CHRISTIAN RUFF: So the AHA ACC recent guidelines on lipids is very important for two reasons. One, it re-emphasizes the fact that LDL is important, and the numbers are important, and what thresholds we use, and LDL achieved is critical. So we now know, and it's been re-incorporated to the guidelines that LDL is a causal factor and a key driver in atherosclerosis, and the lower your LDL, the lower your risk of atherosclerotic cardiovascular disease. So in the guidelines, it's sort of re-established, especially for patients with prior atherosclerosis, a target and a threshold, really, of 70, saying that in patients who are at high risk, who's had prior disease and risk factors, that you really want to probably drive down the LDL. Certainly less than 70.

There's nothing magic about 70 as a number. In fact, we know the risk of atherosclerosis and events really spans the full spectrum of LDL. There is no lower limit, so probably getting people at 50, or 40, or even lower is better than 70, but at least saying that we should pay attention to LDL and be more aggressive, certainly, getting patients who are at high risk to less than 70.

The other, I think, key part-- but it's a little more nuanced in the guidelines-- we can't pay attention to LDL as some binary trigger and holy grail, that it's really sort of the patient and their co-morbid characteristics that are equally as important. I would actually argue more important in driving risk. So we know that it's not just the presence of having vascular disease. You know, if you're certainly older, if you've had a recent MI or multiple heart attacks or stents, you have chronic kidney disease, diabetes, peripheral arterial disease, all of these factors really drive risk. And as you accumulate multiple of these factors, your absolute advantage rate goes up substantially as does your benefit for more intensive lipid lowering therapy. And these are patients are going to really benefit-- get bigger bang for your buck-- about adding agents such as PCSK9 inhibitors, Ezetimibe, et cetera, on top of statin.

And so people shouldn't say, oh, you know, I just pay attention to 70 or 100, and I'm done. In fact, if you took a patient who had a reasonable LDL and high intensity statin, maybe even less than 70, who has a lot of these other risk factors. They have chronic kidney disease, diabetes, multi-vessel coronary disease, they've had two or three MIs in the last five years, that patient's still at really high residual risk. And just because their LDL happens to be less than some number doesn't mean that we shouldn't be very aggressive in driving that particular patient's LDL lower.

So I think the guidelines are just meant to be a general framework, saying pay attention to the LDL. It matters. Drive that lower. Certainly, patients at the higher end of LDL are going to derive greater benefit, but the clinical factors are equally as important. And, I think, if you start to accumulate a lot of those high risk factors-- whether you're using the TIMI risk score for secondary prevention, or you're just using sort of common clinical factors-- if those really are high risk patients, it's not just the number. You really want to probably be adding on additional agents to drive that LDL even lower than those thresholds that are espoused in the guidelines.