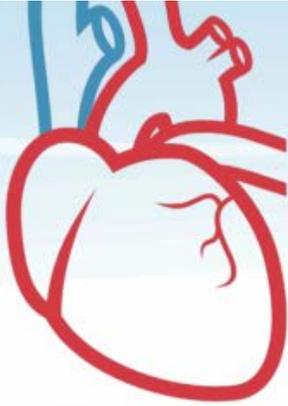


Secondary Prevention of Cardiovascular Disease (CVD)

1 Secondary Prevention of Cardiovascular Disease (CVD)



Heart Health Now!
The North Carolina Cooperative for AHRQ's
EvidenceNOW
Advancing Heart Health in Primary Care

**Secondary Prevention of
Cardiovascular Disease (CVD)**

Funded by the Agency for Healthcare Research and Quality (AHRQ)
in the U.S. Department of Health & Human Services

 **UNC**
THE CECIL G. SHEPS CENTER
FOR HEALTH SERVICES RESEARCH

 **NCHQA**
North Carolina Healthcare Quality Alliance

 North Carolina
AHEC

 Community Care
of North Carolina

LENGTH: About 12 minutes

Updated on 12/15/2015

2 Welcome by Michael Pignone, MD, MPH



Welcome by Michael Pignone, MD, MPH

Professor of Medicine and Chief, UNC Division of General Internal Medicine; Director, UNC Institute for Healthcare Quality Improvement

Hi. My name is Dr. Michael Pignone. I'm a general internist and faculty member of the University of North Carolina Chapel Hill. In this Webinar I'll provide a discussion and update on secondary prevention of cardiovascular disease, also known as CVD. This presentation is one in the series of Webinars developed by our evidence team at the University of North Carolina.

3 Objectives

Objectives

1. To review specific issues in medical therapy for patients with a history of CVD:
 - Lipid lowering therapy
 - Antiplatelet agents
 - Blood pressure control
2. To review specific lifestyle interventions for patients with a history of CVD:
 - Cardiac Rehabilitation / Exercise
 - Diet

Our objectives today in this Webinar will be: Number one, to review specific issues in medical therapy for patients with a history of CVD. This will include lipid-lowering therapy, antiplatelet agents, and blood pressure control; and, secondly, to review specific life-style interventions for patients with a history of CVD. This will include cardiac rehabilitation or exercise and dietary changes.

4 Mrs. Jones

Mrs. Jones

- A 59 year old woman with myocardial infarction 4 months ago, received drug-eluting stent to LAD.
 - Ejection fraction was normal
- She is in your clinic today for follow up.
- Medications: clopidogrel 75 mg daily, lisinopril 20 mg daily, metoprolol 25 mg twice daily, pravastatin 40 mg daily, and aspirin 81 mg daily
- BP 122/68 mmHg, HR 60 bpm
- TC 215 mg/dL, TG 200 mg/dL, HDL 40 mg/dL, LDL 135 mg/dL, fasting glucose 112 mg/dL

Let's start with a typical case. Mrs. Jones is a 59-year-old woman with a myocardial infarction four months ago. She received a drug-eluting stent to her LAD artery, and her ejection fraction at that time was normal. She's in your clinic today for follow up. Her medications include Clopidogrel 75 mg daily, Lisinopril 20 mg daily, Metoprolol 25 mg twice a day, and Pravastatin 40 mg daily, as well as aspirin 81 mg daily. Her blood pressure is 122/68 mmHg. Her heart rate is 68 BPM, and her total cholesterol is 215 mg per deciliter. Her triglycerides are 200 mg per deciliter. Her HDL cholesterol 40 mg per deciliter, and her LDL cholesterol 135 mg per deciliter. Her fasting blood glucose is 112 mg per deciliter.

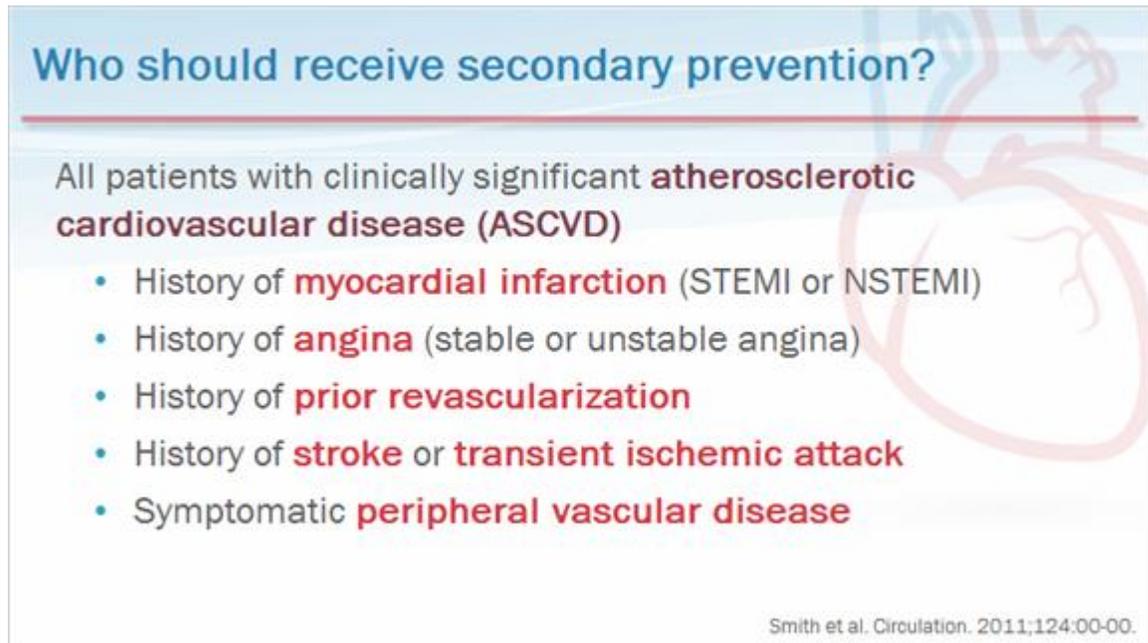
5 Question



Question

Based on that information, what change, if any, would you make to her medication regimen? Would you add Eplerenone 25 mg daily, add Niaspan 500 mg daily with a titration to 2K mg as tolerated, discontinue Pravastatin and add Atorvastatin 80 mg daily, increase her aspirin dose to 325 mg daily, or make no change?

6 Who should receive secondary prevention?



Who should receive secondary prevention?

All patients with clinically significant **atherosclerotic cardiovascular disease (ASCVD)**

- History of **myocardial infarction** (STEMI or NSTEMI)
- History of **angina** (stable or unstable angina)
- History of **prior revascularization**
- History of **stroke** or **transient ischemic attack**
- Symptomatic **peripheral vascular disease**

Smith et al. Circulation. 2011;124:00-00.

This is not an easy question. But, fortunately, there's a good bit of guidance available to help us answer this question of Mrs. Jones, and for other patients like her in our practices. To start with, before we examine recommendations for secondary prevention, let's review who should receive secondary prevention and why this topic is important. The recommendations in this presentation on secondary prevention are directed to patients with a history of clinically significant atherosclerotic cardiovascular disease including a history of myocardial infarction, a history of angina, a history of prior revascularization – either stenting or bypass surgery, a history of stroke or transient ischemic attack or TIA, and a history of symptomatic peripheral vascular disease.

7 What are the goals of secondary prevention?



The slide features a light blue header with the title 'Topics Not Covered in this Presentation' in a dark blue font. Below the header is a photograph of a man with dark hair and a light beard, looking slightly to the right. Overlaid on the left side of the photo is a semi-transparent grey box containing a bulleted list. At the bottom left of the slide, there is a teal progress bar with the word 'PROGRESS' and the percentage '25%'.

Topics Not Covered in this Presentation

- The management of patients with acute coronary syndromes
- Recommendations for patients with symptomatic heart failure

PROGRESS 25%

We will not cover the management of patients with acute coronary syndromes in this presentation, nor will we provide recommendations for patients with symptomatic heart failure.

8 What are the goals of secondary prevention?

The slide features a light blue header with the title 'What are the goals of secondary prevention?'. Below the title, four rounded rectangular boxes are arranged in a 2x2 grid. The left column contains two red boxes: '1. Prevent recurrent events' (top) and '2. Prevent death' (bottom). The right column contains two blue boxes: '3. Improve symptoms' (top) and '4. Improve quality of life' (bottom). At the bottom left, a blue progress bar shows 'PROGRESS' and '25%'.

What are the goals of secondary prevention?

1. Prevent recurrent events
2. Prevent death
3. Improve symptoms
4. Improve quality of life

PROGRESS 25%

So, what are the goals of secondary prevention? Number one, to prevent recurrent events like heart attacks or strokes; secondly, to prevent death; third, to improve symptoms; and, fourth, to improve quality of life.

9 Topics



Topics

Interventions covered include:

- Lipid lowering therapy
- Antiplatelet therapy
- Blood pressure control
- Cardiovascular rehabilitation/exercise
- Diet modification

Smoking Cessation
will be addressed in a separate webinar

The main interventions we'll cover today include: lipid-lowering therapy, anti-platelet therapy, blood pressure control, cardiovascular rehabilitation, and dietary modification. Smoking cessation is very important in secondary prevention, but it will be addressed in a second Webinar.

10 Lipid Lowering Therapy



First, let's look at the use of lipid-lowering therapy in secondary prevention.

11 Statins are Effective in Secondary Prevention

Statins are Effective in Secondary Prevention

- For patients with previous CVD events, statins (compared with placebo) reduce:
 - All cause mortality by **19%**
 - CHD mortality by **27%**
 - Myocardial infarction by **27%**
 - Strokes by **16%**
- High-dose statins (c/w moderate dose) reduce:
 - Combination of non-fatal MI and CHD death by **10%**
 - Stroke by **14%**

Mills EJ, O'Regan C, Eyawo O, Wu P, Mills F, Berwanger O, Briel M. Eur Heart J. 2011;32(11):1409
Gutierrez et al Arch Int Med 2012; 172: 909-19

Statins are effective in secondary prevention. Evidence from multiple randomized trials show that statins reduced the risk of CVD events in patients with a history of cardiovascular disease. They reduce all-cause mortality by 19%, CHD mortality by 27%, myocardial infarction by 27%, and strokes by 16%. High-dose statins, when compared with moderate-dose statins, further reduce the combination of nonfatal myocardial infarction and CHD death by 10% and stroke by 14%.

12 Statin Prescribing in Secondary Prevention

Age \leq 75	Age > 75 Or high intensity statin not tolerated
<p>Initiate high intensity statin:</p> <ul style="list-style-type: none">▪ Atorvastatin 40-80 mg▪ Rosuvastatin 20-40 mg <p><i>once daily</i></p>	<p>Initiate moderate intensity statin:</p> <ul style="list-style-type: none">▪ Atorvastatin 10-20 mg▪ Simvastatin 20-40 mg▪ Pravastatin 40-80 mg▪ Lovastatin 40 mg▪ Rosuvastatin 5-10 mg <p><i>once daily</i></p>

So, here's a table of statin-prescribing and secondary prevention. For patients under age 75, we recommend that you initiate high-intensity statin for secondary prevention such as Atorvastatin 40 mg daily. For patients over age 75, or in whom high-intensity statin is not well-tolerated, we recommend that you initiate moderate-intensity statin using any of the recommended agents on the right side of the table.

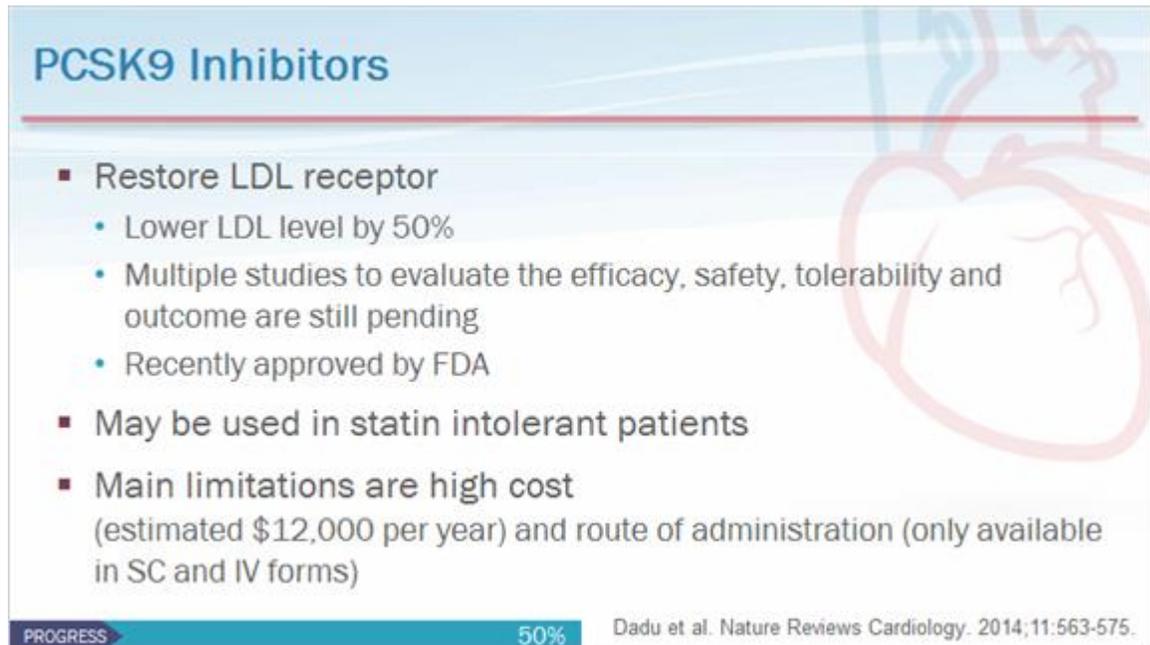
13 Recommendation

Recommendation

- Do not routinely add other lipid lowering therapy to statins because it provides little benefit with higher costs and greater potential for adverse effects
- Consider alternative agents (like PCSK9 inhibitors) for patients at very high risk who cannot tolerate moderate dose statins

We do not routinely recommend that you add other lipid-lowering therapy to statins, because it provides little additional benefit with higher costs and greater potential for adverse effects. For those patients at very high risk who cannot tolerate statins, you can consider using alternative agents. One new, but unproven, option is the use of PCSK9 inhibitors.

14 PCSK9 Inhibitors



PCSK9 Inhibitors

- Restore LDL receptor
 - Lower LDL level by 50%
 - Multiple studies to evaluate the efficacy, safety, tolerability and outcome are still pending
 - Recently approved by FDA
- May be used in statin intolerant patients
- Main limitations are high cost (estimated \$12,000 per year) and route of administration (only available in SC and IV forms)

PROGRESS 50% Dadu et al. Nature Reviews Cardiology. 2014;11:563-575.

PCSK9 inhibitors are a new class of injectable drugs that were recently FDA approved. They lower LDL cholesterol level by 50% or more. However, their safety and efficacy for CVD event reduction are still being evaluated. They may be a reasonable option for patients at high risk who are not able to tolerate statins. Their biggest limitation is cost which is estimated at over \$12,000 per year.

15 Antiplatelet Therapy



Now, let's review the use of anti-platelet agents for secondary prevention.

16 Aspirin in Secondary Prevention

Aspirin in Secondary Prevention

- Mechanism:
 - Non-selective and irreversible cyclooxygenase inhibitors
 - Reduce platelet aggregation
- Dose: 81 mg once daily
- Duration: Life long
- Benefit: Long-term aspirin monotherapy reduces recurrent ASCVD (20% relative risk reduction)
- Risk: Major bleeding (>1% annually in older adults), bruising



Smith et al. Circulation. 2011;124:00-00.
Antithrombotic Trialists' Collaboration. BMJ. 2002;324(7329):71.

Let's start by looking at aspirin. Aspirin works by selectively and irreversibly inhibiting cyclooxygenase and, thus, reducing platelet aggregation. Daily 81 mg aspirin effectively reduces recurrent CVD events by 20 percent or more. The main risk of aspirin, and other anti-platelet agents is bleeding, mostly gastrointestinal. The risk of GI bleeding varies with age, and is greater than 1% per year in the elderly. Patients may also experience annoying bruising and dyspepsia, or upset stomach.

17 P2Y12 Inhibitors in Secondary Prevention in Patients with Prior Stents

P2Y12 Inhibitors in Secondary Prevention in Patients with Prior Stents

- Used along with life long aspirin 81 mg once daily
- Mechanism: Reduce platelet activation and aggregation
- Drugs and dose:
 - Clopidogrel 75 mg once daily (generic cost), or
 - Prasugrel 10 mg once daily, or
 - Ticagrelor 90 mg twice daily
- Duration: **At least 1 month post bare metal stent or at least 1 year post drug eluting stent**
- Benefit: Reduced CVD events, reduced stent thrombosis
- Risk: Bleeding (Clopidogrel<Prasugrel<Ticagrelor)

Smith et al. Circulation. 2011;124:00-00.

Now, let's examine the other main class of anti-platelet drugs, the P2Y12 inhibitors such as Clopidogrel. First, we'll review the use of these drugs in patients who have stents. These patients, along with their high general risk of secondary prevention patients, are at particularly high risk for stent-related thrombosis. For patients with stents, P2Y12 inhibitors are used, along with aspirin 81 mg once daily. They reduce platelet activation and aggregation by different mechanism than aspirin. There are three P2Y12 inhibitors available. Clopidogrel is available generically and is the preferred agent for most patients. The prescribed P2Y12 inhibitor should be taken for at least one month post the implantation of a bare-metal stent or for at least one year post the implantation of a drug eluting stent. P2Y12 inhibitors reduce stent-related thrombosis and also reduce the risk of recurrent events. However, the addition of these drugs also increases the risk of bleeding. If non-life-threatening serious bleeding occurs, consult with the patient's cardiologist about whether to withdraw therapy. Similarly, providers should query for medication cost-related nonadherence and treat it by prescribing generics or seeking medication assistance program.

18 P2Y12 Inhibitors in Secondary Prevention in Patients without Prior Stents

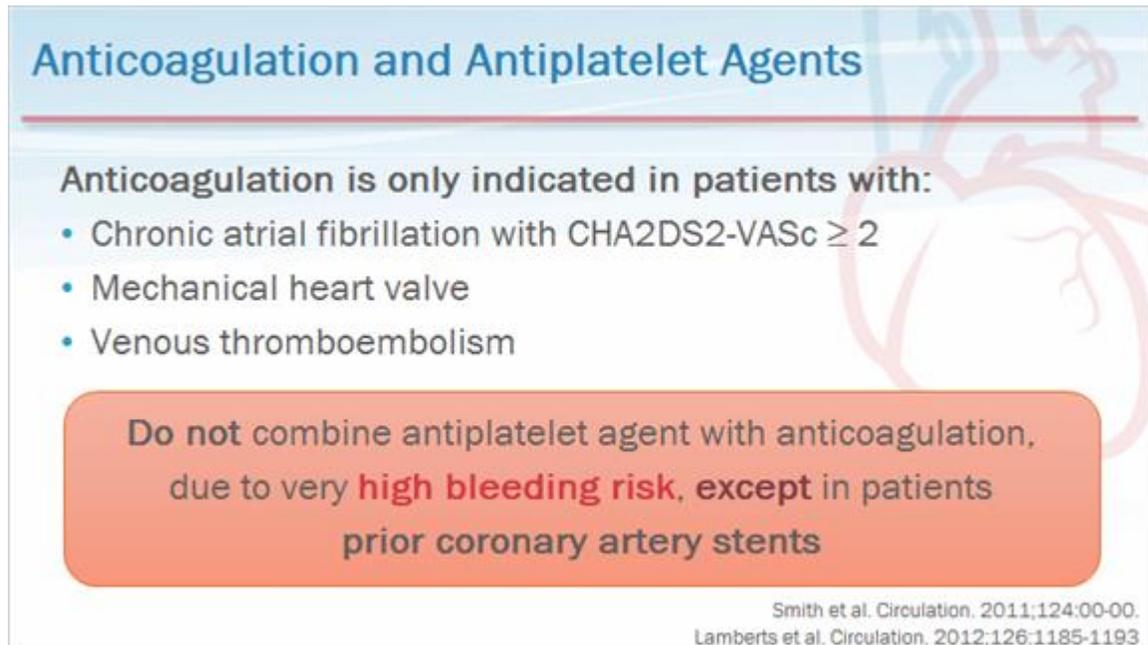
P2Y12 Inhibitors in Secondary Prevention in Patients without Prior Stents

- Use of P2Y12 inhibitors instead of aspirin had **minimal** benefit with much **higher** cost
 - **P2Y12 inhibitor monotherapy** should **only** be used in the patients who cannot tolerate aspirin
- Using P2Y12 inhibitors with aspirin compared to aspirin alone did not show important benefit and was associated with increased bleeding

Antithrombotic Trialists' Collaboration. BMJ. 2002;324(7329):71-86. Diener et al. Lancet. 2004;364(9431):331-7. Bhatt et al. N Engl J Med. 2006;354(16):1706-17.

Now, let's look at the use of P2Y12 inhibitors in patients without prior stents. Compared to aspirin, the use of a P2Y12 inhibitor showed minimal improvement in terms of benefit with much-higher costs. Thus, P2Y12 inhibitor monotherapy should only be used in patients who cannot tolerate aspirin. Adding P2Y12 inhibitors to aspirin had minimal incremental value in terms of benefit with much-higher costs and increased risk of bleeding. So, we don't routinely recommend that.

19 Anticoagulation and Antiplatelet Agents

A slide titled "Anticoagulation and Antiplatelet Agents" with a light blue background and a faint anatomical illustration of a heart and blood vessels. The slide lists indications for anticoagulation and includes a prominent warning box.

Anticoagulation is only indicated in patients with:

- Chronic atrial fibrillation with CHA₂DS₂-VASc ≥ 2
- Mechanical heart valve
- Venous thromboembolism

Do not combine antiplatelet agent with anticoagulation, due to very high bleeding risk, except in patients prior coronary artery stents

Smith et al. Circulation. 2011;124:00-00.
Lamberts et al. Circulation. 2012;126:1185-1193

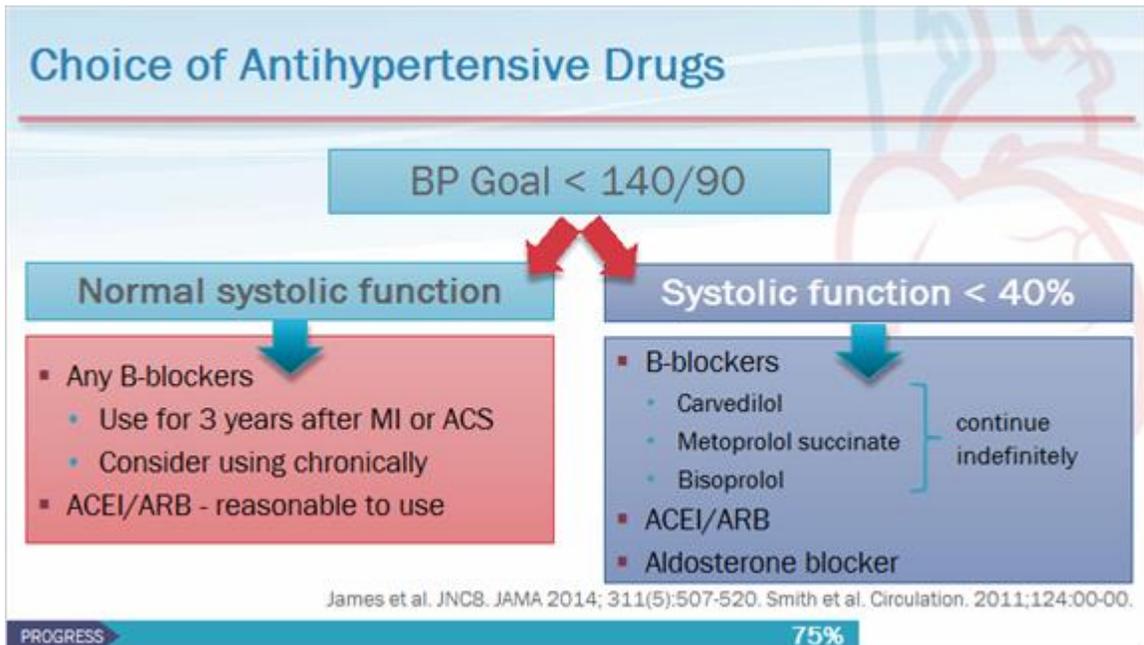
Some secondary prevention patients may be taking an anticoagulation medication like warfarin, or one of the novel anticoagulants, for another condition such as atrial fibrillation or venous thromboembolic disease. In patients receiving anticoagulation, we do not recommend that you add an antiplatelet agent due to very high bleeding risks, except in patients with prior coronary-artery stents.

20 Blood Pressure Control



Now, let's turn to blood pressure control.

21 Choice of Antihypertensive Drugs



Blood-pressure controlled patients with prior CVD events is only slightly different than for primary prevention. Patients with elevated blood pressure, prior history of myocardial infarction, and normal systolic function, should consider use of Beta blocker like Metoprolol, especially within three years of the event. Angiotensin blocking drugs have also shown effectiveness for secondary prevention. For those with a reduced ejection fraction, Beta blockers and angiotensin blocking drugs are both generally indicated. Treatment should aim to reduce blood pressure at least under 140/90 mg of mercury. These agents may also improve cardiovascular symptoms.

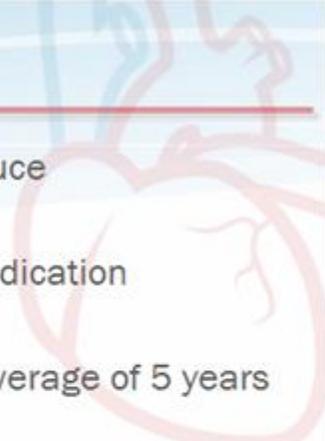
22 Lifestyle Modifications



Now, let's examine the role of life-style modifications in secondary prevention. We'll discuss two main areas: cardiac rehabilitation and dietary modification.

23 Cardiovascular Rehabilitation

Cardiovascular Rehabilitation



- Multidisciplinary approach to stabilize or reduce cardiovascular disease
- Structured exercise and coping skills and medication adherence support
- **Reduces mortality by up to 25%** over an average of 5 years compared to medical therapy alone
- Indications: Patients with coronary heart disease (angina, myocardial infarction, or coronary revascularization)
 - Patients with prior stroke benefit from stroke specific rehabilitation

Martin et al. Circulation. 2012;126:677-687.

Cardiac rehabilitation uses a multidisciplinary approach to reduce the impact of cardiovascular disease and prevent future events. It usually involves structured exercise, as well as coping skills and medication adherence support. Rigorous studies suggest that cardiac rehabilitation can reduce mortality by up to 25% compared to medical therapy alone. Cardiac rehabilitation is indicated for patients with coronary heart disease such as angina, myocardial infarction, or coronary revascularization. Patients with a prior stroke benefit from stroke-specific rehabilitation.

24 Cardiovascular Rehabilitation

Cardiovascular Rehabilitation

Cardiac Rehabilitation Facilities in N.C.

- Please visit North Carolina Cardiopulmonary Rehabilitation Associate (NCCRA) website: <http://nccraonline.org/>



The map displays the state of North Carolina with numerous pins indicating the locations of cardiac rehabilitation facilities. The pins are color-coded: green pins are concentrated in the western and central regions, purple pins are scattered across the central and eastern parts, and blue pins are primarily located in the southeastern coastal area. Major cities and geographical features are labeled on the map, including Asheville, Charlotte, Raleigh, and the Atlantic coast.

This slide shows a map of cardiac rehabilitation facilities throughout North Carolina. Visit:

[Http://nccraonline.org](http://nccraonline.org) to locate a facility near you.

25 Dietary Change

Dietary Change



- **Lyon Diet Heart Study**
 - Randomized, single-blind secondary prevention trial
 - Compared Mediterranean diet and Western diet
- **Mediterranean diet group showed reduced all-cause and cardiovascular mortality**
- **We recommend a diet that is:**
 - High in fruits, vegetables, beans, nuts, seeds and olive oil
 - Low to moderate amounts of fish, poultry, eggs
 - Small amounts of red meat
 - Low in simple carbohydrates and added sugars
- Nutritionist support key to making changes

De Lorgeril et al. Circulation. 1999;99:779-785.

Perhaps the best evidence for dietary intervention for patients with known cardiovascular disease comes from the Lyon Heart Study. In this trial patients were randomized to Mediterranean-style diet compared with the more-traditional Western-European diet. The Mediterranean diet group showed reduced all-cause in cardiovascular mortality. Based on this trial, we recommend a diet that is high in fruits, vegetables, beans, nuts, seeds, and healthy oils like olive oil. We recommend low-to-moderate amounts of fish, poultry, and eggs; limited amounts of red meat, and a diet that is low in simple carbohydrates and added sugars. Working with a skilled nutritionist can help the patient make and sustain changes in his or her diet. See our Website for links for additional helpful materials about dietary change.

26 Summary of Secondary Prevention

Summary of Secondary Prevention

- Use moderate or high intensity statin
- Aspirin is main antiplatelet agent, with addition of second agent for patients with recent stents
- Blood pressure control important - choice of agent depends on type of CVD event and ejection fraction
- Cardiac rehabilitation and dietary change important

In summary, in secondary prevention, we use moderate or high-intensity statins in patients who can tolerate them. Aspirin is the main antiplatelet agent with the addition of second agents for patients with recent stents. Blood pressure control is important. The choice of agent depends on the type of CVD event and injection fraction. Finally, cardiac rehabilitation, including an exercise program, and dietary change are both important other steps to take to reduce recurrent events.

27 Congratulations

Congratulations on Completing the Module

Click *Exit* at top right of screen

Please review the attachments and begin the next course.

28 The Evidence Team

The Evidence Team

Weeranun Bode, MD

Assistant Professor, Division of Cardiology, UNC – Chapel Hill

Crystal Wiley Cené, MD, MPH

Assistant Professor, Division of General Internal Medicine, UNC – Chapel Hill

Sam Cykert, MD

Professor, Division of General Internal Medicine and Director, Program on Health and Clinical Informatics, UNC – Chapel Hill; Associate Director for Medical Education, NC AHEC Program

Adam Goldstein, MD, MPH

Professor, Department of Family Medicine and Director of Tobacco Intervention Programs, UNC - Chapel Hill

29 The Evidence Team

The Evidence Team

Jacque Halladay, MD, MPH

Associate Professor, Department of Family Medicine, UNC – Chapel Hill

Michael Pignone, MD, MPH

*Professor of Medicine and Chief, UNC Division of General Internal Medicine
Director, UNC Institute for Healthcare Quality Improvement*

Carol Ripley-Moffitt, MDiv, CTTS

Director, Nicotine Dependence Program, UNC Department of Family Medicine

Stacey Sheridan, MD, MPH

Associate Professor, Division of General Internal Medicine, UNC – Chapel Hill

Anthony Viera, MD, MPH

*Associate Professor, Department of Family Medicine
Director, Hypertension Research Program, UNC – Chapel Hill*