MICHAEL WALSH: I just want to start off by thanking a Dr. Cohen for allowing me the opportunity to present this topic to you guys today. It's an honor and a privilege to be able to speak. I don't have any disclosures or conflicts of interest.

So you may be wondering, what does immigrant health and screening for congenital heart disease have in common? And probably, not much on the surface. But we will be talking about screening a high-risk population for a significant disease. And we'll have a pretty significant advocacy slant toward the end. So maybe a few things. But I really enjoyed the talk. Dr. Linton, thanks for sharing that with us.

So let's start out with the idea that in 2015, congenital heart disease is being diagnosed in a much different way than it was, say, 20 years ago in 1995. And when I say different, I mean for the better. It's being diagnosed earlier. And so with that, there's been a significant improvement in the morbidity and mortality associated with delayed diagnosis of congenital heart disease. And the two biggest factors that go into that is the advancements made in fetal echocardiography, and a more recent development of mandatory pulse oximetry screening in the nurseries. And so we'll talking about those two topics primarily today.

So we'll start out just kind of looking at the scope of the problem. So when it comes to birth defects, the most common type of birth defect is congenital heart disease. When it comes to mortality from birth defects, the most common cause of mortality from birth defects is also congenital heart disease.

Congenital heart disease affects about 8 in 1,000 live births. A few more other pregnancies that don't lead to live births, you could kind of think of the number 1%, 1 out of 100, you wouldn't be too far off. And of those, 25% of these heart defects are going to be called critical congenital heart defects. And I'm going to use that term throughout the talk today. You probably all have a sense in your mind of what that means-- critical congenital heart defect-- but for the purpose of this talk, we're going to be talking about lesions that would lead to the need for surgery, transplantation, or death within the first 12 months of life, just so we're all on the same page.

So whenever you were a medical student, you probably learned that significant critical congenital heart defects present in this area right over here. This time period between, say, 24 hours and 7 days of life, maybe especially in the 48 to 72 hour time frame. And that, of course, is when the ductus arteriosus closes. And these babies with ductal-dependent blood flow become very sick in a kind of crash into the local emergency room.

You know that the patients with systemic outflow tract obstruction, like critical aortic stenosis, aortic coarctation, or hypoplastic left heart syndrome will become acidotic and shockey, gray, multisystem organ failure when their ductus discloses. The other subset is those that have outflow tract obstruction to the pulmonary side. They may have tricuspid atresia, hypoplastic right ventricles or pulmonary atresia, and those babies are going to get extremely cyanotic whenever they have ductal closure.

So what we're talking about here is the idea that the time frame for diagnosis of these lesions has moved a little bit to the left. And that's the big goal here. Certainly, fetal echocardiography usually kind of comes into play around the second trimester here, around 18 to 24 weeks, a lot of these diagnoses are being made. And certainly, a lot more diagnoses can be made here in the first couple of days of life. We kind of consider this a latent period, where babies are still reasonably well, despite the fact that they have critical congenital heart disease. And so between physical exam and now mandatory pulse ox screening, some of these babies can be picked up before they're discharged home.

This is a study that was published last year in *Pediatrics*, that kind of looks at the venue by which congenital heart defects are diagnosed. And so what they've done here is it's a study out of Boston that looked at a birth defect registry for the state of Massachusetts. And they looked at each year from 2004 to 2009, to look for temporal trends in the way the diagnoses were made. So they kind of found three different, venues where critical congenital heart defects could be diagnosed.

The top line here relates to diagnoses made in utero by fetal echocardiography. And you can see, very encouraging, this number has gone up each year from 45% to 64%. The second line is diagnoses that are made during the birth admission. So in the nursery or in the NICU, before the baby actually goes home. And kind go along with this top trend, this one has kind of gone down by the same amount, fewer diagnoses being made there in the nursery.

Of some concern, though, is this bottom line. The bottom line after a little tick down, has been pretty stable over the course of these last four years in this particular study. And this suggests that about 10% of babies with critical congenital heart defects-- again, those that are going to need surgery within the first 12 months of life-- about 10% of these are going to be sent home without a diagnosis.

So we'll talk a little bit about the logistics of fetal echocardiography. We kind of find the best acoustic windows for a gravid mother are between 18 and 24 weeks. And so that's when we're doing most of our initial fetal echo assessments, often done after the anatomy scan, which the OBs typically perform 18 to 20 weeks. At Wake Forest, we have the ability to scan down to maybe 15 or 16 weeks to provide early cardiovascular imaging. Our sense is that they were able to get some information, but usually not be able to complete a full anatomic survey of the heart during that time period. But for various reasons, sometimes, families or obstetricians want us to look early, and we have the ability to do that. It's a little counterintuitive, but as the babies get bigger and move closer to the time of delivery, sometimes, it gets harder to see things.

So it would be great if every pregnant lady could have a fetal electrocardiogram. It would be great for my RVU production, which is really the most important thing. It would be great, because the sensitivity of a fetal cardiologist to pick up these defects is very, very, very high. But unfortunately, that's not the best utilization of health care resources. And so there are indications that have been put out by the American Institute of Ultrasound Medicine, the American College of OB/GYN, and The American Society of Echo, that basically says that these people listed here ought to have a fetal echocardiogram.

And so there are fetal indications, if the baby is going to have an extra cardiac anomaly like an omphalocele, if they have Down Syndrome or some other genetic defect that has been diagnosed, they should get a fetal echo. And then there are also maternal indications. If mom has diabetes, if she's been exposed to a teratogen like alcohol or anti-epileptic drugs. Or if there's a family history of cardiovascular disease, then those patients should all get fetal echo. And then another important reason that we get patients in is because during their anatomy scan between 18 and 20 weeks, somebody saw something with the heart that they didn't like. And they want us to take a more complete evaluation.

So besides making just an earlier diagnosis, what are we really doing out here with fetal echo? So the primary goal of fetal echocardiography is to provide an accurate diagnosis of complex congenital heart disease. But in so doing, we're able to do so many more things. And certainly, fetal echocardiography is not as important and is not really designed to capture the small muscular VSDs, or the bicuspid aortic valves, but more the lesions that are going to have hemodynamic significance after separation from the placenta or with ductal closure. So the ductal-dependent lesions, the single ventricles, the transpositions, that's where we can't afford to miss these babies.

We also are able to counsel families. After we make a diagnosis of significant heart disease, we're able to sit down with families for 30, 60 longer minutes and speak with them. We're able to draw them pictures of their baby heart defect, try to get them to a place where they understand the anatomy, the expected physiology, try to give them a sense of what's going to happen after the baby's born.

We talk about outcomes data, both for our own institution and kind of national standards. And we try to get them to a place where they can understand their child's heart defect better, so that they can become better advocates for their children. Also, get them to a place where they can really accept the idea that they're going to bring home a sick child from the hospital, and they probably will be able to bring that baby home in the first couple of days of life.

We can also kind of make other decisions about delivery. Certainly, if a baby is going to be born with transposition of the great arteries, that family lives in Salisbury, we don't want them to deliver at Rowan Medical Center. We would like for them to deliver somewhere closer to a place where an intervention can be done in a timely fashion. And we'll get into that a little bit more. Also, some families will elect to terminate pregnancies, or kind of pursue a palliative care approach after birth. And so we speak with them about that as well.

There are in utero therapies that are available, especially for patients with fetal arrhythmias and certain valvulopathies. It's a little bit beyond the scope of this talk, but there are other options that can impact overall health. Probably most importantly, though, we can establish a perinatal strategy. And this is something that ideally, we're documenting in our notes that all of the other people that are involved in the child's care will have access to. The NICU should have access, pediatricians that are going to be involved in the baby should have access, and certainly, the obstetricians and maternal fetal specialists. We want these babies-- especially those with significant heart disease-- to be born in a place where all the resources are assembled cardiology, intensive care, NICU, PICU, a cardiothoracic surgeon an interventional cath doctor, depending on their particular need.

So I'll speak a little bit about one lesion-specific pathway, and give you this illustration of why prenatal diagnosis is so important for these kids. So transposition of the great arteries. One of the things that you see here-- I'm going to come back to this a little bit later-- is this is a four chamber view of a heart that's done in utero. And I'll kind of give you a little sense. In this baby, the spine is down here, sternum is up here. This is the right ventricle, the right atrium, the left ventricle, and the left atrium. And you don't have to be an OB expert to say that this looks pretty normal. And that's really the case in transposition of the great arteries, the atria, the ventricles are normal. There's no real hypoplasia. There's no valve atresia. The four chamber view of the heart looks normal.

And it turns out, that a lot of times, whenever OBs do their anatomy scan from 18 to 20 weeks, they scan the baby head to toe. They look at all the different organ systems. They look at the brain, the palate. They get down to the heart, they look for a four chamber view. And if it's normal, they move on. And so transposition is kind of one of these lesions that can be missed. It can be missed on anatomic ultasound if you don't look at the aorta and the pulmonary artery. And it can also be missed, because a lot of these babies don't have a family history of cardiovascular disease. They don't have extra cardiac anomalies. They don't have genetic syndromes, they just have transposition. And so as a result, this is one that can squeak by. But I'll kind of let you know the importance of prenatal diagnosis.

So just to review, transposition physiology, this is something that you know. I'm sorry, I'm kind of having to pick one side or the other. But I'll try to keep it even. So what happens in transposition is oxygenated blood comes back from the lungs to the left atrium, this pink, oxygen-rich. It flows across the mitral valve and into the left ventricle. Now, as you remember, there's transposition. So the LV gives off the pulmonary artery, blood goes back to the lungs, picks up more oxygen and comes back to the left side of the heart.

Meanwhile, on the right side of the heart, the blue blood comes back in the SVC and the IVC to the right atrium. It flows across the tricuspid valve and into the right ventricle. And again, since the great arteries you transposed, the RV gives off the aorta. The deoxygenated blood goes back to the body, even more oxygen is extracted, and it comes back to the right side of the heart even more blue than it started.

So the only way that this is compatible with life is to maintain some communication between the pink side and the blue side. Now, certainly, one of the things that we could do for these babies after they're born is to start prostaglandins. Umbilical lines are placed, prostaglandin infusion is started. But oftentimes, that's not enough. Despite the fact that some of these babies could have open PDAs and even some VSDs, the mixture really has to be at the atrial level. Now, nature gave all these babies patent foramen ovales, but sometimes, the PFO was not big enough to adequately support mixing between these two sides.

So on fetal echo, we have ways to predict which of these foramen ovale are going to become problematic, in the sense of which ones are not going to allow adequate mixing. Whenever we anticipate that there's going to be a problem, that there's not going to be adequate mixing, that there's going to be severe cyanosis, or if we just can't really tell the very good because our windows aren't that good, then we need to prepare for the fact that these babies may need a procedure done shortly after birth to promote adequate mixing.

The nature of that procedure is a balloon atrial septostomy. Essentially, what's being done here is for these babies that are very cyanotic that have restrictive PFOs, a catheter is placed in the femoral vein under flouroscopy. It's run up IVC into the heart, into the right atrium. It passes across the foramen ovale into the left atrium. And once the balloon on the tip of the catheter is in the left atrium, the balloon is blown up and pulled back across the atrial septum. The balloon is inflated to a size that's bigger than the foramen ovale was. Whenever it comes across the atrial septum, it tears some tissue, creates a larger atrial septal defect and promotes adequate mixing. This allows the baby to kind of come out of this severely cyanotic state, be stabilized before definitive neonatal repair is taken on.

So does fetal echo affect outcomes? And certainly, you know the answer is going to be yes. This is a study from a circulation in 1999 that looked at a number of prenatally-diagnosed transposition patients and compared them to this neonatal group, which is to say that they were diagnosed post-natally. Looked at their experience over 10 years or so, and they found that the group that was prenatally diagnosed had less acidosis and less multisystem organ failure than those that were post-natally diagnosed.

But what really stands out is the difference in mortality. A number of patients that were not prenatally diagnosed, that were post-natally diagnosed, we're too sick to even make it to their arterial switch procedure. And so 6% died before they even got to the arterial switch. Another 9% died after the arterial switch. And presumably, the idea is because they had some multisystem organ failure, they were acidotic, they were not stable candidates for surgery.

Meanwhile, those that were diagnosed prenatally, they all survived, 68 for 68. So a remarkable difference in both morbidity and mortality. We also have some data that I haven't included here that speaks to the neurocognitive development of those that were diagnosed prenatally versus post-natally.

For a different lesion, hypoplastic left heart syndrome, another study that was published in circulation in 2001. This basically looked at the results of the same type of set up, those diagnosed prenatally versus those that were diagnosed post-natally, and looked at the outcomes. Those that were diagnosed prenatally had less acidosis, less tricuspid regurgitation, less ventricular dysfunction. And those that were prenatally diagnosed that went on to have surgery all survived. Just kind of highlight those areas here, those that were prenatally diagnosed and did not elect palliative care, all of them survived. Whereas the number was much lower in those post-natally diagnosed.

So where are our gaps in this? What are we missing with fetal echo? It really comes down to the screening ultrasound. And I mentioned to you earlier with that four chamber view of the heart in transposition, that there we really rely on OBs to send us patients that have abnormalities that they see as being abnormal. And so it's crucial for OBs not to just look at the four chamber view, but also the outflow tracks. Look at the aorta of the pulmonary artery. That's going to help them diagnose and kind of find more conotruncal abnormalities like the transpositions, the truncus's, tetralogy of Fallot.

And so this is something that's very recently been recommended by the American College of OB/GYN, but that hasn't quite caught up with the practice. It's been recommended that they look, but the sonographers haven't been trained. The physicians haven't been trained. Now, this is part of kind of their fellowship residency program. And so we hope that over the years, the recommendation to look at outflow tracks will catch up and improve prenatal diagnosis.

So this is research that was put together by my colleague, Mike Quartermaine. He surveyed a database of over 30,000 infants with congenital heart disease that was put on by the Society of Thoracic Surgeons. It was presented at the American College of Cardiology, and very recently accepted for publication in *Pediatrics*. What we're looking at here is we've broken down diagnoses by whether they are visible on a four chamber view of the heart, or whether they're not. The yellow bars represent diagnoses that are made with a four chamber view, and the white bars like transposition and total anomalous pulmonary venous return are usually not diagnosed with a four chamber view. And we found-- or they found-- that the difference in prenatal detection rate varies significantly between those two.

And so one of their conclusions was that outflow track views are crucial to improve our diagnosis. So just of interest, this isn't limitations of the study. This really is just more limitations of fetal echo. So here in North Carolina, the prenatal detection rate again for critical congenital heart defects is only 45%. And so they concluded that one of the reasons for that is because the quality and access to care is so variable, and that a lot of OB docs don't routinely use the outflow tract views whenever they're screening the fetal heart.

So the bottom line here, is that over half of the babies with critical congenital heart defects are going to be born without a diagnosis. So we still have to be on our game, despite the advances of fetal echo. So we'll talk a little bit about the role of pulse oximetry screening-- which I imagine if you're a community pediatrician-- has really kind of risen to a regular part of your practice over the last two or three years or so. So we'll talk a little bit about the basics of screening in general, and then we'll talk a little bit more about the advocacy process that went into making pulse oximetry screening the norm here. And we'll talk a little bit about the early results.

So whenever you talk about what's a good screening test, like what makes a good screening test, we think of PKU as kind of the original. But epidemiologists have kind of put out Wilson's criteria from the 1960s as something that people still look at as an example or kind of a cheat sheet to look and see what a good screening test is. And it has to do with the diagnosis, the condition that we're treating. We want to make sure it's an important public health issue. And as I said, congenital heart disease is the most common birth defect, so it fits that. There has to be a significant latent period, where we can make a diagnosis before the babies get sick. And we spoke to that already.

The treatment has to be available. There has to be a treatment for the condition, otherwise there's no real reason to screen for the disease. It has to be acceptable and reasonably affordable. And then there's a lot of issues with the test itself. It has to be sensitive, it has to have a reasonable cost benefit analysis from the health care economists. It has to be just kind of acceptable, and not too invasive.

So I won't go into these studies in detail, but essentially, the take home message of this slide is that two studies were performed that suggest that 1 to 2 out of every 100,000 live births will die because of delayed diagnosis of congenital heart disease. So these are babies that aren't diagnosed, that are going to die strictly because their diagnosis was not made in a timely fashion. If you figure that there's about 4 million live births in the United States every year, the estimation from these studies is that 40 to 80 babies will die each year because of the later misdiagnosis of congenital heart disease.

So this study was published a couple years ago in *Pediatrics*, to look at the economics of mandatory pulse oximetry screening. They used a conservative estimate of $6 plus per newborn screen with pulse oximetry. This, however, takes into account labor estimates as if we were hiring new people to do this pulse oximetry screening. But probably, most nurseries are not doing that. That's just kind of lumped into the work that the nurses are already doing.

There's also hope that eventually, we can use re-usable pulse oximeters. And so going through here, you can see the number of lives saved and some other data about pulse oximetry screening.

This is a study I wanted to highlight from 2009 *British Medical Journal*. This is really a landmark study when it comes to pulse oximetry screening. And this study really, I think, kind of pushed our country toward making this happen. I think this is one of the big studies that kind of pushed us in the right direction. This is a map of Sweden, in case you didn't recognize it. This is Sweden. And essentially, what's going on here is the green region up here does not use pulse oximetry screening. And the red region does you pulse oximetry screening. The red region also happens to be where the tertiary care center is, such that all the babies in Sweden that a congenital heart defect come down to the red region to have surgery.

So they looked at the number of ductal-dependent circulation lesions that were missed prenatally, that weren't picked up. Babies that went home from the hospital that weren't picked up. And that number was 28% for the green region, and it was only 8% for the region in red that had done pulse oximetry screening. So this is one of the first big studies that really showed us that pulse oximetry screening can make a difference.

So you will notice that five babies where pulse oximetry screening was in place had ductal-dependent circulation that was not picked up by pulse oximetry screening. And so we'll come back and try to figure out who those babies were.

So essentially, this false positive rate was very low, 0.2%. 2 out of 1,000 babies were false positives and needed an echo based on this. False negatives, who was missed? Who were those five babies that had pulse oximetry screening and were missed? Well, turns out, pulse ox caught all the transpositions, all the babies with ductal-dependent pulmonary blood flow. But it did miss coarctation, aortic arch obstruction. And so we kind of keep that in mind, and well we'll come back to that. Aortic arch obstruction is something that could be missed by pulse ox screening.

So the New Jersey Experience. New Jerset was the first state to institute mandatory pulse oximetry screening. And so they present a little bit of their data in pulse oximetry screening. Essentially, they had pulse oximetry done for 75,000 babies that were born, and kind of looked at the results of the screening. There were 30 babies that were screened that had-- excuse me, let me just make sure I say this right-- that had a positive screen that got an echo, and they wouldn't have gotten an echo because of their physical condition. Which is to say they weren't that sick, they weren't especially cyanotic, but they failed their screen. And three of those had a positive diagnosis. So three otherwise not picked up lesions of congenital heart disease were picked up based on pulse oximetry of these 75,000. And the false positive rate really was not too bad.

So I'll speak briefly about the advocacy process. I think that mandatory pulse oximetry screening has been a huge win for the child advocates out there. So I'll kind of breeze through this, because I know that I'm kind of running late on time. But it is interesting. Essentially, the way that screening tests on the newborn screening panel are put out is the states have to decide for themselves which tests they're going to institute, which conditions they're going to screen for. But it's not really practical for each state to do their own exhaustive research of the health benefit, the cost benefit analysis.

And so the Department of Human Health Services has this secretary advisory committee that will do all the exhaustive research, and kind of make this list. And so in 2010, they nominated congenital heart disease to be on this list to be discussed for possible inclusion. And so all these different people from different agencies got together. The National Institute of Health, the American Academy of Pediatrics, the American College of Cardiology, several patient advocacy groups all got together to kind of hammer out whether this was going to be something to be included or not.

And in 2011, they published their results in *Pediatrics*. And this is kind of a landmark study that suggests that yes, this is absolutely a good idea that has to happen. It reviewed some cost benefit data. It talked about different protocols that may be used. And this launched some further efforts going down the line so. The Secretary's Advisory committee put mandatory pulse oximetry screening on the list of recommended screens. And then it was up to the states to decide whether they were going to put it into practice.

And so this is a picture of a number of family members, of patients with congenital heart disease, and then Greg Olsen-- the tight end for the Panthers, whose family has been affected by congenital heart disease-- they went to Raleigh to lobby for the inclusion of pulse oximetry screening on the North Carolina panel. And in May of 2013, Governor McCrory signed that into law.

It should be noted that the hospitals around here, Forsyth Medical Center, implemented pulse oximetry screening well before May, 2013. A group of pediatricians and cardiologists, neonatologists here in Winston-Salem kind of went together and decided that they wanted to institute that even before. And so I think that most of the hospitals in the Novant system, certainly Forsyth, were doing this long before it became law. Currently-- and this is within the last year, currently-- there are 38 states where pulse oximetry screening is done.

This is the protocol that was published in 2011 in that *Pediatrics* article. And I won't belabor this point, because it's probably posted in all of your nurseries. But I will highlight a couple of things. One is that we don't screen in the first 24 hours of life. In the first 24 hours of life, some babies have a little bit of right-to-left shunting across the PFO, a little bit of right-to-left shunting across the ductus arteriosus. And so this really improves our specificity. We have a lot fewer false positives by waiting for the first 24 hours to pass before we start the screening.

Also, we don't just do a hand pulse ox, but we do hand and foot. And this increases our sensitivity. There are some conditions in which the right arm sat will be normal, but the right leg sat will be a little bit lower. And so I'll kind of give you an example of this differential cyanosis.

So this a little cartoon of a baby with severe coarctation of the aorta. You can see the ascending aorta giving off the three head neck vessels and nominate artery, left carotid, left subclavian. And then this aortic isthmus becomes profoundly small, long segment hypoplasia, here. In this particular baby, the ductus arteriosus is still open.

So imagine you've got a pulse oximeter on the right hand. That pulse oximeter is going to reflect blood that has come from the subclavian artery, which is attached to the innominate artery, which is attached to the ascending aorta. This is going to be richly oxygenated blood that's being pumped from the LV. Sat's going to be 98%, 99%. That's wonderful.

But think about the blood that's being looked at by the pulse ox probe on the foot. So it's going to reflect blood flow from the descending aorta. And a lot of that blood flow coming from the descending aorta crossed over the ductus arteriosus, here. It didn't come from up here, it came from the ductus arteriosus, which came from the main pulmonary artery, which came from the right ventricle.

So what the pulse ox probe on the descending aorta side, the leg, the foot is seeing is a lot of deoxygenated blood. And so in patients with significant coarctation, you may see normal sats high, and decreased sats low. Certainly, we still encourage four extremity blood pressures. And certainly, I also mentioned to you earlier, that this can slip by a pulse oximetry screening. But this is the reason for doing a hand and a foot is it'll pick up more of these lesions.

So what does pulse oximetry miss? We kind of always want to think like where are your vulnerabilities? We've got fetal echo, we've got mandatory pulse oximetry screening. So where are we still vulnerable? Well, left sided obstructive lesions, like maybe non-critical coarctations can be missed. Aortic stenosis can be missed. And then left-to-right shunts. That's not really going to show up on a pulse ox probe. So VSDs, ASDs, AV canal defects, those are going to be missed.

So what does this mean for the pediatrician? It's just important for sure, to know where you're vulnerable. Know these great things have been added onto our ability to screen for congenital heart disease, but there are still some gaps. And so it's important to be aware of those. Also, it's important to be able to counsel families whenever it comes to. If they have a positive screen, you can give them a sense of the rate of false positives, and kind of the rationale for doing what we're doing here. And it's also important to think about the babies that are missed out of hospital and home births.

So in summary, critical congenital heart disease is still a significant public health issue. It's still the most common birth defect. But fortunately, we are catching these a little bit earlier. And fetal echocardiography certainly has had its advantages. It allows us to plan for infant delivery. And this mandatory pulse ox thing has been a huge victory for children. And it's largely due to the advocacy efforts of the American Academy of Pediatrics, local groups like the ones that I highlighted in North Carolina. And it's just a big win for pediatrics, always nice to celebrate those.

So I guess the only final thing I would say is if there's ever anything that we can do for you, particularly, when it comes to I was kind of thinking if you guys have patients that have had a fetal diagnosis of some form or fashion, you're anticipating a delivery of a baby that has known heart disease. Whether you're in a NICU setting or a community pediatrician, or you're just expecting the baby to come and see you afterwards. We're always, always willing just a phone call away, to discuss some of the anticipated physiology. And we'll always be glad to talk to you about any of these guys. So please, just let us know how we can help. Thanks a lot for having me.