancy. Craniofacial morphology, think of your patients that are non-Caucasian. Your minority population tends to have a different way of their genetics, and they look different, and it may increase their risk for having obstructive sleep apnea. Or your person who has that big overbite, that recessed jaw. And then we have fat deposition, right?

We talk a lot about neck circumference and fat deposition around the neck. That is a biggie, and its actually part of the criteria for the STOP-BANG questionnaire, which I'm going to show you in a little bit. But your tongue muscle also gains fat when we gain weight, and that is an awfully big muscle in our mouth that can restrict our airway. And then there's some very specific things to women to keep in mind. Dr. Aurora is going to be sharing with you hormonal influences that can affect the patency of our airway. And one other one that we don't think about often is the fact that we, as women, have smaller diaphragms, which means we have less traction on our trachea, which means our airways may be more prone to collapsing.

So what is the actual OSA disease burden in women? Globally, it is estimated that all-comers, there are 1 billion people on this planet with obstructive sleep apnea. Specific to women, the latest statistics tell us roughly 23% of women have obstructive sleep apnea. There was just a recent publication looking at the projection into the future of where we're going to be in 2050, and it is projected that specifically for women, we're looking at a 65% increase in OSA. That equates to 30 million women within 25 years. And just to clue you in, there's around 7,500 board-certified sleep specialists in the United States.

So we need all hands on deck in finding these patients, diagnosing them, and treating them. The male-to-female ratio, we used to think was a little bit bigger. It is a little bit more common in males, but probably about a 1.5: to 1 ratio.

And around 6% of women have that AHI greater than 30. That's severe sleep apnea that portends worse health impact.

So what is the impact? It's not only a health impact; it's also a socioeconomic impact. All right. Common things associated with obstructive sleep apnea: hypertension, stroke, arrhythmias, heart disease, diabetes, obesity. Mental health issues are commonly a symptom of obstructive sleep apnea. And then we have comorbid sleep disorders that we can't forget about that are very common in women, including restless legs and insomnia.

In terms of the socioeconomic impact, more health care utilization, less employment, higher disability, and if there's nothing that you leave home without, just take that 360 view and know that women with obstructive sleep apnea are 28% higher mortality risk. They do not live as long as their female counterparts that don't have sleep apnea. This is a bad thing and we've got to do better at being able to diagnose these women because 90% of women remain undiagnosed. We are capturing 10% of that population. That's crazy. We got to do better.

There are many reasons for this, including some of your patients who may be reluctant to actually acknowledge their own symptoms of OSA. But there's other things that we can do to poke around and try to understand about the nonspecific symptoms that your female patients may be coming to you and complaining about. What I mean is, they may not complain of sleepiness. They may say that they feel unrested or they're fatigued. They may have insomnia complaints primarily, and there is COMISA. COMISA is comorbid insomnia with obstructive sleep apnea, so you can have 2 things going on at once. They may have the mental health issues like depression and anxiety that pop up, as I mentioned before, morning headaches, nocturia. And please, the low-hanging fruit is if they're presenting just like many of our male counterparts, they're snoring, they have excessive daytime sleepiness, et cetera, you got to get those patients tested.

And part of it's because they have a different pathophysiology. Again, alluding to what Dr. Aurora is going to be talking about, hormonal fluctuations, premenopausal, tends to stabilize the airway, and as our hormones change and we age, we see that the risk factors increase and we see more obstructive sleep apnea, as noted in the graph. Women also tend to wake up a little bit easier, so they have a lower arousal threshold, which can impact what we find. There also is something called REM-related obstructive sleep apnea, and hopefully Dr. Wells may have some time to talk to you about that.

So let's talk about screening here, all right? If you are not using screening tools, I want to share with you some of the common ones. The first being the Epworth Sleepiness Scale. There are some issues with it. Your patients need to actually answer the question appropriately and read the directions and be honest, but it can be a very, very helpful scale. It's basically measuring how sleepy you are during the day. And a score greater than 10 means that you have excessive daytime sleepiness. This actually can be used with pregnant women as well.

I want to share with you a quick story, which is I interviewed Kristen Cascio, who's a patient advocate for Project Sleep on the Sleep Is My Waking Passion podcast, and what she disclosed to me is that she was diagnosed with obstructive sleep apnea at the age of 31 after having 15 years of symptoms and being dismissed. You know what she said to me? I just wish somebody had given me the Epworth Sleepiness Scale. That's what she asked.

So food for thought. You can do this even before the patient enters the office. The STOP-BANG questionnaire is something I have used a lot. It is not perfect. All of this stuff is available free online. You can find this. It is most expensive. This is one of the tools that has been most validated and studied in midlife women. A score of greater than 3, which is different than men, is very important to tip you off to start to look at sleep apnea in these folks.

Another one is the Berlin questionnaire. I brought it up here because it highlights the fact that we live in a multi-ethnic society, and not all questionnaires are going to be good for everyone. There was a study looking at low-income Black Americans, and essentially, it didn't work so great for them. It wasn't the best screening tool for them. However, another study looked at Hispanics over the age of 40, and it was a pretty good tool, no matter what gender. There also happened to be a Greek study. So if you have a lot of Greek patients, they tend to do pretty okay with the Berlin questionnaire. So you just need to understand there's some caveats associated with these.

Last but not least, I wanted to talk to you about the Insomnia Severity Index. I use this routinely because, again, insomnia is such a common complaint with our female patients and can be associated with obstructive sleep apnea. Completion time is 5 minutes, it's validated in women, and it's super easy to do. Again, like I said, I use it all the time.

So OSA screening in real life. What I want you to take home from this is that there are a multitude of questionnaires that you can use. Ask yourself, remember, what is the risk of screening your female patients for obstructive sleep apnea? Personally, I really don't see a downside, and I don't think any of the ladies up here on the panel think that either. Okay? Ask about those atypical symptoms. And you can even go to the Society of Women's Health Research. This is a great tool. It has a lot of the questions that are common. You could print this out. You could have it in your office while they're waiting to see you. And that may clue you into a conversation that could change the quality of your patient's life.

So how do we go from screening to action? Well, this is where we really need to be focused on creating a collaborative environment. We can no longer practice in silos where the OBs are over here, and the PCPs are over here, and the sleep doctors are over there. We've got to all work together to make this work. There's a lot less of us up here than there are of you, but we can help each other out.

Home sleep apnea testing is available. I just want to point out that it's convenient. You can do it at your home. But you run the risk of missing cases, especially of mild sleep apnea, so think about that in-lab sleep study and coordinate with a sleep specialist. There are many options for you. It doesn't just need to be the 6-month wait to go to the local academic center or the local private practice. You can think outside the box. You can think about concierge if you really need an acute visit. You can think about telemedicine options that are now available that can be both using insurance. So there are lots of things that you can do. And if any of you ever have any questions about where you find a sleep specialist, I guarantee you it is a small and loving community. We all really care about each other. We can find someone in your neck of the woods to help you out. Okay?

And thank you so much. I'm going to hand it over to Dr. Aurora.

Dr. Aurora:
Hi, I'm so excited to be here. This is such a cool venue, and I love giving a talk from a sofa. I've never done that before. It's amazing. I might take a nap.

Okay, so I'm going to get going. So oftentimes when I'm presenting, I have to first convince the audience of why we should care specifically about the sleep of women in their midlife. But I feel like I have to do that less here. So that's kind of neat for me. But just in case you want to know, 2022 was a really big year for sleep medicine because the American Heart Association recognized good, healthy sleep as a key pillar of good health. Okay? So they went from Essential 7 to Essentials 8. How cool is that? But even besides that, I think Alison's already talked about this, but just to briefly remind everybody, societal consequences of poor sleep in midlife women are very different than in men or young adults. We are often taking care of not just the kids or the grandkids but aging parents as well. We are the sandwich generation. And when we have sleep disorders, we actually have higher cost of chronic diseases like cardiovascular disease, diabetes. That's been shown in economic reports. And finally, many of us are hitting our peak career stride, right? We're getting into leadership roles and poor sleep can lead to more absenteeism, early retirement can actually affect the global economy.

So just so that we're all on the same page, and you cannot talk about midlife in the woman without talking about menopause. Menopause is basically the cessation of estrogen and progesterone. You don't have a menstrual cycle for a year, then you're in

menopause. And perimenopause is the time, obviously, leading up to that. It can be 3 to 8 years. And all of that combined is the menopause transition. And we've really got to pay attention to sleep in midlife women because if you look at the life expectancy by 2022 data, the life expectancy of a woman in the United States is about 80 years. So we're going to spend over 30% of our lives in this sort of menopausal state. And there are a lot of us out there, and guess what else? There's a lot of sleep complaints. So this is something that's going to happen. It's unavoidable. It's natural. And when you compare it to the men who decline in their reproductive hormone testosterone at about 1% to 2% per year, the women, we kind of lose all our reproductive hormones in a span of 8 years. And while that sounds like a very long time, in the grand scheme of life, it's kind of abrupt for us.

So here's a man, they go up when they're in puberty, testosterone comes down nice and slowly and stable, and look at us, we are so complicated. So the first one is just every month, okay, where I'm going through this. Then we have pregnancy, and then we're going into perimenopause. We're complicated, but that's what makes us so interesting and why we should be studied. Okay? So I just like to show that slide. And if you want to talk about why sleep apnea comes on during menopause, you have to step back and look at the anatomy and differences in the anatomy between men and women.

So the upper airway of the woman, especially pre-menopause, is actually more stable than the man's. And that is because if you think about the upper airway, it's anchored on both sides by bone, but the middle portion is just tubing, and it's not anchored to anything. So the longer that tubing becomes, the more likely it is to collapse. And so men's upper airway is longer. That's a post-pubertal phenomena. Women tend to have a more stable upper airway, which is manifested by something we call pharyngeal closing pressure. So we have a lower peak rate up to menopause. And then men also have more fat deposition around their upper airway.

But with menopause, the OSA prevalence just skyrockets compared to pre-menopause, especially moderate to severe. And although it's kind of difficult to tease out the aging effect, the BMI effect versus the hormonal effect, when we look at surgical menopause, which is younger women that for some reason have lost their reproductive hormones, maybe by surgery, even then, the prevalence of sleep apnea is higher and we know that it is associated with more apnea frequency, and their estrogen and progesterone both seem to play a role. And we also see, of course, increased fat mass, especially around the neck, happen in post-menopause, but also it moves around in the body. And interestingly, that lengthening of the upper airway occurs more in older women post-menopause than older men. So we start to catch up to them.

Okay, so here you can see just outlining the importance of estrogen and progesterone and the loss of that. Estrogen, especially, is extremely important in the development of the upper airway, in protecting the upper airway when it faces an insult, especially chronic intermittent hypoxia. So when it's facing that, its ability to protect and recruit muscles to help keep that airway patent is very important. And estrogen is a major, major antioxidant defense system. So when we lose that in menopause, we are already more prone to diabetes, to cardiovascular events. When you add sleep apnea on top, which is a major anti oxidative stress burden, you really escalate the risk.

Progesterone is a respiratory stimulant. We have receptors in our central nervous system across many respiratory control areas. And what's really kind of interesting is progesterone binds to GABA receptors in our brain, and those are like sleep-inducing receptors. So you can imagine that with the loss of these, we have more insomnia, we have more sleep apnea, et cetera.

And our body changes, as I mentioned. You get a shift in the body composition with fat and adiposity going more central, going more around the upper airway. And don't forget, adipose tissue is in itself an inflammatory organ and creates atherosclerosis risk.

Okay. Now, putting aside what we know about sleep apnea and menopause, let's talk about the future. And you can't talk about the future of medicine without talking about precision medicine. And here, I want to say this is an opportunity to set a new paradigm with precision medicine to treat and address sleep apnea in postmenopausal women. So if you don't know, precision medicine, what they try to do is identify small subgroups within a disease process and then, each subgroup may have different symptoms, different presentations, different demographics. Try to understand what is the mechanism of that subgroup, okay? And what that allows us to do is really get the right therapy to the right person at the right time. So don't just give steroids for all asthma. Asthma field has done a great job of setting their phenotypes and endotypes, which I'm going to talk about.

So a phenotype is basically the disease expression, the symptoms, the demographics, how they deal with outcomes, what the treatment response is. And an endotype is the underlying mechanism that results in that disease expression. And biomarkers kind of link the 2, okay? So in precision medicine in OSA, very sorely needed, because what we've done so far is give a singular therapy, the dreaded machine, to treat a singular metric, the AHI, and not much success. So one size does not fit all.

So we've kind of done the same. We've sort of set our OSA phenotypes and endotypes. And this is based – I'm sorry, the references aren't on here – but this is based on a study in 2014 on the Icelandic cohort that came out of UPenn. And basically, they sort of did a great job of identifying 3 basic phenotypes of obstructive sleep apnea: those that didn't have many symptoms; people with a lot of

disturbed sleep, those insomnia symptoms; and people with excessive daytime sleepiness.

And then, we've done decades and decades of very tedious mechanical studies and experiments, physiological studies, to show there are 4 main endotypes: anatomic compromise of the pharyngeal airway, but also that reduced muscle responsiveness, and something called high loop gain or unstable ventilatory control, where your brain and your lungs, your airway, are overreacting almost to an insult. And then there's low arousal threshold, what Alison referred to, with waking up too easy. The insomnia phenotype, where your airway's almost too sensitive. Even the slightest decrease in its patency or dimension leads to an arousal.

So this is a very nice study that I wanted to alert you all to. This kind of brought everything together: endotype, phenotypes, and specifically for sex-based differences and what we can learn from the in-laboratory sleep study.

So this is a study out of Yale published in 2020. This was based on a very large cohort, the MESA cohort. They had over 2,000 in-laboratory studies and over 50% women. And what they were trying to do was trying to sort of see what the findings on that in-laboratory study were, how it related to the phenotype, how it related to the endotype, and how there were sex-based differences.

I know you can't see this slide, but I just love this slide, so I have to put it up because it's like, men and women were different on each and everything,

total sleep time, the stages, how much sleep apnea they have, until they got to REM sleep. Then they were equal. So it's kind of fascinating because I know Dr. Kole was talking about possibly REM sleep apnea being a phenotype, maybe, that occurs in women.

So what they found, that overall, women had less oxygen desaturations. They had more of those hypopneas, less of that partial collapse. Men had more apneas, complete collapse. And this was especially prominent in non-REM. And men had more supine, on their back, sleep apnea. And overall, they were different in every way except for REM sleep. So there were really important sex differences.

And guess what? When you relate this back to the phenotype, this may explain some of the things we're seeing. So Dr. Kole talked about COMISA. So that lower arousal threshold that you see with women, that could be that COMISA manifesting. And we know now that COMISA is actually associated with worse cardiac outcomes and lower quality of life when that is the phenotype. So that's something really important to think about.

Now, I put this laundry list up here because it just, I'm so proud of the field in some ways because we've been looking at sleep apnea and the difference in outcomes between men and women, and there are important differences in outcomes. Whether you look at endothelial function, whether you look at biomarkers of cardiovascular function, whether you look at large databases, Medicare epidemiological studies, women, there's a lot of evidence women seem to do worse with sleep apnea.

And I'd just like to share this with you because I was super excited about this. This is a publication we had earlier this year, just in the spring of 2025. Oxidative stress, which is a major intermediate pathway towards cardiovascular disease. We looked at this in 84 patients overnight—83, rather. And what you can see here is on that little graph on the left, the y-axis is nitrate levels overnight. So when you go to sleep, if you have nice, healthy, good sleep, your nitrate levels, which are signifying oxidative stress burden, should go down overnight, okay?

And here, we're comparing men and women. Women on the left, men on the right. So morning minus night nitrate levels, overnight oxidative stress burden.

And each of those bars, the circle is mild sleep apnea, the square is moderate, and the triangle is severe. And look at what you see in the differences in overnight oxidative stress. The women almost had a dose response with OSA severity and their oxidative burden overnight, but the men stayed stable.

So we're trying to get to the root of this because that's how you kind of address endotypes and get targeted therapy. So this is just some of the work that we've been doing.

And you know what? I'm really proud of the NIH as well because they finally, in 2018, recognized that sex is a major, major variable that modifies and affects health outcomes in men versus women. So kudos to that. And now we have to look at women and we need to have enough women in trials, which gets me to my last slide.

So this is a slide that I absolutely love to show my patients. This is 8 big randomized controlled trials in sleep apnea over the last 2 decades. In gray are the women—the percentage of the women. In the middle is written out the percentage of the women that participated in each study: 20%, 16%, 16%, 3%. I show my women these when I'm recruiting for my studies in sleep apnea, and they get so excited to participate. We need to get our women involved in our studies to make sure that they get the treatment, they get diagnosed on time, and that what we give as recommendations going forward, that we have considered them, and that we have really personalized and targeted therapy towards them.

So with that, I'm going to stop. Thank you all very much.

Dr. Bourjeily:
All right. Now we're going to move back in a woman's lifetime and we're going to talk about pregnancy and the role of sleep apnea in pregnancy. So I want to start by talking about the prevalence of sleep apnea in pregnancy. One would think that pregnant women are usually younger. We talked about how age is a risk factor for sleep apnea. But in fact, pregnancy is a risk factor for sleep apnea. And as you could see in this slide, the prevalence of sleep apnea in women tends to vary, but in the lowest estimates in low-risk populations, the prevalence of having sleep apnea is about 8.6% to 9%. In higher-risk populations, so populations complicated by gestational diabetes or obesity or even growth restriction, you could see that that prevalence goes up significantly to about 70% or so. So this is a common problem, much more common than we think would be happening in such a young population.

So why do we think it happens? What is it about pregnancy that might predispose to it? We heard about some of the mechanisms that predispose the happening of sleep apnea. So what is it that is specific in pregnancy? You could see in here that the functional residual capacity decreases in pregnancy in part because of ligamental relaxation. In another part, later in pregnancy, because the abdominal contents are pushing against the diaphragm and then lifting the diaphragm up, so the functional residual capacity of the lung becomes lower. And that increases the risk because it reduces the traction on the upper airway.

Another possible thing is the fact that with pregnancy, as you all know, oncotic pressures tend to go down. So like they develop swelling in their hands and feet and everything, the swelling happens in other parts of the body. So that can tend to lead to an increase in the resistance of the upper airway and then a reduction in the cross-sectional area of their pharyngeal tissue, and that increases the risk for sleep apnea as well.

And as we heard, progesterone is a respiratory stimulant, and levels of progesterone go up about 8 times or so in the course of pregnancy, so that might impact as well the women's arousal and their ventilatory control, et cetera. And then, pregnant women tend to have a lowered oxygen reserve. So in response to apneas, they may retain more CO2 and drop their O2 levels quicker than women that are not pregnant.

And there are some other factors that you could see in here, but I'm not going to dwell about them.

So why should we care about sleep apnea in pregnancy? One of the reasons we care is because, and you all know, maternal mortality is an issue in the United States. So when we compare the data about maternal mortality in the US to other industrialized nations, we are at about 3- to 4-fold the rates in France and Canada and the UK and Australia, for instance. And there are many reasons for it. There are areas where there are pregnancy deserts, where access to care might be an issue. But that also tells us that we need to think creatively about things that we can modify to improve the health of these pregnant women.

Another important factor, in thinking that in about 2021, maternal mortality had peaked, COVID had something to do with it, but many other reasons as well. We started to do a little bit better since. We're not at where we were even in 2018, which was a high rate, but we're getting close there. But as you could see in this slide, so even though we have achieved some improvement in maternal mortality, there remain some disparities there. So the improvement, you could see it in white women, but in black women, there wasn't much of a change. So that follows on the theme that we talked about today about the disparities in care and how certain populations experience more disparities than others.

And when we think about pregnancy-related deaths, for instance, you could see in here in the lighter blue color, these are conditions that we're going to talk about and how they could be associated with obstructive sleep apnea. So some metabolic and endocrine conditions, cerebrovascular accidents, cardiomyopathy, embolism. So indirect causes of mortality. And then there's hypertensive disorders of pregnancy, and then there are mental health conditions and suicide. And suicide is one of the leading conditions of maternal deaths, as well.

So as we think about these main causes of maternal mortality, we know that obstructive sleep apnea is associated with many of these things in the course of pregnancy. So probably all of you know by now that sleep apnea has been associated with hypertensive disorders of pregnancy. You can see in this study by Dr. Judette Louis, that the association is significantly elevated. So the association is elevated for gestational hypertension, eclampsia, and preeclampsia. And the association is also there for gestational diabetes. And that's the information that most people know by now. But I think what is even more important is that there are some associations with causes of severe maternal morbidity. So things like pulmonary edema, cardiomyopathy, congestive heart failure, et cetera, that have been demonstrated in this really large database from the nationwide inpatient sample, and it has been reproduced by many other studies, as well.

So we have been able to show a similar association with the things that we just talked about, except for mortality, but we also

demonstrated in data from the National Perinatal Information Center that women that have sleep apnea are at a higher risk of getting admitted to the intensive care unit, almost a 3-fold increase in the risk. And these women also have an increase in hospital stay. So they have a significantly longer hospital stay if they have a diagnosis of sleep apnea.

And then, when we looked at women that had preeclampsia in that National Perinatal Information Center, we had about 75,000 women that had a diagnosis of sleep apnea. Then we divided them into a group that had obstructive sleep apnea and the group that doesn't have obstructive sleep apnea, and what we were able to demonstrate is that women that had obstructive sleep apnea had about 2-fold an increase in the risk for severe maternal morbidity, for severe cardiovascular morbidity, and for increased healthcare utilization. So not only does sleep apnea increase the risk for preeclampsia, it seems to increase the risk for significant complications that are associated with preeclampsia, and that's important to know.

And then, obviously, we have to think about the baby when we think about complications because we all know that the in utero environment is really important for fetal development and for the offspring outcomes. So it would make sense to think about growth in babies after sleep apnea, because we heard about sleep apnea being associated with these drops in oxygen levels and then increases, and then the sympathetic activation, the endothelial dysfunction. So it's natural to think that sleep apnea might impact placental development and placental perfusion and how that might impact the baby's health.

So there have been a few studies that have looked at this association. And it's not a straightforward answer; it's a little bit complicated. And as you can see in here, depending on how sleep apnea was defined, so whether it's subjective, objective, or based on ICD-9 codes, there had been an association with either small for gestational age or large for gestational age. And that really depends on multiple factors. I won't get into them, but one of them is whether women have other comorbidities as well that might impact them. But the data is also very heterogeneous. When we examined the way they look, there had been, I think, about 20 different definitions of fetal growth. So that makes the data very homogeneous, but it tells us that there is something important here that we need to think about.

We also demonstrated when we linked moms' records to babies' records in about 1.5 million pregnancies or so, we were able to demonstrate an increase in the risk for congenital abnormalities. So we looked at major congenital abnormalities, any of them. There was about a 26% increase in the risk after we adjusted for multiple comorbidities. You can see them in the bottom, there. And then, we looked at some individual congenital abnormalities, as well, and you could see the ones that were associated.

So when we first found this out, I was a little nervous about publishing this. I'm like, no one had talked about this before; this could be really terrifying. But so we did publish it and after that, there had been a few studies that have confirmed that association. So it seems like it is real, and it may be related to some inflammatory changes or endothelial dysfunction that happens that might predispose to the development of these congenital abnormalities.

So what can we do about this? I'm going to talk about CPAP because that's the only thing that has been really studied in pregnancy. There was a little something about mandibular advancement devices, but not a lot of data on that in pregnancy. So I'm just going to talk about CPAP, but later we're going to hear about all the other alternative treatments to sleep apnea.

So even though this has been the most studied thing, it hasn't been studied enough, and there are some data here and there that some of them are non-randomized studies. Some randomized studies that were small, that do demonstrate an improvement in hemodynamics and in nocturnal cardiac output in women that have preeclampsia and have evidence of obstructive events, where CPAP improves these hemodynamic measures compared to no CPAP. And then in a randomized controlled study, there was a lower diastolic pressure in women that were randomized to CPAP and a lower risk for preeclampsia.

Adherence to CPAP is an issue. This is a young population. There are some racial disparities in adherence to CPAP as well, again, keeping with the theme that we talked about earlier.

So how do we identify sleep apnea in pregnancy? I am not going to go through details of this, but this is a set of guidelines that we published about 2 years ago in obstetrics and gynecology about who to screen and how to treat people with sleep apnea. But basically, not all pregnant women need to be screened for it. Obviously, if they have symptoms, you ask them further questions.

But definitely women that have an elevated BMI or that have a history of a metabolic disorder or a cardiovascular condition or hypertension. And then when do we screen these women in pregnancy? This was a little bit harder to address because screening early may identify less women with OSA but provide us with an opportunity to intervene early so that we can modify pregnancy outcomes. Screening a little bit later in pregnancy may identify more women with OSA, but then we might lose that window where placental development is happening so that we can make a difference. So we settled on 14 to 26 of gestation where we still have time to make a diagnosis and make an intervention to make somewhat of a difference.

And I want to show you an example in here really quickly. This is a study. If you look at the one that says flow, right here, you could see

that there's evidence of flow limitation where the top part is flatter, as you could see. So this was a participant that came early in pregnancy, and her apnea-hypopnea index was only 3.3 in early pregnancy. We repeated her study in the third trimester, and she now had 69 events per hour. So think about this, going from 3 events per hour, which is normal, to 69 events per hour. So that tells you that what happens in pregnancy definitely predisposes to it. And this is just an image where you see the flat lines in like the third or fourth line. If you can't see my pointer in here, these are all apneic events and they are associated with drops in oxygen level.

So how do we implement the identification and the treatment of sleep apnea in pregnancy? There are some factors that influence this implementation. So some of these are system-level factors. So we need appropriate access to screening and testing. And we did talk about how few sleep doctors there are and even less behavioral sleep clinicians that are available in case we get into trouble, so that may be something that we need to address in the system. There are some individual-level factors. We talked about the social determinants of health, the gender role, where women have a lot of responsibilities in the home and they may not prioritize sleep. Some pregnancy-related factors like access to prenatal care, and then, again, the prioritizing of the sleep discussion in prenatal care and sending the message that sleep is an important thing in the course of pregnancy. And then some treatment-related factors, some that are nonspecific to pregnancy and common to the general population and others that are specific to the course of pregnancy.

Which brings me to my next point, and we heard this theme again over and over that we need to collaborate so that we can make a difference in women's life. So we need multidisciplinary teams. We need to involve the families and the partners because partners' role in women using treatment and addressing their sleep disturbances is really important. We need to involve communities about solutions that work for everyone and then policymakers and advocate for better sleep health so that we can treat all the women that we would want to treat.

Many gaps do remain, so we need to focus on fetal and neonatal health, and we need to consider the unique physiology of pregnancy and then advocate for sleep.

Dr. Wells:
Thank you very much, and a pleasure to be here, everyone. I'm Dr. Audrey Wells, and I am tasked with giving you an overview of innovative therapies for sleep apnea in women. I don't have a lot of time, so I want to be really clear about my objective, which is to give you a sense of what's on the treatment menu along with a sense of hope that there are many things that can be deployed for sleep apnea treatment so that you can communicate that hope for effective therapies to your patients. We've talked about how you can be a scout for sleep apnea in your patients. And paired with that is giving them a solution because a lot of times women do not present for testing, thinking I don't want the machine; I don't want the mask, right? I call that the PAP slap.

So let's talk about why PAP is the gold standard treatment for sleep apnea. There's really 4 reasons. PAP therapy creates a multilevel air stent. And when we talk about levels of airway obstruction, this is one way where CPAP alternatives fall short because they are only addressing 1 level of potential airway obstruction. Secondly, the CPAP pressure is customized or titrated, so just enough air pressure to hold the airway open. And it's the most reliable, effective treatment for sleep apnea, whereas alternatives are not necessarily 100% effective and don't necessarily work for every single person. Finally, PAP therapy is noninvasive, so it makes sense to try it first because of the 3 factors above, but also if you decide that it doesn't work for you, you have not undergone a surgery, you have not had an implant, you can discontinue CPAP without any permanent effects.

On the nonsurgical treatment menu, there's also oral appliance therapy. This is also called a mandibular advancement device. There's weight loss, which I'm going to spend a little bit of time on. And there's multiple other treatments that are not surgical that can be applied in a layered fashion or tested by someone who has sleep apnea.

The key is you have options. And it's never been my style to say that CPAP is for everyone. When someone tries it, though, there are multiple adjustments that can be made for settings. You can have support for acclimation, because you are bringing a machine home to live at your bedside, and there's some mind chatter that comes with that. So mindset reform is often effective in helping someone acclimate. But if it's simply not working, it may be time to move on to an alternative, alternate, or combine therapies.

I mentioned oral appliance treatment briefly. Basically, the idea is the jaw is moved forward to pull soft tissue out of the airway for better breathing. There's 2 main points on this slide that I want to hammer home. One is that an oral appliance for sleep apnea needs to be custom made by a dentist who knows what they're doing. This is someone who has experience and can handle the complications that may arise. But the second point is that experienced dentist is going to recommend testing for sleep apnea with the oral appliance in place to confirm that it's working, because the absence of snoring doesn't necessarily mean that that oral appliance is effective.

Let's move on to talk about weight loss as a therapy for sleep apnea. It is a myth that only overweight people or only people who have clinical obesity have sleep apnea. The truth is sleep apnea can be the result of multiple contributing factors, and about a quarter of the people who have sleep apnea have a normal or near-normal BMI, so this is not just a weight issue. When you think about sleep apnea

contributors, though, body fat percentage and the pattern of distribution is currently the number one risk factor for sleep disordered breathing. Number two is age, and there is an inflection point at about the 50-year mark. So this is especially true for women where incidence of sleep apnea increases. And the third risk is sex, male sex, or post-menopausal status.

Sleep apnea and obesity have a bidirectional relationship. So the presence of obesity increases the risk for obstructive sleep apnea. OSA also increases the risk for obesity because it is a driver for appetite, sedentary behavior, and untreated or undertreated sleep apnea makes it harder to lose weight. So if both conditions coexist in your patient, it really makes sense to treat 2 birds with 1 stone.

What do we know about weight loss or weight gain in the context of sleep apnea? Well, even before the highly effective anti-obesity medications came out, this has been studied, and it's been shown that even a 10% weight loss can reduce the severity of your sleep apnea by about 26%.

Interestingly, a 10% weight gain has a little bit bigger effect in the opposite direction. So 10% weight gain can make your sleep apnea worse by about a third. Now, tirzepatide is a GLP-1 injectable medication that was approved late last year as a treatment for obstructive sleep apnea in the presence of obesity. And there was a 1-year study called the SURMOUNT-OSA study where hundreds of people with moderate to severe sleep apnea and clinical obesity were studied. Two arms in the trial. In one arm, patients were using CPAP. In the other arm, they were untreated.

In this study, about 30% of the participants were women, and fabulously, women tended to lose a little bit more weight. Now, consistent with other trials, the weight loss was about 18% to 20%. This communicated a 50% to 60% reduction in sleep apnea severity. And for about half of the patients who were studied, they enjoyed a sleep apnea remission.

That term remission, I'm using very deliberately instead of cure. Because remember, the second risk factor for sleep apnea, it's age. So even if your sleep apnea goes into remission with weight loss, you are still susceptible to the effects of age. You may acquire sleep apnea in the future.

Even for those who did not experience remission, many had a significant or clinically significant reduction in their sleep apnea severity, which opened up treatment options for them. Now, I want to underscore the idea that for anyone undergoing a weight loss journey, whether it's with a highly effective anti-obesity medication or not, you should not quit your sleep apnea treatment prematurely. This is because untreated or undertreated sleep apnea means you are not sleeping as much as you can, you are not sleeping as well as you can. You may still have low oxygen, deployment of inflammatory mediators, and increased oxidative stress, and a stress burden on your day-to-day life, which is an obstacle for implementing the behaviors necessary to sustain weight loss or continue to lose weight.

It's very clear that for people who have a good response to anti-obesity medication, that that medication, or at least some form of medical intervention, is going to be necessary for the long term. So when an anti-obesity medication is stopped, research demonstrates that the weight comes back on, and with that, your sleep apnea will return, potentially worse than it was before. So these medications are meant to be long term. Both obesity and obstructive sleep apnea are chronic conditions.

In summary, the idea that you can kill 2 birds with 1 stone, I think, is really sexy. And in this room, I know everybody likes to be productive and efficient. So this is like, aah, but you have to emphasize the nutrition, the exercise, the behavioral changes that are all going to support that medication response. And this is all on a foundation of healthy sleep, which makes weight loss easier and more permanent.

In terms of surgeries, historically, the uvulopalatopharyngoplasty was the main upper airway surgery, which is essentially a debulking procedure of the upper airway. Hypoglossal nerve stimulation surgeries are very popular now, and that's with an implant that stimulates tongue movement forward. You can have some nasal procedures or even bariatric surgery to treat sleep apnea.

I won't spend too much time on surgical procedures, but I want to point out that one of the benefits of surgery is that even if a surgical procedure is only partially effective, it is with you nightly and throughout the night, which is different than some of the other devices and things that I've discussed so far.

We're short on time, so I'm going to leave you to read some of the information about surgical procedures. There's a new HDNS procedure, called Genio out, which is a bit similar to Inspire. On the horizon, there is a medication that shows promise—it's in phase 3 clinical trials right now—in increasing the upper airway muscle tone. Unclear whether or not this is going to be completely effective during REM sleep, but we're accumulating more and more tools to apply the principles of personalized medicine and make this a better and more comfortable experience for people with sleep apnea.

So in summary, there are multiple options available. And as your sleep medicine colleagues, we're here to collaborate with anybody who's having patients that need attention. And again, that may be your sister, you. It may be your parent or even your child. So when you listen to talks like these, I know that you're thinking about people in your life who are struggling with sleep.

The presence of REM-predominant sleep apnea matters a lot to women, and treatments are only effective if used nightly and used throughout the night, because a lot of REM sleep occurs in the second half of the night, so you want to make sure that period is covered with your sleep apnea treatment.

There's a QR code on this slide that will take you to sleepeducation.org where you can input your zip code and find a brick-and-mortar sleep center near you. There's also many online platforms for sleep intake and testing.

Lots of benefits from improving sleep. In the short term, you're looking at issues related to quality of life, function, and self-actualization. In the long term, healthy sleep is effectively the compound interest of longevity and health. So this is all foundational to a person's whole-body health.

Thank you very much for your attention.

Announcer:
You've been listening to a replay of a live broadcast discussing women's life stages–specific factors in OSA diagnosis and management to improve sleep and cardiometabolic outcomes. This activity was provided by Omnia Education and is supported by Eli Lilly & Company

To receive your free CE credit or to download this activity, go to ReachMD.com/CME. This is CE on ReachMD. Be Part of the Knowledge.