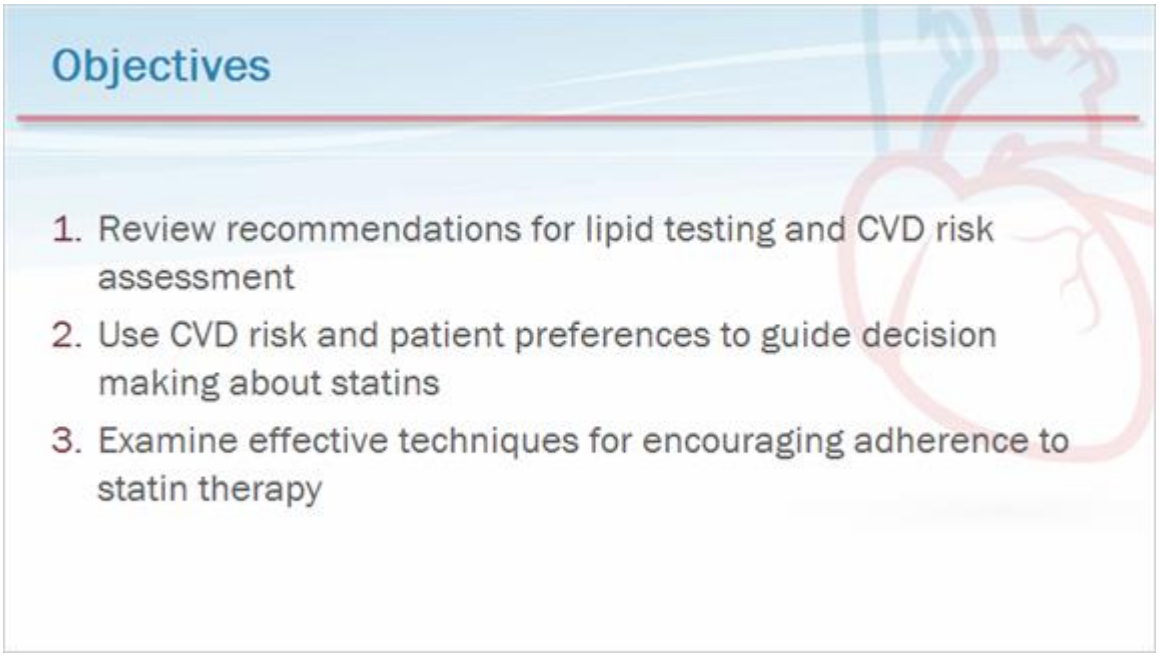
Primary Prevention of Cardiovascular Disease (CVD) Events with Statins

1 Primary Prevention of Cardiovascular Disease (CVD) Events with Statins

2 Welcome by Michael Pignone, MD, MPH

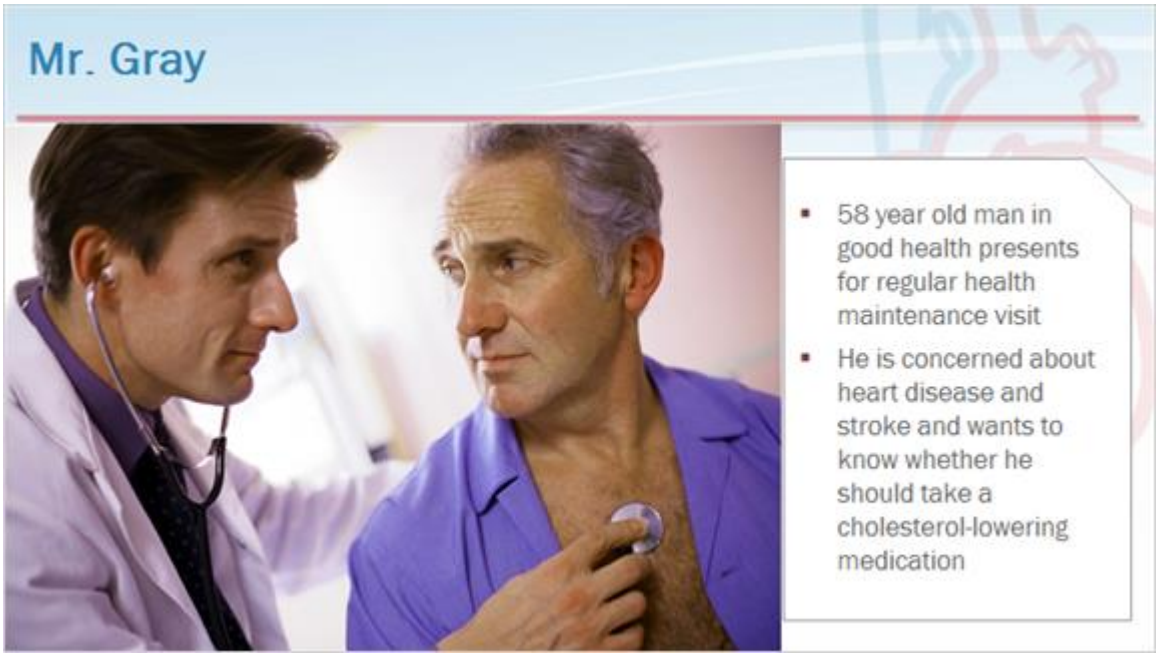
Hi, my name is Dr. Michael Pignone. I'm a General Internist and faculty member at The University of North Carolina - Chapel Hill, School of Medicine. In this Webinar I'll provide a discussion and update on the use of statins for primary prevention of cardiovascular disease, or CVD. This presentation is one in a series of Webinars developed by our evidence team at the University of North Carolina.

3 Objectives



Our objectives in this Webinar will be, first, to review recommendations for lipid testing and CVD risk assessment. Next, to use CVD risk and patient preferences to guide decision-making about statins. And, finally, to examine effective techniques for encouraging adherence to statin therapy.

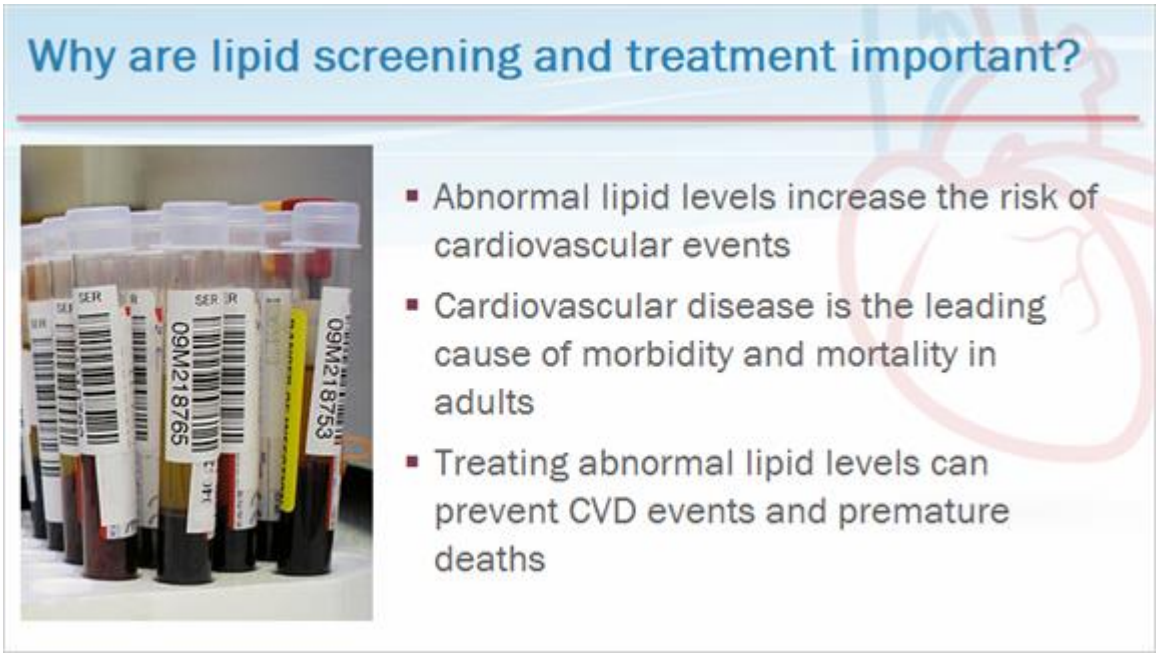
4 Mr. Gray



Let's start with a typical case. Mr. Gray is a 58-year-old white man in good health who presents for a regular health maintenance visit. He's concerned about heart disease and stroke and wants to know whether he should take a cholesterol lowering medication. He has no history of diabetes. He's a nonsmoker, and he likes to walk daily. His Body Mass Index is 27. His blood pressure is 124/82 mmHg. He's taking no medications. His total cholesterol is 210 mg per deciliter. His HDL cholesterol 40 mg per deciliter, and his LDL cholesterol is 130 mg per deciliter. Would you recommend a statin for CVD risk reduction in this patient? How would you decide?

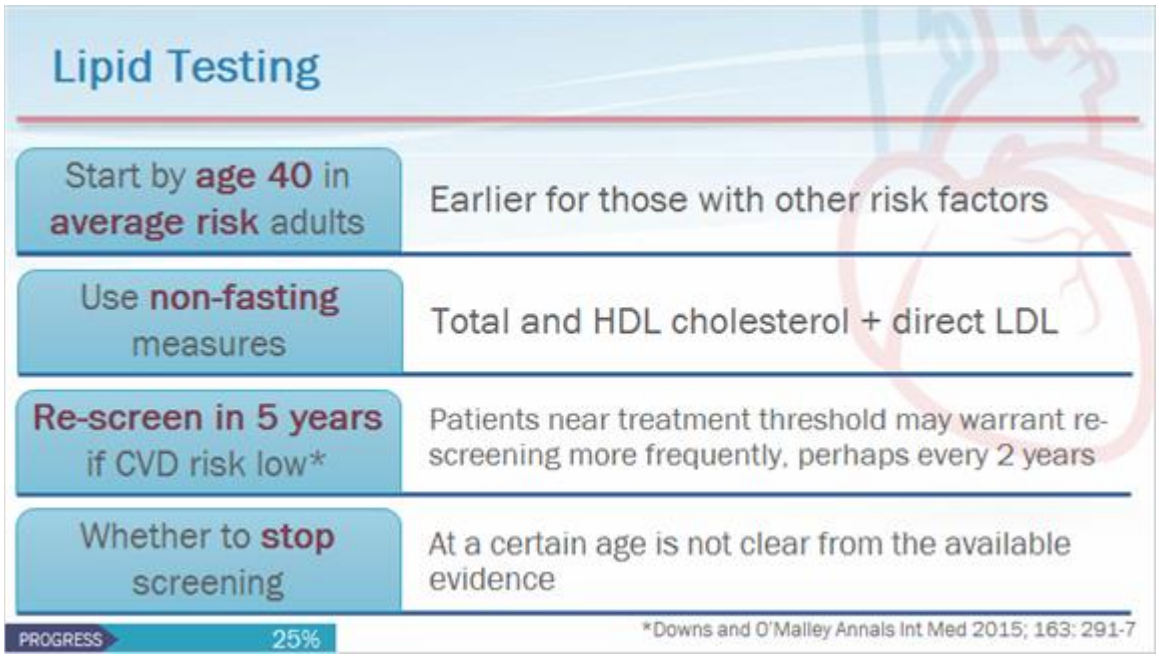
This is not an easy question. But, fortunately, there's a good bit of guidance available to help us answer this question for Mr. Gray and for other patients in our practices.

5 Why is lipid screening and treatment important?



Before we examine recommendations for lipid screening and treatment, let's review why this topic is important. Abnormal lipid levels increase the risk of cardiovascular events including heart attacks and strokes. Cardiovascular disease is the leading cause of morbidity and mortality in adults in North Carolina and across the United States. Identification and treatment of people with increased CVD risk but no prior history of CVD events, which we call primary prevention, has the opportunity to prevent many heart attacks, strokes, and premature deaths.

6 Lipid Testing



First of all, let's briefly review recommendations about lipid testing. Because the risk of cardiovascular events increases with age, we recommend that all adults ages 40 and older have regular lipid testing. You may want to start earlier in those with other cardiovascular risk factors or a family history of lipid disorders. Importantly, lipid screening does not require fasting. Patients should have at least a total and HDL cholesterol measured. Neither of these lipid measures is affected by whether the patient is fasting. These two measures are sufficient for estimating CVD risk. If you want to check an LDL cholesterol level to assist in deciding about treatment, you can order a direct LDL measurement which also does not require fasting. This is nice for patients, particularly those who see you in the afternoon. If lipid levels are very favorable and overall CVD risk is low, retesting in 5 years is reasonable. For those with borderline levels, or who may be near a level at which you would consider treatment, they should be tested sooner, perhaps in two years. Whether to stop screening at a certain age is not clear from the available evidence.

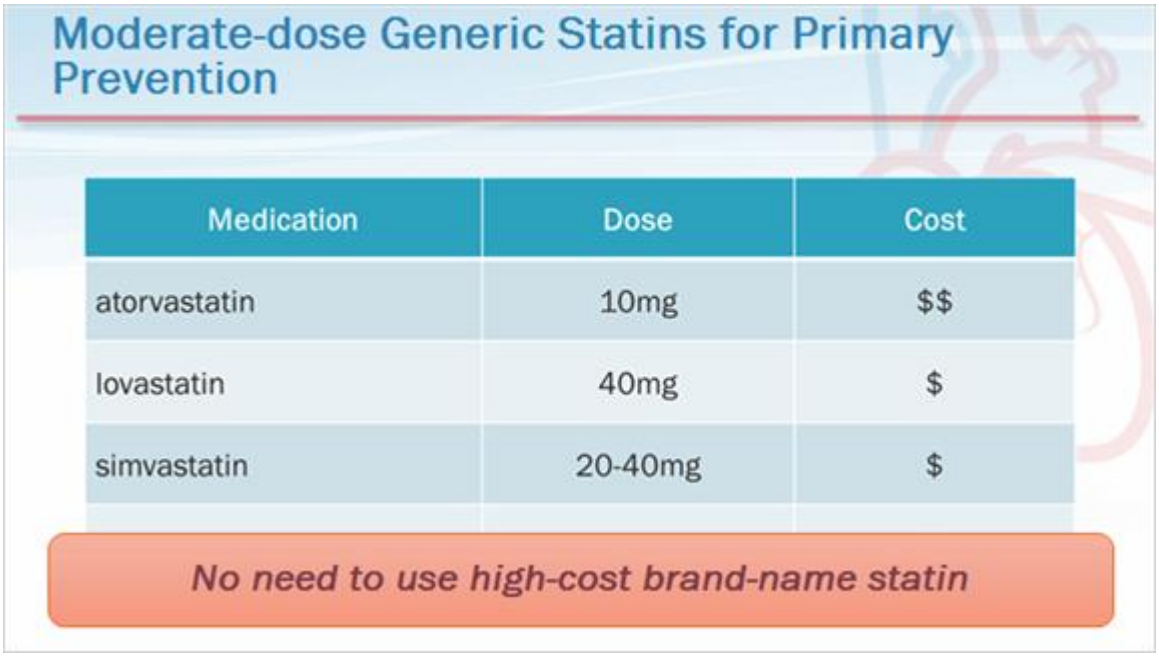
7 Statins are Effective for Primary Prevention

Now let's turn to decision making about the use of statins for primary prevention. Statins are effective. Systematic reviews based on evidence from multiple randomized trials suggest that statins reduce the risk of CVD events by 25% or more. This includes reductions in the risk of myocardial infarction and stroke. Moreover, these reductions in CVD events also lead to a reduction in the risk of all-cause mortality. The effect of diet and exercise counseling are independent of the effect of statins and should be considered separately.

8 Statins for Primary Prevention

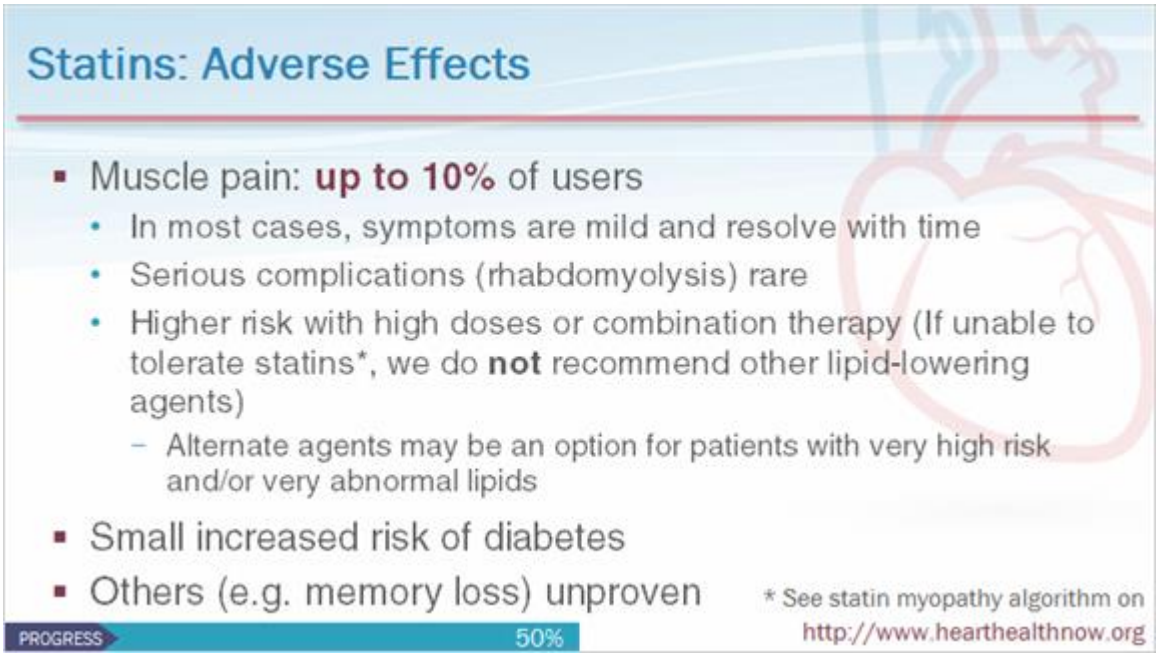
Across studies, reduction in CVD events appear to be proportional to the reduction in LDL observed. This suggests that higher doses of statins are more effective than lower doses. Importantly, however, studies of primary prevention have not examined the effect of treating different goal lipid levels. Lipid goals are recommended in earlier lipid treatment guidelines like ATP3 but have been deemphasized in the most-recent guidelines from the AHA ACC. As such, we recommend that you initiate a moderate dose generic statin for primary prevention. If the initial moderate dose is well-tolerated, and the patient reports good adherence, you don't need to check lipid levels more than once per year.

9 Moderate-dose Generic Statins for Primary Prevention



This next slide shows several options for moderate-dose generic statins. Many of these options are available on the $4 drug list from major pharmacies. There is no good reason to use a high-cost brand name statin.

10 Statins: Adverse Effects



Although statins are effective for primary prevention, they do have some downsides. The most important adverse effect of statins is myopathy, or muscle pain, which is reported in about 10-percent of users in observational studies. In most cases, symptoms are mild and resolve with time or with stopping or changing the statin. The more serious cases of myopathy, or even rhabdomyolysis are rare. They're most likely to occur in patients on high-dose statins, along with other lipid-lowering drugs, or in patients who have conditions that interfere with statin metabolism. See our Websites for frequently asked questions for a list of such drugs and conditions and for an algorithm for addressing statin-related muscle pain. Recent studies have shown that a small increase in risk of diabetes occurs with statins, particularly high-dose statins, but the effect does not appear to be clinically significant. Other hypothesized adverse effects such as memory loss have not been confirmed when they've been examined rigorously.

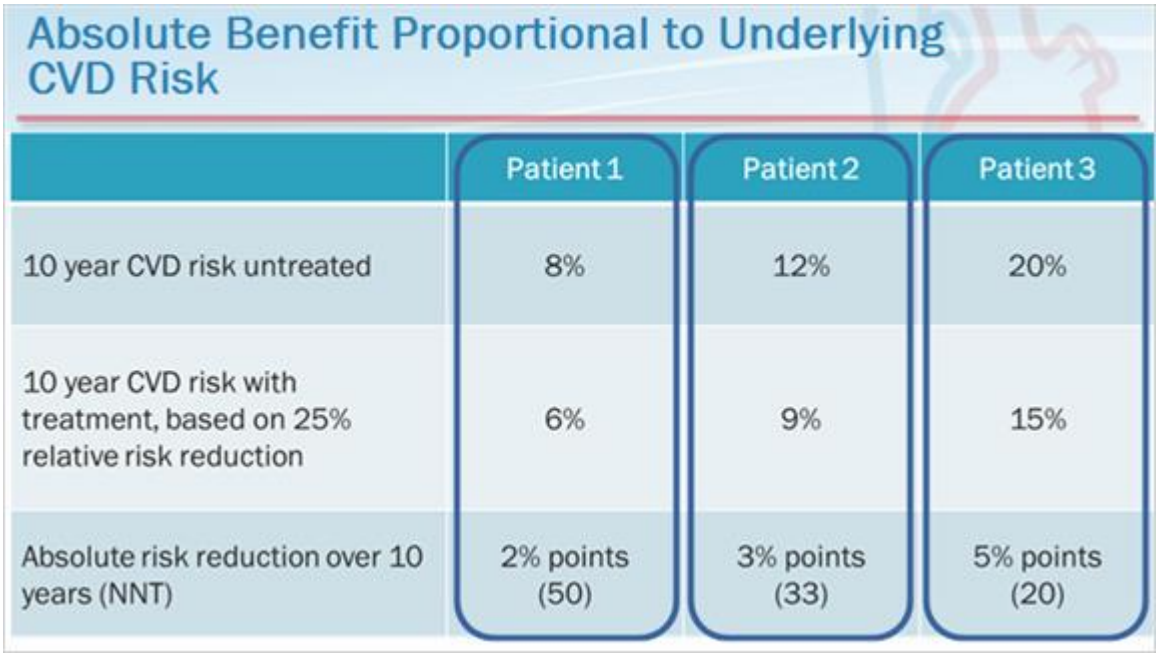
11 Who should be treated?

So who should be treated with statins? Given the potential benefits and downsides, current guidelines suggest the decision about whether to use a statin should be based on the patient's global CVD risk. The rationale for risk-based approach is based on the fact the absolute benefits of treatment are proportional to the patient's absolute CVD risk. On the other hand, the adverse effects appear to be relatively independent of CVD risks. As such, the net benefit is proportional to the patient's 10-year CVD risk. As we discussed in our Webinar in risk estimation, our preferred measure of risk is the 10-year global ASCVD risk from the ACC AHA pooled-risk equations.

12 Reference

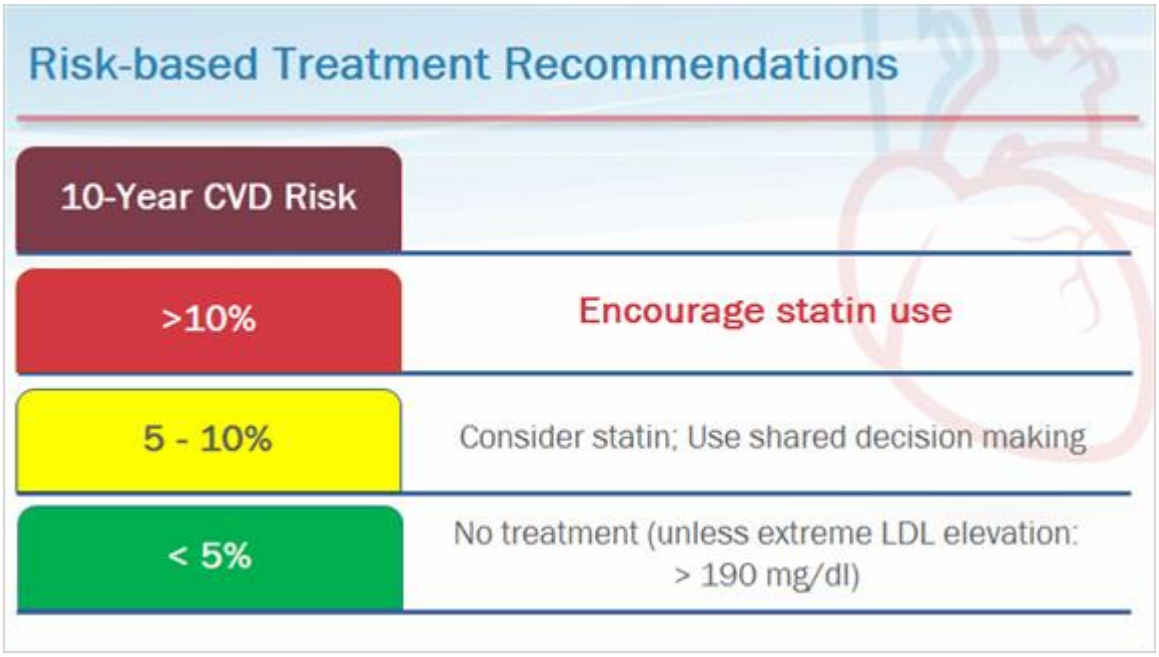
Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PW; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014 Jul 1;63(25 Pt B):2889-934.

13 Absolute Benefit Proportional to Underlying CVD Risk



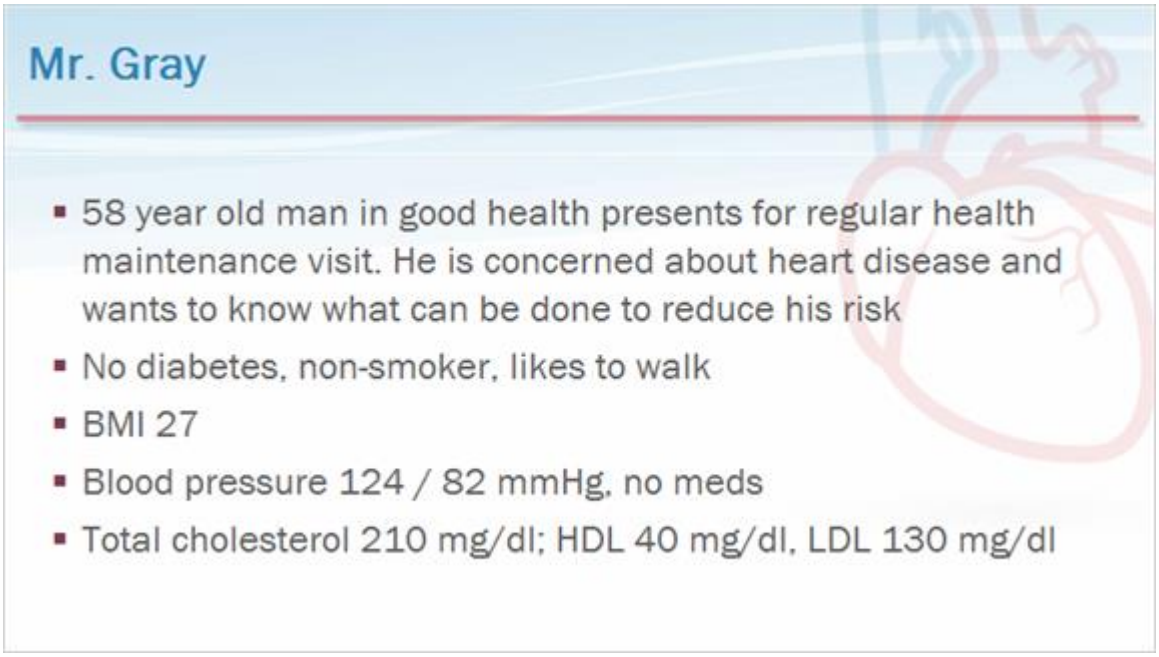
This slide illustrates the difference in benefits for three patients with different levels of underlying CVD risks. It assumes a relative risk reduction of 25% with statin therapy. For the first patient who has a 10-year CVD risk of 8%, treating with a statin would reduce that risk by 2% points over 10 years. Put another way, you'd have to treat 50 patients like this for 10 years to prevent one major CVD event. This is often referred to as the number needed to treat or NNT. For the second patient who has a 12% CVD risk over 10 years, treating would reduce the risk by 3% points. The NNT in this case is 33. This means that because the treatment effect is larger, you'd have to treat fewer patients to prevent one event. Finally, for the patient with a 10-year risk of 20%, the effect is even greater: a 5%-point reduction and an NNT of 20.

14 Risk-based Treatment Recommendations



Different guidelines have made slightly different recommendations for what CVD risk is high enough to justify treatment. Or put another way, what risk level is high enough such as the expected benefits outweigh the potential adverse effects, hassles, and cost of treatment? In our view, patients with a 10-year CVD risk over 10% should generally receive a recommendation for treatment. On the other side, those with a 10-year risk under 5% probably do not warrant treatment. For those in the middle, we suggest the providers briefly describe the potential benefits and potential downsides of treatment and share the decision with the patient in light of how the patient feels about the potential benefits and downsides.

15 Mr. Gray

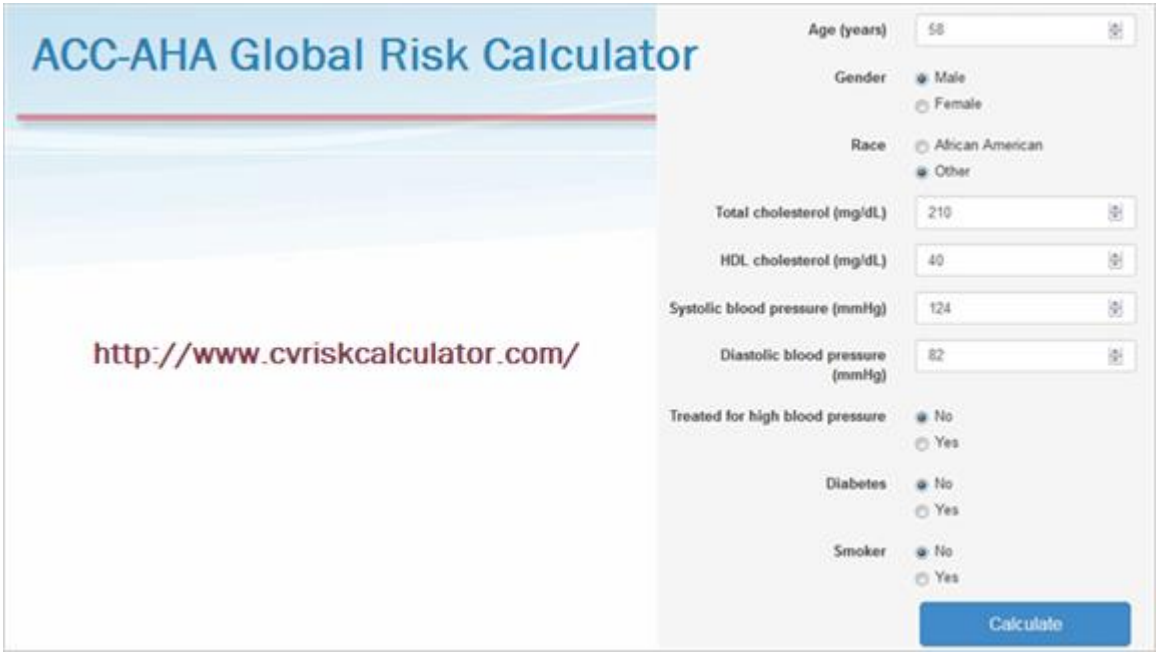


Now let's return to our example of Mr. Gray to see how this approach can be used. Mr. Gray is a 58-year-old white man in good health who presents for a regular health maintenance visit. He's concerned about heart disease and stroke and wants to know whether he should take a cholesterol lowering medication. He has no history of diabetes. He's a nonsmoker, and he likes to walk daily. His Body Mass Index is 27. His blood pressure is 124/82 mmHg. He's taking no medications. His total cholesterol is 210 mg per deciliter. His HDL cholesterol 40 mg per deciliter, and his LDL cholesterol is 130 mg per deciliter.

16 What is his risk of a CVD event over the next 10 years?

Without using the calculator, what do you think his 10-year risk level would be? Is it less than 5%, 5-10%, 10-15%, 15-20%, or greater than 20%?

17 ACC-AHA Global Risk Calculator



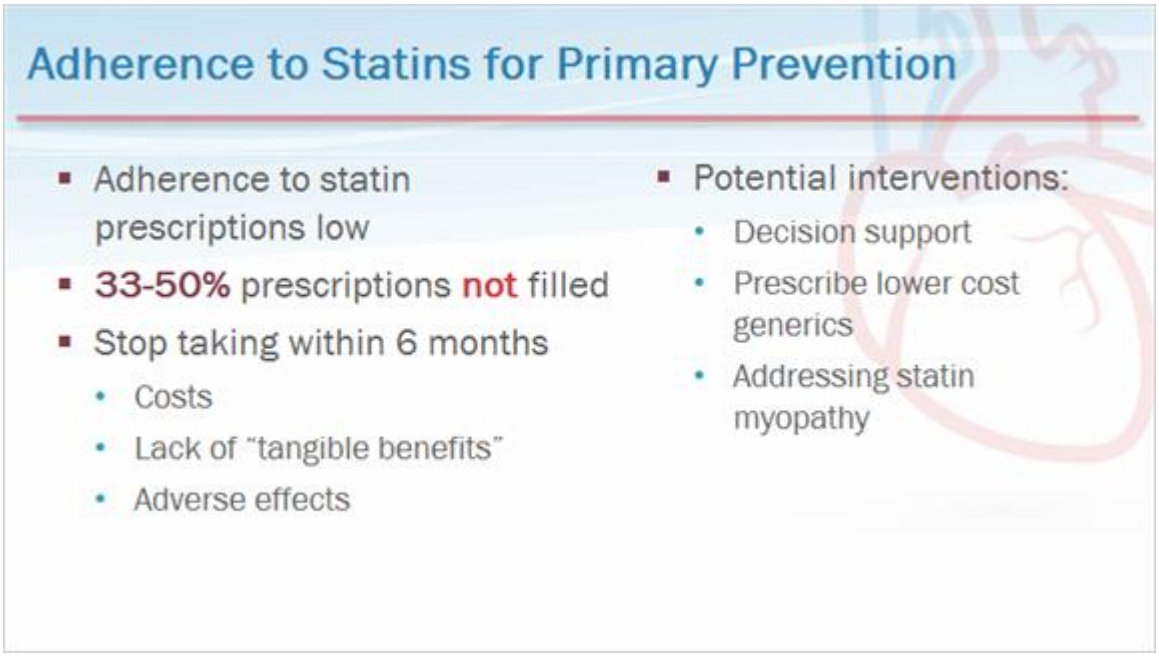
The next slide shows Mr. Gray's information entered into the ASCVD risk calculator. This should take you about 30-45 seconds.

www.cvriskcalculator.com

18 CVD Risk Output (and Treatment Recommendation)

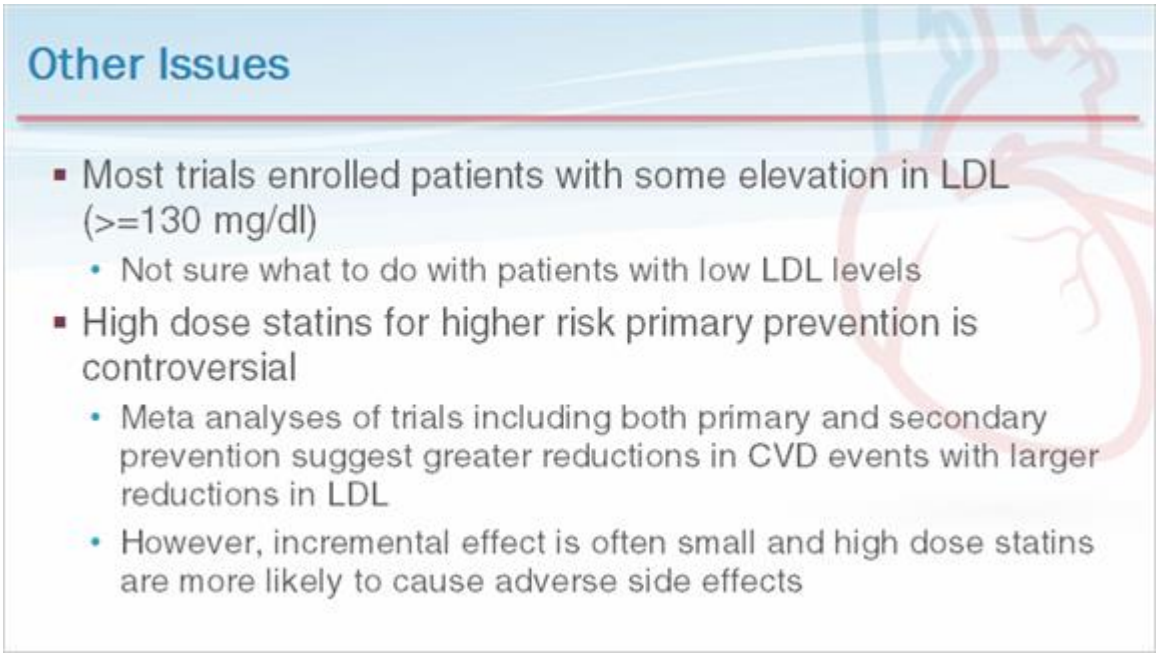
On the following slide, we see that Mr. Gray's 10-year CVD risk is between 8-9%. Using our approach, he is someone who you would engage in shared decision making with. You would describe the potential benefit, a 2% reduction in risk over 10 years, and the potential downsides including the risk of muscle pain, and elicit his opinion about the relative importance levels. In this case, Mr. Gray felt the potential benefits outweighed the downsides, and he agreed to a prescription for generic Pravastatin 40 mg daily which he obtained from his mail-order pharmacy.

19 Adherence to Statins for Primary Prevention



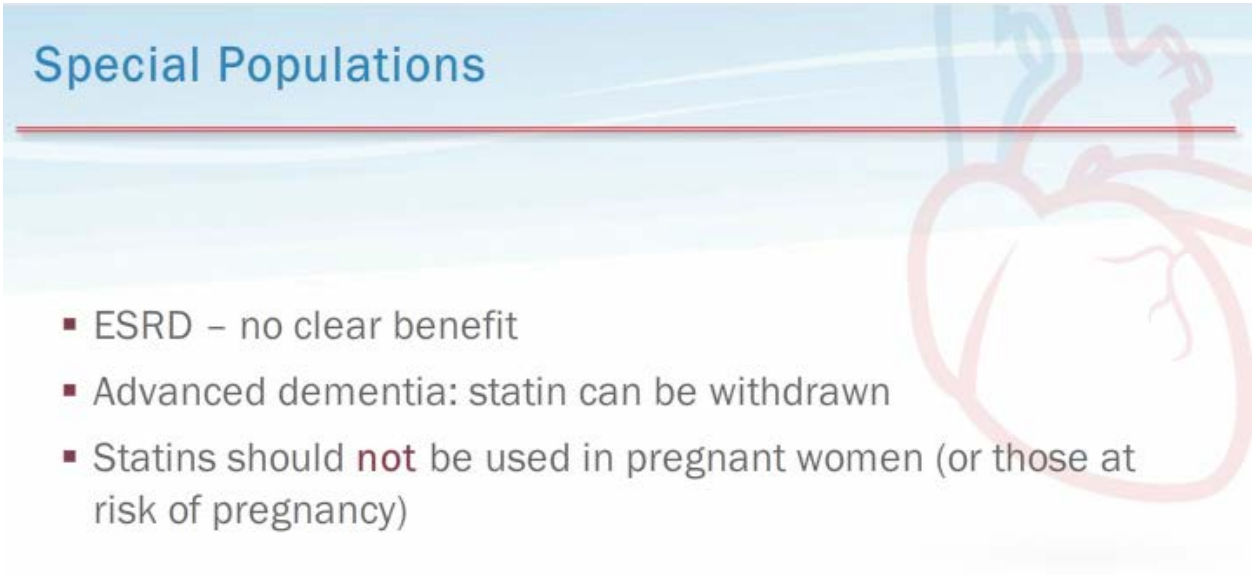
But once you and your patient have decided the statin therapy makes sense, the next challenge is to ensure that it is adhered to effectively. Studies suggest that 33-50% of statin prescriptions are not filled, and that many patients stop taking their statin medication within six months. There are several potential reasons for incomplete adherence including costs, the lack of benefit that a patient can see or feel, and the occurrence of adverse effects, particularly muscle pain. Thankfully, there are several techniques that can help support adherence. These include: decision support. Research from UNC suggested when patients are actively engaged in their decision about taking a statin, they're more likely to be knowledgeable and adherent. Prescribing low-dose generics can help reduce medication cost-related nonadherence. And for patients who experience mild-to-moderate muscle pain without large elevations in CK, we can use our statin myopathy algorithm to reduce or eliminate such symptoms.

20 Other Issues



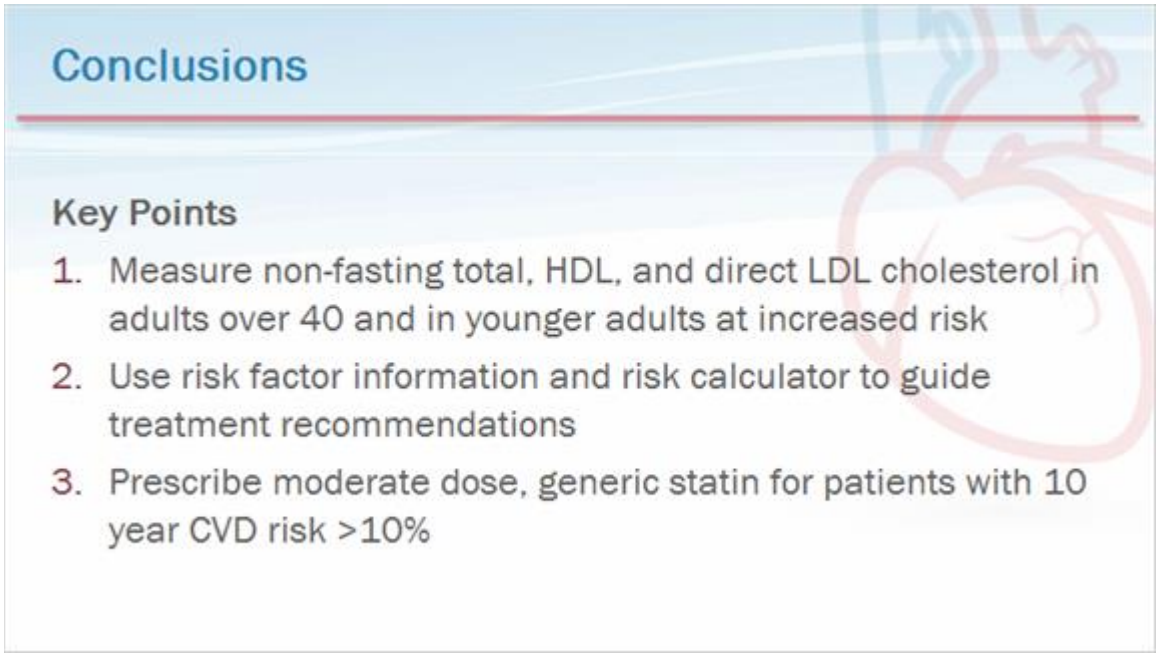
Just a few other salient issues in statin therapy. Most trials enrolled patients with some elevation in LDL or who had elevated risks due to diabetes. We're not sure what to do with the patients at low LDL levels. Whether to use high-dose statins, for example, Atorvastatin 80 mg daily, in higher-risk primary prevention is controversial. Meta analyses of trials that include both primary and secondary prevention suggest greater reductions in CVD events with larger reductions in LDL. However, the incremental absolute effect is often quite small and higher-dose statins are more likely to cause adverse effects.

21 Special Populations



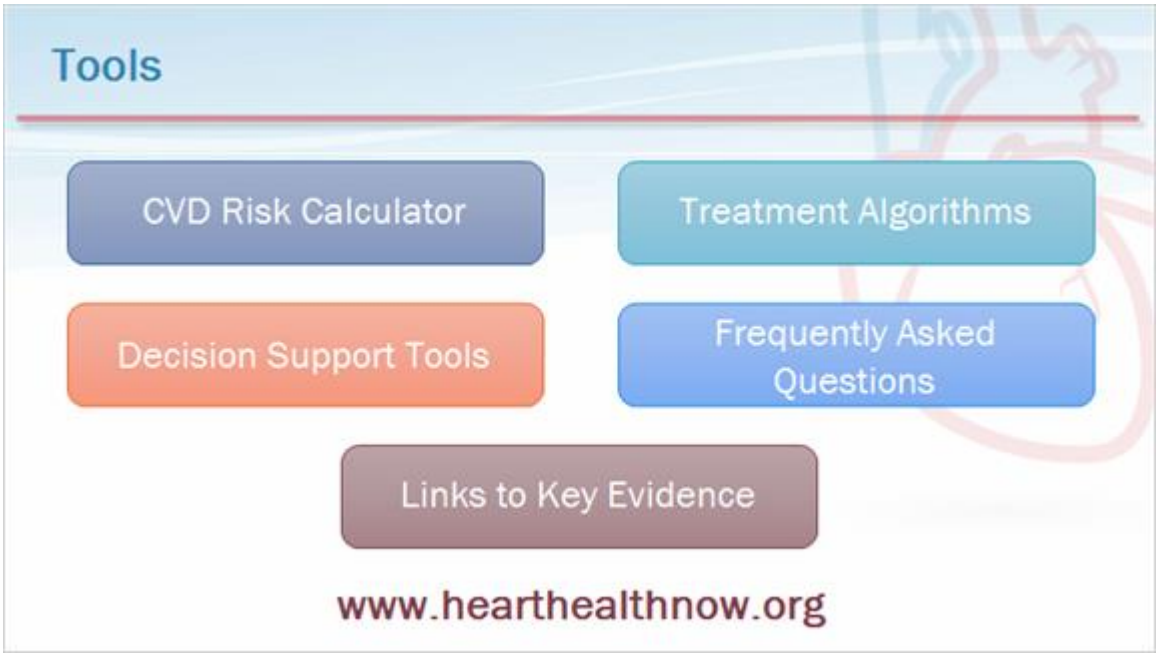
Finally, just some information about a few special populations. Patients with end-stage renal disease do not appear to benefit from statins. Patients who develop advanced dementia can have their statin medication withdrawn, especially if pill taking is distressing or difficult. And statins should not be used in pregnant women or those at risk of pregnancy.

22 Conclusions



OK. We've covered a good bit of material in the Webinar. Here are my key take-home points. First, you should measure non-fasting total HDL and direct LDL cholesterol in adults over 40, and in younger adults at increased risk. Secondly, you should use a risk-based approach to treatment decision making. For those adults at 10% risk or greater, prescribe moderate-dose generic statins. Use shared decision making in patients at moderate risk.

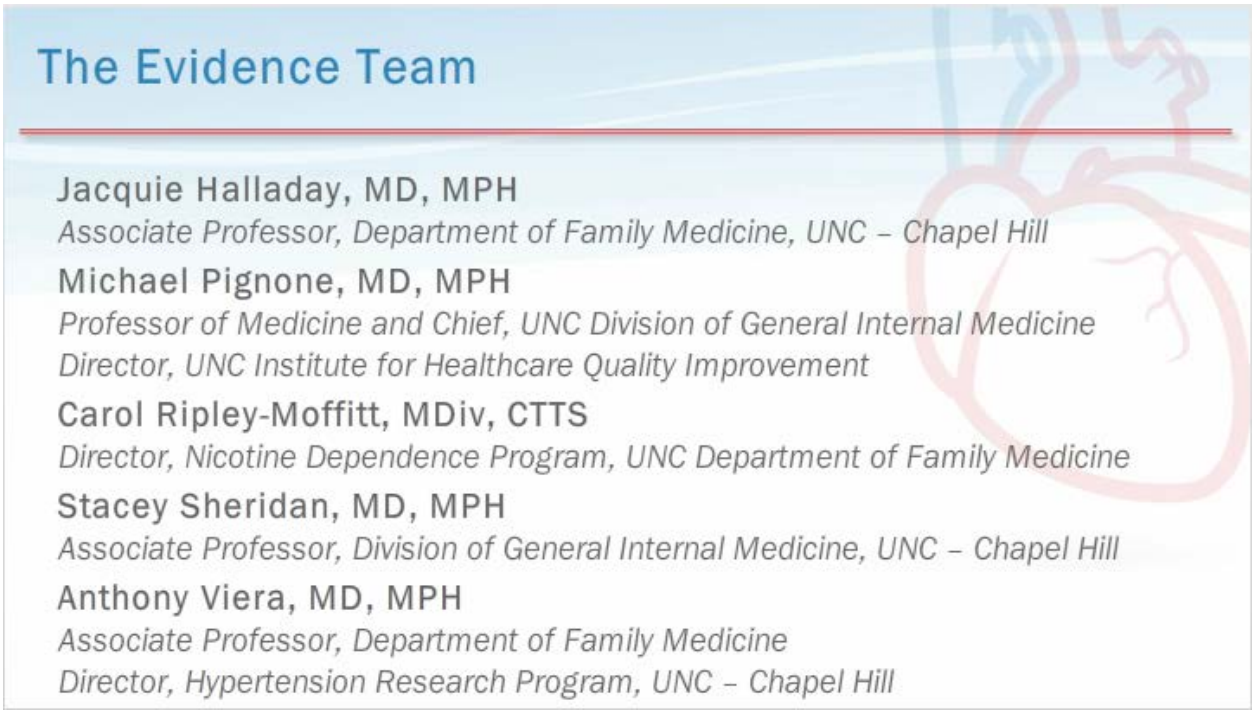
23 Tools



Remember to go to our Website for other resources to help in decision making about the use of statins for primary prevention. The Website has links to the ASCVD risk calculator, treatment algorithms including ones for addressing statin-related muscle pain, decision support tools for patients and providers, a list of frequently asked questions, and a way for you to ask questions of the evidence team, and links to key sources such as systematic reviews and evidence-based guidelines.

www.hearthealthnow.org

25 Congratulations

26 The Evidence Team

27 The Evidence Team