

[MUSIC PLAYING]

**DANIEL
FORMAN:**

Hi, everyone. My name is Daniel Forman. I'm at the University of Pittsburgh, as well as the VA Pittsburgh Healthcare Center, as you see by my affiliations below. I am so pleased to be speaking in this program on Geriatric Update, with a particular focus on cardiology. My focus today is on tailoring hypertension management for older patients.

And I do want to start this talk, as I start many, with this focus on the likelihood of developing cardiovascular disease in older age. We see here a slide that shows age across the x-axis. And we see the higher prevalence of cardiovascular disease and correlation with aging. And for many years of my career, and many of you in the audience, I imagine, this was thought as an epidemiological phenomenon, with the thought that what an interesting coincidence that as people live longer there's more disease.

But we now know at Pittsburgh, and really throughout the world, there's this notion, this insight about geroscience, these mechanisms of aging. And this is a very classic schematic by Carlos Lopez-Otin, that depicts various mechanisms that change on a subset of the level and the gene, and the gene expression, the telomeres with protein-folding with prosthesis, mitochondrial changes-- a variety of constituents that drive the likelihood of cardiovascular disease as a function of living longer.

And now as people are living longer-- the average length of life is about 80 now throughout much of the world, and that's about 30 years longer than it was even 50 years ago-- it means that people are living long enough for these changes in the cells and the subcellular mechanisms to have downstream effects that are pretty profound in how our bodies work.

So whereas, one time really even in my career and many of your careers we thought of vascular aging is predominantly wear and tear, your heart pumping 24/7, the vasculatures working 24/7. And there are downstream effects that are well-known in terms of changes of blood pressure-- systolic blood pressure going up, changes in diastolic blood pressure, and downstream effects in the kidneys in the heart and the brain, we now know that it's really driven not only by the mechanical stresses that I described, but by the mechanical stresses in the context of changing biology.

So, again, this Carlos Lopez-Otin schematic really showing that there are molecular changes that profoundly changed the way the vasculature works with elastin breakdown, and changes in endothelium with fibrosis and amyloid, and changes of the vascular smooth muscles, and changes of intima-medial thickening. So all of these things are contributing to the fact that we do have changes of blood pressure-- a number.

But it's not just a number. It's a number that really reflects a very significant change on all levels of the vasculature and how things are working physiologically. And this notion then that we have changes that are pretty fundamental in how our kidneys and our heart and our brain work in association with the vasculature, that goes right down to a molecular level in each cell as a function of aging. And that's really where we are, as we think about blood pressure now in the context of our sophisticated insight.

So, again, this notion that has been around for decades-- arterial stiffening with aging, with higher blood pressure and widened pulse pressure-- yes, that's well known. But we now know it's not just that. It's that the entire vessel has changed.

And this is a busy slide, and I'm not going to go through it in detail, but just to emphasize that the endothelium, the intima, the media, and the adventitia-- all these layers of the vasculature are changing as a function of aging, function of geroscience and these mechanistic principles on a subcellular level.

It's not only the fact that our vessels changed in terms of the architecture, it's that the architectural changes are occurring in the context of greater ambient changes-- changes of the cellular processes with diminished mechanisms of autophagy and cell repair, and changes of cellular senescence with higher inflammation, and the tissue properties where the inflammation, the oxidative stress, is really profoundly changing the whole mechanisms that really are directly impactful on the endothelial dysfunction and the way our bodies work.

And if that was not complicated enough, it occurs in the context of multimorbidity. Cardiovascular disease is compounding on themselves in the midst of additional noncardiovascular diseases, fundamental changes with frailty and polypharmacy and falls. And that is, in itself, increasingly complex for the patients and for our roles as caregivers caring for our patients.

But it's compounded even more by effects of hydration-- the fact that the thirst of patients is diminished in many cases; changes of heat, especially with global warming and diminished access in many cases to air conditioning and other ways of keeping body temperatures cool. So, again, if we think about just blood pressure, we're really missing the complexity that we were there challenged by.

That all said, so why is it important to treat blood pressure in our older patients? Maybe it's too much. But I want to go back to the fact that we already know that the downstream effects of blood pressure are profound in terms of increasing cardiovascular risks, neurological risks, renal risks, and others.

So we have this constellation of risk that compounds with blood pressure, heart failure, ischemic heart disease, atrial fibrillation, strokes, diminished cognition, renal disease, and even more insidious through things like exercise intolerance, which in many cases compound all the other diseases as people become more sedentary.

And then really to emphasize the fact these things rarely occur as single problems. They're usually in aggregate with heart failure and diabetes compounding on themselves, and other constellations of dyads and triads and other groups of diseases. And so when you have a person with this many risks, the absolute benefit of treating blood pressure, treating risks, is greater because the downstream risks are so high.

So better to intervene and treat blood pressure perhaps, knowing that you may have some benefit in modifying this progression to bad outcomes. And that's been a driving thought process in many of the hallmark trials or the landmark trials of blood pressure, to see whether we can moderate this otherwise likely progression to downstream bad outcomes.

So then the more fundamental question is, what is blood pressure? We know that normal aging involves stiffening of the vessels. We've seen that. I've tried to show that quickly, but I think it gives you a pretty strong sense that the vessels are stiffer, and there are many associated biological effects that occur with that, and it's progressive.

So we know that blood pressure-- systolic blood pressure tends to go up throughout a lifetime up until one's 80s. Diastolic blood pressure tends to go up until the 60s, and then it tends to fall. So there is this predictable pattern. And within that pattern we have this notion of trying to treat this phenomenon and it leads to many questions.

Is treating blood pressure the same at every point of time? If someone is 80, is it the same as when they're 70? If they're 80 and active, is it the same as when they're 70 and sedentary? There are many different idiosyncrasies of each patient. There are many different idiosyncrasies of a person over time that are relevant when we think about treating blood pressure.

What I do also want to emphasize is the vessels get stiffer, there are fundamental risks of treating blood pressure too greatly. If we drive down blood pressure too much, especially for vessels that are stiff, we can lose fundamental perfusion through the vessels to the heart and to the rest of our bodies. And if we drive down diastolic pressure, we lose fundamental ability for the vessels to fill.

So it's been shown this is a complicated literature, but if you treat people with stiff blood vessels, such as those with diabetes or ischemic heart disease with systolic blood pressures below 120, you can do them a disservice. If you treat diastolic blood pressure is usually below 60, people usually have worse outcomes. So, again, many conceptual reasons to treat blood pressure; many conceptual reasons to be concerned.

I go back to the premise that blood pressure elevation is endemic with an aging population. It is normal physiology. So then when you want to identify hypertension, pathological blood pressure, it becomes complex in that normal aging constellation or perception. And when one thinks about what's the point to treat blood pressure, it can really vary, depending upon the studies that have been used to justify treating blood pressure.

And the notion of high prevalence of blood pressure can shift on a dime if a study decides that 140 is the right cut point, if 160 is the right cut point, if 130 is the right cut point. So we know that blood pressure prevalence is high. We saw that slide earlier, and many that you've probably seen. But the notion of how high-- is it 40% of the population or 70% of the population varies from study to study, depending on who is being studied.

So I think of blood pressure myself, and for the sake of this talk, with a challenge for each patient. So this is a patient that's in front of you. I frequently use this picture. It's Google. It's no one I know particularly, but she represents what I think is typical.

You have a population that is fundamentally predisposed to blood pressure, hypertension, abnormal blood pressure as a function of aging for which there is risk. We know that people who have this problem are fundamentally predisposed to cardiovascular disease, to brain disease, to kidney disease. But it's in a context of multimorbidity where these diseases can compound themselves with associated polypharmacy, with associated frailty and falls and vulnerabilities.

And it also occurs in the context of fluctuating health status. People will have viruses. They'll have COVID. They'll have various things that can really suddenly confound the plans of treating them. Different medications can work against them with polypharmacy. Fluctuating circumstances with weather, diet, alcohol intake.

And then as you're trying to treat them, this notion of how long till benefit and how long to harm. Benefits I think you probably heard yesterday in these talks the benefits for treating orthostatic hypotension. We know there's benefits for renal failure. There's notion of treating cardiovascular disease to be sure, diminishing dementia and other types of cognitive impairment.

But likewise, on the opposite side of the same coin, orthostatic hypotension can be exacerbated by treating blood pressure. And renal failure can be exacerbated by treating blood pressure. And falls and fatigue and other types of downstream effects can also occur, depending particularly on the rapidity with which we treat blood pressure, and the fluctuating status of patients through the course of a normal lifetime.

So as we think about blood pressure, I've mentioned that the notion of what is abnormal blood pressure has varied from trial to trial. We see that the predominance of trials-- this is a slide that was taken from a European study that shows the overview from-- through Europe, China, and Japan, showing that the trials have tended to target systolic blood pressure, particularly. An aging population with stiffened vessels tends to have a higher systolic pressure, and showing numbers of 150 to 140 predominantly.

And then we have suddenly the SPRINT trial, which is looking at patients-- or treating blood pressure to 120-- a very dramatic difference as targets of blood pressure with a notion of what is abnormal blood pressure to treat. So the SPRINT trial of systolic blood pressure intervention was really a huge trial-- much different target of blood pressure therapy; enrolling people that had a systolic blood pressure greater than 130 and treating them to see the benefits of lowering blood pressure to 120.

So a much more aggressive treatment, and it included a subgroup of over 3,000 people that were aged over 75, and showing these predominant benefits that were true in the population overall, which is over 10,000, as well as the subgroup that was over 75% of a very significant improvement of a composite of MI acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes, as well as all-cause mortality, with the benefit of this more aggressive blood pressure therapy.

So this was somewhat of a game-changer in showing in this huge trial, published in *New England Journal*, that we could treat blood pressure to this degree even in a very old population with downstream effects. And this is what has driven guidelines, which I think you probably all think about as you treat your patients.

But who are the patients in SPRINT? So this becomes very controversial. This by Jeff Williamson-- a study highlighting the fact that these patients included blood pressures at enrollment that were on the average of only one 141.6; diastolic blood pressure is 71.2. This, to me, is particularly significant. The number of hypertension entry were 1.9. So that we see that this is not a population that to me is among those that I would consider the most challenging when I care for my own patient. This is a relatively select population.

It also had controversial elements in SPRINT that the blood pressure was taken using this automated system. It involves having patients sit. There was a great deal of rigor, but rigor that seems to be somewhat exceptional compared to what most offices use to assess their blood pressure. And it creates some elements of confounding the results with a variety of measurements that were perhaps exceptional and not routine.

And this is probably the most important element. When one thinks about the SPRINT trial-- I mentioned that the population did not have that many meds. They did not have blood pressure that was that high. But this beautiful slide by Michelle Odden really highlights many other features, that when you think about this SPRINT exclusion criteria, it included patients that had-- the exclusion-- those that had strokes, those that had diabetes, those that are from nursing homes, those with dementia, heart failure, those with severe functional limits, those that were homebound, those with orthostatic hypotension, for which we think that blood pressure is good-- or blood pressure management is good. But here we just excluded those in enrollment.

So 1/3 of the people that were screened were ultimately admitted into SPRINT. And to me, that's probably accurate, that among the patients that I treat, this blood pressure criteria is probably reasonable for about 1/3 of my super healthy senior adults, or older adults that are 75 and over. And that was the conclusion of Michelle Odden, and that's been the conclusion of many people who look at SPRINT as being somewhat of an important trial of showing one type of aging demographic that will benefit from this treatment.

But this work by Adam Bress really points-- even within the SPRINT population, higher incidence of hypotension, higher incidence of syncope, higher incidence of electrolyte abnormality, higher incidence of acute kidney injury or acute renal failure. So even with this super healthy population, or relatively healthy population, we see these problems arising among those treated aggressively to get the greater blood pressure reduction in an older population.

The overriding benefit in that population still persisted. It was still the predominant benefit. But if you take SPRINT, and you generalize it to the broader population that includes those with diabetes, that includes those with ischemic heart disease and other issues that make vessels stiffer, one wonders whether these types of adverse effects will be disproportionate in the midst of those greater risks.

So to me, SPRINT is really very narrow in its implications for about 1/3 of my patients, not for everyone. And it really flies in the face of what I think we all live with. The guidelines were driven in 2017 by the SPRINT trial.

And so they came out with a 1A recommendation of less than 130 millimeters of mercury. They were compromising. It was a consensus. We are not going to go to 120 like they did in SPRINT, because we're not sure about how they measured blood pressure and such. But we're going to go to 130 for everyone.

So that was-- and this was very well-intended because they thought this has a predominant benefit in lowering risks, as I highlighted earlier, in terms of these powerful mortality and morbidity risks. And then for the vast majority of patients, I would argue, that were over 65, there was this description of those that you would not treat with for high blood pressure, including those with comorbidity and limited life expectancy. And they asked the physicians to use judgment and patient preference and a team-based approach. These are all very well-meaning words, but to me they're somewhat ambiguous of what you do.

And my issue with these guidelines is that when I have a daughter or a son or a spouse saying that the guidelines say 130, Dr. Forman, and you're using a cut point of 150, you're missing the best care for my loved one, I feel like these guidelines become a very great stress for me as a caregiver because they don't really incorporate what I would say is the more important elements for each individual patient.

I'm very fond of this work by Daniela Anker. She's published many accounts. This is one in which-- just highlighting that there's about 15 studies here that she juxtaposes next to SPRINT. And she shows that in each one of them-- and there are a variety of excellent studies, and she's shown more in other subsequent publications-- that those that are treated-- those that are very old, those with diabetes, those with ischemic disease who are old don't do well with the blood pressure stringencies of SPRINT.

So it raises this notion of equipoise about what really is the best blood pressure, and this notion that tailored care becomes more important. Anker's work really is encapsulated in this one type of representation of the ACC/AHA guidelines, that are the American guidelines, that show the value of treating older adults to a blood pressure target of 130-- less than 130 or-- particularly 130-- less than 130, including those that are 65 and over.

And she compares that to the European guidelines which came out a year later, which typical for most of the world, stratifies blood pressure in those that are older. And in this case, it shows that those that are 80 or over, the cut point is targeted as less than 160 over 90, with the goal of treating blood pressure to about 130 to 139 for those that are 65 and over. And even having a higher cut point for those that are-- clinical or therapeutic cut points for those who are 80 and over. So, again, tailoring care relative to the relative age and complexity of patients.

I want to emphasize this. Canadian guidelines-- for those that are very frail, they suggest treating blood pressure between 160 and 190-- very high targets, vastly different from those that would be in the American guidelines, and certainly different from SPRINT. The Chinese guidelines recommend treating blood pressure to less than 150-- systolic blood pressure less than 150. So, again, really providing the perspective that there's an international difference of what we think is the right cut points to treat blood pressure.

If we go back to our patient, that individual patient before you, I would say that this notion of treating the guidelines-based target can be, I think, a little bit misleading and precarious. But that said, I do want to just highlight that *New England Journal* published yet another landmark article, a public study, in this case, called STEP-- Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients from China.

Again, a younger population, relatively-- 60 to 80 years old-- mean age 66, 20% with diabetes in this case, but showing a powerful endpoint to reducing a composite outcome that included stroke and ACS, heart failure, revascularization, atrial fibrillation, and others. And we see all of these benefits individually with stroke and such, as well as the composite that are quite powerful and really rejuvenate the notion of very aggressive blood pressure therapies.

And I want to yet highlight another perspective. This is an international study from the Blood Pressure Lowering Trialists Collaboration. And it highlights the fact that if you treat blood pressure based upon aggregate risks. This is a cardiovascular risk index. Rather than the treating to a number, that there's a greater benefit in improving care and avoiding unnecessary events.

Going back to that slide that depicted all the possible side effects of overaggressive blood pressure therapy, this article would really argue that if you treat to the risk and not just to a number, you will have a way of refining that-- or offsetting some of those possible events with greater efficacy of care.

So, again, this is not definitive. This is a very provocative study that really highlights a concept that I would really argue is very relevant for each patient that's in front of you as you treat their blood pressure changes with aging. Treat risk, don't just treat a number.

And with that perspective, I really want to emphasize this notion of the relevance of frailty. Frailty will really profoundly change the value and the effect of treating blood pressure. But this has been hard to incorporate into clinical practice because we don't really have a uniform way of thinking about frailty. And this is a topic, which I think many of you know well.

And I'm not going to spend too much time just to mention-- but just to mention that some people think about frailty as a phenotype characterized by this weakening or slowing or weight loss and exhaustion in activity. Some would think of it as an index based upon a deficit accumulation index. And the way that that is assessed, and the way it's-- and what it actually measures varies. So there's been a little bit of an ambiguity about how to best employ this notion of frailty to treat blood pressure.

This is a landmark study by Michelle Odden. Again, I'm very fond of her work. This one really, I think, kind of changed the field. That she looked at people-- about 2,500 people over 65. And she really showed that those that had a high gait speed, looking at frailty in terms of a phenotype, high gait speed-- high blood pressure was associated with risk.

But if she looked at people that had slower gait speeds or who really couldn't walk in that same group-- so they were matched in many other clinical variables, but they had a higher degree of frailty, there was-- the risks of high blood pressure were diminished.

So she really argues from that, that if you use-- if you look at frailty, in this case, with gait speed, you can really subdivide and figure out who would best be treated for their blood pressure and who would not benefit. And this is kind of a controversy.

Going back to Jeff Williamson, one of the lead investigators in SPRINT, they looked at frailty using a deficit accumulation index-- completely different way of looking at frailty. And they looked at it within their SPRINT select population. And they divided out the population-- those that were fit versus those that were frail. And it showed that everyone benefited in this case from treating to a very aggressive blood pressure lowering target.

So Jeff Williamson, a geriatrician, preeminent, would argue, yes, in spite of frailty, we should be treating blood pressure. Michelle Odden would say, no. If you have frailty, you shouldn't be treating blood pressure. So, again, this controversy rages.

And I'm going to finish on yet a kind of a redundant theme, because I'm very fond of this study. This looked at frailty and older adults with diabetes, comparing those that were nonfrail to those that were frail, and really highlighting the fact that in the nonfrail population, treating blood pressure aggressively was associated with increased survival. But in the frail population on the right, treating blood pressure aggressively was associated with diminished survival. So, again, really highlighting the fact that not everyone is the same.

There's a very well-known concept of reverse causality, that as one gets older and one has downstream effects of whatever blood-- if someone has heart failure, for example, and they have a resultant hypertension in the midst of their heart failure, by treating blood pressure aggressively, in that point you're actually-- the overriding effects of the heart failure are exacerbated by treating blood pressure too greatly, and you can actually cause harm. And so this notion is really, I think, the underlying concept of treating blood pressure too aggressively in older age that you can actually contribute to harm inadvertently rather than improving outcomes.

So there are many people that are trying to think about screening our patients. This is a Chinese study-- I'm really not riveting on the study as much as the concept-- that basically argues that if you use frailty as a screen, you should diminish or change your interventions accordingly. Don't just treat the number. Think about the patient. In this case, think about the patient in terms of frailty.

I'm not going to go into details about how you measure frailty because that's still controversial. But you should also be looking at multimorbidity and combinations of meds. So, again, it's hard to generalize. But this is the concept that I think about when one of my patients is in front of me.

So tailoring care to the best suit each patient-- thinking about their aggregate risks in the circumstances, their other meds, their vulnerability to falls; thinking about their preferred goals and this construct that I'm sure you've heard about in the course of this seminar, in terms of the four Ms-- what matters to the patient, their mentation, their mobility, and their other medications. These become very important considerations when I'm thinking about treating blood pressure and to what goal.

And thinking about the medications, but also thinking about their lifestyle. Are there things that we could do beyond just giving them a pill, with all of its associated risks, with improving their lifestyle? So I'll talk a little bit about some of the lifestyle concerns.

But just in terms of generalization, I want to say when we think about patient-preferred care, blood pressure is more than a number. And I think it's incumbent on us as providers, as clinicians, to really think about that with our patients, or to educate them, that blood pressure is a means to vitality. It's not a number. It's the means to preserve cognition and well-being and self-efficacy.

And when we think about a blood pressure, it's not blood pressure itself, it's blood pressure in the midst of other risks. Blood pressure becomes more significant in the context of diabetes, in the context of ischemia and other types of risk that we think about-- in the context of frailty.

And it's important to think about the fact that blood pressure is not static, that it is important to check it in the office, perhaps. But even more important to check it at home and the variety of circumstances throughout a day that it fluctuates. And if we miss the point that it can go down or up, we really may be missing the most important element that will be impactful on management and outcomes.

And one other point is the cadence of management. It's best to treat blood pressure incrementally. I've mentioned orthostatic hypotension. It's a big concern of mine. So if you use a short-acting pill, if you use something that's too aggressive too quickly, you can really exacerbate orthostatic hypotension.

The long-term effects of blood pressure management can improve orthostatic hypotension, but it's really the cadence with which therapy is administered and watching it over time. So having modest targets initially, progressing over time-- that's a strategy. It requires really having trust of your patient's adherence and long-term relationships.

I've mentioned lifestyle. I do want to emphasize that we used to always think of exercise as aerobic because we thought it was predominantly vascular responses that were driving blood pressure. But we now know it's more complex, with inflammation and a variety of other components, along with hallmarks. So strength and aerobic training are both beneficial. And behavioral interventions are also beneficial with Tai Chi and yoga and meditation.

Diet is very important. We know the value of vegetables and fruit and low sugar, low saturated fats. It's not just salt, but salt reduction has been shown in the TONE trial and others to be beneficial-- moderating alcohol intake, diminishing tobacco. All of these things are important-- not just the number. It's really an overall lifestyle.

It's thinking about pain. It's Thinking about stress. It's thinking about sleep quality, especially sleep apnea. It's thinking about weight loss, but not just driving down weight when you can lose muscle mass, but weight loss and exercise in combination. In my mind these things are all important to emphasize when we're thinking about blood pressure.

Likewise, sex differences are different. Women lose the hormonal components of their physiology through menopause, and these can be impactful on blood pressure later. Some of these changes between men and women diminish over time in older old age. But still, they're important dimensions to consider.

Ethnicity, in terms of people's thoughts about pills, about blood pressure, about their cooperation, the socioeconomics, the trajectories of lifelong care-- again, these are all topics in and of themselves, but they're relevant. Rather than just throwing a pill from the guidelines at a patient, these are relevant.

There's a whole literature, and this is true in my practice, to think about assessments at home. And increased use of ambulatory blood pressure monitoring is a way of enhancing perspective of care, really emphasizing the fact that there's hypertension that can occur at home, which has been associated with bad outcomes.

But particularly for my older patients, your older patients, I worry more about masked hypotension. That's less prevalent in the literature, or less focused on in the literature. But the fact is when you have stiff vessels, and you're driving down blood pressure, the fact that patients can have hypotension with associated falls, diminished cognition, and even strokes, that's a profound risk of treating blood pressure. So I think the benefits of ambulatory blood pressure monitoring are really very significant, especially when you're titrating meds.

But I also want to emphasize surveillance is important, but the trauma of surveillance can also be disproportionate in older patients. I have had patients where their family members are waking them up in the middle of the night to check their blood pressure. And it's disruptive. It's caused stresses. So I think that we have to have a nuanced touch about how we emphasize the value of surveillance without making it an end unto itself that's more trouble than benefit to many patients.

And I do want to emphasize, without going into detail, the value of new technologies to improve surveillance, increasing ease to patients and to clinicians to track blood pressure. And I think this is the future. If this can be done in a way that's seamless to patients, then even people with cognitive impairments, or who have some inability to use electronics easily, if they could still be able to incorporate telehealth mechanisms to follow up blood pressure and provide those data to their clinicians, I think that will be an improvement of care.

The Chinese study that I mentioned earlier-- the STEP trial-- was one of the first to incorporate some of these values of technologically enhanced care. And that's going to be one of the results of their trial that I suspect they champion.

And then this notion of channeling care by improving the actual administration of medications. There's a controversy-- do we try to reduce the number of meds for patients that are prone to polypharmacy? Or there really is a countervailing rationale to using combined meds, because you have lower doses, lower side effects. And there are many advantages to lower doses, especially for older adults with changes of pharmacokinetics and pharmacodynamics.

And so my own strategy, and what I would recommend-- and I think this is the predominance of literature, but there's no trials as such that really prove this definitively-- is to use single doses, even with multiple pills, and try to find the best combination for my particular patient. And then trying a combined pill if it matches the doses that I've ultimately come upon for my patient.

So mixing a calcium channel blocker with an ACE inhibitor to find the best dose possible, and then finding the right polypill that combines those would be my strategy. But, again, this is also controversial. And it depends on your patient and your own frequency with which you see your patients. And so this becomes very easier said than done. But it's important to at least consider.

This is a very interesting trial. I think it took probably extraordinary work by Lillian Min, who's been one of the thought leaders in anti-- or the blood pressure lowering literature for older adults. And it looked at a huge VA population. And it really compared those that were treated with one single medication with a higher dose versus changing the strategy to give two medications at lower doses, and really showing some benefits of each, really emphasizing that when you emphasize the maximizing dose, you can achieve improvements of care. But you actually have a better blood pressure lowering effect by giving two doses of medications-- or two medications at lower doses.

So, I mean, her conclusions I think were just to describe that and the relative benefits of each of one pill at a higher dose, acknowledging trade-offs with a higher dose in an older population with the pharmacodynamics and kinetics that I mentioned, versus the difficulty of two pills-- again, knowing this is a complicated step in a complicated field, and treating blood pressure is not simple.

So in summary, I mean, what is the right-- what is blood pressure? Blood pressure is part of what-- elevated blood pressure is part of normal aging. What is hypertension? It's somewhat of an arbitrary cut point based upon this continuum of blood pressure changes over age. And whatever number we pick probably has rationales and also has trade-offs.

Again, guidelines say treat blood pressure to less than 130. And it gives a very ambiguous rationale as to why you wouldn't do that for people that are complex, which is the vast majority of people that are over-- an older population certainly over 75. So I think the guidelines become a little bit difficult for me to best apply to my patients.

So is the right cut point 140? Is it 160? I've highlighted that in different guidelines in different countries at different ages, these are all appropriate cut points based upon the same literature. Everyone looks at the same basic literature and comes to different conclusions about what's right for their country or their population.

So blood pressure is more than a number. It's a phenomenon of aging. And thinking about it in terms of each patient becomes important to see it in terms of that aggregate complexity. And so I see it as there's fundamental changes of physiology, of architecture, and we have to really think about what management is going to be best for each patient.

So I think it's important to listen to the patients, but also to teach them. Listen to their goals of care, to think about their trajectories of aggregate health, but also to teach about the value of treating blood pressure and ways that you're going to try to minimize the risks and maximize the benefits, knowing that for many patients this notion of diminishing cognitive impairment, diminishing stroke risks are overwhelming priorities. Also, the benefits to reduce cardiovascular disease, renal disease, increase longevity-- they're all there, but it's not simple.

So treating blood pressure starts with lifestyle. It's best, I would argue, to avoid short-acting medications and to advance incrementally, or else you may inadvertently exacerbate problems, and to really follow the literature as it's evolving rapidly now for technological adjuncts that may have the benefit for improving surveillance and adherence. And acknowledging that monitoring blood pressure at home has distinctive advantages, particularly in an older population that's prone to stiff vessels and associated risks of hypotension and associated falls and other types of impairments.

So thank you very much. I hope that was useful. And I look forward to answering questions in the following discussion with all the cardiologists.