American Heart Association
Ischemic Stroke Etiology Update
December 5, 2016

- [Will] It is now my pleasure to turn today's program over to Mary Paulsen, Senior Consultant for the American Heart Association. The floor is yours.

- [Mary] Thank you, Will, and welcome, everyone, to today's webinar. We are pleased to have Dr. Lee Schwamm present. He is Professor of Neurology at Harvard Medical School, Vice Chairman and the C. Miller Fisher Endowed Chair and Director of Neurology at Massachusetts General Hospital. He's also Director of Acute Stroke Services. He acts as the Director of the Partners in TeleStroke Center. Dr. Schwamm is a recognized leader in the field of acute stroke treatment, stroke advocacy, and in the use of telemedicine and other technology strategies to improve the quality of stroke care. He's played a pivotal role in the development and leadership of the Get With the Guidelines-Stroke program, and is currently Chair of the National Steering Committee. Dr. Schwamm has also served as a consultant and technical expert to the Massachusetts Department of Public Health, to the CDC's Paul Coverdell National Acute Stroke Registry, the Joint Commission Primary Stroke Center program, and the National Quality Forum. Thank you, Dr. Schwamm, and please begin.

- [Dr. Schwamm] Great, thank you so much, Mary. And thanks everybody for joining. My goal for our session today will be to walk you through some of the science behind our understanding of Cryptogenic Stroke and to marry that science and understanding with some of the new elements that you may have noticed in the PMT and help you understand why we're making a push into this very important area now as a focus of quality improvement for this year. In terms of my Disclosures, I just want to make it clear that I'm a clinical trials consultant to Medtronic for three different stroke prevention trials, the VICTORY AF, REACT AF, and the Stroke AF. Stroke AF is the newest of these trials. It just started recently and it is looking at trying to detect occult atrial fibrillation in patients where we think we know the cause and that it wasn't cardioembolic to help us understand the rate of background detection of atrial fibrillation and whether or not in some cases, atrial fibrillation may be occurring in an unsuspected manner. I'm also the DSMB member for a large influence stroke prevention trial and a catheter-based thrombectomy trial. And as Mary said, I chair the Stroke Clinical Workgroup for AHA. So we'll talk about what or when is a stroke quote, unquote cryptogenic. We'll talk about the nature of the stroke workup and what a complete stroke workup looks like. We'll review the current data on occult causes of stroke and then review the role of occult AF in cryptogenic stroke itself. So that's what we'll try to accomplish today. So Secretary of Defense Donald Rumsfeld was famous for this quote about threats to the United States from a military perspective. But I think there's something very appropriate about this when we think about the issue of cryptogenic stroke. So, "Reports that say that something hasn't happened "are always interesting to me, because as we know, "there are known knowns, "these are the things that we know we know." For example, we see a lacune in the pons, we know it's a lacune in the pons, we feel

comfortable with it. "We also know there are known unknowns, "that is to say we know there are some things "that we don't know." And they are, for example, I would say is cryptogenic stroke. We know there's a stroke. We're not sure what the cause is. And we know that we, at a certain point in our workup, are unable to determine the etiology at that point in time. "But there are also the unknown unknowns, "the ones we don't know that we don't know. "And if one looks throughout the history of our country "and other free countries, it is the latter category "that tend to be the difficult ones." And here I would say is an example of, we think it's a lacune, but it's actually not, it's cardioembolic. But we have dismissed the possibility that it could be anything other than a lacunar stroke because of our certainty, and those are the unknown unknowns. And that's an example of a patient who, if they really did have cardioembolism from atrial fibrillation and we thought it was a lacune, we have not provided the best therapy to prevent that. So what is a Cryptogenic Stroke? Well, it really depends on who you ask and how hard you look. And the caption here says, "Doc, enough with the English, "just give it to me in plain medical "academic medical terminology." So let's try to walk through this a little bit together. So Ischemic Strokes are about 85% of all strokes, 15% being hemorrhagic, and the majority of those being intracerebral hemorrhage. And as you probably know, about 20% are due to large-vessel atherosclerosis, so the basal artery, the carotid artery. About 25% are small-vessel disease due to small penetrating arteries in the brainstem and the basal ganglia. About 20% are cardioembolic from a high-risk source. So we would recognize atrial fibrillation or valvular disease. And 30% are cryptogenic after a thorough workup. And by that we mean either more than one potential cause or no obvious causes. So how do we classify stroke etiology? Well this is probably the most well-known. It was developed for a clinical trial that was looking at the effectiveness of a blood thinner called orgeron, which is a direct thrombin inhibitor, on preventing recurrent stroke. It was given in the acute setting. And they developed this classification system called TOAST. So Large Artery Atherosclerosis, just like I showed you before, Cardioembolism, using high and medium risk sources, Small Vessel Occlusion, Stroke of Other Determined Etiology, that's things like dissection or endocarditis, or antithrombin three deficiency, so a hypercoagulable state, dissection, or Stroke of Undetermined Etiology, that became known as cryptogenic. So two or more causes identified, a negative evaluation, or perhaps an incomplete evaluation. You know, CAT scan, ultrasound of the neck, and you're done, doesn't really exclude a lot of causes but would leave you with uncertainty about the diagnostic etiology. Another popular one, moreso in Europe, is something called this Oxfordshire Community Stroke Project, or OCSP, Stroke Classification System. And this is based on the clinical presentation. So Total Anterior Circulation, that's the MCA plus ACA, so ICA territory. Partial Anterior Circulation, that's either MCA or branch of MCA. Lacunar, a small vessel, as we said. Or Posterior Circulation. And if you put a suffix of I, so PACI, TACI, LACI, or POCI, it means there's infarction on brain imaging there. If you use an S, it's for syndromic classification and that's done either prior to imaging happening, or if imaging was not performed, or if it was performed but it's indeterminate. And those are the two most popular. There is a third which has really been used extensively in research classifications and that's the so-called CCS, or Causative Classification of Stroke. And this stroke subtyping mechanism starts with five basic categories very similar to TOAST, but then subdivides them into increasingly more specific subcategories and levels of certainty. And so this has Supra-aortic, meaning above the aorta, large-artery athero. It then combines cardiac causes of embolism and aortic causes of embolism, which many people would have actually put into the large artery category. So there's a little controversy with where the aortic plaque is classified in this system. But then the other three, Small-artery occlusion, Other uncommon causes, and Undetermined look very familiar. But then, if you go to the eight subtype approach, the Undetermined

can be undetermined because it's truly cryptogenic, because it's unknown-other cryptogenic but not embolism, not cryptogenic embolism, unclassified, or incomplete evaluation. So you can have a cryptogenic stroke, which is a small-vessel stroke, and not be sure where it came from because the person has no hypertension, diabetes, or atherosclerosis. So it's not just embolism that can be cryptogenic, although many times people will refer to cryptogenic stroke really as a surrogate for cryptogenic embolism. And then the eight subtypes can be further delineated by calling them either evident, probable, or possible. And so you end up with, based on a large amount of data that you input into a website that defines the results of various testing, you end up with a classification that is very robust between raters so that everyone agrees on what the diagnosis would be. So this is obviously a Wheel of Fortune joke, where you can see we've got the names of various stroke subtypes here and you want to know how much certainty you need before you say you're ready to guess and stop having Vanna White keep turning over letters. But how certain do you have to be before you're willing to call something established or not? So common things are common, right? And atrial fibrillation is increasingly common as people age. So Afib prevalence increases with age. It increases the stroke risk. Several risk scores exist right now to determine the likelihood of stroke and to help select the most antithrombotic therapy. And once a patient has had an ischemic stroke and has Afib detected, all of our guidelines recommend use of an anticoagulant if it's safe to use that. So in a patient with Afib and prior lacunes, would you call this a cryptogenic stroke? So on the right here, you can see a diagram of the lacune with the small penetrating arteries there. And you can see in B, there's a little area of black dot there, that's a prior lacune, it's now a chronic lesion on DWI. And you see the new lesion here in the thalamus in A. So that person has atrial fibrillation but they have a lacune. So is it embolism? Is it small vessel stroke? And, you know, it's hard to know. If I showed you that they had a stroke in the cerebellum at the same time in the opposite hemisphere, you would say, "Oh, it's clearly embolic." But in its current form, there's some uncertainty there. Is a stroke in a young patient with a PFO cryptogenic? Well I would have said, last week I would've told you, or a couple weeks ago I would've said that everyone would agree that was cryptogenic. But recently, the FDA approved a PFO closure device with a FDA expert panel providing some mixed guidance on whether or not they thought PFO closure was effective. But clearly here, we have a putative mechanism. This is actually something you won't see very often. This is a blood clot trapped across the tunnel of the PFO from the right atrium to the left atrium. This PFO is clearly the culprit in embolic stroke in this patient. But for most of our patients, it remains uncertain whether that is the true cause of the stroke. We know that stroke subtype differs across all age groups. This is some data from MGH back from a couple years ago showing that in the 75+ category, many of the strokes, or almost half, are cardioembolic and the rest are large artery with some degree undetermined. When you're 18 to 49, cardioembolic is a pretty small proportion of strokes. But other determined causes, dissection, hypercoagulability, that kind of thing, they make up almost 40%. So age matters quite a bit in terms of our thinking about this. Now when it comes to thinking about finding, when you're looking for something, finding it positive on a test, a tremendous amount depends on how prevalent the condition is before you look for it. So Rule number one is just cause it's hard to find, doesn't mean it's not there. You may have to looK for a long time and very hard to find it. Rule number two, though, is just cause you found it, doesn't mean it's the cause. Just cause you find something, a mitral calcification, or maybe PFO, or left atrial smoke, it's called, doesn't mean that it's causative. And the last rule is just cause it isn't the cause, doesn't mean you can ignore it. So even if you found Afib after a stroke that you were convinced had nothing to do with Afib, you just can't ignore the Afib. You still have to factor in your decision-making. So this is the impact on a nearly perfect test. This test had

99% sensitivity and 10% specificity. And if the disease exists in the population, at a 1% rate, when a test is positive, it will only indicate the true presence of disease 17% of the time. Meaning if the disease is rare, a positive test is more likely to be a false positive than a true positive. If the disease is present at a 10% rate, it's likely to be accurate 69% of the time. And if a disease is present 20% of the population, then a positive test predicts the presence of disease 83% of the time. So you can see how important it is to know what the background rate might be. So stroke workups are not one-size fits all. And that's part of what we have to really think about is how do we tailor the workup in a way to be maximally thoughtful about the appropriate evaluation? So here's a really nice summary paper about unusual causes of stroke. This is published in the New England Journal of Medicine as part of a CPC. But it gives you a list of all of the unusual things that you might want to think about when you're thinking about stroke. And you want to think about illicit drug use, particularly stimulants. If you're in parts of the country with a large population of African-American patients, you might think about sickle cell. If someone is of particular genetic heritability, some of the hypercoagulable states make more sense to test for than others. And cardiac disease can sometimes present with very rare and unusual causes of embolism. But these are the needle in a haystack. 90% of what we see, the etiologies are much more straightforward than that. So here's a suggested algorithm from a couple of years ago to think about the cardiac workup for patients with ischemic stroke or TIA. So if you have a stroke, you have an H&P, you have regular carotid imaging, telemetry to rule out Afib, brain imaging, EKG, and a chest x-ray. And if you have no clinical signs of heart disease, a normal EKG, normal chest x-ray, meaning heart dimensions, and telemetry, and a clinical picture that suggests a non-cardiac mechanism of stroke, they're suggesting you might not even need an echo or extended cardiac monitoring at all. However, if you have clinical signs of heart disease, then you need at least a transthoracic echocardiogram. And if you find the source of embolism, you're done. However, if you don't find the source of embolism, and you have a strong suspicion of embolism, they recommend doing a transesophageal echo and extended rhythm monitoring to increase the sensitivity for detection. And patients who have a cryptogenic stroke, meaning they don't have any other signs that indicate a high risk for atherosclerotic disease, or they have a high clinical suspicion for a cardiac source of embolism, end up in that same bucket. So that's sort of an interesting way of thinking about risk-stratifying the workup. AHA Guidelines are pretty clear around secondary prevention and they highlight the importance of atrial fibrillation because it's the only situation for which anticoagulation is recommended as a Level one indication. Carotid dissection, there's, I think, reasonable to use short-term anticoagulation or antithrombotic therapy. The PFO classification has not changed. And for true hypercoagulable disorders, patients will be placed on anticoagulation. But it obviously has a big big difference if you find a high-risk cardioembolic source. Young patients with cryptogenic stroke or TIA and a PFO should be evaluated for a lower extremity or pelvic DVT, which itself would be an indication for anticoagulation. So about 10% of patients with an acute stroke or TIA will have new atrial fibrillation detected during their hospital admission. And patients with stroke or TIA who have an indication for a pacemaker, meaning they've had a pacemaker in place already, interrogation of the device identified about a 28% incidence of occult atrial fibrillation during the first year. Now you could say, "Well, but they had a pacemaker, "so clearly there's something wrong with their heart "to begin with, so is that number really believable?" Interestingly, a similar rate of occult AF has been reported among high-risk, non-stroke patients with implantable devices. So there are patients walking around with intermittent atrial fibrillation who haven't had a stroke who have these long-term monitoring devices. And if you do detect it, there is an increased risk of stroke, not surprising. So there's a systematic review and met-analysis from 2015 that looked at 31 studies looking at the

proportion of new fibrillation diagnosed using EKG monitoring for greater than 12 hours in patients with a recent stroke or TIA. The longer you monitored, the greater the rate of detecting Afib. And you can look at that either in a less than three day, greater than three days versus three months or as a continuous variable. But if you look here, just at less than three days, you'd pick up about 5%, seven days, you get about 15%. If we go up to three months, you get 29%. So you're starting to see this sense that about 30% of these patients who have a cryptogenic stroke will show some fibrillation during the three to 12 months after they have their monitoring beginning. So it looks like there's about a sevenfold increase in the odds of detecting Afib if you use long-term monitoring in three randomized control trials they did. So the other question is, what's the importance of Afib? Is there sort of a dose response? And if you look here at the figure on the right, the Observed Rate of Ischemic Stroke by Risk Group with atrial fibrillation, you can see that Paroxysmal Afib, meaning coming and going versus Sustained Afib, there was no difference in the actual occurrence of stroke in these Low, Medium, and High-Risk patients. Their annualized stroke rates were about 1%, 4%, then about 6%. And actually in the Moderate-Risk patients, if anything, the risk attributed to Paroxysmal Afib is higher, although they're not significantly different. You can also see that when you look by Rate Control or Rhythm Control, both have stroke risk in the five to 7% range without a statistically significant difference, which means that just because you think you're controlling the rhythm, you're not controlling the rhythm. Or even if you are, you're not eradicating the stroke risk. So rhythm control is not an acceptable strategy once someone has been shown to be a fibrillator. So the other question is duration. How long do the fibrillation episodes have to be for you to be convinced that they're meaningful? And if you look at Afib lasting greater than or less than five minutes, greater than or less than one hour, greater than or less than six hours, greater than or less than 12, and greater than or less than one day, there's not a lot of difference, meaning if you pick it up, it's real. And if it's real, it increases the risk of stroke. And this is greater than 10,000 patients, data from 10,000 patients from the SOS AF project, which was information from implanted devices. Well, what if you say, "Well, maybe you're not doing "as good of a stroke workup as I am "and if I do a really good workup, "maybe the yield in my patients is lower." So a group in Chicago looked at this issue and looked to see what the yield of 30-day ambulatory monitoring would be in cryptogenic stroke patients who have extensive cardiac imaging before the monitoring is performed. So they looked at 85 patients. 89% had a transthoracic, 68% had a transesophageal echo, and 38% had a cardiac MRI. And only 4.7% of those patients were found to have Afib on a 14 to 30-day ambulatory monitoring. That confidence interval goes from one and a half to 11 and a half because it's a small number of patients. But their experience was that the more intensive the investigation of the heart, the less enriched the pool was of patients who would end up having occult Afib detected on this ambulatory monitoring. And they also recognized that longer monitoring might be needed in this population of patients. So how much Afib do you need to have a stroke? 24 hours? So this is, the top line here in black is you have no fib at all or your atrial fib episodes are shorter than a day. You can see there's still some risk in those patients. If you had Afib that lasted longer than a day, you clearly had a significant increased risk of stroke in the first three months. But if you look at the ASSERT trial, six minutes of pacemaker or implanted device detected Afib, in this case atrial tachycardias increased the risk of stroke or arterial embolism with a ratio of about five. So this was any arrhythmia present for six minutes or more. So it's not 24 hours, might be six minutes. The other thing that increases the risk of stroke is a risk score called the CHADS score. And you can see that if you look at the risk of stroke, the CHADS score, using the CHADS2, increases the risk of stroke whether or not you were able to detect these atrial tachyarrhythmias. So normally, we think about the CHADS score as being useful for saying once you have Afib, how likely is it you're gonna have an

embolism. This is a way of saying, "Well what if we just go with the CHADS score "and assume that subclinical arrhythmias are happening?" So geez, that might increase the risk even further. So maybe the CHADS score is what we ought to be paying attention to. So the burden does appear to matter. So if you look at the risk of events by duration and CHADS score, the two are additive. And if you have really low CHADS scores, then it seems like your chances of embolism are pretty low. So you can have Afib of even 24 hours duration, but if your CHADS score is zero, 0.8% of those patients had a stroke of these 568 patients. Whereas, if you have no Afib but a CHADS score of greater than or equal to three, you have a risk of stroke that's approximately 5%. So I think this is a really useful way of thinking, both of these matter. The duration of Afib matters, but your associated comorbid risk matters. So CRYSTAL AF, this is my picture of the crystal ball. CRYSTAL AF was a randomized controlled study of about 400 patients to see whether long-term monitoring with a small insertable cardiac monitor that was made by Medtronic was more effective than conventional follow-up, meaning the control was you got a telemetry while you're in the hospital, maybe you got a little bit of a Holter monitoring afterwards, in terms of trying to find cryptogenic stroke. They had to be 40 years or older with no Afib beforehand. And you had to be randomized within three months of having had a stroke. And the primary endpoint was the time that you first were detected to have atrial fibrillation lasting at least 30 seconds within the first six months of the trial. And then they also looked out to 12 months. Oh, and here's the randomization. And what they found was the baseline characteristics were pretty similar. There were no major imbalances. There was a bunch of PFOs, not surprisingly. And what you can see here is at six months, so the first green arrow, and at 12 months, the second green arrow, there's a substantial difference in the rate of Afib detection in the arm that has the implanted device. And it was 8%, almost 9%, of patients were found to have Afib versus 1.4% in the controls, which is a ratio of about six and a half. And if you go out to 12 months, it's 12% of these patients had fibrillation that was not suspected versus only 2% had it detected by conventional methods. What this suggests is not that the patients in the control group are different, but they're having intermittent fibrillation that we're just not picking up on our very very brief sampling that happens during an EKG or a little bit of monitoring. And the detection rate rises continuously. If you go out to 36 months, the hazard ratio gets to be almost eight and a half or nine and now you're getting close to 30% of patients. So you go out to three years, you've got 30% of patients and that rate just looks linear and it actually reminds you a lot of the CHADS score, which sort of predicts risk over time. And we know that every year, the risk of Afib is increasing. So it's quite, I think, striking and perhaps occult fibrillation is an important explanatory variable for a lot of patients who we currently discharge from the hospital with a stroke of uncertain etiology. If you look at the CRYSTAL AF data, half pf the patients had a duration of fibrillation that was less than 12 hours. And 25% had it lasting less than one hour on continuous monitoring. Now what that means and the relationship between that risk exposure and stroke still remains to be determined. But it's important to know that it's not the case that these patients are having fib all the time. They're actually going in and out and in and out. So if you try to predict who's gonna have fibrillation, age is a big one, every decade almost doubles the risk. If your EKG shows the prolongation of the PR interval, the time between the atrial impulse and the ventricular impulse, you can see that if you're on medicine that makes that interval longer to begin with, there's a modest increase in risk because maybe it's the medication. But if you are not on the medicines that do that and you have a long interval between the, you have evidence of a delay in conduction, that risk goes up by one and a half-fold, if not more, and is highly significant. So how might atrial tachycardia or atrial fibrillation and stroke be related? Well there can be mechanical effects, there could be altered gene expression, there could potentially even be a reverse relationship where the stroke triggers atrial

fibrillation. There are reciprocal innervation from the heart and the brain. The right side of the hear in the peri-insular area simulates sympathetic fibers and can cause tachycardias when stimulated in the form of seizures and bradycardias when lesions in the form of stroke. And the opposite is true on the left side. You can also think about mechanical factors, you know, you have fibrillation, you don't have the blood moving around as much, you get a clot in the left atrial appendage, that's sort of the classic teaching. But newer thinking has been going on about atrial tachycardias and atrial cardopathies and whether or not there might be changes in gene expression or coagulation environment inside the left atrium that are independent of the actual mechanical effects. We just don't know, we need a lot more research on that. So can you have just a little AF? And if so, what do you do about it? So is it real? Is it signal or is it noise? Is it the cause of the stroke or an effect of the stroke and does it matter? So if you find someone with a stroke, who then has a few minutes of atrial fibrillation in the background a month later, is that an indication for anticoagulation? We don't know. How much AF is enough to justify lifelong anticoagulation? Again, we don't know. And is ablation sufficient? If I see that and if I ablate the focus and the Afib goes away, have I actually reduced the risk or does that risk still endure? I think these are all really interesting and important questions and we're gonna have to study these carefully because as we get better and better about detection, we are gonna have more and more patients in whom we detect these rhythms. So I want to thank you for your attention up to this point. And I want to remind us of two very famous thinkers. Mahatma Gandhi who said, "It is unwise to be too sure of one's own wisdom. "It is healthy to be reminded "that the strongest might weaken and the wisest might err." So our understanding of this field is in flux. Our understanding of PFO and its contribution is in flux. I think we have to be open to the data and, as Albert Einstein said, "A true genius admits that he knows nothing." Admit that what we have right now are conjectures and hypotheses and much of that is circumstantial, much of that thinking. So we have to really keep our minds open to the possibility that both that fibrillation is much more common than we thought and is contributing to and explaining a tremendous amount of the unexplained risk of stroke and recurrent stroke. It's also possible that, in some of these patients, it's an innocent bystander and that it doesn't require aggressive treatment if it's particularly brief or it's unrelated to the primary mechanism. I don't want you to leave this talk thinking that I know those answers. I'm just saying we have to keep our minds open to lots of possibilities. And so, all of this, I think, is really forcing us, driving us to get a better understanding of what kind of workup is actually being done in our hospitals for our patients? Are we evaluating the causes of stroke thoroughly? And what can we learn about the practice across our sites to better inform us about when we should be doing some additional rhythm monitoring? Are the workups really complete? Or are they temporarily cryptogenic but they're soon going to be established because additional parts of the workup are going to be performed after the patient leaves the hospital? So a cryptogenic stroke is a presumptive diagnosis until a complete workup has occurred. So at this point, I'm gonna transition to the Coding Instructions and the changes in the forms. But before I do that, I think now might be a good time to pause and encourage people to ask questions before we transition to this part of the talk. So let me check in. Christine and Mary, are you on the line?

- [Christine] We are.

- [Dr. Schwamm] Great, so do I take questions now only in the Q&A portal or are people also gonna have a chance to unmute and ask their questions verbally?

- [Mary] Our only option is through the portal.

- [Dr. Schwamm] Okay. So if you want to ask a question, you've gotta actually, you can't just be on the phone, you have to sit down and type something into the portal. So I have one question here which is, would an MCA ischemic stroke, without other documentation of etiology, be classified as large-artery, small-vessel stroke, or undetermined cryptogenic stroke? So this is a great example of how, as an abstracter, you're not necessarily gonna see the word cryptogenic. And we're gonna get into that in a minute. But the answer for this would by cryptogenic embolism. So if you were convinced that the blockage in the middle cerebral artery was not due to atherosclerosis, how would you tell that? Well one thing might be that there's no atherosclerosis anywhere else and after the blood clot dissolved, you see that the blood vessel is totally normal in its appearance, then it would by cryptogenic embolism. Usually when people have atherosclerosis of the middle cerebral artery, they have it on both sides. Sometimes one is worse than the other and they often have it in other places inside the brain, if not in the carotid arteries or the vertebral basilar system, or the heart. But that would be a situation where you might call it cryptogenic because you can't determine whether it's due to large-artery athero or embolism of unknown source. It's not a small vessel disease if it's an MCA ischemic stroke affecting the large territory of the MCA. But if it was a penetrating artery off of the middle cerebral, say in the putamen or the basal ganglia or the subcortical white matter, then it might very well be small vessel disease. So I can't answer, that's a great question, and I can't answer it explicitly in the context of just saying MCA stroke. Although I think many people, when they use the term MCA stroke, were probably referring to MCA embolism. But you need a little more information than that. The next question here is, we must have physician nurse practitioner or PA definition for, oops, it jumped on me, for identification of etiology of stroke plus testing performed correct. So I'm gonna defer that question until we get into the next section, which talks explicitly about the coding instructions. Roberta Has asks, "Will you please address three different examples "regarding whether or not etiology is clearly documented? "CVA, appears embolic, no source of embolism found." So I would consider that to be a statement as to that the etiology has been documented. So they're saying that it appears to be embolic with no source. So that would be cryptogenic embolism, is how I would classify that. "Acute CVA, Afib, anticoagulation best option "to prevent future stroke." That would be cardioembolism because atrial fibrillation is a high-risk source for cardioembolism. And then number three, "CVA, nothing significant on echo, MRA, carotid doppler." So there, oops, it just jumped here. So there I would say that's a little bit trickier. You'd probably want to have something a little more clear. CVA, by the way, not a great term, really should be ischemic stroke. But... That is likely going to be cryptogenic stroke, as well, but I'm a little less comfortable with that. Okay. "If the patient has a PFO "and they believe that there is an embolism, "then is it cryptogenic or cardioembolism?" Yeah, that's a tough one. I think the answer there is, in today's world, we would still consider that cryptogenic until the guidelines change and we recognize that PFO is now a recognized cause of cardioembolism, we would probably not treat that as cardioembolism unless the patient has a concomitant deep vein thrombosis or has evidence of a clot visualized in the heart. So that would be a tricky one. But I think, again, an excellent question. I'm going to pause in the

questions for a moment and I'm going to shift back to the slides, and then I think, because many of these look like they're gonna be potentially answered by the slides. So the first new element is, was the stroke etiology documented in the patient medical record? So, you select Yes in patients with evidence that the etiology was investigated even if no cause or multiple causes were identified. So that includes patients with cryptogenic stroke. So it doesn't have to be that the stroke etiology was documented and definitively identified as one of these potential causes. If they look for a cause and they found more than one or they couldn't find any, then there was documentation would be present. And it does have to be by a physician, nurse practitioner, or a physician's assistant indicating that a potential underlying cause was identified. This option should be selected when there is evidence in the medical record that stroke etiology was investigated, even if no cause was identified despite the investigation or multiple causes. If they didn't do an investigation and therefore they don't know what caused it, then that wouldn't count as that the stroke etiology was documented. And you can see here now that under the choice of stroke-related etiology, it only becomes active if it's ischemic stroke. And now, rather than multi-select, which was causing a lot of confusion for people, it's single-select radio buttons. However, if you select number four, Stroke of other determined etiology, you're able to identify dissection or a clotting disorder with one of those radio buttons, or Other. So it's some other cause. But those dissection and clotting disturbances are by far the most common. And then in Cryptogenic Stroke, before we had you ticking off all of the other possible etiologies and it was getting very confusing for people. So now we just say, was it cryptogenic because there were multiple etiologies? Was it cryptogenic because it was an undetermined etiology? Or are you just unsure? They say cryptogenic stroke but you can't get any further sense from the record than that. Then you would pick the Unspecified button. So what are the Coding Instructions help us to identify cryptogenic stroke? Again, multiple potential etiologies identified versus a stroke of undetermined etiology, versus unspecified, when there's no documentation of the results of a diagnostic evaluation. So appropriate testing for most strokes includes a cardiac ultrasound, extracranial arterial vessel imaging, like a carotid artery ultrasound, CTA, or MRA. Obviously, if the stroke is in the back part of the brain and the territory involved is the vertebral basilar system, having a carotid imaging may not be sufficient to address that the vessels have all been visualized. And patients with an undetermined cause of stroke, such as PFO, heart failure with a preserved ejection fraction, mitral annulus calcification, other atrial or ventricular arrhythmias other than fib or flutter, we don't know what the role is of these risk factors and so they roll up under this cryptogenic category. So what are the testing that we're gonna be talking about? So we want to understand, are people performing cardiac ultrasound? Was it performed during this admission or in the past few months? Because you don't have to repeat it if it's just been done. Was it planned after discharge or was it neither performed nor planned to be done, it's simply not going to be done? Similarly, for the carotid artery imaging, was it done during this admission or in the last three months? Because things don't change that quickly for these kinds of fixed lesions, by and large. Is it planned after discharge or not performed or planned? And then we want to know about carotid revascularization. Was the carotid found to be the culprit? And if so, was the carotid treated during the admission and planned for after discharge or not performed or planned? And then is there heart rhythm monitoring that's been planned that's gonna last greater than seven days, so extended rhythm monitoring? And that could be done during the admission, that could be done after discharge, or that could not be planned to be done at all. Same thing with extended implantable rhythm monitoring, which is sort of the final option when it comes to duration of monitoring. And that might be a pacemaker, if they already have a pacemaker, or they got one during this admission. It could one of the small implanted devices. And then hypercoagulability testing, imaging

of the intracranial vessels, so more than just the ultrasound of the carotids. And then there's short-term cardiac rhythm monitoring, so basically less than or equal to seven days of monitoring, which in many instances is like a Holter monitoring. And again, performed during or in the prior three months, I think pretty clear. Planned post discharge, if there's documentation that the test or intervention was not done during the admission but is planned after hospital discharge. And so for example, if a transthoracic echo was performed during the admission but a repeat study or a TE is planned after discharge, don't select that option because you did perform an ultrasound during the admission. And then neither performed nor planned when there's no mention that this is going to be addressed as part of the workup of the stroke. So we have about just under 10 minutes left. Christine and Mary, do you think we should keep going through the questions or do you think there's something else you'd like me to address at this point?

- [Mary] Let's go through a few more questions that I pulled over for you.

- Okay. So let's see here. Some of these are really more like management questions. But, so here, let's see here. In Get with the Guidelines, during the data submission, when you have to answer the question about whether or not anticoagulation was prescribed for Afib, will they ever adjust the options for reasons why a patient would not receive anticoagulation at discharge? Currently, the options are very limited and generally only ask about allergies or risk of bleeding. I think the data for stroke prevention is pretty strong when it comes to fibrillation. And patients or families might refuse the medication, so that's always an option. But other than the risk of bleeding, it's hard to imagine other contraindications to anticoagulation because that is the main downside to anticoagulation. It would be interesting to hear if you're coming across other reasons. Again, we're trying to pick reasons that are actually valid scientifically for why you might not want to provide patients with fibrillation because it's so incredibly powerful at reducing the risk. And people who fall down a lot, for example, the reason we worry about that is that they will bleed, not that coumadin makes them fall or that one of the rivaroxaban makes them fall, but the consequences of falling. So I don't think so. I think that one is probably gonna stay the way it is. Doreen says, "I'm requesting a better list for each category, "I feel like I'm guessing a lot of the time." I think this is a really good way to frame this and I think this is gonna be an iterative experience between the abstracters, which is I think most of who's on the call right now, and the stroke directors, and the vascular neurologists at the hospital. Getting your teams to use the TOAST categories in their discharge summaries as a statement on what they think the cause of the stroke was will not only help you, it'll help everybody who comes after you in the care of that patient. And it will help drive whether or not the appropriate therapies are actually being provided. So I think in the beginning you may need to be asking for help or, rather than guessing, I think you should just say, "No, there is not clear documentation of a stroke etiology." And then bring those cases back to your stroke director and say, "I'm not really sure what to do here. "Can't we get folks to start using "one of these five categories from the TOAST classification "so we can all make sure we're using the same language "to talk about what caused this stroke?" Someone asked, "Should a patient remain on anticoagulation after ablation?" I think patients who've had a stroke and have atrial fibrillation and get ablated should remain on anticoagulation after the ablation because we know that the ablation does not eradicate the risk of recurrent fibrillation, it's more about symptom control and reducing the burden of AF. But there is a

Stroke and Fibrillation guideline from the American College of Cardiology and AHA, which I'd recommend that you take a look at. I guess the question, why the data of stroke etiology does not say that it needs to be explicitly documented tied to cause as you require reasons for treatment not administered for other measures, it seems you are asking us to make a clinical determination of whether an adequate workup was done and to infer etiology if the physician does not specifically document it. It will reduce abstracter burden and give you more reliable data. As it is, it seems very subjective and beyond the scope of an abstracter. I think what we're really asking you to do is to say, if it's clearly documented, say Yes and put down what it is. And if it's not clearly documented, don't guess, just say No to this element here. Was the stroke etiology documented in the medical record? I think the answer you say is No. I don't see any of these words, I don't see anything like this. I'm not sure. And so in that circumstance, that will help drive quality improvement at your organization and we will be constructing a performance measure for people to look at. It'll be in the reporting category or the quality category initially, which says, "How often was the stroke etiology clearly documented?" And I think that will help all of us do a better job. I think we have time for maybe one or two more.

- [Mary] Can I read one Dr. Scwhamm that keeps coming up and I haven't pulled it over but there's a lot of questions on does telemetry monitoring count as short-term monitoring?

- [Dr. Schwamm] I'm just gonna go to this section here. So does telemetry in the hospital, so we have to pull open the Coding Instructions relevant to that and I don't have those here in front of me. In general, I'm sorry, I apologize, but I don't remember. I think short-term monitoring is generally what we're thinking about in the form of like a Holter monitoring. But I have to defer to you or Christine on that. Do you have the Coding Instructions open in front of you?

- [Christine] I'm looking right now, let me just.

- [Dr. Schwamm] I know we've designed that to capture things like a 24 or 48 hour Holter monitor.

- [Mary] While she's looking, there's one more that has a theme to it.

- [Dr. Schwamm] Yup.

- [Mary] Go ahead Christine.

- [Christine] Found it. So, it does look like for the short-term monitoring includes continued monitoring lasting less than seven days, includes 24 to 72 hour Holter monitors or equivalent, does not include heart rate monitoring without rhythm detection. So I would say that that means to me that telemetry monitoring would count. Correct, Dr. Schwamm?

- [Dr. Schwamm] Yup, yup, I think so. Because remember there are a lot of hospitals also that don't admit stroke patients to a monitor telemetry bed. So they might have an oxygen probe on them or they might have heart rate monitoring, but not actual rhythm detection so that you can see the heart rate blinking up at the central station, but you don't get any arrhythmia detection or alerts. So if you don't happen to be looking at the monitor when the patient goes into fibrillation, you won't see it. What was the last thing, Mary, that you were gonna say?

- [Mary] The last theme looks like if there are multiple etiologies documented, is there a hierarchy of which note should be considered, i.e. the neurologist is the highest note considered?

- [Dr. Schwamm] I think that the best approach there is the final note, either the discharge summary or the final note from the neurologist which summarizes the information. So sometimes I think someone might write a note where they think they saw fibrillation but after careful review, people decide that it's actually PACs or some other form of maybe it's an SVT but not Afib. So I think just being a single note that identifies a possible cause, you really want to looK for a note that synthesizes the information. And some of those examples I read you out before, those snippets I felt were very helpful, where at the end of the day it's like, carotid stenosis but also question fibrillation, embolism of uncertain etiology, or cardioembolism possible but not definite, should have continued rhythm monitoring. Again, that would be cryptogenic embolism. Just cause it's embolic, does not mean it came from the heart. I mean we think of it as coming from the heart, and potentially many of those do come from the heart, but we're really talking about embolism in the presence of a high-risk cardiac condition. So if you have fibrillation but you also have a 90% stenosis of the carotid artery and there's a stroke on that same side, you really can't know which of those two it is. And so it's cryptogenic for a different reason. And that's, again, part of why we try to pull out multiple etiologies versus I don't know what the etiology is under cryptogenic, so that we can distinguish between those two because they will likely have very different outcomes. So I think we're at the very top of the hour so maybe I'll turn it back to you, Mary, to close.

- [Mary] Yes, go ahead, Will, and get the closure but thank you everyone for attending today and thank you, Dr. Schwamm. Will?

- [Will] Thank you. I would like to say thanks to all our participants for joining us today. We hope you found this webcast presentation informative. This concludes our program and you may now disconnect. Everyone, have a great day.