All right, I think the trials are convincing really when you look at the subgroups about which patients benefit the most. For example, my patients who have atherosclerotic cardiovascular disease, particularly people who've had recurrent events, who have residual LDL that's higher, for example, above 100, let's say you have complicated coronary anatomy, multiple stents, distal disease, et cetera, multiple myocardial infarctions despite good medical therapy. All those patients, the patient's-- peripheral vascular disease is another one that I try to treat as low as possible. So those are the patients who have secondary prevention level risk but are in the highest risk group within that group that I try to treat as aggressively as possible.

Now, in my particular practice, I treat patients in primary prevention who've advanced subclinical atherosclerosis just as aggressively. So for example, I get referred a patient with a high calcium score at say, calcium score is 800 in a 55 year old man. I'm going to treat that patient in my practice just as aggressively as I treat my secondary prevention patients. So I'm going to take that patient too and drive that LDL down very low. So that's my approach.

So I think within primary prevention, there's extreme high risk patients. Within secondary prevention, there's some stable patients who maybe who had a right coronary stent three or four years ago and are doing fine. And then there's the patient of recurrent events, who have residually high LDL, peripheral vascular disease, multiple PCIs so the anatomy is complicated, those patients I treat as aggressively as possible. And I think the secondary analysis from the clinical trials bears that out. For example, in FOURIER-- repeated MIs, peripheral vascular disease, recent demise-- another one. All those patients are the highest risk group for me within that secondary prevention group.

So you can kind of start to parse out who you need to treat the most aggressively and get that LDL down literally as low as possible.

I'm pretty persuaded by data, particularly from the Glagov Study that shows that when you get the LDL below 70, for example, and even further than that, you start to see plaque regression. That's what we saw on top of a high dose of statin, and you give evolocumab, Get that LDL below 70 and that curve that they did after the trial was published showed that you get plaque regression below an LDL of 70.

So I'm pushing for LDLs below 70 in essentially all my high risk patients. But an important part of those studies, the big clinical trials as well as the Glagov Studies, show that as you continue to lower the LDL, you continue to get benefit. So even down to LDLs of 50, 40, 30, 20, the more you lower it, the better the risk reduction is.

So while there's not a single number that I can say that I have to patients to this number, I do say, I want to get them as low as possible with effective therapies particularly when their LDL's above 70. That's the threshold to add additional therapies, for example, like a PCSK9. So if I have sort of 70 in my head as a number that I'm going to potentially start achieving plaque regression as a, I gotta get below that. And then I try to push it as low as possible as I can get with statins, ezetimibe, PCSK9 inhibition, realizing that the data doesn't show any lower level of LDL that puts you at higher risk of side effects.

This has been vetted by the FDA carefully and the peer reviewed literature from the clinical trials, as well as from ezetimibe studies and statin studies. That there's no lower level of LDL where you get more side effects like neurocognitive side effects have not borne out, cataracts and things have not really borne out. So I find that getting the LDL down very low is extremely safe, biologically plausible too. The LDL receptor saturates at a very low LDL. So being above that is excess LDL. So getting LDL down to evolutionary norms makes sense without side effects. So it's safe. I tell my patients that. I've personally observed no side effects of these low LDLs myself in practice.

So I'm thinking 70 is a number got to get below and as low as possible after that. So if they start at 71, I'm pushing down. And I can usually get patients down into 30, 40, 50 easily, hopefully, in those patients.

Now there's always the patient, for example, say with statin intolerance who has an LDL that starts in the range that I want to treat with a statin. Let's say they start at 170, for example. And they've got statin intolerance, or maybe what we should call it with the new guidelines, statin associated symptoms that we maybe it's for sure statins, may not be. But it's a barrier to the use of statins.

I will definitely try two, three statins to try to get that patient on a statin-- sometimes a rosuvastatin dose twice a week, long half life, you can do that. But you're not going to get to your LDL-- you're going to be above your LDL threshold at that point.

So that's a great patient to get them on a little bit of a statin, as much as they can tolerate, because that's evidence based care. And then, particularly if the LDL is considerably above our threshold, I choose a PCSK9 inhibitor there knowing that, for example, ezetimibe is not going to get me to where I need to be. So PCSK9 is the next best choice, I think, in those patients. That might be a patient who has just a high LDL and subclinical disease, maybe has ASCVD and can't tolerate a full dose statin, or especially those patients who have, let's say, heterozygous FH and can't tolerate a full dose statin. I'm really going to be pushing with, for example, monoclonal antibody there to get their LDL down very low.

So that's why I work in the idea of thresholds and as low as possible because they both kind of apply. There's a threshold at which I have to treat. And I want to go as low as possible after that with effective therapies knowing that there's not one number I want to achieve. It's just as low as possible. And I think most of my patients in my practice I can get into the, I don't know, 50 range or something like that with the available therapies.

So it's really a wonderful time to be treating. So that's the way I think about the numbers. And I like to tell patients that, you know, I want to get your LDL well below 70 because I can start to see plaque regression. And they all want to know that. They all want to know if I can kind of reverse this process in my body. Now, I tell them, of course, you still need to do all the other right things, and exercise, and diet, and take your blood pressure pills.

But you get better regressing particularly the plaque laden, the lipid laden, part of that plaque and dilapidate that plaque when you get that LDL down low. So I think that's where the numbers connect with the biology and then connect with clinical practice and how I talk to my patients and a rationale for being aggressive.