**Operator:**

It is now my pleasure to turn today’s program over to Mary Paulsen, national senior program manager. The floor is yours.

 **Mary Paulsen:**

Thank you, Ginneen. Welcome to the American Heart Association and American Stroke Association’s Get With The Guidelines-Stroke National webinar. During toda’'s session, our panel will share detailed information about the advancements made in our Target: Stroke Phase II program. For our call today, we’re fortunate to have our presenters, Dr. Gregg Fonarow, Dr. Lee Schwamm, Dr. Jeffrey Saver, and Dr. Eric Smith. Dr. Fonarow serves as the Eliot Corday Professor of Cardiovascular Medicine and Science and co‑chief of Clinical Cardiology UCLA, Division of Cardiology. Dr. Lee Schwamm is professor of Neurology at Harvard Medical School and vice chairman of Neurology at the Massachusetts General Hospital where he’s the director of acute stroke services. Dr. Jeffrey Saver is professor and senior associate and vice chair of neurology at UCLA and director of the UCLA Comprehensive Stroke Center. And finally, Dr. Smith is associate professor of neurology in the Department of Clinical Neurosciences at the University of Calgary and a member of the Calgary Stroke Program.

Again, as a reminder, you may post your Q&As via the icon at the right of your screen and our panelists will take the opportunity to answer questions towards the end of the program. Thank you for your participation today. Dr. Fonarow, I hand off to you.

 **Gregg Fonarow, MD:**

Great, thank you so much for joining us today to discuss the important advances made with Target: Stroke and an update on where we stand with Target: Stroke Phase II. I think as all of you are aware, acute ischemic stroke reperfusion therapy is critical for improving outcomes for patients presenting with acute ischemic stroke and the benefits of ischemic stroke treatment with both intravenous tPA as well with endovascular therapy are highly time‑dependent. The shorter onset to treatment times are associated with really markedly better functional outcomes, lower complication rates of treatment and in some studies, lower mortality. So for really more than a decade, national and international guidelines have really recommended that treatment with intravenous tPA be administered as soon as possible and with the goal of a door-to-needle time within 60 minutes. Yet a number of studies had shown prior to Target: Stroke becoming available, that fewer than 1/3 of patients that were treated with intravenous tPA for their acute ischemic stroke, at least in the United States, were meeting this goal and that's a substantial opportunity to improve the quality of care being offered to patients with acute ischemic stroke. This review from Jeff Saver highlighted that in the typical acute ischemic stroke patient, really every minute counts, every minute until reperfusion in the brain there is a loss of 1.9 million neurons, 14 billion synapses, and 7.5 miles of myelinated fibers. So tremendous damage is being done with every minute of delay and again emphasizing how important time to treatment is, in particular that door‑to‑needle time which is under the control of hospital‑based systems of care for treating the acute ischemic stroke patient.

Now, randomized clinical trials have demonstrated that the effects of intravenous IV tPA are highly time‑dependent. So with every 15 minutes of treatment delay, we’re seeing loss of effect as far as achieving a good outcome of a modified rank and score of 0‑1. And there is nice data that was generated in real‑world patients from Get With The Guidelines: Stroke that again, onset to treatment time strongly related to clinical outcome and we nicely demonstrated this same thing holds with regards to door-to-needle time being a critical determinant of outcome for these patients, both functional outcomes as well as complications of tPA use. So there have been strong recommendations in the guidelines from the AHA and ASA with regards to establishing standard operating procedures, having standardized protocols to identify eligible patients with acute ischemic stroke for tPA expeditiously and targeting a treatment time of within 60 minutes of arrival to door time of administering IV tPA. And this guideline recommendation dating back to 2009 and even before then it's been reinforced in every guideline since.

Now with participation in Get With The Guidelines-Stroke during this time period of 2003‑2009, there had been really substantial improvements observed with regards to the percentage of eligible patients arriving within two hours and treated within three hours, arriving at three and a half hours treated within 4.5 hours. But interestingly, when we analyzed it this during this time period as far as the percentage of patients treated with door-to-needle times within 60 minutes, among those being treated with tPA we see really very little improvement year‑over‑year and a very substantial opportunity and this is part of the rationale behind why Target: Stroke Phase I was launched. So you can really see year‑over‑year here very little change overall in 2009, just 27.4 percent of patients with door‑to‑needle times within 60 minutes. And again, this is a framework of all of the national guidelines calling for this as a standard of care evidence of improved outcomes, it’s being part of the criteria for being a primary stroke center, and yet this tremendous unmet need and substantial opportunity to improve the timeliness of IV tPA administration.

So this was the rationale behind the launch of Target: Stroke in January 2010. A multifaceted initiative of the AHA to really in a national collaborative with a broad alliance of hospital, hospital teams, clinicians to work together to address this goal of improving the timeliness of tPA administration for acute ischemic stroke patients aiming for a door‑to‑needle time within 60 minutes and at least 50 percent of the patients treated with tPA. An expert group working together performed a literature review, the 10 key evidence‑based strategies were developed, a whole variety of clinical decisions and support tools that you are all familiar with were released. This slide shows the Target: Stroke initial Phase I 10 key best practice strategies that you’re familiar with and were part of the key emphasis of Target: Stroke Phase I. There were customized implementation tools, time trackers, as well as a variety of educational opportunities and all of these that can be customized and adapted each local hospital.

So what was the impact of Target: Stroke Phase I? We studied this. This was part of the JAMA 2014 publication that just shows how we drill down to the eligible population, the primary analysis population were those treated with IV tPA in the first three hours and then a secondary population looking at the 83,000 patients with onset times of within 4.5 hours, which at least in part of the time of Target: Stroke Phase I was a two way recommendation in the guidelines.

So did Target: Stroke Phase I have an impact on the timeliness of tPA administration, and this slide illustrates, rather than that slow very minuscule rise occurring in the percentage of patients with door‑to‑needle times within 60 minutes? You can see within that first quarter of initiation of Target: Stroke Phase I that there was this increase in door-to-needle times within 60 minutes and that continued acceleration. The P value for comparison of the two strokes actually had eight zeros followed by one, so highly statistically significant, and you can see by third quarter of 2013, that in fact, the goal for Target: Stroke Phase I of at least 50 percent of patients with door‑to‑needle time within 60 minutes was met. So due to the collective tremendous effort of participating hospitals and Get With The Guidelines-Stroke and Target: Stroke this goal was able to be achieved. We had estimated if the secular trends that we had seen before the initiation of Target: Stroke continued, it would have actually taken 12 years before getting to that 50 percent of patients treated. So truly bending the curve and the true impact on the timeliness of tPA treatment.

So just to look at this categorically. So the percentage of patients with door‑to‑needle times within 60 minutes increased from 29.6 percent immediately prior to the launch of Target: Stroke in quarter 4 of 2009 to 53.3 percent in quarter three of 2013. This was highly significant. That median door‑to‑needle times dropped from 74 minutes down to 59 minutes. This is an absolute difference at the national level among participating hospitals of 15 minute decline in this period of just 15 quarters. Remarkable improvement.

And if we look at the hospital level, prior to initiation of Target: Stroke only 15.6 percent of Get With The Guidelines-Stroke hospitals had door‑to‑needle times within 60 minutes of 50 percent of more of their treated patients, whereas in 2013 this had now been met, the benchmark for honor roll, by 46.7 percent of participating hospitals. Highly significant.

So when improving the timeliness, this is also had more patients actually become eligible so with more efficient reliable systems for identifying appropriate candidates, treating them in the time -- triaging them and treating them in a timely fashion. So we actually saw that actually tPA use among eligible patients arriving within two hours, treated within three increased from 64.7 percent to 85.2 percent. For 3.5 treated within 4.5 hours, this increased markedly from 22.5 percent to 63.9 percent. That's almost a threefold increase in patients being treated. And overall among all acute ischemic stroke patients, regardless of time of arrival or contraindications, total percentage increased 5.7 to 8.1. So really remarkable improvements in eligible patients being treated and at least in the way that we could surveil this, there was no evidence of unintended consequences of people becoming more focused on time rather than treating eligible patients, so avoiding treatment in those with less favorable door‑to‑needle times being anticipated. So a remarkable impact on the timeliness of treatment bit by having well performing systems actually more eligible patients were able to be treated with this beneficial therapy.

So what happened to clinical outcomes? And what we can see here is looking in the pre‑ and post-Target: Stroke phase that outcomes improve substantially. I'll draw your focus to a 1 percent absolute decrease in symptomatic intracranial hemorrhage when we treat patients earlier with tPA. This translates to greater safety that ultimately led to less in‑hospital mortality, about a 1 percent absolute decrease. More patients able to go home, ambulatory status being independent, and even after you adjust for any hospital patient characteristics and secular trends in that regard, we can see this holds up to rigorous statistical adjustment. We are also able to show that this was up and above any secular trends and improvement in outcome. We did not see comparable improvements and other types of strokes during this timeframe or in patients being hospitalized with ischemic stroke without being treated for tPA, again hoping to isolate that this was most likely a direct result of Target: Stroke rather than just reflecting overall secular trends and outcomes that would have occurred anyway during this time period. The national impact of Target: Stroke then we could estimate more than 18,000 patients with acute ischemic stroke as a result of Target: Stroke were now treated with tPA. Clinical outcomes close to 1,000 additional lives saved, quality of life close to 6,000 patients reducing their long‑term disability. So really remarkable collective impact by all of the hospitals and clinic teams working on Target: Stroke and having national level impact not just on quality of care, but meaningful clinical outcomes for stroke.

Now, some could speculate well maybe this wasn’t all just a result of Target: Stroke and that there were other efforts or other findings and a national evolution and international evolution that would have occurred anyways. But there is some interesting data from international registries, so this is from the 750 clinical centers greater than 40 countries, 45,000 patients treated with tPA during this time period of 2002‑2011. And at least, you know, to the last two years or a period where we were seeing remarkable improvements in reductions in door‑to‑needle time in Target: Stroke, but at least among these European countries you can see, if anything, door‑to‑needle times as far as median here were heading in the wrong direction. So it looks like what we are seeing with Target: Stroke was far more than just secular trends.

So what were the winning strategies that were helping to drive the improvement? We were really interested in this and this is the rationale behind the Target: Stroke Phase II survey that has been recently published to tell us of the participating states, what are the strategies that were uptake and implemented in the hospitals and then how did that relate to the door‑to‑needle times and ultimately clinical outcomes. So this was published in circulation, cardiovascular quality of care and outcomes, and I really urge you to read through this. I will give you just some of the highlights but there's a wealth of detail here regarding the uptake and use of the strategies as well as how that associates with door‑to‑needle time. So this shows the frequency of the hospital strategies used and you’ll see for actually the majority of the 10 best practice strategies, most hospitals were utilizing them highly. So this accounts for that overall 15 minute reduction in door‑to‑needle time seen with Target: Stroke Phase I. There were some strategies though where there were opportunities for greater use, so transporting patients by EMS directly into the CT or MRI scanners we can utilize pre‑mixing tPA administration of the tPA while the patient is still in the brain imaging suite. So we do see there is some opportunities for greater uptake for some of these strategies. So next we'll look at how the strategies were associated with door‑to‑needle times.

And this is a busy slide, but it shows for each of those strategies the time association, which order door‑to‑needle times after adjusting for patient in‑hospital characteristics. And so to really summarize here, you can look at each of the strategies and the magnitude or benefit but what we were able to demonstrate is essentially 16 of these strategies were associated with shorter door‑to‑needle times. So this reduction on average for each of these strategies is modest at 1.25 minutes could be saved with each strategy, but cumulatively what this represents is the potential to reduce door‑to‑needle times by as much as 20 minutes if all of the strategies were being applied at all hospitals. And so at the patient level, a reduction ‑‑ further reduction of 20 minutes in door‑to‑needle time would save potentially 36 million neurons, reducing the risk of mortality, symptomatic intracranial hemorrhage, and increase the chance of a functional independency. At the national level, a reduction in 20 minutes could bring the median door‑to‑needle times in Get With The Guidelines: Stroke participating hospital towards 30 minutes. So together collectively applying more of these best practice strategies could really have a substantial additional impact beyond what was achieved with Target: Stroke Phase I in driving what we’re hoping Target: Stroke Phase II.

So as you know, we launched in 2014 Target: Stroke Phase II, the national goal to achieve door‑to‑needle times within 60 minutes now for 75 percent of eligible patients and an additional goal of achieving door‑to‑needle times within 45 minutes for 50 percent of eligible patients. We updated the honor roll criteria to have the Honor Roll Elite and Honor Roll Elite Plus recognition for hospitals aligned with these goals as well as updated the Target: Stroke resources with the updated time tracker, additional tools, and two additional best practice strategies based on these survey results that we just told you about. So you can see there are now 12 best practice strategies. I want to emphasize the time or clock attached to the chart, clipboard or bed that is associated with shorter door‑to‑needle times as well as transfer directly to the CT/MRI scanner. So applying these additional strategies that were incompletely applied we see in the Phase II survey could have really substantial impact and we’d urge all participating hospitals to really re-look through this list of the 12 best practice strategies, see where you are with regards to utilization, whether there are opportunities to update your systems of care for patients with acute ischemic stroke to integrate these practices and further improve your time to treatment for the patient population.

So here you can see is where we scanned recently with regards to Target: Stroke Phase II. This was data presented at the ISC 2017. I would caution you, preliminary data has not yet been published so should not be reproduced or distributed. But what you can see plotted here, this is percentage of patients treated with IV tPA with door‑to‑needle times within 60 minutes and you can see, again with the launch of Target: Stroke Phase I, that marked slope change in 2010 and here we have the arrow highlighting when Target: Stroke Phase II initiated in the beginning of 2014 and we can see that steady progress and continued growth continuing since the launch of Target: Stroke Phase II. So rather than everybody resting on their laurels and just being happy at 50 percent of patients with door-to-needle times within 60 minutes collectively, we are seeing making progress toward that Target: Stroke Phase II goal of 75 percent. So you can see the estimated slopes here going from 1.2‑6.2 and 6.3.

Now on the other hand, we could say there was not further acceleration being observed here, so I would take this as an opportunity to apply the learnings from Target: Stroke Phase I, the additional learnings from Target: Stroke Phase II survey and really collectively work towards accelerating our progress towards the Target: Stroke Phase II goal. But you can see that 75 percent goal is within reach and should hopefully be getting there within a few more quarters, but we would love to accelerate that if at all possible.

This next slide shows the progress update towards door‑to‑needle times within 45 minutes looking at Target: Stroke both pre‑Target: Stroke, Target: Stroke Phase I, and then post-Target: Stroke Phase II. In contrast, where we see the marked slope change that occurs as we go from pre‑Target: Stroke to Target: Stroke Phase I with the launch of Target: Stroke Phase II, we do see some not just continued increase, but actually acceleration and increase in achieving door‑to‑needle times within 45 minutes. So here we’re getting close to 50 percent of patients having crossed at least 40 percent and if we look at the estimates, you can see that there is very little increase occurring pre‑Target: Stroke. Target: Stroke Phase I, the estimate was 3.5, but almost a doubling of that of 7.7 on the slope change estimate in Target: Stroke Phase II. So we’re really making some excellent progress here and would like to see, if possible, even further acceleration and percentage of patients with door‑to‑needle times within 45 minutes. And we’re starting to see some hospitals actually reach, in a proportion of their patients, door-to-needle times within 30 minutes. So really impressive progress in that regards. But more to be done to get to our Target: Stroke Phase II goal of 50 percent of patients having door-to-needle times within 45 minutes.

This now looks at the hospital level where you can see that with regards to Target: Stroke Phase I versus Phase II, the percentage of hospitals with door‑to‑needle times within 60 minutes or 50 percent or more of patients going from 46.2 to 71.5 percent. So this is a 25 percent absolute increase with 75 percent of patients. This was only being achieved in 8.9 percent of hospitals in Target: Stroke Phase I. This is now up to 21.7 percent. And with regards to door‑to‑needle times within 45 minutes in at least 50 percent of patients, only 4.6 percent of hospitals now up to 16.8 percent. And those with door‑to‑needle times, that Elite Plus goal of within 60 minutes and 75 percent of patients and 45 minutes within 50 percent of patients, this was only 3.6 percent of hospitals during Target: Stroke Phase I, but now 14.6 percent of hospitals have met that goal. So we’re really seeing remarkable improvements at the hospital level, but further work to be done and we would, of course, love for 100 percent of participating hospitals to meet that Elite Plus Target: Stroke Honor Roll status.

So in conclusion, the findings from Target: Stroke really compellingly support the favorable impact of applying the performance improvement techniques, identifying best practices, clinical decision support, guideline driven care improvement tools, educational outreach, collaborative support, performance profiling, feedback and recognition. The tremendous impact that the collective work that all of those involved with Target: Stroke have done to really drive this remarkable improvement in care. So programs such as Target: Stroke that can markedly improve care, but importantly, this translates to meaningful improvements in clinical outcomes for patients with acute ischemic stroke and in every setting these patients are cared for should be aggressively applied and we should really be doubling and tripling down on these efforts, given the tremendous benefits in improving quality of care and outcomes that can be achieved. As I’ve highlighted for you in the preliminary data, significant progress is being made towards the Target: Stroke Phase II goals. Reaching those goals on the national level is within reach. I would highly urge all of you to double and triple down on your efforts to help us reach these goals as soon as possible. So, ongoing quality improvement efforts and really additional efforts are going to be required to meet these national goals of greater or equal to 75 percent of patients with door‑to‑needle times within 60 minutes and 50 percent or more of patients having door‑to‑needle times within 45 minutes.

So with that, let me thank you for your attention. I want to really acknowledge the tremendous work that all of you have done, the site champions, the hospital teams, the data abstractors in participating in Target: Stroke and Get With The Guidelines: Stroke. Without your tremendous collective efforts none of this would have been possible. Also want to acknowledge all of the Target: Stroke and Get With The Guidelines-Stroke national staff, field staff, as well as volunteers to help create this program and make it so successful. Of course, the unwavering support of the AHA and American Stroke Association towards stroke quality of care, systems of care and outcomes and our analytics center, DCRI.

So with that, let me again, thank you for your attention and let me turn it over to Lee for comments as well as moderating the Q&A. Thanks again.

 **Lee Schwamm, MD:**

Great. Thank you, Gregg, so much for that terrific presentation and summary of sort of where we’ve been. Let me just also confirm that Dr. Saver has been able to join us. Jeff, are you on the line.

 **Jeffrey Saver, MD:**

I’m here. Hi, everyone.

 **Lee Schwamm, MD:**

Terrific. And I think, unfortunately, Dr. Smith is unable to join us on the webinar today so it will be myself, Dr. Saver and Dr. Fonarow. Now, I’d like to open the Q&A panel to folks on the webinar. We've had a bunch of questions come in. I’ll be reading them out and trying to get your answers of them. So let me start with one of those. Was there a comparison done on door‑to‑needle times for hospitals that were not using Get With The Guidelines during the same timeframe? So this is a question, Gregg, of do we have a control population that we can compare to that were not using with Get With The Guidelines? Why don’t you take that one, Gregg.

 **Gregg Fonarow, MD:**

Yes, so it's a real great question, and unfortunately you could say for those hospitals that are not part of Get With The Guidelines-Stroke, there really has not been any systematic way of tracking door‑to‑needle times or any publicly available data set to where they could be compared. So that's why we were interested in the international registry to get some data in that contemporary timeframe. So that would be of interest, but we at least have not had any access to that. I will say that when we did look at some analyses within Get With The Guidelines-Stroke with regards to kind of the type of hospitals having the largest improvements, we really found the improvements over time were kind of collectively across the board. So as hospitals that even if they’re not primary stroke centers that were participating, we saw really substantial improvements. Those that started off with relatively high performance saw further improvements, those with relatively low performance at baseline also significant improvement of hospitals large and small, teaching and non‑teaching, rural and urban, so there was really a collective improvement. But unfortunately we don't have a direct U.S. based analysis of door‑to‑needle times in the same timeframe in non-participating hospitals. Actually estimate close to about 70 percent of patients getting IV tPA in the U.S. for acute ischemic stroke is in one or more of the Get With The Guidelines-Stroke hospital, so it is a vast majority of hospitals that are participating in the U.S.

 **Lee Schwamm, MD:**

Great. So let me ask a question to Jeff. Jeff, you have published a lot on the issue of the shape of the time benefit curve for tPA and we know a lot about what it looks like from 60 or 90 minutes after onset out to four and a half, five, six hours. What do you think the shape of the curve look like in these earlier and earlier time points so that if we are consistently treating within say 30 or 45 minutes and patients are arriving right away at the hospital, do you think that the benefit of tPA will be even greater during that early time point? What are your thoughts?

 **Jeffrey Saver, MD:**

I think there is reason to hope that the benefit increases when you get into the Golden Hour in the first 60 minutes after onset, both because of, as usual, there is more brain to save, but also because the clots are less well organized and may respond to tPA more frequently if tPA arrives earlier. As you said, Lee, the treatment within the first 60 minutes of onset was somewhat incognito for us in the past. There were no patients who got tPA in the pivotal NIMMS trial in that time window, and when we looked at the Get With The Guidelines experience through 2016, only about 1.2 percent of patients had been treated within the first 60 minutes of onset to date. But we’re beginning to see more and more patients treated as Target: Stroke takes hold even after hospital arrival and the new mechanism of giving tPA in mobile stroke units is allowing patients in those special facilities to be treated in that timeframe. And we did see in the Get With The Guidelines analysis that for the most sensitive outcomes, the discharge Rankin 0-1 that we have in the Get With The Guidelines data set, there was an accelerated effect of time in the first 60 minutes delay in hour one by a minute seemed to matter more than delay in hour two or hour three which means the more we climbed the mountain of getting closer to onset, the better we’ll do for our patients.

 **Lee Schwamm, MD:**

Great. I'm going to ask a few more questions, but we’re going to come back to the issues around how to get EMS more engaged and talking about endovascular therapy because there's a lot of interest about endovascular therapy, but here is something that Gregg is not on the best practice list because I don’t think it occurred to us to put it there, but one folk asks: “One of our challenges is family decision. When possible, we give the patient and family information shortly after arrival. We’re moving away from getting signed consent but still families struggle with this decision. Do you think that we should add to one of the best practices to not get written informed consent?” I think it is not in the guidelines. And I think informed decision‑making is important, but that does not equate to the need for a signed written consent form. Gregg, what are your thoughts?

 **Gregg Fonarow, MD:**

Yeah, so actually with Target: Stroke Phase I, we did have in the hospital toolkit a discussion around this issue and that depending on local policy that some hospitals do in fact allow no need for written informed consent and highlighted those decision making components that should go into that and some of the discussion points and examples and what have been previously published. So I think we’re very attuned to this concept of shared decision‑making, but this is such a critical decision where it is highly time‑dependent. This is a standard of care. Any potential delay has consequences with regards to a worse outcome as well as greater complications. And so really trying to very rapidly communicate the benefits and really trying to proceed under that banner that this is standard of care unless there are strong objections. And I know Jeff and others have worked on clinical decision support tools to try and convey that risk and benefit equation very simply to patients and families in this time critical decision period. So I think bringing all of that to bear on the issue of moving even beyond any discussion about risk and benefits I think gets a step too far, but that the default should really be around verbal communication, not necessarily requiring informed consent to be in writing.

 **Lee Schwamm, MD:**

Jeff, any thoughts?

 **Jeffrey Saver, MD:**

Yes, I fully agree and I think it's briefly discussed in the last guideline that it's not formally iterated or stated as a recommendation that it's very reasonable and appropriate for this particular time sensitive decision to have the discussion occur verbally and consent occur verbally and document that. I will note that some of our centers, colleagues internationally in Europe are beginning tPA without any discussion of consent. They do a deferred consent for the start of tPA because they consider the amount of brain lost while deciding the cost of deliberation to be too high and that the beneficence, our instruction to do good for our patients outweighs the autonomy ethic to respect patient identity to get things started. I don't think in the U.S. practice climate we’re quite ready there, but I do think that it is very acceptable and desirable to use a verbal documentation ‑‑ verbal consent rather than written consent to get things started.

 **Lee Schwamm, MD:**

Yeah, I strongly support that position. In fact, I wrote an editorial maybe a year ago, a little bit more, in circulation quality of care and outcomes that really we should be shifting to informed refusal. That any reasonable patient when given the information about the likelihood of improvement with tPA would only refuse this treatment if there was a clear‑cut medical contraindication or previously expressed wishes about what should happen in this circumstance in the presence, say, of another debilitating disease like dementia or medical disease. So I agree, I think that I would encourage any of you on the webinar who are still requiring written informed consent to really review carefully the indications for why that is required. And my guess would be that you’re not getting written informed consent for defibrillation, for cardiac arrest, or for thrombolytic therapy for MI when it's not occurring in the setting of a center that can do PCI. So I think that's a really important and substantial time savings that’s possible.

So here's another question. Are there any strategies to make up for potentially time lost with CT angiography in the initial imaging plan? So I’ll respond first to that and then maybe turn it over to Jeff. The recommendations are that advanced functional imaging should never delay the initiation of intravenous tPA. So at our hospital and in the guidelines, if the patient is eligible for tPA and the noncontrast CT supports the diagnosis and initiation of treatment, that you should interrupt the sequence between the CT and the CT angiogram if they have to stop anyway to go in and set the pump up. Go in and give your bolus and then do your CT angiogram and then immediately start your infusion so that you don't delay tPA initiation while the CT angiogram is being processed, and being read and people are thinking about endovascular treatment. Jeff, would you add any comments to that?

 **Jeffrey Saver, MD:**

I agree with that completely. I will note that the CTA acquisition takes 20 or 30 seconds post-processing may take time. So if the patient is ready to go with the acquisition, then I think we can afford to get that 20‑30 second acquisition done, especially if you're getting the tPA ready to hang. So sometimes we will roll right through the CT and CTA, but certainly not wait for the processing to start. But if we’re ready to go, then just go ahead and interrupt and hang the tPA in the imaging suite rather than back in the ED.

 **Gregg Fonarow, MD:**

I will just emphasize that we definitely found in the Phase II survey, that really represents a big opportunity that not all sites are taking advantage of about administering the tPA while their patient is still in the imaging suite.

 **Lee Schwamm, MD:**

Yes. So a question, Jeff, and then Gregg, if you know it, and I can answer as well. How does your single page activation system actually work? So Jeff, at UCLA, how does that actually work? What's the process?

 **Jeffrey Saver, MD:**

Sure, we have a three level group page. The first is a code stroke one where when there's a patient who may be having a stroke is known to be heading for the ED is sent off, it usually occurs when we get pre‑arrival notification by paramedics that they’re on their way with a likely stroke patient and our radio room nurse will send off the group one page and that goes to the stroke team attending and stroke fellow and stroke resident and stroke nurse coordinator. And they will go to the ED and meet the patient on arrival. That also alerts the CT and MR text that we have a case coming in. After that, after they have clapped eyes on the patient, if it does look like a stroke, if it's a major stroke it might be an endovascular case, one of those people will set off a ‑‑ escalate to a code stroke level 2 page, which indicates a possible large artery occlusion. That's before imaging and that tells our interventionalist and anesthesiologist to get ready. And then if in the angio‑suite it turns out to indeed be in LVO then they’ll set off a code stroke level three page indicating it's a confirmed LVO and we’re on the way to the angio‑suite and anesthesia and interventional list should be on the case.

 **Lee Schwamm, MD:**

So I have to say it's typical of Jeff's team that you have to have like a Ph.D to implement that because that is way too complicated for the simple-minded stroke team at Mass General Hospital. We have a single call activation, which we only have two flavors. Ours is if we get pre‑arrival notification of a suspected stroke, we give a heads up page that just says incoming stroke patient. No information confirmed, but possible case. And then when they arrive, and any member of our stroke team can send out this page, as soon as they actually arrive, a second page goes out to inform everybody with a little more clinical detail as the patient is being rushed back to angiography. The people who are on our single call activation is actually quite a large list. Anyone can subscribe to the group page if they want to. And what we have are the ED‑based neurology residents, our stroke fellow who responds to all tPA potential treatment cases, the neuroradiologist on‑call in the emergency department, the technologist for CT and MRI, because we have acute MRI in the emergency room as well and they need to know in case a patient might be transported to them, as well as a bunch of our research fellows and coordinators who screen for research studies so they can also understand what type of patient it is. We usually try to include an NI stroke scale score or some measure of stroke severity as well as age so they know whether or not this person might be a candidate for an acute trial like Diffuse 3 or something, for example. And then ED nursing, pharmacy, and our triaging nursing supervisor who’s the person who determines bed allocations in the hospital. So we try to give everybody -- sorry, of course the neuroendovascular team. Everybody who might need to know if the case were going to be treated with tPA or given endovascular treatment is on that heads up page. And we don't ‑‑ we tried for a while the experiment of calling off one of these pages. We actually have a five digit code for the pages, it’s called ED2CT. So it’s ED2CT because the main focus is getting the patient to the scanner for the decision-making. Gregg, anything else you’d like to comment on?

 **Gregg Fonarow, MD:**

I think those are both excellent examples that really illustrate what that initial page, the multiple disciplines that are being activated is not just a call going to, say, the stroke resident who then is dependent to activate everybody else, but imaging is being informed, nursing, every one that would need to be involved in the care of the patient to timely assess their eligibility for tPA and administer it are there and then additional components like research or going into endovascular therapy.

 **Jeffrey Saver, MD:**

Lee, let me also note that we are beginning to see, and I’m sure many of the sites on the call are beginning to see, that the term “page” and “group page” is becoming old‑fashioned as texting and smart phone apps that replace pagers are becoming available, which gives more flexibility for what can be communicated and who communicates. So I think when we got to Target: Stroke Phase III and IV we will be talking about ‑‑ I think we used the term “group alert” which allows us to be technology agnostic but we are moving to a smart phone world with this, thankfully.

 **Lee Schwamm, MD:**

Yeah, we are actually working on a mental telepathy stroke transmission system here on Mass General just to keep you on your toes.

Here's a really great question. “Outside of major metropolitan areas, neurologists can be in short supply. While tele‑neurology is available, it can be too expensive for hospitals to utilize. What is your opinion on using hospitalists with appropriate education to run a primary stroke program and make decisions on tPA treatment?” Gregg, do you want to take that?

 **Gregg Fonarow, MD:**

I'm going to kick that back to you and Jeff as the experts, but I will say this, that anything that can be as part of the system with proper decision support is really critical and being flexible in the standards for rural hospitals I think is important in that regard. But let me ask you since you are clearly one of the leaders in tele-stroke efforts.

 **Lee Schwamm, MD:**

I guess the way I would answer this is I think it really depends what you're trying to accomplish. I think if you’re looking to be established as what we would consider an acute stroke ready hospital, which means you’re going to provide initial stabilization and early treatment for stroke, but you’re not going to admit the majority of these cases. You’re going to be transferring them forward to a primary stroke center. Then I think it is very reasonable for having hospitalists or emergency physicians be the ones who make these decisions. And the Michigan Network that is run by Phil Scott, the INSTICT trial, they used telephone support from emergency physician to emergency physician to support treatment of suspected stroke with tPA. So I think it can be done. My only concern is that when hospitalists are told they’re going to do this or ED physicians rather than actually feeling it's a practice they want to take on, they tend to be understandably very conservative, slower to respond, and much more cautious. So I think it may limit the range of patients who get treatment. Now, if you said to me, no that's not what I mean. I mean we want to be a primary stroke center but we don't have a neurologist so we’re just going to have our hospitalists run the stroke program and provide care for complex stroke patients, I worry a little bit about that because I think that it requires some specialized training to manage the later phases of stroke care, particularly diagnosis and management for stroke patients where it’s not the straightforward run‑of‑the‑mill case. But Jeff, what do you think? You have a lot of actually smaller and rural hospitals in California, despite the large cities that are also there. What's been your experience?

 **Jeffrey Saver, MD:**

I agree with what's been said. I think if you have motivated hospitalists who are willing to take this on, they can learn the essentials and be able to make good enough decisions and there have been reports from centers that have used just emergency physicians alone or hospitalists that showed good outcomes, but they are very scattered reports because most practitioners are not comfortable with the type of complex decision‑making in neurologic patients, in emergencies with the risk of hemorrhage that tPA decision‑making requires. So it tends not to be a sustainable strategy.

 **Lee Schwamm, MD:**

Great. “Do you find that hospitals use the field point of care measurement done by EMS?” I think what they mean there is the stroke screen in the triage portion to facilitate faster imaging studies. So I think this question is asking, do you rely on EMS’ diagnosis of suspected stroke to facilitate getting the scanner ready for those patients or are you requiring an in-person physician at the facility to open the gates to imaging? Jeff, what do you do at UCLA?

 **Jeffrey Saver, MD:**

Well, we are using the field identification of likely stroke with the pre‑arrival notification, activate our scanners, and clear the scanners so when the patient hits the door, the scanner will be ready for them. We hold the line so the stroke patient can come in, but we are currently still having the physician see the patient and make sure they’re appropriate first. But as part of Stroke Phase II, and this is one of the differences or intensive approaches as a Target: Stroke program has evolved, there's now a recommendation for the direct to CT delivery by EMS or stop for a pit stop in the ED in the hallway, make sure the patient is stable, but let paramedics bring the patients directly to the CT on the paramedic gurney so you don't take them off one gurney onto another and then a third to get to imaging and don’t get stuck in the ED room. And that direct to CT approach is entirely dependent on paramedic recognition of likely stroke in the field and certainly for the centers that are getting door‑to‑needle times of under 30 minutes, which is occurring in some centers in the U.S. and some in Europe, they often are using direct to CT approaches.

 **Lee Schwamm, MD:**

One of the challenges that we have is we were on EPIC now, which as many of you know, is a very large electronic health record system, we have a record number before we can protocol to CT. We didn't used to have that problem but we do. And we actually find that stopping in the ED just for a few moments to get registered with a think we call Quick Registration allows us to still get to CT very quickly, but be there, give the CT folks a minute or two for the medical record number to process so that when the patient arrives there the scan can be ordered. The other thing we do is we draw blood either off of an existing IV if EMS has placed one or place a large bore antecubital IV for the CT angio as the patient either passes through the ED or when they hit the CT scanner so we can have bloodwork starting to cook and we find that parallel processing has been helpful for us.

 **Jeffrey Saver, MD:**

And Lee, for the registration number issue, which is an issue at many places, another approach we’ve been doing is to assign the patient a John Doe number when we get the pre-arrival notification and use that initially and then reconcile that number with the final assigned number when the patient's full ID is known. That used in our trauma team so we adapted it and it helps with that aspect. But it does create a little bit more workflow for the registration folks.

 **Gregg Fonarow, MD:**

I will just add in the Phase II surveys, so 46 percent of the sites reported for their patient's transport by EMS directly to CT and MRI scanner and that strategy was associated with faster door‑to‑needle times.

 **Lee Schwamm, MD:**

That's great. Here is one quickie. “Premixing tPA, how often should this be done? We typically get the scan, look at the image for a bleed, but most often we take the tPA with us but don't mix it.” So Jeff, do you premix the tPA before you see the CT scan or just have it at hand? What’s your approach?

 **Jeffrey Saver, MD:**

I think it is case dependent. We usually try to premix before we see the CT, but if the patient has had three hemorrhages before and we have reason to think it's happening again, we might hold off a bit. So I haven’t thought before about -- you should be premixing and not using if you’re never failing to use, you’re not premixing enough. But what is the proportion of mixes that you should be using versus having overmixed? I don't know what the optimum is? I haven’t thought about that question before. It probably depends on patient ‑‑ on your patient mix and population.

 **Lee Schwamm, MD:**

All right, we are getting close to the top of the hour and there are -- not hundreds, but there’s a lot of really interesting questions. I'm just going to ask one question that's not on the list, but because I think it's probably in everyone's mind, which is, Jeff, I will ask you. You get to close this out because you’re one of the big endovascular trialists. Now that we know DAWN is a positive trial by report at the European Stroke Conference though not yet published, should we just be going directly to endovascular and skipping tPA altogether? Or does tPA actually increase the response rate of subjects who go on to get thrombectomy?

 **Jeffrey Saver, MD:**

Well, right now, patients who are tPA eligible should be getting tPA on their way to thrombectomy and all of the randomized trials in which thrombectomy was proven of benefit eligible for tPA patients got tPA. So our entire dataset currently rests on that. There are reasons to think that tPA may help thrombectomy, it might open some patients faster, improving their outcome. Get my clean up distal thrombi improving outcome, it might soften the clot. On the other hand, it could hurt by causing more bleeding and slowing you down to the endovascular suite. So there are trials underway in Europe where some patients are going to skip tPA, be randomized to skip tPA versus get tPA as bridging therapy to thrombectomy. Until they come in, patients should be getting tPA. And we have our work cut out for us, rather than skipping a non‑tPA on shortening the door to puncture time for a thrombectomy and making that be as fast as possible, which will be the natural fit for Target: Stroke Phase III or the next program to come which we look forward to putting together and launching.

 **Lee Schwamm, MD:**

Gregg, you get the final one. Is it time for the performance measure to change to arrive by two and a half, treat by three?

 **Gregg Fonarow, MD:**

That is a really terrific question, and I think one that we need to cross because the standards really have evolved. And so as we think about the impact of Target: Stroke Phase I, the impact we’re seeing preliminary on Target: Stroke Phase II, it really does raise that question of whether our standard performance metrics regarding tPA use need to involve recognizing that the majority of patients can now be treated within 45 minutes and perhaps even 30 minutes, is now approaching with what our standards should be.

 **Lee Schwamm, MD:**

Great. Well, thank you both, Gregg and Jeff, so much for this hour of question and answer and Gregg, for your wonderful review on the Target: Stroke data. Mary, I'll turn it back to you.

 **Mary Paulsen:**

Thank you all for presenting today. That was some great information. And on behalf of the American Heart Association, I want to think our attendees for your valuable time and participation. You’ll notice that a survey will be pushed out and we appreciate you taking part in that survey so we can give really good education moving forward. So again, thank you, everyone, for joining.

**Lee Schwamm, MD:**

Thanks, everybody. Have a great day.

 **Jeffrey Saver, MD:**

Thank you.