So there are about maybe less than 20 clinical trials that looked at the efficacy of combination therapy versus monotherapy. And you have different formats. These trials have been done in Japan, in Europe, in the United States, in Brazil, in South America, in different places. The bottom line is that if you take them as a group, it's inconclusive.

What is inconclusive? It's inconclusive that combination therapy is better than levothyroxine. Is it worse? No, combination therapy is not worse than levothyroxine. Combination therapy is not better than levothyroxine. That's what the conclusion. But the conclusion is also that's not worse. So you would say, it's possible to say they're equivalent, because the outcomes were the same.

Now, because there's all this potential risk associated with combination therapy, if they're equivalent, you better stick to levothyroxine. Now, when you look at these trials, the problem is, which I alluded in the beginning, not all patients are symptomatic to start with. In fact, the vast majority of the patients on levothyroxine are fine. Thank you very much.

So if you take those patients, and put them on a clinical trial, and give combination therapy, since they were not symptomatic to start with, what are they going to tell you? Oh, I feel much better, but I was OK before as well. So unfortunately, we did not do a good job with these trials that are available to look for patients that are symptomatic. We should have 600, 700 patients symptomatic, and in those patients try to use combination therapy. We haven't done that in a consistent way.

So what should we look for these patients? Assuming that those patients do respond to combination therapy, how do we know they're responding? We don't have a good way of knowing that. But I can tell you the number one thing it's the preference. When you say, it doesn't seem that it did a lot of good for you. Let's go back to levothyroxine. They say, no, no, no, I want to keep this one. I don't want to change. I do feel better.

So the preference is the one thing that pops up from the clinical trials, and from my personal experience as well. Patients will tell you that they prefer. They can't put a finger why they prefer. And even if you look at the trials, there are a lot of questionnaires that are used. But the questionnaires don't match the preference. Patients will prefer combination therapy. But when you go and look at the details in the questionnaires, then it's inconclusive.

Well, why do you like to eat steak as opposed to shrimp, as opposed to fish? I mean, it's a kind of preference. You feel better doing one-- or eating one or the other. I guess if I had to answer a questionnaire about food preference, it might not conclude that I really like steak, or shrimp, or fish. So patients do have a preference for this. And I think that that's what the physicians need to talk to the patients is, do you prefer this one, or do you want to go back to the other one?

Now, no one should be on combination therapy if they are not clearly preferring the combination therapy. If the trial that you did didn't work, just go back to levothyroxine. It's fine. So you will see that it wasn't helpful. You did your best, and it didn't work. And patients will appreciate that, will appreciate the trial, and the attempt, and the intensive care that you gave to that patient as opposed to say, there's nothing I can do. Your TSH is normal. Go see a therapist.

That's the thing that we should not do, because that patient will not understand and will be mad at you and will go to the other doctor, and to the other doctor. And they repeat up to 10, 15, 20 different doctors, until they find one that will show that extra care and will show that they care for what the patients are feeling.