Host: Welcome to the *ANESTHESIOLOGY* journal podcast, an audio interview of study authors and editorialists.

Dr. BobbieJean Sweitzer: Hello, I'm BobbieJean Sweitzer, Professor of Anesthesiology at Northwestern University and an associate editor for *ANESTHESIOLOGY*, and you are listening to an *ANESTHESIOLOGY* podcast; designed for physicians and scientists interested in the research that appears in our journal. Today we are speaking with two authors of publications that appear in the December 2020 issue of the journal. With us is Dr. Kamal Maheshwari. Dr. Maheshwari is the lead author of an article titled "Hypotension Prediction Index for Prevention of Hypotension during Moderate to High Risk Non-Cardiac Surgery; a Pilot Randomized Trial." Dr. Maheshwari is in the department of general anesthesiology and the department of outcomes research at the Cleveland Clinic in Cleveland, Ohio. Welcome Dr. Maheshwari.

Dr. Kamal Maheshwari: Hello Dr. Sweitzer. Thank you for the invitation and glad to be here.

Dr. BobbieJean Sweitzer: And joining Dr. Maheshwari is Dr. Charles W. Hogue. Dr. Hogue wrote an accompanying editorial: "Preventing Intraoperative Hypotension; Artificial Intelligence Versus Augmented Intelligence." Dr. Hogue is the James E. Eckenhoff Professor and Chair Department of Anesthesiology, Northwestern University Feinberg School of Medicine in Chicago, Illinois, and he's my chairman. Welcome Dr. Hogue.

Dr. Charles W. Hogue: Thank you BobbieJean.

Dr. BobbieJean Sweitzer: So let's start with you Dr. Maheshwari. Maybe we can start by your telling us what the hypotension prediction index is.

Dr. Kamal Maheshwari: Sure. Let me first say hello to Dr. Hogue and thanks for joining us. So yes, with regards to hypotension prediction index, let's first define what is hypotension. So we know that hypotension is associated with worse outcomes. And multiple retrospective studies and some prospective studies have shown even a few minutes of hypotension is bad. But the current blood pressure management is reactive. What we see in our clinical practice, we see a low blood pressure; we treat it. So there's always some amount of hypotension which is there in any anesthetic case. The question is can we prevent hypotension all together. And that leads us to a proactive approach that means can we predict hypotension and prevent it by treating it even before it is happening. And that's what the primary reason why hypotension prediction index was developed is that if you predict hypotension, you will be able to treat it and thus prevent hypotension all together.

Dr. BobbieJean Sweitzer: So how does this index actually work?

Dr. Kamal Maheshwari: There are in the past people have tried to predict hypotension just based on experience that, you know, I know the blood pressure is going to go down because in these kinds of cases this is what happens. This particular hypotension prediction index is based on an algorithm which uses arterial pressure waveform. And what it does is it dissects the arterial pressure waveform into numerous features, and ultimately uses those features to predict the probability of hypotension in coming minutes. And the coming minutes is up to 15 minutes for this particular algorithm. What it does is when it senses that the patient is going to go into hypotension, it gives a score from zero to 100, which becomes the index, and that is zero to 100% probability of having hypotension. One other thing is whenever you have a probability of zero to 100, you have to decide at what level you're going to say please treat it. And in this particular algorithm a level of 85% was decided arbitrarily as an alert for the treatment.

Dr. BobbieJean Sweitzer: I want to ask you a little later about the algorithm itself, but just to clarify, for this index to work you need to have an invasive blood pressure monitor, is that correct?

Dr. Kamal Maheshwari: You need to have arterial pressure waveform, which can be generated both from invasive and noninvasive sources.

Dr. BobbieJean Sweitzer: Okay. And is this index as good – I mean, you know, sometimes the blood pressure drops I can predict, as you mentioned, because we're trending downward or I know that, you know, so I'll have one blood pressure is a bit lower than the previous one, but what about those sudden drops in blood pressure that may be more unexpected? Is this index equally good at predicting both of those situations?

Dr. Kamal Maheshwari: Apparently not, and that's what we will discuss. You need some time for the prediction to work. And the sudden drops in blood pressure, which is mostly happening because of either surgical manipulation or sudden blood loss, those are difficult to predict.

Dr. BobbieJean Sweitzer: Got it. So Dr. Hogue, I know there have been a number of manuscripts in recent years identifying the occurrence of intraoperative hypotension and the consequences of it. Can you summarize for our listeners maybe how commonly hypotension does occur during anesthesia and the associated outcomes that are important?

Dr. Charles W. Hogue: Yes, well I think it depends on the patient population. So this paper we're limited to non-cardiac surgery and not, you know, cardiac surgery. But in non-cardiac surgery it also depends on, you know, the patient you're looking at. But I think it'd be safe to say that in adults undergoing non-cardiac surgery under general anesthesia that hypotension is indeed frequent, but depends on the definition and the definition not only of the threshold but how long the hypotension persists to be called hypotension.

So if you looked at drops of, you know, below 65 mmHg for one minute, it would probably happen in 70 or so patients; 70% of patients or more. I think a definition that certainly is becoming more prevalent a MAP, mean arterial pressure, of less than 65 lasting for 10 or 15 minutes, I think that it would probably occur in 30% of patients, or somewhere in that neighborhood. So it is prevalent. There's no question that it's prevalent. And we all know that. I mean we take care of patients and we know that the pressure drops after induction or after various other events.

Dr. BobbieJean Sweitzer: And what about the consequences? Do we have evidence that this is truly harmful to patients, these different both levels of hypotension as well as duration, as you mentioned?

Dr. Charles W. Hogue: Well I think what's really been a great development over the last several years, maybe decade, is the electronic health record has allowed big data analysis of this question. That is is there an association between hypotension, how you define it, and adverse events? And there are now a fair amount of data that suggests that there is an association between a MAP below 65 lasting ten minutes or so and some adverse events, including acute kidney injury, myocardial infarction and maybe even mortality.

I caution, though, first that there are now data that also shows that hypotension after surgery may even be a more important predictor of myocardial infarction, but let's just say that there are data to suggest that a MAP below 65 for some period of time is associated with organ injury. I think that we have to realize that these are associations and not cause and effect. In terms of, you know, associations could be just they co-locate statistically with other things that could cause these same injuries. So there is this growing concern that this is, indeed, a potentially modifiable risk factor for adverse events after non-cardiac surgery in adults.

Dr. BobbieJean Sweitzer: Now Dr. Maheshwari, as Dr. Hogue has alluded to, there are various definitions of hypotension. He mentioned, I believe, just the one MAP of 65, but for different time periods, but others have, you know, suggested other definitions. And I want to ask Dr. Hogue to expound on that a little bit more later, but for this study how did you define hypotension?

Dr. Kamal Maheshwari: So for this study we defined hypotension based on our work and the work of multiple other groups using the threshold of 65. And we also had to define a duration, and so we used one minute as the duration. So what we were predicting from the HPI alert is that can it predict MAP less than 65 for one minute.

Dr. BobbieJean Sweitzer: So can you tell us a bit about the cohort of patients that you enrolled and the types of surgeries they were having?

Dr. Kamal Maheshwari: The hypotension, as Dr. Hogue alluded to, does happen in pretty much all surgeries. It is the extent of hypotension which is different among them. So given this was the first study and a pilot study, we focused on high risk patients in which the likelihood of hypotension will be higher. So that's why we chose ASA III and IV patients, and the other absolute requirement was they had to have invasive pressure monitoring, because that was required from this algorithm to work for this particular set. And we focused on moderate to high risk surgery patients that all in line basically and going towards the patient who is likely to suffer from hypotension. Then we did have to exclude some patients, especially with fever, (inaudible), arrhythmias. Because some part of the algorithms, especially in the treatment side, depend on normal sinus rhythm.

Dr. BobbieJean Sweitzer: So in addition to the use of this hypotension prediction index to predict the hypotension, as you've noted, you also employed a treatment algorithm. Can you tell us more about that treatment algorithm?

Dr. Kamal Maheshwari: The treatment algorithm was a slightly difficult part because there's no algorithm which is fully defined or, you know, evidence based to say that if hypotension happens, do this. We usually go by three basic principles that we define the status of pre load, after load and contractility. And then based on that we go for treatment that should we give fluid, should we give inotropes and should we give vasopressors.

So based on these principles we made a treatment algorithm which was based on advanced hemodynamic parameters, including stroke volume variation, (inaudible) and dP/dt, which is a measure of contractility, SVR. We utilized all this to take us through a definite of treatment. The goal was to reduce the variability in treatment that once the alert happens the clinicians do some predefined things, and which are evidence based and which are guided by the data.

Dr. BobbieJean Sweitzer: Dr. Hogue, do you have any comments about that treatment algorithm?

Dr. Charles W. Hogue: Well, I think that it's appropriate and it's, you know, I think kind of like it might help clinicians get to the bottom of things. But I think clinically what many of us do, right or wrong, is we typically would treat the hypotension with a vasoconstrictor or open up the fluids and give a bolus of fluids while we're trying to sort through what the causes are. That's a little bit more difficult to do in a clinical study, I think. But I think the algorithm is appropriate, and having this data would be useful if it's, you know, derived and give you, like, an indication like stroke volume is low, then you might just open up the fluids. All these things take time, though, right. So, you know, we often just give a vasoconstrictor or something to get the pressure up while we're addressing the underlying cause. But I think that the algorithm looked very appropriate, in my view.

Dr. BobbieJean Sweitzer: I want to come back to what defines hypotension. And as we've heard now from Dr. Maheshwari, they defined it as a MAP of less than 65 for just a single minute. So I know, Dr. Hogue, in your editorial you did raise concerns about what defines hypotension, and you discuss that a little bit, but can you elaborate a bit more?

Dr. Charles W. Hogue: Yes, I think that the definition is based on evidence that's sound in retrospective studies that indeed that this is what people have found. But our group has been involved for the last, I hate to say nearly 15 years now, looking at monitoring patients more precisely with cerebral blood flow auto regulation at the bedside. Not to elaborate too much on that, but we can monitor patients now and determine the lower limit of auto regulation in real time, or near real time.

And the idea being that you could precisely pick that blood pressure which best profuses the brain. And what we've found is that the lower limit of auto regulation, despite what we've been taught, that is 50 mmHg, in everybody it's not. And it varies markedly. Our data is mostly from cardiac surgery; not exclusively. We do have data from shoulder surgery, from lumbar spine surgery. But by and large what we found is that this lower limit varies markedly between, like, 40 and 90 mmHg. And when we look back at some of the older data that have looked at the lower limit, they've noted this, too, in the past that it varies markedly between individuals.

So to say that one blood pressure fits everybody will never be 100% precise. It may be best evidence at the moment. Our belief is that this is an individual definition, if we want to be entirely precise. Unfortunately, our monitors aren't available yet. They will be, eventually, to clinicians so, you know, we have to do something in the meantime.

Dr. BobbieJean Sweitzer: And I assume that some of these prediction indexes could be programmed such that the alerts could be personalized for a particular patient…

{Crosstalk}

Dr. Charles W. Hogue: Absolutely.

Dr. BobbieJean Sweitzer: So Dr. Maheshwari, what do we already know about this hypotension prediction index or was this the first study to evaluate this clinically?

Dr. Kamal Maheshwari: The hypotension prediction index was developed in 2017-18 and the first paper was published for validation based on retrospective data. So there's few other retrospective studies in different cohorts where validation was done, in which what you do is you apply the algorithm, you report the sensitivity and specificity of your prediction. The next step is that when you use arterial pressure waveform, with the recent advances you can generate arterial pressure waveform using noninvasive. And so we did one study in our group in which we validated using noninvasive arterial pressure waveform, this algorithm, so it does work with reported sensitivity and specificity around, you know, 85-90%.

And so that's the data that, yes, it does predict what it's designed to predict. And that design is important, as Dr. Hogue mentioned, that whatever your target of blood pressure that you want to predict, that can be changed and there's, yes, huge individual variability that which blood pressure will be harmful for that particular patient and for how long it's going to be harmful. And this work on auto regulation is very good. And then you have to look into different organs. Is it because of brain or cardiac or myocardial injury or kidney injury? So there's a lot of complexity, {laughs} if you will, into defining the endpoint or the target of any algorithm. But to get the work started here, to start at one definition and we chose the definition of MAP of 65 based on some available evidence.

Then the next step is, if it is validated, how does it work in the prospective setting or in prospective trials? So there's two randomized trials which have happened, and both were published this year. The one was from our friends in the University of Amsterdam. They randomized 60 patients with or without the use of hypotension prediction index, and they showed almost 400% improvement in blood pressure, that means a four time reduction in hypotension with the use, which is remarkable. And our group with the study which we are talking about, we found something different. So that's the current state of literature regarding the use of hypotension prediction index.

Dr. BobbieJean Sweitzer: What outcomes did you address with this study?

Dr. Kamal Maheshwari: In this study, this was a pilot study designed to see how does the prediction index work and change of clinical care. And we wanted to understand the treatment effect and how people utilize it. So that's a predefined pilot study. We used just the blood pressure as our primary outcome. And we used a time weighted average less than 65, area under the curve less than 65 and minutes less than 65. We used all these three definitions, because they can affect your treatment (inaudible) which you're going to record. And we also looked at different thresholds. That not only 65, we used lower threshold 60 and even lower threshold 50 in both groups, so to get our full understanding of the amount of hypotension happening in both groups. And that was the goal of the whole prediction system is that we will be able to reduce hypotension. And as an exploratory basis, we also looked into multiple different hard outcomes including myocardial injury, kidney injury, death, stroke and a whole host of postoperative morbidity outcomes.

Dr. BobbieJean Sweitzer: I guess this index prediction tool is essentially a artificial intelligence tool. Dr. Hogue, we know there from other studies artificial intelligence tools have been shown to augment decision making, and even improve safety and outcomes in some medical situations. Can you maybe tell us {laughs} a bit about where we are today with AI in medicine and maybe specifically in anesthesia.

Dr. Charles W. Hogue: In two minutes or less? {Laughs}

Dr. BobbieJean Sweitzer: Sure. {Laughs}

Dr. Charles W. Hogue: No, I think that artificial intelligence – I mean this is a very exciting time in medicine that we can have the capacity to help our clinical decision making and have predictive analytics. And the hypotension prediction index I think is an excellent use of artificial intelligence. But, you know, does the artificial intelligence completely take over medicine so we can basically do artificial intelligence to give an anesthetic by a robot? People may be working on that, but I think what we're looking at in 2020-2021 is more like can we use artificial intelligence to enhance our clinical decision making?

And there's lots of interesting things, and I must preface this by saying that I'm not a machine learning engineer; I'm just a clinician. It's really very interesting. I'll give you a couple of examples {clears throat} where I think that this is just sort of, like, epitomizes how this could be used. One example is in pediatric cardiac surgery. My colleague Ken Brady who is now at Lurie Children's Hospital here in Chicago Northwestern helped develop an algorithm. Children after single ventricle surgery have a high incidence of ventricular tachycardia. They used big data derived from the EKG, from the arterial waveform and from other information in the medical record, and things you cannot see with your eyes, to develop a predictive analytic model to predict VT in these kids. And they were able to predict it an hour before it happened with an area under the curve of the predictive model of, like, .91.

Dr. BobbieJean Sweitzer: Wow.

Dr. Charles W. Hogue: So they put this into use. They send this information to the nurses, to the physicians on their iPhones or whatever, and they've dropped the incidence of ventricular tachycardia in these children astronomically. And it's soon to be the standard of care, I think, in these kids. Which we were very, very – you know, there's no room for error; margin of safety. So this is an example where the predictive analytics is going to make a difference to patients.

I think another example is, you know, members of our department, you know BobbieJean, have worked very carefully with some major information companies—and I'll just leave it at that and not give their names—who have the computing wherewithal to do big data analysis, because to do these things you need a lot of data. I mean a lot of data. And they've helped build algorithms to look at CT scans and mammograms. On the CT scans they looked for tumors and from mammograms the development of tumors. And what they've done is they built models that can enhance the ability of radiologists to find tumors, even up to a year before they actually happen. So can you imagine somebody who is going to have a breast tumor one year from now gets a mammogram and the computer says, you know, you might want to look a little bit closer here, how that might change their lives.

So there's tremendous ability that I think (is) available, but we have to temper this with, you know, how we set our expectations. But it's all very exciting and I think this is going to enhance health of populations.

Dr. BobbieJean Sweitzer: Yes, it is very exciting and very cutting-edge. Dr. Maheshwari, can you explain the options that these clinicians had to choose from in the treatment algorithm that was used in your study?

Dr. Kamal Maheshwari: The treatment algorithm, as we were talking earlier, was primarily based on figuring out if it is a preload state or after load state or contractility state, which is a problem. And our thought process was to identify responsiveness of fluid responsiveness with the use of stroke volume variation, adjust the tone, but using SVR and dynamic last and contractility using dP/dt. And based on these parameters we made an algorithm.

And what it ended up is resulting into six different treatment options for clinicians, which is either that they would be giving fluid plus vasopressor, fluid plus inotrope, fluid only, vasopressor only, inotrope only, and we also kept an observe, you know, to give the decision making to the clinician that, you know, you have an option not to do anything. And that's how we approached this treatment algorithm.

Dr. BobbieJean Sweitzer: So Dr. Hogue, you previously raised this issue about the occurrence of hypotension in the postoperative period, and I believe you also wrote about that in your editorial. And that that may be more dangerous than intraoperative low blood pressure, especially related to, I think, cardiac outcomes. What do we know about that?

Dr. Charles W. Hogue: I don't think we know as much, but we do know that hypotension after surgery, particularly in patients in intensive care units, is common and maybe not detected as well, particularly if you don't have an arterial line as we do intraoperatively where there's an anesthesia team watching the monitors continuously. And the paper that we reference showed that hypotension after surgery was more predictive of myocardial injury than the intraoperative hypotension. We have data in cardiac surgical patients that we've published and are about to publish looking at hypotension using our auto regulation endpoints. And we've shown that sort of the magnitude and duration that blood pressures below the lower limit of auto regulation in patients after cardiac surgery predicts brain injury biomarker release.

So, you know, I think that we have to look at the big picture that it's not just what happens in the ORs, but what happens afterwards in the PACU and the intensive care units. And I think that that's another area that we're going to have to include these tools to enhance the care of patients.

Dr. BobbieJean Sweitzer: Yes, and I assume that, you know, just as you mentioned with Dr. Brady's study and the study of Dr. Maheshwari, that these devices can likely be used to predict, you know, future events. And particularly in settings where perhaps you don't have the watchful eyes of anesthesia providers so closely. Dr. Maheshwari, what did you find in your study?

Dr. Kamal Maheshwari: Based on our study in which we used HPI guidance, which is hypotension prediction index guidance in one group and no guidance in another group, we did not find any difference in the amount of hypotension in both groups. Specifically, when we used the definition of time weighted average of MAP less than 65 or area under the curve map less than 65, or even the duration of the minute. And there was no difference even using different thresholds. So it's fair to say that our primary goal was not achieved, which we thought that we would be able to reduce hypotension.

When we try to understand the reason for this lack of difference, and we did a post doc analysis, what other (inaudible) which we learned from this study was that around half of the 1,500 alerts which were there, they were not followed by treatment. That means there was an alert and half of the time there was no treatment which was given. So those are the findings which are going to help us understand why we did not see a difference and what should be done going forward in the future.

Dr. BobbieJean Sweitzer: Dr. Hogue, were you surprised by these findings and why or why not?

Dr. Charles W. Hogue: Well, yes and no. I mean given the prior publication that showed such great prediction in advance of the hypotension, I was a little surprised. But when you look at it, what Kamal just said about half of them were not acted upon; there's many hypotensive episodes that happen during anesthetic that we are looking at the field and we know that the surgeons just, you know, lifted up – impeded venous return by putting pressure on the IVC, or they've done the, you know, a maneuver during a hepatectomy or whatever that we know that they're temporary and they'll reverse.

So the HPI algorithm looks at characteristics of the arterial waveform, along with other things, to develop the algorithm predicting hypotension. But this algorithm would not be able to detect when a surgeon's going to lift up the liver, right, and cause venous return. And during cardiac surgery we see this all the time when they pick up the heart or move the heart or whatever. These would not be necessarily picked up by changes ahead of time in the arterial waveforms or the dynamics of arterial waveforms. So it's not surprising.

And I think that clinically we know this. As clinicians we're looking at the field. And so I think that in future studies, and like they looked at their analysis and the hypotensive episodes that were acted upon, their HPI index actually performed better when they looked at their appointed time weighted average of hypotension. So I think that there's still going to be a need for clinicians to filter through; to put in the results into the clinical context. And in that case, this can probably augment our intelligence, but it's not necessarily – you couldn't necessarily build an (sounds like: aserval) pump with phenylephrine, maybe, to treat a surgeon doing the Pringle maneuver, for example, or whatever.

Dr. BobbieJean Sweitzer: Yes, and I guess if a goal is to prevent rather than treat, there's sort of different goals there, right. Even if the surgeon is going to lift it up. Is it possible that perhaps the design of the study such that it was also predicting such a short duration of hypotension, just one single minute, influenced these results heavily?

Dr. Charles W. Hogue: Well, yes. I guess, you know. So if you would have made it a longer duration, five minutes or so, versus just the one minute, you know, I'm sure they could have. But, you know, I think it was a well thought out, well designed study. Very interesting to read. The data are very interesting. But it's still these observed versus acted upon hypotensive events I think is the distinguishing feature between this and prior publications.

Dr. BobbieJean Sweitzer: Um-hum [affirmative]. Dr. Maheshwari, what was the average time between the warning from this prediction index and the actual development of hypotension? And how do you think this impacted results?

Dr. Kamal Maheshwari: I want to clarify one thing and that is the alert and event episode. So in any prediction system you're predicting at a particular time that is the alert time. And the event which we are predicting, this is hypotension in less than one minute, and that's the difference from the alert/event episode we are talking about.

So the alert was at 85 when HPI index went to the level of 85, and that becomes our alert threshold. Then the event was whenever hypotension happened and it lasted for at least a minute, right. So on an average, this difference of time was four minutes. You had four minutes from alert to the event. But that's an average. That means that we did have a lot of patients or a quarter of patients in which the warning time was less than two minutes. And then the question is even if the clinician wanted to intervene, they wanted to give fluid and they started hanging up fluid, was that enough time for the treatment for avoiding hypotension altogether?

So that is a critical issue for any prediction system; that how much time you are giving for intervention and what intervention will be done. And sometimes, you know, as we did not see any difference in hypotension, one of the things which we are trying to figure out is that can we increase this time that alert of an episode?

Dr. BobbieJean Sweitzer: How often did the index predict hypotension that did not occur, or how often did it not predict hypotension that did occur? Were you able to tease this out and measure?

Dr. Kamal Maheshwari: Sure. It's a good question, and we have to give a background or context of one lab test in which nothing is changing from the time you took a test and you obtain saying positive or negative. Compared to hypotension index where you took a test, that means alert was given, but before it became positive or negative we are intervening. We are changing the surrounding situation. And that's an important difference which makes it difficult to answer your question directly. What is the positive predictive value of this test based on your predicted and observed value for outcome?

And it's an important question, because the false positive test or a false positive alert can lead to some unnecessary treatment. But when you use the HPI as an alert and you give the clinician – the clinician intervenes and that complicates the assessment or evaluation of the data based on positive and negative predictive values, and trying to figure out the true false positive results.

Having said that, what we have to look into this system is what we were trying to achieve. If the goal was to use this alert system and reduce hypotension, then we can focus on did we actually achieve reduction in hypotension or not, irrespective of the performance of that alert in this prospective fashion. And that, I think, is a better way to approach this problem or to answer this question. And then you can say that okay, you had a validated alert. You put it into the place, but it did not achieve our desired outcome, or it did achieve our desired outcome, for example hypotension.

Dr. BobbieJean Sweitzer: Dr. Hogue, what do you think we need to help clinicians avoid or limit intraoperative hypotension?

Dr. Charles W. Hogue: I think this is the right approach. Should we limit hypotension? I think that it's a very important goal to have. Is it easy? No. I mean it's not easy because there are so many variables, measured and unmeasured. I always like to give the example of somebody with diastolic dysfunction and hypertension on an ACE inhibitor that they took on the morning of surgery. They're going to be difficult to manage, likely, anyway.

So I think that the tool is probably a great first step and I think that we could probably refine it; get better. And if we could, you know, keep up with euvolemia, we could, you know, keep up with (sounds like: astertone) and inotropy and cardiac filling to prevent it, I think the tools would be very useful and could have the potential of improving outcomes.

Dr. BobbieJean Sweitzer: So Dr. Maheshwari, at the end of your manuscript I believe you write that a planned future full trial will use a lower alert threshold and a simpler treatment algorithm. Sounds like you're already working on this next step. Is this trial underway and can you tell us more about it?

Dr. Kamal Maheshwari: Yes, given our pilot trial, that was our primary goal to understand what's going on when we use this kind of predictive software to change clinical outcomes. You know, we hoped that we would be able to show the process outcome, which is hypotension was different, but unfortunately not. And what we learned is that as we talked about the time to treatment, you know, in some cases which is only two minutes, and as you mentioned earlier in some cases it's so sudden that there's no time to intervene. So even if we take those conditions of sudden events of hypotension away, there's still a lot of hypotension which can be avoidable. And I think the time to event, if you give more time to the clinician that can help, and reducing the threshold from 85 to let's say 60% probability or 70% probability that will give clinicians more time. It might result in a slightly higher negative predictions, but definitely will give more time for the clinician to act.

That's one. The second is the treatment algorithm. As we mentioned, the treatment algorithm was not validated with high quality science, but definitely we learned from the treatment algorithm that the observe component should not be there. We plan to remove that, and we think that all alerts should be treated in one way or the other.

And third is the compliance, which was the bigger issue. If there's an alert and there's good data that alerts usually follow with hypotension, education regarding this data can help improve the compliance on the treatment; that they will intervene. So based on, you know, giving more time to the clinician for treatment and making sure that they do treat most of the time will be the two major changes which we are trying to do for the future trial. That was the learning from this pilot.

And yes, this planned but did not start, as you know, unfortunately because of the coronavirus infection and epidemic. You know, most of the research plans are being delayed or postponed. {Laughs} We are in that situation.

Dr. BobbieJean Sweitzer: Yes, it's unfortunate times, isn't it. But I hope today's discussion will interest many of our listeners and lead you to read this important article and editorial to learn more. Thank you Drs. Maheshwari and Hogue for discussing your work with us today. I wish you well as you continue your efforts to enhance the practice of anesthesiology and strive to improve the care of our patients.

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