

[MUSIC PLAYING]

**DANIEL E.
FORMAN:**

Thank you very much. It's a great pleasure for me to come here, now, for the last few years and to speak about this interplay, as you just heard, between geriatrics and cardiology. I want to highlight that one of my co-speakers, Deirdre O'Neill, is also one of those rare people who is bordered in geriatrics and cardiology.

In fact, there are a growing number of cardiologists who've embraced geriatrics and geriatricians who have embraced cardiology. And many geriatricians who-- perhaps, many of you-- who are embracing many other specialty fields, because the interplay between aging and every other dimension of medicine is so powerful. And I think you all live it clinically, and perhaps many of you live it research-wise, but it's here, and it certainly has defined my career over many years now.

So today, for me, and for the second year in a row, this session is particularly special because I've been allowed by the meeting organizers to-- and I'm really grateful to them, to emphasize that-- to have not only my own voice discussing this interplay between aging and cardiology, but having colleagues who are kind of kindred spirits.

I mentioned Deirdre O'Neill's background as double-boarded, but you'll hear all the other speakers as well have tremendous interplay of geriatrics into their cardiovascular careers. We're really a different breed of cardiologist than I think has been typical, but I will say that we're really not going to be so exceptional in years to come, because I do think-- and I'm very proud of saying this-- we're changing mainstream cardiology.

I think you are seeing myself as more of the senior guy and these junior colleagues, who are really not so-- I mean, they're preeminent. And they're all moving forward and really changing the cultures locally, nationally, and even internationally. And how cardiologists and other specialists are regarding older adults that have many disease patterns.

So I'm going to be focusing on statin therapy. I think last year I talked about hypertension. You'll hear some of the same themes today. This whole notion, I would say you can generalize-- and I'll speak about one thing, but you can generalize about this interplay between the cardiovascular issues and the broader constellation of issues that we all struggle with with our older patients. So statin therapy and older adults evolving concepts of management.

And I really always start with this picture, because I think it's really the way that I think of most of my career. But if you look at who has cardiovascular disease, it is not in 50-year-old men, which is where most of the data used to be. It's in older adults, older women and men. Women outlive men, and, therefore, they tend to have more cardiovascular disease as we reach old age.

And as you think about the demographics, soon 1 out of 5 will be over 65, the population over 85 is the most rapidly-growing demographic in the world, certainly in the US. So who is getting cardiovascular disease? It's this explosion of older adults, and what is our thought process? Where is our refinement? It really has been wanting.

So I'm speaking about statins, and if you think about atherosclerotic disease, in this case, coronary heart disease, you see the prevalence data shows it's skyrocketing with age. And I really want to emphasize this is an under representation of the problem. Because this is looking at coronary heart disease kind of a very narrow perspective of many cardiologists and many other practitioners.

But it's really atherosclerotic disease. It's peripheral arterial disease. It's strokes. It's even more insidious, perhaps. It's functional capacity. It's issues of frailty. They're all interplayed with vascular changes and the influence of atherosclerotic disease in aging.

So we have a big problem. And it really leads to this mindset, perhaps, which is somewhat provocative still, that when someone is 75, 80, this may be the time to really think the most about prevention. It's not really just adding another pill to somebody who already has polypharmacy, but there's really perhaps a very thoughtful, well-intended goal of trying to modify this great prevalence, this predisposition, and all of these effects.

Perhaps-- when is the key time to start? Maybe in your 50s and then driving it even more in your 60s and 70s. Not to back off. Not to back off the way the geriatrician precepts have been, but to be more aggressive in the face of these kinds of biological constructs.

So age itself is now targeted, and I've mentioned the last few years in Pittsburgh and really throughout the world, there's this focus on generalist science, trying to figure out what are the mechanisms of aging. Perhaps they could be modified, and we're doing some tremendous research in Pittsburgh.

But then looking at issues that you'll hear this morning of hypertension, issues that I'm going to talk about with LDL with statins, and other types of risk modification as a geriatric priority. And then you think about, perhaps, as do I, what are your patients-- what are they worried about? Your 85-year-old patient.

Why in the world would they want a pill for cholesterol? What are the risks, Doctor? When they say, well, what's the risk of a fatal MI? It's not so bad. Maybe this is not the thing I want to worry the most about at 85, because the risks don't seem to be that overwhelming compared to the other things that they may be worrying about.

But these are the kind of data that I think are really very compelling. You say, who is most vulnerable to an event? To going to the hospital? To having chest pain? And these numbers really do skyrocket with age. And if there is a mentality of secondary or primary prevention in this population to avoid those otherwise predictable events, they become really very compelling to many adults, even someone who might be on a bunch of pills. Who doesn't like pills. Who doesn't want to deal with the co-payments.

They suddenly may find it interesting if you phrase it that way. And if you start saying, well, maybe you could have less-- you have more functional capacity, more ability to walk, maybe your thinking will be a little bit sharper. These types of-- these are the kinds of considerations that I would argue are worth considering.

So this is the conundrum. You have increased longevity. That is a fact. People are living longer. That's really the driving thought process. It's associated with a biological construct. There's more likelihood of atherosclerotic disease, and there are more systemic effects. People could rip it on the cost and the cost efficacy.

And then you have these happy pills, so to speak. The statins, they've been around for decades now. They raise the issue, the possibility, of ineffective-- excuse me, effective, inexpensive prevention, diminishing events, and really, perhaps, diminishing the more insidious disability cognitive declines and frailty that we worry about with so many of our patients.

And I want to highlight this. This is a very important concept, which is like a driving home theme, prevention in older adults. When you look at aging, it drives up the likelihood of having, in this case, atherosclerotic events, or many events in general.

And if you talk about, in this case, statin therapy risk reduction, 40% risk reduction on the orange-red bar, and then it's 20% risk reduction. Even less effective risk reduction if you juxtapose it to the number of events. The relative efficiency of risk reduction is greater, because more people benefit by risk reduction. Even 20% risk reduction has greater numbers.

The actual effect of what you're doing grows with aging, so your 85-year-old patient may get disproportionate benefit by statin therapy. It's not just torturing him or her. It's really giving them something to really benefit from. And then if you could then refine your thought process and give it to the patients that are going to benefit the most, you don't have to treat necessarily everyone, but if you could really figure out who's going to benefit the most, you're likely to have much greater benefit.

The number needed to treat goes down because the efficacy is so great. Again, this-- you could talk about every other aspect of prevention, beyond just statins. You could have the same kinds of principles.

So this is the backdrop, and it drives a lot of research. The research has really been wanting, but there's still a good deal of it in terms of, what are the benefits of statin therapy for an older population, an aging population.

And this has really been growing over the last 10 years or so, and there's been a variety of meta-analyses, and what they've done, and this is just one of several as I keep emphasizing, is that they've taken data from large trials in a broader population, and they find the subset that are usually over 70 or sometimes over 65, and they make general comments about the elderly. The older subsets of adults.

And data like this are certainly compelling. Perhaps not definitive, but you see a variety of big trials, and you see everything seems to favor statins, in terms of heart attacks and in terms of strokes. And so this is for primary prevention. I really want to emphasize these are people who have been healthy their whole lives, and they're saying, why are you bothering me, Doctor Forman, talking about a pill? Another pill that I don't want, that might even have side effects.

But these are the kinds of data that become at least compelling. Something to perhaps talk about. Like, in this case, about 25,000 people, the younger subsets of older adults as I see it, 73, but they reduce statins. Are associated with reduced events in a primary prevention application.

It didn't increase or cause death in this population, but it reduced events. So it goes back to that graph that I showed earlier. Reduced hospitalization, reduced costs, reduced cascade of progressive hospitalizations, re-hospitalizations, and disability. And on these data, there were no differences in myalgias in changes of the liver, diabetes. So the argument is it's predominately beneficial effects.

So one could criticize this and say, well, these are trial data, and these are subsets of the older adults that are perhaps not typical for my patients. They're perhaps on fewer meds, less complicated, so it's not perfect. But there are many data, and they are accumulating.

This is a study that was-- again, these are prominently published. The first one I just showed was in JACC, a big journal in cardiology. This one's in circulation, very high profile. Paul Ridker, a big voice in the cardiology world, and he took data from the Jupiter trial, the trial where he was the principal investigator, and the Hope trial, kind of a sister trial.

And he looked at the subsets, again, of older adults. He had relatively young subsets of older adults and came to very similar principles, but an even more powerful emphasis. Pulling together about 6,000 people from the Jupiter trial, about 3,000 from the Hope 3 trial, and he comes up to this conclusion of a 26% relative risk reduction for those greater than 70.

So in a combined endpoint of being beneficial for non-fatal MI, non-fatal stroke, and for cardiovascular death. Powerful. Again, trial data. Subsets. What's the meaning-- how does this relate to my patient? How am I going to make this compelling to my patient who is complicated in my office today, tomorrow?

I want to highlight these data. [INAUDIBLE], who's a friend of mine, who did this work in the VA population. And if any of you cared for VA patients, these are not subsets of super healthy people. VA patients are complicated. They usually have many different diseases in addition to their cholesterol.

And so here she looked at, with a variety of other people, over 300,000 individuals in a primary prevention analysis and showing across the board benefits. All cause mortality. Cardiovascular death. Myocardial infarction strokes. CABG.

In a population that's mean age is 81 years old and breaking it down even further, this is perhaps the most interesting slide. Hard to see, but the general points is that if you break down into these older age strata, they're all-- most of them are quite significant.

Showing that if they were stratified by sex, race, age, ethnicity, the benefits of statins were huge, even in diabetics. This is going to publish in JAMA, and it is big because even as a retrospective analysis, this is a huge endorsement of the benefits of statins in the very old population.

So this is the dilemma. This is going to happen to you, perhaps, this week. Perhaps, next week. Perhaps, it's spinning in your head right now, that you have an older population prone to atherosclerotic disease and a lot of other diseases, but it's really embedded in an a construct with multi-morbidity.

They're taking many pills with many pill interactions. They have concomitant frailty and all these issues of muscle pain may be exacerbated by taking a statin or any other pill. They have sarcopenia, less muscle mass. They're weak to begin with in most cases, so you're giving them a pill that might compound that.

How long are they going to live? Is this really worth the bother in any way, shape, or form? And so, are you giving them a pill that's going to help or hurt?

And I do want to highlight what the Palliative Care fund has really emphasized, is that there may be a benefit for discontinuing statin. I could talk about all the trials that say there may be a benefit. There may be a signal. This is Jean Kudner's data. It's been heralded by many people. It's really important because it shows that if you take away statin, people live longer in certain populations of older adults.

In fact, her data goes on to show that if you take away statins, quality of life improves, symptoms improve, and the whole sense of satisfaction of care improves. Often, statins in a population that she explored. So what's the right answer?

This, to me, is every patient. This encapsulates the dilemma that anything you do has multiple effects. If you give someone statins, you could say you're well-intended. You're trying to reduce cardiovascular events. You're trying to reduce mortality, reduce claudication, increase function, diminish frailty, and even increase cognition.

I would say there are data that really suggest this is happening for all of our patients that are older that you treat with statins. This is an evidence-based kind of statement. But so is this. That you have greater likelihood of benefit in the association with age, but you have greater likelihood of risk.

So with that same pill, you might be inducing myalgias, diminishing function, increasing frailty, undermining cognition, increasing polypharmacy, and increasing costs. So are you torturing your patients or helping them? And I think this is really very difficult.

And then you have to ask these related issues of what's the time to benefit, which usually can take two or four years for MI and stroke, respectively, and what's the time to harm. That could be like tomorrow, next week, and what's really the most important to your patient. And how long are they going to live that they really want to deal with this new pill and this set of challenges that you're bringing to them? Lots of questions.

So I've been someone who's been very critical of guidelines. I've always felt that guidelines may do more harm than benefit to my patients when they start dealing with older patients that have cardiac disease and, why do I want a number or something for me to do?

So I was asked to be on the guidelines, and I accepted with some ambivalence, but I really love the process of people that really deeply cared about doing the best thing for patients and trying to find-- distill rules based upon the data such as it is to best direct practice.

So these are the guidelines that just published for older adults and statins, and I really am proud of them because it embraces the complexity that I've been really emphasizing, and it puts the onus back on you and your office to think about it and not just be too prescriptive based upon something that somebody else said a year or two ago.

It's saying that statins, they may be reasonable to prescribe to my older patients 75 and over. They may be-- and I've showed you some of those data. They may be. It's considered a 'to be' recommendation, which is generally considered weak, but those are the data. There are data, and they may apply, and you have to think about it.

But it also includes and embraces the spirit of Jean Kudner's work, that may be reasonable to take away a statin. So what's the right answer? You have to really think about it. You have to think about that patient, and you have to talk, perhaps, with that patient and really weigh it with them. You have equipoise. You really don't know, and that's really the take-home point of the guidelines.

It's really saying-- and it's really-- this is the whole pivot point for geriatric cardiology-- it's saying you have to share the decision. I think what's really the emphasis of my career is that it's-- the cardiologists are not just talking down to the patient and saying, this is what you have to do. You know, snap to it.

It's really, we don't really know what's the best thing for everyone. We know-- we can think about it with you and guide you and do an excellent job based upon your choice. And that's where we are.

It also leads to the premise of new-- the importance of more data. I've showed you some things. If you listen to Dr. Ridker, he is particularly-- he's got a lot of bravado when he says, the Jupiter trial solved it all. I've been a little bit skeptical, and so have many other people, because that was a subset of a big trial, and it really didn't perhaps generalize the patients that many of us care for.

So the NHLBI, a big part of the NIH that's embraced cardiovascular disease and the NIA, National Institute of Aging have really agreed to that. They say, with the population shifting, older population prone to cardiovascular disease, we have to think of older adults.

It led to, at this point, a \$40 million investment in the preventable trial. It's about to start. It's going to be in Pittsburgh. It's going to be all over the country, and it's going to look at the utility, in this case, of Lipitor, in a population that's 75 and over. To really change the premise of care where we don't know exactly what we're doing, we have this kind of, perhaps, unstructured contr-- or, not unstructured, but, perhaps, disturbing, contract that you have to really think about each patient in a way that's based upon their own idiosyncrasies, to something where we have more and more data to help inform that decision with precision.

The primary endpoint, in this case, is cognitive changes, and the associated endpoint is going to be functional changes. Only on a tertiary level are we thinking about cardiovascular events. It's really flipping the whole notion of what's important for a trial that's funded by the NHLBI to think about these patient-centered domains of care, perhaps a little bit in front of just disease-specific domains of care or endpoints.

So again, cognition is the main endpoint. Function, an associated endpoint. And the composite of cardiovascular disease as an endpoint after that. All important, all being prioritized, but really trying to make this more patient-centered and more, perhaps, useful to you as clinicians caring for patients.

This trial is just getting off the ground. It's going to go into implementation in August. It's a five-year trial. It's a very aggressive recruitment, intending to recruit 20,000 people. Again, it's Atorvastatin versus placebo. It's designed to be very user-friendly for patients to participate from home and get evaluated predominantly from home with a very aggressive team orchestrated through Duke as the main center.

In the meantime, what do you do? What are you going to do this afternoon for your patients? Or tomorrow or next week? So I want to highlight this work. Again, Dr. O'Neil, who I'll introduce in a minute. She was visiting-- or, doing work in Pittsburgh last year, training in geriatrics, and worked with me on this paper.

It really talked about the fact that while we wait for trials like preventable to perhaps inform us a little bit more with our patients, we still have a dilemma. What do we do for our patients? And it really tries to highlight the utility of shared decision-making.

And this is not just one paper. This is really the theme of the American Heart Association and the American College of Cardiology saying we have to really drive this notion of shared decision-making and patient-centeredness. This is just giving example. So with what Dr. O'Neil did, I think just developed this concept with multiple patients and really showed how we used the data the best way possible in each patient's case.

So patient AG, highlighting a woman who has multi-morbidity and all kinds of issues and concerns about statins. She says, she's heard dreadful things about statins from her friends and family and television. She compares that, and we compare that, to another patient, an 82-year-old gentleman who is super healthy.

He's involved in travel and all kinds of athleticism, but he has a strong family history of cardiovascular disease, and he wants to do everything he possibly can to prevent cardiovascular disease. In fact, he's already taking statins, and he feels, why should I stop them? I'm doing fine with them.

Compares that with another person, in this case, an 80-year-old woman who shows all these elements of frailty. She's in a wheelchair. She's losing weight, and she's becoming weaker. I don't want to go through the details of the case, but I want to emphasize this notion of cases.

These are, I suspect, every one of your patients having their own set of issues and their own set of challenges and then the importance then of applying the principles of prevention and seeing which fits best for that patient. Do they want to take a pill? Do they not want to take a pill? What are the benefits and what are the risks?

We can really start saying this is complicated. You know, who's young? Who's the young-old? Who's the old-old? Who's going to benefit? You might start having ideas. And I think, again, for many cardiologists, this has really not necessarily struck them as being that important, as something they struggle with.

But I would really argue-- as you think about who our elderly are, who are the older adults, and what are the effects of statins on their mentation and on their physical capacities? I think these issues are mainstream, and I think the imprecision of what the medicines do and how we talk about them and how we really affect best care is front and center. Something that we should be prioritizing.

So this notion of shared decision-making is exploded, and my talk is not on shared decision-making today, but I wanted to really highlight the fact that there are many people at the Mayo Clinic and throughout the country and world who are now trying to really hone the techniques to do this in a very rigorous way.

Having the visualization of what percentages mean and really trying to understand what the benefits and risks are. And really trying to make this accessible to people with multi-morbidity, to people with limited cognition. Executive cognitive decline is really likely when someone has atherosclerotic disease, so how do we help people, who are likely to have difficulty with decisions, deal with these difficult decisions? This is the challenge, I think, of mainstream medicine, as we deal with an aging population.

We have this other concept, which is also coming along, that there are tools to help us as clinicians and help our patients make the best choices. The bioimage trial highlighted the utility of the coronary artery calcium score. So if you see calcium, it really can often indicate someone who is most likely to have cardiovascular disease.

When you're doing primary prevention, and you see no calcium, it really is an indication this person is not likely to have cardiovascular disease, and it may not be beneficial to treat that individual with a zero calcium score with a statin. It may not be worth the headache of being on the statin.

This was a very important trial in helping us to make better decisions and inform better decisions, particularly having, in an older population, this CAC score, the coronary artery calcium score, of zero. In this particular trial, in a population that included the subset 75 to 80, the CAC score of zero was prevalent in about 30% of people. 30% of people could be told, you're going to get no benefit from being on a statin.

That made it somewhat easy. So, are you doing your CAC score? They're relatively cheap, but it's another test. Someone has to schlep to the hospital and get a scan and raise all those questions. Is it worth it? Maybe. And I think this kind of highlights the utility.

What about someone who's 85 and 90? This trial doesn't answer that. We need more data. And, actually, within that preventable trial, which has just got funded, the first thing that they're doing is they approved an ancillary study to look at the CAC score in this population that's going to be 75 and over.

It's going to be randomized to include disproportionate numbers of people that are in their 80s and even in their 90s. So you'll have those data. We'll have those data shortly, and it may be worth thinking about getting CAC scores routinely. I'm not a big believer that we should be scanning all our patients for everything, but here's a very important tool that's evolving.

It also opens up the even bigger door to think about other metrics. Are there other biometrics that could identify greater risk of our older patients, who may have cardiovascular disease, likely or less likely depending on what we find. So in addition to the imaging kinds of modalities, like CAC, there may be others. This is a hot field of research within cardiology as we try to refine our management.

In addition to the recommendations that I've already highlighted, in terms of, there may be benefits-- reasonable benefits for being on a statin or taking away statins. There also may be reasonable benefits to using a CAC score to help inform those decisions. That's where we are really with primary prevention.

Someone who, again, often looks at me and says, I've been healthy my whole life. Why do I suddenly have this disease? You have it because it's a function of aging. It's biologically-driven. We have this reality, a dimension of care for someone who is in his or her 70s, 80s, and 90s.

Secondary prevention is really a little bit different in that the preponderance of data, again, through many different trials, shows everything going in the same direction. It's beneficial if you've had an event, and events are likely in an older population, to be in a statin therapy to lower your risk.

This is John Afilalo's work. He did this a while ago, but the data have not changed. All cause mortality in all these subsets of benefit are all significantly positive of showing the utility of a statin therapy. It goes on. There's been some data that looks specifically in older population. The prosper trial, population about 6,000. Patients were recruited to be older to begin with, and it showed over time that the benefits, the cardiovascular benefits, were significant, even in an older population, particularly for secondary prevention.

There are even data-- this is Fatima Rodriguez looking at a VA population, another complex population, showing that the utility of higher intensity statin therapy. This has been another raging controversy. Do we just give a little bit of pravastatin? Relatively weaker statin? Be easier tolerated? Or do you push the dose? And her data suggested that higher dose works better, in terms of mortality endpoint, at least.

Again, with that trade-off. Higher dose may have more myalgias and more side effects, but in terms of cardiovascular endpoints, there's certainly a compelling rationale.

Then, in a randomized controlled trial, Chris Cannon, showing the benefits of adding ezetimibe to a statin and showing that the combined effect with more potent LDL-lowering, more potent statin benefit official effect reduced cardiovascular endpoints. Again, arguing not only are statins beneficial for secondary prevention, but they're beneficial at the higher doses.

Compelling until it's your patient who's complaining about her myalgias, fatigue, or other side effects. So, even for secondary prevention, the new guidelines acknowledge the relatively stronger data, and they say, it is now reasonable. A higher emphasis. It is reasonable to give a statin for secondary prevention, even in an older population, and even a higher dose statin.

There is certainly an endorsement of what the data show, but it doesn't literally just say we should put it in the water. It stops short because it also highlights, and, again, these are really different in the guidelines this year, it acknowledges in the same sentence that you have to think about the adverse effects, the drug-drug interactions, the frailty, and the patient preferences.

So the onus is on the clinician in your offices to really engage with your patients and not just to say its guidelines. The guidelines are really meant to emphasize patient-centeredness in every step of the way.

So in adults over 75, primary prevention is reasonable, and the CAC score may be helpful in making that decision. And secondary prevention is even more reasonable, and it should be endorsed as an important concern. But in the same breath, without being the least bit dismissive, the possibility of myalgias, all the concerns about polypharmacy, they're prevalent. And they're growing.

So I think that this notion of sharing the decision and engaging with your patients is absolutely tied to anything we do for our patients. This is true probably for everything you think about with your older population. But when you think about statins and cardiovascular care, I want to emphasize that is an important theme.

I would say that many times when patients are referred to cardiologists, they don't hear this. By the time they're referred, I think the cardiologists think it's incumbent on them to do something. That's why their patient's been referred. But I do think that's a little bit too quick to the draw. I think that there's much more that cardiologists have to do as part of best care for our population.

I want to highlight to end that as I start to introduce my colleagues, that there's a group of us who are really invested in cardiology, as I've emphasized, to changing the whole culture of cardiovascular care. When I started my career, there was a geriatric cardiology section that had about 20 or 30 members, and when it joined the ACC officially, it grew into almost 3,000 members. 3,000 cardiologists across the country had this interest in aging.

So it's really a change of culture, and today, you'll meet some of the other people that are part of this. This grant - this is the bridge. Geriatric cardiology is just being reviewed or being submitted and about to be submitted. And it's being heavily reviewed in its final phases talking about the infrastructure that's needed to really integrate geriatrics with cardiovascular research.

To really bring this forward and to try to bridge the different campuses where there's one or two geriatric cardiologists, so that they have a community. They're working cohesively the way mainstream cardiology does, and we're really trying very hard to leverage the energy and the enthusiasm that I think you'll hear with all of our speakers, into a national- and international- effective movement.

I hope that the spirit of statins and the aging really is compelling to you and thought-provoking, and I hope it leads to a whole series of conversations with our other speakers that even expand that further. So, thank you very much.

[APPLAUSE]

