Speaker 1: It is now my pleasure to turn the webcast over to Sara Camp. Sara, the floor is yours.

Sarah: Thank you. This is Sara Camp, Director of Quality Research and Marketing at the American Heart Association. I, along with the entire AHA and ASA, welcome you to the Young investigator Webinar Series.

This webinar series highlights the work of the investigators who are early in their career development and have an interest in cardiovascular or stroke research. Before we introduce our speaker for today, I’d like to introduce you to the Young Investigator Research Grant Opportunity.

The Council on Clinical Cardiology, the Stroke Council, The Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, and The Council on Basic Cardiovascular Science greatly value the development of young clinical investigators. To further this effort, these councils offer a limited number of seed grants for young investigators for meritorious research projects based on the data gathered from Get With The Guidelines.

Young investigators who are eligible for these seed grants may be current residents or fellows in training or students within five years of completing residency or fellowship, or other doctoral prepared professionals who are early in their career development and have interest in cardiovascular or stroke research.

The seed grants provide adequate funds to allow initial project design, access to the Get With The Guidelines data and statistical analysis; and to cover travel expenses of the recipient to travel to a National scientific conference to present the results. These grant opportunities are paired with valuable mentorship for members of the American Heart Association Get With the Guidelines Steering Committee and Science Subcommittee who oversee the database as well as national conference opportunities for young investigators can publicly present these findings.

For many professionals, these grants serve as stepping stones for future opportunities in research, collaboration, and scientific advancement. For the AHA and ASA they provide a step forward in our mission of building healthier lives free of cardiovascular diseases and stroke. You can find more information and details on applying for these grants twice yearly at our website heart.org/younginvestigators.

On today's session, we'll have the opportunity to hear from Dr. Lisa [Leffert 00:02:11]. Dr. Leffert is the senior member of the Department of Anesthesia,
Critical Care and Pain Medicine at the Massachusetts General Hospital in Boston where she serves as the Chief of Obstetric Anesthesia Division and vice chair for faculty development. She is Secretary Member of the Board of Directors of [SOAP 00:02:28] or Society of Obstetric Anesthesia and Paritionology. She lectures nationally and internationally on diverse topics, such as pericardial stroke, the anesthetic management of patients with intracranial lesions, strategies for placing neuraxial anesthetics, and patients with diverse comorbidity, [inaudible 00:02:45] and perio-delivery care of patients with substance abuse.

Recently, Dr. Leffert was delivered the honorary [Ostomer Westnoon 00:02:51] Obstetric Anesthesia Lecturer at the 2013 SOAP Annual meeting in Toronto, and the 2014 San Hughes Lecture at the Sol Shnider meeting in San Francisco.

Dr. Leffert's clinical focus is on the care of pregnant patients with high risk comorbidity with the particular interest in comorbid neurological disease. Her research investigates the epidemiology and approach to anesthetic management of these complex patients in collaboration with colleagues at the Centers for Disease Control and American Heart Association. Dr. Leffert is a Young Investigator Grant recipient from Spring 2013.

One final note for today's presentation, we have recently heard that some were not aware that pregnancy is actually captured through The Get with the Guidelines Stroke. However, you can find that within the past medical history section where it states current pregnancy up to six weeks postpartum.

And now it's my pleasure to turn over today's presentation to Dr. Lisa Leffert.

Dr. Leffert: Thank you. And thank you for that lovely introduction. Let me just say it probably bares a moment of explanation. I am not young, but my research career is young and I am very grateful for, on behalf of me and my collaborators across the country in the CDC, and many with affiliation with the American Heart Association, for this opportunity and for this Young Investigator Database Research Seed-Grant.

Today I want to talk to you about pregnancy related stroke. I'm going to give you some background on the topic and talk about some of the prior research. Then talk about how our investigation of The Get with the Guidelines Stroke really has enabled us to learn more about this incredibly important subset of patients with stroke. We'll talk about an overview of these patients, our stroke sub-type analysis, and then what we've learned about ischemic stroke therapy.

Let's begin with the background. Stroke is certainly a catastrophic event in pregnancy and the postpartum period. It can be associated with significant morbidity and mortality. Residual deficits can impact not only the quality of life of a pregnant or postpartum woman, but also her decisions about future pregnancies. Fortunately pregnant woman are generally healthy, and this can
certainly obscure timely stroke diagnosis. You'll find that pregnant woman are excluded from studies about most things, and this is certainly true related to stroke and stroke therapy.

Much of prior research has focused on case series, and I'll highlight for a moment the [Waiver 00:05:30] case series. This was basically the first time that incidence data was attempted to be looked at. Before that there were small collections of patients and someone would notice that one or two of the patients would have an ischemic stroke or hemorrhagic stroke. This was published in [JAMA 00:05:48], this basically looked at all the patients and the Catchment area of Rochester Minnesota and the institutions around it. They said, "Look, one patient had an ischemic stroke in these twenty-six thousand patients. Is that what we can expect in terms of stroke?"

When we begin to look at other investigations, we began to learn more as we looked at large data sets. Now, some of you may be familiar with the nation wide in patient sample, and other of you may not. This is the largest US in patient payer patient data base; this collects 20% of the non-federal community hospital discharges. These are actually collected based on ICD-9 codes for billing, but can tell you a lot administratively about patients, you cannot get patient level detail. I'm going to present to you a few of these studies, including one of ours.

This payer study had twenty-eight hundred pregnancy related discharges and show the stroke rate of about thirty-four per ten thousand deliveries. It was the first that began to characterize "What were the risk factors in this group?" African American women were at increased risk, as were women greater than thirty-five years of age. There were some stroke associated medical conditions; migraine headaches with a greatly increased [dodge 00:07:15] ratio of almost seventeen, thrombophilia, heart disease and hypertension, which you'll see a theme throughout. Complications that were particular to pregnancy; postpartum infection with a very high odds ratio, transfusion, gestational hypertension, and postpartum hemorrhage.

The UK collects very clinically detailed patient data, but also in a large database form; this has been extremely helpful in stroke and other things. This was a look back at from 2007 to 2010 at almost two million delivering woman, thirty cases in antenatal stroke and incidence in this population of 1.5 cases per hundred thousand. Here we learned, poor outcomes are more frequent than we previously thought; 30% of survivors were discharged not home, but to another facility, 45% of survivors with significant disability. And care? Sort of all over the place, only 20% admitted to an acute stroke unit, 67% with aspirin, 42% with an anticoagulant and none with thrombolysis.

With the same data, looking back now over a longer period of time from the UK 1979 to 2008, these looked at the worst stroke outcomes, that of death. What they found were about 1.6 stroke deaths per hundred thousand maternities.
Just to put this in context of overall maternal deaths, about one in seven maternal deaths. If you look at the graph on the right, when you’re talking about stroke death in pregnancy, you’re talking mostly about hemorrhagic strokes, a predominance in this case. More ICH than SAH and a smaller percentage, smaller number in this case; thirty-five out of the three hundred and forty-seven of cerebral infarction. They looked down and drilled down on the particular cases, again this familiar theme, management of hypertension. In this case, what they deemed as substandard care.

This paper was extremely influential in the obstetric community, although only twenty-eight patients and case ascertainment was in a very unusual way. These were cases that were actually across the country and what brought them in common were there were cases on which a lawsuit was pending. Really not good for incidence data, but some interesting blood pressure reflections. 92% of these patients have hemorrhagic stroke, again we’re getting the sense that these were perhaps the most deadly strokes in pregnancy.

What these authors observed were that of the patients who died in this cohort, the systolic pressure was greater than 155 in more than 100% of the patients. But in terms of the diastolic blood pressure, which really had been a lot of the focus prior to this, diastolic pressure only greater than 110 in about 12% of the patients. This was significant because 110 is the cut for severe pre-aclampsia. Realize that in the obstetric community, much of the focus on stroke prevention in pregnancy is on a very short period of time, that’s when the patient is in the hospital having her baby, and really around the parameters of preeclampsia, 140/90. Above that is preeclampsia at all, and greater than 160/110, beyond that is severe preeclampsia.

Certainly the initial post-stroke blood pressures were significantly higher than the pre-stroke values in these patients, this is going to be an important observation when we look at our Get With the Guidelines Data, the maternal mortality was more than 50%, so it was significant. Another national, nationwide inpatient sample study, looking now at ten thousand delivery hospitalizations, more recent tells us that the pregnancy related stroke incidents, albeit low, the prevalence is increasing. In particularly, for the times when the patient are not in our view; antenatal hospitalizations for stroke when the woman is pregnant, but not expected to be delivering, and postpartum hospitalizations, in particular, an 83% increase. This is when a woman is home, she’s with her new baby, and no one is focusing on her. These trends are thought to be largely driven by concomitant prevalence changes in hypertensive disorders of pregnancy, and in heart disease over all.

What is the obstetric community doing about this? Well, in the United States, in Canada and the UK, there’s been a real focus on changing guidelines of management of hypertensive in pregnancy. The American Congress of OBGYN, called ACOG, came out with a new set of guidelines in 2013, I'm going to take a minute to focus on them.
Early recognition of hypertensive disorders of pregnancy, or preeclampsia, extremely important, so important, that they took one of the major criteria, which was having protein in your urine measured over twenty-four hours, and said, "If you have the hypertension, and other signs of preeclampsia; a headache, renal dysfunction, liver dysfunction, don't even wait the twenty-four hours to count the protein, just start treating the patient. Don't worry about calling them mild preeclampsia, always be on the lookout for patients being severe." Interesting. Not really espousing the treatment of moderate hypertension, less than 160/110, again, this is going to turn out to be important. They did give an important nod to monitoring these patients postpartum. How they chose these specific days is not particularly clear. What's particularly important about day one, three, seven, and ten, but in acknowledgement, that the patients are particularly at risk then.

Then came the guidelines for prevention of stroke in women, these guidelines, this audience is probably very familiar with, there was a subsection on pregnancy. Severe hypertension should be treated in pregnancy, no questions about it. Then a statement that's much stronger than the obstetric community has really embraced, the goal of blood pressure management in pregnancy, is to maintain systolic blood pressure between 130 and 155, and diastolic pressure between 80 and 105. With the lower target ranges in the context of comorbidity.

This really got us to thinking. What is really important about blood pressure? Which patients are really most at risk? How much more at risk are the patients with hypertensive disorders of pregnancy? Just to make sure that we know what we're talking about, hypertensive disorders of pregnancy include; preeclampsia and eclampsia, they include gestational hypertension, those who become hypertensive during their pregnancy, they include those who have underlying chronic hypertension and don't become preeclamptic, and those who do.

The [gradations 00:14:42] between them, it's hard to distinguish in the stroke population and their influence, because we're talking about rare things. Which is why it's so important to look at large data, or large registries, like Get With the Guidelines. Before we did Get With the Guidelines analysis, we too looked at the nationwide inpatient sample. Our aim was to evaluate the trends and associated stroke risk and complications of stroke in pregnant women, with and without these hypertensive disorders of pregnancy. We did a cross sectional study, as you would, with this data; eighty-one million pregnancy hospitalizations, we looked over time because we wanted to look at trends. We looked at the rates of stroke hospitalization with or without these diseases, with adjusted odds ratios with a logistic regression analysis.

Our study population, we got the reasonable numbers because of the power of this database. In terms of stroke with these hypertensive disorders, we had ninety-eight hundred patients. Stroke without these hypertensive disorders, twenty-one thousand seven hundred patients. Then for the comparison group,
hypertensive disorders without stroke, over six million. The most general category of all, no stroke no hypertensive disorders of pregnancy, but all pregnant, seventy-five million patients.

What did we find? I began by saying we were really interested in looking at trends over time. That's what this graph is about; the study period on the X axis, 1994 - 5 is the earliest time period, 2010 to 11 is the latest time period. At the top we have overall pregnancy related stroke, on the Y axis the rate per ten thousand pregnancy hospitalizations. In the middle, the pregnant women without hypertensive disorders of pregnancy. On the bottom, those with hypertensive disorders of pregnancy.

The first thing you notice is that they're all increasing. However, those at the bottom with those that pregnancy related hypertensive disorders of pregnancy are increasing at the most rapid rate; 102% increase in this patient population, the first observation. The second, what if these particular pregnant patients also have risk factors that are traditional stroke risk factors. Postpartum hemorrhage, as we learned from the nationwide inpatient sample, congenital coagulation defects, valvular disorders, SLE atrial fibrillation, the adjusted odds ratio are significantly increased above the pregnant patients without these hypertensive disorders.

When you look at complications; things like mechanical ventilation, pneumonia, seizures, and death during hospitalization. Even in the adjusted odds ratio, we’re still getting either truly increased odds, or a trend toward increased odds. What did we find in summary from this analysis? Much greater increase in stroke rate in all cases in pregnancy related stroke, but particularly those with hypertensive disorders of pregnancy, still small numbers. A trend increase from .8 to 1.6 in these patients, and particularly in the patients with hypertensive disorders. These were only partially explained by the changing trends and some of the common risk factors; advanced maternal age, heart disease, the increase in hypertensive disorders of pregnancy, preeclampsia overall, which is certainly occurring, and other comorbid maternal conditions.

Patients with these diseases were five times more likely to have a stroke than those without. If you also had increased stroke risk factors, that greatly increased your stroke risk. Clearly the complications were also increased. We really yearned for more detailed data, and this has limitations, as you know. We’re relying on billing codes, there's missing information on pregnancy, lack of clinical detailed unmeasured confounders, and we certainly could not, by the study design, impute causality.

We were so pleased to be able to look at the Get With the Guidelines and really be able to look first in general at pregnancy related stroke, and then get more into stroke sub-types and therapy. Our initial aim in our first analysis was to elucidate patient in hospital characteristics and stroke sub-types and pregnancy related stroke. If any of you are not familiar with Get With the Guidelines stroke
method, this program design is incredible, as I've learned more and more about it. It's a voluntary observational registry and continuous quality improvement program. It features a web-based patient management tool with decision support, on demand patient reporting, and even patient education features.

The eligibility of all stroke admissions is confirmed prior the chart abstraction is done by trained hospital personnel, so the integrity of the data is really good. We were able to analyze patient level data from nine-hundred Get With the Guidelines hospitals that participated from our study period 2008 to 2013. We defined pregnancy related stroke as stroke in a woman who was pregnant, or less than six weeks post partum. This was per convention and we selected women of child bearing age and we got them both through ICD-9 codes, a medical history of pregnancy, or the two together.

We used descriptive statistics of this portion, they were both were prevented as perportion with means or medians, and patient in a hospital characteristics were compared by [Chi Squared 00:21:01]. The categorical variables and will [inaudible 00:21:04] for continuous variables.

In terms of case assertion, overall we had six hundred and sixty-eight pregnancy related stroke, where fifty-seven percent were from medical history and ICD-9 codes twenty-five percent and eighteen percent from both. Overall, women with pregnancy related stroke were young, with a median age of 31. The majority were not in the health care setting when their stroke occurred, only twenty percent arrived by EMS, so it was only thought to be an emergency a minority at the period of time. These patients overall had a low incidence of traditional stroke risk factors, hypertension seventeen percent, smoking twenty percent, prior stroke five percent, and very few were diabetic, and not surprisingly few were on associated medications.

If you look at their initial first post stroke laboratory values, very little glucose derangement; ninety-eight. Now was that because of their [physiologic mulher 00:22:09], was that because of the fact that glucose is very highly regulated in pregnant patients? Not clear. Surprisingly normal vital signs, median systolic blood pressure of 134 with not too big of range, and median diastolic blood pressure of 81. Again, was not too wide a range.

What did we find from this initial analysis? About 1.5 % of all strokes, among these child bearing aged women were pregnancy related. About 50% of them were hemorrhagic strokes. Most patients were out of the hospital and about half of them presented with reasonably low blood pressures, below the levels of preeclampsia, or the recommendation for high anti hypertensive therapy. Perhaps these patients with moderate to severe hypertension in pregnancy had particularly compromised central cerebral vascular autoregulation. Certainly it's seeming like stroke can occur at moderately elevated blood pressures and maybe that the current treatment thresholds, at least in the obstetric community, potentially needed to be reevaluated.
I'll say up front, and then present the other analyses, there were limitations in this analysis as well. It's contingent on the accuracy of documentation and abstraction of the medical details, the hospitals are not audited, there may be enrollment bias, we don't have long-term maternal and fetal outcomes and pregnancy details are not part of the registry. Although, the fact that pregnancy itself was part of the registry, made this whole thing possible, which was wonderful. The Get With the Guidelines hospitals are voluntary and may attract larger and better preforming hospitals. Despite the fact that this is by far the largest sample of pregnancy related stroke, it still is a relatively small sample size. There were some residual measured and unmeasured confounders.

Let’s look now, what we found out in our sub-population analysis. We looked at ischemic and hemorrhagic stroke, our aim was to describe the distribution of stroke sub-types for pregnant patients, and to compare differences in patient in hospital characteristics between pregnancy related ischemic stroke and pregnancy related hemorrhagic stroke. You’ll see separately that we’ll also compare each of these in the pregnant and the non-pregnant population.

In the registry, we found, pretty much evenly split between ischemic and hemorrhagic stroke. When you further break down hemorrhagic stroke, pretty evenly split between intracerebral hemorrhage and subarachnoid hemorrhage. I’m going to show you these two charts, not for you to read the details, but just to see that there were actually a lot of significant differences between pregnancy related hemorrhagic stroke and pregnancy related ischemic stroke. Let’s highlight a few of them.

When you’re looking at the hemorrhagic versus ischemic stroke in pregnancy, the hemorrhagic stroke patients were less likely to have recurrent stroke. Perhaps not surprising, they were less likely to be white, and they were less likely to have traditional stroke risk factors; diabetes, dyslipidemia, coronary artery disease, prior MI. Perhaps associated, unless likely to have into hypertensive agents anticoagulants prior to their stroke. These hemorrhagic stroke patients, however, were more likely to be in a health care setting at their stroke onset. They were more likely to be treated at larger academic hospitals, and more likely to be hypertensive on arrival to the emergency department. Their systolic blood pressures of median 43, with the interquartile ranges 123 to 164, versus 127 for the ischemic stroke patients. Again, the interquartile range is 115 to 146. The diastolic blood pressures median of 84 versus 78.

If you actually looked at the hemorrhagic stroke sub-types, that is intracerebral hemorrhage versus subarachnoid hemorrhage, the patterns were similar. They had similar initial blood pressures recorded post stroke on arrival. Close, again, to the threshold for preeclampsia, and pretty much below the threshold at least for more than 50% of them for initiating anti-hypertensive therapy. Now if we look at pregnancy related subarachnoid hemorrhage versus non-pregnancy related subarachnoid hemorrhage, and the same for intracerebral hemorrhage,
we start to see more differences in the pregnant population versus the non-pregnant population.

They look reasonably similar, the subarachnoid and intracerebral hemorrhage pregnant patients to each other. They’re younger than their non-pregnant cohorts. In this case, subarachnoid hemorrhage more likely to be black, more likely to be on Medicaid, less stroke symptomatology, less likely altered level of consciousness. In this case, less likely to be hypertensive, have altered glucose levels when they first come in, a little bit higher systolic and diastolic blood pressures, less likely to be on medications and less likely to use emergency services.

Again, now intracerebral hemorrhage pregnant versus not. Again, younger than their non-pregnant cohort. More likely to be on Medicaid, and very similar story; less likely to be in a- excuse me, more likely to be in a health care setting for the intracerebral hemorrhage patients. Less likely to have pre existing stroke risk factors, and deranged glucose levels, and to be on the associated medications for their stroke risk factors.

How about outcomes? In many cases, that's what we care about the most. This is the result of a regression analysis, in terms of the most important outcomes that Get With the Guidelines tracks. Here we see when you compare pregnant subarachnoid hemorrhage patients to non, in hospital mortality was much, much lower with an odds ratio of .17. More likely to be discharged to home and more likely to have independent ambulation at discharge. How about for the intracerebral hemorrhage patients, pregnant versus not. A little less striking but still lower in hospital mortality.

What does this tell us? In this largest most clinically detailed series, pregnant hemorrhagic stroke patients fared better in outcome measures than their non-pregnant counterparts. Perhaps because the pregnant hemorrhagic stroke patients presented with fewer traditional stroke risk factors and only moderate hypertension, and may be more challenging to identify at risk patients, and provide prompt and appropriate care. Certainly beginning with arriving to the hospital with emergency services, and taking it from there.

I'll tell you from some work that we have done that I didn't present in the nationwide inpatient sample, that we have shown that these patients are less likely to have an aneurysmal etiology to their subarachnoid hemorrhage than non-pregnant patients. We really have to begin to think of other etiologies. There certainly seems to be some evidence for disruption for cerebral autoregulation in the hypertensive patients. Perhaps at a lower blood pressure than we're used to thinking about.

How about ischemic stroke? In this analysis we compared the base line patient in hospital characteristics, as well as the difference in care delivering short term outcomes looking at pregnant versus non-pregnant ischemic stroke. Again, we
analyzed the Get With the Guidelines hospitals that were at our disposal with the very similar ascertainment strategy that we had before. We added a sensitivity analysis, which I'll describe to you, and use the same statistical analysis that we did in the other populations. Overall what we found were that the pregnant ischemic stroke patients were less likely to have traditional stroke risk factors and less likely be black. They were significantly younger, more likely to be insured by Medicare, more likely to be in a health care setting at stroke onset. Although still, the majority by far, were not. They were more likely to be admitted to a stroke center and had somewhat higher systolic and diastolic blood pressures, although still, in this range that we've been talking about.

Both groups had similar initial stroke severity in exam findings. We really wanted to peak and go under the surface in terms of age, because what we notice was, that the pregnant patients, delineated in pink, had a very different distribution in stroke and age, than the non-pregnant patients who were very much distributed more to the right. We wondered were all these differences just based on the difference in age of the population. We did two things; one is we looked at the distribution of age and pregnancy using some CDC data, and our stroke distribution mirrored the age and pregnancy. Two, we did a sensitivity analysis and stratified by age; 18 to 34, was one group, an older group, 35 to 44, and not much changed.

Most of the patient characteristics were very similar when we compared the two age groups, pregnant and not. There were small changes, only the younger group had differences and rates in diastolic blood pressure. Only the older group had differences in patient location, stroke symptom onset. The major differences and findings were the same. In this case, the outcomes and quality of care measures between the pregnant and non-pregnant ischemic stroke patients were very similar. Just a trend toward an increase length of stay more than four days than the pregnant patients. You should know that four days is the maximum that pregnant patients usually stay in the hospital, those are patients that have [cesarean 00:33:03] delivery.

We had some data on 145 of the cases on timing of stroke. We found what others have, about 44% of them antepartum, about 52% of them postpartum. Again, a highlighted period, these patients were more likely to have hypertension beyond anti-hypertensive meds pre-stroke, and have higher blood pressures; 140 versus 118, and 82 versus 70 for the diastolics. These were the patients that were supposedly following and working on, and not particularly having high blood pressures; again the theme.

We still have uncommon pregnancy related ischemic stroke, fewer traditional risk factors. Again, it may be that because they're pregnant, and they're otherwise healthy, and because their blood pressures (at least the initial stroke post blood pressures), we unfortunately don't have pre-stroke blood pressures, are relatively low, that they're just not as much in our mindset. What about treatment, because ultimately diagnosis facilitates treatment. We know that
thrombolysis is the gold standard for ischemic stroke treatment in non-pregnancy adults. Pregnancy and obstetrical delivery have just been removed as a warning in the FDA label for Alteplase 00:34:26.

What are the kind of things people have worried about? They worry about [tradelegenicity 00:34:32], although you should know that [Alteplase 00:34:34] is a very large molecule and does not cross the placenta. They worry about placental hemorrhages. We'll talk about the data, the little data we have. Certainly pregnant women have been excluded for all clinical trials.

What I will say is that ... women in the few case reports have done pretty well; no major complications. Very small hemorrhages that have not been that significant, except for one. The mothers in general have done well, with rare exception, and the infants have done well with a couple of medical terminations. This subject has been highlighted in a recent subject in stroke with a very eloquent point counterpoint discussion, should these women have treatment? We can tell you that if you're talking about any thrombolytic treatment in Get With the Guidelines. We did a similar analysis to the other people, the other Get With the Guideline stroke analyses, if you're talking about any thrombolysis, forty of our three-hundred and thirty-eight patients had any thrombolysis. No difference in terms of the basic percentage of patients.

There were some difference in their characteristics, the pregnant patients were less likely to arrive by EMS, less likely to be hypertensive, less likely to be on cholesterol meds, more likely to be younger, and to have actually a higher [NAIHF score 00:36:13]. But, no difference between groups in race, health insurance, complications or outcomes, IV TPA only, less likely. The reasons for non-treatment? Pregnancy itself, recent surgery, stroke severity too mild in rapid improvement were actually less likely. The results; they basically had a trend, one patient had a more symptomatic intracerebral hemorrhage, a trend toward a longer length of stay. Comparative discharge outcomes; low rates of in hospital mortality, zero versus two percent, and high rates of home discharge, so they did well.

Let me conclude, pregnant related ischemic stroke patients underwent IV thrombolysis infrequently and less often than their non-pregnant IS counterparts. There was less frequent use of IFs, EMS, despite the higher [NIHFF 00:37:13], the complication rates and short term outcomes generally appeared to be favorable. There were limited data size, and therefore, more study needs to be warranted. But, I'm very interested in knowing your questions and your comments, but it looks as though the armamentarium intentionally for these pregnant patients has greatly expanded. That, in addition to endovascular therapy, intravenous therapy which often precedes endovascular therapy, is really a possibility in these patients. We have an incredible opportunity to not only identify patients at risk, but to deal with their potential bleeding complications from an obstetric point of view, to identify which of these patients are particularly high risk from an obstetric point of view, to tailor what
kinds of thrombolysis is most appropriate from a neurologic point of view, and to really work together as a community to offer these patients reperfusion therapy.

Thank you so much, and please, I welcome your comments and your questions.

Speaker 1: To submit a web question, use the green Q & A icon on the lower left hand corner of your screen, type your question into the open area, and press send to submit.

Sarah: Dr. Leffert, we do have a couple of questions. Here, I'll just read them off to you.

First question is: If you could talk about blood pressure you're recommended into hypertensive for pregnant patients? What's the range you're really shooting for?

Dr. Leffert: I think probably the best advice comes from your guidelines, from your task force, published in January, I think it was of 2015. Guidelines for recommendations for women for stroke prevention. We can back up. There's a really nice paragraph on pregnant women. It recommends on the order of 130 to 155, for systolic blood pressure. I will tell you, the obstetricians concern is for the affect on the fetus. That data is a little bit difficult to interpret because of confounding by indication. A lot of times it's difficult to separate when women are being treated for hypertension and they have fetal outcomes like intrauterine growth retardation. Whether the result of intrauterine growth retardation is because of the treatment for hypertension, or it's because the hypertension itself.

I am aware from some of my colleagues of some very good studies that are coming out now, that separates that out to some extent. The reason why that's so important is, if it's the hypertension itself and not the treatment for hypertension that's effecting the fetus, that's all the more reason to feel comfortable being a little bit more aggressive treating hypertensive women when they're pregnant, than if you're worried that you're going to harm the fetus in some way. You know, I really look to your community to say what's going to be most helpful from a neurologic standpoint for the women.

When you're talking about postpartum women then, I think it's really the recommendations that I just mentioned that you have put forth in terms of stroke prevention. Clearly these women are at risk for stroke, not only immediately postpartum, but thereafter. Then, you do not have any fetus in situ, so all of the concerns that people have about worrying about the two patients and treating maternal hypertension are no longer an issue in this very vulnerable postpartum period.

Sarah: Another question for you: Where is this study published and how can people find it?
Dr. Leffert: Thank you for asking that question. This data was presented, some in oral format, some in post presentation at ISC 2015 and it's currently submitted for publication. So, I hope I can answer that publicly in the relatively near future.

Sarah: We'll make sure from an AHA standpoint that we put that in an email. Plus, when it is published and get it out to everybody here on the phone.

Dr. Leffert: Thank you. [crosstalk 00:42:01]

Sarah: Yeah. Next question: For the pregnant patient with stroke, what type of clinical evaluations are recommended? Would you do CT, CTA, MRI?

Dr. Leffert: My teaching from your community, and I am speaking like this because I'm actually trained as a high risk obstetric anesthesiologist. I joke, I am marr- this is not a joke, this is the truth. I'm married to a neurologist for more than twenty-five years, so I have absorbed from osmosis, and have really been fortunate to bring together a bunch of people, wonderful people to work on this issue. What I've really learned from you is that when a women has high risk neurologic disease, she needs to be evaluated basically like anyone else would be. There will be some extreme cases where you're talking about gadolinium, where maybe it's better not to give gadolinium. In general, the obstetricians will tell you that you need to evaluate her from a neurologic point of view.

I'll give you a one moment antidote; we had a patient recently who was treated with IV TPA for her stroke, it was a relatively mid-level, I'd say obstetrician, who made the recommendation go ahead with the IV TPA. She had had a cesarean delivery twelve days before. I asked her afterwards, "How did you make that decision? How were you so brave as to say, this is surgery, it's been twelve days, it's a little risky." She said, "It was quite obvious to me. We know how to treat obstetric hemorrhage, but, this is her brain." She didn't quite use the term "time is brain" because she wasn't as familiar with that terminology, but she got it. What I find, working closely with these folks is that's their basic feeling, do what you need to do from a neurologic point of view, and we can work together and deal with obstetric hemorrhage. Clearly there will be patients for whom it doesn't make sense from either a neurologic or an obstetric point of view, or particularly high risk patients. Let's think of, at base line, these are patients for reperfusion in some way. If it makes sense from a neurologic point of view.

Sarah: Perfect. There's another one: If pregnant with ischemic stroke are less likely to be treated with TPA, when is it more likely that they would be treated with?

Dr. Leffert: Nothing. You know, [inaudible 00:44:47] it's hard to sort of make any kind of generalization, but as someone who has sort of scoured the literature, and various interacting with all kinds of folks that work with this population, what I have gleaned is that they're less likely to be treated with much of anything. I think, in general, maybe an aspirin, but I think people are terrified of touching pregnant women, they don't want to ruin anything. They don't want to ruin
anything with the pregnancy. They certainly don't want to be liable for anything, not that their hearts aren't in the right place. I completely understand that. I think the issue is just that potential downside, if they have a real disability, is large. That's where the risk benefit comes in to play.

Not to trivialize, if there is a complication, or what the complications could be, part of the problem is we know so little because there has been so little treatment. The Get With the Guidelines has helped us hugely increase the number of patients that we can put out there who have been treated. It's dramatically improved, but clearly we need much more patient history and case history to be able to really get an idea of what the complications could and will be.

Sarah: Another question is that: You noted some of the signs and symptoms of pregnancy related stroke were non-typical, can you review those one more time for this group?

Dr. Leffert: Yes. I think that's one of the trickiest things. My guess is that, that is true for stroke in the young in general. That's not something I'm an expert on. Women come in sometimes with more subtle symptoms, they can have ... Depending on the stroke sub-type and such, hopefully all of this will be out in the public venue sometime reasonably soon, and that will be hopefully helpful to folks. I think a lot of times these things can be mis-thought of as atypical migraine. Although, atypical migraine is absolutely something that shows up in pregnancy with some sensory symptoms, particularly that women have never had. I think one of the basic messages is certainly if there are things like aphasia and motor deficits, those kinds of things need to be taken very seriously in this population.

Particularly, in the postpartum period, I can't stress enough; this is a time when women are often very tired, under slept, when they present with intractable headaches, they absolutely need to be paid attention to. Plus, any of these other sorts of symptomatology, that's a very vulnerable time when women, everything is sort of ascribed to just being postpartum and tired and un-slept. And/Or, they had an epidural, maybe they have a postdural puncture headache. We know that postdural puncture headache have some pretty traditional cardinal signs, and when headaches really are persistent, have no positional component at all, are worse when they lie down, various different things. We certainly should have increased radar, particularly in patients who have been hypertensive.

Sarah: Many people are asking, they say this is a great presentation: Will we be able to get a copy of the power point slides?

That's a yes. We are going to put this on our website so people can learn more, because this is a really important subject. We're really excited to see so many great questions coming through.
Let me see if there is any more for you Dr. Leffert.

Is there a difference in [inaudible 00:49:00] scales at discharges versus non-pregnant? [crosstalk 00:49:05]

Dr. Leffert: We didn't have that information. You know, we were so fortunate that [inaudible 00:49:10] it was with such forethought that Get With the Guidelines had the information that they had, given that certainly pregnancy was not the reason for which the registry was designed. But, there were- We had certain data, we didn't have certain data, we were specifically focusing on a subset of patients that were pregnant. So, you know, those were the patients we went with and we went with the data where we had some numbers that were reasonable to look at.

Sarah: Perfect. [crosstalk 00:49:51]

Dr. Leffert: I will just point out to the attendees who are doing wonderful work in this area, that actually getting detailed neurological data on pregnant patients is one of my goals, to sort of spur interest in that, because that's something that I think is really lacking. You folks are the ones to make tremendous contributions in that area.

Sarah: I think that that's the last of the question that has come through, unless we have any audio questions that have come through. Let me ask the operator.

Operator: Hello, there are no further questions at this time. [inaudible 00:50:37]

Sarah: Okay. We'll say on behalf of the American Heart Association, American Stroke Association, thank you so much Dr. Leffert for presenting today.

Thank you to our attendees for your valuable time and we will make sure to get this information out to everybody and make sure this is an important that we all focus on.

Thanks everybody so much.

Dr. Leffert: Thank you.

Speaker 1: Thank you for joining us today, this concludes today's presentation. You may now disconnect.