ROBERT ROSENSON: The greatest challenge that we have with regards to statin adherence is adverse muscle events. These symptoms may be perceived by the patient, based on news reports, reports of family members, reports of neighbors. But they also may be real. As a clinician, we need to listen to our patients and we need to understand their concerns, address some of their fears, review the data from the clinical trials that support that statin are very effective and well tolerated. We also have to recognize that there are about 5%-8% and maybe as much as 20% of individuals who cannot tolerate a statin due to adverse muscle events.

When one deals with a symptom in the absence of a biomarker, the evaluation becomes more challenging. We had the opportunity through the National Lipid Association 2014 Statin Muscle Task Force that I led, as well as additional work on international working group on statin muscle intolerance to develop a clinical tool. The Clinical Myalgia Index that helps us stratify individuals based on people with true statin intolerance in randomized, double blind, placebo crossover study design. In other words, individuals who had a adverse muscle event upon blinded re-challenge.

And our score's very effective. Because if you score low, you have a 91% certainty of not having true statin muscle intolerance. So evaluating the clinical pattern, the symptoms are symmetric. They're often proximal. They disappear with the drug de-challenge or drug withdrawal. And the same symptoms occur with drug re-challenge.

If you've identified somebody who you feel is statin muscle intolerance, what you would do is lower the dose of the statin or choose a different statin. Why would you choose a different statin if somebody failed one statin? Not all statin are the same with regards to the pharmacokinetics, pharmacodynamics, and pharmacogenomics. We often find that an individual can tolerate one statin but not another.

What if they fail a second agent? We might try a third and then consider those individuals for ezetimibe PCSK9 inhibitor therapy. There are clinical trials that have shown that individuals with statin muscle intolerance have marked reductions in LDL cholesterol with PCSK9 inhibitors. And the individuals that we're talking about are ones who had LDL cholesterol levels averaging 200 mg per deciliter, many individuals with familial hypercholesterolemia.

We recently reported that in individuals who had a myocardial infarction who down-titrated or discontinued the statins, they had a higher cardiovascular event rate. At two years, they had a 50% greater likelihood of having a myocardial infarction, 51% greater likelihood of having hospitalization for a cardiovascular event.

So this is not a benign condition. This is not a population that one would ignore if they have high risk characteristics such as myocardial infarction. We also know from a high risk population that was conducted in the Partners Health Group that followed individuals for four years that those individuals that down-titrated or discontinued the statin also had a higher mortality.

When we think about PCSK9 inhibitors in those individuals, clearly the most challenging population to receive insurance approval, one has to be aware of our recent analysis from Medicare beneficiaries. That the medical expenditures in the first year for people that down-titrated or discontinue are $14,000 higher than individuals that are highly adherent to a statin. So the cost to society, a cost to the health care system, if we don't properly and effectively address individuals of statin muscle intolerance and provide them another solution. That's our obligation not only to the patient but our obligation to society is to treat the highest risk individuals with whatever tools are available to us.