SPEAKER: You know, when we look at cholesterol and lipid management, obviously, we've been dealing with this, whether it's primary care, it's general cardiology, sub-specialty cardiology, we've certainly been aware of this for a long time. But if you look really since the previous guidelines and in the last five years, there's really been a transformation in how we understand risk and also the therapies that we can bring to bear.

There are a couple of important things that have really transpired in the last few years. One is that we know that it's not simply good enough to be on a high-intensity statin. High-intensity statins are a great start. But we know that often patients who are taking high-intensity statins still have LDLs that are not optimal. And I think one of the things we've learned from whether that's the IMPROVE-IT trial, with ezetimibe or the two PCSK9 trials with ODYSSEY and the FOURIER is that LDL matters. And the lower you drive the LDL, the better patient outcomes even going below 70 to 60, 50. And there is even a sub analysis with FOURIER that patients who get down to LDLs in the 20s or teens do even better.

So we want to bring all of these medications to bear to drive the LDL down. So using a high-intensity statin is great, but we should be adding on additional agents to try to get the LDL as low as possible in high-risk patients.

The second thing that we've learned is that by doing so-- and particularly in the PCSK9 inhibitor trials-- you know, they both showed significant reductions in major adverse cardiovascular events. But even over a relatively short period of time, one of the trials, the ODYSSEY Outcomes trial shows a reduction in mortality. And so I think that's important that even over a very short time horizon that being much more aggressive in lowering LDL through non-statin additional therapy is reducing their cardiovascular risk, but patients are living longer.

And remember these are clinical trials that were less than a three year duration. So when you have a patient sitting in front of you, though, you're not just thinking about three years where one of the PCSK9 inhibitors demonstrated a mortality reduction. Think about what you're going to see in five years, 10 years in that patient. And so likely, when we treat populations, we're going to see even magnified benefits because we'll be treating these patients over much longer periods of time.

Now the science is incredibly strong. We should be as aggressive as possible in driving the LDL as low as possible in as many patients as we can. Now because we live in a health care system that we have to incorporate the economics, a challenge has been that these new therapies which are more expensive to manufacture, often their price points made it very difficult to prescribe these agents. In practice, there were a lot of prior authorizations. And so although we had many patients we wanted to use these drugs on, it really wasn't very practical to get it approved because there was a lot of resistance for approval because of the cost.

And one of the things really in the last 12 months, 18 months, is that the prices have dropped astronomically. And we're now really-- even after the guidelines-- so the current guidelines really didn't even incorporate this latest significant price drop. We're really now at a point even from a pharmaco economic analysis-- and there was a very nice recent publication in the *New England Journal*-- that these drugs as currently priced are cost effective and you know the standard kind of quality adjusted life year metric that we use of $100,000 with a price point of these drugs around somewhere between $3,000-$7,000 that not only do we have the clinical data, which is incredibly robust, but even in the health care sort of system that we work on, they are actually cost effective. And so that should make it much easier for us to justify additional non-statin therapy in a much larger percentage of patients than we currently have been able to do.

And I know even in my practice when I get home from Chicago, when I start to see these patients again in clinic, I'm going to be prescribing PCSK9 inhibitors to a significantly increased fraction of my patients because I think it's going to be a lot easier based on the new guidelines and also the new cost of the drugs to justify that these patients are going to benefit. And as a health care system, if we're reducing mortality as well as cardiovascular events, there's no reason why we-- shouldn't be denying them a potentially life saving therapy.