

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

I'm joined by my colleague Dr. Thomas Allison, Dr. Ronald 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. Thomas. Would you mind telling us a summary of the guidelines and the major restraints?

**DR. RONALD THOMAS:** The new blood cholesterol guidelines in the American College of Cardiology and 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. The 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.

Then, the final group would be-- and this is perhaps the most controversial-- and that is a group that has a 10 year risk of an atherosclerotic cardiovascular disease event of at least 7.5%, based on a new risk calculator known as the pool cohort calculator.

So the idea is to use the evidence base from randomized controlled trials to direct our use of the statins of medications, recommending either moderate or high newstands, depending upon which of these subgroups that people fall into.

**DR. 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?

**DR. 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 utilized 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. And 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 limited 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 or 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.

**DR. FRANCISCO** Great. Thank you. Good. Dr. Simha, would you treat a young patient? Because the other side of the coin, which is the younger individual who has high cholesterol, not too high to qualify, but is 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 39-year-old man with an LDL cholesterol, let's say 170, with family history of premature coronary disease?

**DR. VINAYA** Well, probably not right off the bat. But then, in this person who is 38-year-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 control trial to show benefit in this age group, nonetheless I think, to my mind at least, I think I have enough data from other lines of evidence which support the benefit of lower 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 the least likely to have side effects from statin therapy. And safer 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 reservations 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 then, 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 in therapy.

**DR. FRANCISCO** 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.

**DR. THOMAS** 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 gonna 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 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, particularly in these younger patients, at least the second time before you launch therapy.

**DR. FRANCISCO** And that takes me to the next question. And that's for DR. THOMAS ALLISON: Dr. Thomas. So for how long do you think is 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 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.

**DR. RONALD THOMAS:** That's a good question. And I agree with Tom and with Vinaya that it's a matter of discussing with the patient to decide what's gonna be best in each individual case. But I would say, generally, the higher the risk to 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's at a pretty high risk, I would probably go ahead and start them on statin therapy at the same time we initiate lifestyle therapy too.

**DR. THOMAS ALLISON:** Vinaya's 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.

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

**DR. RONALD THOMAS:** 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. 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 could help people control their risk without medication, then that's the way we should really push and use the medications as needed.

**DR. 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. Dr. Simha, what is your take on that? Would you treat every single patient with diabetes with statins?

**DR. 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 in people with diabetes about who would benefit, like 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 that 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.

**DR. FRANCISCO** I was looking at the calculation the other day. And it is really possible for our diabetic patient to have an estimated 10 years 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 a statin treatment.

And now, so the other thing to consider, is the risk potential or real, to cause diabetes by statin therapy. So whether statin therapy made impair the control of the diabetic patient is something that has yet to be determined, something else to consider.

**DR. VINAYA SIMHA:** Well, I think we have very likely 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 a family history of diabetes. I'm not so much worried about the statin effects on glycemic control.

But I think you bring up a very good point about the new cohort [INAUDIBLE] question. Has diabetes incorporated it in any way? 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 will benefit from statin therapy.

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

**DR. RONALD 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.

**DR. FRANCISCO** Good. Something else?

**DR. 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 epidemiological or observational data for it.

**DR. FRANCISCO** I'm sure that many experts in the field will want to see a clinical trial comparing the all approach of targeting and 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 of 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.