AMERICAN HEART ASSOCIATION

Moderator: Jeanne Rash

March 29, 2016

2:13 p.m. ET

Operator:

This is Conference #: 31034977.

Hello and welcome to today's webcast. My name is (Lauren) and I will be your event specialist today.

All lines have been placed on mute to prevent any background noise and please note that today's webcast is being recorded. During the presentation, we will have a question and answer session. You can ask text questions at anytime. Click the green Q&A icon on the lower left hand corner of your screen. Type your question in the open area and click submit. If you would like to view the presentation in a full screen view, click the full screen button in the lower right hand corner of your screen. Press the skip key on your keyboard to return to your original view.

If you would like to download materials associated with today's event, please click the blue files button on the lower left hand side of your screen. For optimal viewing and participation, please disable your pop-up blockers. And finally, if you need technical assistance of the best practice, we suggest you first refresh your browser. If that does not resolve the issue, please click on the support option in the upper right hand corner of your screen for online troubleshooting.

It is now my pleasure to turn this program over to Jeanne Rash from the American Heart Association. The floor is yours.

Jeanne Rash: Thank you, (Lauren). Welcome everyone on behalf of the American Heart Association and the American Stroke Association. I'd like to welcome you to today's webinar to review upcoming enhancements to the Get With The Guidelines Stroke Patient Management Tool. And we thank you for your participation in the Get With The Guidelines Program.

Before I turn things over to today's speakers, I'd like to remind everyone that a recording of this webinar will be posted on the heart.org Web site for viewing it a letter date. The enhancements reviewed in today's presentation are scheduled to be implemented on March 26 and I'll get with the guideline users. We'll be receiving e-mail communications about the updates.

We do aim to have time for your questions following today's presentation. We are extremely fortunate to have Dr. Lee Schwamm and Eric Schmidt with us today. Dr. Schwamm is executive vice chairman of neurology at Massachusetts General Hospital. He's director of stroke services and medical director of TeleHealth Massachusetts General, director of Partners TeleStroke Center at Massachusetts General Hospital and chair of the Get With The Guidelines Stroke Committee.

Dr. Schmidt is the associate professor at the Department of Clinical Neurosciences, Radiology and Community Health Sciences. He's a member of the Hotchkiss Brain Institute, Cumming School of Medicine at the University of Calgary, medical director of the Cognitive Neurosciences clinic, stroke neurologist and member of the Calgary Stroke Program.

Thank you, doctors, for being with us today and Dr. Schwamm, I will tell the presentation over to you now.

Lee Schwamm: Great. Thank you so much, Jeanne and welcome everybody. So, I think we have a really fun and exciting hour ahead for you. I'm going to start things of by talking a little bit cryptogenic stroke and giving you some clinical background around that topic and then talk a little bit about how we've modified the PMT to try to help us capture this very important aspect of the stroke workup which is something we're really haven't stepped into in the past

but we think will be increasingly important as we try to focus on and improving the value of healthcare and thinking about what it means to identify the cause of the stroke in our efforts to reduce the likelihood of a recurrent stroke which as you know, affects up to 25 percent of stroke patients.

After that, Eric will walk you through some additional changes, in particular one focused on the reasons for non-treatment with tPA which all of you think about everyday as you do the abstractions and I think that that we'll be also a useful section and I'm sure one where you'll have some questions. So, let me start out by emphasizing the fact that the Heart Association, Stroke Association has been focused for the last year on really addressing topic that is one of, I think, deep concern to patients but also to providers which is the question of what do we say to patients and what should we do when the patient presents with a stroke and we need to decide what's the appropriate evaluation to determine the cause of the stroke.

What you can see here is slide showing you that we have about 700,000 ischemic strokes every year. It's the fifth leading cost of death. It's one of the leading causes of serious long-term disability in the U.S. and it's quickly becoming – stoke is quickly becoming the leading cause of death in developing countries in the world. As we've done a better of fighting communicable diseases, so people are living longer because they're getting appropriate and effective treatment for infectious or communicable diseases, non-communicable diseases like stroke particularly as a consequence of long, untreated, long standing hypertension really have become a global epidemic.

So of those 700,000 strokes, about 30 percent of patients are discharged from the hospital without a clear likely cause being identified. And I'm going to talk a little bit more about what we mean by cryptogenic in a minute. And so, about 30 percent are large vessel, 15 percent maybe or so are lacunar and another 10 percent or so, maybe less are a bunch of other very rare causes.

So one of the questions is what do you do for those patients? And current guidelines don't suggest anything beyond anticoagulation, a bit on the antiplatelets therapy for these patients unless they have a clear indication for

chronic anticoagulation. And recently, there has been increasing interest in trying to understand whether with shorter hospitals stays, whether longer monitoring of those patients or more extensive in-patient evaluation will yield a better understanding of the risk of stroke in these patients.

So I really am so fond of this quote which has been often repeated but I think misinterpreted. This was Donald Rumsfeld and he wasn't actually really talking about cryptogenic stroke. He was actually talking in general about threats in the United States but he said, "Reports that say that something hasn't happened are always interesting to me because as we know, there are the known knowns. There are things we know that we know. We also know there are known unknowns, that is to say, we know there are some things we don't know. But there are also unknown unknowns, the ones we don't know we don't know. And if one looks throughout the history of our country and other free countries, it is the latter category that tends to be the difficult ones."

So what I would say about cryptogenic stroke is they are the known knows. Those are the strokes where we really feel we understand the cause. They have AFib. Their vessels are clean. They have no other suggestions. Otherwise, their cholesterol is normal and we see a small bit of clot in the left atrium. We call those strokes due to AFib. We have patients with severe carotid stenosis or occlusion. They have an infarct in the appropriate territory. It's cortical. It's correlated with the stenosis. There is thromboses on the plaque, on the imaging. We say those are the known knowns. That when we assign a ideology.

And then we have this sort of known unknowns. We know that we can never approve for sure that anyone of these things really because the stroke and we factor that knowledge in about what we can't know. We know there are hypercoagulable disorders that we can't measure, right? So there are times when we assume something is a (clotting) disturbance even though we can't measure it.

But then we have the sort of unknown unknown. So you have a stroke with maybe more than one cause so there's no identifiable cause. But what does

that mean? And what is the significance of some of the findings that we have where there are associations that are loosely associated with stroke? Mitral annulus calcification, left atrial smoke, PFO, what are those mean and what don't we know about those?

And so I would argue that cryptogenic stroke is actually, it's kind a strange term. It really means – it happened for some reason but I'm not sure why and the I'm not sure why could be for many different reasons. I'm going to walk you through at it a little bit. So, doc, enough with the English, just give it to me in plain academic medical terminology.

So, you know, that's kind of to me what cryptogenic is. It doesn't actually convey any more information. And so to be given the diagnosis of cryptogenic stroke is, to me, a little but of a tautology. Really what we're saying is the good news is we found no obvious high risk cause but we're not exactly sure which of the following potential causes could have explained your stroke.

So again, these numbers vary and this is a slide from a couple of years ago. But, remember, 85 percent of strokes are ischemic. Only 15 percent are hemorrhagic. And of those, we can generally explain about 65, 70 percent of strokes in a very straight forward way from their imaging and the history. Although I will say that we're not always perfect. And so, we do have to ask ourselves, especially with the 25 percent recurrent rate how we really figured it out.

So there are a bunch of different classification systems for deciding what cause the stroke. And probably, the most popular is one called the TOAST criteria which was actually from a trial invented for a clinical trial many years ago which was a trial of a drug that (inaudible) was called Orgaran and it was a trial of Orgaran in acute stroke treatment to see of early anticoagulation could reduce the risk of recurrent stroke. It did not in this trial and it's one of the reasons why we don't have a guideline recommendation for early anticoagulation.

So large artery atherosclerosis, that's cholesterol with stenosis or occlusion in the carotid artery. The very origin of the middle cerebral artery or the basilar artery. There's cardioembolism and there, we talked about high and medium risk sources and the high risk sources are things like atrial fibrillation valvular disease, LV aneurysm, et cetera.

Small vessel occlusion sometimes called lacunar infarction is when an infarct usually less than one centimeter maximum in diameter often located in the deep white or gray matter of the brainstem or the internal capsule or corona radiata in the center of the brain.

Then stroke of other determined ideology. These are all of the uncommon things all rolled into one, dissection, hypercoagulability, vasculitis, sickle cell, all sorts of relatively uncommon. But when you rolled them on together, not that uncommon as a group.

And then the last stroke of undetermined ideology, i.e., cryptogenic and that can be produced by either you found two or more causes. They've got 90 percent carotid stenosis and AFib. I'm not sure which of those was the culprit. Or a negative evaluation. I evaluated them thoroughly, (inaudible), every test you can imagine, nothing came back positive. Or you got a CAT scan or an ultrasound in the emergency room and he was sent home. And, really, very little evaluation was done. Any one of those could lead to an undetermined ideology.

So the NINDS stroke data bank had a similar set of criteria. You'll notice some of the terms are similar but there was this issue of tandem arterial pathology, the idea of being sort of artery to artery embolism there, but basically, not a system that's been used very often.

And then interestingly, the Oxford Community Stroke Project looked at trying to develop classification system that could be used worldwide. And the idea here was you could use this even when you just have the syndrome but no imaging. So this can be used in any country. So there's a total anterior circulation or partial anterior circulation. I don't think most of you are finding

this in the charts in the U.S. but in Europe, you still might see some of these and particularly in the developing world compared to lacunar infarction or posterior circulation.

So these are different patterns that we would expect to see clinically so that total anterior circulation is the full hemisphere syndrome. It's hemiplegia and aphasia with a gaze preference with the left hemisphere stroke or neglect hemiplegia with a right hemisphere stroke. The partial anterior circulation are the subset syndromes, the Wernicke's or Broca's aphasia or the less profound nephritic syndromes.

Lacunar infarctions, the clumsy hand and dysarthria of the pure motor hemiparesis, the ataxic hemiparesis or some of the brainstem syndromes. And then the posterior circulation isolated visual cut for example. If you append that with an I, it means that you did imaging and there was infarction in that territory. If you append it with an S, it means it was for the syndrome prior to imaging or if the imaging was indeterminate.

By far, the most complex but reliable and valuable from a research context is the Causative Classification of Stroke, the CCS, which you can see here with the reference published in neurology but also access online. And this gives a very precise, as precise as you want it to be classification. So the first five groups look very similar to TOAST except that the cardioembolism also has aortic embolism mixed together because it's embolism from a proximal source.

If you want to break that down further, you can get into eight subtypes where the undetermined has unknown cryptogenic, unknown other cryptogenic so non-embolism cryptogenic, unclassified or incomplete evaluation. And then if you want to get even fancier, you can get to 16 subtypes where it's evident, probable or possible as a modifier for each of these. This turns out to be extremely important in genetic studies where you really want to classify the phenotypes as precisely as possible. And I would say that at some point in the future when we all live in one electronic health record world, we may be able

to do automated classification of stroke which I think would be a tremendous boon to our understanding of stroke.

So we talked about the sort of classification of cryptogenic stroke and if you think about the classification scheme, the required workup is actually not specified for the TOAST scale. It was really just the investigator's opinion. Whereas, some of the other imaging based classification schemes are quiet specific about the type of evaluation that needs to be performed and you can see that at minimum, brain imaging and electrocardiogram and echocardiogram and some from of vascular imaging is sort of the minimum workup needed to really understand what might be driving the stroke subtype and cardiac monitoring for some period of time is likely to play an important role here.

So there are, as we said, sort of the four basic stroke types, five really but I'm not going to spend too much time on the rare causes. And to some extent, it is a little bit like Jeopardy or Wheel of Fortune. You know, we're kind of doing test, trying to put the pieces together and get more and more confident that there's only one answer to, you know, to the word puzzle.

So here's an example of a case that I think is troubling. This patient has known carotid artery stenosis but in the imaging on the right, you see what we would normally call a thalamic lacune. So this patient has a lacune on the same side as carotid artery narrowing. We think it's in the thalamus but maybe it's in the internal capsule adjacent to the thalamus just like the one that's identified as letter B which is an old infarct. So is this a symptomatic carotid and this is large artery athero or is this is penetrating artery lacune similar to this previous lacune in a patient for whom this carotid is not symptomatic? This is difficult and experts will disagree.

So this could end up being classified as lacunar if you believe is it's in the thalamus, as large artery if you believe it's in the anterior circulation or as cryptogenic because we really don't know which of these possible ideologies was the cause.

Similarly, is stroke in a young patient with a PFO always cryptogenic or is it always cardioembolic or is it paradoxical as we say, embolism? Here's a rare instants of a patient with a trend thoracic ultrasound showing a clot straddling across the PFO with the PFO indicated by one arrow in the edge of the clot now in the left atrium, the LA? You'll never see this in your whole career that's why if you see this, you can publish it. We don't really know. We do know in multiple clinical trials that closing a PFO after stroke did not reduce the risk of recurrent stroke compared to aspirin or Coumadin.

So I would say PFO is still at the moment a culprit but a prisoner, someone you arrest on circumstantial evidence and you don't have enough evidence to keep him in jail. You got to let him go until you're share they're the culprit.

So the two approaches to thinking about stroke care are round up the usual suspects and 90, 80 percent of the time, that's going to give you the answer. And then for a small number of cases, you got to call in the crime scene investigators do a whole bunch of more test.

And so where do we live between these two approaches? So it's a lot of information that we could potentially be gathering from patients. We could be doing expensive and extensive and invasive testing in everybody. You know, is that really (warranted)?

So the guideline for secondary prevention make it very clear that anticoagulation is recommended for patients with high risk cardioembolic sources. Young patients with cryptogenic TIA or stroke with a PFO should be evaluated further for lower extremity or pelvic venous thrombosis which would be an indication for anticoagulation, not the PFO, the venous thrombosis. And for patients with PFO at the moment, there's no evidence to support closure or anticoagulation. So antiplatelet therapy is the mainstay of treatment in the current guidelines.

So what are the detection and monitoring strategies that should be used in patients with cryptogenic stroke where the pattern of the stroke on imaging suggests embolism but there is no obvious abnormality on the echocardiogram

to explain this? So what can we do? Well, the first thing we do is an ECG, a simple EKG on arrival that can tell us whether there is a presence of any overt structural heart disease such as left atrial enlargement, left ventricular hypertrophy or prior coronary disease leading to ST changes or Q waves.

The yield of echocardiograms in those patients is much higher than it is in patients with a normal cardiogram. Telemetry is an important part of the hospital admission and should be done in all stroke patients where there is a question of cryptogenic embolism and in those patients on occasion. I was just on service for two weeks. We admitted about, I don't know, 50 or 60 patients during that period of time who had strokes and several of them went into atrial fibrillation with rapid ventricular response while we were – while they were in the hospital in the first few days, thereby, likely revealing the cause of their stroke.

I will raise this question a little bit later but I'll just preview it now. You know, the stroke could -- has been due AFib or the stroke could actually cause the AFib. So we have to always be thoughtful about that.

Holter monitoring, we used to do it in the hospital all the time. I think there has been some recent changes in reimbursement such that it's not necessarily paid for anymore in the hospital so we do much less of it now. And what we have shifted to relying on is ambulatory monitoring for up to 30 days based on some recent studies that suggested high rates of atrial fibrillation detected in those patients.

And then for patients with a pacemaker, you have an automatic. If it's a recent pacemaker indwelling cardiac monitor or if not, there is the opportunity now to implant very small minimally invasive cardiac monitors that can allow for prolonged rhythm monitoring.

So about 10 percent of patients with acute ischemic stroke who are hospitalized will have AFib detected during the admission on monitoring as I said. And in patients who have an indication for a pacemaker, interrogation of the device found about 30 percent incidents of occult atrial fibrillation during

the following year but these are patients with abnormal hearts to begin with because they had pacemakers.

A similar rate of occult atrial fibrillation has been reported among high risk non-stroke patients with implantable rhythm devices. So AFib exist in a lot of people who have implantable rhythm devices and during pacemaker interrogation in stroke free population. If you find it, there is an increased risk of stroke.

But what about detecting it after ischemic stroke or TIA? So this is a recent meta-analysis looking at 31 studies that looked at the proportion of new AFib diagnosed using EKG monitoring for more than 12 hours in patients with a recent stroke or TIA. The longer you monitor, the more you saw atrial fibrillation as they continue as variable or when you look at less than three days versus seven days versus three months, then you can see it goes from five to 15 to 30 percent.

So, 30 percent of 30 percent is about 10 percent of patients. So 10 percent of all strokes could potentially have a cryptogenic embolism due to atrial fibrillation. And if you look at the odds of detecting AFib in the three randomized controlled trials that were relatively similar with a seven-fold increased odds of detecting AFib if you did prolonged monitoring.

Now, a big part of that data was the CRYSTAL AF study that looked at the outcome of six months but I'm showing you here the outcome of 36 months which is the duration of the battery in the current devices. And that arm was 30 percent detection over 36 months compared to 30 percent where you took the patients who had the implantable monitor and pretended that it was actually an external monitor and showing you what the rates of expected detection would be.

If you look at the predictors of who has AFib in this cryptogenic population, you can see that every 10 years of increased age increased the likelihood of finding AFib by almost two-fold. And then looking at the duration of the

interval between the P wave and the QRS complex was a sign of dysfunction of the AV node and associated with an increased risk.

So at this point now, I'd like to kind of turn things over to Dr. Schmidt who is going to talk to you a little bit about the relevance of what we've just talked about, where we need to go in terms of thinking about what we capture in the PMT and some additional changes that are forthcoming. So at this point, let me turn it over to Eric and I'm going to pass control of the mouse to Eric and, I think, Eric do you have it?

I think your of mute, Eric.

Eric Schmidt: OK, thanks, Lee. Great. I got it. So you can hear me OK I hope.

Lee Schwamm: Yes.

Eric Schmidt: All right, fantastic. So, I think I'll present just a few slides on new scientific statements, recommendations in stroke and cardiovascular medicine and the relevance of the PMT and then we'll get to the PMT and new data elements in the PMT for – about cryptogenic stroke as well as some changes to tPA contraindications and warnings and a new stat in reporting measure. So, some exciting changes and I'll just go ahead and move on to address contraindications and warnings to tPA.

So some of you may have had the opportunity to be on a webinar about three weeks ago where we went over this in a lot of detail. But now 20 years after FDA approval of tPA in 1996, you know, we have both accumulated new evidence on how well tPA works in certain subgroups as well as a new statement on the rationale for the inclusions and the exclusions for tPA. And finally, a change to the FDA label as well which has also reorganized some of the contraindications and warnings trimming, some of them and citing accumulating evidence for safety and effectiveness and certain important patient subgroups. So I'll just review that briefly.

On the slide here you see the 2013 American Heart Association guidelines that include both exclusions and relative exclusions to tPA and it's these guidelines that are the basis for the contraindications and warnings section in the PMT.

And then just fairly recently in December 2015, AHA commissioned a group to produce a scientific statement on the rationale for the different inclusion and exclusion criteria. They reviewed all of the contraindications and warnings in the FDA label as well as several additional clinical scenarios that come up less commonly but are still part of, you know, kind of yearly practice in a large stroke referral center to address what evidence there was on safety, effectiveness of tPA in certain subgroups and also the rationale for some of the warnings and contraindications, like prior warnings around treatment of severe stroke or patients with advanced age.

Both Lee and I were participants in generating this statement and there were a couple of major things that came out of that statement including new recommendations with level one evidence or level 1A level evidence, meaning data from randomized controlled trials that, in contrast to prior years, have now accumulated, I think, sufficiently such that our evidence review show that tPA can be considered effective now really regardless of age, accepting a lack of (data) in the pediatric population.

Subgroup analysis of the individual tPA trials like the NINDS trial, the ECASS III trial and the subgroups treated within three hours and IST-3 trial, as well as a pool of meta-analysis of individual patient level data from all of the tPA trials so including those as well as ECASS II and (inaudible) and others has shown that there really is a tPA effect even in patients with advanced age.

Now of course, older patients, you know, generally have worse prognosis from stroke and that remains true. However, at each age strata where you look at the age, you find that the tPA treated patients do better than placebo treated patients. And for example, at the last International Stroke Conference, we took a look at the outcomes in patients who are 90 years old and older who

are treated with tPA and entered in to get with the guidelines. We found more than 2500 such patients. So uncommon overall, but not exceedingly rare that these patients would be treated.

Patients over 90 were slightly more likely to have warnings and contraindications to tPA. But the treated patients had a similar risk of intracranial hemorrhage, patients in their 70s and 80s. And the data from the trials indicates that they do better over all with tPA than when given placebo, again, assuming there are another contraindications or exclusions present.

So the best data we have now suggest that although patients in their 80s and 90s over all have a worst prognosis, including both the tPA and placebo treated groups that the patients treated with tPA will have better outcomes than patients not treated with tPA.

The other area were subgroup analysis of the patients in the trial is showing that their preserved effectiveness is in patients with severe stroke symptoms. So in the past, there were warnings relative to the exclusions for severe stroke which maybe define as stroke skill score of 25 or higher.

However, breaking down those patients in the tPA trials shows again that, although, the prognosis is worst for patients with high stroke severity compare to patients with milder stroke over all, that the tPA treated patient, nonetheless, have a better chance of a good outcome even though the odds may be (stuck) against them than patients not treated with tPA.

So, in the news scientific statement from December 2015, treatment in both patients with advanced age as well as patients with severe stroke is now recommended with level 1A evidence. And that has some implications for the PMT as you'll see later on and that we've removed those two factors, old age and severe stroke, are no longer sufficient by themselves to be a reason for non-treatment and to move a patient out of the denominator for the (arrive) by two or by three measure.

And then, I'll let you read the statement yourself for all the other good information that's in there. There are lot of other clinical scenarios, for example, what you do at extracranial or intracranial arterial dissection, what about patients that have had recent lumbar puncture or recent major surgery and so fort. And there are great summaries of the evidence and there are recommendations for where the treatment may be considered or might be considered reasonable but with lower grades of evidence because there aren't data from randomized controlled trials.

But, still, very useful advice where scenarios were clinical judgments, you know, might be needed to determine whether treatment should be provided or not, but also, where reasonable clinician might document in the charts that, you know, tPA was considered but not given because of this recent surgery and so fort.

And so, here are the exclusion criteria and relative exclusion criteria that are in the 2013 AHA guidelines for management of acute ischemic stroke. And these are the guideline recommendations that the PMT warnings and contraindications are based on.

And so, one question we get sometimes is, you know, what are warnings and contraindications based on? Are they based on the FDA label? Are they based on the AHA guidelines? And our policy is that the reasons for non-treatment with tPA that would take you out of the (arrive) by two, three by three measure or based on the AHA guidelines. That's our primary source of the evidence.

Moving on a little bit to talking about cholesterol. As you may be aware, there were 2013 guidelines from the American Oncology and Cardiology and American Heart Association, all treatment of cholesterol to reduce cardiovascular risk including both risk for myocardial infarction, stroke.

These guidelines generated a lot of press and a lot of interest because they represented a philosophical switch from an LDL targeted approach to an approach to treatment of cardiovascular disease that was based more on

predicted risk of cardiovascular events rather than achieving a specific LDL target emphasizing that patients that were at high risk according to the cohort equations should be treated with Statin, with intensive lipid- lowering effects and to respond to changing treatments patterns as the results of those guidelines. And because they are risk-based, a patient that has had an event like TIA or stroke related to atherosclerosis would pretty much, you know, always fall into the category of requiring intensive Statin treatment regardless of LDL level.

We are now implementing a new measure. It's a reporting measure only, so not related towards Statin and the measure of Statin prescribed discharged. And in contract to prior Statin measures, this new reporting measure includes removal of two exclusion criteria, the first being removal of no document prior cholesterol reducing therapy and removal of LDL less than 100 and allows you to look at the 12 portion of your ischemic stroke patients that are going to be treated with Statin.

Of course, they documented reason for not prescribing a Statin at discharge would continue to be an exclusion for this measure population. So that could include allergy to Statin and tolerance to Statin or a non-atherosclerotic cause of stroke.

Lee Schwamm: Right. So (Eric, just to clarify for folks and necessary, the first part of the webinar now where we're talking about the changes for the tool that you're going to be seeing in response to the background we've just been presenting. So before you were – if the person had no documented prior cholesterol treatment or their LDL was already less than 100, they used to be out of the measure. Now, it's just basically asking, did you give him a Statin discharge or did you document why a Statin is not appropriate in this patient? The other formulaic approaches are no longer relevant because a Statin – an LDL of 95 still is an indication for more aggressive lipid-lowering therapy in this population.

Eric Schmidt: Absolutely, thanks.

OK. So, we'll move on to patient management tool updates. So we're moving to part of the webinar where we'll show the implications for this new data, guidelines and approaches on the PMT. And we'll start with stroke ideology. Did you want to go through this, Lee, or?

Lee Schwamm: Well, why don't we talk about it together, actually?

Eric Schmidt: Yes.

Lee Schwamm: So this is one of the big challenges that we held of for many years on putting this into the PMT because we were uncertain about how successful (sites) would be at trying to abstract this information. And we finally came to the conclusion recently that this is something we need to teach all of our sites how to do a better job documenting.

When we first started, 80 percent of the charts or 70 percent just had CVA. That was the only diagnosis. And over time, we were able to teach sites that CVA is not a specific diagnosis and that with the presence of imaging, they should really be classifying this as ischemic or hemorrhagic strokes. And I'm happy to say that the rate of CVA and 436 of the ICD-9 code is now vanishingly small.

So by the same token, we think it's really important for the care of the patient that people put their nickel down as to what they think the cause of the stroke was because that should dictate and be linked to the treatment they prescribed at discharge.

So if you think it's a lacune, you should not put that patient on anticoagulation. We've never really had the ability to link diagnosis with the treatment decisions before. So that's going to be the effort here.

And so, the first item here is really if you pick the ischemic stroke as the final clinical diagnosis, if – the question is, if there is stroke related diagnosis, so if you said, was the stroke ideology documented in the patient's medical record? If you say yes, then you're asked to select one of these check boxes as to what

was the impression of the clinical team. If there is no clear ideology documented, you'll just say the ischemic stroke start aspirin, then you can't check that box yes. You have to say no.

And if the radiology report says, you know, lacunar infarction and the left basal ganglia, but the doctor's notes don't reflect lacunar infarct, small vessel inclusion, you know, something to that affects and the coding instructions have those synonyms, then you can't check it. But you could check of large artery athero, cardioembolism, small vessel occlusion, stroke of other determined ideology. That's rare strokes or cryptogenic. And here, it would be stroke of undetermined ideology.

Now, if you think you're not sure and you think it could be either or say from all vessel or large artery, you would check those two boxes. You wouldn't check cryptogenic because here, we have restricted cryptogenic really to I have no idea. But if you thought it was one of these other two, you will just check two of them and that would be your way of saying, it's one of this, but I'm not sure versus cryptogenic would be, I really don't know.

And, I think, Eric, we have a slide on the next slide that shows the rates of that already.

Eric Schmidt: Is that the case?

Lee Schwamm: Oh, sorry. No, this is the, what tests were done. Yes, so let's go to this for a second. So we can tell, we started making this available as an overlay to some of you in the end of 2015. And these are all the cases that have been entered so far. And about 70 percent of all cases in 2015 and 2016 didn't have any chance to answer this question or didn't answer it. But among the 2500 or so cases that were entered, we see 23 percent were large artery, 34 cardio embolism, 21 small vessel, six percent other and 16 percent cryptogenic.

And so, it'll be interesting to see as we go forward whether those percentages start to change and level off closer to the 20 to 30 percent that's been seen these larger studies or whether Get With The Guidelines hospitals do a more

thorough workup. And therefore, I have lower rates of cryptogenic stroke because more workup is being done.

So based on that, if you want to go back one slide, Eric, we can talk a little bit about our efforts to capture the work of that's been done. And you want to talk through that, Eric?

Eric Schmidt: Absolutely, yes. So maybe a few questions for you Lee so we can talk it through.

Lee Schwamm: Yes.

Eric Schmidt: You know, so if you see documented in your record, you know, something like, you know, 50 – the clinician rights, moderate carotid stenosis and nature of, you know. But probably, the cause of stroke was atrial fibrillation. How would you fill out the PMT in that case? So, I guess, would you defer to what the clinician thinks is the most likely cause even if there are alternate causes?

Lee Schwamm: I think our job here is – and the job of the abstractors is not to outthink the clinician, but is to actually capture what the clinician – if the clinician said, "I believe, this is the cause of the stroke," then that's what should be listed as the cause. If the clinician says, difficult to determine whether this is due fibrillation or the carotid, so I'm going to recommend Coumadin plus endarterectomy, I would clearly put both of them down.

Where I think it will be a little tricky is if somebody writes embolism, likely due to EFib but need to rule out, you know, carotid disease or small vessel stroke and that's in the admit note, that doesn't matter because that's before the workup. But if in the summary, it says, likely due to fibrillation but can't exclude carotid disease, I would probably mark that as both of those being selective. I would probably put both check marks on both of those. And I think this is a learning process. So we're going to get a lot of feedback from those of you in the field.

And I would encourage you. Maybe, Jeanne, you can make a suggestion for how people can feedback to us the challenges they're having as they start abstracting this which they're going to be doing on every single patient now because every patient has a diagnosis of stroke is going to need this to be address.

So let's figure out how to make this the most effective and constructive that we can. And also, make sure the coding instructions are designed to answer the questions that are likely to come from the field. Is that helpful, Eric?

Eric Schmidt: Yes. I think all of these will be easy for abstractors if clinicians are using these terms in the chart. I mean, do you use these terms in your own progress notes, Lee?

Lee Schwamm: I probably say cardioembolism all the time and small vessel or lacunar infarction when I believe it's the case. For dissection or vasculitis, I probably wouldn't say stroke of other determined ideology. I would say the specific ideology I was concerned about. And I cannot use the word cryptogenic. I tend to say cardioembolism of, you know, uncertain source or I would say, you know, unable to determine if this is due to carotid atherosclerosis or atrial fibrillation.

Eric Schmidt: Yes. I try to use these terms in my note. I use the cryptogenic term. I guess, another term that you describe that a subset of cryptogenic stroke is what's been called, ESUS. I don't know if you use that term, embolic stroke of undetermined source. It's in the title of some of the randomized controlled trials that are, you know, looking at normal or anticoagulant versus antiplatelet therapy in this population. Do you want to describe that term and do you use that term, ESUS?

Lee Schwamm: I do actually. And so, I think it's important to make a distinction of what is the appearance of the stroke on imaging. And so, strokes that are small in the center of the brain like we showed you before are sort of, I think, thought of in a slightly different way as cryptogenic from these strokes that are out in the periphery of the brain, near the cortex and are clearly from a clot that came

from somewhere and got stuck there. And those could come from an artery that's more proximal like the middle cerebral and get stuck out indistinctly. They could come from the carotid, they could come from the – or they could come from the heart, they could come from the veins paradoxically through the heart.

So I think most people when they heard cryptogenic are thinking about embolic appearing stroke of uncertain source. I would say, though, that the small vessel stroke in the territory of a symptomatic – of a moderate or severe carotid stenosis is also a challenging one because it's putting you between antiplatelet therapy and surgery. The reason why this embolic stroke of uncertain source got so much attention is trying to decide between antiplatelet with therapy and anticoagulation.

But I think we'd all be better off if in every discharge summary, we got our providers just to start classifying patients according to these five categories and it may be, that down the road, we have a tool that we recommend that people really create and try to use as a way to summarize the admission. And just like we have a time tracker and best practices for the use of tPA for timely care, maybe it's time for us to think about an admission tracker that help to structure the data elements that are the hardest for abstractors to find reliably and embed those into the electronic or paper chart prompt.

I know there's a lot to work going on right now to help with – try to create something like this in Epic that would make it again easy for the doc to doc or the nurse practitioners to document according to these terms. But I think that's an area of fruitful investigation.

Eric Schmidt: Thanks, Lee. Should we move on to the next slide on the diagnostic testing?

Lee Schwamm: Yes. I think that's a great idea.

Eric Schmidt: OK. So I'll get started on this one. So these are the discharged tab and the diagnostic testing is really important obviously because it's based on this test that you can assign at the cause of stroke and classify the (source) in the

TOAST criteria which is so important for determining what the right secondary prevention is.

So we'll just walk briefly through the different options here. Cardiac ultra – so there's cardiac ultrasound, there's carotid imaging to identify larger artery atherosclerosis or the carotid revascularization was performed which applies the carotid source of the stroke, extend surface, cardiac rhythm of monitoring and implantable rhythm monitoring, hypercoagulability testing, intracranial vascular imaging and short-term cardiac rhythm monitoring.

And as you can see, for each these diagnostic testing options, there are three sub-options for either perform during the submission. Plan post-discharge because we understand that sometimes patients may be referred, you know, for example for longer term rhythm monitoring with the plan and place at time of discharge but where they thought that it cannot be completed during the admission.

And then finally, a box for report. As I said, you know, it's really important to do this kind of test to figure out what the cause of stroke is. We're not implying that all of these tests need to be done in every patients but rather this allows you to record, I think, all of the common diagnostic investigations that would be ordered as part of the clinical workup.

And this kind of information is important too, you know, for us to understand, you know, patterns of care, what types of hospitals or regions, like for example have loss access to some of this testing. It also allows us to put the final diagnosis or stroke ideology and context because one of the challenges was determining the ideology of stroke is that (inaudible), how hard you look for the, you know what, I guess, it's the known and unknowns or unknown unknowns. I'm not sure which. I think it's for the known and unknown.

So, Lee, do you want to add any comments on this slide?

Lee Schwamm: Yes. I want to make that really clear to folks that we're not suggesting that every patient needs everyone of this. So this is not an example of where you

want to be feeding this forward back to your docs. It's really trying to understand what kind of workup is being done. We don't really have a good way to understand and link it to the clinical information.

So this will allow us if we're successful, to start giving you feedback about the appropriateness of some of the evaluations and interventions. So if you had a patient who came with an ischemic stroke that you thought was due to large artery athero, you did a carotid imaging but there was no plan to carotid revascularization, that's the kind of chart you may want to look at again and say, "Hey, maybe there is a reason."

Now we haven't developed any measures yet for this but in the future, I can imagine the measure that says if larger artery athero was detected, was there a plan to do coronary revascularization? Or if the patient was diagnosed as cryptogenic stroke and you did short-term rhythm monitoring in the hospital, was there a plan for extended rhythm monitoring, you know, for example. Or, you know, if it's a young patient under the age of 45 with the ischemic stroke and a prior history of stroke, was hypercoagulability testing done?

Now, it might have done, you know, three months ago with their last stroke or it may never have been done. But I think we want to try to move beyond some of the simple adherence measures to start capturing some of the more nuance issues that are still level one recommendations but which we haven't been able to give you information and feedback on yet.

So this really reflects Get With The Guidelines kind of phase two of really thinking about appropriateness and the plans that might be happening after discharge.

Eric Schmidt: One clarification on the data element, so the difference between the short-term cardiac rhythm monitoring and the extended surface or implantable cardiac rhythm monitoring is based on but there's more or less than 72 hours of recording so the 24 for Holter would be short-term cardiac rhythm monitoring, whereas 30 day of that monitor for example would be extended surface cardiac rhythm monitoring.

Lee Schwamm: Right. And an extended implantable monitoring could be a pacemaker, an AICD, an implanted monitor solely for the purposes of monitoring for cardiac arrhythmia. It might be that the patient has syncope, you know, as part of the presentation and you are concerned about more than just fibrillation. But the time frame of monitoring and the nature of the monitor here are kind of joins together because, in general, we don't do extended surface rhythm monitoring for continuous periods of time beyond this 14 to 30 day adventures. If you're going to do a continuous monitoring for more than 30 days, it really is not feasible to do that continuously with external surface monitoring at least for the technology we have currently.

Eric Schmidt: Very good, Lee. Should I move on?

Lee Schwamm: I think in the interest of time, we have about 5 minutes left. So why don't we try to move through the remaining slides?

Eric Schmidt: Absolutely. So we're almost done. So now we're looking at documented inclusions or (routes) of exclusion. We're not initiating I.V. tPA and the main change here is related to the new recommendations that tPA should be given to patients with advanced age and severe stroke. So those reasons have moved out of relative exclusion criteria to other reason, hospital related or other factors that you can still document it there but it will be no longer take the patient out of the denominator for the (arrive) by two to three by three hours.

Of course we understand that not every older patient will be eligible for treatment. However, ineligibility should no longer be based on chronological age but rather other comorbidities associate with aging.

So we understand that as you get older, there is more chance for, in particular, life expectancy less than one year or severe comorbid illness, comorbid dementia, for example, would be one example of a severe comorbid illness that if documents would be a sufficient reason not to get tPA and to be out of the (arrive) by two three by three measure.

The difference from the path that it would longer simply be good enough to check advanced age, you know, because the patient is 95. But if a clinician documented, for example, no tPA because age 95, that would be insufficient to move out of the denominator. But if the clinician documented no tPA because age 95 and severe dementia, the patient would come out of the denominator by checking the severe comorbid illness box.

Lee Schwamm: Right. And I guess two things I would say, one is, there is nothing shameful about having an adherence of less than 100 percent. There are some patients who aren't appropriate for treatment and it's not always possible the patient who presents and you don't know it's a stroke and you think it's a UTI because they're in their 90s and you find out afterwards it was small stroke.

The other things I would say is that exclusion criteria, we use (call) contraindications and warnings, that haven't really changed very much. We've just realigned them with the latest guidelines because we are Get With The Guidelines not Get With The PMT. So when the guidelines get updated, it's our job to try to update this as well.

And someone had asked a question in the question box about whether use of novel oral anticoagulants would be a reason for (not) treatment and you can see here under item C5 acute bleeding diathesis and one of those is use of a NOAC. So current use of a NOAC is a concern.

Eric Schmidt: And so the previous contraindications and warnings prior to April 1 coming up will be moved to the historic tab.

Lee Schwamm: Great. So, Erick, maybe we can just jump over to the question and answer tab and perhaps we can just grab maybe one or two of the most recent questions and try to answer them before we sign off.

And here is a question, 135, what is your recommendation for anticoagulation in the presence of PPMA ICD with AFib flutter?

The guideline recommendations are clear in that regard that in-patients with the AFib flutter, anticoagulation is indicated with the CHA2DS2-VASc score of two of higher. And so, a pacemaker in ICD don't prevent the stroke risk associated with AFib nor does the (inaudible) in most patients. And so, the important step there is to prepare the risk of stroke with the CHA2DS2-VASc, the risk of bleeding with the HAS-BLED or a similar risk score to determine whether anticoagulation is appropriate.

And, Eric, here is a question for you. Do the M.D. still have to link the reason for no tPA to advanced age or stroke severity?

Eric Schmidt: Those are no longer sufficient reasons to come out of the denominator for the (arrive) by two by three measure so there are remained tick boxes for those but they're under hospital or system related factors now. Yes, advanced age, you know, it usually is as a surrogate, you know, for other comorbidities that may prevent the use of tPA like dementia or comorbid illness, high risk of –.

Lee Schwamm: I think the question, they were asking if all the treatment done is the age and the doc didn't say that age was the reason they didn't treat. Should they still check that box as the reason or is it only if they have a clear connection from the M.D. or the P.A. or N.T. as to why the treatment wasn't provided? Can they infer that or do they have to have it explicitly documented?

Eric Schmidt: Well, generally, we try to limit the amount of inference on (inaudible). It's almost kind of, by definition, takes you out of an inclusion criteria. So I believe that there were need to be documentation of a link between the advanced age and the rationale for non-treatment. Do you agree with that, Lee?

Lee Schwamm: Yes. I think that's the goal. Sometimes it's not documented, like delay in stroke diagnosis, someone's doesn't right whatever the delay which is why we didn't treat it such that you can see that the patient wasn't recognized to have a stroke till beyond when the time had relapsed. So I think we can try to clarify that in the questions – in the coding instructions.

Let's end with one for you, Eric. What – at baseline, what initial testing that you think should be performed on all patients presenting with the presumptive diagnoses of stroke or DIA.

Eric Schmidt: Well, I guess, in my practice, the answer is a little bit nuisance. The most common test that we order and we often order all of these tests in probably in most patients would be vascular imaging to exclude carotid stenosis which would be an indication for revascularization, a cardiac ultrasound and some sort of rhythm monitoring, you know, Holter monitor or prolonged rhythm monitoring to exclude cardioembolism. Of course, just you know baseline EKG as well in the initial screen. And of course we do cholesterol testing, you know, other blood work and the A1c.

There may be scenarios where the cause of the stroke can be inferred, you know, without necessary doing all those test. Perhaps, the most common would be a patient who comes, the EKG shows atrial fibrillation. Perhaps it's unknown. There's unknown history of atrial fibrillation. There are multiple embolic appearing strokes in both hemispheres. Meaning, it can't be just, you know, carotid stenosis on a single (tab).

The patient like that, we may end up just ordering vascular imaging and an EKG. Prolonged rhythm monitor is not needed because the EKG already shows AFib. Patient had an acute heart failure as known diagnose based that we not – might not order the cardiac ultrasound.

So that would be our general approach would be, you know, cardiac investigations and vascular imaging unless the cause of stroke and, you know, kind of evident and the rest can be excluded based on the pattern of infracts and documentation of a sufficient source. What do you think? What is your practice, Lee?

Lee Schwamm: I like that, Erick. I think I would say, at minimum brain imaging, vessel imaging and some evaluation of the heart ideally within echo but sometimes just an EKG could be enough. And I think sad so say that we hit the top of the hour and I think it's time to turn it back to Jeanne because the time is up.

Jeanne Rash: Thank you, Dr. Schwamm and Dr. Schmidt. I really appreciate your presentations today. There were several other questions unanswered and we'll try to compile this and provide responses for everyone. There were several questions regarding the slide. Just one let everyone know, the slide will be available for viewing when the webinar recording is posted to the heart.org Web site and also all Get With The Guidelines users will receiving release notes that outline all the changes reviewed today. And we are expecting a smooth software update on the 26.

If you have any questions regarding access to the program, please call the Get With The Guidelines help desk either by telephone or e-mail. Again, thank you all for your participation today. We had nearly 14,000 participants, so truly exceptional turnout today. And again thank you Dr. Schwamm and Dr. Schmidt for your presentations. This concludes our presentation for today.

Lee Schwamm: Thanks everyone. Bye.

Eric Schmidt: Thank you.

Operator: Thanks to all participants for joining us today. We hope you found this webcast presentation informative. This concludes the webcast and you may now disconnect. Have a good day.

END