RAY GIBBONS: Hi. I'm Ray Gibbons from the Mayo Clinic in Rochester, Minnesota, where I'm a senior cardiologist in the Department of Cardiovascular Diseases. And I'm here to talk about the ischemia trial.

In the past, we would refer most patients with an abnormal stress test to early coronary angiography to see if they would benefit from stenting or bypass surgery. However, Mayo participated in the BARI 2D and COURAGE randomized trials, which found that there was no advantage of early revascularization compared to optimal medical therapy. And on that basis, we've referred only patients with the most severe stress tests because there was evidence in the literature from an observational study that patients with ischemia involving 15% of the left ventricle would do better with revascularization.

To further explore this issue, the National Institute of Health funded the ischemia trial. And the baseline data from that trial are published this week in *JAMA Cardiology.* They show that the patients in that trial received excellent baseline medical therapy, which was good for the patients and good for the trial design.

However, the paper also shows some cautionary information. About one in four patients randomized in the trial was randomized on the basis of an exercise electrocardiogram. And those patients appear to have clinical characteristics that place them at lower risk. In addition, some of the patients randomized on the basis of stress imaging by the individual centers did actually not have as much ischemia as they should have on core lab review.

So about one in seven patients randomized by stress imaging actually didn't meet the criteria set out by the trial design. Thus, it is possible that there are not enough patients to answer the original question, and only 18.7% of the patients randomized in the trial actually had 15% ischemia of the left ventricle.

Why did the trial have trouble enrolling patients with severe ischemia? Well, one factor was the poor support in the United States. Although Mayo enrolled patients in the trial, US enrollment only constituted about one in six patients in the study. And only one US center was among the 10 leading enrolling centers. US interventionalists apparently were not comfortable randomizing their patients to optimal medical therapy, even though three published reviews, one by a leading US interventionalist, argued in support of the trial design.

Another factor is the declining prevalence of moderate to severe ischemia on stress test, which has been reported in several studies, including one from Mayo. The results of the ischemia trial will be published later this year. They will set a new standard in the treatment of chronic coronary artery disease. But they may not actually have enough patients with moderate to severe ischemia to answer the original question because those patients are declining.

If the trial is negative, and if the event rates are low, I suspect that it will be criticized for not enrolling the right patients. However, I believe it potentially should be viewed more as a success of optimal medical therapy when it is consistently delivered as it was judged by the baseline data from this trial. Thank you.