PAUL RIDKER: Between early 2017 and today, we've come an enormous distance. We've known for a long time that lowering LDL cholesterol with statins is highly effective. But the first two major PCSK9 trials reported in early 2017, Marc Sabatine with the FOURIER data, my group with the SPIRE-1 and SPIRE-2 data. Those trials told us very clearly that if you took the LDL cholesterol down, well beyond the range we could do with a statin alone, we got 15% to 20% reductions further in MACE and MACE+. And most importantly, it was terrifically safe. I think we saw that the safety signal was almost absent.

> And so the real issues were how do different monoclonal antibodies differ? In the Pfizer-sponsored bococizumab trials that my group was associated with, there was an anti-drug antibody issue. And that's the reason that agent is no longer available. The good news was the FOURIER drug and now the Regeneron drug don't have that problem. So alirocumab and evolocumab are both highly effective.

And more recently, we've gotten finally the publication of the ODYSSEY outcomes trial. And again, almost identical results, excellent efficacy, excellent safety. And so we now are in an era where we know we can take LDL cholesterol very low. And we should be doing that for the vast majority of our patients.