

## BroadcastMed | Drilling Down on the Cholesterol Treatment Guidelines

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**FRANCISCO LOPEZ-JIMENEZ:** Greetings, I'm Dr. Francisco Lopez-Jimenez, the Director of the Preventive Cardiology Program at Mayo Clinic. Today we'll be convening a roundtable review on the 2013 American College of Cardiology, American Heart Association guidelines on the treatment of blood cholesterol.

I'm joined by my colleagues Dr. Thomas Allison, Dr. Randal Thomas, and Dr. Vinaya Simha. They are consultants at Mayo Clinic, from cardiology and endocrinology. Welcome, everybody. Well I would like to discuss some questions with you. And I will start with Dr. Tomas. Would you mind telling us a summary of the guidelines and the major restraints?

**RANDAL THOMAS:** Well the new blood cholesterol guidelines in the American College of Cardiology, American Heart Association attempted to take more of the evidence from randomized controlled trials to make things potentially simpler for the clinicians to manage cholesterol. They group people according to risk groups and then recommended medications, statin medications in particular, according to the risk of the certain groups.

So for example, one group was a group of patients who already have known cardiovascular disease, atherosclerotic cardiovascular disease. Second group would be those that have an elevated LDL cholesterol above 190. Another group would be those who have diabetes, whether they have a low or a high risk according to a risk calculation. And the final group would be one that's perhaps the most controversial.

And that is a group that has a 10-year risk of atherosclerotic cardiovascular disease event of at least 7.5% based on a new risk calculator, known as the Pooled Cohort Calculator. So the idea is to use the evidence base from randomized controlled trials to direct our use of the statin medications, recommending either moderate or high-dose statins depending upon which of these subgroups people fall into.

**FRANCISCO LOPEZ-JIMENEZ:** Thank you. Good. Dr. Allison, what do you think about the recommendation to treat patients at high-risk for cardiovascular disease regardless of the cholesterol, whether it is 80, 90, 120, 140, where the risk is the most important factor.

**THOMAS ALLISON:** Well I think there are some serious limitations to that. First of all, just a quick comment, is although the guidelines were very definitive about being evidence-based, none of the clinical trials that I'm aware of utilize the Framingham Risk Score to recruit patients. None of them published the Framingham Risk Scores. And none of them analyzed their final results by Framingham Risk Score.

And yet, that is the basis of the guideline. So it's just kind of an interesting point. I'm not trying to be critical. But back to your question, specifically. Very limited data, only the JUPITER study had significant numbers of patients with an LDL cholesterol at baseline, below 130. And all of the patients in this study had other risk factors.

Everyone had elevated CRP. And many patients had hypertension, insulin resistance, obesity. The principle analysis was not performed based on the baseline cholesterol levels, or LDL cholesterol levels, although there is a subsequent paper that looked to that to some degree.

So my feeling is that young patients with high lipids whose risk scores are in the 7.5% range or above or even slightly below it, would benefit from statin therapy because they have lipid abnormalities. And they have many years, which to develop cardiovascular disease. At the other end of the spectrum, older patients with normal lipids who by age 60 or 64, 65, have not developed cardiovascular disease, are very unlikely to benefit in their lifetime from statin therapy when their LDL is already less than 100.

**FRANCISCO LOPEZ-JIMENEZ:** Great, thank you. Good. To Simha, would you treat a young patient? Because the other issue is the other side of the coin, which is the younger individual who has high cholesterol, not too high to qualify but it's still high enough to worry the patient and the provider. But the guidelines are not very clear on what to do in the younger individual. So for example, would you treat a 38-year-old man with an LDL cholesterol, let's say, 170 with family history of premature coronary disease?

**VINAYA SIMHA:** Well probably not right off the bat. But then in this person who is 38 years old, has a high cholesterol, bad family history, after a reasonable period of lifestyle intervention if his LDL cholesterol still remains in that range of over 160, I would strongly consider recommending pharmacotherapy in him.

Of course, given the fact that we don't really have any randomized controlled trial to show benefit in this age group, nonetheless I think to my mind, at least, I think we have enough data from other lines of evidence which support the benefit of lowering LDL burden over an extended period of time. And I think that that would be very beneficial. And then again, what's the downside of treating them?

After all, patients like this are least likely to have side effects from statin therapy. And say for low to moderate intensity statin therapy that is generic, cost, I don't think, is a big issue. So my own bias would be to treat him. The only thing, the reservation that I would have is probably what are the patient values.

Now there are some patients who would probably feel very reassured to be on statin therapy. But there are probably others who feel kind of burdened by having a label of having a disease that needs lifelong pharmacotherapy. So I would discuss these issues with him. My own bias, as I already said, would probably be to encourage him to pursue pharmacotherapy, statin therapy.

**FRANCISCO LOPEZ-JIMENEZ:** Thank you. So yeah, I think that highlights the issue of the importance of recognizing that younger individuals will rarely have a high-- 10-year risk because they are just young. But the 30-year predictor might give us a better estimation of the long-term probability to develop the disease. And that might help the patient and the provider to share the decision about what to do. Yeah?

**THOMAS ALLISON:** He brings up a very good point. And that is the guideline stresses the primacy of lifestyle modification as the first line of risk reduction. But it's not particularly precise about how long we should wait with lifestyle and if we're allowed to recalibrate the risk score based on some lifestyle modification results. So a patient who might have an 8% or 9% risk when we first see them with-- say if they quit smoking, that risk is going to drop dramatically.

And even if smoking isn't involved, if their blood pressure is improved, they lose weight, they might get under the 7.5% at a subsequent evaluation. And that, I think it's kind of inherent in there. But it's not maybe spelled out as correctly to say you should reassess the risk in the-- particularly in these younger patients, at least the second time before you launch therapy.

**FRANCISCO LOPEZ-JIMENEZ:** Yeah, that takes me to the next question. And that's for Dr. Thomas. So for how long do you think it's reasonable to wait in a patient that is labeled as high-risk, has an elevated LDL cholesterol, has an elevated 10-year risk-- for how long will it be reasonable to recommend lifestyle changes, retest, before we prescribe medications? Should we just do both at once and then reassess the need for the statins later on?

**RANDAL THOMAS:** Yeah, that's a good question. I agree with Tom and with Vinaya that it's a matter of discussing with the patient to decide what's going to be best in each individual case. But I would say, generally, the higher the risk of the patient the more likely we would start on both therapies.

If a patient is kind of borderline level on the risk, say, between 7.5% and 10% 10-year risk then I would probably give them three to six months to see if through their efforts and lifestyle change they can get their 10-year risk to below 7.5%. On the other hand, if it's someone with known cardiovascular disease who is at pretty high risk, I would probably go ahead and start them on statin therapy at the same time we initiate lifestyle therapy too.

**THOMAS ALLISON:** Vinaya has brought up that important point about that in the younger patient and statins at lower doses, this is a very safe, very well tolerated therapy. And maybe a few people need to be backed off because of side effects. But it won't be a huge burden.

**FRANCISCO LOPEZ-JIMENEZ:** Yeah, and maybe also relevant to identify the real potential to decrease the risk. Because in some patients maybe-- they're very high risk that even after modify some factors, they will still be at high risk.

**THOMAS ALLISON:** Francisco, I guess I'd say one more thing too. And that is although the risk does appear to be low in that group of individuals, we don't really have good 30-year data to see how safe statins are at that length of time. And we assume that they're safe.

We've had really good results clinically as well as in research studies for relatively long periods of time. But we still don't really know. So I think my bias still would be if we can help people control their risk without medication then that's the way we should really push and use the medications as needed,

**FRANCISCO LOPEZ-JIMENEZ:** Now let me move to a different area, which is on diabetes. The guidelines recommend statin treatment for every patient with diabetes, either type 1 or 2, older than 40 years old. What is your take on that? Would you treat every single patient with diabetes with statins?

**VINAYA SIMHA:** Well obviously, no. I wouldn't do that. But before finding fault with the new guidelines about such sweeping recommendations, I would actually like to commend them for at least not labeling diabetes as a cardiovascular risk equivalent as many of the earlier guidelines had almost led us to believe. I think that was a gross mischaracterization.

I think it's very good that the guidelines at least have more restrictions on who should be treated. That being so clearly, I don't think that if you have somebody who is, say, 45, has just had type 2 diabetes that was diagnosed six months ago, has no other risk factor, has a non-HDL cholesterol of 110, clearly I don't think he needs statin therapy, at least based on the available evidence.

We really have very little evidence in terms of primary prevention and people with diabetes about who would benefit, especially those who would have a lower LDL cholesterol. Probably the only large-scale primary prevention trial in diabetes was the CARDS. And the mean LDL cholesterol in this group was 120.

So for the guidelines to say that people with, say, between 70 to 100, to give them all a statin, I don't think we have any data to show that. I do feel that probably a large majority of these patients will benefit from statin therapy. But we clearly don't have that evidence in.

**FRANCISCO LOPEZ- JIMENEZ:** I was doing the calculation the other day. And it is really possible for a diabetic patient to have an estimated 10-year risk way below 5%. And therefore, in one side, according to one of the main recommendations of the guidelines, that patient will not benefit from statin treatment.

And also the other thing to consider is the risk potential are real to cause diabetes by statin therapy. So whether that may impair the control of the diabetic patient is something that is yet to be determined, something else to consider.

**VINAYA SIMHA:** I think we have very little data to suggest that statins impede diabetes control. Yes, most of the new onset diabetes seems to occur primarily in people with impaired fasting glucose or people with family history of diabetes. I'm not so much worried about the statin effects and glycemic control. But I think you bring a very good point about the new Pooled Cohort Equation. Has diabetes incorporated it in anyway.

So we could just very well base our decision to start statin therapy looking at the estimated risks. So we could probably-- so if somebody has diabetes, whether or not has diabetes, as long as the estimated risk is less than 5% or whatever we decide on, and if their non-HDL cholesterol is below a particular-- say, below 130-- then I don't think they would benefit from statin therapy.

**FRANCISCO LOPEZ- JIMENEZ:** Good. Well we would like to finish with a general question for everybody. If you have to pick up one randomized trial that is hardly needed, what would you want?

**RANDAL THOMAS:** Well I guess I would probably go back to that question we were discussing for those people who are kind of in that borderline level of risk. If we go with lifestyle therapy, first and foremost, compared to going with statin therapy first, which approach would be better? That'd be interesting for me to see.

**FRANCISCO LOPEZ- JIMENEZ:** Good. Something else?

**THOMAS ALLISON:** Yeah, and of course, although, we can say we should do this trial, but the trial in the lower-risk patients with better lipids-- but of course, it's a very expensive and very long-term trial. It may not be feasible to do that. And similar to exercise trials, or smoking trials, or things like that, we may be forced to use epidemiologic or observational data for it.

**FRANCISCO LOPEZ- JIMENEZ:** I'm sure that many experts in the field will want to see a clinical trial comparing the old approach of targeting a specific number versus just giving a dose or intensity according to the risk. Well thank you, everybody, for your participation. And thank you, all you, for your attention. And we hope you continue to follow our roundtable review series at [theheart.org](http://theheart.org) on Medscape. Thank you.