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Closing Gaps in ASCVD Prevention: Lipid Management Insights from AHA 2025

Announcer:
You're listening to *Heart Matters* on ReachMD, and this episode is sponsored by the Family Heart Foundation. Here's your host, Dr. Laurence Sperling.

Dr. Sperling:
This is *Heart Matters* on ReachMD. My name is Dr. Laurence Sperling, and I'm the Katz Professor in Preventive Cardiology and Founder of the Center for Heart Disease Prevention at Emory University School of Medicine. I also serve as the Chief Medical Officer of the Family Heart Foundation.

Today, I'm joined by Dr. Eugenia Gianos, who's a friend, colleague, and leader in cardiovascular disease prevention, to discuss new data on cholesterol management that was presented at the 2025 American Heart Association Scientific Sessions. Dr. Gianos is the System Director of Cardiovascular Disease Prevention at Northwell Health in New York.

Dr. Gianos, welcome to the program.

Dr. Gianos:
Thank you, Dr. Sperling, it's an honor to be here with you, and I'm a big fan of the Family Heart Foundation.

Dr. Sperling:
Well, wonderful. We have an important conversation today. It was a very vibrant American Heart Association meeting, and one of my take-homes was that prevention of cardiovascular disease is really front and center. It's very powerful.

So, to start us off, you served as one of the co-chairs of the opening late-breaking clinical trial session. But in general, what stood out to you most about the presentations on lipid management at this year's AHA Scientific Sessions?

Dr. Gianos:
For starters, just the fact that the entire opening session of the American Heart Association meeting was dedicated to lipidology is a big win in prevention. Really exciting content was shared on newer therapies that are emerging, all atherogenic lipoproteins, new technologies, a big shift in terms of thresholds and where we want to get targets to that potentially could shift guidelines and are very exciting, and also data in high-risk populations who don't have established events for cardiovascular disease—questioning where those targets need to be at this point.

Dr. Sperling:
It truly is a pivotal time in cardiovascular disease prevention. And the meeting highlighted frontiers, new possibilities, and new therapies. But importantly, as we start out our conversation today, let's dive into some sobering and hopefully activating findings—some real-world data from the Family Heart Database. This database brings forth over 340 million U.S. individuals related to de-identified medical claims across diagnosis, medications, procedures, and surgeries. And a third of the cohort has cholesterol-related lab data.

The key findings from this study were: in over three and a half million individuals living with ASCVD in the years 2022 to 2023, there were major gaps in care. The gaps in care reported that many—28 percent—received no therapy at all related to their LDL cholesterol. 40 percent reported LDLs less than 70. Only 30 percent had dispensed high-intensity LDL-lowering therapy that predominantly included high-intensity statin monotherapy. Unfortunately, use of combination therapy, as well as non-statin therapy, was quite limited.

Two other important findings from the study were that only 35 percent were dispensed LDL-lowering therapy throughout this two-year duration 20 out of 24 months. There were disparities in care that mirrored disparities in care that we know of treating those with ASCVD:

greater gaps in care for women, Black individuals, those less than age 50, and those living with PAD and cerebrovascular disease. And then for the clinician prescribing data, 50 percent of the clinicians—over 250,000 clinicians—prescribed only statin monotherapy.

This study highlights gaps and opportunities to improve use of any therapy—high-intensity statins and non-statins—and a greater focus on optimizing consistent therapy in this high-risk population.

So, Dr. Gianos, I'm going to come back to you because the excitement of the meeting was in pioneering thoughts, science, new therapies, and more tools in our toolbox. But can you react to this data?

Dr. Gianos:
Absolutely. I think it's important for us to start with the data that you're presenting, to understand the gaps, and to understand that as much exciting technology as there is out there, we have to understand that although we believe lower for longer is better, we're not achieving that at the moment.

So some of the key highlights here—one is implementation of the basics. Sometimes we're missing the boat on statin use, et cetera, but could a lot of these advanced therapies and newer technologies help us in achieving lower for longer, in fact, in these populations as well? Could there be different ways to approach this in our populations?

Dr. Sperling:
For those just tuning in, you're listening to *Heart Matters* on ReachMD. I'm Dr. Lawrence Sperling, and I'm speaking with Dr. Eugenia Gianos about key findings on cholesterol management from the 2025 American Heart Association Scientific Sessions.

So, Dr. Gianos, let's turn now to what many thought was the most impactful study presented at AHA Scientific Sessions: the VESALIUS trial. Can you walk us through the objective and design of this study?

Dr. Gianos:
Absolutely. We had already known about the fact that evolocumab has proven benefit in terms of reducing major adverse cardiovascular events in high-risk populations that have had stroke or MI. And now we were looking at a very different subgroup of patients who did not have a prior cardiovascular event.

So how you got into this study was essentially if you either had established cardiovascular disease, either through coronary calcium scoring, on CT, or on different imaging, or if you had high-risk diabetes. So a completely different population was on this risk continuum of cardiovascular disease.

And what they saw as they randomized the populations to the two groups is a very significant difference of 25 percent reduction in 3-point MACE and 19 percent reduction in 4-point MACE. And with the different subgroups, they got the median LDL that was achieved down to about 45. The results were consistent across different subgroups and also showed a nominal reduction in all-cause death. So extremely impressive results for this study that was very well awaited after 4.5 years.

Dr. Sperling:
Yeah, I really think it was a well-designed study. It's extending the concept of high-risk cardiovascular disease prevention.

So as we look at this study, what are the implications? How should we think about LDL targets? And then especially in patients who haven't had a prior ASCVD event? Because the whole concept of primary prevention as a different population for secondary prevention—I often say that the difference between primary and secondary prevention, it overlaps. And somebody can be a primary prevention patient, and then they're in the hospital and they're a secondary prevention patient. So how do we distill these findings? And how do we bring forth to our listeners how they should consider therapies for their patients?

Dr. Gianos:
It confirms the way we've been practicing. Most of us in preventive cardiology have been more aggressive with treating patients who have established coronary calcification or non-obstructive disease or high-risk diabetics. But interestingly, it shows that getting patients to a much lower LDL than perhaps we expected is what translated into this 25 percent relative risk reduction in 3-point MACE. It was an LDL achieved of a median approximately down to the 40s.

Really interesting to think about where we've been guiding our patients to get their LDL, and perhaps where we should now be striving to get them maybe even lower.

Dr. Sperling:
What about very low LDL cholesterols? Is that a concern? I know I get these questions frequently from my patients and referring clinicians. How do you address that question when you're helping to take care of patients and committed to optimizing comprehensive

cardiovascular disease prevention?

Dr. Gianos:
It's a great question, and one that we come across very frequently in our offices, predominantly, I think, because of social media, to be honest. So we really need to be prepared with the right answers for our patients.

In this study, they got the median LDL down to about 45. And again, the safety profile was excellent in this study, and we have so many years of data to confirm that getting your LDL to a very low level does not increase harm over time. As a matter of fact, if anything, it is likely to reduce your risk of things like vascular dementia, which patients are very concerned about when they're asking these questions. So extremely safe and important that we achieve those low LDLs.

Dr. Sperling:
I look back to see who Vesalius was, and there was a great editorial published along with the paper in the *New England Journal of Medicine*. Vesalius was an anatomist who focused a lot and taught us a lot about vascular anatomy.

So looking forward, do you think this study, adding to the data we've had, might impact future guidelines? And without being specific, how do we think broadly now about high-risk cardiovascular disease prevention, and maybe targets or goals?

Dr. Gianos:
For me—and I agree that editorial was excellent, highlighting the fact that not only did it reduce events in patients who have evidence of subclinical atherosclerosis without events—those are patients I think that are a little more obvious to us, that these are patients who need a low LDL to prevent progression—but also patients with cardiometabolic disease, with diabetes and at high risk, really benefited. So they confirmed the fact that risk calculators and the recognition of cardiometabolic disease, of diabetes as being high risk, and of non-HDL and ApoB as targets—all of that confirmed what we've learned in prior guidelines.

The low LDL target is the question. Now that we've achieved that low an LDL, should we be thinking about changing where we aim to get our patients, in general, in the primary prevention setting?

Dr. Sperling:
Time flies as you and I dedicate our careers to cardiovascular disease prevention. PCSK9 inhibitors were first FDA approved a decade ago. And so here we have data that extends the potential utility of PCSK9 inhibitors above and beyond the original populations and FOURIER and ODYSSEY outcomes. But the study I shared on behalf of the Family Heart Foundation database shows how—I'm going to say—nominally, clinicians are prescribing non-statins and even ezetimibe or combination therapy, let alone PCSK9 inhibitors.

What are some of the opportunities we have, even beyond the clinician–patient risk discussion?

Dr. Gianos:
Yeah, the clinical inertia is discouraging—to see that this is not happening more frequently, even in the easier—you would think—target of a drug that should be easy to get. And even PCSK9 inhibitors, over the years, even prior to this study coming out—it's been fairly reasonable to get them approved by insurance if you have valid reasons to be on them, and that process has gotten much easier.

So I think it's multifaceted. We have to educate patients, right? They need to understand, where should their LDL go? Is it safe? Making sure that they know their options. We have to educate clinicians even further, making sure they know how to use these drugs. We need to support those clinicians to have enough time in clinic to have that conversation with their patient and to make sure they have processes in place to get the authorizations and help them.

So it's definitely at multiple levels, but we absolutely need to do a better job at this.

Dr. Sperling:
Yeah, I fully agree. And we talk about team-based care, but we need to understand the value of team-based care and who are the critical members of the team. At our program at Emory, we have an amazing clinical pharmacist as part of our team and a nurse practitioner, and, of course, our preventive cardiologist, but our nurses and our medical assistants—everybody's part of this team.

Dr. Gianos, there were many trials and scientific presentations focused on cholesterol-related agents, but also new frontiers that were highlighted at AHA Scientific Sessions. One of the ones that really caught not only my attention but the attention of many—and I'd say half pun intended, splashed big—was the CORALreef trial. CORALreef Lipids, and there was also CORALreef heterozygous familial hypercholesterolemia. Can you comment on this?

Dr. Gianos:
Sure. It's a simple trial and very important one. There definitely is a category of patients where the patient themselves is just not that comfortable with injectables. Perhaps it's just not as feasible for them to do it. Or clinicians are not as comfortable prescribing them

where there is a need for oral PCSK9 inhibitors.

It was a relatively small, about 3,000-person trial with a diverse population looking to see the efficacy and safety of this. So there was about a 52 percent reduction in LDL at the end of the trial with this oral PCSK9 inhibitor, just really adding to another therapy that might help with that clinical inertia. So whatever the limitations are in your practice, we have another answer essentially. So many therapies out there.

Dr. Sperling:
Well, Dr. Gianos, you have been a true champion of cardiovascular disease prevention. You've mentored many, and you have been a leader across the nation.

What key takeaways can you share that can both be implemented tomorrow? Because that's most important. But we also talked about some new frontiers. Please share with our healthcare professionals that are managing cholesterol-related risk—how should we think in clinic this coming week? And then what do we have to look forward to in terms of emerging therapies and opportunities?

Dr. Gianos:
Well, first of all, it's an honor to be part of the preventive society—it's just a wonderful society overall across the organization—and then to be a mentee of yours as well.

And the way I advise my trainees and other clinicians out there is, number one, think about where you need to get to, and you just have to exhaust the armamentarium until you get there. But you should always do it in a specific pyramid. You'd have to start with lifestyle. You then go with the studied therapies that have been out there, including statins, and give them a good try and make sure that your patients are getting them.

And then really, we've got so many other therapies, and it's wonderful to see that that's the case now. With appropriate risk assessment, recognizing the patients at risk, and then using these therapies, we should be able to get all of our patients to goal.

And the earlier a treatment, as you're learning from these particular trials that went out, the earlier we start in the disease process, the lower we get the LDL for a longer period of time, the better patients do.

So there's a lot of exciting things out there—gene therapy on the horizon and other types of mechanisms. So this field will continue to expand. I think we just need to keep up with it and use it for our patients.

Dr. Sperling:
Really important final comments. And so with those key takeaways in mind, from my heart to yours, I want to thank our guest, Dr. Eugenia Gianos, for joining us to discuss the advances in cholesterol management that were presented at the 2025 American Heart Association Scientific Sessions.

Dr. Gianos, it was really great having you on the program.

Dr. Gianos:
My pleasure. Great to be here.

Announcer:
This episode of *Heart Matters* was sponsored by Family Heart Foundation. To access this and other episodes in our series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!