Piedmont WellStar HealthPlans, Inc.
CARDIOVASCULAR RISK FACTORS AND CORONARY ARTERY DISEASE CLINICAL GUIDELINE

Relevance to Population: An estimated 1 in 3 American adults have some form of cardiovascular disease. Cardiovascular disease includes high blood pressure, coronary heart disease, heart failure, and stroke. Studies among people with cardiovascular disease have shown that lowering high blood cholesterol and high blood pressure can reduce the risk of dying of heart disease, having a non-fatal heart attack, and needing heart bypass surgery or angioplasty. Studies among people without cardiovascular disease have shown that lowering high blood cholesterol and high blood pressure can reduce the risk of developing cardiovascular disease.

Population Covered by Guideline: All adult members without known CAD whose symptoms suggest chronic stable angina, members with known chronic stable angina, asymptomatic members with evidence suggesting CAD on previous testing or with risk factors that predispose them to CAD, and those who have had a past MI or coronary artery revascularization procedure.

Clinical Indicators Measured by Piedmont Wellstar HealthPlans:

1. Persistence of beta-blocker treatment after a heart attack. HEDIS®
2. The percentage of members discharged on or prescribed a statin within 30 days post-hospital discharge within the measurement year.
3. The percentage of members who received persistent statin treatment for six months after discharge.

Goals specific to preventing heart disease and stroke:

- Prevention, detection, and treatment of risk factors
- Early identification and treatment of heart attacks and strokes
- Prevention of recurrent cardiovascular events

Clinical Classification of Chest Pain:

- **Typical angina (definite):**
  1) Substernal chest discomfort with a characteristic quality and duration that is
  2) Provoked by exertion or emotions and
  3) Relieved by rest or nitroglycerine.
- **Atypical angina (probable):** Meets 2 or less of the above criteria.

Clinical Classifications of Angina:

- Classic angina – a sense of choking, pressure, heaviness, or tightness deep in the precordium of the chest, usually brought on by exertion or anxiety and relieved by rest.
- Anginal equivalent – exertional dyspnea, breathlessness, or fatigue without chest pressure, which results from myocardial ischemia and is relieved by rest or nitroglycerine.
- Variant or Prinzmetal's angina – angina occurring at rest or in atypical patterns such as following exercise or at night. It is caused by coronary artery spasm and is associated with ECG changes (usually ST segment elevation) during symptoms.
- Unstable angina – anginal pain/discomfort that is new or changed in character, becoming more frequent and/or severe. It may be a precursor to MI in certain cases.

Evaluation Using Clinical Variables in Symptomatic Persons			
Assess Angina/Chest Pain	Assess Cardiovascular Risk Factors	Assess Comorbid Conditions	Assess Other Potential Causes of Chest Pain
Descriptive Information Characteristics of chest pain: • Quality, location, duration, and the presence of factors that trigger and relieve the pain	• Smoking • Hyperlipidemia • Diabetes mellitus • Hypertension • Metabolic syndrome • Physical inactivity • Poor diet • Family history of premature CAD • Postmenopausal status in women	• Systemic atherosclerosis (TIAs, claudication, bruits) • Hyperthyroidism • Hyperthermia • Cocaine use • Aortic stenosis • Severe uncontrolled HTN • Anemia • Hypoxia secondary to pulmonary disease	• Pericarditis • Aortic dissection • Pulmonary embolism • Pleuritis

Diagnostic Tests and Procedures:

Non-Invasive Testing for Diagnosis of Cause of Chest Pain				
Resting ECG	Echocardiography	Exercise ECG	Stress Imaging Studies	Computed Tomographic Angiography (CTA) – 64+ slice or higher*
All patients with symptoms that suggest angina or coronary artery disease.	Patients with a heart murmur of unidentified etiology or who have clinical evidence of previous MI.	Patients with a low to intermediate pretest probability of CAD based on age, gender, and symptoms, and normal baseline ECG (RBBB is acceptable if there are no other abnormalities).	Patients with clinical presentation suggestive of CAD including all patients with baseline abnormalities in ECG.	May be effective for emergency evaluation of acute chest pain, cardiac evaluation of chest pain syndrome as an alternative to cardiac cath, and for evaluation of anomalous coronary or pulmonary vessels. CTA is not indicated for screening or asymptomatic patients.

* The ACC/AHA chronic angina guideline update, current as of October 19, 2010, states that present state-of-the- art performance for CTA is not considered achievable with less than 64-channel CT scanners. Full coverage indications and limitations are in the Piedmont WellStar HealthPlans, Inc. P&P Manual, Policy number: Pay.044

Invasive Testing: Coronary Angiography	
• Patients with uncertain diagnosis after non-invasive testing. • Patients who cannot undergo non-invasive testing because of disability, illness, or morbid obesity. • Patients with an occupational requirement	• Patients who, by virtue of young age at onset of symptoms, non-invasive imaging, or other clinical parameters, are suspected of having a non- arterosclerotic cause for myocardial ischemia. • Patients with a high pretest probability of left

Treatment Mnemonic	
A	**A**spirin, Antianginal therapy and ACE inhibitor
B	**B**eta-blocker and Blood pressure
C	**C**igarette smoking and Cholesterol
D	**D**iet and Diabetes
E	**E**ducation and Exercise

Goal	Interventions and Recommendations
Smoking: Goal: Complete cessation. No exposure to environmental tobacco smoke.	• Assess tobacco use for cigarette smoking, smokeless tobacco, or any use of nicotine at every visit. • Advise patient and family to stop smoking and to avoid second-hand smoke. • Provide counseling, pharmacological therapy (including nicotine replacement and bupropion), and formal cessation programs as appropriate. • Urge avoidance of exposure to environmental tobacco smoke at work and home. • Consider utilizing a stepwise strategy for smoking cessation – ASK, ADVISE, ASSESS, ASSIST, ARRANGE (see page 6).
BP control: Goal: < 140/90 mm Hg or < 130/80 mm Hg if renal insufficiency or diabetes	• Initiate and/or maintain lifestyle modification (weight control, physical activity, alcohol moderation, limited sodium intake, and maintenance of a diet high in fruits, vegetables, and low-fat dairy products). • For hypertensive patients with well-established coronary artery disease, add blood pressure medication as tolerated, treating initially with beta blockers and/or ACE inhibitors with addition of other drugs as needed to achieve target blood pressure.

Lipid management: Primary goal: LDL < 100mg/dL (optimal goal of <70 mg/dL in those at high risk of CAD)	*Dietary therapy* for all patients should include: • Reduced intake of saturated fats (< 7% of total calories), trans-fatty acids, and < 200 mg/dL cholesterol per day. • Adding plant stanol/sterols (2 g/day) and/or viscous fiber (> 10 g/day) is reasonable to further lower LDL-C. • Promote daily physical activity and weight management. • Encourage consumption of omega-3 fatty acids in the form of fish or in capsule form (1g/day) for risk reduction. For treatment of elevated TG, higher doses are usually necessary for risk reduction. Lipid management includes assessment of a fasting lipid profile: • LDL-C should be less than 100 mg/dL. • Reduction of LDL-C to less than 70mg/dL is an option for patients with known CHD or equivalent and high-dose statin therapy to ↓ LDL-C by ≥ 50%. • If baseline LDL-C is ≥ to 100 mg/dL, LDL-lowering drug therapy should be initiated in addition to therapeutic lifestyle changes. When LDL-lowering medications are used in high-risk or moderately high-risk persons, it is recommended that intensity of therapy be sufficient to achieve 30% – 40% reduction in LDL-C levels. • If on treatment, LDL-C is ≥ to 100 mg/dL, LDL-lowering drug therapy should be intensified. If baseline LDL-C is 70 – 100 mg/dL, it's reasonable to treat LDL-C to < 70 mg/dL.
Lipid management: Secondary goal: If TG ≥ 200 - 499 mg/dL non-HDL-C should be < 130 mg/dL (Non-HDL-C= total cholesterol minus HDL cholesterol)	If TG 200-499 mg/dL, non-HDL-C should be less than 130 mg/dL. Further reduction of non-HDL-C to less than100 mg/dL is reasonable if TG is ≥ 200 to 499 mg/dL. Options to reduce non-HDL-C are: • Niacin *after* LDL-lowering therapy** • Fibrate therapy *after* LDL-lowering therapy If TG ≥ 500 mg/dL: • Consider fibrate or niacin *before* LDL-lowering therapy.** • The goal is to achieve non-HDL-C less than 130 mg/dl if possible • *The following lipid management strategy may be beneficial:* • If LDL-C < 70 mg/dL is the target, consider drug titration to achieve this level to minimize side effects and cost. • When LDL-C < 70 mg/dL is not achievable due to high baseline LDL-C levels, it is usually possible to achieve reductions of greater than 50% in LDL-C levels by either statins or LDL-C-lowering drug combinations. • Drug combinations are beneficial for patients on lipid lowering therapy who are unable to achieve LDL-C < 100mg/dL. (Monitor combination therapy closely for potential side effects; avoid combination or use cautiously with underlying renal or hepatic insuffiency.) • **The use of resin is relatively contraindicated when TG > 200 mg/dL.

Physical activity: Minimum goal: 30 to 60 minutes 5 days per week Optimal: Daily	• Physical activity of 30 – 60 minutes, 7 days per week (minimum 5 days per week) is recommended. • All patients should be encouraged to obtain 30 – 60 minutes of moderate-intensity aerobic activity, such as brisk walking, on most, preferably all, days of the week, supplemented by an increase in daily activities (such as walking breaks at work, gardening, or household work). • The patient's risk should be assessed with a physical activity history. Where appropriate, an exercise test is useful to guide the exercise prescription. • Medically supervised programs (cardiac rehabilitation) are recommended for at-risk patients (e.g., recent ACS or revascularization, heart failure). Expanding physical activity to include resistance training on 2 days a week may be reasonable.
Weight management: Goal: BMI 18.5-24.9 kg/m²	• BMI and waist circumference should be assessed regularly. • On each visit, it's useful to consistently encourage weight maintenance/ reduction through a balance of: ➢ Physical activity, ➢ Caloric intake, and ➢ Formal behavioral programs when indicated to achieve/maintain a BMI of BMI 18.5-24.9 kg/m². If waist circumference is ≥ 35 inches in women or ≥ 40 inches in men, it's beneficial to initiate lifestyle changes and consider treatment strategies for metabolic syndrome as indicated. • Some males can develop multiple metabolic risk factors when the waist circumference is only marginally increased (37 to 40 inches). ➢ Such persons may have a strong genetic contribution to insulin resistance. ➢ They should benefit from changes in life habits similar to men with categorical increases in waist circumference. • *Initial goal* for weight loss therapy is to gradually reduce body weight 10% from baseline. Further weight loss can be attempted if indicated through further assessment.
Diabetes management: Goal: HbA1c < 7%	• Diabetes management should include lifestyle and pharmacotherapy measures to achieve a near normal HbA1c. • Vigorous modification of other risks (e.g., physical activity, weight management, BP, and cholesterol management) as recommended should be initiated and maintained. • Also refer to "Anti-Platelet Therapy

Antiplatelet agents/anticoagulants	• Primary Prevention with Aspirin: The USPSTF recommends low dose aspirin, 75-162mg, in men ages 45-79 and women ages 55-79 with or without diabetes. • Primary Prevention with Aspirin in Persons with Diabetes: The ADA/AHA jointly recommends low dose aspirin in persons with diabetes at increased CV risk (age > 40 with 1 or more risks as follows: family history of CVD, HBP, smoking, dyslipidemia, or albuminuria; 10 year Framingham CV Risk > 10%). It might also be considered for diabetes with intermediate risk (age < 40 with 1 or more risks; older patients without risks; 10-year risk 5-10%). • Secondary Prevention with Aspirin: Aspirin should be started and continued indefinitely at 75 to 162 mg/d if not contraindicated. • Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with increased risk of bleeding and should be monitored closely. • FDA warning on clopidogrel: The FDA has warned physicians to be aware of genetic variations or drugs affecting CYP enzymes that can alter clopidogrel metabolism and activity. Current evidence is insufficient to recommend routine genetic or platelet function testing. Consideration of alternative therapy or dose adjustment is recommended in known poor metabolizers. <u>Post CABG:</u> • Aspirin 100-325mg should be started within 48 hours after surgery to reduce saphenous vein graft closure. <u>Maintenance treatment for Unstable Angina/Non-ST_Elevation MI (UA/NSTEMI):</u> • Medical treatment Only: ○ Aspirin should be prescribed indefinitely and clopidrogel 75mg/day or ticagrelor 90 mg Bid should be prescribed up to 12 months. • Post percutaneous coronary intervention (PCI) and stent placement: ○ Aspirin should be continued indefinitely and ○ Clopidrogel 75mg/day, Ticragelor 90mg Bid, or Prasugrel 10mg/day should be given as follows (unless bleeding risk outweighs benefits): ▪ Bare metal stent – up to 12 months ▪ Drug-eluting stent – at least 12 months; treatment can be considered beyond 12 months • Other KEY POINTS regarding $P2Y_{12}$ Receptor Inhibitors: ○ Clopidrogel 75mg/day, Ticragelor 90mg Bid, or Prasugrel 10mg/day should be given to patients recovering from UA/NSTEMI when ASA is contraindicated

Goal	Interventions and Recommendations
	○ There is mixed study evidence suggesting PPI medications may reduce the effectiveness of clopidrogel, which led to an FDA warning about the concomitant use of these drugs. An ACCF expert consensus statement highlighted the potential risks and benefits of PPIs and clopidrogel, especially in elderly patients with high-risk of GI bleeding, and did not prohibit use of this combination in appropriate clinical settings. Other options may be considered, such as use of the H2-blocker ranitidine with clopidrogel in high-risk patients. ○ After PCI, an ASA dose of 81 mg/day is preferable to higher doses ○ Because prasugrel is only indicated after PCI and stent placement, it should not be given routinely for UA/NSTMI before angiography ○ Prasugrel and ticagrelor had increased bleeding risks compared to clopidrogel in clinical trials ○ Although clopidrogel resistance may occur, information regarding strategies to use newer agents remains unclear at this time ○ The FDA issued a warning concerning genetic resistance to clopidrogel and noted that testing exists to detect it, but current evidence does not support routine genotype testing for clopidrogel resistance. Expert consensus is that it may be considered on a case by case basis. For additional guidance refer to Holmes DR et al. (Refer to the 2006 AHA/ACC guideline update for secondary prevention for patients with CAD and atherosclerotic vascular disease and the 2012 ACCF/AHA Focused Update of the Guideline for Unstable Angina/Non-STEMI.)

Renin-Angiotensin-Aldosterone Inhibitors	ACE Inhibitors: • Start and continue indefinitely in all patients with LVEF ≤ 40% and in those with HTN, diabetes, or chronic kidney disease unless contraindicated (the HOPE and EUROPA trials showed moderate benefit of ACE inhibitors in CAD with normal LV function). • Start and continue indefinitely in patients who are not lower risk (lower risk = those with normal LVEF in whom cardiovascular risk factors are well controlled and revascularization has been performed), unless contraindicated. • It is reasonable to use ACE inhibitors among lower-risk patients with mildly reduced or normal LVEF in whom cardiovascular risk factors are well controlled and revascularization has been performed. Angiotensin receptor blockers (ARBs): • Recommended for patients who have HTN, have indications for but are intolerant of ACE inhibitors, have heart failure, or have had an MI with LVEF ≤ to 40%. • May be considered in combination with ACE inhibitors for heart failure due to left ventricular systolic dysfunction. o CHARM-Added Trial: Significant decrease CV death and CHF hospitalization and trend toward decrease in all-cause mortality with combined ACE/ARB therapy in patient with LVEF ≤ 40%. Aldosterone Blockade: Recommended for use in post-MI patients: • Who are already receiving therapeutic doses of an ACEI and beta blocker and • Have a LVEF ≤ 40% and • Have either diabetes or heart failure AND

Goals	Interventions and Recommendations
	• Do not have significant renal dysfunction (creatinine > 2.5 in men or > 2.0 in women) • Do not have hyperkalemia (serum potassium > 5 mEq/L)
Beta-blockers	Start and continue beta-blocker therapy indefinitely in all: • Post-MI and acute coronary syndrome, or • Left ventricular dysfunction with or without heart failure symptoms, unless contraindicated.
Inactivated influenza vaccination	An annual influenza vaccination is recommended for patients with cardiovascular disease.
Pneumococcal vaccine	Recommended for all patients with chronic cardiovascular disease. A one-time revaccination is recommended for individuals > 64 y/o, if they were previously immunized < 65 y/o and it has been > 5 years from the previous immunization. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and other immunocompromised states.
Chelation therapy	Chelation therapy (intravenous infusions of ethylenediamine tetraacetic or EDTA) is not recommended for the treatment of chronic angina or arteriosclerotic cardiovascular disease and may be harmful because of its potential to cause hypocalcemia.

Principles of Patient Education	
• Assess patient's baseline understanding. • Elicit the patient's desire for information. • Use epidemiologic and clinical evidence. • Use ancillary personnel and professional patient education. Refer to Piedmont WellStar HealthPlan Cardiology Health Management Program.	• Use professionally prepared resources, when available. • Develop a plan with the patient. • Involve family members in educational efforts (if given permission by the patient). • Give written instructions to the member and family members directly involved in the care of the patient (if given permission by the patient). • Remind, repeat, and reinforce.

Five Questions to Ask During Follow-up
• Has patient decreased the level of physical activity since last visit? • Have anginal symptoms increased in frequency and become more severe since last visit? • How well is patient tolerating therapy? • How successful has the patient been in reducing modifiable risk factors and improving knowledge about ischemic heart disease? • Has the patient developed any new comorbid illnesses or has the severity or treatment of known comorbid illnesses worsened the patient's angina?

Tobacco Cessation Strategy	
ASK about tobacco use.	Identify and document tobacco use for cigarette smoking, smokeless tobacco, or any use of nicotine for all patients.
ADVISE to quit.	Offer clear, strong, and personalized advice to quit to all smokers at least yearly.

ASSESS willingness to quit.	Is the user willing to make a quit attempt at this time? Also, assess the user's level of addiction and whether there are any complicating factors, such as depression, other addictions, schizophrenia, attention deficit, etc. If the person is not ready to quit, let him or her know you will help when he or she is ready.

Principles of Patient	
ASSIST in quit attempt.	Use practical counseling and pharmacotherapy to help the tobacco user to develop problem-solving skills and an effective quit plan.
ARRANGE follow-up.	Schedule follow-up contact, preferably within two weeks of the quit date.

Clinical practice guidelines are designed to assist clinicians by providing a framework for the evaluation and treatment of patients.

Additional Resources for Piedmont WellStar HealthPlans, Inc. Members

- ***My*Health Advice Line** is staffed by experienced Registered Nurses and is available 24/7 to provide telephone support to members. Call 855-514-3679.

- **Online** interactive preventive health programs and resources are available in partnership with WebMD by logging in at www.pwplans.org/individuals.

Scientific Evidence Sources:

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Sandhu HS. A practical guide to tobacco cessation in dental offices. J Can Dent Assoc 2001; 67: 153-7. http://www.cda-adc.ca/jcda/vol-67/issue-3/153.html